POSTER SESSIONS

SESSION: POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC MONDAY, SEPTEMBER 7, 2015

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-001 Pembrolizumab for Advanced NSCLC: Patterns of Response and Progression Jenny H. Lee[1], John J. Park[1], Val Gebski[2], Raymond Tangunan[3], Matthew M. Chan[4], Bo Gao[1], Rina Hui[1] [1]*Department of Medical Oncology, Crown Princess Mary Cancer Centre, Westmead Hospital, Sydney/NSW/Australia,* [2]*Nhmrc Clinical Trials Centre, University of Sydney, Sydney/NSW/Australia,* [3]*Clinical Trials Unit, Crown Princess Mary Cancer Centre, Westmead Hospital, Sydney/NSW/Australia,* [4]*Department of Medical Oncology, Central Coast Cancer Centre, Gosford Hospital, Gosford/NSW/Australia*

Background: Anti-PD1 therapy has activity in patients with NSCLC, as assessed by RECIST or immune-related response criteria (irRC) on selected index lesions. Baseline tumour size was reported as an independent predictor of response to pembrolizumab in melanoma, but little is known about NSCLC. Tumour burden varies depending on number and size of lesions. We investigate the relationship of treatment response and baseline disease burden using comprehensive lesion-specific analysis on imaging at a single centre from a large multicentre Phase I study. **Methods:** Clinicopathologic characteristics of patients with advanced NSCLC enrolled from May 2012 to April 2014 at Westmead Hospital on the phase I pembrolizumab (MK-3475) KEYNOTE-001 were collected, including age, ethnicity, smoking status, histopathology (squamous or non-squamous), stage and prior treatments. Patients were treated with pembrolizumab until disease progression determined by irRC on index lesions or intolerable toxicity. Bi-dimensional measurements of individual lesions on computed tomography scans at baseline, week 9 and thereafter were performed. Every metastasis ≥5mm (up to 30 lesions per organ, excluding bone) and every lymph node ≥15mm in the short axis were assessed. Overall response was determined by change in sum of the product of longest perpendicular diameters (SPD) and categorised as complete response (CR, 100% reduction SPD), partial response (PR, ≥50% reduction SPD), progressive disease (PD, ≥25% increase in SPD) or stable disease (SD, neither CR/PR/PD) using comprehensive lesion-specific analysis. **Results:** Of 25 evaluable patients with at least one post-baseline imaging, 12 were treatment-naïve, 21 were PD-L1 positive (≥1% staining of cells) determined by prototype assay using 22C3 antibody and 4 were unknown. A total of 226 lesions were evaluated, 196 at baseline and 22 new lesions by first scan. Objective response (OR, ≥50% reduction SPD) was achieved in 9/25 patients (36%) by first scan, with 1 out of the 9 patients subsequently achieving CR. The patients with treatment response by first scan had a lower median number of lesions at baseline, 4.0 (range 2-8) vs 8.5 (range 4-30) and a lower median SPD per patient at baseline, 2516 vs 4178.5 Clinical benefit (CR/PR/SD) occurred in 15/25 patients (60%) with median treatment duration of 18.4 months (range 2.8 – 33.5 months). At the time of analysis on 11 April 2015, 10/25 patients were still receiving ongoing treatment. Clinical benefit was seen in 14/17 Caucasians and 1/8 non-Caucasians; 14/16 current or former smokers and 1/9 non-smokers. However, all Asians but one were non-smokers and this ex-smoker was the only Asian patient who achieved SD as best response. No differences were found in histopathology, stage, number of prior treatments or age. **Conclusion:**Fewer lesions or lower tumour burden at baseline as determined by comprehensive lesion-specific analysis may predict treatment response to anti-PD1 in advanced NSCLC. More responses were also observed in Caucasians and current or former smokers. Due to small sample size, these results need to be interpreted with caution and warrant further investigation. **Keywords:** NSCLC, Response pattern, pembrolizumab

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P1.01-002 Response Evaluation and Predictors in NSCLC During Treatment with AntiPD-L1 Alessandra Bearz, Eleonora Berto, Luca Cancian, Tiziana Perin, Ivana Sartor, Umberto Tirelli *Medical Oncology, CRO-IRCCS, Aviano/Italy*

Background: Treatment of metastatic NSCLC patients with immune-checkpoint medicine is intriguing for the potential efficacy, even in difficult setting such as smokers or squamous-carcinoma; however it may be difficult to evaluate the clinical response due to the lack of reliable immuno-monitoring markers and the possibility of radiological pseudo-progression. **Methods:** not applicable **Results:** Herein we report five cases treated with antiPD-L1(MPDL3280A, Genentech): four patients were male and one female, all of them were ex-smokers, affected by metastatic NSCLC; 4 adeno- and 1 squamous cell carcinoma- in progression after one cycle of platin-based combined chemotherapy, median age 60 yrs (58-64), renal function after cisplatin was normal. They received anti-PD-L1 i.v. every 3 weeks in a clinical trial. Two patients had progression of disease, while 3 patients showed a clinical benefit. Patient #1 had stable disease at the pleural and right lung disease in the CT-scan after 6 weeks of treatment. He had low Magnesium values at basal and at every further control during PD-L1 therapy. Patient #2 showed progression of mediastinal lymph nodes and liver metastases in the CT scan after 6 weeks of treatment and progression was confirmed by CT-scans 4 and 8 weeks later; eventually a biopsy of the liver metastasis confirmed that there was a massive neoplastic invasion with tumor infiltrating lymphocytes (Tils) <5%. His basal Magnesium values were always normal. He stopped anti-PD-L1 therapy due to progression. Patient #3 had a volumetric increase of bilateral lung nodules in the CT-scan after 6 weeks while mediastinal lymph nodes were stable; lung nodules again and lymph nodes were both in progression 12 weeks later. His basal and further on Magnesium values were always normal. Patient #4 showed partial response in the CT-scan after 6 weeks of treatment, and benefit was confirmed later on by CT-scan after 12 weeks; he reported a clinical benefit for decrease of fatigue and chest pain; his basal Magnesium value was lower than normal and it has been always abnormal at every further blood check during PD-L1 treatment. Patient #5 showed partial response in the CT-scan after 6 weeks of treatment; she reported a clinical benefit for decrease of fatigue and increase of appetite; her basal Magnesium value was lower than normal and she continued to have low magnesemia at every further blood check during anti-PD-L1 treatment. **Conclusion:** evaluation of response may be difficult with immune checkpoint inhibitors and in one case we performed a biopsy to study tumor infiltrating lymphocytes to decide whether pseudoprogression or real progression. Data about PDL1 expression were not available because patients in a clinical trial. In our experience lower basal Magnesium value may predict a clinical benefit with anti-PD-L1, although we do not know its possible explanation. **Keywords:** response, immune checkpoint, NSCLC

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P1.01-003 Co-Expression of Programmed Death Ligand-1 (PD-L1) and CD3 in Patients with EGFR Mutant NSCLC Treated with EGFR Tyrosine Kinase Inhibitors (TKI) Ross Soo[1], Hye Ryun Kim[2], Bernadette Asuncion[3], Zul Fazreen[3], Mohd Feroz Mohd Omar[4], Macy C. Herrera[3], Joey S. Lim[3], Grace V. Chia[3], Richie Soong[3], Byoung Chul Cho[2] [1]*Haematology-Oncology, National University Health System, Singapore/Singapore,* [2]*Medical Oncology, Yonsei Cancer Center, Seoul/Korea,* [3]*Cancer Science Institute of Singapore, National University of Singapore, Singapore/Singapore,*[4]*Department of Pathology, National University of Singapore, Singapore/Singapore*

Background: Recent reports have suggested an association between non-small cell lung cancer (NSCLC) and epidermal growth factor receptor (EGFR) gene mutations. Other studies have indicated that EGFR signaling can activate PD-L1 expression and immune escape in mutant *EGFR* driven NSCLC. Furthermore PD-L1 expression is down-regulated by EGFR TKI. In this study, we aim to determine the association between tumoral and immune cell PDL1 expression and clinical characteristics and outcome in EGFR mutant NSCLC patients treated with first line EGFR TKI. **Methods:** Tumors from 90 patients with advanced stage NSCLC with EGFR mutations and treated with first line EGFR TKI were analyzed. Double staining for CD3 and PDL1 was performed by immunohistochemistry. PDL1 expression in tumour membrane, and PDL1 and CD3 expression in tumor and stromal immune cells were segmented and quantified using the Vectra slide imaging system (Perkin Elmer, Waltham, MA). **Results:** The median age of patients was 62 (range 34-88) years, 64 (71%) were female, 69 (77%) were never smokers, and 43 (48%) harbored EGFR exon 19 deletion. Most immune cells were CD3-ve and PDL1-ve in the tumor (median 99%) and stroma (median 86%). PDL1 tumor membrane expression was associated with PDL1 expression in CD3+ve immune in the tumor and stroma. There was no association between PDL1 or CD3 expression with response rate or time to progression. **Conclusion:** This is the first study to characterize PDL1 expression in immune cells in advanced stage NSCLC harboring *EGFR* mutations. PDL1+ve immune cells are rare in this patient population. PDL1 expression in tumor membrane and immune cells may not be associated with outcome in NSCLC patients harboring *EGFR* mutations and treated with EGFR TKIs. **Keywords:** immune cell, programmed death ligand 1, EGFR mutations, EGFR Tyrosine Kinase Inhibitors

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-004 Updated Results and Efficacy Analysis According to EGFR Mutation Subtypes for Gefitinib plus Carboplatin and S-1 of the Phase II Trial Akihiro Tamiya[1], Motohiro Tamiya[2], Takayuki Shiroyama[2], Taisuke Tsuji[1], Naoko Morishita[2], Naoki Omachi[1], Norio Okamoto[2], Hidekazu Suzuki[2], Kyoichi Okishio[3], Tomonori Hirashima[2], Shinji Atagi[3] [1]*Internal Medicine, Kinki-Chuo Chest Medical Center, Sakai/Japan,* [2]*Thoracic Oncology, Osaka Prefectural Medical Center for Respiratory and Allergic Diseases, Habikino/Japan,* [3]*Thoracic Oncology, Kinki-Chuo Chest Medical Center, Sakai/Japan*

Background: Good efficacy and survival was observed in patients with advanced non-small cell lung cancer harboring epidermal growth factor receptor (EGFR) mutation. And the phase II study treated with gefitinib plus carboplatin and S-1 previously demonstrated the good efficacy in terms of progression free survival (PFS) and response rate (RR) as the first-line treatment of advanced NSCLC harboring activating EGFR mutations. **Methods:** This trial was multi-center, open rabel, single arm trial. All patients had a dvanced non-small cell lung cancer (Stage IIIB / IV) harboring activating mutations.A total of 35 patients received carboplatin on day 1 plus oral S-1 on days 1–14 and gefitinib daily. Updated results and subgroup analysis according to EGFR mutations are presented. **Results:** All patients had lung adenocarcinoma with activating EGFR mutations, namely, deletion (exon 19; *n* = 22), L858R (exon 21; *n* = 12), and T790M/L858R (exons 20 and 21; *n* = 1). Almost all patients had stage IV disease. The updated analysis revealed response rate of 85.7 %, a median PFS of 17.6 months (95% CI: 13.4 - 23.0 months), and a median overall survival (OS) was not reached (95% CI: 27.8 months -). Response rate and median PFS and median OS were 90.9 %, 18.7 months (95% CI: 15.5 - 28.4 months) and not reached (95% CI: 27.8 months -) in the exon 19 del+ arm, and 83.3 %, 13.4 months (95% CI: 6.2 - 18.5 months), and 27.9 months (95% CI: 10.1 - 32.4 months) in the exon 21 (L858R) arm. The common toxicities related to gefitinib were skin rash, elevated transaminase and diarrhea. And the common toxicity in the present trial was neutropenia. No interstitial lung disease or treatment-related deaths occurred. **Conclusion:** This triplet chemotherapy showed good efficacy and prolonged PFS. And this analysis showed the different efficacy in terms of PFS and OS of gefitinib plus carboplatin plus S-1 in patients with advanced NSCLC between EGFR mutation subtypes.

Keywords: gefitinib, non-small cell lung cancer, epidermal growth factor receptor mutation, combination therapy

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P1.01-005 Early versus Late Brain Metastases in Wild Type and Mutation Positive EGFR Patients Ren Yuan[1], Andrew Yamada[2], Britta Weber[3], Cheryl Ho[2] [1]*Diagnostic Radiology, BC Cancer Agency, Vancouver/BC/Canada,* [2]*Medical Oncology, BC Cancer Agency, Vancouver/BC/Canada,* [3]*Aarhus University Hospital, Aarhus/Denmark*

Background: Brain metastasis (BM) in NSCLC is a negative prognostic indicator. Historically, the median survival from diagnosis of BM has been reported as 6 m. The prognostic significance of BM however, may be altered in the setting of EGFR mutated disease. The timing of BM development may also influence survival outcomes. We evaluated the difference between early (<= 6 months from diagnosis) versus late (> 6 months) BM, in EGFR wild type (WT) and mutant (MT) with respect to radiographic patterns and the impact on survival. **Methods:** The British Columbia Cancer Agency provides cancer care to a population of 4.6 million. A retrospective study was conducted of referred patients with stage IV non squamous NSCLC who underwent whole brain radiotherapy and/or surgical resection of brain metastasis with known EGFR mutation status from Mar 2010 - Dec 2012. The data was analyzed by WT and MT, early and late BM groups to characterize the radiographic patterns and overall survival (OS) from initial NSCLC diagnosis (dx) and BM dx. **Results:** 430 patients were identified: 327 WT patients (206 early vs 121 late) and 103 MT (65 early vs 38 late). Pattern of BM in WT early vs late showed no difference in size of largest BM, number of metastases, cerebral edema. Leptomeningeal disease was more frequent in WT late disease (2% vs 8% p=0.01). Pattern of BM in MT early vs late showed no difference in size of largest BM, cerebral edema or leptomeningeal disease. There was a trend to miliary pattern disease in MT late BM (p=0.058). Median OS from initial dx in EGFR WT was early: 7.1 m vs late: 24.9 m (p<0.001) and OS from BM dx early: 6.3 m vs late: 4.9 m (p=0.67). Median OS from initial dx in EGFR MT was early: 19.9 m vs late: 25.6 m (p=0.39) and OS from BM dx early: 19.2 m vs late: 3.9 m (p<0.001). Cox proportional hazards (CPH) model showed in the EGFR WT receipt of chemotherapy and late BM were associated with better survival. CPH in EGFR MT demonstrated that good PS and systemic treatment but not BM timing were predictive of better outcomes. **Conclusion:** Brain metastases in EGFR WT disease is a significant negative prognostic indicator with early dx associated with poor survival. In contrast, in EGFR mutation positive disease, the overall survival from diagnosis is the same regardless of the development of early or late brain metastases. This outcome may reflect the importance of systemic control and the penetrance of EGFR TKIs across the blood brain barrier. **Keywords:** EGFR, brain metastasis, timing, TKI

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P1.01-006 Targeted Drug Selection for Advanced NSCLC Treatment Jun Ni, Li Zhang *Peking Union Medical College Hosptial, Peking Union Medical College & Chinese Academy of Medical Sciences, Department of Respiratory Medicine, Beijing/China*

Background: The efficacy of traditional cytotoxic drugs that treat the Advanced Non-Small Cell Lung Cancer (ANSCLC) has reached a plateau. Recently, the targeted therapy has become a new option for ANSCLC treatment. The most representative targeted therapy is tyrosine kinase inhibitor (TKI) aimed at the genetic mutations of epidermal growth factor (EGFR). Currently, three TKI drugs, namely Gefitinib, Erlotinib, and Icotinib, are available in Chinese market. This article compared the molecular structure, pharmacokinetic parameters, clinical data, adverse reactions, and contraindications of the three drugs to guide the optimal selection in clinical practice. **Methods:** Not Applicable. **Results:** Not Applicable. **Conclusion:** Presently the pros and cons of the three drugs are inconclusive. Taken together, TKI can be used as the first-line drug among patients with EGFR mutations. Of these TKIs, Gefitinib is convenient and safe with fair tolerability, and consequently recommended. Icotinib needs to be administered t.i.d without meal. However, in ICOGEN study, it was safer than Gefitinib, and therefore also recommended. Erlotinib needs to be taken without meal, requires quitting smoke and has narrow therapeutic windows. The occurrence rate and severity of its adverse reactions are relatively high. Therefore Erlotinib is not recommended. Among the non-selective patients, TKI can be used as the second- or third-line treatment. Erlotinib apparently has better survival benefit and therefore is recommended. Icotinib has certain efficacy among the Acian female non-smokers with adenocarcinoma or lung adenocarcinoma. Its safety and tolerability are the best. Therefore, Icotinib is the next recommended drug. Gefitinib only has certain efficacies among the Asian female nonsmoking lung adenocarcinoma patients, and therefore is recommended to only the appropriate population. **Keywords:** Targeted drug therapy, Optimal Selection, Advanced Non-Small Cell Lung Cancer

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P1.01-007 Treatment with EGFR-TKIs in Non Small Cell Lung Cancer Patients. The Impact of EGFR Mutations Teresa Garcia Manrique, Rosario Carrillo De Albornoz, Ana Milena Vargas, M.Carmen Alamo De La Gala, Ana Maria Grueso Lopez, M.Mar Barros Perez, David Vicente Baz *Medical Oncology, Hospital Virgen Macarena, Seville/Spain*

Background: Patients with advanced stage of non small cell lung cancer (NSCLC) have been treated with few platinum-doublets in first-line. Most of them are observed for disease progression wich is followed by second-line therapy in proper patients. Maintenance therapy were introduced, with either biologic or chemotherapeutic agents, given after first line treatment, trying to prevent progression and increasing progression-free survival (PFS). Ten years ago, somatic mutations in epidermal growth factor receptor (EGFR) were identified in patients with NSCLC, those targeted agents, used previously as maintenance, were seen to inactivate specific mutated proteins, and treatment of them has changed. For patients with lung adenocarcinoma and activating EGFR mutations who received EGFR TKIs median overall survival (OS) ranges between 24 and 30 months contrasts with the plateau of 10 months reached with first line platinum-based chemotherapy in populations not selected by molecular profiling. **Methods:** We analyze all patients attended in our hospital with NSCLC, who had received EGFR-TKI since 2010. Continuous variables were summarized as arithmetic means, medians and standard deviations. Categorical variables were reported as proportions with 95% confidence intervals (95% CI). OS were measured from the day of EGFR TKI treatment to the date of death and analyzed with the Kaplan-Meier technique, **Results:** The amount of patients were 53. EGFR mutation was detected in 46 (86,8%) patients. The median patient age was 62.8 ± 19 years, 58.5% were women, 41.5 % had a history of non-smoking and 73% had adenocarcinoma histology. Six types of EGFR gene mutations were found: delection in exon 19, exon 18 (G719), exon 20(T790 and S768I),exon 21 (L861Q and L858R). There were 17 (32%) patients with exon 19 delection, 7 (13.2%) patients with exon 18 G719 mutation, 4 (7.5%) and 13 (24.5%) patients with exon 21 L861Q and L858R respectively, 4 (7.5%) with double mutation (two combinations of G719 and L861Q, one combination of G719 plus S768I, and one combination of delection in 19 exon and T790 mutation). Delection in exon 19 and L858R exon 21 mutations were higher in non-smoking patients (31.8% and 40.9%) and in women (35.5% and 32.3%). Mutations in exon 18 (G719) and delection in exon 19 -also- were higher in patients with smoking history (19.4% and 29%) and in men (18.2% and 22.7%). 79.2% received ITK as first line treatment and 1.9% as maintenance therapy. 50.9% had erlotinib, 43.4% had gefitinib and 3.8% received dacomitinib. 13 patients (24.5%) have recieved further lines of therapy including: chemotherapy, immunotherapy and second generation EGFR TKIs. Prognosis was worse in unkwoun mutations and in wild type tumors. OS was 25.8 months [11.4-40.2; IC 95%] **Conclusion:** Treatment of patients with advanced NSCLC should be individualized, based on the molecular and histological features of tumours. When harbouring an activating EGFR mutation, first-line treatment should be with an EGFR TKI. Any avalilable agent can be used, until data from comparative studies may better guide TKI selection. **Keywords:** EGFR- tyrosine kinase inhibitors, non-small cell lung cancer, EGFR- mutations, Targeted agents

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P1.01-008 Second Line Erlotinib for NSCLC Patients with EGFR Mutation: Our Experience Simonida Crvenkova[1], Meri Pesevska[2] [1]*Lung Cancer, University Clinic of Radiotherapy and Oncology, Skopje/Macedonia,* [2]*Lung Department, University Clinic of Radiotherapy and Oncology, Skopje/Macedonia*

Background: As regards lung cancer patients who have relapse on platinum-based chemotherapy, there is a significant need for effective, well-tolerated treatment. Targeted agents such as orally active epidermal growth factor receptor EGFR tyrosine kinase inhibitor TKI (Erlotinib-Tarceva) and (Gefitinib-Iressa) offered a new therapeutic approach. Discovering of somatic EGFR mutations in some patients with NSCLC was a very significant breakthrough in the understanding of this disease. EGFR mutations occur almost within exons 18-21 of the gene of the receptor. The aim of this study was to evaluate tumor response, QoL and adverse effects of erlotinib, as a second line therapy for patients with EGFR mutation in NSCLC, after failure on previous first line therapy. **Methods:** During the year 2010-2011, 5 patients were enrolled in this study for testing EGFR mutations, after conditions for testing were created in Macedonia. We screened 5 patients for EGFR mutations by direct sequencing of axons 18 to 21, by retrospective analyzed their previous biopsy samples. Three of the patients were men and two of the patients were women. Previous smokers were two of males and one male and both female were never-smokers. All of the patients who were enrolled in the study were with histological proven adenocarcionoma. Patients started with erlotinib 150 mg, one tablet per day, after failure on previous first line platinum based chemotherapy, with or without surgery and radiotherapy. Assessment of tumor response was according RECIST criteria on the follow-up visits every 4 weeks. We analyzed tumor response from the beginning with erlotinib until tumor progression or detected severe toxicity. Assessment was performed only for those patients with EGFR mutations. Assessment of QoL was performed by patient's subjective answers, as subjective improvement and without subjective improvements. Adverse effects were performed according to WHO criteria. **Results:** Tissue was available for all 5 cases, two (40%) of which were found to harbor an EGFR mutation, identified axon 19 deletions. The both two patients responded to therapy. Complete response was seen in female patient for 37 months. Progressive disease was reason to stop with erlotinib after 37 mounts and start with third line therapy. Partial response in male patient was assessed for 30 mounts and is still in follow up. This patient is still alive with good condition. The two patients reported subjective improvements during treatment with erlotinib. Skin rash was grade 2-3, and diarrhea was grade1-2. Both patients complained for hair loss, but without complete alopecia. **Conclusion:** Considering our clinical results, we recommend target therapy with erlotinib for patients with NSCLC and EGFR mutations as a second line treatment. Our excellent results encouraged to require prospective tissue procurement for all patients in Macedonia. This may in fact require a shift in diagnostic practice, from the current emphasis on fine-needle aspiration, which often provides insufficient material for molecular analysis, to obtaining more substantial biopsies and to provide this treatment as a first line for selected patients. **Keywords:** epidermal growth factor receptor mutation, erlotinib for second line therapy, Tumor response, Adverse effects

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P1.01-009 Combination of Angiogenesis Inhibitor and EGFR-TKIs in Advanced NSCLC Patients Who Developed Acquired Resistance Xia Song, Ruifen Tian, Yi Guo, Rong Wang, Xia Zhang, Wei Guo, Haibo Zhu *Department of Pulmonary Oncology, Shanxi Cancer Hospital, Taiyuan/China*

Background: Several randomized clinical trials have shown that erlotinib and Bevacizumab combination improved the survival of patients with EGFR mutation-positive Non-small cell lung cancer (NSCLC) . The aim of this study was to evaluate the clinical activity of another angiogenesis inhibitor Endostar (rh-endostatin) in combination with continued EGFR-TKIs (including erlotinib, gefitinib and Icotinib) for advanced NSCLC patients who have developed acquired resistance to prior EGFR-TKIs treatment. **Methods:** Advanced NSCLC patients with disease progression who had partial or complete response to prior EGFR-TKIs treatment received 2-8cycles of Endostar plus EGFR-TKIs. Endostar was administered at a dose of 15mg q.d intravenously for 14 days, each at 3-week intervals; combined with continued EGFR-TKIs (erlotinib 150mg PO daily, or gefitinib 250mg PO daily or Icotinib 125mg PO t.i.d); until unacceptable toxicity or disease progression. The response was assessed using Southwest Oncology Group (SWOG) criteria after 6 weeks. **Results:** A total of 17 NSCLC evaluable patients were enrolled, including 9 women and 8 men. The presence of EGFR status were exon 21 L858R point mutation in 7 cases, exon 19 deletion in 5 cases, wild type in 2 cases and unknown in 3 cases. Median number of treatment cycles was four. It showed a 76.47% (13/17) disease control rate and had a prolonged stabilization of disease (>6 months). Median PFS was 6.9 Months. Treatment benefit and overall survival was noted both in activating EGFR mutation patients, EGFR stated unknown patients and even in wild type patients. One stage VI patient with EGFR wild type, developed resistance after 6 months 2nd line erlotinib treatment, received 8 cycles of Endstar and erlotinib combination, and had 46 months overall survival time. Endostar in combination with EGFR-TKIs were generally well tolerated. The most common adverse events were rash 35.29% (6/17), decreased appetite 29.41% (5/17), dry skin29.41% (5/17). No grade 3 or greater adverse events were seen in this study. **Conclusion:** Endostar with the addition of continuation of EGFR-TKIs has demonstrated promising clinical activity in NSCLC patients selected for acquired resistance to previous use of EGFR-TKIs. Treatment with this combination exhibited a good safety profile. Our results strengthen the evidence that angiogenesis inhibitor may be a valid option for NSCLC patients who have progressed on EGFR-TKIs. The optimal clinical combination and activity warrants further investigation. **Keywords:** Angiogenesis Inhibitor, EGFR-TKIs, NSCLC, Acquired resistance

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P1.01-010 Development of Skin Rash within the First Week Is a Potential Surrogate Marker of Effect in Afatinib for EGFR Mutant NSCLC Kenichiro Kudo[1], Katsuyuki Hotta[1], Akihiro Bessho[2], Shinobu Hosokawa[2], Kazuya Nishii[2], Naoyuki Nogami[3], Toshiyuki Kozuki[3], Shoichi Kuyama[4], Koji Inoue[5], Shingo Harita[6], Toshiaki Okada[6], Kenichi Gemba[7], Masanori Fujii[8], Nagio Takigawa[9], Naohiro Oda[1], Mitsune Tanimoto[1], Katsuyuki Kiura[1] [1]*Respiratory Medicine, Okayama University Hospital, Okayama/Japan,* [2]*Respiratory Medicine, Japanese Red Cross Okayama Hospital, Okayama-Shi/Japan,* [3]*Pulmonary Medicine, National Hospital Organization, Shikoku Cancer Center, Matsuyama/Japan,* [4]*5. Department of Respiratory Medicine, NHO Iwakuni Medical Center, Iwakuni/Japan,* [5]*6. Department of Respiratory Medicine, Ehime Prefectural Central Hospital, Matsuyama/Japan,* [6]*Medicine, Chugoku Central Hospital, Fukuyama/Japan,* [7]*National Hospital Organization, Fukuyama Medical Center, Fukuyama/Japan,* [8]*9. Department of Respiratory Medicine, Kobe Red Cross Hospital, Kobe/Japan,* [9]*General Internal Medicine, Kawasaki Medical School, Okayama/Japan*

Background: Epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) are now key agents in EGFR-mutant non-small-cell lung cancer (NSCLC). In gefitinib or erlotinib monotherapy, its efficacy could be predicted by development of skin rash, however, it has not been fully evaluated if this is similarly the case with afatinib monotherapy. **Methods:** We retrospectively studied consecutive 49 patients with EGFR-mutant NSCLC who received afatinib therapy between 2009 and 2015. Relationship with several toxicities and tumor response was examined. **Results:**

Table 1 Toxicity profile

	Grade 1	2	3	No. of pts who developed ≥ Grade 2 within the first week
Hepatitis	11 (22%)	1 (2%)	1 (2%)	1 (2%)
Skin rash	24 (49%)	13 (27%)	4 (8%)	5 (10%)
Diarrhea	22 (45%)	10 (20%)	8 (16%)	12 (24%)
Paronychia	9 (18%)	13 (27%)	4 (8%)	0
Mucositis	10 (20%)	13 (27%)	2 (4%)	4 (8%)
Gastritis	1 (2%)	2 (4%)	0	0
Dysgeusia	3 (6%)	3 (6%)	0	0
ILD	2 (4%)	0	1 (2%)	0

Abbreviations: ILD, interstitial lung disease

Table 2 Relationship with early development of adverse events and response

	No. of patients (%)		
	Response (-)	Response (+)	P
≥ Grade2 hepatitis			
yes	1	0 (0%)	0.382
no	27	21 (44%)	
≥ Grade2 skin rash			
yes	1	4 (80%)	0.077
no	27	17 (39%)	
≥ Grade2 diarrhea			
yes	6	6 (50%)	0.565
no	22	15 (41%)	
≥ Grade2 paronychia			
yes	1	0 (0%)	0.382
no	27	21 (44%)	
≥ Grade2 mucositis			
yes	2	2 (50%)	0.763
no	26	19 (42%)	
≥ Grade2 gastritis			
yes	0	0 (0%)	
no	28	21 (43%)	
≥ Grade2 dysgeusia			
yes	0	0 (0%)	
no	28	21 (43%)	
≥ Grade2 ILD			
yes	0	0 (0%)	
no	28	21 (43%)	

The Grade 2 or worse common adverse events (AEs) included skin rash in 17 patients (35%), diarrhea in 19 (39%) and mucositis in 15 (31%). Of these, number of patients who developed ≥ Grade 2 AEs within the first week was 5 (10%; skin rash), 12 (25%; diarrhea) and 4 (8%; mucositis). As for objective response, 21 (43%) of the 49 had partial response. In association with AEs and antitumor effect, those who had Grade 2 or worse skin rash within the first week tended to have better tumor response as compared with those who did not have (80% vs. 39%; p = 0.077). **Conclusion:** Our small study demonstrated that early development of skin rash might predict the response to afatinib monotherapy. **Keywords:** lung cancer, afatinib, skin rash

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P1.01-011 Response to Erlotinib in Metastatic Lung Adenocarcinoma with a Rare Double Epidermal Growth Factor Receptor (EGFR) Mutation Syed H.R. Jafri[1], Angel Blanco[1], Bonnie A. Labdi[2], Shan Guo[1] [1]*Internal Medicine, Division of Oncology, UT Houston Medical School, Houston/TX/United States of America,* [2]*Department of Pharmacy Service, Memorial Hermann Texas Medical Center, Houston/TX/United States of America*

Background: Erlotinib is an EGFR tyrosine kinase inhibitor (TKI) which is approved as a first line treatment in patients with metastatic lung cancer with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations. Here we are reporting use of erlotinib in a patient with a rare double EGFR mutation **Methods: Case history:** Patient is a 52 years old Hispanic female with12 packs/year history of smoking who quit few years prior to diagnosis. She was evaluated for gradually worsening vision of one year duration and regular headaches for one month. MRI brain showed a 2 cm cystic lesion in right posterior temporal /parietal region. She underwent surgical resection which showed metastatic adenocarcinoma cells positive for CAM 5.2, CK 7, napsin and TTF-1 and negative for CK 20 consistent with lung primary. Staging PET/CT scan showed increased FDG uptake in a left upper lobe 2.5 cm perihilar mass (SUV 12.3) with several satellite lesions and hilar nodal metastasis giving her a final stage of T3N2M1. **Next generation sequencing**: Resected metastatic brain lesion was sent for next generation sequencing which showed presence of EGFR p.L858R and p.H870R mutations and increased EGFR copy number. Other mutations identified included Tp53 p.R175H and CDKN2Ap.H83Y. Tumor was negative for KRAS mutation. EML4-ALK and ROS1 rearrangement were also negative by FISH. **Results: Treatment:** Patient received adjuvant gamma knife to the tumor bed of resected brain lesion and in consideration of her oligometastatic disease was started on concurrent thoracic chemo-radiotherapy. She received a total of 60 Gy radiation to the chest with 2 cycles of cisplatin-etoposide. At the completion of chemo-radiotherapy re-staging CT scan chest and abdomen showed no improvement in chest disease with appearance of new metastatic lesion in liver. MRI brain done at that time also showed a new metastatic lesion in parietal calvarial bone for which she received whole brain radiation therapy. At that time she was stared on erlotinib at 150mg/day. Initially patient had poor tolerance to erlotinib with excessive vomiting. Erlotinib dose was reduced to 150mg every other day and once tolerance improved the dose was gradually increased back to 150mg/day. Re-stating CT scan at 2 months showed partial response in primary thoracic tumor as well as almost complete resolution of metastatic lesion in liver. Patient remains on erlotinib at 150mg/day and most recent re-staging CT scan chest /abdomen as well as MRI brain performed 7 months after starting erlotinib show stable disease. **Conclusion:** Previous reports have shown poor response to EGFR TKI in patients with double EGFR (L858R + p.H870R) mutation (1,2).This case report shows poor response of platinum doublet chemotherapy but good response to EGFR TKI eroltinib in a patient with double EGFR (L858R + p.870R) mutation.**References:** 1. Pas TD, et al. Activity of Epidermal growth factor receptor-tyrosine kinase inhibitors in patients with non-small cell lung cancer harboring rare epidermal growth factor receptor mutations. Journal of Thoracic Oncology.2011.6(11)1895-1901 2. Tam IY,et al. Double EGFR mutants containing rare EGFR mutant types show reduced in vitro response to gefitinib compared with common activating missense mutations. Mol Cancer Ther. (2009); 8(8):2142-51
Keywords: Erlotinib, rare EGFR mutation, lung adenocarcinoma

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-012 Kinase Domain Mutation Positive Lung Cancers Are Sensitive to Intrapleural Perfusion with Hyperthermic Chemotherapy (IPHC) Complete Treatment Lei Yu[1], Liang Chen[2] [1]*Department of Thoracic Surgery, Beijing Tongren Hospital, Capital Medical University, Beijing City/China,* [2]*National Institute of Biological Sciences, Beijing, Beijing City/China*

Background: Lung cancer is the global leading cause of cancer-related deaths. A significant portion of lung cancer patients harbor kinase domain mutations in the epidermal growth factor receptor (EGFR). While EGFR tyrosine kinase inhibitors (TKI) effectively shrink tumors harboring mutant EGFR, clinical efficacy is limited by the development of TKI resistance. As such, effective alternatives are desperately needed. **Methods:** We have been treating M1a lung cancer patients through intrapleural perfusion with hyperthermic chemotherapy (IPHC) followed by cycles of systemic chemotherapy (we termed this procedure IPHC complete treatment, IPHC-CT). Tumor shrinkage was analyzed in mutant EGFR-positive patients after IPHC-CT treatment. Furthermore, patient-derived cell lines driven by mutant EGFR were treated with hyperthermic chemotherapy to study the mechanisms of effect of IPHC-CT on cancer cells. **Results:** Tumor shrinkage was detected in patients whose tumor harbored EGFR kinase domain mutation. Hyperthermia and cisplatin synergistically downregulated EGFR protein levels in tumor cells, which ultimately elicited apoptosis. **Conclusion:** IPHC-CT is effective in treating EGFR kinase domain mutation positive lung cancer patients.
Keywords: Kinase domain mutation, intrapleural perfusion, hyperthermic chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-013 EGFR Mutations and Targeted Treatment Reverse the Bad Prognosis of Stage IV NSCLC Associated to Liver Metastasis Eduardo Castanon[1], Christian Rolfo[2], David Viñal[1], Ines Lopez[1], Juan P. Fusco[1], Patricia Martin[1], Leire Zubiri[1], Jose I. Echeveste[3], Ignacio Gil-Bazo[1] [1]*Oncology, Clinica Universidad de Navarra, Pamplona/ Spain,* [2]*Thoracic Oncology, Multidisciplinary Oncology Centre Antwerp, University Hospital Antwerp, Edegem/Belgium,* [3]*Pathology, Clinica Universidad de Navarra, Pamplona/Spain*

Background: Liver metastases appear in 20-30% of patients diagnosed with non-small cell lung cancer (NSCLC) and represent a poor prognosis feature of NSCLC and a possibly more treatment-resistant condition. Potential clinical outcome differences in NSCLC patients with liver metastases harboring molecular alterations in EGFR, KRAS and EML4-ALK genes are still to be determined. This study aims to evaluate the incidence of liver metastasis in a single population and look for potential correlations between molecular profile, liver infiltration and response to treatment. response to Liver metastases appear in 20-30% of patients diagnosed with non-small cell lung cancer (NSCLC) and represent a poor prognosis feature of NSCLC and a possibly more treatment-resistant condition. Potential clinical outcome differences in NSCLC patients with liver metastases harboring molecular alterations in EGFR, KRAS and EML4-ALK genes are still to be determined. This study aims to evaluate the incidence of liver metastasis in a single population and look for potential correlations between molecular profile, liver infiltration and response to treatment. **Methods:** A total of 236 consecutive stage IV NSCLC patients treated at the Clínica Universidad de Navarra were analyzed. **Results:** At onset, liver metastases were present in 16.9% of patients conferring them a shorter overall survival (OS) compared to those with different metastatic locations excluding liver infiltration (10 mo. vs. 21 mo.; p =0.001). Patients with EGFR wild-type tumors receiving standard chemotherapy and showing no liver involvement presented a superior median OS compared to those with liver metastases (23 mo. vs 13 mo.; p=0.001). Conversely, patients with EGFR-mutated tumors treated with EGFR tirosin-kinase inhibitors (TKI's) presented no significant differences in OS regardless of liver involvement (median OS not reached vs. 25 mo; p=0.81). **Conclusion:**Overall, liver metastases at onset negatively impact OS of NSCLC patients. EGFR TKIs however, may reverse the effects of an initial negative prognosis in first-line treatment of EGFR mutated tumors and, more interestingly, in patients with EGFR wild-type NCSLC receiving EGFR TKIs after progression to chemotherapy. **Table 1. Multivariate regression model.**

Variable	HR	p
Sex	1.28	0.32
Age	1	0.9
N	1.28	0.06
EGFR	0.24	0.001
TKIs (after progression)	0.44	0.03
Liver metastases at onset	1.5	0.28
Liver metastases during disease	1.28	0.43
Bone metastases at onset	1.6	0.22
Bone metastases during disease	1.19	0.64
Skin metastases at onset	2.2	0.31
Adrenal metastases at onset	1.37	0.29

Keywords: Liver Metastasis, Epidermal growth factor receptor, Tyrosin Kinase Inhibitors, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-014 Long Term Clinical Benefit of EGFR wt in Advanced NSCLC Patients Treated for Long Time with Salvage Erlotinib. A Retrospective Analysis Athanasios Kotsakis, Alexandra Voutsina, Aristea Kalikaki, Nikolaos Kentepozidis, Filippos Koinis, Athanassios Pallis, Panayiotis Katsaounis, Kostas Kalbakis, K. E Dermitzaki, Dora Hatzidaki, Vassilis Georgoulias *Hellenic Oncology Research Group (Horg), Athens/Greece*

Background: Erlotinib (E) has been approved for the management of NSCLC patients (pts) after failure of the first or subsequent line of chemotherapy. Although the efficacy of E is clearly associated with the presence of drivers EGFR mutations, there is a subset of pts with EGFR wild type (EGFR wt) tumors who impressively respond. We retrospectively analyzed the clinical and pathological characteristics of a group of pts with unresectable EGFR wt NSCLC treated for a prolonged period with salvage (≥ 2nd line setting) E. **Methods:** Patients with unresectable EGFRwt NSCLC who received ≥ 2nd line treatment with E without disease progression for at least 6 months, were sought from the database of HORG. Pts with available tumor material were molecularly (KRAS, BRAF, PI3K, HER2 mutations and ALK-EML4 translocation) characterized. **Results:** Among 1450 pts treated in different HORG's collaborating centers (from 2004-2013), 44 (3.03%) received E for >6months (median: 10.1 mo; range, 6.0-36.5). 17 were women, 57% had no history of smoking, 42 had a PS (ECOG) of 0-1; 16% had squamous cell histology and 73% adenocarcinoma. KRAS mutations were detected in 20.5% (9/42 tested) of the pts, PI3K mutations in 9% (3/30 tested) and ALK-EML4 translocation in 9.5% (2/21 tested); there was no patient with HER2 or BRAF mutated tumor. 11(25%) pts experienced a partial response and 26 (59%) stable disease (Tumor growth control rate 84%). The median PFS and OS was 10.1 (6.0-40.6) and 24.1 (6.0- 89.1) months, respectively. Pts with KRAS wt tumors had a significantly (p=0.018) better OS compared to pts with KRAS mutant tumors. There was a trend of improved PFS (p=0.083) and OS (p=0.053) in favor of pts with adenocarcinoma compared to pts with squamous cell carcinoma. **Conclusion:** Treatment with E significantly improves the clinical outcome in a subset of NSCLC pts with EGFR wt tumors. Pts with non-squamous pathology and no smoking history seem to benefit most from such therapy. KRAS mutation was the

only molecular alteration correlated with the clinical outcome. Further molecular analysis of these pts could help to more appropriately define this particular group of patients. **Keywords:** EGFR, wt, metastatic, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-015 Clinical-Pathological and Survival Analysis of Patients with Advanced NSCLC and EGFR Mutation Treated With a Drug Therapy Anti-T790M
Jesús Corral, Antonio Cervera, Pilar Maiquez, Miriam Alonso, Maria Dolores Mediano, Maria José Flor, Lucia Jiménez *University Hospital Virgen Del Rocio, Seville/Spain*

Background: Multiple phase III trials have demonstrated the benefit in terms of RR and PFS of the EGFR TKIs versus platinum-based chemotherapy in patients with advanced NSCLC and EGFR mutation. Median PFS of these patients ranges from 9-13 months, time where a new therapy approach is needed, the most commonly chemotherapy nowadays. The main resistance mechanism described in this clinical situation is the development of T790M resistance mutation. There are no comparative efficacy data among chemotherapy and T790M targeted therapies. Our research included data from 15 patients treated in our Institution Phase I Unit with a T790M inhibitor analyzing the effectiveness according to their clinical features and mutational profile (T790M carriers or not) **Methods:** Descriptive clinico-pathological and efficacy analysis from October 2013 to March 2015 of patients with advanced NSCLC and EGFR mutation in progression and receiving T790M targeted therapy in the context of a phase I clinical trial performed in our Clinica Trial Unit. **Results:** Fifteen patients were included. The median age resulted 60 years (range 37-80 years) with a proportion of 8 (55%)/7 (45%) female/men. The entire study population was Caucasian and had an histological diagnosis of stage IV NSCLC with the presence of activating mutation of EGFR (66% L848R and del19 44%). In relation to smoking exposition, most of the patients were past-smokers (55%) or active (13%). All patients received a specific T790M inhibitor, 7 of them (45%) with a confirmed T790M mutation by local and/or local analysis. The average of prior lines of therapy before the experimental T790M inhibitor was 1,9. No grade 3/4 toxicities were reported. After an average follow up of 17 months, PFS of the overall population was 4,73 months, with a statistically significance difference between T790M positive patients (8,14 months) versus negative or unknown (1,8 months). We have no outcome at present of the OS for the active treatment of most the patients. **Conclusion:** Despite the limitation of the number of patients and follow-up time, our research suggested a clear survival benefit with the T790M inhibitor in the context of advanced NSCLC patients harboring T790M resistance mutation versus non in progression after EGFR TKI first line therapy. **Keywords:** T790M, inhibition, phase I unit, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-016 Treatment Outcomes among Elderly Lung Cancer Patients > 65 Years following Clinical Use of EGFR Tyrosine Kinase Inhibitor
Wan-Teck Lim[1], Li-Lian Kwok[2], Daniel S.-W. Tan[1], Chee-Keong Toh[1], Eng Huat Tan[1], Mei-Kim Ang[1], Ravindran Kanesvaran[1] [1]*Department of Medical Oncology, National Cancer Center, Singapore/Singapore,* [2]*Division of Clinical Trials and Epidemiology, National Cancer Center, Singapore/Singapore*

Background: Elderly patients (pts) with lung cancer pose significant challenges in cancer treatment because of concurrent comorbidities and age. We examined treatment patterns and outcomes in elderly pts with advanced lung cancer prior to and after introduction of epidermal growth factor receptor (EGFR) inhibitors into clinical use. **Methods:** Clinical data for pts > 65 yrs derived from two databases, cohort 1(1998-2003) and cohort 2(2004-current), were used. Demographics, clinical characteristics and treatment outcomes were compared between these 2 cohorts with stage III/IV lung cancer. Chi-square and Mann-Whitney-U tests were used to compare differences between cohorts. Overall survival (OS) from the time from diagnosis to death from any cause was estimated using Kaplan-Meier method and differences were defined using the logrank test. Pairwise comparisons were analyzed with Sidak's adjustment applied to account for multiple testing. The Cox proportional hazards model was used to model the association between survival end-points and patient cohort, with the resulting hazard ratios assessed using the Wald test. The proportional hazards assumption was verified by fitting an alternative model with inclusion of a covariate-by-time interaction term and inspection of the p-value of the interaction term for categorical variables. A 2-sided p-value of <.05 was considered statistically significant. **Results:** There were 397 pts (cohort 1) and 1584 pts (cohort 2) with complete data for analysis. The median age of diagnosis was not significantly different between the cohorts (72.5 yrs vs 72.8 yrs), p: 0.252. Median follow-up times were comparable. Cohort 1 had poorer ECOG at diagnosis, more males and a higher proportion of current smokers. For cohort 1, cytotoxic chemotherapy was standard of care and EGFR TKI use was minimal. In contrast, for cohort 2, 50% of pts received EGFR TKI monotherapy in 1st line, 30% of pts in 2nd line and 33.3% of pts in 3rdline and beyond. There was a significant difference in OS between the both cohorts (p <.001), HR 0.75 in favor of cohort 2. Specifically women, good ECOG, never smoker status, and adenocarcinoma were associated with significantly reduced hazard of death. **Conclusion:** Routine EGFR TKI use in elderly > 65 yrs of age clinical setting has improved OS over the last decade. This benefit is reflected in the reduced hazards of death for specific patient subsets. Elderly pts where targeted therapies are indicated should not be deprived of therapy. **Keywords:** lung cancer, Tyrosine kinase inhibitors, treatment outcomes, elderly

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-017 Two Cases of NSCLC with EGFR Exon 20 Insertions with Major Clinical Response to Cetuximab-Containing Therapies
Chad M. Vanderbilt[1], Erin C. Fulchiero[2], Robert J. Hoyer[3], Dara L. Aisner[1], Robert C. Doebele[4] [1]*Department of Pathology, University of Colorado Som, Aurora/CO/United States of America,* [2]*Department of Internal Medicine, University of Colorado Som, Aurora/CO/United States of America,* [3]*Medical Oncology & Hematology, Memorial Hospital, Colorado Springs/CO/United States of America,* [4]*Division of Medical Oncology, University of Colorado Som, Aurora/CO/United States of America*

Background: Lung tumors with EGFR Exon 20 mutations, particularly insertions between the amino acids Y764 and V774, present a major challenge for treatment. These mutations are known to confer resistance to current EGFR specific tyrosine kinase inhibitors (TKI). The mechanism of this resistance is described by Yasuda et al. as a "wedge" formed by the aberrant amino acids locking the C-helix in an inward, active position. This structural aberration prevents the TKI from accessing the critical pocket within the protein and inhibiting kinase activity. Without the ability to treat these tumors with TKIs, alternate treatments need to be pursued. **Methods:** We present, as index cases, two patients with metastatic lung adenocarcinomas demonstrating TKI unresponsive insertions in exon 20. Both patients had exuberant clinical and radiographic responses to cetuximab, an EGFR specific monoclonal antibody. **Results:** The first patient is a 39 year old male never-smoker with lung adenocarcinoma. The disease had progressed prior to molecular identification of the EGFR mutation, and the patient developed bilateral lung disease and metastatic lymph node and brain lesions. An exon 20 EGFR mutation (p.N771_P772insPHGH c.2313_2314insCCCCACGGGCAC) was identified. Following 4th line therapy with combination chemiotherapy plus cetuximab, the tumor burden was dramatically decreased and the patient had markedly improved functional status with the ability to return to employment. The second patient is a 71 year old male never-smoker with lung adenocarcinoma. The disease progressed and the patient developed widely metastatic disease. An exon 20 EGFR mutation (P770_N771insNPP) was identified. The patient was treated with combination cetuximab and afatinib therapy and experienced a dramatic decrease in lung and metastatic tumor burden with improved functional status. **Conclusion:** Cetuximab-containing therapeutic regimens may be a viable therapy for what previously have been considered treatment resistant molecular insults. Additional cases of these mutations and treatment with cetuximab are needed to demonstrate that these results are reproducible and that they warrant study in prospective clinical trials. **Keywords:** EGFR Exon 20 Insertion, Cetuximab, TKI resistant mutation

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-018 Response Rate and Outcomes in Crizotinib Treated Advanced ALK-Positive NSCLC Patients
Keith L. Davis[1], James A. Kaye[2], Shrividya Iyer[3] [1]*RTI Health Solutions, Research Triangle Park/NC/United States of America,* [2]*RTI Health Solutions, Waltham/MA/United States of America,* [3]*Pfizer Inc, New York/NY/United States of America*

Background: Crizotinib is an oral small-molecule tyrosine kinase inhibitor, which was approved in the United States (US) in August of 2011 for the treatment of anaplastic lymphoma kinase (*ALK*)-positive advanced non-small cell lung cancer (NSCLC). In clinical studies, crizotinib has demonstrated robust response rates and significantly greater efficacy than chemotherapy. However, there is currently limited data on crizotinib treatment and related outcomes in real-world practice settings. The main objective of the current study was to assess the treatment patterns and outcomes of *ALK*-positive advanced NSCLC patients treated with crizotinib in regular clinical practice. **Methods:** Physicians in the US (N= 107) and Canada (N= 40) were recruited from cancer centers/teaching hospitals (48%) or free standing oncology clinics (47%), to abstract data retrospectively from medical records of adult (≥18 years) patients diagnosed with *ALK*-positive advanced NSCLC and treated with crizotinib as first or later line therapy between August 1, 2011, and March 31, 2013 (for the US) or April 1, 2012 and March 31, 2013 (for Canada) in non-clinical trial settings. IRB approval was obtained. A secure web-based form was used by physicians to abstract data and all patient data were de-identified and anonymous. Descriptive analyses were conducted to assess treatment patterns and objective response rate (ORR). Progression-free survival (PFS) and overall survival (OS) were descriptively analyzed using the Kaplan-Meier method. **Results:** Data were extracted from 212 patient records in US (N=147) and Canada (N=65). The mean (SD) patient age was 58.9 (9.5) years and a majority were male (69%), Caucasian (79%), current or former smokers (67%), ECOG status 0 or 1 (75%), adenocarcinoma histology (90%) and initially diagnosed at the metastatic stage (71%). Cough, fatigue, and dyspnea were the most common symptoms present (71%, 65%, and 55%, respectively) at the time of metastatic NSCLC diagnosis. Approximately 65% (n=137) of patients initiated crizotinib as first-line therapy and the mean ± SD duration of crizotinib treatment was 8.7 ± 4.9 months. Approximately 37% of the patients were deceased at time of medical record abstraction. Disease progression following initial response was the most frequently reported (59%) reason for treatment discontinuation and 35% received additional systemic chemotherapy post-crizotinib. Approximately 90% of patients had no changes (reduction or escalation) in crizotinib dose. Among patients experiencing progression during crizotinib treatment, the most common sites of progressive metastases were liver (35%), bone (30%), and contralateral lung (28%). The crizotinib ORR was estimated to be 66% for the overall cohort (69% first line and 60% for later line). The median (95% CI) PFS from crizotinib initiation was 9.5 (8.7, 10.1) months in the overall cohort. Median (95% CI) OS from crizotinib initiation was 23.4 (19.5, –) months for the overall cohort. Based on Kaplan-Meier estimation, 1- and 2-year survival rates from crizotinib initiation were 82% and 49%, respectively. **Conclusion:** Response rates in patients treated with crizotinib in real world settings seem to align with data reported previously from clinical studies. Median OS in patients treated with crizotinib in the real world

settings examined here was approximately 2 years from crizotinib treatment initiation.
Keywords: crizotinib, lung cancer, outcomes, response rates

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-019 Czech Experience with Crizotinib in the Personalized Treatment of NSCLC Vitezslav Kolek[1], Milos Pesek[2], Jana Skrickova[3], Ivona Grygarkova[1], Jaromir Roubec[4], Leona Koubkova[5], Marketa Cernovska[6], Karel Hejduk[7], Jana Skrickova[8] [1]*Respiratory Medicine, University Hospital, Olomouc/Czech Republic,* [2]*Pulmonary Medicine, University Hospital, Plzen/Czech Republic,* [3]*Pulmonary Medicine, University Hospital, Brno/Czech Republic,* [4]*Pulmonary Medicine, University Hospital, Ostrava/Czech Republic,* [5]*Pulmonary Medicine, University Hospital,, Praha/Czech Republic,* [6]*Pulmonary Medicine, Thomayer Memorial Hospital, Prague/Czech Republic,* [7]*Biostatistics, Iba Institute, Brno/Czech Republic,* [8]*Institute of Biostatistics and Analyses, Masaryk University Brno, Brno/Czech Republic*

Background: Crizotinib is a highly selective drug used in the treatment of anaplastic lymphoma kinase (*ALK*) gene re-arrangement positive non-small cell lung cancer (NSCLC). In the Czech Republic it was used in frame of compassionate cases program and now is reimbursed in pretreated tumors with EML 4/ALK gen translocation verified by FISH and/or IHC testing. The recommended dose is 250 mg bid/ day. Crizotinib is used since 2011, data are evaluated according to the National Reference Centre Registry. **Methods:** Present study evaluates 26 patients (pts), 14 males,12 females with mean age 60 (31- 75) years. Out of them 11 (42.3%) were non-smokers, 8 (30.8%) ex-smokers and 7 (26.9 %) smokers. All of them had NSCLC with EML4/ALK gene translocation, 23 had adenocarcinoma, two NOS and one patient had adenosquamous cancer. Stage in the time of treatment was IIIB in 3 and IV in 23 pts. Crizotinib was applied in 2nd line in 17 pts, 3rd line in 5 pts, 4th line in 3 pts, 5th in one patient. PS was 0 in 3 pts, 1 in 20 pts and 2 in 3 pts. **Results:** On the date of evaluation, 14 pts continued the treatment, 6 died and 6 stopped treatment due to progression. Crizotinib effectiveness was assessed in 15 pts: CR in 3 (20%) pts, PR in 3 (20%) pts, SD in 5 (33.3 %) pts, DP in 4 (26.7 %) pts. CR was associated with long response duration (10.7, 31.8, 34.1 months). Grade 3 adverse events (gastrointenstinal discomfort and liver disease) were observed in two (7.7 %) pts, grade 2 problems with visus appeared in two patients. Dose of crizotinib was reduced in 3 pts. Median of progression free survival was 15 months, median of overall survival was not reached. **Conclusion:** Interim analysis of present series shows, that crizotinib has very good tolerability and promising effectiveness even in heavily pretreated patients with EML4/ALK gene translocation. Long term survival analysis is running. Supported by national grant IGA MZ ČR NT/13569
Keywords: ALK gene, crizotinib, survival, advanced NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

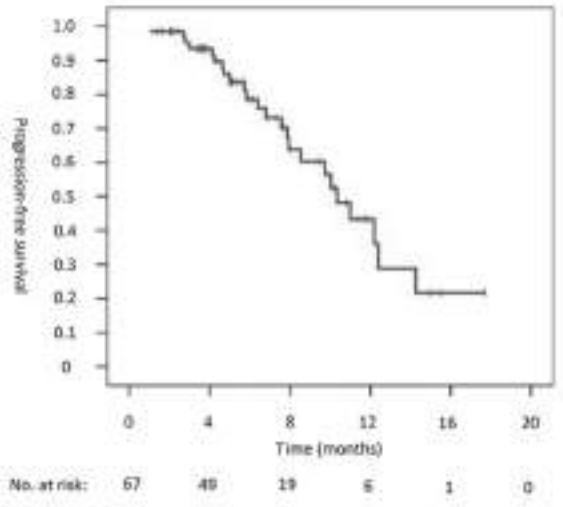
P1.01-020 Symptoms of Bone and Liver Metastases in Patients with ALK+ Non-Small Cell Lung Cancer (NSCLC) Annie Guerin[1], Medha Sasane[2], Roy Nitulescu[1], Jie Zhang[2], Kenneth W. Culver[2], Eric Q. Wu[3], Alexander R. Macalalad[3], Anand Dalal[2] [1]*Analysis Group, Inc., Montreal/QC/Canada,* [2]*Novartis Pharmaceuticals Corporation, East Hanover/NJ/United States of America,* [3]*Analysis Group, Inc., Boston/MA/United States of America*

Background: Among patients with *ALK*+ NSCLC who develop metastases, common metastatic sites include brain, bones, and liver. Although the symptomatic profile of *ALK*+ NSCLC patients with brain metastases is well documented, information remains limited for patients with bone metastases or liver metastases. **Methods:** Data from 2 large US administrative claims databases—IMS LifeLink Health Plan Claims (01/2001 – 03/2014) and Truven Health Analytics MarketScan (01/2002 – 09/2012)—were pooled for this retrospective study. Among adult patients with a lung cancer diagnosis, *ALK*+ NSCLC patients were identified based on prescription fills for crizotinib. Patients were analyzed if they had ≥60 days of follow-up before and ≥30 days after the bone metastasis or liver metastasis diagnosis date. **Results:** A total of 231 *ALK*+ NSCLC patients were selected: 191 had bone metastasis and 104 had liver metastasis. For the bone metastasis sample, median age was 54.9 years, 39.3% were male, and median time from first lung cancer diagnosis to the bone metastasis diagnosis was 30 days. The frequency of symptoms frequently associated with bone metastasis increased after bone metastasis diagnosis compared to before. Common skeletal-related events included pathologic fractures (before: 0.5% vs. after: 12.6%), spinal cord compression (2.6% vs. 5.2%), and bone radiation therapy (12.6% vs. 62.3%).Other common symptoms were weakness/fatigue (before: 24.6% vs. after: 46.6%), anemia (10.5% vs. 33.0%), back pain (8.4% vs. 22.5%), bowel dysfunction (6.8% vs. 20.9%), and neoplasm-related pain (0.0% vs. 14.1%). For the liver metastasis sample, median age was 54.0 years, 42.3% were male, and median time from first lung cancer diagnosis to first liver metastasis diagnosis was 151 days. The frequency of symptoms frequently associated with liver metastasis also increased compared to before liver metastasis diagnosis, where most common symptoms were nausea/vomiting (before: 21.2% vs. after: 42.3%), abdominal pain (20.2% vs. 34.6%), fever/sweating (6.7% vs. 27.9%), edema (6.7% vs. 25.0%), jaundice (0.0% vs. 3.8%), and fatigue (29.8% vs. 46.2%). **Conclusion:** *ALK*+ NSCLC patients experience an increased symptomatic burden after developing bone metastasis or liver metastasis. Further research is warranted to analyze the impact of the symptomatic burden on patient quality of life and other outcomes as well as the potential benefit of instituting second-generation *ALK*-inhibitors earlier in the treatment course. **Keywords:** ALK, ALK Inhibitor, non-small cell lung cancer, Metastatic Disease

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-021 Crizotinib Efficacy in ALK-Positive Advanced NSCLC Chinese Patients Shaohua Cui[1], Yizhuo Zhao[1], Aiqin Gu[1], Xiaoxiao Ge[1], Yanyan Song[2], Wei Zhang[1], Yuqing Lou[1], Lili Dong[1], Baohui Han[1], Liyan Jiang[1] [1]*Department of Pulmonary Medicine, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China,* [2]*Department of Biostatistics, Shanghai Jiao Tong University, School of Medicine, Shanghai/China*

Background: Anaplastic lymphoma kinase (ALK) is a new tyrosine kinase target that has been validated recently in NSCLC. Crizotinib, an oral, small-molecule, tyrosine kinase inhibitor that targets ALK, MET and ROS-1, has been reported to be particularly effective and to have acceptable toxicity in advanced anaplastic lymphoma kinase (ALK)-positive non-small-cell lung cancer (NSCLC). In a phase 1, open-label, multicenter trial evaluating the efficacy and adverse event profile of crizotinib in a cohort of 82 ALK-positive lung cancer patients, treatment for a mean duration of 6.4 months achieved an overall response rate (ORR) of 57%, and the estimated probability of 6-months' progression-free survival (PFS) was 72%. Mild gastrointestinal disturbances were the main adverse effects observed in this study. Subsequently, updated data from a study involving 143 patients confirmed the durable response and tolerable adverse effect profile of crizotinib in patients with ALK-positive NSCLC. **Methods:** A total of 72 patients with ALK-positive NSCLC who received crizotinib between June 1, 2013 and October 15, 2014 at Shanghai Chest Hospital, Shanghai JiaoTong University, were prospectively enrolled in the study. All were histologically diagnosed and staged as clinically advanced (stage IV, or stage IIIB with pleural effusion) NSCLC. All patients received oral crizotinib 250 mg twice daily in 28-day cycles. The tumor response was assessed after the first cycle of crizotinib therapy and subsequently after every 2 cycles using the Response Evaluation Criteria in Solid Tumors (RECIST), version 1.0. Tolerability was assessed at least twice per cycle until crizotinib was discontinued. **Results:** The patients tended to be young (mean age 55 years, range 31-83 years), never or light smokers (smoking index <400), and to have an adenocarcinoma histology. Most (49/72; 68.1%) had received previous anticancer treatment before crizotinib therapy. Sixty-seven patients (93%) were able to be assessed for efficacy. The objective response rate (ORR) and disease control rate (DCR) were 52.2% (95% CI 40.5%-63.9%) and 64.2% (95% CI 52.75%-75.7%), respectively. The estimated median progression-free survival (PFS) for all 67 patients was 10.3 months (95% CI 8.6-12.0 months). Mild visual disturbances, nausea, vomiting, diarrhea and constipation were the most commonly reported adverse effects.



Kaplan-Meier curve of progression-free survival for 67 patients. Tick marks represent censored observations.

Conclusion: crizotinib was well tolerated and showed promising efficacy in Chinese patients with ALK-positive, advanced NSCLC. Further prospective, multicenter studies with a larger sample size are needed to confirm these findings. **Keywords:** Anaplastic lymphoma kinase, efficacy, Non-small-cell lung cancer, crizotinib

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-022 Radiologic Features of Advanced ALK-Rearranged Lung Cancer Kakeru Hisakane, Eri Sugiyama, Keisuke Kirita, Shigeki Umemura, Shingo Matsumoto, Kiyotaka Yoh, Seiji Niho, Hironobu Ohmatsu, Koichi Goto *Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Chiba/Japan*

Background: Reportedly, the radiologic features of most primary resectable lung cancers harboring an anaplastic lymphoma kinase (ALK)-fusion do not exhibit a ground-glass opacity (GGO) component when viewed using CT. However, little is known about the features of advanced ALK-rearranged lung cancer. **Methods:** The radiologic features of 21 advanced ALK-positive lung cancers treated at the National Cancer Center Hospital East between January 2012 and June 2014 were retrospectively investigated. ALK-fusion was confirmed using IHC and FISH or RT-PCR methods. The primary tumor's diameter

and characteristics (i.e., presence of a GGO component, notch, spiculation, and pleural indentation) as viewed using CT and the SUVmax observed using PET before treatment were evaluated. The radiologic features of 181 EGFR/ALK-negative non-sq NSCLCs treated during the same period were also evaluated as a control group. In addition, sites of distant metastases were evaluated. **Results:** The median age of patients with ALK-positive lung cancer was 58 years (range, 25-83 years). Of the 21 patients, 8 (39%) were female and 11 (52%) were never-smokers. The proportion of primary tumors smaller than 3 cm was significantly higher among the ALK-positive tumors than among the EGFR/ALK-negative tumors (48% vs. 21%, P = 0.01). Notches (71% vs. 41%, P = 0.01) and pleural indentations (81% vs. 55%, P = 0.03) were significantly more common among the ALK-positive tumors than among the EGFR/ALK-negative tumors. No significant differences in peripheral GGO (4.8% vs. 6.1%, P = 1.00) and spiculation (71.4% vs. 54.7%, P = 0.17) were observed. The median SUVmax values of the primary tumors were not significantly different (9.33 [range 4.56-28.81] vs. 10.54 [range 1.20-38.18], P = 0.91). Regarding the sites of distant metastases, liver (33% vs. 8%, P < 0.03) and pleural dissemination (48% vs. 24%, P = 0.03) were more frequent among patients with ALK-positive tumors than among patients with EGFR/ALK-negative tumors. **Conclusion:** We identified the radiologic features of advanced ALK-positive lung cancer, which include smaller-sized primary tumors and higher frequencies of notch and pleural indentation, compared with EGFR/ALK-negative tumors. These findings might be useful for the selection of patients with advanced ALK-positive lung cancer. **Keywords:** site of distant metastases, advanced ALK-rearranged lung cancer, Radiologic features

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-023 Discrepancy of ALK Status in Lung Adenocarcinoma Subtypes According to the IALSC/ATS/ERS Classification in Chinese Patients Shun Lu[1], Yongfeng Yu[2] [1]*Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China,* [2]*Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai/China*

Background: This study aimed to determine the relationship between ALK status and predominant subtype, according to the IALSC/ATS/ERS classification. **Methods:** A reclassification of 638 surgically resected adenocarcinomas was performed in Shanghai Chest Hospital. ALK Status was detected by immunohistochemistry (Ventana Medical Systems) in these patients.All of the cases were confirmed by two independent pathologists.**Results:**Themostprevalentsubtypewasacinarpredominant(46.0%),followed by papillary predominant (25.2%), solid predominant (9.2%), micropapillary predominant (8.7%), variants of invasive adenocarcinoma (5.5%), lepidic predominant(5.3%), minimally invasive adenocarcinoma(2.0%), and adenocarcinoma in situ(1.0%). ALK positive was identified in 29 of 638 tumors (4.5%). The ALK positive frequencies were: 3.0%(8/284) for acinar predominant, 1.9%(3/156) for papillary predominant, 12.3%(7/57) for solid predominant, 5.3%(3/54) for micropapillary predominant, 17.6%(6/34) for variants of invasive adenocarcinoma, 3.0%(1/33) for lepidic predominant, 7.7%(1/13) for minimally invasive adenocarcinoma, and 0%(0/7) for adenocarcinoma in situ, respectively. ALK positive was significantly associated with the solid predominant subtype (p=0.003) and variants of invasive adenocarcinoma(p=0.0002). **Conclusion:** The ALK positive frequencies of solid predominant subtype and variants of invasive adenocarcinoma were higher than other subtypes. **Keywords:** lung adenocarcinoma, histologic classification, ALK status

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-024 Case Report of a Patient with Non-Small Cell Cancer Treated in Two Consecutive Randomized Clinical Trilas. Safety of Imaging Procedures Ewa Chmielowska[1], Maciej Studzinski[2], Marcin Świezynski[3], Przemyslaw Szlezak[4] [1]*Clinical Oncology, Oncoogy Center, Bydgoszcz/Poland,* [2]*Oddział Kliniczny Onkologii Chemioterapiii, Szpital Onkologiczno Kliniczny Magodent, Warszawa/Poland,* [3]*Clinical Oncology, Oncology Center, Bydgoszcz/Poland,* [4]*Radiology, Oncology Center, Bydgoszcz/Poland*

Background: Severala rates for patients with adenocarcinoma of the lung who cannot be treated with targeted therapies due to lack of EGFR gene mutation or EML4-ALK translocation are relatively poor. Clinical trials with a new compounds pose a chance to improve treatment outcome, but also expose patients to many additional and potentially risky-related diagnostic procedures **Methods:** Case study analysis of 57 - years old male patient diagnosed in 2008 with metastatic adenocarcinoma of lung cT2N0M1. Patient was in good condition without any significant comorbidities.Patient has been qualified to A6181058 clinical trial- he received 6 cycles of Paclitaxel and Carboplatin chemotherapy with subsequent maintenance therapyconsisting of 72 Bevacizumab infusions.Partial remission has been achived with reduction of tumor size by 60%. Subsequently, due to disease progression, patient have been enrolled into another clinical trial - EC-FV-07 - 9 cycles of Docetaxel and 26 injections of folate receptor inhibitor EC145 has been applied. After 71 months since treatment initiationdisease has progressed.Upon disease progression paliative radiotherapy has been started. During treatment period, because of clinical trial scheduling requirements, contrast-enhanced computed tomography (CE-CT)scans were performed every 6 to 8 weeks. During whole disease course neither lung cancer itselfnor applied treatment did not impaire patient's daily activity. Aim of this report is to analyse a disease course and risks of repeated contrast enhanced computed tomography in patient treated with potentially nepfotoxic drug with long lasting maintenace treatment. **Results:** During seven years of treatment contrast-enhanced chest CT scans has been performed 57 times. Effective radiation dose patient has received was 395mSv and 4560 mg of iodine-based contrast was injected.Cumulative doses of chemotherapeutic agents was as folows- Bevacizumab -87480 mg; EC145(Vintafolide) - 90 mg, Carboplatin 3700 mg, Paclitaxel -2508 mg, Docetaxel -1710 mg. Baseline renal function described by glomerular filtration rate (GFR) was 78 ml/min and during treatment GFR never dropped below ml/min. Patient developped sensory peripheral neuropathy, CTC grade 2.Use of ACE inhibitor therapy due to arterial hypertension has been initiated.No other clinically significant toxicity has been observed, including myelotoxicity and renal toxicity other than non-significant transient proteinuria. **Conclusion:** By presenting this case report we would like to bring attention to long -term survival in patient with metastatic NSCLC treated with two lines of chemotherapy that included taxane and targeted molecular therapy. Despite potentially nephrotoxic regimens and rigorous iodine- based CT disease monitoring scans no significant toxicity has been observed. A matter of discussion is a significance of ACE inhibitor for renal protection in contrast-and chemotherapy -induced toxicity. **Keywords:** toxicity, clinical trials, long survival, lung adenocarcinoma

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-025 Radical Resection for Supraclavicular Lymph Node Metastasis (N3-Stage IIIB) Adenocarcinoma of the Lung Jun Zhang, Changyu Wang, Shichun Xie, Xueshan Qiu *China Medical University Lung Cancer Center, The First Hospital of China Medical University, Shenyang/China*

Background: In China, lung cancer is increasing rapidly, of which 80% are non-small cell lung cancer, and most belong to Stage IIIB and IV when diagnosed, losing opportunity of surgery, and the prognosis is worse, the average survival time is about 6-12 months. Recently we perform radical resection for part N3-Stage IIIB non-small cell lung cancer, hope to improve the prognosis of these patients. A typical case is discussed here. **Methods:** Case1: Man, aged 43 in Dec 2012, found right supraclavicular lymph node swollen, CT showed right lower lobe tumor 7X6X5cm3, invading right inferior pulmonary vein and pericardium, regional and mediastinal lymph node 11,10,7,4R,3,2R,1R swollen badly; right supraclavicular lymph node biopsy revealed the diagnosis of lung adenocarcinoma; no other distant metastasis was found in brain, liver, and bone; cT3-4N3M0 Stage IIIB, which is usually contraindication of surgery. Three cycles' preoperative chemotherapy of Pemetrexed and cisplatin (DDP) was conducted, the lung tumor shrunk 1/3, mediastinal lymph node shrunk significantly, and the right supraclavicular lymph node disappeared. PET-CT showed right lower lobe tumor and part mediastinal lymph node positive, however, showed negative in the neck and other part of the body; cT2aN1-2M0 Stage IIA-IIIA, prepared for operation. **Results:** Standard "large-incision" right posterolateral thoracotomy was performed, pleural adhesion, tissue edema, fragile, easily broken, easy bleeding were encountered. Right lower lobe lobectomy, systematic lymph node dissection including No.2R,3A,3P,4R,7,9,10,11,12 group lymph node and surrounding adipose tissue were en block dissected. Tumor size 4X4X3cm3, postoperative pathology diagnosed as lung adenocarcinoma, No.12 lymph node metastasis, others were negative, pT2aN1M0 Stage IIA. Two cycles' postoperative chemotherapy was followed. Regular follow-up showed the patient recovered very well. Now he is in his 3rd year postoperatively, living a healthy man's life. CT, Ultrasound, ECT, and blood tumor markers' test showed no sign of recurrence and metastasis. **Conclusion:** Part supraclavicular lymph node metastasis N3-Stage IIIB non-small cell lung cancer, if prepared carefully, could gain the opportunity of receiving surgical resection, could achieve a much more better prognosis, even to get cured as usual Stage IA-IIIA lung cancer patients who receive regular radical resection of lung cancer. **Keywords:** supraclavicular lymph node metastasis, N3 Stage IIIB, preoperative chemotherapy, lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-026 Post-Treatment Effects of Lung Cancer on Spinal Fracture Malcolm O. Tagbarha *Public Health, University of Abuja, Abuja/Nigeria*

Background: Studies have shown the relationship between cancers and bone diseases. Observations have also shown that the spine, rib and pelvis are more susceptible to cancer for riches in marrow that fosters tumor growth. We particularly examined the relationship with spinal fractures and cancer **Methods:** The medical records of more than 100 lung cancer survivors were assessed from six Teaching Hospitals in Eastern (Ethiopia and Tanzania) and Southern African countries from 2003-2013. We checked for osteolytic lesions and osteoblastic lesion as the patients have undergone several kinds of screening during and after cancer treatment including DXA (Dual-energy X-ray Absorptiometry), plain X-ray or magnetic resonance imaging (MRI) to screen for metastatic bone disease **Results:** We found that an estimated 30-40% of the lung cancer patients developed bone metastases and disrupted the balance between bone breakdown and repair which caused reduction of bone in some areas and increased density in others. As a result, the bone was weakened and became more prone to spinal fracture after treatment **Conclusion:** As lung cancer has spread thereby causing spinal fractures, treatment needs to be focused on disease control with chemotherapy. The treatment of bone metastases will be primarily dependent on an effective treatment against lung cancer itself **Keywords:** bone metastases, lung cancer, spinal fracture, bone diseases

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-027 Prognostic Impact of Cytological Fluid Tumor Markers in Non-Small Cell Lung Cancer Arthur Cho[1], Jin Hur[2], Yoo Jin Hong[2], Hye-Jeong Lee[2], Young Jin Kim[2], Sae Rom Hong[2], Young Joo Suh[2], Dong Jin Im[2], Yun Jung Kim[2], Jae Seok Lee[3], Hyo Sup Shim[3], Byoung Wook Choi[2] [1]*Nuclear Medicine, Yuhs, Seoul/Korea,* [2]*Diagnostic Radiology, Yuhs, Seoul/Korea,* [3]*Pathology, Yuhs, Seoul/Korea*

Background: Serum tumor markers CYFRA 21-1, CEA, and squamous cell carcinoma antigen (SCCA) are useful in non-small cell lung cancer (NSCLC) diagnosis and prognosis. Cytologic tumor markers obtained during needle aspiration biopsy (NAB) of lung lesions help in NSCLC diagnosis. This study investigated the incremental prognostic value of cytologic tumor markers compared to serum tumor markers. **Methods:** This prospective study included 253 patients diagnosed with NSCLC by NAB with cytologic tumor marker analysis. Cytologic CYFRA 21-1, CEA, SCCA and serum counterparts were followed up for survival analysis. Optimal cut-off values for each tumor marker were obtained for overall survival (OS) and progression free survival (PFS) analysis. **Results:** All patients were followed up for median 22.8 months. Using cut-off value of 0.44ng/ml for C-SCCA, 2.0ng/ml for S-SCCA, and 3.3ng/ml for S-CYFRA, multivariate analysis revealed that high S-CYFRA (Hazard ratio (HR): 1.573), high S-SCCA (HR: 1.999), and high C-SCCA (HR: 1.744) were independent predictive factors for OS. The 3 year overall survival was 55% vs 80% for high and low C-SCCA. **Conclusion:** Cytologic tumor markers are poor prognostic factor in NSCLC patients as serum tumor markers, with C-SCCA showing a strong prognostic factor for overall survival. **Keywords:** cytologic tumor marker, serum tumor marker, NSCLC, Prognosis

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-028 Pathological Characteristics of Lung Cancer Patients in Colombian Coffe Zone Gustavo Rojas[1], Marco Kimmel[1], Jaime A. Echeverri F[2], German A. Moreno[1], Jose W. Martinez[1], Paula Londno[1] [1]*Oncologos Del Occidente S.A., Pereira/ Colombia,* [2]*Pulmonary Medicine, Oncologos Del Occidente, Pereira/Colombia*

Background: During 1998 and 2013 at the "Colombian Coffee Zone" (conformed by three states Caldas, Quindio, and Risaralda) had an increase of 105 mortality cases of Bronchi and lung malignant tumors, as reported in death certificates. **Methods:** This is an observational, descriptive study, that was made in patients at Clínica Oncologos del Occidente in the year 2014. Information was taken from the Clinical History Administration System (SAHICO). Thereafter, pending data was collected, by phone calls to patients or patient's family, according to every case. Patients were interviewed to know their actual performance status and, in case of death, date and basic cause of death was asked **Results:** SAHICO reported 178 patients with lung cancer. From these patients, 33 did not have a correct diagnosis. Basically, they did not have a histology report. This happens in patients that consulted with a clinical presentation compatible with a pulmonary origin neoplasia and radiologist reports concluding thorax tumors, which had a lung dependency. But patients had a very low performance status, because they did not assist to the second appointment or never started treatment; finally they died by the disease. The prevalence of these tumors was slightly more common in men. 50% of the patients were between 60.7 and 74 years old. The median age was 69.1 years for males and 64.1 for women. This age median differences were statistically significant (F=9,121 p value=0,003). Also, 90.8% of the patients were from urban areas. 85.3% of tumors treated during 2014 corresponded to NSCLC, meanwhile 10% were Small Cell lung cancer. It was also observed a relationship of 1.7 patients with Squamous cellular carcinoma for every patient with Adenocarcinoma. 28 patients were tested for the EGFR mutation analysis, from these, 5 were mutated. Squamous cellular carcinoma patients were older than Adenocarcinoma patients. Besides this, patients with Small cell had a Media and Median age higher than the squamous cellular carcinoma. Although, Squamous cellular tumor patients were more frequent, the median survival time was inferior to adenocarcinoma patients and the Non-Small cell lung cancer. And neuroendocrine tumor patients had also a longer survival than Squamous cellular patients. **Conclusion:** Pathological characteristics of Lung cancer patients in Colombian Coffee Zone are in general similar than the other latitudes, predominating the squamous cellular carcinoma and with an incidence around 10% of the small cell carcinoma; it is striking the sex relationship close than 1:1, presumably for the early incorporation of the female population to smoking habit and to others known risk factors like the expose to combustion biomass smoke. The epidermic growth factor receptor (EGFR) mutation was observed in same proportion than in other studies. **Keywords:** Lung Neoplasms, Surveillance, Survival, Carcinoma Bronchogenic

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-029 Dutch Radiotherapy Lung Audit: Results of 2014 Jose Belderbos[1], E. Troost[2], M Ten Berge[3], Iris Walraven[1], B. Reymen[2], C. Tissing-Tan[4], J. Widder[5], F. Koppe[6], E. Vonk[7], I. Coremans[8], J. Bussink[9], K. De Jaeger[10], N. Van Der Voort Van Zyp[11], S. El Sharouni[12], H. Knol[13], J. Peer-Valstar[14], A. Van Der Wel[15] [1]*Department of Radiation Oncology, The Netherlands Cancer Institute – Antoni Van Leeuwenhoek Hospital, Amsterdam/Netherlands,* [2]*Department of Radiation Oncology (Maastro Clinic), Maastricht University Medical Center, Maastricht/Netherlands,* [3]*Department of Surgery, Leiden University Medical Center, Leiden/Netherlands,* [4]*Department of Radiation Oncology, Institute for Radiation Oncology Arnhem, Arnhem/Netherlands,* [5]*Department of Radiation Oncology, University Medical Center Groningen, Groningen/Netherlands,* [6]*Department of Radiation Oncology, Verbeeten Institute, Tilburg/Netherlands,* [7]*Department of Radiation Oncology, Radiotherapeutisch Instituut Stedendriehoek En Omstreken (Riso), Deventer/ Netherlands,* [8]*Department of Radiation Oncology, Leiden University Medical Center, Leiden/ Netherlands,* [9]*Department of Radiation Oncology, Radboud University Nijmegen Medical Center, Nijmegen/Netherlands,* [10]*Department of Radiation Oncology, Catharina Hospital, Eindhoven/Netherlands,* [11]*Department of Radiation Oncology, Medical Center Haaglanden, The Hague/Netherlands,* [12]*Department of Radiation Oncology, University Medical Center Utrecht, Utrecht/Netherlands,* [13]*Department of Radiation Oncology, Medical Center Alkmaar, Alkmaar/Netherlands,* [14]*Department of Radiation Oncology, Medical Spectrum Twente, Enschede/Netherlands,* [15]*Department of Radiation Oncology, Radiotherapy Institute Friesland, Leeuwarden/Netherlands*

Background: The Dutch Radiotherapy Lung Audit (DLRA) is an outcome registration that provides the local health professionals with an instrument to compare and improve their lung cancer treatments. It ensures transparency regarding clinical outcome, quality and safety of lung cancer treatments in the radiotherapy departments throughout the Netherlands. Patients receiving thoracic radiation treatment with curative intent for (primary or recurrent) stage I-IIIB Non-Small Cell Lung Cancer (NSCLC) were included in the registry. The results of the DLRA on the first fully registered year, 2014, are reported. **Methods:** Information collected included patient, tumor and treatment characteristics, the incidence and severity of acute toxicity, mortality within three months after radical radiation treatment and the time interval between diagnostic work-up and start of the radiotherapy. The adherence to the waiting time (time between referral and start of the irradiation) and throughput time (time between planning CT scan and start of the irradiation) guidelines were registered and analyzed, as well as the use of modern treatment techniques such as stereotactic irradiation and image-guided radiotherapy. **Results:** 14 out of 21 radiotherapy institutes included patients in the DLRA database. A total of 1350 patients were entered from January-December 2014. Patients were treated with concurrent (32%) or sequential chemoradiation(20%), radiotherapy only (13%) or stereotactic ablative body radiotherapy (SABR [35%]). On a patient record level, there was a high level of completeness. The mean age was 69 years (range 32-91, 59% males). Charlson comorbidity index ≥ 2 was present in 42% of patients. Most patients (45%) were cN+ with 20% cT4 tumors. Fifty eight percent of all patients started irradiation within 21 days after referral (range 0-89%). For 68% of the patients SABR started within 10 days after the planning-CT scan was acquired (range 17-100%) (fig 1). There was no correlation between the number of patients treated and the throughput times. Most patients received IMRT or VMAT irradiation. All registered patients had position verification during irradiation, mostly 3D (94%). Three-month (calculated from the end of RT) acute esophagus toxicity (grade≥ III) and pneumonitis (grade≥ II) of concurrent treatment were 12.4% and 3.9%, 6.1% and 4.1% for sequential chemoradiation, 3.3% and 4.3% for radiotherapy only, and 0.4% and 2.3% for SABR, respectively. Three-month mortality rates were 8.2%, 8.5%, 9.6%, and 1.7%, respectively. **Conclusion:** The Dutch Radiotherapy Lung Audit on outcomes after (chemo)radiotherapy is directed towards an improvement of care for lung cancer patients. There's room for improvement in the waiting and throughput times. **Keywords:** non-small cell lung cancer, Clinical audit, waiting times, throughput times

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-030 Curable Bulky T4 Right Lower Lobe Tumours Invading Diaphragm and Liver: A Distinct Entity? Noelle O'Rourke[1], Fiona Roberts[2] [1]*Clinical Oncology, Beatson West of Scotland Cancer Centre, Glasgow/United Kingdom,* [2]*Pathology, Southern General Hospital, Glasgow/United Kingdom*

Background: One third of patients with non-small cell lung cancer present with unresectable stage III disease. The median survival for all stage III(A and B) tumours with optimal chemoradiation in published series ranges 17-24 months. Using platinum doublet neoadjuvant chemotherapy as primary treatment the expected response rate is modest at 30-40%. In patients presenting with bulky T4 tumours with direct extension to diaphragm and beyond into liver, the expected outlook would be extremely poor. We report here a series of four such cases over a five year period in our practice which challenge our understanding of this disease **Methods:** Our regional lung cancer network presents all new patients at multidisciplinary tumour meetings to agree staging and management plan. We record data on all new patients registered with demographic data, performance status, results of staging and pathology investigations, treatment proposed, treatment delivered and outcomes in terms of progression free and overall survival. **Results:** Between January 2009 and end 2013 we recorded four cases of bulky right lower lobe lung cancers which showed radiological evidence of invasion into diaphragm (1 case) or beyond to liver (3 cases). There were 2 men and 2 women with ages 34, 51, 52 and 68. Three had squamous carcinoma and in one tumour was poorly differentiated, no subtype. Two were staged radiologically T4N2 and two were T4N0 but both with gross visible extension into liver. All patients were fit and received induction chemotherapy (2 carboplatin/paclitaxel and 2 cisplatin/vinorelbine). All had extraordinary responses to chemotherapy and proceeded to microscopically complete surgical resection. One patient had no viable tumour at operation including within the necessary liver resection. Another had only necrosis in the liver but small area viable residual tumour at right hilum and proceeded to post-op radiotherapy. All are alive with no evidence of recurrence with follow-up ranging 22, 34, 64 and 71 months **Conclusion:** This series although small is remarkable for the exquisite chemosensitivity of locally very advanced squamous cancers which have been apparently cured by neoadjuvant chemotherapy and surgical resection. We are undertaking additional pathological analysis of these specimens to determine whether there is a linking characteristic. **Keywords:** Bulky T4, liver, neoadjuvant chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-031 Feasibility of Median Sternotomy Approach for Locally Advanced Lung Cancer Hiroki Sato, Takeshi Kurosaki, Shinji Otani, Yuho Maki, Kentaro Miyoshi, Hiromasa Yamamoto, Seiichiro Sugimoto, Junichi Soh, Masaomi Yamane, Shinichi Toyooka, Takahiro Oto, Shinichiro Miyoshi *Departments of Thoracic, Breast and Endocrinological Surgery, Okayama University Graduate School of Medicine, Okayama/Japan*

Background: Trimodality therapy is one of therapeutic options for local advanced lung cancer. While a posterolateral thoracotomy was used as the standard approach, a median sternotomy with or without transverse thoracotomy is applied if necessary. In our institution, we have applied median approach for patients who need dissection of contralateral mediastinal lymph nodes or clamp of great vessels, mainly pulmonary artery, for a safe resection. The purpose of this study was to evaluate the feasibility and clinical outcome of median sternotomy approach for locally advanced lung cancer after chemoradiotherapy. **Methods:** Between March 2002 and December 2014, 35 non-small-cell lung cancer patients underwent radical surgery with median sternotomy approach after induction chemoradiotherapy . The medical records were reviewed to investigate clinical outcomes including perioperative complications. **Results:** The median patient age was 59 years (range: 41–77 years). There were 28 men and 7 women in the series. The histological subtype was adenocarcinoma in 21 patients, squamous cell carcinoma in 14. 16 patients had stage IIIA disease, and 19 had stage IIIB disease. The median postoperative hospital stay was 23 days. As notable perioperative complications, 12 patients revealed tachycardia that needs medication, 6 pneumonia, 3 radiation-induced pneumonitis, one wound ablation, one bronchial stump fistula, and one chylothorax. All of them were manageable. There was no treatment-related death in this cohort. As patients' survival, the 3-year and 5-year overall survival rates were 77.7 % and 67.1 %, respectively. The 1-year and 3-year recurrence-free survival rates were 75.4 % and 63.4 %, respectively. **Conclusion:** Our experience indicates that median sternotomy approach for locally advanced lung cancer after ChRT is feasible procedure after chemoradiotherapy. **Keywords:** median sternotomy, induction chemoradiotherapy, locally advanced lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-032 Surgical Resection for Lung Adenocarcinoma after Afatinib Treatment Hirofumi Suzuki[1], Motohiro Nishimura[1], Asuka Okada[2], Junichi Shimada[3] [1]*Thoracic Suregery, Saiseikai Suita Hospital, Osaka/Japan,* [2]*Respiratory Medicine, Saiseikai Suita Hospital, Osaka/Japan,* [3]*Thoracic Suregery, Kyoto Prefectural University of Medicine, Kyoto/Japan*

Background: Afatinib, an irreversible ErbB family blocker, has shown superiority to chemotherapy in patients with epidermal growth factor receptor gene (EGFR) mutated non-small cell lung cancer. However, there has been no report about the preoperative Afatinib treatment. We report a case of surgical resection for lung adenocarcinoma after Afatinib treatment. **Methods:** A 33-year-old female with a chronic cough was referred to our hospital because of an abnormality on a chest radiograph. Computed Tomography (CT) displayed consolidation in left lower lobe. On bronchoscopic examination, her disease was diagnosed as adenocarcinoma of the lung, harboring EGFR mutation (exson19 deletions). Contrast-enhanced brain magnetic resonance imaging showed 4 brain metastases. Positron emission topography (PET) revealed abnormal accumulation in left lower lobe, lymph nodes (station 1, 4R, 5) and plevis. Her clinical staging was IV (T4N3M1b). Stereotactic radiotherapy for brain metastases (total 35Gy:7Gy/fraction) was done, and Afatinib was administered for 6 months. **Results:** These treatments resulted in a down-stage (T1aN0M1b) ; CT showed that the consolidation shrank and a single nodule (20mm) remained in S8 of left lower lobe. 3 of the brain metastases lost and the rest one diminished. PET revealed slight FDG uptake only in the nodule in S8 but not regional lymph node or in a distant site. We performed surgical resection for the nodule. Pathological examination revealed no cancer rest. The postoperative course was uneventful. She has been continuing Afatinib for 3 months without any recurrence after the surgery. **Conclusion:** We report the first case, to our knowledge, of a patient who obtained significant response to Afatinib and was proved no cancer rest by surgical resection. Although more observation period for this patient and prospective study are needed, this report provides insight into the efficacy of surgical resection after Afatinib treatment. **Keywords:** afatinib, Surgical resection, lung adenocarcinoma, preoperative treatment

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-033 Multiple Organ Metastasis Could Be Identified as Poor Prognostic Factors for NSCLC Zhenrong Zhang, Deruo Liu, Hongxiang Feng *China-Japan Friendship Hospital, Beijing/China*

Background: Metastatic spread of cancer to distant organs is the reason for most cancer deaths.Lung cancer frequently metastasize to bone, brain, lung, andliver, causing a shorter survival. Therefore, increased knowledgeof metastatic patterns is crucial in the treatment of patients. In this article, we evaluate the prognostic significance of postoperative metastasis organ in NSCLC. **Methods:** The relationship between postoperative metastasis and survival was investigated. Patients who underwent curative lobectomy and pathologically diagnosed with NSCLC between 2005.1 and 2011.12 were included in our study. SPSS 20.0 software was used for analysis. Survival rates were calculated using Kaplan-Meier survival plots and analyzed using the Cox regression. The variables with statistical significance in univariate analysis were included in multivariate analysis. Significant difference between groups could be found if p value was less than 0.05. **Results:** Finally 94 patients including 53 male and 41 female were enrolled in our study. The average age was 62 years old. Metastasis occurred during early stage (less than 2 years postoperatively) in 45 patients, and during late stage (more than 2 years postoperatively) in 49 patients. Single organ metastasis and multiple organ metastasis were found in 85 and 9 patients separately. the most popular metastatic site was pulmonary, and then bone and brain. The overall survival (OS) of all included patients was 41.5%. The median survival time was 43 months and 29 months for single metastasis and multiple metastasis groups separately. There was significant difference in the OS between GS and GM group (45.9% Vs 0, P<0.001). The median survival time was 50 months and 32 months for early metastatic patients and late metastatic patients separately. Significant difference could be in the OS between GS and GM group (53.3% Vs 30.6%, COX P=0.130, Breslow P=0.014). Cox regression showed age TNM stage (P=0.003), and single organ metastasis (P<0.001) were significant prognostic factors for NSCLC. **Conclusion:** Lung, bone, and brain were the most popular metastatic organ for postoperative NSCLC. The presence of multiple organ metastases could be identified as an independent poor prognostic factor in NSCLC. **Keywords:** non-small cell lung cancer, Prognosis, metastasis

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-034 Is There A "Physician Effect" in Medical Oncology? Hannah Jonker[1], Khalid Al-Baimani[2], Tinghua Zhang[3], Glenwood Goss[1], Scott A. Laurie[1], Garth Nicholas[2], Paul Wheatley-Price[2] [1]*Medical Oncology, The Ottawa Hospital Cancer Centre, University of Ottawa, Ottawa/ON/Canada,* [2]*Medical Oncology, The Ottawa Hospital Cancer Centre, University of Ottawa, Ottawa/Canada,* [3]*Ottawa Hospital Research Institute, Ottawa/Canada*

Background: Non-small cell lung cancer (NSCLC) is the commonest cause of cancer death globally, with a 5-year survival of 16%. Known prognostic factors include stage, performance status (PS) and gender, but does the choice of physician affect patient outcome? We assessed practice variations of four medical oncologists treating advanced NSCLC, investigating this impact on overall survival (OS). **Methods:** Following ethics approval, a retrospective analysis was undertaken of all newly diagnosed stage 4 NSCLC patients seen in out-patient consultation at our institution between 2009 and 2012. All physicians accepted unselected lung cancer referrals and all patients are included. Baseline demographics, systemic therapy received, reasons for not receiving therapy, and OS data were collected. Cox regression analyses (univariate and multivariate) were employed to assess determinants of OS. The physicians were blinded to the results. **Results:** Overall 528 patients were included. Baseline characteristics are shown in table 1. A significant variation was noted in the proportion receiving any systemic chemotherapy (p≤0.01) [D(60%), L(65%), R(43%), M(52%)] (Figure 1A). However OS was not statistically significantly different among all patients (p=0.47), among treated patients (p=0.18) or among untreated patients (p=0.22)(Table and Figure 1B). In multivariate analysis, factors associated with survival were PS (p<0.01), weight loss (<5%, ≥5%)(p<0.01), WBC (<11, ≥11)(p=0.0588) and platelets (<400, ≥400)(p=0.0374).

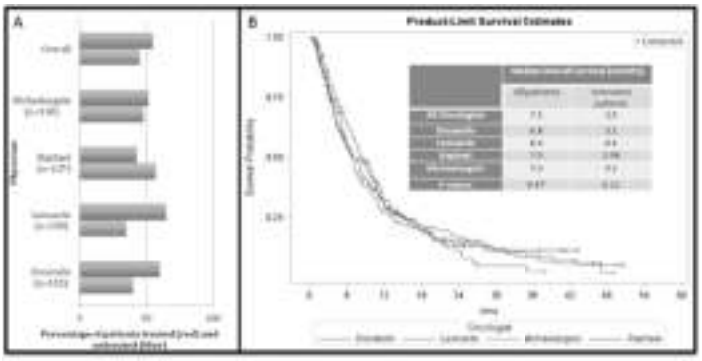

Figure 1. A) Proportion of patients receiving systemic therapy
B) Overall survival for all patients by physician

Demographic	Overall (n=528)	Physician R (n=137)	Physician M (n=118)	Physician D (n=115)	Physician L (n=158)	p-value
Median Age	68	70	68	67	67	0.23
Gender (male)	55%	58%	58%	49%	56%	0.42
PS (0-1)	50%	47%	48%	50%	55%	0.01
Hg (<100)	6%	11%	3%	4%	4%	0.01
LDH (<250)	28%	21%	30%	27%	33%	0.09
Platelets (<400)	71%	64%	75%	78%	70%	0.12
Weight loss (>5%)	48%	49%	48%	46%	49%	0.87
WBC (<11)	62%	56%	68%	68%	60%	0.11
Received ≥ 1 line systemic therapy	55%	43%	52%	60%	65%	<0.01

Conclusion: While practice size and proportion of patient treated did vary between oncologists, these did not translate into significantly different survival. There were statistically significant differences in the distribution of baseline characteristics between the 4 oncologists and this could cause the differences in proportion of patients treated. We hypothesize that as long as the oncologists are well trained and display good practice, survival is not dependant on the individual. This research does not measure other valuable characteristics or outcomes such as rapport, compassion, and quality of life, which may differ between physicians. **Keywords:** outcome, advanced, NSCLC, physician

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-035 Clinico-Epidemiological Features and Survival Outcome in Patients with NSCLC: Ain Shams Clinical Oncology Department 5-Year Data Ahmed A. Nagy, Mohamed Kelney *Clinical Oncology and Nuclear Medicine, Ain Shams University Faculty of Medicine, Cairo/Egypt*

Background: Primary lung cancer is the most common malignant neoplasm worldwide. In spite of the fact that in Egypt, according to various institutional and hospital-based data, bronchogenic carcinoma is the fifth most common malignancy among males the seventh most common cancer in females, its incidence continues to increase with no improvement in treatment outcome. This study aims to analyze the epidemiological factors and clinicopathological features of NSCLC in egyptian patients and evaluate the various lines of treatment and their impact on survival. **Methods:** This study included the examination and analysis of data collected retrospectively from the medical records of 504 patients diagnosed with NSCLC who were treated at Department of Clinical Oncology and Nuclear Medicine, Ain Shams University, Cairo-Egypt in the period from January 2008 till December 2012. **Results:** The median age of the cohort was 59 years (Range 33-80)with male predominance (74.4%) and 59.1% were of urban residence. The most common symptom at presentation was dyspnea (49.2%). Most patients were stage IV at presentation (73.2%) and adenocarcinoma was the most common histology (52.6%). About 85% of the patients received active treatment. The Median PFS after first,second and third lines was 3, 4 and 2 months respectively and the median OS was 8 months. Factors which were associated with a statistically significant difference in median OS were age <60 years versus ≥ 60 years (10 and 7 months respectively, $p<0.001$), female versus male gender (10 and 8 months respectively, $p<0.001$), urban versus rural residence (9 and 8 months respectively , $p=0.03$), smokers versus non-smokers (8 and 10 months respectively, $p<0.001$), patients presenting with non-neurological symptoms and those presenting with neurological symptoms (9 and 6 months respectively, $p<0.001$) and the receiving treatment versus no treatment (10 and 5 months respectively, , $p<0.001$). Cox regression analysis showed that the factors that were associated with shorter OS were age≥ 60 years, not receiving any line of treatment, patients presenting with neurological symptoms and male gender. **Conclusion:** This study shows that the active treatment of patients with NSCLC continues to have an important impact on survival. The fact that rural residence could be associated with worse OS warrants further investigation. We recommend large multicentric prospective studies comparing multimodality treatment approaches and including quality of life assessment. **Keywords:** NSCLC, Adenocarcinoma

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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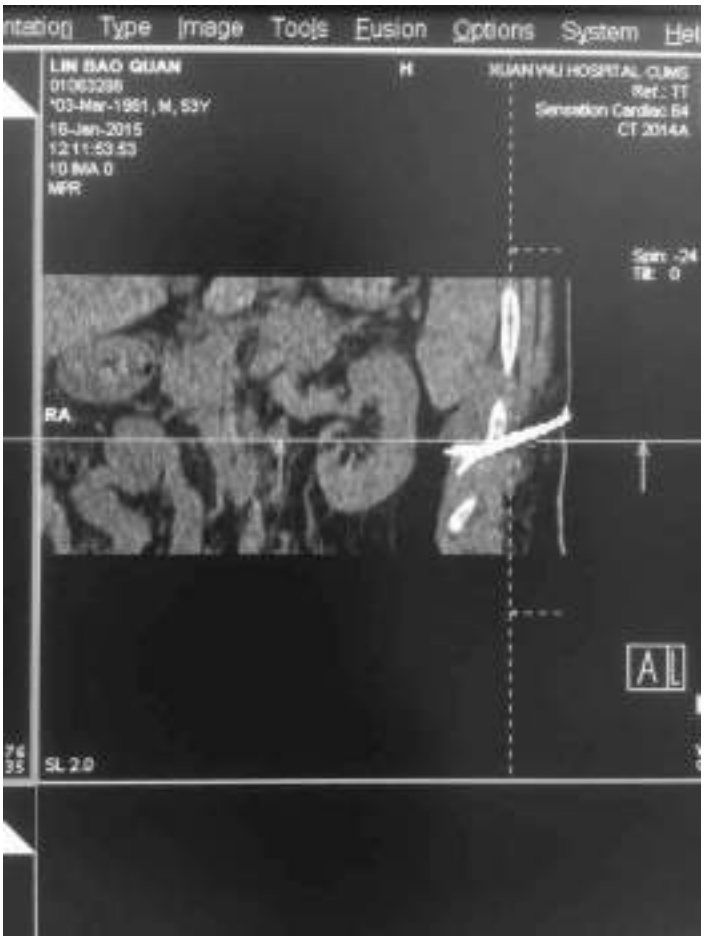
P1.01-036 RFA for Palliative Treatment of NSCLC Rib Painful Metastasis: Experience in 12 Patients Hu Mu *Thoracic Surgery Department, Xuanwu Hospital Capital Mediacl University, Beijing/China*

Background: Painful rib metastasis is common in NSCLC. Pain sometimes was partially or totally refractory to analgesic medications or the side-effects of medication were unacceptable. We report the safety and efficacy of a new method: radiofrequency ablation in treating painful none small cell lung cancer (NSCLC) rib metastasis. **Methods:** treating painful none small cell lung cancer (NSCLC) rib metastasis. Methods radiofrequency ablation procedures were completed in 12 patients with painful rib metastasis. Patient age ranged from 66 to 83 years (mean 74.8 years, Standard Deviation (SD) =5.3).Pathology: squamous-carcinoma 4 cases, adeno-carcinoma 7 cases and large cell carcinoma 1 case. Pain causing neoplasm size, pain levels pre- and post-procedure (as assessed using the Visual Analog Scale), time length and target temperature of radiofrequency ablation (RFA) treatments were documented.



Results: Radiofrequency ablation (RFA) procedures were performed with 100% technical success. The mean pre-procedure and post-procedure pain, as measured by the Visual Analog Scale (VAS), was 7.9 (SD=0.90) and 3.4 (SD=0.99) respectively. No symptomatic complications occurred. Non-symptomatic complications included 1 case of pneumothorax, 1 case of hemoptysis. **Conclusion:** RFA appears to be safe, practical and effective in the palliative treatment of none small cell lung cancer (NSCLC) chest wall painful metastasis. **Keywords:** palliative treatment, rib painful metastasis, Radiofrequency ablation, none small cell lung cancer

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P1.01-037 Successful Treatment of Non-Small Cell Lung Cancer with Erlotinib throughout Pregnancy Yongli Ji[1], Joanna Schwartz[2], Alan Hardford[3], Jon Ramsey[4], Julie Phillips[5], Claire Verschraegen[6] *[1]University of Vermont Cancer Center, Burlington, Vt/United States of America, [2]Albany College of Pharmacy, Albany/ United States of America, [3]Dartmouth-Hitchcock Medical Center, Lebanon/NH/United States of America, [4]University of Vermont Cancer Center, Burlington/United States of America, [5]Maternal Fetal Medicine, University of Vermont Medical Center, Burlington, Vt/VT/ United States of America, [6]University of Vermont Cancer Center, Burlington/VT/United States of America*

Background: Erlotinib is the standard of care for epidermal growth factor receptor (EGFR) mutated lung adenocarcinomas in the USA. However, in pregnant patients with lung cancer, chemotherapy is recommended, irrespective of EGFR mutations, given the lack of experience and uncertainty for fetus' safety with Erlotinib. **Methods:** A patient, with twin pregnancy after in-vitro fertilization, was intentionally treated with Erlotinib. Pharmacokinetics of Erlotinib and its active metabolite (OSI240) were measured in mother's plasma and twins' cord blood which were collected at delivery. Times of gestation, fetal growth, transplacental pharmacokinetics of Erlotinib, and cancer outcome were recorded. The pharmacovigilance of Erlotinib during pregnancy was analyzed by accessing Roche/Genentech global database. **Results:** A 47 year old woman, ten-weeks pregnant with twins, was diagnosed with stage 4 lung cancer which harbored an exon 19 deletion. She had brain metastases which were treated with stereotactic surgery during

the first trimester. Erlotinib -150 mg daily - was intentionally administered at the start of the second trimester. She was treated for 130 days. Growth retardation was noted in one fetus at week 33 and delivery was planned at week 37 by cesarean section. Drug concentrations in mother's plasma and twins'cord blood are shown in the table. Erlotinib and its metabolite cross the placenta, but only at 10-25% of blood concentrations. Side effects included a lower than expected birth weight (87% of normal) and transaminitis in both newborns that resolved within 3 months. The mother sustains an ongoing partial response to Erlotinib with minor skin rash and fatigue from treatment. The infants are normal at 10 months. **Table 1. Erlotinib Concentrations in Mother and Twins**

Sample	Erlotinib concentration (ng/mL)	%	OSI-420 concentration (ng/mL)	%	Newborn weight (g)
Mother plasma	54.31	100	16.25	100	-
Newborn A cord	13.67	25.2	2.12	13.0	2353
Newborn B cord	12.18	22.4	1.5	9.2	2438

OSI-420, Desmethyl-Erlotinib.
Conclusion: Erlotinib administration is feasible during late pregnancy and yields improved cancer outcome. **Keywords:** lung cancer, Erlotinib, Pregnancy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-038 Endosonographic vs Surgical Staging for Mediastinal Nodal Staging of Lung Cancer: A Systematic Review Prakash Balakrishnan[1], Casey Lo[2], Sean Galvin[2], Barry Mahon[2] [1]*Cardiothoracic Department, Wellington Regional Hospital, Wellington/New Zealand,* [2]*Cardiothoracic Surgery, Wellington Regional Hospital, Wellington/New Zealand*

Background: Endosonographic staging techniques mainly endoscopic (EUS-FNA) or endobronchial (EBUS-TBNA) with needle aspiration modalities has been increasingly described and used in many established centres since the early year 2000 as 1st line mediastinal staging compared to surgical staging (video / cervical mediastinoscopy) . Its minimally-invasive nature , with low complications rate , excellent diagnostic accuracy and ultimately cost-effectiveness are some of the main deciding factors involved .The aim of this review is to evaluate the diagnostic yield of endosonographic staging compared to surgical staging for mediastinal lymphadenopathy in lung cancer patients. **Methods:** A thorough extensive electronic literature database search in PUBMED ,EMBASE ,MEDLINE and ISI web of Science was conducted systematically , emphasizing endosonographic staging modalities vs surgical staging ,ranging from year 2000 up to April 2015 . These search engines were not confined to English-literature language only . Lung cancer patients were identified as a separate unit of analysis ,as well as these endosonographic staging methods at the level of mediastinum and its diagnostic yield (positive lymph nodes) were clustered in a different analysis group. In this review , the methodological analysis used was the Quality Assessment of Diagnostic Accuracy Study (QUADAS-2) as a tool to allow transparent rating of potential bias and application of primary diagnostic accuracy study. The primary end-point was the number of positive successful mediastinal nodal biopsies ,which was grouped according to the American Thoracic Society (ATS) classification . **Results:** A total of 10 major trials & reviews pertaining to this topic were extensively reviewed . Approximately nearly 1000 patients were grouped in this study ,who underwent either EUS-FNA staging with or without EBUS-TBNA and mediastinoscopy following diagnosis of lung cancer , either in a small or large , single or multiple centres across the world . The sensitivity , specificity , positive (PPV) & negative predictive values (NPV) and diagnostic accuracy or yield for endosonographic staging vs surgical staging modalities were cross-examined . **Conclusion:** According to the systematic analysis , these groups are moving forward for endosonographic (EUS-FNA or EBUS-TBNA) modalities compared to solely surgical staging (mediastinoscopy) in most cases . It seems to be a more promising ,successful & cost-effective method for sampling mediastinal nodes in lung cancer patients . **Keywords:** Endoscopic ultrasound-guided fine needle-aspiration, lung cancer, endobronchial ultrasound-guided transbronchial needle aspiration, lymphadenopathy

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P1.01-039 Lung Cancer in Kidney Transplant Recipients: A Case-Control Retrospective Study of 30 Patients Claire R. Gazaniol[1], Séverine Fraboulet[2], Louis-Jean Couderc[2], Henri Kreis[3], Raphaël Borie[4], Leila Tricot[2], Dany Anglicheau[3], Marie-Ange Massiani[2], Pierre Bonnette[2], Hélène Doubre[2], Francois Mellot[2], Gaelle Pelle[2], Edouard Sage[2], Patricia Moisson[2], Michel Delahousse[2], Magali Colombat[2], Alain Chapelier[2], Leila Zemoura[2], Philippe Puyo[2], Elisabeth Longchampt[2], Christophe Legendre[3], Sylvie Friard[2], Emilie Catherinot[2] [1]*Hôpital Foch, Suresnes/France,* [2]*Hopital Foch, Suresnes/France,* [3]*Hôpital Necker, Paris/France,* [4]*Hôpital Bichat, Paris/France*

Background: Kidney transplantation has dramatically increased during last decades. As significant progress has been made in the prevention and treatment of infections, cancer has become a major cause of concern. Limited data exist about lung cancer after kidney transplantation. **Methods:** The data from 2003 to 2012 of all transplanted patients with lung cancer in three French kidney transplant centers were retrospectively reviewed. 30 cases were included. Lung cancer incidence was determined in two centers for the 2008-2012 period. Each case was matched with two controls. Controls were patients without solid organ transplantation matched with the cases for age (<30; 30-50; 50-65; >65 years), gender and diagnosis date of lung cancer. **Results:** Lung cancer incidence in renal transplanted patients was 1.89/1000 person-years for the 2008-2012 period. Our cohort was mainly formed of male smokers around 60 years old, all current or former smokers. 43% were diagnosed by routine exams. Histopathological distribution was different with more squamous cell carcinoma. As expected, hypertension and ischemic heart disease were more prevalent but the other comorbidities and characteristics were the same in both groups. 60% had a stage IV cancer. Surgery was performed as often as in controls if the stage allowed it and advanced stage received full dose chemotherapy. Palliative care only was given to 20% of the patients. Hospitalization for infectious complications was somewhat higher in the cases group but global survival was similar. **Conclusion:** Kidney transplant recipients are likely to develop lung cancer. Despite frequent radiologic examinations, the majority of patients had advanced stage disease at diagnosis. Therapeutic management and prognosis did not differ between patients and control. As current or past smoking habit was present in all cases, a screening strategy should focus on smokers in this high-risk population. Our study was not designed to determine if other risks factors could be identified. **Keywords:** lung cancer, Kidney transplantation

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-040 Determining Completeness of Case Ascertainment to the Victorian Lung Cancer Registry: A Quantitative Case Finding Audit Rob Stirling[1], Peta Mclaughlin[1], Meera Senthuren[1], Baki Billah[1], Lise Hales[2], Mark Molloy[3], Chris Bain[2], Sue Evans[1] [1]*Epidemiology and Preventative Medicine, Monash University, Melbourne/VIC/Australia,* [2]*Health Information Services, Alfred Health, Melbourne/VIC/Australia,* [3]*Health Information Services, Epworth Health, Richmond/VIC/Australia*

Background: The Victorian Lung Cancer Registry (VLCR) pilot project aims to recruit all lung cancer cases diagnosed across participating Victorian sites. Case ascertainment derives from institutional ICD-10 coding. A quantitative, case finding audit was employed to evaluate the case ascertainment methodology and assess capture completeness at a Victorian public and private metropolitan hospital. **Methods:** Lists of lung cancer patients recorded for the period 01/07/2011 and 30/06/2012 were requested from institutional departments including; Radiotherapy, Palliative Care, Day Procedure Unit, Oncology Lung Multidisciplinary Team Meeting (MDM), Cardiothoracic Surgery (CTS), Pathology and the Victorian Cancer Registry (VCR). Comparisons were made between VLCR administrative capture versus clinical capture achieved by the use of clinical databases compared with mandated VCR capture. **Results:** The VLCR registered 125 new cases in Site A and 100 in Site B. A total of 10 (7.5%) patients in Site A and 13 (11%) patients in Site B had not been recruited by the registry. Investigations indicated that the underreporting of these cases was attributed to:

- Use of the ICD10 *R91* Code (when lung cancer is suspected but not confirmed)
- Non coded patients (e.g. day admissions, direct admission to palliative care or MDM)

Conclusion: The completeness of capture of incident cancers occurring in a population and included in a registry database is a vital attribute of a cancer registry. Current capture is approximately 90% and inclusion of the R code and an attempt to capture uncoded patients will ensure registry incidence rates are close to their true value.

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-041 Prognostic Significance of CT Emphysema Score in Patients with Advanced Squamous Cell Carcinoma of the Lung Young Saing Kim[1], Eun Young Kim[2], Min Young Baek[1], Hee Kyung Ahn[1], Eun Kyung Cho[1] [1]*Division of Hematology and Oncology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon/Korea,* [2]*Radiology, Gachon University Gil Medical Center, Incheon/Korea*

Background: Although the contribution of emphysema to lung cancer risk has been recognized, no study has focused the prognostic impact of CT emphysema score for advanced stage of lung cancer. The aim of our study was to analyze the prognostic value of CT emphysema score in patients with advanced squamous cell carcinoma of the lung (SCCL). **Methods:** We analyzed 84 consecutive patients with advanced stage (stage IIIB and IV) of SCCL who underwent palliative chemotherapy. The severity of emphysema was semi-quantitatively scored using baseline chest CT images according to the Goddard scoring system, ranging from 0 to 24. Data on clinical characteristics and survival were retrospectively collected. Survival was estimated by the Kaplan-Meier method and compared with the log-rank test. A multivariable Cox proportional hazard model was used to identify prognostic factors. **Results:** Most patients were male (89%) and current/ex-smokers (90%). The median CT emphysema score was five (range, 0 to 22). In univariable analysis, patients with higher CT emphysema score (> 6) showed a trend toward poor survival(6.3 months vs. 11.4 months in those with lower score, p=0.076). In the multivariable model, higher CT emphysema score was a significant independent prognostic factor for poor survival (HR,1.85; 95% CI, 1.14 to 3.00; p=0.012) along with response to first-line therapy (p=0.001) and second-line therapy (p<0.001). **Conclusion:** The CT emphysema score is significantly associated with poor prognosis in patients with advanced SCCL. **Keywords:** CT emphysema score, Squamous cell carcinoma, Prognosis

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-042 Maintenance Therapy with Pemetrexed after Induction Therapy with Pemetrexed plus Cisplatin for Advanced Pulmonary Adenocarcinoma Ho-Kee Yum, I-Nae Park *Department of Internal Medicine, Seoul Paik Hospital INJE University, Seoul, Korea, Seoul/Korea*

Background: Recently, continuation maintenance with Pemetrexed after induction therapy with pemetrexed plus cisplatin for advanced pulmonary adenocarcinoma has been approved in Korea. Therefore we retrospectively evaluated the activity and feasibility of continuation maintenance with Pemetrexed in Korean patients. **Methods:** Stage IIIB/V patients with pulmonary adenocarcinoma were evaluated from 2006 to 2015 April. We analyzed 12 cases with maintenance therapy with Pemetrexed. All patients received an induction phase which consisted of 4-6 cycles of induction pemetrexed (500 mg/m^2) plus cisplatin (75 mg/m^2) on day 1 of a 21-day cycle and maintenance therapy with pemetrexed (500 mg/m^2) every 21 days) plus best supportive care until disease progression. **Results:** Mean age was 61 years; 9 were men. Median number of total pemetrexed cycles was 18 (8-42). The mean overall survival time and the mean progression free survival were 46±12.3 months and 21.1±5.8 months, respectively. The median overall survival time and the median progression free survival were 29±20.8 months and 12±7.1 months, respectively. Discontinuations due to drug-related adverse events occurred in one (8%) patients. **Conclusion:** Continuation maintenance with pemetrexed is an effective and well tolerated treatment option for patients with advanced pulmonary adenocarcinoma with good performance status who have not progressed after induction therapy with pemetrexed plus cisplatin in Korea. **Keywords:** pemetrexed, advanced lung ca

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-043 Prognostic Factors in the First-Line Chemotherapy of Advanced Non-Squamous Non-Small Cell Lung Cancer Patients with Performance Status 2 Shinobu Hosokawa, Akihiro Bessho, Kazuya Nishii, Nobuaki Fukamatsu, Yoshiko Ogata, Makoto Sakugawa *Department of Respiratory Medicine, Japanese Red Cross Okayama Hospital, Okayama/Japan*

Background: To evaluate prognostic factors in the first-line chemotherapy of advanced non-squamous non-small cell lung cancer patients with Eastern Cooperative Oncology Group(ECOG) performance status(PS) 2. **Methods:** We retrospectively analyzed clinical and laboratory characteristics of patients with advanced non-squamous non-small cell lung cancer patients with ECOG PS 2 who received the first-line chemotherapy in our institute. We examined the various clinical values such as gender, age, clinical stage, histology, immunohistochemistry, chemotherapy regimen, underlying diseases, metastasis sites, data of blood test. **Results:** A total of 31 patients aged 45 to 80 years (median 65) were treated from August 2006 to February 2015(male/female;23/8, adenocarcinoma/non-small cell carcinoma;15/16). They were received single agent or combination chemotherapy(carboplatin and pemetrexed(CP);17, others;14). In univariate analysis, median survival times were 9.56 months in adenocarcinoma vs 3.26 months in non-small cell carcinoma(P=0.0011) , 16.77months in Thyroid Transcription Factor-1(TTF-1) expression positive(n=10) vs 4.96 months in TTF-1 expression negative(n=9) (P=0.0166), 2.59 months in 7.0ng/ml and over of CYFRA21-1 vs 9.56 months under 7.0ng/ml of CYFRA21-1(P=0.0236), 8.53 months in CP vs 2.20 months in others(P=0.0003). Objective response rates were 29.4% in CP and 0% in others. **Conclusion:** Our results show that patients who were diagnosed adenocarcinoma pathologically had significantly better prognosis than the others, and CP may attributes to good prognosis of the patients with advanced non-squamous non-small cell lung cancer patients with ECOG PS 2. **Keywords:** Prognostic factors, performance status 2, Advanced Non-Small Cell Lung Cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-044 Cost-Effectiveness of Chemotherapy Based on the Tumor Genetic Profile in Elderly Patients with Advanced Non-Small-Cell Lung Cancer Federica Capano[1], Tiziana Vavala[2], Valentina Monica[2], Teresa Mele[2], Andrea Filieri[1], Carlotta Lerda[1], Daniela Ielo[1], Paolo Cortesi[3], Silvia Novello[2] *[1]Pharmacy, Aou San Luigi, Orbassano (Turin)/Italy, [2]Department of Oncology, University of Turin, Orbassano/Italy, [3]Research Centre on Public Health (Cesp), University of Milan-Bicocca, Monza/Italy*

Background: *Platinum-Based* chemotherapy is still the cornerstone in the treatment of Non-Small Cell Lung Cancer (NSCLC), in non oncogene-addicted patients (pts). Therapeutic algorithm is established on the basis of patient and disease characteristics, such as histology and radiologic features. Pharmagenomic-driven trials are investigating the role of different markers in predicting efficacy and toxicity in NSCLC pts. A better selection of a right therapy for the right patient would improve outcomes ameliorating tolerability and optimize the resources available. The aim of the present study is to carry out a cost-effectiveness analysis, in order to evaluate the economic efficiency of 1st line chemotherapy within a clinical trial (EPIC eudract N 2012-001194-81), in elderly pts affected from advanced NSCLC, looking at efficacy and tolerability. **Methods:** The study population consisted in Elderly Patients Individualized Chemotherapy (EPIC) trial enrolled at San Luigi Hospital (Orbassano-Italy, coordinating centre) from July 2012 to August 2014. Main recruitment criteria: chemotherapy-naïve pts diagnosed with stage IV NSCLC, aged≥70 years, no activating EGFR mutations. We evaluated 48 pts randomised (2:1 ratio) to receive pharmacogenomics-driven chemotherapy assessed according to the genetic profile of primary tumours based on expression of ERCC1, RRM1 and TS evaluated by "Real-Time PCR" (arm A) or standard chemotherapy (arm B). Costs of treatments were calculated using National Health System (NHS) direct costs and 12 months time-horizon. Effectiveness was estimated as Progression Free Survival (PFS). The Incremental Cost-Effectiveness Ratio (ICER) was calculated and pharma-economic analysis was performed setting the Willingness To Pay (WTP) threshold value at 40,000€ per free-disease month gained. The reliability of results was assessed by a probabilistic sensitivity analysis based on "Monte Carlo" method (10,000 simulations) changing the costs and effectiveness variables simultaneously. Number and grade of adverse events were used to determine the tolerability profile. **Results:** The average cost per patient was 10,278.38€ (arm A) and 8,659.53€ (arm B). Related ICER was 4,496.80€ per free-disease month gained and 53,961.73€ per year gained (over the WTP threshold). The scatterplot generated in the sensitivity analysis indicated that higher densities of ICERs, calculated for each simulation, took place at the cross over of the Cartesian axes indicating that there is no clear prevalence of treatment cost-effectiveness. Moreover, the Cost-Effectiveness Acceptability Curve (CEAC) was calculated. This curve demonstrated that treatment A had 35% of probability to be cost-effectiveness. **Conclusion:** This preliminary evaluation, conducted in a subgroup of pts, suggests the relevance of pharmacoeconomic analysis within a clinical trial looking at the best way to identify a tailored treatment in non-oncogene addicted NSCLC pts. Further data will be collected in a larger simple size. Personalised chemotherapy is a potential method addressing both the optimisation of the effectiveness of therapeutic agents and the minimisation of adverse events, objectives even more relevant for elderly and fragile patients, given the possibility to optimize the use of scarce resources available.

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-045 Drug Fever After Cancer Chemotherapy Is Most Commonly Observed on Post-Treatment Days 3-4 Minoru Fukuda[1], Daiki Ogawara[2], Shiro Ueno[3], Yoshihiro Ohue[4], Hiroshi Gyotoku[5], Hiroaki Senju[5], Shinnosuke Takemoto[5], Hiroyuki Yamaguchi[5], Katsumi Nakatomi[5], Yoichi Nakamura[5], Takuya Honda[1], Kazuma Kobayashi[1], Daisuke Nakamura[1], Hideyuki Hayashi[1], Mikio Oka[4], Kazuto Ashizawa[1] *[1]Clinical Oncology Center, Nagasaki University Hospital, Nagasaki/Japan, [2]Internal Medicine, Isahaya General Hospital, Isahaya/Japan, [3]Ikeda Hospital, Kagoshima/Japan, [4]Respiratory Medicine, Kawasaki Medical School, Okayama/Japan,[5]Respiratory Medicine, Nagasaki University Hospital, Nagasaki/Japan*

Background: Fever during cancer chemotherapy is require attention using antibiotics to prevention severe infection. On the other hand, it should be avoid using antibiotics to non-infectious fever such as drug and tumor fever with the object of development of resistant bacteria, exacerbation of drug fever, and medical economics. **Methods:** Retrospectively, 1,016 consecutive cycles of cancer chemotherapy were analyzed. Fever was defined as a temperature of ≥37.5°C. Age, sex, tumor histology, the treatment regimen, the timing of fever onset, the number of days for which the fever persisted, the cause of the fever, and the presence or absence of radiotherapy were examined. **Results:** Seventy-four percent of the patients (748 of 1016) were males, the patients' median age was 68 years (range: from 29 to 88 years), and lung cancer was the most common disease (93%). Fevers occurred in 36% of cycles (367 of 1016) including 37% of those involving males and 32% of those involving females. There was no difference in the frequency of fever among the sexes (p=0.146). The incidence of fever according to age were 33% (≤60), 41% (61-65), 36% (66-70), 33% (71-75), 41% (76-80), and 33% (≥81); it did not differ significantly with age (p=0.424). In incidence of fever according to the drugs administered, gemcitabine was the drug that was most frequently associated with fever (41%; 43/106), followed by irinotecan (40%; 108/272), amrubicin (39%; 29/75), and docetaxel (36%; 47/131). Post-treatment days 4 (8.3%), 3 (6.8%), and 12 (6.7%) were the days on which fever was most common. The distribution of fever exhibited a bimodal distribution; i.e., whilst it peaked on post-treatment days 3 and 4; otherwise, it generally gradually increased until day 12 and then gradually decreased. The peak on post-treatment days 3-4 was considered to be due to adverse drug reactions, and the latter peak was considered to represent neutropenic or infection-based fevers. Fevers occurred on post-treatment days 3-4 in 11% of all cycles (113 of 1016) including 11% (84 of 748) of the cycles involving males and 11% (29 of 268) of those involving females. The incidence of fever on post-treatment days 3-4 according to age were 12% (≤60), 13% (61-65), 10% (66-70), 8% (71-75), 13% (76-80), and 10% (≥81); however, this parameter did not differ significantly with age (p=0.427). The incidence of fever on post-treatment days 3-4, gemcitabine was the drug that was most commonly associated with fever (20%), followed by docetaxel (18%), nedaplatin (12%), and carboplatin (11%). The patients' fevers were caused by infections (47%), adverse drug reactions (24%), unknown causes (19%), and tumors (7%). The causative infections included febrile neutropenia (50%), pneumonia (18%), unidentified infections (9%), and colitis (7%). The incidence of fever was significantly higher among the patients treated with radiotherapy than among those that did not receive radiotherapy (46% vs. 34%, p=0.001). **Conclusion:** The febrile episodes that occurred on post-treatment days 3-4 were considered to represent adverse drug reactions after cancer chemotherapy. Physicians should be aware of this feature of chemotherapy-associated fever and avoid unnecessary examination and treatments including prescribing antibiotics. **Keywords:** drug fever, Radiotherapy, cancer chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-046 Characteristics of Complete Remission Cases in Advanced Non-Small Cell Lung Cancer Takuya Aoki[1], Kazuki Harada[1], Jun Tanaka[1], Masako Sato[1], Yukihiro Horio[1], Hiroto Takiguchi[1], Hiromi Tomomatsu[1], Katsuyoshi Tomomatsu[1], Takahisa Takihara[1], Kyoko Niimi[1], Naoki Hayama[1], Tsuyoshi Oguma[1], Takeshi Akiba[2], Tetsuya Komatsu[2], Tomoki Nakagawa[3], Rhota Masuda[3], Hitoshi Itoh[4], Hiroshi Kajiwara[4], Jun Nishiyama[5], Tetsuya Urano[1], Etsuo Kunieda[2], Naoya Nakamura[4], Atsushi Tsugu[5], Mitsunori Matsumae[5], Jill E. Slansky[6], Tullia C. Bruno[6], Masayuki Iwazaki[3], Koichiro

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Background: Various types of chemotherapies have been extensively investigated in advanced non-small cell lung cancer (NSCLC). Although median survival times have been getting long, the outcomes remain poor. This study aimed to analyze the characteristics of those with complete remission among advanced NSCLC patients. **Methods:** Based on our hospital database, 1,699 patients who were registered as lung cancer between August 2004 and April 2011 were examined, and Stage III or IV NSCLC patients, whose treatment began between September 2004 and April 2011, were retrospectively evaluated at September 2014. We defined complete remission as a continuous complete response observed in spite of the treatment initiation over three years ago, regardless of treatment continuation. **Results:** Seven patients were observed. Two patients were at stage IIIA, one at stage IIIB, and four at stage IV. The treatment modalities included cytotoxic chemotherapy only (one patient), chemotherapy and EGFR-TKI followed by surgery (one patient), radiosurgery for brain metastasis followed by surgery and chemotherapy (one patient), and chemoradiation (four patients). Three patients had adenocarcinoma, three squamous cell carcinoma, and one large-cell carcinoma. The numbers according to survival time since the date of treatment initiation were two (between three and four years), three (between four and five years), and two (over five years). All cases had complications of inflammatory diseases. In case 1, an acquired immunological response against lung cancer was suggested. The patient had rheumatoid arthritis and stage IV adenocarcinoma with massive pleural effusion, treatment was only 1 course of vinorelbine, and sepsis occurred after chemotherapy. After that, complete remission has been achieved. Acquired cancer immunity was also suggested in case 2, who had stage IV adenocarcinoma with cardiac tamponade. Pericardial drainage was done and three courses of cisplatin and gemcitabine were administered, followed by EGFR-TKI. Gefitinib have continuously been used for four years, however the tumor in the right upper lobe had gradually getting large. The tumor was resected, while EGFR mutation was negative and many inflammatory cell infiltrations were observed. In case 3, oligo-metastatic states have been controlled by surgery and radiation. The patient had stage IV large cell carcinoma with a brain metastasis, the primary pulmonary lesion was surgically removed after cyber-knife therapy. Chemotherapies were started. Oligo-metastatic new brain lesions were firstly cyber-knife therapies, and the relapsed or new lesions were removed by brain surgeries. After the brain surgery, encephalitis and meningitis developed. Many inflammatory cells were observed around and inside the brain tumor. Finally, the brain tumors and the pleural dissemination disappeared. In case 4, who had stage IIIA adenocarcinoma with bulky N2, PET-assisted three-dimensional conformal radiation therapy was used to control oligo-metastases. The tissue types of chemoradiation-induced complete remission were squamous cell carcinoma in three patients and adenocarcinoma in one patient. **Conclusion:** These results suggest that complete remission can be achieved for several types of advanced NSCLC by employing combinations of treatment modalities. Oligo-metastatic states could be controlled by surgery and radiation therapies with or without chemotherapies. The acquired immune response against lung cancer might be important to induce complete remission. **Keywords:** Advanced Non-Small Cell Lung Cancer, complete remmision, Tumor immunology, Oligo-matastatic states

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-047 Pemetrexed in Treating Advanced NSCLC Mivael Olivera, Roxana Ticona, Gerson Mejia, Jhoana Muniz, Luis Mas *Medical Oncology, Instituto Nacional de Enfermedades Neoplasicas, Lima/Peru*

Background: In advanced NSCLC, the goal of maintenance therapy is to prolong overall survival of first line platinum based combination chemotherapy. Maintenance Pemetrexed was associated with statistically and clinically significant improvement in both PFS ans OS. Objective was to determine the response rate, progression-free survival (PFS), overall survival (OS). **Methods:** Between January 2011 until July 2014, Peruvian patients with advanced NSCLC (IIIB, IVA) received four to six cycles of Carboplatin (AUC 6) - Pemetrexed 500mg/m2 day 1. Patients who achieved a complete response (CR), partial response (PR) o stable diase (SD) were to received maintenance Pemetrexed (500mg/m2 day 1) in 21 day cycles until disease progression. All patients recevied vitamin B12, Folic acid supplement. **Results:** 83 patients received induction chemotherapy and maintenance therapy, median age was 61 years (26 - 84), > 70 years 15.7%, female:male 1.5, no smoking:smoking 2.6, exposure to wood smoke 25 (30.1%), ECOG 1 98.8%, EC IIIB 8.4%, EC IV 91.6%, hystology Adenocarcinoma 100%. Sites of metastasis: pleural 36 (43.4%), bone 20 (24.1%), brain 7 (8.4%), liver 4 (4.8%). 40 (48.2%) received 4 cycles, 27 (32.5%) 6 cycles of induction chemotherapy; median of cycles of maintenance 5 cycles (1-16). Response to treatment: 4 (4.8%) RC, 42 (50.6%) RP, 30 (36.1%) DS, 7 (8.4%) PD. The median time to progression was 11 months, estimated PFS was 86.5%, 39.6%, 13.8% at 6, 12, 30 months respectively. The estimated OS was 68.8%, 51.4% and 41.5% at 12, 24 and 30 months respectively, median time to OS was 28 months. None variables are significantly associated with OS. **Conclusion:** Induction chemotherapy and maintenance therapy with Pemetrexed improves PFS and OS in patients with advanced lung cancer without compromising the quality of life. There is a need for better ways of identifying patients most likely to benefit. **Keywords:** PFS and OS, pemetrexed, advanced NSCLC, maintenance

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-048 Cost-Effectiveness of Pemetrexed for Advanced Non-Squamous Non-Small Cell Lung Cancer (nsNSCLC) in Patients Treated in a Spanish Institution Xabier Mielgo Rubio[1], Ruth Martínez Cabañes[2], Alejandro Velastegui[1], Adriana Rosero[1], Leticia Ruiz-Giménez[1], Cristina Aguayo[1], Maria Garcia Ferron[1], Jorge Silva[1], Elia Perez Fernandez[3], Carlos Jara[1] [1]*Medical Oncology, Hospital Universitario Fundación Alcorcón, Alcorcón/Spain,* [2]*Medical Oncology Research Unit, Hospital Universitario Fundación Alcorcón, Alcorcón/Spain,* [3]*Research Unit, Hospital Universitario Fundación Alcorcón, Alcorcón/Spain*

Background: Pemetrexed (Pem) is a widespread used drug as standard treatment option in patients diagnosed of nsNSCLC in different settings: first line combined with platinum, maintenance or second line treatment. The aim of this study is to assess the cost-effectiveness of Pem-based chemotherapy in routine clinical practice from the perspective of the Spanish National Health System. **Methods:** We evaluated retrospectively clinical outcomes, in terms of overall survival (OS) and progression free survival (PFS), in patients diagnosed of advanced nsNSCLC from 2005 to 2014 who were treated with Pem-based chemotherapy, and we performed a cost-effectiveness analysis. We assessed the cost-effectivenss of the use of Pem-based treatment in routine clinical practice calculating the cost per life years gained (LYG) from the first time the patient received Pem, based on the price established in Spain and the number of cycles received. We calculated OS from the start date of Pem to the death or last contact with the patient, and PFS from the start date of Pem to first tumor progression after Pem. **Results:** 114 patients treated with Pem-based chemotherapy were reviewed, 78.9% men and 21.1% women. Mean age at diagnosis was 64 (range 36-81). 80.7% were smokers or former smokers. 90.4% were stage IV and 9.6% IIIB. The predominant histology was adenocarcinoma (69.3%), followed by large cell carcinoma (22.8%), NSCLC-NOS (7%) and pleomorphic carcinoma (0.9%). 59.6% of patients received Pem in first-line and/or maintenance (1L - Maint.), and 40.3% in second or successive lines. The majority of them had a good functional status; ECOG 0 25,4% and 1 59,6%. Median number of received Pem cycles was 5 (range 1-39). Median number of treatment lines was 3 (range 1-8). Clinical outcomes: 68.6% obtained clinical benefit (46.1% stable disease, 21.5% partial response, and 1% complete response). Median progression free survival (PFS) was 5.16 months in 1L- Maint., and 4.55 months in second or successive lines (p = 0,278). Median OS was significantly better in 1L – Maint. setting than in second or successive lines (17.8 vs 9.8 months (p = 0,033)). The mean cost of Pem-based chemotherapy per LYG was 18988 euros in 1L-Maint. setting and 17095 euros in second or successive lines. **Conclusion:** From the perspective of the Spanish National Health System, Pem-based chemotherapy was cost-effective in both first line and/or maintenance setting, and second or successive treatment lines in our patients. The cost per life year gained (LYG) from treatment with Pem was below the standard threshold of 30000 euros. **Keywords:** pemetrexed, Cost-effectiveness, Life Years Gained (LYG), non squamous Non Small Cell Lung Cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-049 Feasibility of Cisplatin plus Etoposide for Non-Small Cell Lung Cancer Associated with Interstitial Lung Disease on Chest Computed Tomography Masafumi Yamaguchi[1], Takashi Seto[1], Akio Furuya[2], Hinichiro Shimamatsu[1], Gouji Toyokawa[1], Kaname Nosaki[1], Fumihiko Hirai[1], Mitsuhiro Takenoyama Takenoyama[1], Yukito Ichinose[1] [1]*Department of Thoracic Oncology, National Kyusyu Cancer Center, Fukuoka City/Japan,* [2]*Department of Diagnostic Imaging and Nuclear Medicine, National Kyusyu Cancer Center, Fukuoka City/Japan*

Background: Despite the recent remarkable progress in chemotherapy (CTx) regimens, the application of CTx for non-small cell lung cancer (NSCLC) associated with interstitial lung disease (ILD) remains challenging because of the possibility of acute deterioration of the underlying ILD, which can lead to severe respiratory insufficiency, thus decreasing the life expectancy of the patient. To date, no acceptable CTx regimen for patients with ILD has been established. We herein assessed our series of non-small cell lung cancer patients with ILD treated with cisplatin and etoposide (PE). **Methods:** Unresectable NSCLC patients with ILD detected on chest computed tomography (CT) who received PE at our department between December 2006 and December 2013 were retrospectively reviewed. ILD was defined as interstitial opacity on CT, as confirmed by an independent radiologist. Overall survival (OS) was defined as the time from the start date of any treatment to the date of death from any cause. Progression-free survival (PFS) was defined as the time from the start date of PE to disease progression or cancer-related death. **Results:** A total of 32 NSCLC patients with ILD were evaluated. There were 31 males and one female, with a median age of 66 (53-79) years. The ECOG performance status was 0/1/2 in 17/13/2 patients. Seventeen patients had adenocarcinoma, six patients had squamous cell carcinoma and nine patients had NSCLC. Three patients experienced post-surgical recurrence. The clinical stage was IIB/IIIA/IIIB//IV in 2/5/8/17 patients. The subtypes of ILD classified according to the CT appearance were the usual interstitial pneumonia pattern in 22 patients and a non-specific interstitial pneumonia pattern and previous drug-induced pneumonia in five patients each. Oral steroids were administered concomitant with CTx in two patients. Twenty-four patients received PE as the first-line CTx, while the other eight patients received PE after more than two regimens of CTx. Grade 3/4 hematological toxicity of leukopenia was noted in 15 (46.9%) patients, neutropenia was observed in 24 (75.0%) patients, thrombocytopenia occurred in four (12.5%) patients and anemia was detected in six (18.8%) patients. Grade 3 febrile neutropenia was recorded in six (19.4%) patients, grade 3 and 4 acute myocardial infarction occurred in one patient each and grade 3 cerebral infarction occurred in one patient. Two patients experienced grade 2 worsening of ILD and successfully recovered. The response rate was PR/SD/PD in 10/19/2 patients, and one patient could not be evaluated because

of an adverse event. The median PFS was 3.9 months, the one-year PFS was 12.8% and the two-year PFS was 4.3%. Additionally, the median OS for all patients was 11.2 months, the one-year OS was 46.2% and the two-year OS was 14.2%. **Conclusion:** PE treatment for unresectable NSCLC associated with ILD was demonstrated to be relatively safe in our series, with an acceptable tumor response and OS. However, careful patient selection and management during CTx are required. The limitation of the current analysis is its retrospective nature and the fact that there was a single arm of CTx therapy. Hence, future prospective comparisons of other CTx regimens are warranted. **Keywords:** Interstitial pneumonia, cisplatin and etposide, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-050 Clinical Features of Non-Squamous Non-Small-Cell Lung Cancer Patients Treated with Long-Term Pemetrexed Kenichiro Hirai, Hiroshi Yokouchi, Keisuke Azuma, Hiroyuki Minemura, Satoko Sekine, Kenya Kanazawa, Yoshinori Tanino, Mitsuru Munakata *Department of Pulmonary Medicine, Fukushima Medical University, Fukushima/Japan*

Background: It has been generally accepted that pemetrexed (PEM) with platinum followed by PEM maintenance therapy is a standard first-line treatment for patients with advanced non-squamous non-small cell lung cancer (NS-NSCLC). The number of patients treated with long-term use of PEM is increasing, and thus we should know the clinical features including side effects in those patients. Belen et al. reported that skin toxicities were related to PEM maintenance therapy, while Jean et al. demonstrated that 7.8% of patients receiving maintenance PEM had grade 1/2 edema in the PARAMOUNT trial. Further investigation into clarifying the clinical features of these patients is required. **Methods:** We retrospectively reviewed the charts of 13 patients with advanced NS-NSCLC who had been treated with long-term PEM (10 and more courses) in our hospital between July 2009 and December 2014. **Results:** All patients had adenocarcinoma. The median age was 63 years (range: 39-72). Six patients were male, and six were never-smokers. All but one patient were classified as clinical stage IV. Six patients harbored EGFR mutation and one patient had ALK gene rearrangement. Twelve patients received PEM with platinum (cisplatin; seven patients, carboplatin; five patients), and one patient received PEM alone. The median number of courses of PEM was 16 (range: 10-21). Grade 3/4 non-hematological toxicities observed in the 13 patients were anorexia (8%), nausea (8%), and dizziness (15%). Grade 3/4 hematological toxicities observed were neutropenia (46%), anemia (15%), and thrombocytopenia (15%). Two patients had peripheral skin edema; one patient developed eyelid edema at 21 cycles of PEM, and the other developed limb edema and pleural fluid at 20 cycles of PEM. Four patients underwent PEM beyond RECIST PD following platinum-based doublet chemotherapy regimen (CDDP+PEM; 2, CBDCA+PEM; 2). Initial response by the induction chemotherapy was PR in two patients and SD in two patients. The PD sites were lungs in two patients, bone in one patient and adrenal gland in one patient. The median post progression survival (PPS) of each of the four patients was 205.5 days (range; 68-330). All the four patients underwent PEM until "clinical" PD. Progressive sites were lungs in two patients, bone in one patient and esophagus in one patient. The median duration between RECIST PD and clinical PD was 100.5 days (range; 35-210). **Conclusion:** The differential profile of adverse effects, including dizziness and edema, driven by long-term PEM compared with those by conventional use of PEM suggested that we should cautiously select supportive therapies for NSCLC patients who are being treated with long-term PEM. Continuation of PEM beyond PD can be in consideration for selective patients with NS-NSCLC, as observed in patients treated with EGFR-TKI. **Keywords:** Long-term, Beyond PD, pemetrexed, NS-NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-051 Efficiency of Nab-Paclitaxel as a Late Phase Chemotherapy for NSCLC Mitsunori Higuchi[1], Hironori Takagi[2], Yuki Owada[1], Takuya Inoue[1], Yuzuru Watanabe[1], Mitsuro Fukuhara[1], Takumi Yamaura[1], Satoshi Muto[1], Naoyuki Okabe[1], Yuki Matsumura[1], Takeo Hasegawa[2], Atsushi Yonechi[3], Jun Osugi[1], Mika Hoshino[1], Yutaka Shio[4], Koichi Fujiu[5], Ryuzo Kanno[6], Akio Ohishi[6], Hiroyuki Suzuki[1] [1]*Chest Surgery, Fukushima Medical University, Fukushima/Japan,* [2]*Shirakawa Kousei General Hospital, Shirakawa/Japan,* [3]*Takeda General Hospital, Aizuwakamatsu/Japan,* [4]*Fukushima Rosai Hospital, Iwaki/Japan,* [5]*Southern Tohoku General Hospital, Koriyama/Japan,* [6]*Fukushima Red Cross Hospital, Fukushima/Japan*

Background: Nanoparticle albumin-bound (nab) paclitaxel is a biologically interactive nanoparticle, combining albumin with paclitaxel and has a better toxicity profile compared to solvent-based paclitaxel. Recently some studies are reported which show the efficacy of nab-paclitaxel as first line chemotherapy for non-small cell lung cancer (NSCLC), but rarely reported until today to elucidate the efficacy of nab-paclitaxel with carboplatin (CBDCA) as second or later phase chemotherapy for NSCLC. We here evaluate the efficiency and feasibility of nab-paclitaxel plus CBDCA as second or later phase chemotherapy in patients with recurrent or advanced NSCLC in this study. **Methods:** Twenty-five patients with recurrence after radical surgery for NSCLC and unresectable stage IIIB/IV NSCLC who had received previous chemotherapies were treated with nab-paclitaxel 70mg/m^2 intravenously on day1, 8, and 15 with CBDCA area under the concentration-time curve of 4 (AUC4) intravenously on day1, every 28 days. Progression-free (PFS) and overall survival (OS) rates were calculated by means of Kaplan-Meier analysis and statistical significance between the groups was analyzed by using log-rank tests. Disease control rates and toxicity were also evaluated. Disease response in all of the patients was monitored after two cycles of chemotherapy. **Results:** Of 25 patients who participated in this study, 9 were recurrent and 16 were advanced case. 13 were adenocarcinoma, 11 were squamous cell carcinoma and 1 was large cell carcinoma. 13 were performed as second line chemotherapy, 6 were as third line and 6 were forth or later line. EGFR mutation status was positive in 5 patients (20.0%) and they all received EGFR-TKI in their serial chemotherapy. One achieved complete response (CR), 7 reached a stage of partial responses (PR), 10 maintained stable disease (SD) and 7 suffered progressive diseases (PD). The overall response rate (ORR) was 32.0% and disease control rate (DCR) was 72.0%. The median PFS was 4.8 months and median OS was 29.0 months. Common treatment related adverse events were myelosuppression, baldness, peripheral neuropathy and gastrointestinal symptoms, most of which were grade 1 to 2. Grade 3-4 neutropenia was present in 6 patients (24.0%), thrombocytopenia and anemia in 2 patients (8.0%), respectively. No patients experienced grade 3-4 neuropathy. The need of a dose reduction was 26.9% because of toxicity, but there were no adverse effects of grade 5. **Conclusion:** Nab-paclitaxel plus CBDCA as second or later phase chemotherapy offers a small but significant survival benefits for the patients with recurrent and advanced NSCLC, and its adverse effects are tolerable. Further studies including prospective studies of this regimen are required. **Keywords:** nab-paclitaxel, late phase chemotherapy, carboplatin

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-052 Retreatment with Platinum-Based Regimen for Patients with Metastatic NSCLC Is a Reasonable Therapy Rachel L. Mitchell[1], Mary J. Fidler[1], Sanjib Basu[1], Philip Bonomi[1], Shruthi Melinamani[1], Audrey Kam[2], Marta Batus[1] [1]*Hematology, Oncology and Cell Therapy, Rush University Medical Center, Chicago/United States of America,* [2]*Internal Medicine, Rush University Medical Center, Chicago/United States of America*

Background: Standard first-line therapy in stage IV NSCLC patients remains a platinum-based regimen. Currently, there are limited FDA approved agents for second line therapy following progressive disease. The purpose of this study was to evaluate the response to retreatment with platinum-based regimens upon progression in a group of platinum-sensitive patients. **Methods:** Patients with stage IV NSCLC previously treated with a platinum-based first-line regimen were retrospectively reviewed. We examined the outcomes of 52 patients retreated with a platinum-based regimen upon progression between February 2002 and March 2015. Patients were evaluated for response rate, progression free survival, overall survival and platinum reactions. **Results:** Of the 52 patients reviewed, 31 were women (59.6%) and 21 were men (40.4%). Median age was 62.6 (range 42-89) and adenocarcinoma was the most prevalent histology (86.5%). The response rate for retreatment was 21.15%. A notable 57.69% of patients had stable disease. The median PFS for the first line platinum regimen was 9.2 months (CI 95%; 6.28-12.13) and for the retreatment was 4.8 months (CI 95%; 3.17-6.42). The median OS from diagnosis was 23.31 months (CI 95%; 11.76-34.85). A platinum reaction was noted in 9 of the patients (17.3%) though none were fatal. **Conclusion:** Patients with prolonged PFS with frontline chemotherapy appear to benefit from retreatment with a platinum-based regimen. This cohort demonstrated by a PFS of 4.8 months upon retreatment. Patients with prolonged progression free survivals with frontline chemotherapy may be reasonable candidates to consider for retreatment with a platinum-based regimen. **Keywords:** Platinum, metastatic, NSCLC, Retreatment

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-053 Thiol - Disulfide Ratio (TDR) in Blood as a Predictive in Vitro Test for Individualized Targeted Therapy Choice in Patients with Advanced NSCLC Oleksandr O. Obodnikov[1], Genadiy V. Didenko[2], Oleksandr V. Parshikov[3] [1]*Thoracic Surgery and Pulmonology, P.L.Shupik National Medical Academy of Postgraduate Education, Kiev/Ukraine,* [2]*Biotherapy of Cancer, R.Y.Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, Kiev/Ukraine,*[3]*Experimental Treatment, Institute of Pharmacology and Toxicology, Kiev/Ukraine*

Background: Despite the available positive results of targeted therapy (TT) in clinical oncology, more and more actual is a problem of preliminary screening of patients with solid tumors to whom TT will bring success. TDR is an integrated indicator of redox balance in biological cells which reflects dynamics of activity of a set of the thiol-containing cellular enzymes. It is known that the TDR level in a blood of cancer patients has a direct correlation with TDR in cancer cells. It assumes possibility of use change of TDR in a blood under the influence of drugs for indirect research of influence on biochemical processes in tumor cells. The possibility of prognosis of clinical efficacy and choice of effective targeting agents by means of TDR-test in blood in vitro in patients with advanced NSCLC was the purpose of the study. **Methods:** Between 09/11 and 10/14 we enrolled 52 treated patients (M/F - 44/8) with advanced NSCLC (stage IIIB/IV - 44/8); adenocarcinoma -21, squamous-cell carcinoma - 27, large-cell carcinoma - 4. The median number of prior chemotherapy regimens was 3 (range 1-6), median performance status - 1 (range 0 -3). Prior before TT course, patient's blood was tested in vitro with targeting agents: erlotinib, gefitinib, cetuximab, trastuzumab, bevacizumab; the respons was evaluated on the dynamics of TDR during 24- our incubation. All the patients received two 4-week courses of treatment: the standard TT (control group, n=25) or such targeting agent susceptibility to which was confirmed by the TDR-test (study group, n=27). Clinical respons was evaluated by RECIST. **Results:** After the end of treatment, the analysis of in vitro TDR reactions on the targeted agents tested showed direct correlation with the clinical results. According to the TDR-test, a portion of effective drugs was 50% - 100% in 92% of the patients, whose treatment resulted in regression or stabilization of disease. At the same time, in 94% of the patients, whose treatment resulted in progression of disease, a portion of effective agents was only 0 - 49%. Among the two groups of patients, objective clinical effects were observed in 7(26%) pts [(PR - 7(26%) pts, 95% CI: 11,6 - 55,2%), SD - 16(59%) pts, PD - 4(15%) pts)] in the study group

versus 2(8)% pts [(PR - 2(8)% pts, 95% CI: 3,3 - 16,2%); SD - 8(32%) pts, PD - 15(60%) pts.)] in the control group; grade 3 and 4 toxicity was experienced by 1(4,0%) pt and 2(8%) pts, respectively, - in the control group, and by 1(3,7%) pt and 0, respectively, - in the study group. Sensitivity of the method used to choice efficacious targeting agent amounted to 91,8%, specificity (selectivity) was 94,5% in forecasting the cases resistant to targeting agent. **Conclusion:** The determination of individual sensitivity to targeted agents in patient's blood in vitro by means of TDR- test is an effective method both for forecasting clinical efficacy of the treatment and for individual choice of TT in patients with advanced NSCLC. These findings need futher validation in additional clinical studies.
Keywords: Advanced NSCLC, Individualized therapy, Targeted therapy, Thiol-Disulfide Ratio

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-054 To Analyse the Efficacy and Toxicity Profile of Continuation Maintenance Pemetrexed in Advanced NSCLC: An Indian Data
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Background: Continuation maintenance therapy with pemetrexed has been proved to be well tolerated ,offers an overall survival benefit and reduced risk of disease progression in Phase III Paramount trial. Based on same it is approved as a category 1 recommendation for patients with nonsquamous advanced lung cancer, who do not progress after pemetrexed plus platinum induction regimen. However there is lack of data from Indian subcontinent. Here we report the data from a tertiary care cancer centre in North India **Methods:** - In all 280 patients were registered as advanced non squamous lung cancer(stage IV) between JAN 14 to DEC 14. Subsequently 96 patients received pemetrexed plus platinum based initial chemotherapy. 46 patients with no disease progression and ECOG PS 0 or 1 received maintenance pemetrexed (500 mg/m^2 on day 1 of 21 day cycles). Statistical tests were applied to calculate progression free survival. Toxicity profile was evaluated **Results:** The mean number of maintenance cycles was 9.5. Pemetrexed maintenance therapy resulted in progression free survival (PFS) of 5.4 months. PFS on pemetrexed was consistent for all patient subgroups, including induction response: complete/partial responders (n-24) and stable disease (n-22). 3 patients developed grade 3 or 4 toxicity as to cause a delay in cycles.2 patients also developed renal dysfunction during maintenance therapy. 7 patients continue to receive pemetrexed maintenance till date. **Conclusion:** Pemetrexed continuation maintenance therapy is well-tolerated and offers benefits consistent with Paramount trial, demonstrating that it is an efficacious treatment strategy for Indian patients with advanced nonsquamous NSCLC and good performance status who do not progress during pemetrexed-platinum induction therapy
Keywords: continuation maintenance pemetrexed NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-055 Prognostic Impact of KRAS Mutational Status in Patients with Advanced Lung Adenocarcinoma Receiving First-Line Cytotoxic Chemotherapy
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Background: KRAS mutations are among the most commonly encountered mutations in lung adenocarcinoma. Although differential outcomes from cytotoxic agents according to histology have been shown in lung adenocarcinoma, the prognostic and predictive impact of KRAS mutational status is controversial. Recently, a study identified greater dependency on folate metabolism pathways in KRAS mutant (mt) compared to KRAS wildtype (wt) NSCLC (Moran et al, Mol Cancer Ther 2014, 6:1611-24). We sought to evaluate the clinical outcomes of patients with lung adenocarcinoma to first-line cytotoxic chemotherapy according to KRAS mutational status. **Methods:** This IRB-approved retrospective study involved patients from Roswell Park Cancer Institute (RPCI) diagnosed with inoperable stage III or IV lung adenocarcinoma from January 1, 2012 to December 31, 2013. Patients with documented KRAS mutational status who received chemotherapy were eligible. Patients with EGFR mutation or ALK translocation were excluded. The objective response (OR) to chemotherapy was assessed using RECIST version 1.1 criteria. The primary end points were Progression Free survival (PFS) and Overall Survival (OS). Secondary endpoint was the time to achieve OR. OS was estimated by the Kaplan-Meier method and compared using the Log-rank method. The association between study endpoints and variables of interest (age, gender, stage, ECOG performance status [PS], KRAS mutation status) were conducted with univariate and multiple Cox models. SAS version 9.4 (SAS Institute, Cary, NC) were used for statistical analyses. All tests were two-sided and performed at a nominal significance level of 0.05. **Results:** A total of 123 patients were eligible for this analysis. In our study, 53 (42%) patients carried KRAS mutations. Majority of patients had stage IV cancer at presentation (74%). There was no difference in distribution of KRAS mutation status by the stage of disease at presentation. The most common first-line chemotherapy regimen was pemetrexed-based platinum combination (85%). When pemetrexed-based regimen was utilized as first-line therapy, univariate analysis showed correlation between KRAS status, gender, stage and PS with OS, favoring KRAS wt, female, stage III and PS 0, respectively. After controlling for other related covariates, only gender, stage and PS remain independently associated with better OS. Patients with KRAS wt had a longer median OS compared to KRAS mt patients (414 vs 249 days, p=0.027). PFS and time to OR were similarly better in KRAS wt group although these were not statistically significant. There was no imbalance in terms of second-line therapy between KRAS mt vs wt patients. There was no difference in study endpoints according to KRAS mutation status observed in patients who received taxane-based chemotherapy as first line treatment. There was also no difference in survival outcomes according to first-line treatment regimen used when patients were stratified according to KRAS mutation status. **Conclusion:** KRAS mutation status is not correlated with treatment outcomes in patients with advanced lung adenocarcinoma receiving first-line cytotoxic chemotherapy.
Keywords: KRAS, NSCLC, pemetrexed

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-056 A Prospective Audit on Toxicity for Platinum-Based Chemotherapy in Stage IIIB/IV Non-Small Cell Lung Cancer (NSCLC): A West of Scotland Analysis
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Background: The current standard of care for patients with Stage IIIB/IV NSCLC with no activating Epidermal Growth Factor Receptor (EGFR) mutations recommends platinum (carboplatin or cisplatin) doublet chemotherapy in patients who are performance status 0-2. Although a number of options are available, evidence from Phase 3 Randomised Controlled Trials have previously shown no differences in survival outcomes in non-pemetrexed based regimens. We set out to prospectively audit toxicity and efficacy of four commonly offered platinum-based doublets in the West of Scotland with a view to making comparative conclusions from our data. **Methods:** Patients undergoing first line palliative chemotherapy with a platinum doublet in two lung cancer clinics in the West of Scotland (Glasgow and Lanarkshire) between July 2014 and April 2015 were included. Baseline demographics were obtained and entered into a common database. On each attendance for chemotherapy pre-assessment, toxicity data was recorded using CTC version 4.0 and prospectively entered into the database. Requirements for admission to hospital and the need for blood and platelet transfusions were also recorded. **Results:**To date 54 patients have been included. The median number of chemotherapy cycles was 2.7(150). 55% (30) of patients were male and 45% (24) female, with the majority sub-type being adenocarcinomas. The most commonly prescribed agent with platinum was pemetrexed (52%) followed by gemcitabine (24%) and vinorelbine (22%). The use of paclitaxel was lower than anticipated (2%). Toxicity data is available for all 54 patients (see table 1). Survival outcomes will be reported subsequently along with ongoing collated data on toxicity in additional patients in this prospective audit. Table 1

Platinum Doublet	Pemetrexed		Vinorelbine		Gemcitabine		Paclitaxel	
n	28		12		13		1	
Toxicity Grade No. pts (%)	G1/2	G3/4	G1/2	G3/4	G1/2	G3/4	G1/2	G3/4
Nausea	12 (42%)	0	5 (91%)	0	2 (15%)	1(7%)	0	0
Vomiting	3 (10%)	0	3 (25%)	0	2 (15%)	0	0	0
Anorexia	12 (42%)	0	6 (50%)	1(8%)	2 (15%)	0	0	0
Diarrhoea	3 (10%)	0	3 (25%)	0	1 (7%)	0	0	0
Constipation	6 (20%)	0	6 (50%)	0	6 (46%)	0	0	0
Fatigue	18 (64%)	4 (14%)	11 (91%)	1(9%)	13(100%)	0	0	0
Neurotoxicity	1 (3.5%)	0	1 (9%)	0	1 (7%)	0	0	0
Ototoxicity	1 (10%)	0	0	0	0	0	0	0
Alopecia	2 (7%)	0	3 (25%)	0	2 (15%)	0	0	0
Neutropaenia	1 (3.5%)	1(3.5%)	1 (9%)	0	4 (30%)	0	0	0
Thrombocytopaenia	1(3.5%)	1(3.5%)	0	0	4 (30%)	0	0	0

Conclusion: First line treatment of advanced NSCLC with platinum doublets in the West of Scotland is generally well tolerated. Toxicities exceeding Grade 2 were uncommon with any of the 4 platinum doublets. However, hospital admission was more likely in those receiving pemetrexed or vinorelbine doublets. The need for blood transfusion was more common in doublets containing pemetrexed or gemcitabine.
Keywords: non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-057 Gemcitabine plus Platinum versus Other Platinum Doublets in Squamous NSCLC Giorgio V.V. Scagliotti[1], Joseph A. Treat[2], Rafael Rosell[3], Cong Xu[4], Baoyue Li[4], Haidong Chi[4], Mauro Orlando[5], Caicun Zhou[6] *[1]Thoracic Oncology Unit, University of Turin, Turin/Italy, [2]Eli Lilly and Company, Global Med Affairs & Late Phase Prod Dev, Indianapolis/IN/United States of America, [3]Hospital Germans Trias I Pujol, Catalan Institute of Oncology, Barcelona/Spain, [4]Lilly China, Shanghai/China, [5]Emerging Markets, Eli Lilly Interamérica Inc., Buenos Aires/Argentina, [6]Department of Medical Oncology, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

Background: Squamous cell carcinoma is the second most common histologic subtype of non-small-cell lung cancer (NSCLC). Platinum-based doublet chemotherapy regimens remain the basis of front-line systemic treatment. Most studies in NSCLC included all histologic subtypes. Here we present a pooled analysis of gemcitabine in combination with cisplatin or carboplatin, specifically focusing on patients with squamous NSCLC, from three studies for which individual patient data are available. The objective of this analysis was to evaluate the efficacy of first-line gemcitabine plus platinum (GP) compared with other regimens plus platinum (OP). **Methods:** This analysis included squamous NSCLC patients from three randomized, open-label, phase III studies of gemcitabine: 1) gemcitabine plus cisplatin versus etoposide plus cisplatin (n=61), 2) gemcitabine plus carboplatin versus paclitaxel plus carboplatin (n=128), and 3) gemcitabine plus cisplatin versus pemetrexed plus cisplatin (n=473). Patients were grouped into the GP subgroup (n=324) or the OP subgroup (n=338). Efficacy measures included overall response rate (ORR), overall survival (OS), and time to disease progression (TTP). Stratified (by study) Cox proportional hazard regression models were used to analyze OS and TTP by random assignment factors to identify potential prognostic factors and explore their predictive value. **Results:** Baseline characteristics were similar between the GP and OP groups. Median OS was 9.72 months for GP versus 9.33 months for OP (HR=0.898, p=0.223) (Figure 1). There was a significant difference in median TTP (5.52 months for GP versus 4.73 months for OP; HR=0.792, p=0.008) (Figure 2). ORR was 31.5% for GP, and 27.2% for OP (p=0.229). Cox regression model identified three prognostic factors for OS: Eastern Cooperative Oncology Group performance status, prior radiotherapy, and body mass index.

Figure 1. Kaplan–Meier estimates of overall survival

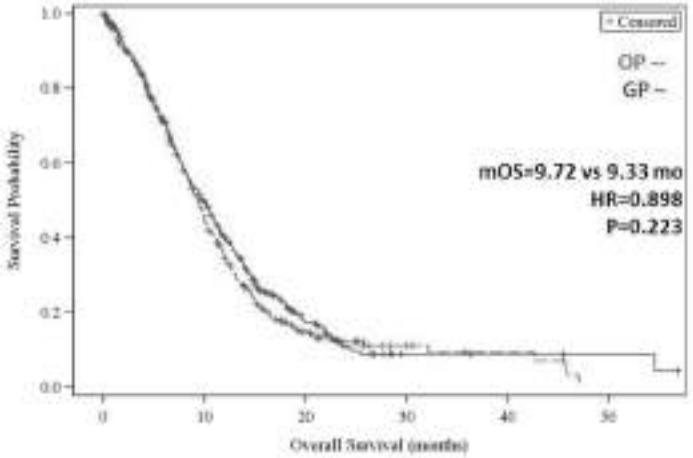
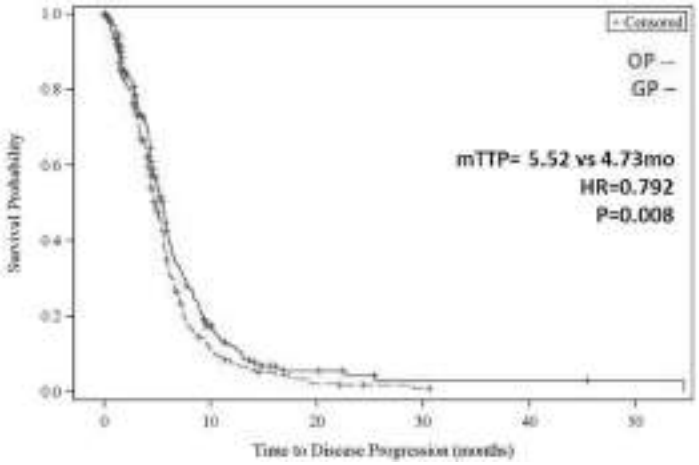


Figure 2. Kaplan–Meier estimates of time to disease progression



Conclusion: This pooled analysis further confirmed the efficacy of gemcitabine plus platinum as first-line treatment of squamous NSCLC. **Keywords:** Gemcitabine, squamous NSCLC, Non-small-cell lung cancer, Platinum

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-058 Impact of Low-Grade Toxicity on Lung Cancer Patient Willingness to Undergo Treatment with Novel Agents Emily H. Castellanos, Hillary Drexler, Sheau-Chiann Chen, Leora Horn *Vanderbilt University Medical Center, Nashville/TN/United States of America*

Background: Targeted therapies have shown clinical benefit in the treatment of solid tumors. The route, frequency, and duration of administration of these agents as well as toxicity profiles differ significantly from traditional cytotoxic chemotherapy. Many studies of targeted therapies report significant numbers of grade 1 or 2 toxicities, which are often regarded as clinically insignificant. We sought to explore whether anticipation of low-grade toxicities and dosing convenience would affect lung cancer patient willingness to undergo therapy. **Methods:** 101 lung cancer patients were surveyed at the Vanderbilt Ingram Cancer Center regarding willingness to comply with treatment based on anticipated efficacy, dosing convenience, and toxicity profiles. All toxicities described were CTCAE V.4.0 grade 1 and 2. Willingness to comply with treatment depending upon toxicity, anticipated benefit, and dosing convenience were compared. **Results:** A substantial number of patients professed unwillingness to undergo treatment due to anticipation of chronic grade 1 and 2 toxicities (Table 1). Gastrointestinal (anorexia, nausea, vomiting, diarrhea, or dysgeusia) and constitutional toxicity (fatigue) had a stronger negative impact on patient willingness to undergo therapy than dermatologic toxicity (rash, hand-foot syndrome, or acne). Willingness to tolerate toxicities correlated with expected benefit in life expectancy and chance of cure. Lengthy travel distance for treatment also negatively impacted willingness to undergo treatment.

Table 1: Percentage of lung cancer patients who stated that they would be unwilling to receive treatment by toxicity type and grade.

Adverse Effect	Unwilling to Receive Treatment
Grade 1 Dermatologic Toxicity	5.2%
Grade 1 Gastrointestinal Toxicity	9.5%
Grade 1 Constitutional Toxicity	6.8%
Grade 2 Dermatologic Toxicity	8.7%
Grade 2 Gastrointestinal Toxicity	18.1%
Grade 2 Constitutional Toxicity	19.4%

Conclusion: Anticipation of chronic low grade toxicities and dosing inconvenience has a negative impact on patient willingness to be treated, which may affect patient adherence and outcomes from therapy. Long-term tolerability should be considered when developing and using novel agents in lung cancer patients. **Keywords:** toxicity, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P1.01-059 Steps to Improve NSCLC Patient Outcomes Utilizing Mobile Apps - Survey Findings Corey J. Langer[1], Patty Peterson[2], Elaine Rudell[3] *[1]Hematology/Oncology, University of Pennsylvania Health System, Philadelphia/PA/United States of America, [2]Projects in Knowledge, Livingston/United States of America, [3]Projects in Knowledge, Livingston/NJ/United States of America*

Background: Integration of mobile devices/health-related apps into medical practice is transforming healthcare. For clinicians treating NSCLC, the addition of a new app, NSCLC @Point of Care, and its patient companion app, are practice-based tools designed to provide content at the time it is actually needed and the ability to sync with patient data, potentially enabling better decisions, outcomes and care. This survey assesses how this mobile dashboard is used in the NSCLC setting, its effect as a learning tool, and how it can improve patient outcomes. **Methods:** To assess how clinicians utilize the NSCLC @Point of Care dashboard and patient companion app, Projects In Knowledge, the CME provider, sent an online survey to its proprietary database of over 53,000 clinicians caring for NSCLC patients. Respondents reported: demographic information, use of EMR technology, frequency and reasons for accessing the NSCLC @Point of Care app, interest in tracking patient-reported data, and use of patient-reported data in institutional EMR reports. **Results:** Overall findings show a large number of responding clinicians use EMR technology, access the NSCLC @Point of Care App daily for relevant disease/treatment-specific information, and want to track patient-reported data. The survey demonstrates many clinicians are in agreement that the clinician app, NSCLC @Point of Care, and its companion app will not only provide important disease- and treatment-specific information that they need and can access at point of care, but also improve communication of critical and accurate patient data in real-time to ensure optimal interventions and patient outcomes, incorporate patient-reported data from the companion app into EMRs and believe this maneuver can streamline time efficiencies in practice. **Conclusion:** Management of NSCLC, a leading cause of cancer-related mortality, is evolving so rapidly that it is difficult for clinicians to keep current and integrate new improved treatment strategies into practice. Many clinicians surveyed believe the NSCLC @Point of Care dashboard provides a desirable approach for busy clinicians to access information needed to support practice change and improve patient outcomes through point of care accessibility. **Keywords:** NSCLC, @Point of Care, patient-reported data, patient companion app

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-060 Value Based Health Care Analysis for Lung Cancer Patients
Ben Van Den Borne, Daphne Dumoulin *Pulmonary Diseases, Catharina Ziekenhuis, Eindhoven/Netherlands*

Background: 'Care for Outcome' is a Value Based Health Care project of Santeon (a cooperation of six leading, top clinical hospitals spread across the Netherlands) in which outcome measures for lung cancer are being measured and reported on a yearly base. In this observational study we report differences in outcome of the 6 participating hospitals. **Methods:** In this retrospective study, data of all lung cancer patients from the Santeon hospitals who were diagnosed between 1-1-2008 and 31-12-2012 was analysed. Primary endpoint in this analysis is mortality. Logistic regression analysis was performed to identify correlating factors for outcome. **Results:** Data of 5922 lung cancer patients was collected. Of these, 3584 (61%) patients had stage IIIB or IV disease. Tumour stage, performance status, age, co morbidity and treatment with or without chemotherapy correlated significantly with survival. Of these factors, treatment with or without chemotherapy had the highest correlation The percentage of patients receiving chemotherapy was significantly different between hospitals, ranging from 36% to 59% (mean 47,6%). The median survival of patients treated with or without chemotherapy (excluding those who died within 45 days and therefore passing the 'immortal time bias' effect) was 124 (95%CI 116-132) and 295 (95%CI 281-309) days (p<0.001) respectively. The difference persisted after correction for tumour stage, performance state, age and co morbidity. **Conclusion:** There is a strong variation between hospitals in the percentage of patients with stage IIIB / IV lung cancer receiving chemotherapy. Our data indicate that chemotherapy is an independent prognostic factor for survival.**Santeon's 'Care for Outcome' team for lung cancer:** Onze Lieve Vrouwe Gasthuis, Amsterdam: A.A.J. Smit, MD PhD, St Lucas Andreas Hospital, Amsterdam: H.J. Smit, MD PhD, Catharina Hospital, Eindhoven: D.W. Dumoulin, MD; B.E.E.M. van den Borne, MD PhD, Medisch Spectrum Twente, Enschede: A.J. Polman MD, Martini Hospital, Groningen: J.W.G. van Putten, MD PhD, Antonius Hospital, Nieuwegein: G.J.M. Herder MD PhD; F.M.N.H. Schramel MD PhD; W.F. van den Bosch PhD, Canisius Hospital, Nijmegen: A. Termeer MD
Keywords: Value Based Health Care, chemotherapy, non-small cell lung cancer, survival

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-061 The Chicago Thoracic Oncology Database Consortium: A Multi-Site Database Initiative
Brian M. Won[1], George B. Carey[2], Yi-Hung Carol Tan[1], James Wallace[3], Mark Kozloff[3], Thomas Hensing[4], Ravi Salgia[5] [1]*Medicine, University of Chicago, Chicago/IL/United States of America,* [2]*The Perelman School of Medicine, University of Pennsylvania, Philadelphia/PA/United States of America,* [3]*Ingalls Memorial Hospital, Harvey/IL/United States of America,*[4]*Section of Hematology/Oncology, Northshore University Health System, Evanston/IL/United States of America,* [5]*Medicine, Section of Hematology/Oncology, University of Chicago, Chicago/IL/United States of America*

Background: An increasing amount of clinical data is available to biomedical researchers, but specifically designed databases and informatics infrastructures are needed to handle this data effectively. Multiple research groups should be able to pool and share this data in an efficient manner. The Chicago Thoracic Oncology Database Consortium (CTODC) was created to standardize data collection and facilitate the pooling and sharing of data at institutions throughout Chicago and across the world. **Methods:** The Salgia Laboratory has implemented the Thoracic Oncology Program Database Project (TOPDP) Microsoft Access, the TORP Velos, and the TORP REDCap databases for translational research efforts. Standard operating procedures (SOPs) were created that document the construction and proper utilization of these databases. These SOPs have been made available freely to other institutions that have implemented their own databases patterned on these SOPs. In order to evaluate the effectiveness of this consortium, we have performed an investigation examining patients receiving erlotinib at three institutions belonging to the CTODC: The University of Chicago Medical Center, Ingalls Health System, and NorthShore University Health System. **Results:** A cohort of 373 lung cancer patients who are taking erlotinib was identified by querying data from all three institutions of the consortium. The patients' demographic and clinical data were compiled. In addition, the EGFR statuses of patients were analyzed, showing that out of the 70 patients that were tested, 55 had mutations while 15 did not have any mutations. The overall survival and duration of treatment were calculated from the data that was provided. It was shown that patients with an EGFR mutation had longer duration of erlotinib treatment and longer overall survival compared to patients who received erlotinib and were EGFR wild type. **Conclusion:** The investigation described herein demonstrates the successful data collection from multiple institutions in the context of a collaborative effort. However, the investigation identified many challenges in this type of collaboration, such as difficulty of transferring data between institutions and potential duplication of patient data. Overall, these issues do not lessen the findings of the investigation or the effectiveness of the CTODC. With greater cooperation and communication between institutions of the consortium, these issues can be readily resolved. The data presented here can be utilized as the basis for further collaborative efforts and/or development of a larger, more streamlined collection of databases within the consortium.
Keywords: consortium, Erlotinib, EGFR, database

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-062 Rash as a Marker for the Efficacy of Necitumumab in the SQUIRE Study
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Background: SQUIRE, a randomized, phase III study (n=1,093), demonstrated that the addition of the EGFR monoclonal antibody necitumumab (N) to gemcitabine-cisplatin (GC) improved overall survival in patients with stage IV squamous NSCLC. Rash is an established class side-effect associated with EGFR-targeting agents. Previous studies have suggested a positive association between rash and clinical outcomes with EGFR-targeted therapy. **Methods:** Pre-emptive treatment for rash was not allowed per protocol until completion of the first cycle of study therapy. For the purpose of this analysis, patients randomized to the N+GC arm were categorized and grouped according to whether or not they experienced rash during the first two cycles of study therapy. Patients who died or were lost to follow-up before completing two cycles of study therapy were not included in this analysis. Overall survival (OS) and progression-free survival (PFS) were measured from the date of randomization, with parameters estimated using the Kaplan-Meier method. Hazard ratios and 95% CIs between subgroups were estimated from stratified Cox proportional hazards models, with comparisons between arms using a stratified log-rank test. **Results:** 505 patients were evaluable in the N+GC arm at the end of cycle 2 of which 69% experienced rash during cycle 1 and/or cycle 2. Patients experiencing rash in the N+GC arm had improved OS (HR=0.738, p=0.0001) and PFS (HR=0.808, p=0.0066) compared with patients in the GC arm. Patients experiencing rash in the N+GC arm had improved OS (HR=0.656, p=0.0001) compared with patients in the N+GC arm who did not experience rash. The difference in PFS between patients in the N+GC arm experiencing rash versus those not experiencing rash was not statistically significant. Median PFS and OS for patients experiencing rash in the N+GC arm was 6.2 mo and 13.6 mo respectively, as compared to 5.6 and 10.2 mo for patients in the N+GC arm without rash and 5.6 and 10.6 mo for patients in the GC arm.

	Patients alive and under follow-up after Cycle 2		
	N+GC with rash N=350	N+GC no rash N=155	GC N=508
Overall Survival, mo (CI)	13.6 mo (11.6, 15.2)	10.2 (8.7, 11.6)	10.6 (9.5, 11.9)
HR* (95% CI)		0.656 (0.529, 0.813)	0.738 (0.631, 0.864)
Stratified log-rank p value*		0.0001	0.0001
PFS, mo (CI)	6.2 mo (5.7, 6.9)	5.6 (5.0, 5.7)	5.6 (5.3, 5.6)
HR* (95% CI)		0.867 (0.693, 1.084)	0.808 (0.692, 0.942)
Stratified log-rank p value*		0.2127	0.0066

*In comparison to the N+GC group with rash **Conclusion:** Rash occurring during the first two cycles of treatment with necitumumab (N+GC) is associated with improved OS in patients with advanced squamous NSCLC.
Keywords: Necitumumab, rash, efficacy, overall survival

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-063 Efficacy and Safety of Erlotinib in Squamous Cell Lung Cancer
Marko Jakopovic[1], Branka Cucevic[1], Sanja Plestina[1], Suzana Kukulj[1], Mihovil Roglic[1], Silvana Smojver-Jezek[1], Nabil Chalfe[1], Marta Korsic[1], Gzim Redzepi[2], Luka Brcic[3], Filip Popovic[2], Sonja Badovinac[2], Miroslav Samarzija[2] [1]*University Hospital Centre Zagreb, Zagreb/Croatia,* [2]*University Hospital Center Zagreb, Zagreb/Croatia,* [3]*Institute of Pathology, Medical University Graz, Graz/Austria*

Background: Erlotinib is epidermal growth factor receptor (EGFR) tyrosine-kinase inhibitor which showed efficacy and tolerability in patients with advanced non-small cell lung cancer (NSCLC), especially in patients which harbor activating mutations in EGFR. However, erlotinib also showed efficafy in patient with unknown or wild type EGFR mutation status. The iam of the study was to determine safety and efficacy of erlotinib in patients with advanced (stage IIIB and IV) squamous NSCLC. **Methods:** patients with advanced squamous NSCLC who had failed prior chemotherapy were treated with oral erlotinib 150 mg daily until disease progression or unaccaptable toxicity. Data was analyzed retrospectively. **Results:** a total of 122 patients (107 men and 15 women, mean age 62±8 years) with advanced squamous NSCLC were enrolled in the study from 2006 to 2012 in 14 centers throughout Croatia. More than 50% of patients were active smokers at time of enrollment. Most of the patients had performance status ECOG 1 and 2 (91%). Vast majority of patients were treated with erlotinib in third line setting. After cycle 2, 10% of patients had partial response (PR), and 45% of patients had stable diseases. In total, 55% of patients had disease control after cycle 2. Progression free

survival (PFS) was 3.7 months in overall population. Statistically significant differences in PFS were recorded according to response to treatment; patients with PR after two cycles had PFS of 6.2 months comparing to patients with progressive disease (PFS 2.0 months, p<0.001). Patients with better ECOG status (ECOG 1 and 2) had trend to improved PFS (3.8 vs 1.9 months) compared to ECOG 2 and patients with rash after cycle 2 also showed trend to improved PFS (4.1 vs 2.4 months) compared to no rash. There were no grade 3 and 4 toxicities noticed during the study. Overall survival in our study was meaningfully prolonged. **Conclusion:** erlotinib as a single agent showed efficacy in treatment of patients with squamous cell lung cancer without significant toxicities. The best predictive factor of response to treatment was response to erlotinib after 2 months of treatment. **Keywords:** Erlotinib, squamous, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-064 A Phase II Study of Gemcitabine-Cisplatin plus Necitumumab for Stage IV Sq-NSCLC Jesús Corral[1], Santiago Ponce[2], Joachim G. Aerts[3], Chun-Ming Tsai[4], Desiree Hao[5], Jacques Cadranel[6], J Thaddeus Beck[7], Sang-We Kim[8], Rocio Varea[9], Grace Chao[9], Susana Barriga[9], Luis Paz-Ares[1] [1]*Hospital Virgen Del Rocio, Sevilal/ Spain,* [2]*Medical Oncology Department, 12 de Octubre´ Hospital, Madrid/Spain,* [3]*Amphia Ziekenhuis, Breda/Netherlands,* [4]*Taipei Veterans General Hospital, Taipei/Taiwan,* [5]*Tom Baker Cancer Centre/ University of Calgary, Alberta/AB/Canada,* [6]*Hôpital Tenon, Paris/ France,* [7]*Highlands Oncology Group, Fayetteville/AR/United States of America,* [8]*Asan Medical Center, Seoul/Korea,* [9]*Eli Lilly and Company, Indianapolis/IN/United States of America*

Background: To report the efficacy and safety results from a study of necitumumab (N), manufactured under process D, modified from Process C, used in the pivotal SQUIRE study, in combination with gemcitabine (G) plus cisplatin (C) as first-line treatment in patients with advanced squamous non-small cell lung cancer (Sq-NSCLC). (NCT01788566) **Methods:** This was an open-label, single-arm, multicenter, phase II study in patients with advanced Sq-NSCLC. Patients were enrolled who were aged ≥18 years and had measurable, pathologically confirmed stage IV Sq-NSCLC without prior chemotherapy. Patients had ECOG-PS 0-1, adequate organ function, and life expectancy of ≥12 weeks. Patients received N (800 mg iv, Days 1 and 8) plus GC (G=1250 mg/m^2 iv, Days 1 and 8; C=75 mg/m^2 iv, Day 1) each 3-week cycle for up to 6 cycles. Patients with at least stable disease (SD) could continue to receive N alone until progressive disease (PD) or other discontinuation criteria. Primary endpoint was objective response rate (ORR) based on RECIST1.1. Secondary endpoints included overall survival (OS), progression-free survival (PFS), disease control rate (DCR), change in tumor size (CTS; % improvement in lesions), and safety. **Results:** Patients (N=61), median age 65 years, heavy metastatic disease burden; approximately 70% of the patients had metastases to ≥ 2 organ systems. Efficacy results, including an ORR of 48.1% are shown in the Table. Survival and PFS findings were similar to those reported in the SQUIRE study in the GC+N arm (SQUIRE results: median OS of 11.5 months, 1-year survival rate of 47.7%, and median PFS of 5.7 months). Median duration of treatment was 12 weeks (4 cycles) for G and C and 16 weeks (5 cycles) for N; the median relative dose intensity was 85% for G and 93% for C and N. Twenty-eight (46%) patients continued on single-agent N (median: 4 cycles). Skin reactions (n=49; 80.3%) and hypomagnesemia (n=21; 34.4%) were the most commonly reported adverse events of special interest (AESIs, all grades). AESI ≥ Grade 3 were skin reactions (n=8; 13.1%), thromboembolic events (n=7; 11.5%), hypomagnesemia (n=6; 9.8%), and hypersensitivity/ IRR (n=3; 4.9%). There were 27 deaths (20 due to PD and 7 due to AEs [5 had no causal relationship to study drug]) at the time of data cut-off.

Table. Efficacy Results

	N=61
ORR*† (CR+PR), n (%) [95% CI]	26/54 (48.1)† [34.34–62.16]
CR	0
PR, n (%)	26/54 (48.1)†
SD	18 (29.5)
PD	9 (14.8)
Not evaluable	1 (1.6)
Not assessable	7 (11.5)
DCR CR+PR+SD, n (%) [95% CI]	44 (81.5)† [68.57–90.75]
Median OS, months (95% CI)	11.7 [7.59–NA]
1-year survival rate, % (95% CI)	47.6% [30.20–63.08]
Median PFS, months (95% CI)	5.6 [3.68–6.87]
Median CTS, (%)	42.1
*Assessed by investigators	
†Patients who had a post-baseline radiological assessment, n=54	

Conclusion: The efficacy results and the safety profile, with N manufactured under process D, are consistent with what is expected for this combination as first-line therapy of patients with metastatic Sq-NSCLC. **Keywords:** Necitumumab, advanced Sq-NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-065 Bevacizumab Combined with Chemotherapy in the Treatment of Advanced NSCLC Patients Hong Tao, Zhe Liu, Junfang Tang, Mingzhi Li, Liang Shi, Wei Wu *Oncology, Beijing Chest Hospital, Capital Medical University, Beijing/China*

Background: Bevacizumab is a monoclonal antibody which selectively binds to human vascular endothelia growth factor (VEGF) .The combination of bevacizumab with chemotherapy has been one of the choices for advanced non-squamous non-small cell lung cancer (NSNSCLC) patients.In this study we evaluate the efficacy,safety and imaging findings of bevacizumab plus chemotheray in patients with advanced NSNSCLC. In addition, the mutation status of EGFR gene and KRAS gene were detected. **Methods:** Patients adimitted in the hospital were treated with bevacizumab (15mg/kg or 7.5mg/kg, d1) plus chemotherapy(paclitaxel 175mg/m2, d1, carboplatin AUC=5 or 6, d1) with 3 weeks in one cycle,up to 6 cycles,followed with maintenance therapy of bevacizumab(15mg/kg or 7.5 mg/kg, d1) till disease progression. Efficacy, safety, tumoral cavitation, therapeutic outcome of malignant pleural effusion and EGFR, KRAS mutation status were analysed. **Results:**

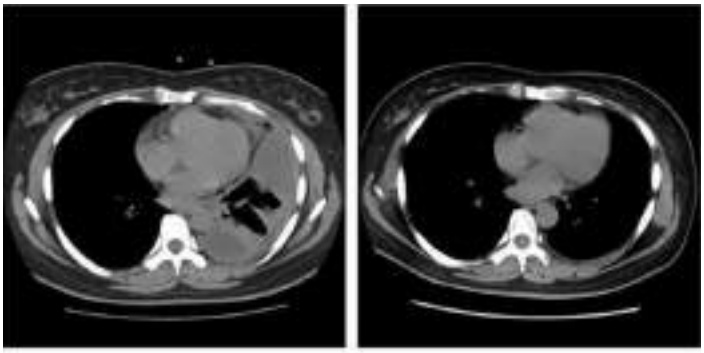

Fig. Imaging changes of pleural effusion before and after treatment. A: Baseline CT of the chest showed plenty of pleural effusion on left side;B: Follow-up CT scan after 4 cycles of therapy demonstrated the pleural effusion had disappeared. 26 Patients were collected.They were all treated with bevacizumab plus chemotherapy.17 patients received maintenance therapy.The median cycle number of chemotherapy was 6, and that of bevacizumab was 8.Partial response(PR), stable disease(SD) and progressive disease(PD) rates were 53.8%, 42.3% and 3.8%, respectively. The median progression free survival(PFS) and overall survival(OS) were11.0 and 25.8 months respectively. Out of 26 patients, 15.4% developed cavitation after treatment.2 years and 3 years survivle rates of cavitation group were lightly higher than those of non-cavitation group(75.0% vs 44.4%, P=0.293, 25.0% vs 12.5%, P=0.509, respectively). Of the 13 patients with malignant pleural effusion, disease control rate of malignant pleural effusion was 100%: complete response(CR) rate was 38.5% and SD rate was 61.5%. EGFR gene ststus were detected in 11 patients. 36.4% showed sensitive mutation. The PR rate of EGFR mutation positive group was higher than that of mutation negitive group (75% vs 28.6%, P=0.262),but not statistically. KRAS mutation has not been found in all the 10 patients whose samsples were capable of being detected. Common adverse effects included myelosuppression, digestive symptoms,epistaxis, ect. Special adverse effects were also observed such as hemoptysis,hypertension,proteinuria etc. Most adverse effects were mild and controllable. **Conclusion:** Bevacizumab with chemotherapy is a promising and safe treatment for patients with NSNSCLC. It was also effective in controlling malignant pleural effusion. Tumoral cavitation were found, but the clinical significance was indeterminate. The relationship of EGFR gene status and efficacy of bevacizumab-based chemotheray is subject to further research. **Keywords:** bevacizumab, efficacy, Cavitation, malignant pleural effusion

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-066 Maintenance Bevacizumab after Chemotherapy with Bevacizumab in First Line Treatment of Lung Cancer. A Single Institution Experience Malika Gamaz Bensaou, Nabila Gheroufella, Maria Gherbi, Kamel Bouzid *Medical Oncology, Pierre and Marie Curie Center, Algiers/Algeria*

Background: Lung cancer is the first cancer in term of incidence and mortality for men in Algeria and a majority of the patients are stage IIIB or IV at the diagnostic. Bevacizumab + chemotherapy as first line followed by continuation maintenance with bevacizumab showed in many phase III randomized trial, an increase of PFS and overall survival. The purpose of this study is the evaluation of efficacy and toxicity of patient after continuation maintenance with bevacizumab in stage IIIB and IV for no squamous lung cancer in single institution. **Methods:** A retrospective study including all patients seen between September 2013 and April 2015, at department of medical oncology in Algiers. • Patients should have advanced or metastatic non squamous

(adenocarcinoma and carcinoma with large cell) lung cancer, and received 4 cycles of induction chemotherapy with platine + pemetrexed + bevacizumab. • All patients with response or stable disease received bevacizumab as maintenance therapy, evaluation by CT scan was done every three cycles. **Results:** Twenty (3 F and 17 M) patients were enrolled, and all are evaluable for response and toxicity. Median age was 61.5 years (range m 31 years – M 74 years). Histology was adenocarcinoma in 19 patients and carcinoma with large cell in 1 patient. Sixteen (16) patients had IV stage and four (4) patients had IIIB stage disease. Response rate (1 CR, 4 PR) was seen in 5 patients (25 %), Stable Disease (SD) was achieved in 5 patients (25 %) and Progressive Disease (PD) in 10 patients (50 %). Among the 20 patients who achieved 4 cycles of induction bitherapy + bevacizumab, 10 patients (50 %) underwent for maintenance therapy. All the ten patients received the first three cycle of maintenance with bevacizumab and well tolerated without toxicity. At this time, two patients achieved one year maintenance with stabilization of disease. One of them developed hypertension and is under treatment. **Conclusion:** Bevacizumab was well tolerated in first line treatment and as maintenance, for patients with advanced or metastatic non-squamous lung cancer. **Keywords:** NSCLC, non squamous carcinoma, bevacizumab, maintenance

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-067 Epidermal Growth Factor Receptor Gene Amplification in Patients with Advanced-Stage NSCLC Ondrej Fiala[1], Milos Pesek[2], Jindrich Finek[1], Marek Minarik[3], Lucie Benesova[4], Zbynek Bortlicek[5], Ondrej Topolcan[6] [1]*Department of Oncology and Radiotherapy, Medical School and Teaching Hospital in Pilsen, Charles University, Pilsen/Czech Republic,* [2]*Department of Pneumology, Medical School and Teaching Hospital in Pilsen, Charles University, Pilsen/Czech Republic,* [3]*Center for Applied Genomics of Solid Tumours, Genomac Research Institute, Prague, Czech Republic, Pilsen/Czech Republic,* [4]*Center for Applied Genomics of Solid Tumours, Genomac Research Institute, Prague/Czech Republic,* [5]*Institute of Biostatistics and Analysis, Faculty of Medicine, Masaryk University, Brno/Czech Republic,* [6]*Department of Nuclear Medicine, Medical School and Teaching Hospital in Pilsen, Charles University, Pilsen/Czech Republic*

Background: Tyrozine kinase inhibitors (TKI) targeting epidermal growth factor receptor (EGFR) represent a novel effective tools in management of advanced-stage non-small cell lung cancer (NSCLC). We aimed to evaluate the incidence and predictive role of *EGFR* gene amplification in patients with advanced-stage NSCLC treated with EGFR-TKIs. **Methods:** The study included 290 patients with advanced-stage (IIIB or IV) NSCLC. Multiplex ligation-dependent probe amplification (MLPA) and Polymerase chain reaction (PCR) were used for detection of *EGFR* mutations and *EGFR* gene amplification, respectively. **Results:** *EGFR* amplification was detected in 26 (9.0%) patients. *EGFR* amplification was found more frequent in patients harboring *EGFR* mutation ($p < 0.001$). No significant corelation between *EGFR* gene amplification and survival was observed. **Conclusion:** The presence of *EGFR* gene amplification is associated with *EGFR* gene mutations. *EGFR* gene amplification is not a feasible predictive biomarker for the treatment with EGFR-TKIs in patients with advanced-stage NSCLC. *This study is supported by Ministry of Health, Czech Republic - conceptual development of research organization Faculty Hospital in Pilsen - FNPl, 00669806 and by the project CZ.1.05/2.1.00/03.0076 from European Regional Development Fund.* **Keywords:** EGFR, amplification, NSCLC, EGFR-TKI

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-068 Randomized Trial of Maintenance Chemotherapy Versus SBRT plus Maintenance Chemotherapy for Advanced NSCLC - Feasibility and Early Outcomes Zabi Wardak[1], David E. Gerber[2], Chul Ahn[3], Randall S. Hughes[2], Grace Raja[2], Saad Khan[2], Jonathan E. Dowell[2], Lorraine Pelosof[2], Suprabha Pulipparacharuvil[1], Robert D. Timmerman[1], Hak Choy[1], Puneeth Iyengar[1] [1]*Radiation Oncology, UT Southwestern, Dallas/TX/United States of America,* [2]*Hematology/Oncology, UT Southwestern, Dallas/TX/United States of America,* [3]*Biostatistics, UT Southwestern, Dallas/TX/United States of America*

Background: Following first-line chemotherapy, maintenance therapy regimens have shown modest yet statistically significant benefits in progression free survival (PFS). To date, there have been no completed, prospective randomized trials examining the role of locally aggressive therapy in limited metastastic, advanced stage non-small cell lung cancer (NSCLC). We hypothesized that stereotactic body radiotherapy (SBRT) prior to maintenance chemotherapy would further improve PFS. This trial also serves to provide prospective survival data for a population with limited metastatic NSCLC. **Methods:** This is a two-arm randomized phase II trial. Eligible patients have stable disease or partial response with limited metastatic disease (defined by six or fewer sites amenable to SBRT) after treatment with up to 6 cycles of first line platinum doublet chemotherapy. Patients are then randomized to investigator's choice maintenance chemotherapy alone or SBRT to all amenable sites followed by maintenance chemotherapy. The primary endpoint of the study is PFS, with 36 patients required to demonstrate an increase from 4 months in the control arm to 10 months in the experimental arm, with 80% statistical power and a 2-sided significance level of 0.10. **Results:** Since May 2014, 11 patients have been enrolled (5 to SBRT + maintenance arm; 6 to maintenance arm). The median number of first-line chemotherapy cycles was four, with the most common regimen carboplatin/paclitaxel followed by carboplatin/pemetrexed. The median number of maintenance chemotherapy cycles was six, the most common agent being pemetrexed followed by bevacizumab. The median number of sites treated with SBRT were two, with the lung the most common anatomic location followed by the adrenal gland. Five patients have progressed to date, three in the maintenance chemotherapy arm and two in the SBRT + maintenance chemotherapy arm. Progression in the maintenance alone arm occurred in original sites of disease in two of three patients. There have been no in-field failures in the SBRT arm. There has been one death due to disease progression in the maintenance chemotherapy arm. No patients have suffered a grade 3 or higher adverse event related to protocol therapy. **Conclusion:** This study demonstrates the feasibility of enrolling patients with limited metastatic lung cancer to a randomized trial of local therapy following first-line chemotherapy. To date, all patients have tolerated the administration of SBRT to multiple sites in between first-line and maintenance chemotherapy without any grade 3 or higher adverse events. Continued follow-up will be necessary to determine the efficacy of the experimental arm. **Keywords:** Oligometastases, SBRT, maintenance

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-069 Reasons for Discontinuation of Treatment with Bevacizumab in Patients with Non-Progressing NSCLC - Retrospective Study Peter Berzinec[1], Maria Cerna[2], Peter Kasan[3], Helena Kuzmova[1], Gabriela Chowaniecova[1], Marian Martak[3], Milada Vesela[3], Lucia Denkova[3], Lucia Dolakova[1], Milan Kroslak[1], Zdenka Cavarova[1] [1]*Specialised Hospital of St Zoerardus Zobor, Nitra/Slovak Republic,* [2]*Slovak Medical University, Bratislava/Slovak Republic,* [3]*University Hospital, Bratislava/Slovak Republic*

Background: In general, bevacizumab is well-tolerated treatment in patients with advanced, metastatic non-squamous NSCLC. Despite this, permanent discontinuations of bevacizumab occur also before progressive disease (PD), both in clinical trials and in clinical practice. Purpose of this study was to find out the reasons for permanent discontinuation of bevacizumab before PD in patients treated in two centers in the Slovak republic. **Methods:** In this retrospective study, approved by the Ethics Committee of the Specialized Hospital of St Zoerardus Zobor, the institutional databases were searched for patients with advanced NSCLC treated with bevacizumab between 2007 and 2013. **Results:** Altogether 161 patients were included into the analysis. Patients' characteristics: M/W: 99/62, age: median 61 years (32 - 83), histologically /cytologically confirmed NSCLC: adenocarcinoma/large cell/adenosquamous: 158/2/1. Number of cycles with bevacizumab (induction and maintenance): median 8 (1 - 52), PFS: median 7 months (1 - 42). Bevacizumab was permanently discontinued before PD in 28 of 161 patients (17,4%), in 18 of 161 (11,2%) due to undesirable effects - Table 1. Table 1: Reasons for permanent discontinuation of bevacizumab in non-progressing NSCLC

Undesirable effects	N	Other reasons	N
Cavitation	3	Lost to FU	2
Pneumothoraces	3	Molecular testing, start of TKI	2
Cerebrovascular event	2	Patients' preference	2
Gastrointestinal perforation	2	Car accident, death	1
Hypertensive crisis	2	Planned surgery	1
Pneumonia	2	Traumatic fractures	1
Proteinuria	2	Other	1
Thrombotic event	2		
All	18	All	10

Conclusion: Permanent discontinuation of bevacizumab in non-progressing NSCLC was seen in this study in the similar rate as in the larger trials (Wozniak AJ et al. Clin Oncol [Coll Radiol]. 2015, 27:187-96.) However, some differences are in the type of undesirable effects, which are in part also chemotherapy related. **Keywords:** NSCLC, bevacizumab, discontinuation

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-070 KRAS Mutations: Does It Mean No Erlotinib? Margarida Dias[1], Rita Linhas[1], José Carlos Machado[2], Luís Cirnes[2], Ana Gonçalves[1], Sérgio Campainha[1], Sara Conde[1], Ana Barroso[1] [1]*Pulmonology, Centro Hospitalar Vila Nova de Gaia Espinho, Vila Nova de Gaia/Portugal,* [2]*Ipatimup, Porto/Portugal*

Background: KRAS mutations are the most common mutations in non-small cell lung cancer (NSCLC). Theoretically those patients are resistant to tyrosine kinase inhibitors, but studies are contradictory. The aim of this study was to compare second-line chemotherapy with docetaxel and erlotinib in patients with NSCLC, EGFR wild-type, depending on their KRAS status. **Methods:** We included 47 patients diagnosed with NSCLC, EGFR wild type, followed in a Lung Cancer Unit and treated with docetaxel or erlotinib as second-line chemotherapy. KRAS mutations in exon 12 and 13 were screened. Patients were divided in two arms: docetaxel arm and erlotinib arm. Time to progression to each second-line chemotherapy and overall survival after second-line chemotherapy was compared between patients with KRAS mutations and KRAS wild-type. In patients with KRAS mutations, time to progression and overall survival after second-line chemotherapy was compared between docetaxel and erlotinib. **Results:** 87% were male, mean age 65±11 years, 77% smokers or ex-smokers, 81% non-squamous tumors, 70% stage IV at diagnosis. Analyzing all patients, there was no statistical difference regarding the time to progression and overall survival between patients with or without KRAS. 14 patients were in docetaxel arm and 33 patients in erlotinib arm. There were no statistical differences between arms regarding gender, smoking status, performance status and

stage at diagnosis. Patients in docetaxel group were younger (60±9 years vs. 67±11 years, p=0.027). In docetaxel arm, 3 patients had KRAS mutations. We found no statistical differences between patients with or without mutations regarding time to progression and overall survival after docetaxel. In erlotinib arm, 7 patients had KRAS mutations. We found no statistical differences between patients with or without mutations regarding time to progression and overall survival after erlotinib. In patients with KRAS mutations, time to progression tends to be slightly higher in erlotinib arm (2 vs. 1 month, p=0.088) and overall survival after second-line chemotherapy seems to be similar. **Conclusion:** Unlike what is reported in some studies, we found no differences concerning KRAS status with respect to overall survival and time to progression. Moreover, it seems that there are no differences between docetaxel and erlotinib in second-line treatment. This questions the non-use of erlotinib in second-line treatment of KRAS mutated NSCLC patients. **Keywords:** KRAS mutations, Erlotinib, docetaxel, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-071 Long-Term Tolerability Among IRESSA Clinical Access Program (ICAP) Participants in the United States (US) Paul A. Bunn, Jr[1], Katherine Pisters[2], Ira Gore[3], Elisabeth F. Croft[4], Diana Devincenzo[5], Dara Stein[6], Klaus Freivogel[7], Frangiscos Sifakis[4], Fred R. Hirsch[1] [1]*University of Colorado Cancer Center, Aurora/CO/United States of America,* [2]*Department of Thoracic Head and Neck Medical Oncology, University of Texas MD Anderson Cancer Center, Houston/TX/United States of America,* [3]*Alabama Oncology - St. Vincent'S Birmingham, Birmingham/AL/United States of America,* [4]*Astrazeneca, Lp, Gaithersburg/MD/United States of America,* [5]*Astrazeneca, Lp, Wilmington/DE/United States of America,* [6]*United Biosource Corporation, Chevychase/MD/ United States of America,* [7]*United Biosource Corporation, Munich/Germany*

Background: Following the gefitinib (IRESSA®) NDA voluntary withdrawal, which previously had allowed for limited commercial distribution of IRESSA, gefitinib became available under the IRESSA Clinical Access Program (ICAP) in June 2011. The ICAP continued to provide drug access to patients who were benefiting or had benefited from treatment with gefitinib through restricted distribution (2005-2011) or through a clinical trial that was IRB approved prior to June 2005. ICAP participants constitute a unique subset of cancer patients in whom long-term use of gefitinib can be studied. Consequently, this is the first study to describe long-term safety and tolerability data for an EGFR TKI in cancer patients outside of the clinical trial setting. **Methods:** This study utilizes 2 data sources: (1) retrospective patient medical chart review of demographics, including safety and tolerability of prolonged treatment with gefitinib as part of the ICAP; and (2) retrospective review of serious adverse event (SAE) reports in the AstraZeneca safety database, as all ICAP investigators are responsible, per protocol, for reporting all SAEs observed for ICAP participants. **Results:** A total of 188 patients were enrolled in the ICAP from 134 sites across the US; 94 patients (50.0%) remain on active treatment. This study aims to include as many sites and patients as feasible. Currently, 46 sites representing 77 patients have agreed to participate; site enrollment and data collection are ongoing. As of July 16, 2015, chart abstractions of 16 patients were completed. These patients have a median age of 68.0 years, are predominantly female (75.0%), non-Hispanic white (87.5%), with a confirmed NSCLC diagnosis (93.8%). More patients received gefitinib in second line (43.8%) followed by first line (37.5%) and third line (18.8%). Median gefitinib duration prior to ICAP initiation was 11.3 years (range 9.1-13.9 years), with median gefitinib duration as part of the ICAP being an additional 3.5 years (range: 0.3-3.8 years). During the ICAP, 93.8% of patients (95% CI: 87.9-99.6) did not experience any dose reductions, interruptions, or discontinuation due to gefitinib-related adverse events. The AstraZeneca Safety Database showed 123 SAEs reported from 54 ICAP patients as of February 26, 2015. The majority of SAEs were consistent with underlying disease conditions and were considered unrelated to gefitinib therapy by investigators. 5.6% of patients (3/54) had potentially causally related SAEs as determined by investigators: one patient had procedure-related bronchitis, lung infection, and exacerbation of preexisting COPD with a fatal outcome; one patient experienced interstitial lung disease, pulmonary alveolar hemorrhage, and acute respiratory and renal failure (patient recovered with sequelae); and one patient developed dermatitis acneiform and pruritus. Of the remaining 51 patients, 20 had fatal outcomes (39.2%). The majority of fatalities (12) had insufficient information to assess cause of death and may have had other alternative causes, including underlying or concurrent diseases (6) and possible disease progression (2). **Conclusion:** Characterization of long-term gefitinib use among this subset of NSCLC patients indicates acceptable long-term tolerability and indicates that some patients have long-term (>10 year) benefit. Clinical and genetic features associated with long-term benefit need further study. **Keywords:** gefitinib, Long-term, NSCLC, EGFR

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-072 Targeted Delivery of a Synthetic microRNA-Based Mimic to Treat Thoracic Cancers Glen Reid[1], Yuen Y. Cheng[1], Kadir Sarun[1], Marissa Williams[2], Michaela B. Kirschner[2], Andrej Despotovski[2], Nancy Mugridge[3], Jocelyn Weiss[4], Himanshu Brahmbhatt[3], Jennifer Macdiarmid[3], Mark Molloy[5], Ruby Lin[2], Nico Van Zandwijk[2] [1]*Asbestos Diseases Research Institute, Sydney/NSW/Australia,* [2]*Asbestos Diseases Research Institute, Sydney/Australia,* [3]*Engeneic Ltd, Sydney/NSW/ Australia,* [4]*Engeneic Ltd, Sydney/Australia,* [5]*Australian Proteome Analysis Facility, Macquarie University, Sydney/NSW/Australia*

Background: MicroRNA expression is commonly suppressed in cancer, contributing to tumor cell biology. Recently we demonstrated that multiple members of the miR-15/16 family are downregulated and have tumor suppressor functions in malignant pleural mesothelioma (MPM), an asbestos-related cancer for which few treatments are available. These results are similar to previous findings in non-small cell lung cancer (NSCLC). As multiple microRNAs from the same family are downregulated in MPM, we investigated whether a single synthetic mimic based on the consensus sequence of the entire family could restore activity of the entire family. **Methods:** Novel microRNA mimics based on the consensus sequence of the miR-15/107 group were designed (con15/107.1 to 4). The effects on growth, migration, target regulation, drug sensitivity and angiogenesis of the con15/107 mimics were compared with native miR-15 and miR-16 mimics using standard assays in MPM and lung cancer cell lines *in vitro*. The regulation of specific target genes was assessed by RT-qPCR, Western blot and luciferase reporter assays. Global gene regulation was assessed by proteomics. Activity of con15/107 mimics was investigated *in vivo* in xenograft models in nude mice. **Results:** The consensus mimics inhibited growth and migration of MPM and lung cancer cell lines in vitro, and effects were greater than with native miR-15 or miR-16 mimics. Growth inhibition was associated with an induction of apoptosis, and downregulation of predicted targets of the mimics. Target gene interactions were confirmed with 3'UTR reporter constructs, and proteomics identified a number of candidate genes involved in consensus mimic-induced growth inhibition. Consensus mimics also sensitized multiple MPM and lung cancer cell lines to chemotherapy agents, and inhibited angiogenic activity in endothelial cells. In a xenograft model, the consensus mimic con15/107.2, packaged in bacterially-derived, EGFR antibody-targeted, EDVTMnanocells, inhibited MPM tumor growth *in vivo*. **Conclusion:** The novel con15/107 mimics based on the consensus sequence of the miR-15/107 group have greater activity than native miR-15 or miR-16 mimics *in vitro* and are active *in vivo*. Increased activity correlates to greater target gene downregulation. These preclinical studies support a Phase I clinical trial has been initiated for patients with MPM or NSCLC failing standard therapy. This represents the first trial of microRNA replacement as a therapy for thoracic cancer. **Keywords:** malignant pleural mesothelioma, non small cell lung cancer, microRNA

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-073 MET and Invasive Function in NSCLC Tamara Mirzapoiazova, Carol Tan, Patrick Singleton, Ravi Salgia *Department of Medicine, University of Chicago, Chicago/ United States of America*

Background: There is molecular heterogeneity of lung cancers, especially non-small cell lung cancer (NSCLC). Even though pathways such as EGFR and ALK are understood much more, we are beginning to understand the role of MET receptor tyrosine kinase (RTK). The initial trial of EGFR with MET inhibitor was no better than single agent, we strongly believe that it is a subset of MET abnormalities that lead to the pathogenesis of lung cancer. In order to better define this, we are studying the MET function in invasion of NSCLC. We are utilizing the novel ECIS method to study biological behavior. **Methods:** Immunofluorescence of Met/pMet staining was performed with the following antibodies: c-MET (NovusBio) and p-METet (Tyr1230,1234,1235, Invitrogen). Immunoblot analyses of MET/pMET and related signal transduction molecules were performed on H1993 (MET amplified cell line) and A549 (KRAS mutated cell line, with activated MET) cell lysates. ECIS instrument (Applied Biophysics Inc) was used for motility assay and proliferation assay. Confluent cell monolayer was electrically abrased at 6V for 30 seconds. Impedance and resistance of the cell layer were immediately recorded for a period of up to 20 hours. For proliferation assay cells were seeded in 8W10E plates without or with inhibitors. Impedance and resistance were measured for 48 hours at 15 kHz. MET inhibitors were also utilized in the study. **Results:** In our study we investigated the inhibition potential of MET inhibitors. Staining with MET antibody resulted in nuclear and perinuclear staining of both of the cell lines. HGF treatment (100 nM, 20 min) increased nuclear staining. p-MET also increased in the presence of HGF and had plasma membrane, perinuclear and nuclear pattern. 48 hours pre-incubation with MET inhibitors reduced cellular MET staining and abolished MET phosphorylation. Moreover immunoblotting assay demonstrated significant reduction of MET phosphorylation in untreated and HGF treated cells. We measured biological activity of the cells in the presence of inhibitors. MET inhibitors significantly reduced growth rate compared with untreated cells as assessed by electrical resistance measurement. Next we did ECIS based wound-healing assay for a quantitative determination of MET inhibitors on migration potential of NSCLC cells. Voltage pulse led to drastic decrease of cell resistance. MET inhibitors delayed for 35% return to resistance value of the resting cells. **Conclusion:** MET inhibitors reduced NSCLC cell motility, migration and invasion. Novel MET inhibitors can be used for therapeutic intervention against NSCLC. The nuclear localization of MET is a novle function and needs to be explored further. ECIS also is a novel technique to study the biology of epithelial cancers. **Keywords:** NSCLC, MET/pMET, RON/pRON, ECIS

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-074 Phase III Study of WBRT with or without Erlotinib for Brain Metastasis NSCLC Zhen-Zhou Yang[1], Rong-Qing Li[2], Bo Zhu[3] [1]*Daping Hospital and the Research Institute of Surgery of the Third Military Medical University, Chongqing/ China,* [2]*Radiation Oncology, The First Affiliated Hospital of Kunming Medical College, Kunming/China,* [3]*Cancer Center of People'S Liberation Army, Xinqiao Hospital, Third Military Medical University, Chongqing/China*

Background: More effective treatment strategies are required for pts with brain metastasis (BM) from non-small cell lung cancer although whole-brain radiotherapy (WBRT) remains the standard treatment. Erlotinib, an effective TKI in EGFR mutant NSCLC, has shown evidence of intracranial accumulation, and has been proven with well tolerability and favorable objective response rate (71%) when concurrent with WBRT. One phase II study (n=80) reported no advantage in median neurological PFS or OS for

concurrent erlotinib (100mg/d) and WBRT (20 Gy/5f) in pts with predominantly EGFR wild-type NSCLC compared to WBRT alone, while another single arm phase II study (n=40) found that pre-treatment with erlotinib (150mg/d for 1 wk) followed by concurrently with WBRT (35 Gy/12f) could extend median OS to 11.8 months in all population and 19.1 months in EGFR mut pts. The optimal administration schedule for erlotinib concurrent with WBRT for BM NSCLC is controversial, which should be confirmed in a randomized controlled trial in a more larger population. This phase III trial is to investigate the efficacy and safety of erlotinib pre-treatment followed by combination of erlotinib and WBRT in comparison to WBRT alone in multiple BM NSCLC pts. **Methods:** This was an open-labeled, randomized, multicenter phase III clinical trial. Pts, aged≥18 and KPS≥70, with at least two BMs of NSCLC from 7 medical centers were recruited began in August 2013. Pts with previous use of EGFR-TKI need to withdraw≥4 weeks if assigned to the experimental arm. ARMs for detection of EGFR mutation in tumor tissue is mandatory. The major exclusion criteria included previous brain radiotherapy, or any uncontrolled or symptomatic major medical illnesses or neurologic/psychiatric illnesses. The enrolled pts would be randomly assigned to either erlotinib (150mg/day) concurrent WBRT (2.0Gy/day, 5 days/week, total dose 40Gy) or WBRT alone group with a 1:1 allocation (Fig.1). Only pts with EGFR sensitive mutation will continue to use erlotinib until disease progression or intolerable adverse events. The primary endpoint is the time to neurologic progression (TTP), defined as evidence of progression of brain metastasis (The total of longest diameter more than 20% enhanced area in MRI) or of emergency of new intracranial metastases. The secondary endpoints include, OS, ORR and QoL and subgroup analyses. Till February 12, 2015, 125 of planned 224 pts have been enrolled. This study is registered in clnicaltrials.gov (NCT01887795).

Figure 1. Study design

Results: not applicable **Conclusion:** not applicable **Keywords:** Erlotinib, whole-brain radiotherapy, Brain metastasis, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-075 Phase III, Randomized, Double-Blind Trial of Bavituximab Plus Docetaxel in Previously Treated Stage IIIb/IV Non-Squamous NSCLC (SUNRISE)
David R. Spigel[1], Joseph Shan[2], Alberto Chiappori[3], Ulrich Keilholz[4], Martin Reck[5], Martin Edelman[6], Manuel Domine[7], Keunchil Park[8], Tae Won Jang[9], Wu-Chou Su[10], Rachel E. Sanborn[11], Leora Horn[12], Rebecca Heist[13], Paul Mainwaring[14], David E. Gerber[15]
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Background: Exposed phosphatidylserine (PS) in the tumor microenvironment is highly immunosuppressive. PS binding to PS receptors on myeloid derived suppressor cells (MDSC) and M2 macrophages leads to production of anti-inflammatory cytokines such as TGF-β and IL-10. Bavituximab, a first-in-class PS-targeting monoclonal antibody, counters these effects, resulting in production of pro-inflammatory cytokines such as TNF-α and IL-12, maturation of dendritic cells and induction of tumor specific cytotoxic T lymphocyte (CTL) immunity. Docetaxel has also been shown to suppress MDSCs while increasing tumor antigens and T-cell mediated cytotoxicity, thereby enhancing bavituximab's immunomodulatory effects. In a prior double-blind Phase II trial in 2nd line non-squamous non-small cell lung cancer, bavituximab 3 mg/kg plus docetaxel was well-tolerated and demonstrated 60% improvement (11.7 vs 7.3 month) in median overall survival (OS) compared to control. **Methods:** SUNRISE is a Phase III, double-blind trial where patients with previously treated Stage IIIb/IV non-squamous, non-small cell lung cancer are randomized in a 1:1 ratio to receive up to six 21-day cycles of docetaxel in combination with either weekly 3 mg/kg bavituximab or placebo, followed by maintenance with weekly bavituximab or placebo until progression or toxicity. Patients will be stratified by region (North America, Europe, or Rest of World), disease stage (IIIb or IV), and previous maintenance/targeted therapy (yes or no). This trial was initiated in December 2013 and accrual of 582 patients across 160+ sites in 14 countries is planned over 24 months. The primary endpoint is OS and two interim analyses are planned. Secondary endpoints include progression-free survival (PFS), overall response rate (ORR) and safety. Radiographic tumor response is centrally assessed every two cycles during combination therapy and every nine weeks during maintenance. Exploratory analysis will include the assessment of changes in circulating immune cells and cytokines to better understand the immunotherapeutic mechanism. **Results:** Trial in progress **Conclusion:** Trial in progress

Keywords: Non-small-cell lung cancer; Bavituximab; Immunotherapy; phosphatidylserine

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-076 TIGER-1: A Phase 2/3 Study of First Line Rociletinib or Erlotinib in EGFR-Mutant NSCLC
Ross Camidge[1], Federico Cappuzzo[2], Jowell Go[3], Jeffrey Isaacson[4], Jason Litten[3], Keunchil Park[5], David R. Spigel[6], Alexander Spira[7], Alain Vergnenegre[8], Jürgen Wolf[9], James Chih-Hsin Yang[10], Tony Mok[11] [1]*Medicine, University of Colorado, Denver/United States of America,* [2]*Ospedali Riuniti, Ancona/Italy,* [3]*Clovis Oncology, Sanfrancisco/CA/United States of America,* [4]*Clovis Oncology, Boulder/CO/United States of America,* [5]*Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/Korea,* [6]*Sarah Cannon Research Institute/Tennessee Oncology, Pllc, Nashville/TN/United States of America,* [7]*Virginia Cancer Specialists, Fairfax/VA/United States of America,* [8]*CHU de Limoges, Limoges/France,* [9]*Universitaetsklinik Köln, Köln/Germany,* [10]*Department of Oncology, National Taiwan University Hospital, Graduate Institute of Oncology & Cancer Research Center, National Taiwan University, Taipei/Taiwan,* [11]*The Chinese University of Hong Kong, Hong Kong/China*

Background: Activating EGFR mutations including the L858R mutation and exon 19 deletions (del19) are key drivers of non-small cell lung cancer (NSCLC) in 10%–15% of patients of European and 30%–35% of Asian descent.[1] Acquired resistance to first-generation EGFR tyrosine kinase inhibitors (TKIs) such as erlotinib can be driven by additional EGFR mutations, with exon 20 T790M accounting for 50%–60% of cases.[2] Rociletinib (CO-1686) was designed to inhibit T790M as well as L858R and del19 while sparing wild-type EGFR and has demonstrated response rates up to 67% in patients with T790M mutations who had progressed on first or later line EGFR inhibitor therapy. Rociletinib continues to be well tolerated by patients in ongoing studies.[3] Given that T790M mutated subclones commonly emerge during treatment with existing EGFR inhibitors, early targeting of T790M along with initial activating mutations is a rational approach to delay progression. **Methods:** TIGER-1 (NCT02186301) is a randomized, open label study of rociletinib vs erlotinib in patients with mutant EGFR NSCLC. Patients with histologically or cytologically confirmed metastatic or unresectable locally advanced treatment-naive NSCLC (no prior therapy in the metastatic setting and no CNS disease), with documentation of ≥1 activating EGFR mutation (excluding exon 20 insertions) and biopsy within 60 days will be enrolled in this 2-part study. All patients will be randomized 1:1 to rociletinib (500 mg twice daily) or erlotinib (150 mg once daily) and treated until death, qualifying adverse events or disease progression. Patients will be stratified by sensitizing EGFR mutation (T790M, del19, L858R, or other) and territory (Asian vs non-Asian geography). The same patient eligibility criteria will be used for the Phase 2 and Phase 3 portions of TIGER-1. The phase 2 portion is currently enrolling and will transition to the Phase 3 portion upon enrollment of the 201st patient. The maturing Phase 2 dataset will contribute to decision-making rules for the Phase 3 interim analyses. The Phase 3 portion will incorporate larger cohorts; the final sample sizes will be determined by interim analyses where the chances of success will be estimated at pre-planned enrollment milestones. The primary endpoint is PFS; secondary efficacy endpoints include objective response rate, duration of response, disease control rate and overall survival. Safety will be assessed via standard adverse event reporting. PFS and OS will be summarized with Kaplan-Meier plots. The stratified log-rank and hazard ratio will compare PFS distributions for rociletinib- vs erlotinib-treated patients. Enrollment is ongoing. 1. Herbst R et al. *N Engl J Med*. 2008 2. Yu H et al. *Clin Cancer Res*. 2013 3. Sequist LV *J Clin Oncol*. 2014 **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** T790M, rociletinib, EGFR, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-077 First-Line Nivolumab + Nab-Paclitaxel + Carboplatin (C) in Advanced NSCLC
David Waterhouse[1], William Derosa[2], Cindy Duval Fraser[3], Martin Gutierrez[4], Amy Ko[3], Teng Jin Ong[3], Daniel Pierce[3], Sotirous Stergiopoulos[3], Karen Kelly[5] [1]*Oncology Hematology Care, Blue Ash/OH/United States of America,* [2]*Regional Cancer Care Associates, Llc-Morristown Carol G. Simon Cancer Center, Morristown/NJ/United States of America,* [3]*Celgene Corporation, Summit/NJ/United States of America,* [4]*John Theuer Cancer Center, Hackensack/NJ/United States of America,* [5]*University of California, Davis Comprehensive Cancer Center, Sacramento/CA/United States of America*

Background: Nivolumab, an anti-PD-1 inhibitor, has demonstrated anti-tumor activity in several solid tumors and is approved for unresectable/metastatic melanoma and disease progression following ipilimumab, and if *BRAF* V600 mutation positive, a BRAF inhibitor; and for metastatic squamous NSCLC in patients with progression on/after platinum-based chemotherapy. Combining a taxane, which can act as a cytotoxic and an immunomodulator, with an immune checkpoint inhibitor has demonstrated improved outcomes over chemotherapy alone in NSCLC. First-line nivolumab and solvent-based paclitaxel plus C (sb-P/C) resulted in a 43% overall response rate and a median progression-free survival of 31 weeks in an interim analyses from a phase I trial in patients with advanced NSCLC (Antonia et al. Presented at ASCO 2014 [Abstract 8113]). *nab*-Paclitaxel (*nab*-P) based therapy has demonstrated improved efficacy over standard treatment in pancreatic and breast cancers, and *nab*-P plus carboplatin (*nab*-P/C) significantly improved the primary endpoint (ORR) vs sb-P/C in a phase III trial of patients with advanced NSCLC (Socinski et al. *J Clin Oncol*. 2012;30:2055-2062) and does not requires immunosuppressive premedication. This phase I, open-label, 6-arm, multicenter trial, will evaluate safety of nivolumab with *nab*-P in 3 cancer types: advanced NSCLC (+ C), advanced pancreatic cancer (± gemcitabine), and metastatic breast

cancer; 2 arms in each disease. The study design for the NSCLC portion is described below. **Methods:** Eligibility criteria include histologically/cytologically confirmed stage IIIB/IV NSCLC, no prior chemotherapy for metastatic disease, prior adjuvant chemotherapy allowed providing completion >12 months before study entry, ECOG PS 0-1, adequate organ function, and preexisting peripheral neuropathy grade <2. NSCLC patients will be treated in 2 arms: 4 cycles of *nab*-P 100 mg/m^{2}on days 1, 8, and 15 plus C AUC 6 on day 1 of a 21 day cycle with nivolumab 5 mg/kg on day 15 starting at cycle 1 or the same *nab*-P/C regimen with nivolumab 5 mg/kg on day 15 starting at cycle 3. In both arms, nivolumab monotherapy will begin at cycle 5. Part 1 will assess the dose-limiting toxicities (DLTs) of the nivolumab dose with *nab*-P/C (≈ 6 patients/arm). If deemed safe, the treatment arms may be expanded using the recommended part 2 dose with an additional ≈ 14 patients/arm (total of 20 nivolumab-treated patients/arm) to further assess safety and tolerability as well as anti-tumor activity. Patients will be allowed to continue nivolumab treatment beyond RECIST 1.1 disease progression (physician discretion). ClinicalTrials.gov number NCT02309177.

Key Endpoints	
Primary	• Part 1: the number of patients with DLTs in each treatment arm • Part 1 and 2: the percentage of patients with grade 3/4 treatment-emergent adverse events (TEAEs) or treatment discontinuation due to a TEAE
Secondary	• TEAEs leading to dose reduction, interruption, or treatment discontinuation • Investigator-assessed progression-free survival* • Overall survival, disease control rate,* overall response rate,* and duration of response*
Exploratory	• Tumor-associated PD-L1 expression prior to treatment • Tumor and peripheral blood immune cell populations and soluble immune factors in peripheral blood • Tumor and nontumor (peripheral blood mononuclear cells) genetic and expression markers of efficacy and safety • Nivolumab serum concentration levels • Anti-drug antibody development after nivolumab treatment

* Based on RECIST 1.1.

Results: Not applicable **Conclusion:** Not applicable **Keywords:** nab-paclitaxel, NSCLC, Nivolumab, carboplatin

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-078 Pembrolizumab vs Platinum-Based Chemotherapy for PD-L1-Strong-Positive NSCLC Julie R. Brahmer[1], Maya Gottfried[2], Xiaoyun Li[3], Margaret Smith[3], Reshma A. Rangwala[3], Mary E. O'Brien[4] [1]*The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore/MD/United States of America,* [2]*Meir Medical Center, Kfar-Saba/Israel,* [3]*Merck & Co., Inc., Kenilworth/NJ/United States of America,* [4]*The Royal Marsden Hospital, London/United Kingdom*

Background: Platinum-doublet chemotherapy with or without maintenance therapy is the standard-of-care first-line therapy for patients with NSCLC that do not harbor *EGFR* sensitizing mutations or *ALK* translocations. Most patients experience disease progression despite treatment with chemotherapy, with median overall survival <12 months. Pembrolizumab (MK-3475), a humanized monoclonal antibody against PD-1, has demonstrated a manageable safety profile and robust antitumor activity as first-line therapy in patients with advanced NSCLC enrolled in the phase 1b KEYNOTE-001 study. Improved efficacy was observed in patients whose tumors strongly expressed PD-L1 (ie, showed membranous staining in ≥50% of tumor cells). The international, open-label, phase 3 KEYNOTE-024 trial (ClinicalTrials.gov identifier NCT02142738) is designed to assess the efficacy and safety of pembrolizumab with those of standard-of-care platinum-doublet chemotherapy in patients with treatment-naive metastatic NSCLC and PD-L1 expression in ≥50% of tumor cells. **Methods:** Patients aged ≥18 years with previously untreated advanced NSCLC without *EGFR* sensitizing mutations or *ALK* translocations, membranous PD-L1 expression in ≥50% of tumor cells, Eastern Cooperative Oncology Group performance status (ECOG PS) 0 or 1, no active autoimmune disease, or history of interstitial lung disease are eligible. PD-L1 expression is determined by immunohistochemistry in newly collected tumor samples at a central laboratory. Patients are randomly assigned in a 1:1 ratio to receive a 200-mg fixed dose of intravenous pembrolizumab every 3 weeks (Q3W) or investigator's choice of up to 6 cycles of gemcitabine 1250 mg/m^2 plus cisplatin 75 mg/m^2, gemcitabine 1250 mg/m^2 plus carboplatin AUC 5 or 6, pemetrexed 500 mg/m^2 plus carboplatin AUC 5 or 6, pemetrexed 500 mg/m^2 plus cisplatin 75 mg/m^2, or paclitaxel 200 mg/m^2 plus carboplatin AUC 5 or 6; patients with nonsquamous histology may receive pemetrexed 500 mg/m^2 Q3W maintenance therapy. Randomization is stratified by ECOG PS (0 vs 1), histology (squamous vs nonsquamous), and region (East Asia vs non-East Asia). Pembrolizumab will be given for up to 35 cycles or until disease progression, intolerable toxicity, or patient withdrawal. Eligible patients may remain on pembrolizumab therapy after initial radiographic disease progression. Patients who complete 35 cycles of pembrolizumab or who stop treatment after achieving complete response may be eligible for 1 year of pembrolizumab retreatment. Crossover to pembrolizumab is permitted for patients who progress on chemotherapy. Tumor imaging is performed every 9 weeks; response is assessed per RECIST v1.1 by independent central review and by modified RECIST by investigator review. Adverse events will be collected throughout the study and for 30 days (90 days for serious adverse events) thereafter; all toxicities will be graded according to NCI CTCAE v4.0. The primary end point is progression-free survival per RECIST 1.1 by central review; secondary end points are overall response rate per RECIST 1.1, overall survival, and safety. Enrollment is ongoing and will continue until approximately 300 patients are assigned to treatment. **Results:** Not applicable. **Conclusion:** Not applicable. **Keywords:** pembrolizumab

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-079 Pembrolizumab Plus Chemotherapy vs Chemotherapy Alone as First-Line Therapy for NSCLC Shirish Gadgeel[1], Leena Gandhi[2], Hossein Borghaei[3], Mark A. Socinski[4], Matthew A. Gubens[5], James Stevenson[6], Lecia V. Sequist[7], James Chih-Hsin Yang[8], Vassiliki Papadimitrakopoulou[9], Jennifer Bourque[10], Robert D. Bachman[10], Joy Yang Ge[10], Ellie Im[10], Amita Patnaik[11] [1]*Karmanos Cancer Institute/Wayne State University, Detroit/MI/United States of America,* [2]*Dana-Farber Cancer Institute, Boston/MA/United States of America,* [3]*Fox Chase Cancer Center, Philadelphia/PA/United States of America,* [4]*University of Pittsburgh Cancer Insitute, Pittsburgh/PA/United States of America,* [5]*University of California, San Francisco, San Francisco/CA/United States of America,* [6]*Cleveland Clinic, Cleveland/OH/United States of America,* [7]*Massachusetts General Hospital, Boston/MA/United States of America,* [8]*National Taiwan University, Taipei/Taiwan,* [9]*University of Texas MD Anderson Cancer Center, Houston/TX/United States of America,* [10]*Merck & Co., Inc., Kenilworth/NJ/United States of America,* [11]*South Texas Accelerated Research Therapeutics, San Antonio/TX/United States of America*

Background: Platinum doublet chemotherapy with or without bevacizumab is the standard first-line therapy for patients with advanced NSCLC without *EGFR* sensitizing mutations or *ALK* rearrangement. Pembrolizumab (MK-3475), a humanized monoclonal antibody against PD-1 designed to block the interaction of PD-1 with its ligands PD-L1 and PD-L2, has shown efficacy and a manageable toxicity profile in patients with NSCLC treated at doses ranging from 2 mg/kg every 3 weeks to 10 mg/kg every 2 weeks. In 45 patients with treatment-naive advanced NSCLC treated in KEYNOTE-001, single-agent pembrolizumab has demonstrated a response rate of 26%. **Methods:** KEYNOTE-021 (ClinicalTrials.gov, NCT02039674) is an international, open-label, multi-arm, phase 1/2 trial of pembrolizumab for advanced NSCLC. After establishing the safety and tolerability of pembrolizumab plus carboplatin and pemetrexed in phase 1, a randomized phase 2 cohort comparing the efficacy of pembrolizumab plus carboplatin and pemetrexed with that of carboplatin and pemetrexed has been initiated. Key eligibility criteria for this cohort are previously untreated stage IIIB/IV nonsquamous NSCLC, no sensitizing *EGFR* mutation or *ALK* rearrangement, and ECOG PS 0-1. Patients will be randomly assigned in a 1:1 ratio to receive pembrolizumab 200 mg Q3W plus carboplatin and pemetrexed at standard doses or carboplatin and pemetrexed alone. Randomization will be stratified by PD-L1 expression determined by immunohistochemistry at a central laboratory (positive [membranous expression in ≥1% of tumor cells] vs negative). Pembrolizumab will be given for 24 months or until progression, intolerable toxicity, or investigator decision. Pembrolizumab may be continued beyond radiographic progression in eligible patients. Carboplatin and pemetrexed will be given for 4 cycles followed by maintenance pemetrexed, alone or with pembrolizumab. Patients allocated to the chemotherapy-alone arm who experience progression may cross over to the pembrolizumab arm of the study. AEs will be monitored throughout treatment and for 30 days thereafter. Response will be assessed every 6 weeks for the first 18 weeks, then every 9 weeks in year 1 and every 12 weeks in year 2. Survival follow-up will occur every 3 months after discontinuation of study treatment. Primary end point is progression-free survival (RECIST v1.1, central review); secondary end points include overall survival, objective response rate, and correlation of PD-L1 expression with antitumor activity. This cohort is currently enrolling patients. **Results:** Not applicable. **Conclusion:** Not applicable. **Keywords:** pembrolizumab

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-080 Treatment Rationale and Study Design for the Phase 3 JUNIPER Study: Abemaciclib vs Erlotinib in Patients with Stage IV NSCLC and KRAS Mutation Jonathan W. Goldman[1], Peipei Shi[2], Martin Reck[3], Luis Paz-Ares[4], Andrew Koustenis[2] [1]*University of California at Los Angeles Medical Center, Santa Monica/CA/United States of America,* [2]*Eli Lilly and Company, Indianapolis/IN/United States of America,* [3]*Department of Thoracic Oncology, Lungen Clinic Grosshansdorf, Airway Research Center, North (Arcn), Grosshansdorf/Germany,* [4]*Hospital Universitario Doce de Octubre, Madrid/Spain*

Background: Abemaciclib (LY2835219) is a potent, selective small molecule inhibitor of CDK4/6, which has been shown to inhibit cell cycle progression by preventing the phosphorylation and functional inactivation of the Rb tumor-suppressor protein. Cell cycle dysfunction due to abnormalities in the CDK4/6 pathway occurs in NSCLC. KRAS mutant xenografts predict for greater sensitivity to CDK4/6 inhibitors. In a phase 1 study with abemaciclib (Goldman ASCO 2014), 16 patients with KRAS mutant tumors (N=29) had a response of stable disease (SD) or better (disease control rate [DCR]=55.2%), and 9 patients with KRAS wild-type tumors (N=24) had a response of SD or better (DCR=37.5%). **Methods:** JUNIPER (NCT02152631) is a randomized, phase 3 study of abemaciclib (200 mg orally q12hrs) + best supportive care (BSC) versus erlotinib (150 mg orally q24hrs) + BSC in patients with stage IV NSCLC whose tumors have detectable KRAS mutations and who have progressed after platinum-based chemotherapy and one other prior therapy or who are not eligible for further chemotherapy. About 550 patients will be randomized to abemaciclib or erlotinib 3:2 ratio using following factors: number of prior chemotherapy regimens (1 vs. 2), ECOG PS (0 vs. 1), gender (male vs. female) and KRAS mutation (G12C vs. others). This design has 80% power to detect overall survival (OS) hazard ratio (HR) of 0.75 (type I error 0.045) and progression-free survival (PFS) HR of 0.67 (type I error 0.005). Erlotinib was chosen as the control arm, as it is the only agent indicated for both 2nd and 3rd line therapy in advanced NSCLC. Treatment will continue until disease progression or unacceptable toxicity occurs, with assessments every 28 days, followed by short-term and long-term follow-up. Primary objectives are to compare OS and PFS of the treatment arms. Enrollment began December 2014. If the primary objectives are achieved, this study will provide results on an alternative treatment option, abemaciclib + BSC, for patients with

NSCLC whose tumors have detectable KRAS mutations, currently a patient population with few treatment options. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** NSCLC, CDK4, CDK6, KRAS

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-081 Patritumab Plus Erlotinib in EGFR Wild-Type Advanced Non-Small Cell Lung Cancer: A 2-Part Phase 3 Study (HER3-Lung) Wallace L. Akerley[1], Joachim Von Pawel[2], Berta Moritz[3], Ling Zhang[4], Susan Macintyre[4], Wenqin Feng[4], Dale Shuster[4], Shuquan Chen[4], Catherine Copigneaux[4], Luis Paz Ares[5] [1]*Huntsman Cancer Institute, Salt Lake City/UT/United States of America,* [2]*Asklepios Fachkliniken München-Gauting, Gauting/Germany,* [3]*Cesar Central European Society for Anticancer Drug Research, Vienna/Austria,* [4]*Daiichi Sankyo Pharma Development, Edison/NJ/United States of America,* [5]*University Hospital Virgen Del Rocío, Seville/Spain*

Background: Patritumab (P) is a fully human monoclonal antibody directed against human epidermal growth factor receptor 3 (HER3) that blocks activation by the ligand, heregulin (HRG), and induces receptor internalization. A Phase 2 study (NCT01211483) demonstrated that addition of P to erlotinib (E) increased progression-free survival (PFS) for the subgroup of advanced non–small cell lung cancer (NSCLC) patients with high HRG mRNA expression (HRG-high); a generally similar safety profile was seen with P+E compared with E monotherapy. To confirm these results, P+E vs. E is being investigated in a 2-part Phase 3 study designed to further evaluate the predictiveness of the HRG biomarker in patients with advanced NSCLC (https://clinicaltrials.gov/ct2/show/NCT02134015). **Methods:** HER3-Lung is randomized, placebo-controlled, double-blind, 2-part (A and B), Phase 3 study. Part A will enroll subjects with any HRG expression (limited to approximately one-third of subjects with HRG-low expression) to confirm efficacy of P+E vs. E in HRG-high disease and to possibly refine the cut-off level of HRG expression. The primary endpoint of Part A is PFS and secondary endpoints are objective response rate, overall survival, and safety. Part B will enroll subjects with HRG-high disease, defined as having a cut-off based upon the results of Part A and previous Phase 2 results. Part B is designed to independently provide pivotal confirmation of the efficacy and safety of P+E vs. E in the biomarker-defined population (n=600). The primary endpoint of Part B is overall survival. For both Part A and Part B, subjects must be aged ≥20 years with advanced NSCLC previously treated with 1 or 2 systemic therapies, and if adenocarcinoma histology, wild-type for *EGFR* and *ALK*. Tissue assessable for HRG expression must be available from archival or recently collected tumor sample. For Part A, subjects will be stratified by histology subtype, Eastern Cooperative Oncology Group performance status (0, 1) and best response to the most recent systemic therapy. Within each stratum, patients will be randomized 1:1 to P (18 mg/kg intravenous loading dose, then 9 mg/kg maintenance dose every 3 weeks) + E (150 mg/day orally) or placebo + E. Patients will be treated until disease progression, unacceptable toxicity, or withdrawal of consent. **Results:** Recruitment commenced in April 2014, and enrollment of Part A is ongoing. Investigational sites are located in Europe, United States and Canada. **Conclusion:** This study employs an innovative design to confirm efficacy in HRG-selected subjects while evaluating the expression cut-off before pivotal confirmation of efficacy and safety in the HRG-high subpopulation of *EGFR* wild-type NSCLC. **Keywords:** Advanced non–small cell lung cancer, Heregulin biomarker, Phase 3 study, Patritumab

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-082 A Phase III Study of MEDI4736 (M) an Anti-PD-L1 Antibody ± Tremelimumab (T), vs Standard of Care (SoC), in Patients with Advanced NSCLC (ARCTIC) David Planchard[1], Mikhail Shtivelband[2], Benjamin P. Levy[3], Maen Hussein[4], Kelvin Shi[5], Ramy Ibrahim[5], Marc Ballas[5], Jean-Charles Soria[1] [1]*Gustave Roussy, Villejuif/France,* [2]*Ironwood Cancer and Research Center, Chandler/AZ/United States of America,* [3]*Mount Sinai Health Systems, New York/NY/United States of America,* [4]*Florida Cancer Specialists, St. Petersburg/FL/United States of America,* [5]*Astrazeneca, Gaithersburg/MD/United States of America*

Background: M is a human IgG1 mAb that blocks programmed cell death ligand-1 (PD-L1) binding to programmed cell death-1 and CD-80 with high affinity and selectivity, and T is a selective human IgG2 mAb inhibitor of cytotoxic T-lymphocyte antigen-4 (CTLA-4). Both PD-L1 and CTLA-4 are regulators, or checkpoints, of T-cell activation. PD-L1 expression may be associated with greater clinical benefit of anti-PD-1/PD-L1 agents. Thus, the subset of patients with PD-L1-negative tumors represent a cohort with limited therapeutic options, and may benefit from the combination of M+T. Preclinical data, including mouse models of transplantable solid tumors, suggest that targeting both pathways may have synergistic antitumor activity. Emerging pharmacokinetics, pharmacodynamics, safety and efficacy data from a phase Ib study of M+T in advanced NSCLC (NCT02000947) has determined the appropriate dose for this combination. **Methods:** This randomized, open label, multi-center, phase III study (NCT02352948) is designed to evaluate the efficacy and safety of M (10mg/kg once every 2 weeks [Q2W] for up to 12 months) vs SoC (gemcitabine 1000 mg/m^2 iv Days 1, 8, and 15, vinorelbine 30 mg/m^2 iv on Days 1, 8, 15 and 22 or erlotinib 150 mg once daily, on a 4-weekly schedule until PD at the investigator's discretion) in NSCLC patients with PD-L1-positive tumors (based on archival tumor sample or recent biopsy) (Sub-study A), and the combination of M+T (M 20mg/kg + T 1mg/kg Q4W for 12 weeks then M alone 10mg/kg Q2W for 34 weeks) vs M or T (10mg/kg Q4W for 24 weeks then Q12W for 24 weeks) vs SoC in NSCLC patients with PD-L1-negative tumors (Sub-study B). PD-L1-positive is defined as ≥25% of tumor cells with membrane staining based on central assessment. Approximately 300 patients will be randomized 1:1 in Sub-study A and approximately 600 patients in a 3:2:2:1 ratio (M+T or SoC or M or T) in Sub-study B. Retreatment with immune-therapy is allowed within the setting of PD. For both sub-studies, an interim analysis for OS (and also PFS for Sub-study B) will be performed. Eligible patients include patients (PS of 0-1) with locally advanced or metastatic NSCLC, who have received at least 2 prior treatment regimens including 1 platinum-based chemotherapy. Patients with brain metastases or spinal cord compression are excluded unless asymptomatic, treated and stable off steroids. Patients with known EGFR activating mutations or ALK rearrangements are not eligible, nor patients previously exposed to any anti-PD-1 or anti-PD-L1 antibody. The primary objective is to assess PFS (per RECIST 1.1 as assessed by the Blinded Independent Central Review) and OS of M (PD-L1-positive) and M+T (PD-L1-negative), compared with SoC, in sub-study A and B, respectively. Secondary objectives include proportion of patients alive at 12 months, objective response rate, duration of response, PFS at 6 and 12 months, safety, tolerability, pharmacokinetics, immunogenicity and health-related QoL. Tumor assessments are performed every 8 weeks (first 48 weeks) then every 12 weeks. A confirmatory scan is required following the initial demonstration of PD. Recruitment in the study is ongoing since January 2015. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** NSCLC, MEDI4736, tremelimumab, PD-L1

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-083 Phase 2 Study of MEDI4736 in Patients with PD-L1+ Locally Advanced or Metastatic Stage IIIb-IV NSCLC Treated with ≥ 2 Prior Regimens (ATLANTIC) Marina C. Garassino[1], Fabrice Barlesi[2], Jamie Chaft[3], Kelvin Shi[4], Ramy Ibrahim[4], Paul Stockman[5], Marc Ballas[4], Naiyer A. Rizvi[6] [1]*Fondazione Irccs Istituto Nazionale Dei Tumori, Milano/Italy,* [2]*Aix Marseille University-Assistance Publique Hôpitaux de Marseille, Marseille/France,* [3]*Memorial Sloan-Kettering Cancer Center, New York/NY/United States of America,* [4]*Astrazeneca, Gaithersburg/MD/United States of America,* [5]*Astrazeneca, Macclesfield/United Kingdom,* [6]*Columbia University Medical Center, New York/NY/United States of America*

Background: The role of third and further line therapies in advanced NSCLC is contentious both for patients harboring EGFR mutations and ALK translocations and for patients without activating mutations. Recent studies have demonstrated that activation of the EGFR pathway induces PD-L1 expression, thereby facilitating evasion of the host's anti-tumor immune response as a potential mechanism of targeted therapy resistance. This evidence suggests a promising and inadequately explored role of immunotherapy in this particular setting of patients in whom only targeted agents were considered of unique interest. For the ~85% of patients with non-squamous NSCLC without ALK/EGFR aberrations, single agent chemotherapy represents the only option with its associated poor results and chemotherapy-related toxicities. Many cancers co-opt the programmed cell death-1 (PD-1)/programmed cell death ligand-1 (PD-L1) pathway to evade immune-mediated tumor rejection. Encouraging clinical activity against several tumor types has been seen for anti-PD-L1/PD-1 monoclonal antibodies (mAbs), including the proven benefit of nivolumab in advanced refractory squamous NSCLC. MEDI4736 is a human IgG1 mAb that blocks PD-L1 binding to PD-1 and CD-80 with high affinity and selectivity. Evidence of clinical activity for MEDI4736 in NSCLC has been observed in a Phase 1 study (Study 1108, NCT01693562), with initial data indicating that PD-L1 expression is associated with a higher objective response rate (ORR). A clinical development program of MEDI4736 in NSCLC is underway. Here we describe the ATLANTIC study (NCT02087423). **Methods:** In this Phase 2, open-label, international, multicenter, non-comparative study, the efficacy and safety of MEDI4736 (10 mg/kg IV every 2 weeks for up to 12 months) is being assessed in patients with PD-L1+ locally advanced or metastatic NSCLC (Stage IIIb–IV). The present study design includes three patient cohorts: 1) Cohort 1 (n=≥94): patients with EGFR mutations or ALK alterations; 2) Cohort 2 (n=≥94): patients with wild-type EGFR and ALK; 3) Cohort 3 (n=≥94): patients with wild-type EGFR/ALK and ≥90% of tumor cells PD-L1+. Cohorts 1 and 2 include patients whose tumor tissue samples have ≥25% of tumor cells with membrane staining for PD-L1. The PD-L1 status was tested according to the VENTANA proprietary assay. At the time the study was conceived, patients were initially included regardless of PD-L1 status. However, based on the observation that PD-L1 expression may enrich response to MEDI4736 (Study 1108), the trial was amended accordingly to include PD-L1+ tumors only. Eligible patients must have an ECOG Performance Status of 0 or 1, and have received ≥2 prior systemic treatment regimens, including one platinum-based chemotherapy and a tyrosine kinase inhibitor if *EGFR* or *ALK* positive. The primary outcome measure is ORR (RECIST v1.1), based on independent central review. Secondary outcome measures will further assess efficacy (including disease control rate, duration of response, progression-free survival and overall survival), safety (CTCAE v4.03), tolerability, pharmacokinetics, and immunogenicity of MEDI4736. Patients will be recruited at ~100–150 sites across North America, Asia, and Europe. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** NSCLC, MEDI4736, PD-L1, Immunotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-084 A Phase 2 Study of TH-4000 in Patients with EGFR Mutant, T790M-Negative, Advanced NSCLC Progressing on an EGFR TKI Stephen V. Liu[1], Charu Aggarawal[2], Corey Carter[3], David E. Gerber[4], Barbara J. Gitlitz[5], Leora Horn[6], Benjamin J. Solomon[7], Thomas E. Stinchcombe[8], Liza Villaruz[9], Howard West[10], Stew Kroll[11], Tillman Pearce[11], Ross Camidge[12] [1]*Lombardi Cancer Center, Georgetown University Hospital Cancer Center, Washington/DC/United States of America,* [2]*Abramson Cancer Center, Univ of Penn Hospital, Philadelphia/PA/United States of America,* [3]*Oncology, Walter Reed National Military Med Ctr, Bethesda/MD/United States of America,* [4]*UT Southwestern, Dallas/TX/United States of America,* [5]*Oncology, Usc Norris Comprehensive Cancer Center, Los Angeles/CA/United States of America,* [6]*Vanderbilt-Ingram Cancer Center, Nashville/TN/United States of America,* [7]*Peter Maccallum Cancer Centre, Melbourne/ACT/Australia,* [8]*Oncology, Unc Lineberger Cancer Center, Chapel Hill/NC/United States of*

America, [9]Oncology, Univ of Pittsburgh School of Medicine, Pittsburgh/PA/United States of America, [10]Swedish Cancer Institute, Seattle/WA/United States of America, [11]Clinical, Threshold Pharmaceutical, Inc., South San Francisco/CA/United States of America, [12]Medical Oncology, University of Colorado, Denver/CO/United States of America

Background: While EGFR-TKI therapy is initially effective for patients with EGFR-mutant NSCLC, eventual resistance to EFGR-TKI therapy is expected. For patients with nonT790M resistance to EGFR-TKIs, the optimal treatment is unclear. Sensitizing mutations in EGFR are often heterozygous with co-expression of both wild type (WT) and mutant EGFR. Tumor hypoxia upregulates WT EGFR signaling through several HIF-dependent mechanisms. Clinical studies indicate that EGFR-mutant NSCLC with WT EGFR present is associated with a poorer response to EGFR-TKIs. NSCLC is known to be a hypoxic tumor; thus, hypoxia-induced activation of WT EGFR signaling may be a mechanism of EGFR-TKI resistance. TH-4000 is a clinical-stage hypoxia-activated prodrug that releases an irreversible pan-ErbB TKI targeting WT EGFR, mutant EGFR and HER2. Hypoxic tumor targeting using TH-4000 may allow a greater therapeutic index with greater intratumoral TKI levels and less dose-limiting systemic toxicity seen with current EGFR-TKIs. In xenograft models of EGFR-mutant NSCLC that coexpress WT EGFR, TH-4000 reverses resistance to current EGFR-TKIs, and is effective as a singleagent. A Phase 1 study was conducted in patients with advanced solid tumors; the maximum tolerated dose (MTD) of TH-4000 administered as a 1-hour weekly intravenous (IV) infusion was established at 150 mg/m^2. The most common treatment-related adverse events were dose-dependent and included rash, QT prolongation, nausea, infusion reaction, vomiting, diarrhea and fatigue. **Methods:** A multicenter Phase 2 trial was initiated to evaluate the safety and activity of TH-4000 as a singleagent in patients with EGFRmutant, T790M-negative Stage IV NSCLC progressing on an EGFR TKI. Hypoxia PET imaging with [18F]-HX4 and molecular analyses of tumor tissue and plasma are incorporated in the study design to identify potential predictors of response to treatment. The primary endpoint is response rate. Secondary endpoints include progression-free survival, duration of response, overall survival, pharmacokinetics and safety, as well as evaluation of imaging, serum, and tissue biomarkers that may be associated with tumor response. Up to 37 patients will be enrolled with recurrent EGFR-mutant Stage IV NSCLC which has progressed while on treatment with EGFR-TKI, absence of EGFR T790M mutation, measureable disease according to RECIST 1.1, and ECOG performance status 0-1. Eligible patients must also have adequate pre-therapy tumor tissue available to enable tumor biomarker assessment. TH-4000 (150 mg/m^2) is administered weekly by IV infusion over 60 minutes. The study design incorporates a Simon two-stage design (alpha = 0.10; beta = 0.10). Recruitment is ongoing. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** wild-type EGFR, tumor microenvironment, tyrosine kinase inhibitor, T790M-negative

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-085 A Multicenter Phase 1B Study of Ceritinib plus Nivolumab in Patients with ALK+ NSCLC Alice Shaw[1], Herbert Loong[2], Daniel S.-W. Tan[3], Kerry Griscti[4], Haitao Gao[4], Friedrich Finckenstein[5], Jeffrey Scott[4], Johan Vansteenkiste[6] [1]*Massachusetts General Hospital, Boston/United States of America, [2]The Chinese University of Hong Kong, Hong Kong/Hong Kong, [3]National Cancer Centre, Singapore, Singapore/ Singapore, [4]Novartis Pharma, East Hanover/NJ/United States of America, [5]Bristol-Myers Squibb Co, Princeton/NJ/United States of America, [6]University Hospital Ku Leuven, Leuven/ Belgium*

Background: Ceritinib is a novel, highly selective, orally active and potent tyrosine kinase inhibitor of anaplastic lymphoma kinase (ALK), and has demonstrated clinical efficacy in ALK-rearranged (ALK+) non-small cell lung cancer (NSCLC) (ASCEND-1; NCT01283516). Nivolumab is a fully human, immunoglobulin G4 programmed cell death protein-1 (PD-1) immune checkpoint inhibitor antibody that selectively prevents interaction with PD-1 ligands (PD-L1 and PD-L2), thereby promoting antitumor T-cell function, and is approved by the United States Food and Drug Administration for treatment of squamous NSCLC patients with progression following platinum doublet (Checkmate-017; NCT01642004). Nivolumab in combination with chemotherapy, other immune modulators and molecular targeted therapy has shown promising preliminary results in Stage IIIB/IV NSCLC patients (CheckMate-012; NCT01454102). The demonstrated efficacy of ceritinib in ALK+ NSCLC, and nivolumab in Stage IIIB/IV NSCLC, provides a rationale to study ceritinib in combination with nivolumab in patients with ALK+ NSCLC. **Methods:** In this prospective, open-label, multicenter phase 1B study (CLDK378A2120C; NCT02393625), the primary objectives are to determine the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) and to evaluate the preliminary efficacy, based on overall response rate of ceritinib in combination with a fixed dose of nivolumab in adult stage IIIB/IV ALK+ NSCLC patients. Secondary objectives include evaluating duration of response, disease control rate, time to response, progression-free survival, overall intracranial response rate for patients with baseline measurable brain metastases, overall survival, and safety profile. In dose escalation phase, patients may have had ≥ 1 prior ALK inhibitors (except ceritinib) or prior chemotherapy regimens. In expansion phase, there will be 2 arms: 1) ALK-inhibitor pre-treated patients with 0 or 1 prior chemotherapies; 2) ALK-inhibitor naïve patients with 0 or 1 prior chemotherapies. Other key inclusion criteria are: presence of ≥ 1 measurable lesion as defined by Response Evaluation Criteria In Solid Tumors (RECIST) 1.1, and a World Health Organization performance status 0-1. Patients with asymptomatic, untreated brain metastases at baseline are allowed. Dose-escalation phase will consist of successive cohorts of patients (3 to 6) receiving increasing doses of ceritinib (starting dose: 450 mg/d with a low-fat meal; 28-day cycles) plus nivolumab (3 mg/kg Q2W) and will enroll a minimum of 12 patients. In expansion phase, approximately 60 patients will be allocated to arms 1 and 2 (30 in each arm) and treated with ceritinib at MTD/RDE plus nivolumab (3 mg/kg Q2W). Material required for central assessment of ALK rearrangement must be either archival tissue or, preferably, a fresh biopsy. Apart from ALK rearrangement, potential predictive markers of PD-L1 and PD-L2 expression and/or additional immunological biomarkers will also be assessed. Patients may continue treatment until unacceptable toxicity, disease progression, discontinuation at the discretion of the investigator, or consent withdrawal. MTD and/or RDE estimation will be based on the probability of dose-limiting toxicities using an adaptive Bayesian logistic regression model guided by the escalation with overdose control principle and an overall assessment of safety and tolerability data. Tumor responses will be assessed per RECIST v1.1 by investigator assessment. **Results:** Not available **Conclusion:** Not available **Keywords:** Ceritinib, Nivolumab, ALK, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-086 TIGER-3: A Phase 3 Open-Label, Randomized Study of Rociletinib vs Chemotherapy in NSCLC James Chih-Hsin Yang[1], Sanjay Popat[2], Lyudmila Bazhenova[3], Collin M. Blakely[4], Robert Dichman[5], Enriqueta Felip[6], Frank Griesinger[7], Harry J.M. Groen[8], Sarada Gurubhagavatula[9], Joseph W. Leach[10], Silvia Novello[11], Maurice Perol[12], Ravindranath Patel[13], Karen Reckamp[14], Panos Georgiou[15], Emiko Miyamoto[16], Jeffrey Isaacson[17], Heather A. Wakelee[18] [1]*National Taiwan University, Taipei City/Taiwan, [2]Royal Marsden Hospital, London/United Kingdom, [3]Internal Medicine, Division of Hematology-Oncology, University of California San Diego, La Jolla/United States of America, [4]Medicine, UCSF, San Francisco/United States of America, [5]Central Coast Medical Oncology Corporation, Santa Maria/CA/United States of America, [6]Vall D'Hebron University Hospital and Vall D'Hebron Institute of Oncology (Vhio), Barcelona/Spain, [7]Pius-Hospital Oldenburg, Oldenburg/Germany, [8]Department of Pulmonary Diseases, University Medical Center Groningen, Groningen/Netherlands, [9]Regional Cancer Care Associates, Morristown/NJ/United States of America, [10]Virginia Piper Cancer Institute, Minneapolis/ MN/United States of America, [11]Department of Oncology, University of Turin, Aou San Luigi, Orbassano/Italy, [12]Department of Medical Oncology, Léon Bérard Cancer Center, Lyon/France, [13]Comprehensive Blood and Cancer Center, Bakersfield/CA/United States of America, [14]Medical Oncology and Therapeutics Research, City of Hope, Duarte/CA/United States of America, [15]Clovis Oncology, Chelmsford/United Kingdom, [16]Clovis Oncology, San Francisco/CA/United States of America, [17]Clovis Oncology, Boulder/CO/United States of America, [18]Department of Medicine, Division of Oncology, Stanford University, Stanford/CA/ United States of America*

Background: Rociletinib (CO-1686) is a novel, oral, irreversible tyrosine kinase inhibitor for the treatment of patients with mutant epidermal growth factor receptor (EGFR) non-small cell lung cancer (NSCLC) that has demonstrated efficacy against the activating mutations (L858R and Del19) and the dominant acquired resistance mutation (T790M), while sparing wild-type EGFR. TIGER-X, a Phase I/II dose-ranging trial, has provided evidence that rociletinib is associated with durable response and is well tolerated in patients with NSCLC and positive T790M status following progression on a TKI.[1] Efficacy has also been noted for patients with T790M negative status in TIGER-X.[2] TIGER-3 is designed to investigate single agent rociletinib vs chemotherapy in patients who have failed EGFR therapy and platinum-based doublet chemotherapy, which is a setting of acquired resistance and high unmet need for targeted therapeutic options. TIGER-3 will evaluate patients with T790M positive and negative status based on tumor biopsies and plasma, and biomarkers of response and/or resistance. **Methods:** Patients with histologically or cytologically confirmed metastatic or unresectable locally advanced NSCLC, with radiological progression on the most recent therapy will be enrolled in this phase 3, randomized, open-label study (NCT02322281). Patients must have documented evidence of a tumor with ≥1 EGFR activating mutations excluding exon 20 insertion, and prior treatment with an EGFR TKI and platinum-containing doublet chemotherapy. Patients will be randomized 1:1 to receive rociletinib twice daily (500 mg) or single agent cytotoxic chemotherapy (investigator choice specified before randomization) until disease progression according to RECIST 1.1. Patients will be stratified by presence or absence of brain metastases, ECOG performance status (0 vs 1), and race (Asian vs non-Asian). The primary endpoint is progression-free survival (PFS). Secondary endpoints include safety, objective response rates, duration of response, disease control rate, and overall survival. Kaplan-Meier methodology will assess time to event variables. The stratified log-rank and the hazard ratio will be used for comparing PFS distributions. Serial assessment of safety will be carried out based on standard adverse event reporting. Planned enrolment is 600 patients; enrolment has been open since March 2015.

- Sequist LV *J Clin Oncol*. 2014
- Soria J-C EORTC-NCI-AACR 2014

Results: Not applicable **Conclusion:** Not applicable **Keywords:** rociletinib, EGFR, T790M, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.01-087 A Phase I Study of Chloroquine with Carboplatin and Gemcitabine in Advanced Solid Tumors and NSCLC Nagla Abdel Karim[1], El Mustapha Bahassi[2], Ahmed Khaled[1], Mahmoud Shehata[2], Trisha Wise-Draper[2], Sue O'Gara[2], John Morris[2] [1]*Internal Medicine/Division of Hematology/Oncology, The University of Cincinnati, Ohio/ OH/United States of America, [2]Internal Medicine/Division of Hematology/Oncology, The University of Cincinnati, Ohio/United States of America*

Background: Autophagy is the catabolic degradation of cellular constituents that can promote cancer cell survival by maintaining cellular energy levels during periods of stress, including exposure to radiation or chemotherapy. The antimalarial, chloroquine (CQ), has received attention as an inhibitor of autophagy. The lysosomotropic properties of CQ are probably responsible for many of its biological effects. Manipulation of autophagy is a potentially exciting area for the development of new cancer treatments. Recently, accumulating evidence suggest that CQ can effectively sensitize cancer cells to the cell-

killing effects of ionizing radiation and chemotherapeutic agents, thus suggesting its use as a sensitizer for conventional therapies. Hypothesis: CQ may sensitize chemotherapy-resistant tumor cells by inhibiting autophagy and enhance tumor response and survival of patients with solid tumors. Patients with non small cell lung cancer (NSCLC) squamous cell carcinoma subtype will be enrolled and followed for possible improved outcome with the addition of choloroquine to platinum doublet especially agents as Bevacuzimab can not be added to their standard doublet therapy. Patients with other advanced solid tumors will be eligible as long as carboplatin and Gemcitabine are considered an acceptable therapeutic option.

Methods:

Dose Level	Patients(N)	CQ mg/dl D-7-D21	Carboplatin AUC D1	Gemcitabine mg/m2 D1 &D8
1	3-6	50	5	1,000
2	3-6	100	5	1,000
3	3-6	150	5	1,000
4	3-6	200	5	1,000
Expansion cohort	10-12	MTD	5	1,000

Primary Objectives: The aim of this phase I study is to determine the adverse events (AE) and maximum tolerated dose (MTD) associated with adding chloroquine (CQ) to carboplatin and gemcitabine (CG) in patients with previously treated advanced solid tumors. Secondary Objectives: To estimate overall response rate (ORR), progression-free survival (PFS), and overall survival (OS); to determine the pharmacokinetics of CQ in combination with CG, and its effect on tumor burden by measurement of circulating tumor cells (CTCs). Methods: A single institution phase I dose-escalation study. Patients with advanced solid malignancies with no available standard of care treatment options, and ECOG performance status 0-2 are eligible. Sequential cohorts of 3-6 patients will be treated with escalating daily doses of oral CQ in addition to carboplatin and gemcitabine (Table 1). The study is ongoing and patient accrual is in the first cohort. **Results:** Not applicable **Conclusion:** Not applicable
Keywords: phase I Clinical trial in progress, Carboplatin and Gemcitabine, Choloroquine, Autophagy

SESSION: POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC MONDAY, SEPTEMBER 7, 2015

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-001 Predictive Factors of Distant and Local Recurrence in Patients with Surgically Resected Stage 1 NSCLC Shinjiro Mizuguchi, Nobuhiro Izumi, Hiroko Oka-Yamamoto, Satoshi Okada, Michihito Toda, Kantaro Hara, Noritoshi Nishiyama *Osaka City University, Osaka/Japan*

Background: Surgical treatment is the most efficient therapy for early non-small lung cancer (NSCLC). However, after radical surgery many patients relapse or progress to systemic disease, even in stage I NSCLC. The objective of this study was to examine the recurrence predictors, especially focused on location of recurrence (local or distant), in patients who underwent potentially curative resection for stage 1NSCLC. **Methods:** The study included 371 consecutive patients who underwent lobectomy with radical mediastinum lymph node dissection from 1998 to 2011 without any preoperative therapy. For analysis of recurrence, 342 patients were enrolled after excluding patients with non-cancer related death or loss of their follow-up within 3 years of resection. Disease recurrence at the surgical margin, ipsilateral pleural dissemination, ipsilateral hilum, and/or mediastinum was considered as local recurrence. The median follow-up was 62 months. There were 205 males and 137 females with a median age of 69 years. Two hundred and forty-four patients had adenocarcinoma, 86 had squamous cell carcinoma, and 12 had other types. On pathologic staging 194 patients were in stage IA and 148 in stage IB. Lymph/vascular invasion were detected in 123, moderate/poor degree of tumor differentiation in 210, and 129 were non-smokers. The patients were divided into two groups: recurrence (n = 70) and non-recurrence (n = 272) within 3 years. **Results:** The 1, 3, and 5-year overall survival was 97%, 85% and 74%, respectively. Postoperative recurrence within 1, 2 and 3 years was observed in 26 (7.1%), 58 (16.6%) and 70 (20.4%) patients, respectively. Recurrence in local tissue only within 1, 2 and 3 years was observed in 4 (15%), 14 (24%) and 17 (24%) cases, respectively. Age, sex, smoking history, pathologic stage (IB), lymphatic/vascular invasion, and the degree of tumor differentiation were also significantly different between recurrence and non-recurrence group. Regarding tumor markers, the serum concentrations of SLX, CEA and CYFRA21-1 in the recurrence group were significantly higher than those in the non-recurrence group (p = 0.003, 0.030, and 0.006, respectively). By multivariate analysis, independent predictors of recurrence within 3 years were age more than 75 years (HR 2.51; 1.27–4.96), lymph/vascular invasion (HR 1.95; 1.06–3.63), stage IB (vs IA; HR 2.17; 1.14–4.18) and SLX (HR 1.04; 1.01-1.08). Although the rate of distant recurrence within 3 years was higher in stage IB (p = 0.032), there was no significant difference in age, sex, smoking history, lymphatic/vascular invasion, degree of tumor differentiation, CEA and CYFRA between distant and local recurrence group. The serum tumor marker SLX was also significantly higher in the distant metastasis group than in the local recurrence group (mean 29.8 and 21.4U/ml, respectively; p = 0.007) **Conclusion:** Early recurrence predictors after complete resection in patients with pathological stage 1 NSCLC were age (over 75 years), lymph/vascular invasion, stage 1B and high serum concentration of SLX. Furthermore, SLX is potentially useful to predict distant metastasis. Adjuvant chemotherapy might be considered in patients who are positive for these predictive factors.
Keywords: stage1 NSCLC, recurrence, SLX, predictive factor

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-002 Interstitial Lung Disease (ILD) Associated Cancer Genesis Is Noble Predictor for Patients with Non-Small Cell Lung Cancer and ILD Ryo Miyata, Mitsugu Omasa, Ryo Fujimoto, Hiroyuki Ishikawa, Yosuke Otake, Minoru Aoki *Department of Thoracic Surgery, Nishi-Kobe Medical Center, Kobe, Hyogo/Japan*

Background: Interstitial lung diseases (ILDs) are at increased risk of developing lung cancer. The purpose of this study is to evaluate the survival and predictors of survival after surgical resection in patients with non-small cell lung cancer (NSCLC) and ILDs. **Methods:** We retrospectively analyzed data from 55 patients with NSCLC with a clinical diagnosis of ILD who underwent pulmonary resection between 1994 and 2010 at our institution. Kaplan-Meier analysis and Cox proportional hazards regression analysis were used. **Results:** Male patients (94.5%) and smokers (98.2%) were in majority. The overall 5-year survival was 15.4%. The 5-year survivals were 9.1% and 31.6% for patients with a predicted percent vital capacity of 80% or less and a predicted percent vital capacity greater than 80%, respectively (log-rank test, P = .036). The 5-year survival of patients in which NSCLC was developed in the ILD positive background was 15.4%. On the other hand, the 5-year survival of patients in which NSCLC was developed in the ILD negative background was 47.5% (P = .033). Surgical procedures had an association with survival (P = .051), the 5-year survival were 0% and 31.3% in the wedge resection and segmentectomy / lobectomy groups, respectively. Multivariable analysis revealed that lower predicted percent vital capacity, ILD-associated cancer genesis, and non-anatomical pulmonary resection were independent poor prognostic factor for survival. Carbon monoxide diffusing capacity and Krebs von den Lungen-6 (KL-6) were not included in the analysis because of missing data more than 5%. **Conclusion:** Anatomical resection is recommended for patients with NSCLC and ILD with predicted percent vital capacity greater than 80%. ILD-associated cancer genesis is noble predictor for patients with a clinical diagnosis of ILD who underwent pulmonary resection for NSCLC.
Keywords: prognostic factor, lung cancer, interstitial lung diease, cancer genesis

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-003 Accuracy of Clinical and Pathologic Staging of Non-Small Cell Lung Cancer in a Residency Education Program Mariam J. Almarashda, Stephen A. Deppen, Joe B. Putnam, Jr. *Thoracic Surgery, Vanderbilt University Medical Center, Nashville/TN/United States of America*

Background: Accurate non-small cell lung cancer (NSCLC) clinical staging (CS) guides treatment options and prognosis. In addition, clinical and quality improvement registries incorporate CS and pathological staging (PS) for patients undergoing pulmonary resection. In residency education programs, CS and PS for NSCLC patients are essential educational components of thoracic surgical care. To determine the accuracy of CS by our house staff, we prospectively collected CS of patients who were treated by lobectomy (traditionally entered by our house staff) and compared those results to CS and PS in our cancer registry for accuracy and concordance. **Methods:** We conducted a retrospective analysis of prospectively collected clinical data between January 2005 and December 2014. Only patients with NSCLC who underwent anatomic pulmonary resection were included. We compared accuracy and Kappa score of preoperative CS entered by our house staff with the CS and PS obtained by our institutional cancer registry. **Results:** A total of 915 patients underwent pulmonary resection operation for known or suspected lung cancer. 582 patients underwent lobectomy, segmentectomy, or sleeve resection for non-small cell lung cancer. The mean age at time of surgery was 65 years (95%CI: 64, 66), and 316 (56%) were women. Histology included adenocarcinoma, 292 (50%); squamous, 181, (31%); carcinoid, 40, (7%); large cell, 36, (6%); and others, NOS 30 (5%). CS by house staff compared to registry CS had 49% agreement and (expected agreement at random was 27% given 7 possible staging choices; Kappa score of interrater reliability of the 7 possible staging levels was 0.31). Agreement was significantly better than random ($p<0.001$) but Kappa score was relatively low. CS by house staff was compared to final PS had 52% agreement of an expected 28% and a Kappa score of 0.34. Final pathological stage by the author [MJA] or pathologist compared to cancer registry final pathology had 87% agreement and Kappa 0.83. House staff clinical nodal staging accuracy compared to pathological nodal staging had a higher absolute agreement (73%) than tumor staging (67%); however, due to fewer levels of nodal disease, higher agreement was expected in nodal staging. Adjusted level of agreement measured by Kappa score was lower in nodal staging, (0.14) compared to moderate agreement in tumor staging, Kappa 0.48. Registry CS absolute agreement for lymph nodes (66%) and tumor (63%) compared to PS was slightly lower than that of house staff (73% nodal and 67% tumor staging). This was largely due to the greater number of unstaged cancers (n=105) found in the registry. **Conclusion:** The cancer registry generally under stages the patient's CS compared to the PS. In addition, CS by trainees was only accurate in 52% of patients. The clinical nodal status had the lowest agreement (42%) after adjusting for the number of choices available by both our house staff and the cancer registry. Additional attention in trainee education, especially in the area of clinical nodal staging is necessary for improving CS and subsequent clinical decision making for our patients with NSCLC.
Keywords: NSCLC, Accuracy, Staging, Education

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

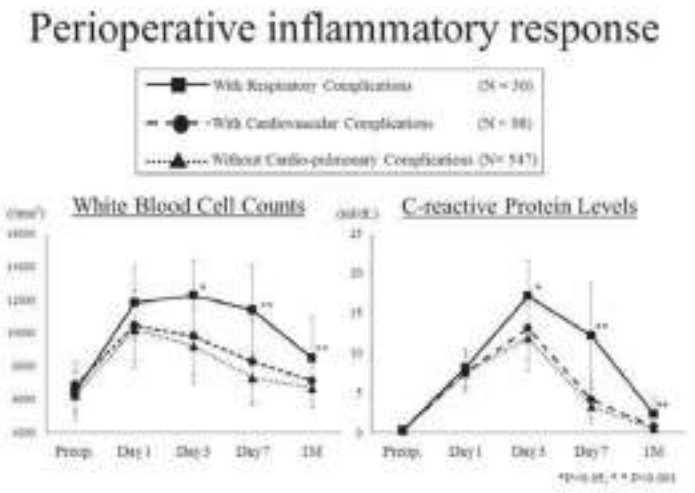
P1.02-004 Accurate Assessment of Vessel Invasion Using D2-40 and Victoria Blue Predicts Recurrence in Patients with Pathological Stage I NSCLC
Satoshi Okada, Shinjiro Mizuguchi, Nobuhiro Izumi, Hiroko Oka-Yamamoto, Michihito Toda, Kantaro Hara, Noritoshi Nishiyama *Osaka City University Hospital, Osaka/Japan*

Background: It is difficult to estimate lymphatic vessel invasion (LVI) and blood vessel invasion (BVI) by Hematoxylin-Eosin (HE) staining for lung cancer specimens. The aim of this study was to compare HE with D2-40 and Victoria blue staining for detection of LVI and BVI, respectively, and to assess the relationship between these measurements and recurrence in patients with pathological stage I non-small cell lung cancer (NSCLC). **Methods:** We retrospectively analyzed 251 patients who underwent complete resection for pathological stage I NSCLC from 1997 to 2008. This study included 152 males and 99 females with a median age of 69 years (range, 20–93 years). Using criteria detailed in the seventh edition of the TNM classification for lung cancer, 129 cases were pathological stage IA and 122 cases were IB. Histologically, 175 adenocarcinomas, 67 squamous cell carcinomas, and 9 other subtypes of carcinomas were found. There were 81 well-differentiated carcinomas and 170 moderate or poorly differentiated carcinomas. The median follow-up across the cohort was 70.2 months and the 5-year survival rate was 72.2%. The paraffin-embedded sections were stained with HE, D2-40, and Victoria blue. Specimens with each staining were reevaluated and classified into three grades according to numbers of vessel invasion in one section: Ly0/V0, no invasion; Ly1/V1, one or two invasions; and Ly2/V2, more than three invasions. **Results:**Assessment of vessel invasion by HE revealed the following distribution of LVI grades: Ly0=125 (49.8%); Ly1=104 (41.4%); Ly2=22 (8.8%), and BVI grades: V0=224 (89.2%); V1=24 (9.6%); and V2=3 (1.2%). In contrast, segregation of patients according to reassessment of LVI and BVI by D2-40 and Victoria blue, respectively, resulted in the following distributions: Ly0=177 (70.5%); Ly1=53 (21.1%); Ly2=21 (8.4%); V0=186 (74.1%); V1=53 (21.1%); and V2=12 (4.8%). After reassessment using D2-40 and Victoria blue, 50% (11 of 22) of Ly2 cases by HE changed to Ly0, and 22.7% (5 of 22) of Ly2 cases by HE changed to Ly1, 66% (2 of 3) of V2 cases by HE changed to V0 and V1, respectively. According to accurate assessment of vessel invasion using D2-40 and Victoria blue, there was no significant difference in disease-free survival between patients who were negative and positive for LVI or BVI (p=0.1062 and 0.1849, respectively); however, when patients were divided according to the intensity of LVI/BVI (Ly0&1/V0&1 vs. Ly2/V2), there was a significant difference in disease-free survival (p=0.0281 and p<0.0001, respectively). A recurrence of lung cancer was discovered in 50 patients (19.9%) within 3 years. On multivariate analysis, the independent recurrence factors were pleural invasion (HR 2.64; 1.40–4.86) and V2 based on Victoria blue (HR 8.54; 3.46–19.1). **Conclusion:** Our study suggests that accurate reassessment of LVI and BVI using D2-40 and Victoria blue staining, used to assess not only presence but also intensity, is important to predict the postoperative recurrence in patients with pathological stage I NSCLC. If the predictive factors of pleural invasion and V2 based on Victoria blue staining were recognized, adjuvant chemotherapy might be considered for these patients.
Keywords: pathological stage I NSCLC, lymphatic invasion, blood vessel invasion, recurrence

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-005 Impact of Postoperative Complications on Cancer Recurrence following Lung Cancer Surgery
Takashi Nojiri[1], Masayoshi Inoue[1], Yasushi Shintani[1], Yukiyasu Takeuchi[2], Hajime Maeda[2], Toshimitsu Hamasaki[3], Meinoshin Okumura[1] [1]*General Thoracic Surgery, Osaka University Graduate School of Medicine, Suita/Japan,* [2]*General Thoracic Surgery, National Hospital Organization Toneyama Hospital, Toyonaka/Japan,* [3]*Clinical Research and Development, National Cerebral and Cardiovascular Center, Suita/Japan*

Background: Recent studies indicate that postoperative complications after various types of cancer surgery are associated with poor cancer-specific survival. Postoperative complications induce severe inflammatory reaction during the perioperative period. Emerging evidence suggests that systemic inflammation can accelerate the adhesion of circulating tumor cells to the vascular endothelium of distant organs, which is the first step of extravasation in hematogenous metastasis. The objective of this study was to investigate the impact of postoperative cardiopulmonary complications on cancer recurrence after lung cancer surgery. **Methods:** From a prospective database of 675 consecutive patients who underwent a lung cancer surgery between April 2007 and March 2012, we retrospectively analyzed medical charts of all patients with curative surgery. The primary endpoint was the incidence of cancer recurrence after surgery between the patients with and without postoperative cardiopulmonary complications. Perioperative white blood cell counts and C-reactive protein levels were also compared. **Results:** Postoperative cardiovascular or respiratory complications were identified in 98 (15%) or 30 (4%) patients, respectively. There were no significant differences in the incidence of cancer recurrence between the patients with postoperative cardiovascular complications and without cardiopulmonary complications (23% vs. 19%; p = 0.26). In contrast, there was significantly higher incidence of cancer recurrence in those with postoperative respiratory complications than those without cardiopulmonary complications (42% vs. 19%; p < 0.05). Multiple regression analysis adjusted age, sex, and pathological staging showed the similar tendency, however there was no significant difference. There were significantly higher levels of white blood cell counts and C-reactive protein levels in the acute phase after surgery in those with postoperative respiratory complications than those without.



Conclusion: Not cardiovascular but respiratory complications following lung cancer surgery might have the negative predictor in the incidence of cancer recurrence. Severe inflammation induced by postoperative complications might be associated with high incidence of cancer recurrence.
Keywords: postoperative complication, cancer recurrence, surgical inflammation, lung cancer surgery

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-006 Visceral Pleural Invasion Was Common in Larger (> 2 cm) Ground Glass Nodules, but Showed No Aggressive Prognostic Impact
Lilan Zhao[1], Huikang Xie[2], Junyan Zha[1], Ke Fei[1], Chang Chen[3] [1]*Department of General Thoracic Surgery, Shanghai Pulmonary Hospital, Shanghai/China,* [2]*Department of Pathology, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China,* [3]*Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

Background: Visceral pleural invasion (VPI) had been demonstrated as an aggressive sign in solid-density non-small-cell lung cancers. However, its incidence and clinical relevance in ground glass nodules (GGNs) has not been clarified. The present study aims to investigate the clinical, radiological and pathological features of GGNs in patients with VPI. **Methods:** All consecutive surgically treated patients with solitary GGNs between 2008 and 2013 were retrospectively reviewed. Inclusion criteria were defined as: lesions < 3 cm and pleura abutting on computed tomography scan; pathologically confirmed non-small cell lung cancers. Patients with and without VPI were compared for clinical, radiological and pathologic parameters and survival. **Results:** A total of 121 patients were enrolled and 38 had pathologically proven VPI. The median patient age was 61 years old (range, 30-81 years old) and 45 (37.2%) patients were male. The mean follow-up duration was 30 months. The incidence of VPI was 43.9% (25/57) if the tumor diameter was > 2.0 cm and 20.3% (13/64) in < 2.0 cm (p=0.005). It was 20.9% (9/43) in pure GGNs and 37.2% (29/78) in part-solid GGNs (p=0.065). In cases with pleura indentation the incidence was 37.5% (24/64). In lepidic predominant, acinar predominant, papillary predominant and mucinous variant adenocarcinomas, the VPI rate was 44.7%, 84.60%, 52.9% and 100%, respectively (p=0.07). There were five lymph node involvement cases and three death cases due to distant metastasis. There was no statistical difference in 3-year overall survival between patients with VPI and without, nor between pure (all alive) and part-solid GGNs (p=0.956). **Conclusion:** VPI was more commonly seen in large (> 2 cm) GGNs and those with pleural indentations. Histologically it was more frequently seen when acinar was also predominant. Although commonly taken as an aggressive sign predictive of poor prognosis, the presence of VPI in GGNs may be associated with less prognostic significance. Therefore, upgrading of the TNM stage on the basis of VPI for such patients needs further verification.
Keywords: non-small cell lung cancer, ground-glass nodules, visceral pleural invasion

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-007 The Histologic Subtype of Lung Adenocarcinoma Should Not Deter Sublobar Resection for Patients with Clinical Stage IA Lung Cancer
Mohamed Kamel[1], Navneet Narula[2], Brendon Stiles[1], Abu Nasar[1], Galal Ghaly[1], Mohamed Rahouma[1], Jeffery Port[1], Paul Lee[1], Subroto Paul[1], Nasser Altorki[1] [1]*Thoracic Division of Cardiothoracic Surgery Department, Weill Cornell Medical College, New York/NY/United States of America,* [2]*Pathology Department, Weill Cornell Medical College, New York/NY/United States of America*

Background: The International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society pathological classification of lung cancer allows for a more comprehensive understanding of the prognostic factors associated with subtypes of lung adenocarcinoma. Micropapillary and solid (MIP/SOL) subtypes have been associated with higher recurrence rates. Some have therefore suggested that sublobar resection (SLR) should be considered a compromise procedure

in patients with MIP or SOL tumors. We conducted this study to examine the effect of the resection type [lobectomy (LO) or SLR] on oncological outcomes of patients with MIP/SOL. **Methods:** A retrospective review of a prospective database (2000-2014) was performed to identify patients with clinical stage IA adenocarcinoma, excluding pure ground glass opacities. Propensity score matching (age, gender, FEV1%, and clinical tumor size) was done to obtain balanced cohorts of patients undergoing LO and SLR. The presence of MIP and/or SOL components (≥5%) was assessed by a single pathologist to avoid inter-observer bias. The SLR group of patients had more comorbidities. Therefore, deaths from causes other than lung cancer were censored and freedom from recurrence was used to assess oncological outcomes. Survival analysis was done using the Kaplan Meier method. Multivariable analysis (MVA) was done using Cox regression. **Results:** This study included 300 patients (150 LO vs. 150 SLR, including 77 segmentectomy and 73 wedge resection). Patients undergoing SLR had higher Charlson comorbidity index (P=0.002) and lower DLco% (P=0.01). Patients undergoing LO were more likely to have nodal assessment (99% vs. 85%,P<0.001). Otherwise, no differences in the clinicopathological characteristics were found between the two groups. The presence of ≥5% MIP and/or SOL components was found in 135 patients; LO (58), SLR (77). The 3-year probability of freedom from recurrence in the whole cohort was: MIP (77%), synchronous MIP/SOL (76%), and SOL (61%), compared to 86% freedom from recurrence for other pathological subtypes (median follow-up 41 months). The probability of freedom from recurrence in patients with MIP/SOL subtypes showed a trend favoring the LO group (P=0.092). However, when we excluded patients with SLR with resection margin <1 cm (n=64), there was no difference between LO (80%-72%) and SLR (81%-75%) at 3 and 5 years respectively (P=0.812)(Fig.1). Also, the type of resection (LO/SLR) was not associated with higher recurrence rates in the MVA of the whole cohort.

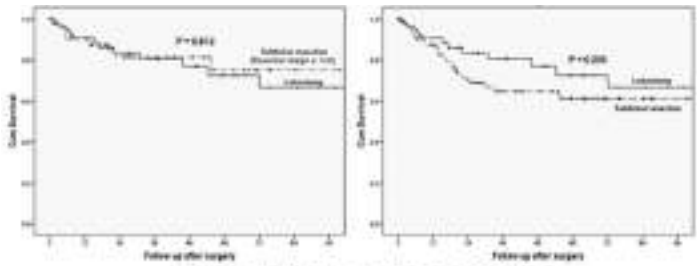

Fig.1 Freedom from recurrence in patients with MIP/SOL

Conclusion: SLR can be safely performed in clinical stage-IA lung adenocarcinoma, regardless of the histological subtype, provided that a resection margin >1 cm is obtained. **Keywords:** lobectomy, Histological Subtype, stage I, Sublobar

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-008 Diagnostic Molecular Testing in Multiple Lung Cancers Jarushka Naidoo[1], Kaitlin Woo[2], Camelia S. Sima[3], William D. Travis[4], Maria E. Arcila[5], David J. Finley[6], Valerie Rusch[7], David R. Jones[8], Mark G. Kris[1], Marjorie G. Zauderer[9] [1]*Thoracic Oncology, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [2]*Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York/United States of America,* [3]*Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [4]*Pathology, Memorial Sloan Kettering Cancer Center, New York/United States of America,* [5]*Department of Pathology - Molecular Diagnostics, Memoria Sloan Kettering Cancer Center, New York/United States of America,* [6]*Thoracic Surgery, Dartmouth-Hitchcock Medical Center, New Hampshire/NH/United States of America,* [7]*Thoracic Surgery, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [8]*Thoracic Surgery, Memorial Sloan Kettering Cancer, New York/NY/United States of America,* [9]*Medicine/Thoracic Oncology, Mskcc, New York/NY/United States of America*

Background: Multiple lung cancers (MLCs) are determined using the Martini-Melamed clinical criteria, and comprehensive pathologic assessment. The underlying biology for why MLCs develop is not known. Herein, we evaluate clinicopathologic data for patients with MLCs, and report clonality between MLC lesions using diagnostic molecular testing. **Methods:** After IRB approval, we conducted a retrospective review of all patients who underwent an R0 resection for stage IA-IIIA LC from 2008-2013 in our institution. Patients with carcinoid tumors, adenocarcinoma-in-situ, multiple ground-glass opacities, intrapulmonary metastases, and cancers not originating from the lung, were excluded. MLCs were defined using Martini-Melamed criteria, and comprehensive pathologic assessment. Clinico-pathologic data was collected for patients with MLCs, including available diagnostic molecular data from sizing assays, Sanger sequencing and mass spectrometry genotyping (Sequenom). **Results:** 2352 pts were identified: one LC (n=2238), recurrent LC (n=348), MLC (n=113). In patients with MLCs, adenocarcinoma histology (n=97) was associated with improved OS (p=0.049) compared to squamous histology (n=13, other n=3). Paired diagnostic molecular pathology was available in 51 patients with adequate tissue from MLCs. MLC pairs stratified by mutation type are depicted in Table 1. In 49 patients, both MLCs were adenocarcinomas (20= extended panel: sizing assays/Sanger sequencing/Sequenom, 29=limited panel: *EGFR/KRAS* sizing assay/Sanger sequencing): 51% (n=25/49) had concordant molecular results, suggesting a common tumor clone, and 49% (n=24/49) had discordant results. In 1 patient, one MLC was an adenocarcinoma and the other was a squamous carcinoma, and had discordant molecular results by limited panel testing. In 1 patient, both MLCs were squamous carcinomas, and had concordant molecular results by limited panel testing. In patients where MLCs both had a *KRAS* mutation (n=11), 3 pairs had the same mutation (*KRAS* G12C, *KRAS* G12D, *KRAS* G12F), and 8 had different mutations.

Table 1: Multiple Lung Cancer: Molecular Data

Paired Lung Adenocarcinomas (n=49)					
	Second Lung Cancer				
First Lung Cancer	*BRAF*	*EGFR*	*KRAS*	*NRAS*	No mutation
BRAF	0	0	1	0	0
EGFR	0	3	0	0	4
KRAS	1	0	11	1	6
No mutation	0	3	7	1	11
One Adenocarcinoma/One Squamous Carcinoma (n=1)					
	Second Lung Cancer				
First Lung Cancer	*EGFR*				
No mutation	1				
Paired Squamous Carcinomas (n=1)					
	Second Lung Cancer				
First Lung Cancer	No mutation				

Conclusion: Martini-Melamed criteria and comprehensive pathologic assessment, are currently used to diagnose MLCs. Assuming separate MLC lesions harbor distinct molecularly defined clones, paired molecular testing using limited panels is not sufficient to diagnose MLCs. Concordant molecular profiles do not necessarily define whether a lesion is an MLC or a metastatic lesion. Paired prospective testing of suspected MLC lesions including broader molecular tests such as DNA, RNA, protein expression and immune correlates, may advance our understanding of the biology of these tumors. **Keywords:** multiple lung cancers, diagnostic molecular pathology, non-small cell lung cancer, clonality

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-009 Prognostic Value of New IASLC/ATS/RES Lung Adenocarcinoma Classification on Dominate Tumor in Synchronous Multiple Primary Adenocarcinomas Chien-Sheng Huang[1], Po-Kuei Hsu[1], Yu-Chao Yu[1], Chun-Ku Chen[2], Yi-Chen Yeh[3], Mei-Han Wu[2], Chih-Cheng Hsieh[1], Han-Shui Hsu[1], Teh-Ying Chou[3], Yu-Chung Wu[1], Biing-Shiun Huang[1], Wen-Hu Hsu[1] [1]*Division of Thoracic Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei/Taiwan,* [2]*Department of Radiology, Taipei Veterans General Hospital, Taipei/Taiwan,* [3]*Department of Pathology, Taipei Veterans General Hospital, Taipei/Taiwan*

Background: The prognostic roles of the dominate tumor and tumor combination pattern in synchronous multiple primary adenocarcinoma (SMPADCs) remain unclear. **Methods:** The predominant histologic pattern of each tumor among SMPADCs was determined according to the new IASLC/ATS/ERS classification system. For recurrence analysis, each tumor was further divided into low, intermediate and high grade prognostic group. The dominate tumor (DT) was representative of the highest prognostic grade in each SMPADCs. **Results:** From 2004 to 2012, there were 108 consecutive nodal-negative patients who underwent surgery for SMPADCs in a tertiary referral center. The median follow-up time was 52.4 months. During follow-up, 38 (35.2%) patients developed recurrence. The pattern of recurrence included local recurrence only in 8 patients (21.1%), distal metastasis only in 11 (28.9%), and both local recurrence and distal metastasis in 19 (50.0%). In multivariate analysis, the percentage of recurrence was significantly higher in older age (p=0.002; odds ratio 6.324) and DT presented with radiologic solid-appearance (vs. pure- , Mixed-GGNs, p=0.032; odds ratio 7.041). In addition, there was no tumor recurrence identified in 17 DTs presented with radiologic pure GGN and 6 DTs in low grade prognostic group. The 5-year overall and disease-free survival of SMPADCs determined by DT in low, intermittent and high grade were 100%, 84.6%, 32.5% (p<0.001) and 100%, 73.9%, 23.3%, respectively (p<0.001). Compared to low/intermediate grade, DT in high grade had significantly worse overall survival (p=0.007; hazard ratio 4.313) and disease-free survival (p=0.045; hazard ratio 2.360) in multivariate analysis. For further combination pattern analysis, high grade DT combined with high grade 2nd dominate tumor had significantly worse disease-free survival than that combined with intermediate and low grade 2nd dominate tumors.

Conclusion:

Risks analysis of disease-free survival				
Variables	HR	p value	HR	p value
Age	3.212	0.001	2.228	0.026
Gender	1.552	0.182	--	--
Smoking Hx	1.443	0.270	--	--
Preop CEA	1.640	0.217	--	--
Tumor size	2.108	0.024	0.967	0.927
Radiologic appearance	10.814	0.001	3.911	0.086
Pleural invasion	2.069	0.050	0.930	0.869
TNM stage	3.405	0.021	1.334	0.669
Histologic differentiation	4.170	<0.001	1.840	0.118
Angiolymphatic invasion	4.089	<0.001	1.773	0.175
Subtyping predominate	5.399	<0.001	2.360	0.045
Tumor distribution	0.523	0.146	--	--
Same lobe	1.269	0.481	--	--
Adjuvant chemotherapy	1.855	0.072	1.391	0.360
Similar CHS	1.251	0.521	--	--

DT analyzed with prognostic grouping of the IASLC/ATS/RES histological classification was an independent risk factor regarding to overall and disease-free survivals in complete resected nodal-negative SMPADCs.

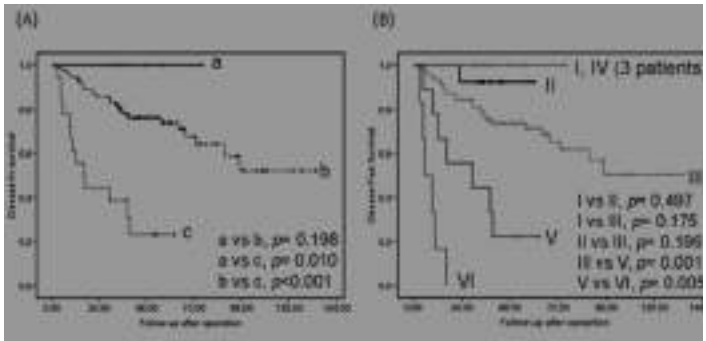

Figure 1 Disease-free survivals of SMPADCs (A) presented as prognc grade of the dominate tumor; a=low; b=intermediate; c= high grade different combinations of prognostic grade of SMPADCs (presente dominate + 2nd dominate tumor); I= low + low grade; II= intermedia low grade; III= intermediate + intermediate grade; IV= high + low gr

Keywords: synchronous primary lung cancers, New lung adenocarcinoma classification, recurrent pattern, dominate tumor

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-010 What Is the Difference between Lung Cancer and Infectious Lung Disease in Predicted Postoperative Pulmonary Function after Pneumonectomy? Takayuki Nakagawa, Kiyomi Shimoda, Miyako Hiramatsu, Tsutomu Yoshida, Yuji Shiraishi *Chest Surgery Division, Respiratory Disease Center, Fukujuji Hospital, Japan Anti-Tuberculosis Association, Tokyo/Japan*

Background: Clinical guideline recommends that spirometry and/or lung perfusion scan be performed for patients undergoing pneumonectomy. Unlike in patients with lung cancer, the affected lungs to be resected have been destroyed due to inflammatory changes in patients with infectious lung diseases. This study was aimed to assess whether there is any difference in predicted postoperative pulmonary function between patients with lung cancer and patients with infectious lung disease. **Methods:** The study was done on 55 patients undergoing pneumonectomy from January 2005 to February 2015, including 22 patients with lung cancer (three right, 19 left) and 33 patients with infectious lung disease (13 right, 20 left). Infectious diseases included 10 pulmonary aspergillosis, 15 multidrug-resistant tuberculosis (MDR-TB), and 8 non-tuberculosis mycobacterial (NTM) infections. In all cases, predicted postoperative pulmonary function was evaluated by spirometry and quantitative lung perfusion scan before operation. We analyzed the differences in patient characteristics and pulmonary function between the two groups, such as percentage of forced expiratory volume in one second (%FEV1), percentage of postoperative FEV1.0 (%ppoFEV1), and estimated postoperative epoFEV1/m2 (epoFEV1/m^2). **Results:** The mean %FEV1 in spirometry was significantly higher in patients with lung cancer than in patients with infectious lung disease (79.5% vs 67.0%; p=0.01). The rate of perfusion to the operative lung was significantly higher in patients with lung cancer than in patients with infectious lung disease (35.8% vs. 19.3%; p<0.01). Consequently, the mean %ppoFEV1 was not significantly different between the two groups (51.8% vs 50.6%; p=0.72). Body surface area of lung cancer patients was larger than that of infectious lung disease patients (1.65m^2 vs 1.50m^2; p<0.01). The mean calculated epoFEV1/m^2 after pneumonectomy in patients with lung cancer and in patients with infectious lung disease were 869ml/m^2 and 993ml/m^2 (p=0.05), respectively. **Conclusion:** Preoperative %FEV1 in patients with lung cancer was higher than that in patients with infectious lung disease. However, %ppoFEV1.0 and epoFEV1/m^2 after pneumonectomy were not different between the two groups. These differences were caused by destructive feature of infectious lung diseases. **Keywords:** lung infectious disease, pneumonectomy, Pulmonary Function, lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-011 The Discordance of Two Major Diagnostic Criteria for Chronic Obstructive Pulmonary Disease Affects Lung Cancer Prognosis after Resection Masaya Yotsukura[1], Takashi Ohtsuka[1], Yasoo Sugiura[1], Yuichiro Hayashi[2], Ikuo Kamiyama[1], Hisao Asamura[1] [1]*Division of Thoracic Surgery, Keio University School of Medicine, Tokyo/Japan,* [2]*Department of Pathology, Keio University Hospital, Tokyo/Japan*

Background: Chronic obstructive pulmonary disease (COPD) has been reported to be associated with the development of lung cancer and poor prognosis after curative surgery for early-stage non-small cell lung cancer (NSCLC). The Global Initiative for Chronic Obstructive Lung Disease defines COPD as a fixed post-bronchodilator ratio of forced expiratory volume in 1 second and forced vital capacity (FEV1/FVC) below 0.7. Age-dependent cut-off values below the lower fifth percentile (LLN) of this ratio derived from the general population have been proposed as an alternative. In patients with obstruction according to the LLN cut-off point but not according to the fixed cut-off point, the prognosis after curative surgery for NSCLC is not known. **Methods:** We enrolled 556 patients with FEV1/FVC ≥0.7 who underwent curative surgical resection for pathological stage I or II NSCLC in our institute between January 2002 and December 2012. The post-surgical prognosis was compared between patients with obstruction (obstructed patients) and without obstruction (non-obstructed patients) according to the LLN cut-off point, using a Cox regression hazards model. **Results:** Of the 556 patients, 42 (7.6%) met the criteria of the LLN cut-off point. The 5-year recurrence-free rate was significantly lower in the obstructed patients (54.4%) than in the non-obstructed patients (77.1%), in univariate analysis (p < 0.01). The 5-year overall survival rate was also significantly lower in the obstructed patients (64.0%) than in the non-obstructed patients (91.1%), in univariate analysis (p < 0.01). Multivariate analysis showed that the obstructed patients had a poor recurrence-free (p = 0.05) and overall survival (p < 0.01) probability. **Conclusion:** Even if COPD is not diagnosed according to the fixed cut-off point, those who meet the criteria of the LLN cut-off point have a poor prognosis after curative surgery for NSCLC. **Keywords:** Early-stage lung cancer, Thoracic Surgery, Chronic obstructive pulmonary disease

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-012 Study for Prognostic Impact of Tumor Volume Instead of Tumor Size for T Staging in NSCLCancer Doosang Kim[1], Jungeun Kim[2], Hyungho Park[2] [1]*Thoracic and Cardio-Vascular Surgery, Veterans Health Service Medical Center, Seoul/Korea,* [2]*Veterans Health Service Medical Center, Seoul/Korea*

Background: Size criteria have been used as a gold standard for a long time in cancer staging of all kinds of solid tumors. However, real tumor mass is usually neither spherical, nor symmetrical in shape. Therefore, single dimension length of tumor does not stand for the tumor volume exactly. We conducted the feasibility test of volume criteria for T staging. **Methods:** From April 1998 to April 2015, 425 lung tumor masses were resected. Among them, 187 masses of completely resected (R0) pT1a,1b,2a,2bN0M0 were enrolled for study. Their survival data were used for comparing log-rank statistics between size-based T(s) stage and volume-based T(v) stage. Tumor volumes were calculated from two-to-three dimension lengths of tumor from biopsy specimen. **Results:** Overall log-rank statistics was p=0.4377 and there was no detectable numerical order for trend among pT1a~pT2b in size-based T(s) stage. However, overall log-rank was p=0.1153 and log-rank for trend was p=0.0241 in volume-based T(v) stage. Cut-off values for volume T stage were selected as V1 (less than 2cc), V2 (more than 2cc and less than 4cc), V3 (more than 4cc and less than 9cc) and V4 (more than 9cc) from log-rank statistics. **Conclusion:**Volume-based T(v) stage shows better discrimination power comparing size-based T(s) stage in T1-2N0 NSCLCa. **Keywords:** T staging, volume staging

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-013 The New Interventional Technique by Photodynamic Therapy Using Composite-Type Optical Fiberscope of 1.0 mm in Diameter Jitsuo Usuda *Thoracic Surgery, Nippon Medical School, Tokyo/Japan*

Background: Ground-glass opacity (GGO) nodules at peripheral parenchyma of the lung noted at thin –section computed tomography (CT) scan have shown to have a histopathologic relationship with atypical adenomatous hyperplasia (AAH)

and adenocarcinoma (AIS) which is newly classified by International Association for the study of Lung Cancer (IASLC). We hypothesize that those early lung cancers in peripheral parenchyma such as AIS, do not need surgical resection may be curred by interventional approach such as Photodynamic therapy (PDT). For peripheral type early lung cancer, it is unable to observe using bronchoscopy nor to treat by PDT. Therefore, we have developed a new minimally invasive laser device using a 1.0 mm in diameter composite-type optical fiberscope (COF), which could transmit laser energy and images for observation in parallel, consisting a laser Doppler blood-flow meter. The use of COF technology was previously used in the field of atomic energy. It enables the acquisition of an image while simultaneously performing laser treatment such as PDT, measuring the blood-flow, estimating the irradiational distance. **Methods:** In this study, we aimed to develop a new endoscopical treatment for peripheral parenchymal cancer by NPe6-PDT and a COF. We administered NPe6, 10mg/kg to pigs and we observed the peripheral parenchyma through the bronchus using COF. One h after the administration of NPe6, we irradiated 664 nm-laser (120 mW, 100J) for normal lesion of the peripheral lung using COF. Seven days after PDT, we extracted lungs and examined pathologically. **Results:** We were able to introduce the 1.0 mm COF into pig peripheral parenchyma of the lungs and observed feasibly and clearly, and then we performed NPe6-PDT safely. We measured the blood-flow at the irradiated area by COF during PDT, and we observed gradually disappearance of the blood-flow. The mean diameter of necrosis in normal peripheral lung caused by NPe6-PDT was 16 mm. **Conclusion:** The 1.0 mm COF was a very useful device of NPe6-PDT for peripheral parenchyma of the lung. In the future, for non-invasive adenocarcinoma such as AIS, NPe6-PDT using COF will become one option of standard treatment and play a important role for the treatment of syncronous or metachronous multiple primary lung cancer lesions. **Keywords:** photodynamic therapy, interventional technique, composite-type optical fiberscope, lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-014 Predictive Factors of Postoperative Acute Exacerbation of Interstitial Pneumonia for Patients with Lung Cancer Haruhiro Yukiue, Hiroshi Niwa, Masayuki Tanahashi, Eriko Suzuki, Naoko Yoshii, Masayuki Shitara, Toshio Fujino *Division of Thoracic Surgery, Respiratory Disease Center, Seirei Mikatahara General Hospital, Hamamatsu, Shizuoka/Japan*

Background: Currently, postoperative acute exacerbation (AE) of idiopathic interstitial pneumonia (IIP) accounts for the most common cause of death after pulmonary resection for lung cancer. Preoperative risk assessment and prevention of postoperative AE is essential for the operative performance improvement. **Methods:** From 2000 through 2013, a total of 1730 patients underwent pulmonary resections for primary lung cancer. One hundred and two patients (5.9%) were diagnosed the lung cancer combined with IIP based on the postoperative pathological findings. Postoperative AE was defined as acute exacerbation within 30 days after the operation. **Results:** Postoperative AE was observed in 9 patients (8.8%), of which 6 patients (66.7%) died of respiratory failure. Although three patients had improved and discharged, two patients of which finally died with re-exacerbation. All of the postoperative AE patients were men having all cases smoking history, and many of them were advanced stage. The AE patients were significantly worse than non-AE patients in following clinicopathological factors. Preoperative serum LDH (248±52IU/l vs 206±45)、CRP (1.6±1.8mg/dl vs 0.9±1.8)、PaO2 (78.1±7.8mmHg vs 84.9±10.5) and %VC (78.9±14.3% vs 94.4±15.1). Moreover, for the postoperative AE patients, the changes of these factors and X-ray or CT findings before operation were analyzed. An exacerbation before operation observed for serum LDH in five patients, CRP in three patients, and increased lung opacity on imaging findings observed in four patients. **Conclusion:** To see the exacerbation of laboratory values (LDH, CRP) and imaging findings (increasing lung opacity) during preoperative time, there is a possibility of selecting high-risk patients of postoperative AE. **Keywords:** Interstitial pneumonia, lung cancer, acute exacerbation

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-015 Pathological Variables in Resected NSCLC Tumours: Predictors of Survival? Matthew Evison, Stuart Britton, Haider Al-Najjar, Rajesh Shah, Philip Crosbie, Richard Booton *Manchester Thoracic Oncology Centre, University Hospital of South Manchester, Manchester/United Kingdom*

Background: Lung cancer recurrence following treatment with radical intent remains a significant problem for thoracic oncology specialists. Identifying novel predictors of recurrence may inform future management strategies including indications for adjuvant chemotherapy and the intensity of surveillance programs. This study used survival analysis, as a surrogate marker of disease recurrence, to assess if pathological variables in resected NSCLC could predict survival. **Methods:** We retrospectively reviewed all pathological reports for patients undergoing surgical resection for NSCLC at the University Hospital South Manchester from 01/01/2011 to 31/12/2013. The following variables were analysed in univariate and multivariate (cox regression) analysis: extra-capsular nodal disease, lymphovascular invasion, pleural invasion (PL0-3), residual disease (R0 vs R1), grade of differentiation, pT-stage and pN-stage. Survival was provided by national death registry data. **Results:** Extra-capsular nodal disease (p=<0.001, Figure 1), Lymphovascular invasion (p=<0.001), pleural invasion (PL3, p=<0.001), residual disease (R1, p=<0.001), pT-stage (pT4, pT3, pT2b, p=<0.001) and pN-stage (pN2, p<0.001) were all associated with significantly lower survival on univariate analysis. A multivariate cox regrerssion model was run with all significant univariate variables. The least significant variable was removed and this was repeated until only those significant at the 0.05 level remained (Table 1).

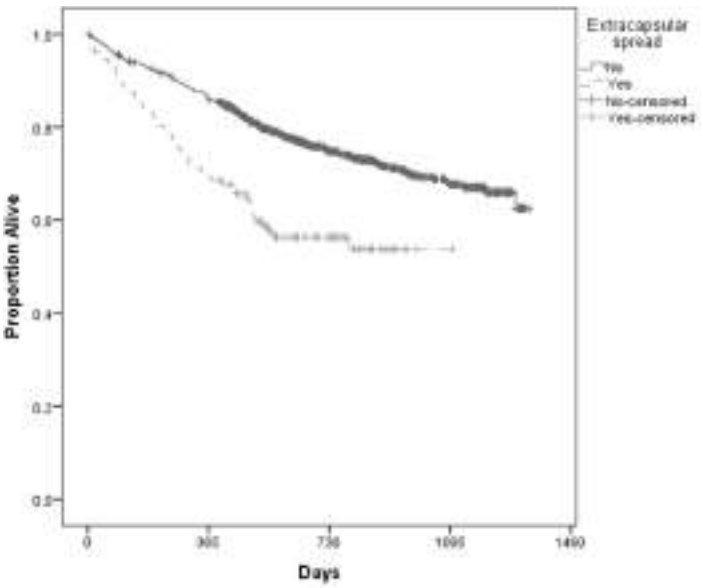

Table 1

Variables	Hazard ratio (95% CI)	p-value	
Extracapsular spread	Yes vs no	1.47 (1.00, 2.17)	0.049
Pleural invasion	PL1 vs PL0	1.37 (0.97, 1.93)	0.002
PL2 vs PL0	1.08 (0.63, 1.85)		
PL3 vs PL0	2.42 (1.53, 3.83)		
T stage	1b vs 1a	1.04 (0.61, 1.79)	0.006
2a vs 1a	1.30 (0.81, 2.08)		
2b vs 1a	1.63 (0.95, 2.81)		
3 vs 1a	2.17 (1.28, 3.66)		
4 vs 1a	2.99 (1.46, 6.11)		
N stage	N1 vs N0	1.30 (0.91, 1.87)	0.005
N2 vs N0	1.80 (1.26, 2.58)		

Conclusion: Pathological T-stage and N-stage are well established predictors of prognosis and inform decisions around adjuvant chemotherapy. Extra-capsular nodal disease and pleural invasion (PL3) are additional independent predictors of survival. The presence of these pathological findings in resected NSCLC may help in the decision making around adjuvant therapy, the appropriate intensity of surveillance programs and the design or stratification of adjuvant therapy trials. **Keywords:** Adjuvant chemotherapy NSCLC, NSCLC surgery, NSCLC recurrence, NSCLC survival

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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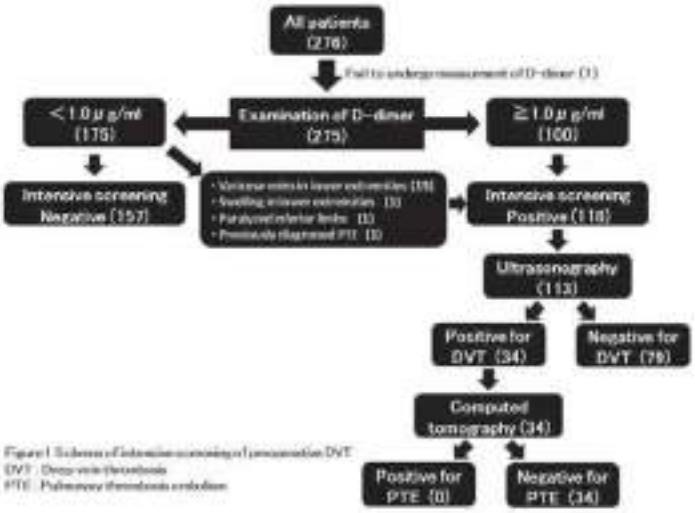
P1.02-016 Prevalence of Preoperative DVT in Japanese Patients Who Underwent Thoracic Surgery by Intensive Screeng Toshiki Takemoto, Yuichi Sesumi, Yoshihisa Kobayashi, Katsuaki Sato, Masato Chiba, Masaki Shimoji, Kenichi Suda, Kenji Tomizawa, Masahiro Sakaguchi, Tetsuya Mitsudomi *Division of Thoracic Surgery, Department of Surgery, Kinki University Faculty of Medicine, Osaka-Sayama/Japan*

Background: Pulmonary thromboembolism (PTE) is a well-recognized potentially fatal complication after thoracic surgery. In Japan, PTE had been relatively uncommon. However, it has recently been increasing probably due to changes in lifestyle. Therefore the first guideline for the prevention of venous thromboembolism (VTE) were published in February 2004 in Japan. In this guideline, the patients with history of VTE are classified as highest risk group for PTE. Recently, it has been reported that the presence of normal D-dimer levels can exclude acute-phase deep vein thrombosis (DVT). Therefore, in our institution, DVT had been intensively screened by measuring preoperative D-dimer. The objective of this study was to investigate prevalence of preoperative DVT in Japanese patients scheduled for thoracic surgery. **Methods:** A total of 276 patients who underwent thoracic surgery from June 2013 through July 2014 in our institution were reviewed. The patients who were deemed high-risk for DVT (those with elevated preoperative D-dimer (≧1.0μg/ml), with past history of thrombosis, or with varicose veins in their lower extremities) were defined as preoperative screening positive. They were examined with venous ultrasonography of lower extremities. Those with DVT underwent contrast-

enhanced computed tomographic scan (CT) for PTE. **Results:** Of all patients, only 1 failed to undergo preoperative measurement of D-dimer because of emergency surgery. Among the remaining 275 patients, a total of 113 patients (95 with elevated D-dimer, 15 with varicose veins in their lower extremities, one with swelling in his extremities, one with paralyzed inferior limbs, and one with previously diagnosed PTE) were examined with venous ultrasonography of lower extremities. Of them, 34 patients (12.6%) were diagnosed DVT (Figure 1) Proximal and distal DVT were diagnosed in ten patients (three with isolated DVT, three with multiple DVT, and four with a wide range of huge clots) and 24 patients (15 with isolated DVT and nine with multiple DVT) , respectively. Of them, none was diagnosed preoperative PTE. For a peri-operative management, all the patients received unfractionated heparin. In addition, of four patients with a wide range of huge clots, three had prophylactic inferior vena cava filter placed. Of 34 patients, one was diagnosed asymptomatic exacerbation of DVT by ultrasonography one week after surgery, but none developed symptomatic PTE.



Conclusion: This study showed an DVT prevalence of 12.6% in patients undergoing thoracic surgery in Japan. However, none developed symptomatic PTE in the peri-operative period.
Keywords: deep vein thrombosis, Thoracic Surgery

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-017 Complications after Lobectomy or Segmentectomy for cT1aN0M0 Non-Small Cell Lung Cancer Takashi Ohtsuka, Yasoo Sugiura, Ikuo Kamiyama, Hisao Asamura *Department of Surgery, Division of Thoracic Surgery, Keio University, Tokyo/Japan*

Background: Although lobectomy is considered the standard surgical approach for clinical T1aN0M0 non-small cell lung cancer (NSCLC), several recent studies have shown segmentectomy could be a substitute for lobectomy for early stage NSCLC. However, the differences of perioperative complications between lobectomy and segmentectomy have not yet been fully evaluated. The aim of this study is to investigate the postoperative complications which occurred after lobectomy or segmentectomy using propensity-matched analysis. **Methods:** Between February 2006 and February 2013, 100 patients underwent lobectomy and 111 patients underwent segmentectomy for clinical T1aN0M0 NSCLC. A retrospective comparison with each group was performed in perioperative mortality, morbidity, operative time, blood loss, length of hospital stay, chest tube duration and clinical parameters including age, gender, preoperative forced expiratory volume in 1 second percentage predicted (preop FEV1%), and Charlson Comorbidity Index (CCI). Data was analyzed for all patients and their propensity score matched pairs. **Results:** The rate of postoperative complications in the segmentectomy group (n = 21, 19%) was significantly higher than that in the lobectomy group (n = 7, 7%) ($p < 0.01$). The majority of complications were prolonged air leak. There was no significant difference in postoperative length of hopital stay and chest tube duration.The average operative time of 263 ± 64 minutes and estimated blood loss of 133 ± 125 ml for segmentectomy were significantly more than those of lobectomy (201 ± 61 minutes and 88 ± 101ml, respectively). In propensity score matched analysis (61 patients each), the average operative time of 270 ± 70 minutes for segmentectomy was longer than that of lobectomy (202 ± 67 minutes). Postoperative complications were more frequent in the segmentectomy group than those in lobectomy group (19.6% and 6.5%, $p = 0.03$). **Conclusion:** Although segmentectomy could offer preservation of pulmonary function, significantly more postoperative complications occurred in the segmentectomy group compared with lobectomy group. The majority of complications were prolonged air leaks in all patients and propensity matched pairs. The operation time was also longer in the segmentectomy group. Surgeons should bear in mind that complications can happen more frequently after segmentectomy than after lobectomy for cT1aN0M0 NSCLC.
Keywords: lung segmentectomy, complications, surgery

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-018 Needlescopic Lobectomy and Segmentectomy for Primary Lung Cancer: Less Invasive Surgery Using Fine Scope and Forceps Michihiko Tajiri, Hiromasa Arai, Kohei Ando *General Thoracic Surgery, Kanagawa Cardiovascular and Respiratory Center, Yokohama/Japan*

Background: If we can maintain a satisfactory technical level, safeness and prognosis equal to conventional surgery, a less invasive procedure will bring more benefits to patients. We have performed thoracoscopic anatomical lobectomy and segmentectomy for primary lung cancer for twenty years. At first we used and slid 10mm-diameter scope and forceps through three or four ports. Later we changed to 5mm-diameter scope and forceps, and presently we start performing the needlescopic surgery (1 port+3 punctures method) using a 3mm-diameter scope and forceps, which we have used since September 2012. Now we would like to explain this operative procedure and effectiveness. **Methods: 【Patients】** One hundred and eleven patients underwent the needlescopic anatomical lobectomy and segmentectomy of the lung between September 2012 to March 2015. They had clinical stage IA or IB lung cancer. We compared the operation time, blood loss volume, post-operative creatinine phosphokinase (CK) and other peri-operative parameters of this method with those of the conventional method using a 5mm-diameter scope which were performed on 73 patients from January 2012 to August 2012. **【Operative procedure】 1.** We make a 2 to 3 cm length skin incision on the 4th or 6th intercostal space of the chest trunk and set the polyurethane-made retractor. We use it as the main port. **2.** We puncture the skin with three 3mm-diameter trocars. Then we insert and slide a 3mm-diameter scope and forceps through them. We observe thoracic lumen and perform various manipulations using them. **3.** Endostaplers, energy devices and electric cautery of which diameters are larger than 3mm go into the thoracic lumen through the main port. **4.** Finally we remove specimens and set the chest tube within the main port incision at the end of surgery. **Results:** We performed 15 segmentectomies and 96 lobectomies of the lung using this method for the lung cancer. We dissected mediastinal nodes in all cases. We had one case that was converted to the conventional method, and one case that was converted to the open method. However we elongated the incision of one puncture from 3 mm to 10 mm in four cases in order to insert endostaplers for dissecting pulmonary veins and arteries. Mean operation time was 220±63 minutes. It was not significantly different from that of the conventional method. Mean blood loss volume was 16.6±22.3 ml. It was significantly less than that of the conventional method. Post-operative peak titers of CK and CRP of this method were significantly lower than that of the conventional method. We had no severe intraoperative accidents or postoperative complications. All patients were smoothly discharged. **Conclusion:** This one plus three method is less invasive than a conventional procedure. We were able to successfully perform the needlescopic lobectomy and segmentectomy for lung cancer as well as conventional thoracoscopic surgery. This method would be the optimal and optional method if and when we appropriately select cases.
Keywords: lung cancer, Surgery, Thoracoscopy, Needlescope

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-019 Effectiveness of Touch Cytology on the Staple Line in the Assessment of Resection Margins for Pulmonary Malignant Tumors Rie Nakahara[1], Ikuma Wakamatsu[1], Seiji Igarashi[2], Haruhisa Matsuguma[1] [1]*Division of Thoracic Surgery, Tochigi Cancer Center, Utsunomiya, Tochigi/Japan,* [2]*Division of Pathology, Tochigi Cancer Center, Utsunomiya, Tochigi/Japan*

Background: Assessing the presence of cancer cells in resected margins following partial or segmental resection of malignant lung tumors is an important step when planning complete resection. When the tumor is deemed proximal to the resection margin, the policy at our hospital is to swiftly conduct touch cytology on the staple line of the resected tissue sample and, when positive, to perform additional resection. In the present study, we evaluated whether or not this strategy is appropriate. **Methods:** From among 161 patients who had a partial or segmental lung resection at our hospital between April 2009 and December 2013, forty-two patients who underwent touch cytology of resection margins were evaluated. Variables investigated were cytodiagnostic findings, tumor size and distance from margin, and subsequent occurrence of local relapse. **Results:** Resection of lung metastasis was performed on 16 of the 42 patients, intentional limited resection for primary lung carcinoma was performed in 13 patients, and conservative limited resection was performed on 13 patients due to issues with their respiratory function and systemic condition. Two patients tested positive on cytodiagnosis of the resected margin; hence, the surgical procedure was modified from partial to segmental resection and from lung lobe and partial resection to resection of both lobes, respectively. Moreover, both of these patients underwent conservative procedures, and both tumors were adenocarcinoma. Mean tumor size (mm) in the metastasis group, intentional limited resection group and conservative limited resection group was 14 mm, 15 mm and 24 mm respectively, and distance to resection margin was 9.3 mm, 11.2 mm and 8.6 mm respectively. None of the 42 patients, including the 2 patients who tested positive, exhibited subsequent local relapse. **Conclusion:** Both the patients who tested positive on cytodiagnosis belonged to the conservative limited resection group and tended to have a larger tumor size than patients in the other groups. Inadequate distance from the resected margin with respect to tumor size increases the risk of a positive result at the resected margin. Of the 42 patients in the present study who underwent touch cytology of resected margins, none experienced subsequent local relapse, which implies the appropriateness of our evaluation method.
Keywords: touch cytology, limited resection, assessment of resection margins

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-020 Physiological Assessment in Thoracic Surgery for High Risk Patients with Lung Cancer; How Do International Guidelines Compare? Haider Al-Najjar, Matthew Evison, Nigel Clayton, Stuart Britton, Rajesh Shah, Philip Crosbie, Richard Booton *Manchester Thoracic Oncology Centre, University Hospital of South Manchester, Manchester/United Kingdom*

Background: Surgical resection is the best curative option in patients with appropriately staged lung cancer. Physiological assessment is vital in selecting patients for surgical resection with particular attention to risk of mortality and morbidity with the planned surgery. This is most crucial in patients deemed high-risk. Physiological parameters employed include spirometry (FEV1%), diffusion (DLCO%), Shuttle walks, Cardiopulmonary Exercise Testing (VO2Max absolute value and %) as well as post-operative predicted values for all of these tests using segment counting to discriminate depending on the planned surgery. However, three major international guidelines exist which advocate different approaches to assessing this patient group (BTS, ERS, ACCP). We aim to assess how these guidelines compare to one another and our local practice in informing decision-making. **Methods:** Patients with operable thoracic malignancy who were candidates for surgery and had CPET were eligible for inclusion. We retrospectively analysed all patients who underwent CPET at the University Hospital of South Manchester, a tertiary Thoracic Oncology Centre, between 01/01/2013 and 31/12/2013. Physiology reports, clinical correspondence and survival databases were analysed. **Results:** 96 patients fulfilled the inclusion criteria. 3 were excluded due to no available pulmonary function data. A further 17 were excluded as they were denied surgery for non-physiology reasons (patient declined surgery, metastatic disease discovered before, small cell histology, adequate resection margin impossible, severe comorbidities). The remaining 74 patients were included in the final analysis. 62/74(84%) underwent surgery (12 pneumonectomy, 3 bilobectomy, 33 lobectomy, 4 segmentectomy, 6 wedge resection, 4 futile thoracotomy due to finding unexpected advanced disease) The overall breakdown of risk classification of patients using the 3 guidelines was as follows. BTS: low-risk 27/74 (36%), medium-risk 31/74 (42%), high-risk 16/74 (22%). ACCP: low-risk 19/74 (26%), medium-risk 52/74 (70%), high-risk 3/74 (4%). ERS: low-risk 47/74 (63%), medium-risk 16/74 (22%), high-risk 11/74 (15%). Of the patients BTS guidelines classed high-risk, we operated on 8/16 (1 pneumonectomy, 3 lobectomy, 1 segmentectomy, 2 wedge resection, 1 futile thoracotomy) with 100% survival at 90 days. We did not operate on any of the 3 patients classed high-risk by ACCP guidelines. Of the patients ERS guidelines classed high-risk, we operated on 5/11 (1 pneumonectomy, 1 bilobectomy, 2 lobectomy, 1 segmentectomy) with 100% survival at 90 days. Of those classed high-risk by ACCP 2/3 would be high-risk by BTS guidelines and of those classed high risk by BTS 2/16 would be high-risk by ACCP guidelines. Of those classed high-risk by ERS 8/11 would be high-risk by BTS guidelines and of those classed high-risk by BTS 2/16 would be high-risk by ERS guidelines. **Conclusion:** From our results a lack of concordance between the three guidelines in classification of high-risk is evident. Also, with the exception of the ACCP guidelines, our local practice has shown that patients deemed high-risk for surgery were operated on (upto and including pneumonectomy) with no cases of 90-day mortality. With this in mind an appraisal of current guidelines is indicated as well as a more consistent approach worldwide to ensure that no potentially fit patients are excluded from surgical resection of lung cancer. **Keywords:** Pulmonary function tests, Thoracic Surgery, Respiratory Physiology, Cardiopulmonary Exercise Test

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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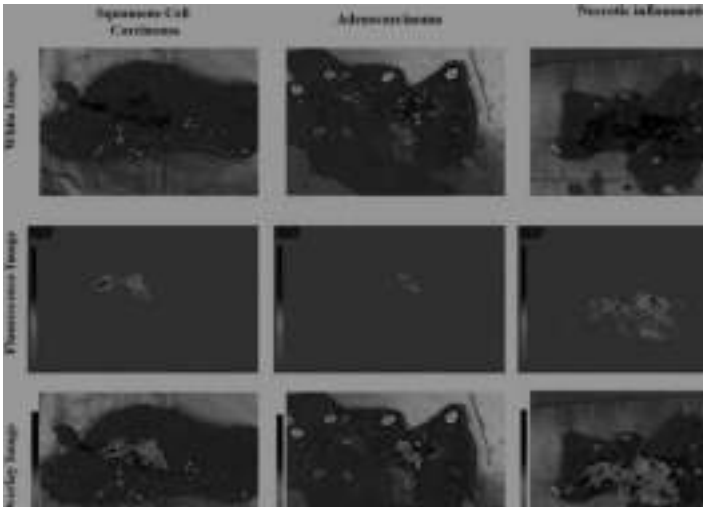
P1.02-021 The Feasibility of Fluorescence Image-Guided Surgery for Pulmonary Nodules Hyun Koo Kim[1], Yu Hua Quan[2], Byeong Hyun Choi[2], Kook Nam Han[2], Young Ho Choi[2] [1]*Thoracic and Cardiovascular Surgery, Korea University Guro Hospital, Seoul/Korea,* [2]*Korea University Guro Hospital, Seoul/Korea*

Background: Recently, fluorescence imaging using indocyanine green (ICG) has been applied to cancer, not only to visualize the sentinel lymph node, but also to identify mass during surgery. We hypothesized that this fluorescence imaging will also be useful to identify and locate pulmonary nodules during surgery. We try to detect pulmonary nodules and measure fluorescence intensity by using reasonable dosage of ICG. **Methods:** We enrolled 11 patients who were diagnosed with a pulmonary nodule. ICG is administered intravenously at a dose of 1 mg/kg prior to operation. Surgical specimens were investigated using a near-infrared light camera system (SPY Elite) at 20 hours after injection. And we examined the histologic characteristics of the specimens.

Results:



ICG-fluorescent imaging was observed 10 out of the 11 patient. 1 squamous cell carcinoma was not detected fluorescent. 2 false – positive nodules (necrotic inflammation) were identified among the 10 fluorescent specimens. Fluorescence signal of nodules (Signal to Background Ratio (SBR)) was 4.3 ± 2.5. There was no significant difference depending on histology, size and tumor grade. However, Fluorescence signal of 2 false – positive nodules was 9.5 ± 0.7 was higher than nodules. **Conclusion:** This study demonstrated that fluorescence imaging using a low dosage of ICG can be useful to identify and locate pulmonary nodules during surgery. However, our results (2 false positive) also show limitation of present fluorescence image guide surgery which used only ICG for passive cancer targeting. Base on this result, we thought that for ideal fluorescence guided surgery, we will need a further study about active targeting by using biomarker as well as passive targeting. We hope that this data will give us some clue to develop fluorescence guided surgery technique in lung cancer surgery. **Keywords:** Fluorescence, Indocyanine green, pulmonary nodule

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-022 Sleeve Lobectomy Is a Safe and Effective Oncologic Procedure: A Single Center Experience over Three Decades Luis Carlos Silva Corten[1], Johnny Moons[1], James Villeneuve[2], Alessia Stanzi[1], Lieven Depypere[1], Hans Van Veer[1], Philippe Nafteux[1], Willy Coosemans[1], Herbert Decaluwé[1], Dirk Van Raemdonck[1], Paul De Leyn[1] [1]*Thoracic Surgery, University Hospitals Leuven, Leuven/Belgium,* [2]*Thoracic Surgery, Ottawa General Hospital, Ottawa/ON/Canada*

Background: Sleeve lobectomy is a parenchyma-sparing technique suitable for treating central tumors, avoiding pneumonectomy. The aim of this study was to assess perioperative and long-term survival outcomes in patients treated by sleeve lobectomy. **Methods:** Data were analysed from a prospectively collected database. All consecutive cases of sleeve lobectomy/bilobectomy (1985 - 2013) were included. Cox-Regression was used to analyse survival outcomes. There were 300 patients available for analysis. Sleeve lobectomy was performed in 272 patients (RUL:153; RML:5; RLL:1; LUL:83; LLL:30), sleeve bilobectomy in 28 (RUM:17; RLM:11). In most patients a sleeve of the bronchus (n=219) or a reversed sleeve of the bronchus (n=19) was performed. Arterial (n=35) or combined arterial and bronchial sleeve (n=27) resections were less common. The most common operative indication was non-small cell lung cancer (254 cases, 85%), less commonly for carcinoid (n=27), small cell lung cancer (n=6) , pulmonary metastasis (n=9) and 4 others. **Results:** Patients were predominantly male (85%) with a mean age of 62.7 years (range 20.1-84.6). Postoperative course was uneventful (Dindo-grade 0/1) in 60%; with minor complications (Dindo-grade 2/3a) in 30% and major complications (Dindo-grade 3b/4) in 7.3%. In hospital mortality (Dindo-grade 5) was 2.7%. Overall median survival was 68 months, with a 5- and 10-year survival of 52.3% and 35.8%. A Cox-Regression model showed five independent prognosticators for survival: asymptomatic at presentation, age, pT, pN and neoadjuvant treatment (see table). Although neoadjuvant treatment showed to be a negative prognosticator for survival, complete responders (n=8 or 14.5% of neoadjuvant treated patients) showed a mean survival of 132 months and a 5-year survival of 80%.

Variables in the Equation

	B	SE	df	Sig.	Exp(B)	95,0% CI for Exp(B) Lower	Upper
pT (ref = pT0)			4	<0,0001			
pT2a	1,24	0,76	1	0,092	3,47	0,82	14,72
pT2b	1,01	0,78	1	0,197	2,75	0,59	12,76
pT3	2,38	0,75	1	0,001	10,80	2,50	46,74
pT4	2,05	1,03	1	0,046	7,77	1,04	58,26
pN (ref = pN0)			2	<0,0001			
pN1	0,61	0,21	1	0,004	1,83	1,22	2,75
pN2	1,16	0,30	1	<0,0001	3,20	1,79	5,74
Asymptomatic	-0,54	0,23	1	0,017	0,58	0,37	0,91
Age	0,07	0,01	1	<0,0001	1,07	1,05	1,10
Neoadjuvant R/ (ref = no)			2	0,001			
Chemotherapy	0,79	0,26	1	0,003	2,20	1,32	3,68
Chemoradiation	1,28	0,53	1	0,016	3,61	1,27	10,26

Variables not in the Equation

	Score	df	Sig.
Previous malignancies	1,263	1	0,871
Active Smoking	1,91	1	0,167
ppoFEV1	1,329	1	0,249
ppoDLCO	1,724	1	0,189

Conclusion: Sleeve lobectomy can be safely performed as treatment for centrally-located lung tumours. A single-institution experience over 3 decades demonstrates acceptable morbidity and mortality rates. Overall survival seems to be mainly determined by oncologic variables (TNM-staging factors). **Keywords:** sleeve lobectomy, broncho-plastic resection, long term, lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-023 The Role of Selective EBUS-TBNA Mediastinal Sampling in Early Lung Cancer Rajaram Burrah[1], Phillip Antippa[1], Daniel P. Steinfort[2], Louis B. Irving[2] [1]*Cardiothoracic Surgery, Royal Melbourne Hospital, Melbourne/ACT/Australia,* [2]*Respiratory Medicine, Royal Melbourne Hospital, Melbourne/ACT/Australia*

Background: Accurate pre-operative staging of the mediastinum in lung cancer is essential to determine the type of treatment. The commonly used investigations are CT scan, PET scan, EBUS-TBNA (Endobronchial ultrasound-guided transbronchial needle aspiration) and mediastinoscopy, and often these tests complement each other to increase the accuracy of staging. With advances in technology and increased experience, EBUS has the potential to replace mediastinoscopy to stage the mediastinum. Surgical mediastinal dissection, though commonly performed, has not been convincingly proven to have a therapeutic value. We postulate that if the mediastinum can be staged accurately with EBUS-TBNA (a low morbid procedure) then a surgical staging of the mediastinum (mediastinoscopy and / or dissection) can be avoided and therefore, avoid the morbidity associated with these procedures. We have studied the use of selective EBUS-TBNA which is sampling abnormal nodes on imaging (CT, PET scan) and compared it with the mediastinal dissection done surgically. **Methods:** This is a retrospective study of patients who underwent surgery (lobectomy/ pneumonectomy + mediastinal lymphnode dissection) for early stage lung cancer (stage I/II).Patients who had negative N2 lymph nodes on EBUS-TBNA evaluation were included in the study. All patients had CT and PET scans which assisted the EBUS study. The results of EBUS-TBNA were compared with that of the surgical mediastinal lymph node dissection. **Results:** A total of 86 patients were included in the study. EBUS-TBNA correctly staged the mediastinum in 78 patients (90.7%, negative predictive value (NPV) = 0.90). Eight patients had false negative (FN) evaluation by EBUS-TBNA. On review, two of these patients had a sampling error. Three patients had incomplete evaluation of the mediastinum. All these 3 patients had left lung cancer whose level 5 lymph nodes could not be sampled, and surgical sampling displayed these nodes to be involved with extracapsular spread. There were three other patients with FN results, and they had mediastinal nodes biopsied by EBUS which with surgical removal showed metastasis. Two of these patients had metastatic deposits < 3mm in size. We feel that diligent and systematic EBUS would have avoided the FN result in most of the above patients except for sampling of level 5 nodes which may not be technically accessible by EBUS. The NPV for right lung cancers, especially right upper lobe (NPV=0.96) was higher as compared to left sided cancers. **Conclusion:** This study shows that selective EBUS-TBNA mediastinal staging in early lung cancer is feasible, has an acceptable NPV and provides evidence to facilitate studies on systematic EBUS. This study draws attention thorough the identified 8 FNs to the real and potentially avoidable limitations of selective EBUS mediastinal lymphnode sampling. The accuracy of systematic EBUS evaluation should be superior to a selective study and can therefore potentially avoid a surgical staging of the mediastinum and its associated complications. **Keywords:** Staging, EBUS, lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-024 Conditional Survival after Surgical Treatment of Non-Small Cell Lung Cancer Takayuki Fukui, Toshiki Okasaka, Koji Kawaguchi, Koichi Fukumoto, Shota Nakamura, Kohei Yokoi *Thoracic Surgery, Nagoya University, Nagoya/Japan*

Background: Conditional survival (CS) is an estimate of survival probability for patients who have already survived at least 1 year after diagnosis or treatment. This study was intended to find some useful informations in postoperative follow-up plan by CS analyses of resected non-small lung cancer patients. **Methods:** We retrospectively analyzed data on the clinicopathological features and survival outcomes of 925 patients with non-small cell lung cancer who had undergone complete resection at Nagoya University Hospital between 2005 and 2012. CS is the probability of surviving additional time (y) after already surviving time (x), and can be calculated from the following formula: CS(y|x) = S(x+y)/S(x), where S(t) is the overall survival at time (t). In this study, two methods of CS analyses were performed. Briefly, CS(5|x), which meant 5-year conditional survival (5Y-CS(x)), and CS(5-x|x), which was the probability of surviving when five years has passed from surgery (CS5(x)), were calculated in the various setting or subgroups. **Results:** The cohort consisted of 624 males and 301 females, ranging in age 26 to 89. The 5-year overall survival rate of all patients was 76%. 5Y-CS(1,2,3,4) was 74, 76, 77, 80%, respecively, showing gradually improvement. This meant that the given treatment for NSCLC including surgery contributed the survival of the patients to some degree. However, the 5Y-CS did not approach 100%, which indicated a certain number of patients coninued to die during the follow-up period. The CS5(1, 2, 3, 4) in all patients were 79%, 84%, 90% and 96%, respectively, which meant the 90% of patients who were alive at 3 years after surgery would survive for next 2 years. The patients with younger female (≤ 70 years), no or light smoker, adenocarcinoma histology, pathologocal stage I and normal serum carcinoembryonal antigen level showed the CS5(3) higher than 90%. Both CS5(3) and 5Y-CS(3) of the patients with all the six favorable factors reached 98%. **Conclusion:** Postoperative follow-up visit after 3 years from surgery might be minimum for the patients with younger female, no or light smoker, adenocarcinoma histology, pathological stage I, and normal serum carcinoembryonic antigen level. **Keywords:** conditional survival, non-small cell lung cancer, postoperative follow-up

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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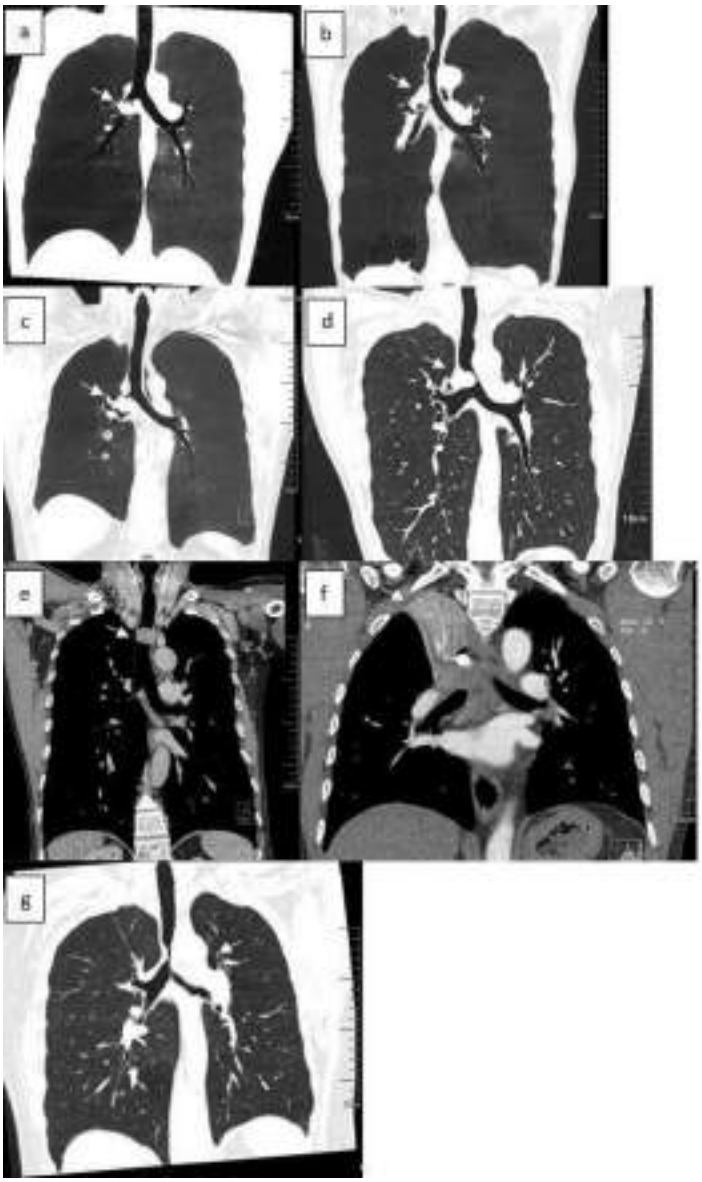
P1.02-025 Complete VATS Resection and Reconstruction of Carina and Trachea for Malignant or Benign Disease Jianxing He, Jingpei Li, Hanzhang Chen, Weiqiang Yin, Jun Liu, Xin Xu, Xin Zhang, Wei Wang *Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China, Guangzhou/China*

Background: General thoracic surgery involving carinal and/or tracheal reconstruction is technically demanding. The aim of this study is to discuss the feasibility of complete video assisted thoracoscopic surgery (VATS) in the surgical treatment of disease involving the carina and/or trachea. **Methods:** Between May 2012 and April 2015, seven cases of malignant or benign disease involving carina and/or trachea were treated via complete VATS resection and reconstruction of carina and trachea in our hospital. Among the seven patients (median age, 47 years; range, 43-60 years), two patients suffered from a malignant tracheal tumor, one from a main bronchial malignant tumor invading the carina, two from right upper lobe malignant tumor invading the carina, and two from benign bronchial stenosis due to endobronchial tuberculosis. A prospective analysis of clinical characteristics, operative data, and postoperative events was performed.



Results: There were five different types of VATS airway reconstruction in our group, including left main bronchus resection and carinal reconstruction, right main bronchus resection and carinal reconstruction, right upper lobectomy and carinal reconstruction, right upper lobectomy and half carinal reconstruction, and tracheal resection and reconstruction. Median data of surgical outcome are as follows: operative time-200 minutes (range, 50-300 minutes); time of airway reconstruction-50 minutes (range, 19-130 minutes); blood loss-100 mL (range, 30-1000 mL). One patient suffered from endobronchial tuberculosis; during the thoracic procedure we observed complete pleural adhesions which led to large volume of blood loss during pleuropneumonolysis. No conversions to thoracotomy were performed. There was no 30-day mortality. Median data of perioperative outcomes are as follows: postoperative hospital stay-12 days (range, 7-15 days); ICU stay -1 day (range, 0-6 days) and duration of thoracic drainage- 2 days (range, 1-5 days). No patient required postoperative mechanical ventilation. One patient had to be assisted with bronchoscopy as a result of insufficient sputum excretion. Median duration of follow-up was 6 months (range, 0-37 months). Minor anastomotic stenosis(less than 1/4 diameter) was found in two patients during follow-up, but no complaints of significant impact on activity were noted. **Conclusion:** Complete VATS for carina and trachea resection and reconstruction is a technically challenging, but feasible procedure for both benign and malignant disease and should be restricted to skilled VATS surgeons. **Keywords:** VATS, carinal reconstruction, trachea reconstruction

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-026 For NSCLC with T3 (Central) Disease, Sleeve Lobectomy or Pneumonectomy? Qianli Ma, Deruo Liu, Yongqing Guo *Thoracic Surgery, China-Japan Friendship Hospital, Beijing/China*

Background: Pneumonectomy has traditionally been the treatment of choice for central lung tumors for which the alternative is sleeve lobectomy. The aim of this study was to compare early and long-term results after sleeve lobectomy and pneumonectomy in focusing on T3 central non-small cell lung cancer (NSCLC). **Methods:** Patients who underwent sleeve lobectomy (n = 58) or pneumonectomy (n = 42) were retrospectively analyzed. For bias reduction, these 100 patients had been selected according to the following criteria: (1) tumor located in the main bronchus less than 2 cm distal to the carina, (2) there was no N2 disease, (3) no induction therapy was applied, (4) a complete resection was achieved. **Results:** Sleeve lobectomy and pneumonectomy patients have had comparable mean ages, gender distribution, mean forced expiratory volume in 1 second, stage and tumor grade. Postoperative mortality (3.4% vs 4.8%, $p = 1.0$) and morbidity (41% vs 38%, $p = 0.74$) were similar between the two groups. Recurrences occurred in 48% of patients after sleeve lobectomy and in 31% of those after pneumonectomy ($p = 0.08$). The 5-year survival after sleeve lobectomy (64.8%) and pneumonectomy (61.4%) was not significantly different ($p = 0.20$). Multivariable survival analysis showed that there were no independent prognostic factors. **Conclusion:** Sleeve lobectomy does not compromise survival for NSCLC with T3 central disease compared with pneumonectomy. It is an adequate oncologic resection and should be treated as the first line intervention whenever complete resection can be achieved. **Keywords:** sleeve lobectomy, pneumonectomy, lung neoplasm

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-027 Thoracoscopic Segmentectomy of Pulmonary Nodules after Computed Tomography-Assisted Bronchoscopic Metallic Coil Marking Takanori Miyoshi, Masayuki Sumitomo, Mariko Aoyama, Naoki Hino *Department of Thoracic Surgery, Tokushima Municipal Hospital, Tokushima City/Japan*

Background: With advances in computed tomography (CT), small pulmonary lesions previously unseen on chest radiographs are being increasingly detected. Among lesions less than 10 mm in size, a considerable number of malignancies have been reported. To localize small and deeply situated pulmonary nodules during thoracoscopy with roentgenographic fluoroscopy, we developed a marking procedure that uses a metallic coil and a coin for thoracoscopic segmentectomy. **Methods:**Thirteen patients underwent video-assisted thoracoscopic surgery for removal of 14 pulmonary lesions. Fluoroscopy-assisted thoracoscopic surgery after CT-assisted bronchoscopic metallic coil marking was performed using an ultrathin bronchoscope under fluoroscopy viewing a coin on a patient's chest wall. The coin was simulated a pulmonary lesion by the CT findings, and it was put on the patient's chest wall. During thoracoscopy, a C-arm-shaped roentgenographic fluoroscope was used to detect the radiopaque nodules. The nodule with coil markings was grasped with forceps and resected in segmentectomy under fluoroscopic and thoracoscopic guidance. **Results:** The marking procedure took 10 to 50 minutes from insertion to removal of the bronchoscope. There were no complications from the marking, and all 14 nodules were easily localized by means of thoracoscopy. The metallic coil showed the nodules on the fluoroscopic monitor, which aided in nodule manipulation. Nodules were completely resected under thoracoscopic guidance in segmentectomy. The pathologic diagnosis was primary adenocarcinoma in 7 patients, a primary adenosquamous carcinoma in 1 patient, pulmonary metastases in 3 patients, an atypical adenomatous hyperplasia in 1 patient, a hamartoma in 1 patient and a nontuberculous mycobacteriosis in 1 patient. One case of a bronchiolo-alveolar adenocarcinoma with an extensive two segments was performed a curative segmentectomy. **Conclusion:** In this study, CT-guided transbronchial metallic coil marking with an ultrathin bronchoscope with a coin on a patient's chest wall after CT-assisted stimulation was found to be feasible and safe. In our previous report, CT had been needed at least three times, but this method needed only twice CT scan. It might be a useful method not only for making a diagnosis but also for therapeutic resection in selected early lung cancers. **Keywords:** VATS, coil marking, CT assisted bronchoscopy, segmentectomy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-028 Surgical Resection for Sarcomatoid Carcinoma of the Lung Tarek Kilani[1], Sarra Zairi[1], Sadok Boudaya[1], Hazem Zribi[1], Mouna Mlika[2], Adel Marghli[1], Aida Ayadi[2], Hammouda Boussen[3], Faouzi Mezni[2], Tahar Mestiri[1] [1]*Thoracic and Cardiovascular Surgery, Abderrahmane Mami Hospital, Ariana/Tunisia,* [2]*Pathology, Abderrahmane Mami Hospital, Ariana/Tunisia,* [3]*Medical Oncolog, Abderrahmane Mami Hospital, Ariana/Tunisia*

Background: Sarcomatoid carcinoma of the lung is not very common. It consists of poorly differentiated non-small cell carcinomas with sarcoma or sarcoma-like differentiation component. The World Health Organization lists five subtypes representing an overall continuum of epithelial and mesenchymal differentiation: pleomorphic carcinoma, spindle cell carcinoma, giant cell carcinoma, carcinosarcoma, and pulmonary blastoma. The diagnosis is pathological and requires a good sampling of the tumor. The purpose of this study was to assess the surgical management of primary sarcomatoid carcinomas of the lung which could benefit from surgery with curative intent. **Methods:** We retrospectively reviewed the 38 cases of primary sarcomatoid carcinoma, which were managed between 2000 and 2012, in the thoracic surgery department of our Hospital. All the included patients had surgical resection. **Results:** There were 33 males and 5 females with a mean age of 59.7 years (42-81). The main symptoms were respiratory. Imaging features showed a pulmonary mass invading pleura or the thoracic wall in 14 cases. The diagnosis was confirmed in all cases on histological examination of the resected tumor. According to the pathological results there were 23 pleomorphic carcinomas, 7 giant cell carcinomas, 1 spindle cell carcinoma, 5 carcinosarcomas and 2 blastomas. Associated treatments were split as follows: neoadjuvant (four cases) or adjuvant (six cases) chemotherapy, and radiotherapy (ten cases). Lobectomy (26 cases) or bilobectomy (2 cases) was performed in 28 patients and pneumonectomy in 9 patients. Chest wall enlargement with costal resection

was associated in 5 cases. One patient had a conservative resection (segmentectomy) because of a history of contralateral adenocarcinoma for which he had a lobectomy (2 years earlier). The tumors were classified as: T1 in 2 cases, T2 in 16, T3 in 16 and T4 in 4. The different stages were: Ia (n=2), Ib (n=8), IIa (n=1), IIb (n=13), IIIa (n=8), IIIb (n=2) and IV (n=4). The margins of the resected parenchyma showed tumoral involvement in 1 case. The median survival of our patients was 9 months. Two patients died in the early postoperative course. **Conclusion:** Sarcomatoid carcinomas are rare, aggressive tumors which require early diagnosis and management. Surgery whenever performed can be beneficial for these tumors which are of bad prognosis compared to other NSCLC. **Keywords:** Surgery, Sarcomatoid Carcinoma, NSCLC

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-029 Long and Short-Term Predictors of Outcome in Elderly Patients (≥ 75 Years) Undergoing Lobectomy for Stage I Non-Small Cell Lung Cancer
Takashi Eguchi[1], Daniel H. Buitrago[1], Marissa Mayor[2], Kyuichi Kadota[3], Nabil P. Rizk[1], Bernard J. Park[1], David R. Jones[4], Prasad S. Adusumilli[2] [1]*Thoracic Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [2]*Thoracic Service and Center for Cell Engineering, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [3]*Department of Diagnostic Pathology, Kagawa University, Kagawa/Japan,* [4]*Thoracic Service, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America*

Background: More than 65% of patients diagnosed with non-small cell lung cancer (NSCLC) are above the age of 65 years. Half of this cohort are ≥75 years who are at higher risk following surgical resection, which is the mainstay of treatment for early-stage NSCLC. The purpose of this study is to determine the factors influencing the outcomes in patients ≥75 years who underwent lobectomy for stage I NSCLC: postoperative complications, short-term (30- and 90-day mortality) and long-term (overall survival (OS) and cancer-specific survival (CSS)). In addition to the routinely used clinical factors, we investigated the utility of lung age, the tool commonly used for smoking cessation. **Methods:** Patients with pathological stage I NSCLC who underwent lobectomy between 2000 and 2011, age ≥75 years at surgery with no induction therapy, and no previous lung resection were included in the study (n =435). We investigated the influence of smoking history, preoperative history of cardiovascular disease (CVD) and chronic obstructive pulmonary disease (COPD), Carlson comorbidity index (CCI), serum creatinine level, lung age (calculated by height and forced expiratory volume in one second), percent predicted diffusing capacity of the lung for carbon monoxide (%DLCO), and p-stage. Outcomes studied were postoperative in-hospital complication (CTCAE grade ≥3), 30- and 90-day mortality, OS, and CSS. Complications and mortality were analyzed by chi-square tests for univariate analysis. OS and CSS were analyzed by Kaplan-Meier methods with log-rank tests for univariate analysis, and Cox proportional analysis for multivariate analysis. **Results:** Median chronological age was 79 years, whereas median lung age was 89 years (female gender n = 334, positive smoking history n = 391, p-stage IA/IB were 282/153). In univariate analysis, low %DLCO and CVD history were significantly associated with postoperative complications (p = 0.032 and 0.018, respectively), and only high serum creatinine level was significantly associated with 30- and 90-day mortality (p = 0.02 and 0.027, respectively). P-stage, lung age, %DLCO, and COPD history were significantly associated with poor OS (p <0.001, p <0.001, p = 0.009 and 0.008, respectively). P-stage, lung age, and COPD history were significantly associated with poor CSS (p =0.003, 0.004, and 0.046, respectively). In multivariate analysis, both p-stage and lung age were independently associated with poor OS (p <0.001 and <0.001, respectively) and poor CSS (p = 0.006 and 0.01, respectively). **Conclusion:** In elderly patients with stage I NSCLC undergoing lobectomy, p-stage and lung age were independent risk predictor for long-term prognosis (OS and CSS); serum creatinine level was associated with short-term mortality; and %DLCO and CVD history were associated with postoperative complications. Our observations from this large cohort are useful for treatment decision making in elderly patients with stage I NSCLC. **Keywords:** lung age, elderly, postoperative prognosis, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-030 Effectiveness of Extended Bilateral Superior Mediastinal Lymph Node Dissection Through a Median Sternotomy in Patients with Left NSCLC
Toshiya Yokota, Shingo Ikeda *Thoracic Surgery, Misui Memorial Hospiral, Tokyo/Japan*

Background: Lymph node dissection plays important role in oncologic surgery. The removal of the whole regional lymphatic system together with primary tumor is one of the fundamental rules in oncological surgery. But, the role of surgical treatment in non-small-cell lung cancer (NSCLC) with clinically manifested mediastinal lymph node metastasis is controversial. Bilateral paratracheal lymphnodes for left side tumors are considered inaccessible through a standard thoracotomy. It is difficult to perform complete dissection of superior mediastinal lymph nodes through the left thoracotomy in the left lung cancer. We had devised Systemic extended bilateral superior mediastinal dissection and lung resection through a median sternotomy (ND3 operation, Hata's method), and reported that ND3 operation can allow for complete dissection of all stations of mediastinal lymph nodes. The aim of this study was to evaluate the surgical outcomes and long term survival in patients of survival of the patient with non-small lung cancer (NSCLC) who underwent our ND3 operation. **Methods:** We retrospectively studied 289 patients (202 male and 87 female, mean ages 59.7 years (range, 38-75)) , underwent ND3 operation due to Left NSCLC, from January 1988 till December 2014. The patients with NSCLC of left side primary who are estimated to be able to conventional radical operation and aged 75 years old or less becomes the adaptation of our ND3 operation. Postoperative survival rates calculated with Kaplan-Meier method. Clinicopathological data were compared according to the p stage. **Results:** Overall 5-year survival rate in the 289 patients of left lung primary was 64.6%. Operative mortality in 289 patients was 3.0%,1.2% from January 2001 till December 2014. Lymph node metastasis to the mediastinum was confirmed in 98 (33.9%) patients (pN2 was 50 patients,pN3α was 29 patients, pN3β was 2 patients, pN3γ was 17 patients). According to pathological stages, five-year survival rate was was 88.7% in stage IA, 75.3% in stage IB, 60.6% in stage IIA, 71.4% in stageIIB, 47.5% in stageIIIA, 39.6% in stageIIIB. Five-year survival rate was 48% in pN2 cases, and 48.8% in pN3α cases. Compere with previouse our reports, this result is more safety and better prognosis. **Conclusion:** Our result suggest that ND3 operation would provide better prognosis in the patients with pN2 and pN3α Lt.NSCLC. And better local tumor control by ND3 operation than conventional lung cancer operation does not increase mortality.Lung cancer surgery should be denied due to clinical N status because patient with N2,N3 disease NSCLC can be operated for curative intent by our ND3 with acceptable surgical risk and long term survival. **Keywords:** Lymph node dissection, mediastinal lymph node, median sternotomy, non small cell lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P1.02-031 Wedge Resection for NSCLC: Does Minimally Invasive Surgery Warrant the Maximum Advantage?
Pietro Bertoglio, Marco Lucchi, Carmelina C. Zirafa, Federico Davini, Alfredo Mussi *Department of Surgical Medical Molecular Pathology and Critical Care, Divison of Thoracic Surgery, University Hospital of Pisa, Pisa/Italy*

Background: Anatomic resections of the lung are firmly considered the gold standard treatment for early stage Non Small Cell Lung Cancer (NSCLC). The role of non-anatomic surgery is still not clear and it is generally used for very selected patients, who cannot undergo an anatomical resection of lung parenchyma for functional reasons. The aim of this study is to analyze whether surgical approach (VATS or open) might have an influence on the long term outcome of NSCLC patients treated by wedge resection. **Methods:** From December 2006 till 2010, 1695 patients underwent surgery for primary NSCLC at our Institution. Among them, 97 patients received a wedge resection either by open or thoracoscopic apprach due to coexisting morbidities or low pulmonary function; 54 were selected for our study. We excluded from our analysis all patients with a previous lung cancer, with suspected (on the basis of CT or PET CT images) or confirmed N2 disease, nodules greater than 5 cm or with involvement of the chest wall or mediastinal structures. Follow-up was carried out at December 2013. **Results:** Out of the 54 wedge resections, 30 were performed through a thoracothomy, while 24 cases by means of a VATS procedures. There were no statistically significant difference among clinical features of the two groups. Mean tumor diameter were 2,1 cm in the open group (OG) and 1,7 cm in the VATS group (VG); mean distance from visceral pleura was significantly higher in the OG (2,1 cm vs 0,8 cm; p=0,02) and so were the stapler edge (2,4 cm vs 1,2 cm; p<0,03). Mean follow-up was 42 months. In the open surgery group 2 patients (6,7%) had a local recurrence and in 10 patients (33,3%) we noticed systemic metasthasis. In the VATS group we had 4 cases (16,7%) of local recurrences and 7 (29,2%) of distant metasthasis. Local recurrence rate was significantly different between the two groups (p=0,048), while no significant correlation was found regarding the distant methastasis rate. Three patients died during the follow up period (two in the group treated with thoracotomy, 1 with VATS). **Conclusion:** Although different deepness of nodule between the two groups may represent a bias, we noticed a significant lower recurrence rate when surgery was performed by thoracotomy. Tumors larger than 1,5 cm are more likely to develop a recurrence, regardless to the kind of surgical approach. Wedge resection may be considered a feasible procedure for highly selected patients affected by NSCLC: open approach may be related to a better long term outcome in patients with small and deep nodules. **Keywords:** Non-small-cell lung cancer, wedge resection, VATS, limited resection

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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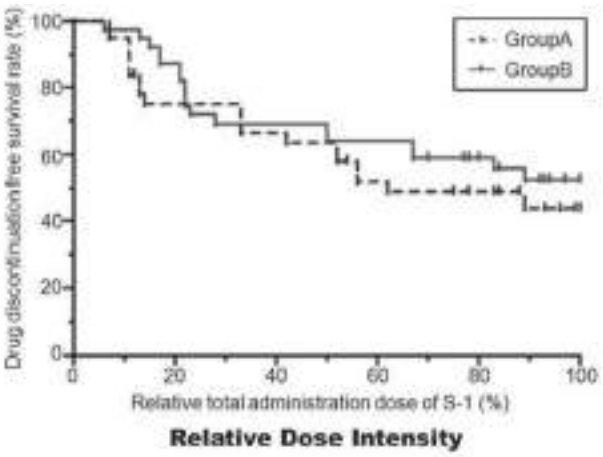
P1.02-032 Randomized Feasibility Study of S-1 for Adjuvant Chemotherapy in Completely-Resected Stage IA Non-Small-Cell Lung Cancer (SLCG 0701)
Norihito Okumura[1], Junichi Soh[2], Masao Nakata[3], Hiroshige Nakamura[4], Minoru Fukuda[5], Masafumi Kataoka[6], Shinsuke Kajiwara[7], Yoshifumi Sano[8], Motoi Aoe[9], Kazuhiko Kataoka[10], Katsuyuki Hotta[2], Keitaro Matsuo[11], Shinichi Toyooka[2], Hiroshi Date[12] [1]*Kurashiki Central Hospital, Kurashiki/Japan,* [2]*Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama/Japan,* [3]*Kawasaki Medical School, Kurashiki/Japan,* [4]*Tottori University Faculty of Medicine, Yonago/Japan,* [5]*Japanese Red Cross Nagasaki Genbaku Hospital, Nagasaki/Japan,* [6]*Okayama Saiseikai General Hospital, Okayama/Japan,* [7]*Uwajima City Hospital, Uwajima/Japan,* [8]*Ehime University Hospital, Touon/Japan,* [9]*Kagawa Prefectural Central Hospital, Takamatsu/Japan,* [10]*Iwakuni Clinical Center, Iwakuni/Japan,* [11]*Kyushu University Faculty of Medical Sciences, Fukuoka/Japan,* [12]*Kyoto University Graduate School of Medicine, Kyoto/Japan*

Background: The aim of this multicenter study (the Setouchi Lung Cancer Group Study 0701) was to determine the feasible administration schedule of S-1, an oral fluoropyrimidine, for adjuvant chemotherapy in patients with completely-resected pathological stage IA (tumor diameter, 2 to 3 cm) non-small-cell lung cancer (NSCLC). **Methods:** Patients were randomly assigned to receive an adjuvant chemotherapy of either 4-week oral administration of S-1 (80 mg/m2/day) followed by 2-week rest (group A), or 2-week oral administration of S-1 (80 mg/m2/day) followed by one week rest (Group B). The duration of adjuvant chemotherapy was one year in both arms. The primary endpoint was feasibility.

Results:



Eighty patients were enrolled, of whom 76 were received S-1 treatment. The treatment completion rates were 49.4% [95% confidential interval (CI), 32.8 to 65.9%] in group A and 52.1 % (95%CI, 35.5 to 68.6%) in group B (P = 0.4). The relative dose intensities were 40.4% (95%CI, 20.3 to 60.5%) in group A and 53.5% (95%CI, 37.7 to 69.3%) in group B (P = 0.4). There were no treatment-related deaths. Patients with grade 3/4 toxicities were significantly more frequent in group A (40.5%) than group B (15.4%, P = 0.02). The 2-year relapse-free survival rates were 97.5% in group A and 92.5% in group B, and the 2-year overall survival rates were 100% in both groups. **Conclusion:** Two-week oral administration of S-1 followed by one week rest for one year may be more feasible for adjuvant chemotherapy in patients with completely-resected stage IA (T diameter, 2 to 3 cm) NSCLC.
Keywords: adjuvant chemotherapy, Non-small-cell lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-033 Pemetrexed plus Platinum as Adjuvant Therapy in Patients with Resected Lung Adenocarcinoma and Exploratory Biomarkers Analysis
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Background: Non-small cell lung cancer (NSCLC) is the leading cause of cancer-related death around the world. Currently, adjuvant platinum-based chemotherapy is recommended as the standard treatment for patients with completely resected stage IB-IIIA NSCLC. Pemetrexed, a multitargeted antifolate agent, has been shown to have definite activity in non-squamous NSCLC and has proven to be efficacious in the first-line metastatic NSCLC. Hence, the aim of this study was to evaluate the efficacy and toxicity of pemetrexed/ platinum in patients with completely resected lung adenocarcinoma and identify prognostic factors in this setting. **Methods:** A retrospective study was performed in patients with completely resected stage IB-IIIA lung adenocarcinoma who received pemetrexed and a platinum as adjuvant therapy. Generally, pemetrexed 500mg/m2 d1 and cisplatin 30mg/ m2 day1-3 were administrated every 21-28 days for 4 cycles. Study endpoints included overall survival (OS), progression-free survival (PFS) and treated-related toxicities. Immunohistochemical (IHC) was used to examine the protein expression of p53, thymidylate synthase (TS), dihydrofolate reductase (DHFR), Lipocalin 2 and nm23-H1 in surgical resection specimens of 23 patients. The associations between protein expression level and clinical outcome were evaluated using cox proportional hazards model. **Results:** Between Feb. 2012 and Jan.2014, 49 patients were treated with pemetrexed-based chemotherapy. Median age 57(range35-79, years), males 47%; stage IB 41%, II 18%, IIIA 41%; ever smokers 35%; lobectomy 92%, wedge resection 8%. The completion of 4-cycle chemotherapy was 67.3%. Grade 3+ hematologic and gastrointestinal toxicities were observed in 5 (10%) patients and 4 (8%) patients, respectively. The median PFS was 39.63 months (95%CI 26.55-52.71 months), and the median OS was unreachable. 1-, 2- and 3-year survival rates were 95.9%, 93.6%, 83.2%, respectively. 1-, 2- and 3-year PFS rates were 93.9%, 75.3% and 56.8%, respectively. Of 23 patients measured by IHC, 19 expressed TS, 9 expressed p53, 10 expressed DHFR, and none expressed Lipocalin 2 or nm23-H1. No significant correlations of these protein expression and clinical outcome were observed. **Conclusion:** The regimen of pemetrexed/platinum showed lower incidence rates of toxicities and promising treatment outcomes in patients with completely resected stage IB-IIIA lung adenocarcinoma. However,no prognostic biomarker was identified in our study, which may be related to the small sample size.
Keywords: lung adenocarcinoma, Biomarkers, pemetrexed, adjuvant chemotherapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-034 Lung v5 Does Not Predict for Lung Toxicity after Fixed-Beam Intensity Modulated Radiotherapy (IMRT)
Clara Chan[1], Paula Mccloskey[2], Linda Ashcroft[1], Philip Whitehurst[1], Jason Kennedy[1], Annalie Shears[1], Michelle Bewley[1], Rhiannon Goldstraw[1], Neil Bayman[1], Corinne Faivre-Finn[3] [1]*Clinical Oncology, The Christie NHS Foundation Trust, Manchester/United Kingdom,* [2]*Clinical Oncology, Belfast Health and Social Care Trust, Belfast/United Kingdom,* [3]*Univ. of Manchester, Manchester/United Kingdom*

Background: Intensity Modulated Radiotherapy (IMRT) facilitates superior dose conformity, due to sculpting of the high dose volume and reduction of dose to normal tissues. However, the use of IMRT for lung cancer in the U.K. remains low, as a result of the paucity of clinical data and concerns about the impact of the low dose bath on toxicity. Our institution has treated 738 lung cancer patients with IMRT since 2008. Here we report the results of 227 patients, focusing on toxicity. Survival will be reported at a later date. **Methods:** A retrospective review of the first 227 patients receiving 6MV inversely planned (6-8 field) step and shoot IMRT for lung cancer from 2008-2013 was carried out. A database was interrogated to correlate planning parameters with toxicity. Toxicity was collected using Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. **Results:** 227 patients with a median age of 66 (36-87) were included. Patients received a dose of 50-68 Gy in 20-33 fractions. One hundred and sixty (70%) had non-small cell lung cancer, 47 (21%) small cell lung cancer, 8 (4%) mixed histology and 12 (5%) no histology. At presentation, 6 (3%), 27 (12%), 184 (81%) and 9 patients (4%) had stage I, II, III and IV disease respectively. Treatment modalities were split evenly between concurrent (37%), sequential (31%) chemo-radiotherapy and radiotherapy alone (32%). Median PTV volume was 502.7 cc (67.3-1297.2). Median lung V20, V10 and V5 were 27.7% (6.8-35.3), 50.4% (9.8-83.1) and 64.3% (12.9-98.9). Mean dose to the oesophagus was 23.8 Gy (3.1-51.0); oesophageal V55 and V35 were 2.9% (0-70.8) and 36.8% (0-79.8). Heart V30 and V5 were 23.6% (0-60.6) and 57.6% (0-100) respectively. Despite 104 patients (46%) with V5 values > 65%, acute G3 pneumonitis was observed in only 7 (3.1%) patients. Acute G3 oesophagitis was observed in 31 (13.7%) patients. Late toxicity was not available in all patients. 6/154 (4%) developed late G3 pneumonitis, 8/154 (5.3%) had late G3 dyspnoea and late G2 cough was reported in 12/154 (8.1%). Grades 1, 2 and 3 pulmonary fibrosis occurred in 68/178 (30%), 13/178 (6%) and 1/178 (0.4%) patients respectively. Oesophageal stricture was evident in 7/173 (3%) and 4 patients developed an oesophageal fistula. There was no significant correlation between lung V5 and acute or late lung toxicity, using >65% as a cut off. Similar results were found with lung V10. There was also no relationship between mean oesophageal dose/V35/V55 and fistula or oesophageal stricture. **Conclusion:** From our experience, IMRT to the thorax is well tolerated, with minimal grade 3 toxicity. Contrary to reports, we did not observe a correlation between lung V5 and acute/late lung toxicity. However the heterogeneous population, retrospective nature of this study and small number of grade 3+ events limit the scope for multivariate analysis of toxicity. The data needs to be confirmed with a larger number of patients and integrated within predictive models of radiation-induced toxicity using patient reported outcome tools to facilitate collection of prospective toxicity data in the routine clinical setting. Data will be updated prior to the meeting.
Keywords: lung cancer, intensity modulated radiotherapy, toxicity

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-035 Radiographic Changes in Lung of Patients Treated with Stereotactic Ablative Body Radiation Therapy and the Dosimetric Correlations
Fen Wang[1], John Park[2], Bruce F. Kimler[1], Rajeev Badkul[1], Parvesh Kumar[1] [1]*University of Kansas Medical Center, Kansas City/KS/United States of America,* [2]*Kansas City Va Hospital, Kansas City/MO/United States of America*

Background: To describe radiographic evidence of radiation pneumonitis (rRP) and fibrosis (rRF) and determine what dosimetric parameters correlate with rRP and rRF after stereotactic ablative radiation therapy (SABR) to the lung. **Methods:** 98 follow up CT scans from 32 patients treated by SABR were retrospectively reviewed for CT appearance of rRP and rRF determined by the Ikezoe (≤ 6 months) and Koenig (≥ 7 months) systems. The correlation of dosimetric parameters such as planning target volume (PTV) and the volume of lung receiving dose of radiation (V2.5, V5, V7, V10, V15, V20, V25, and V30) to rRP, rRF, and fibrotic volume ($V_{fibrosis}$) were analyzed using Spearman's rho. **Results:** The median follow up was 10 months (range 2 – 24 months). There was a 55% incidence of rRP and 59% incidence of rRF. The low dose parameters of $V_{2.5,}$ $V_{5,}$ $V_{7,}$ and V_{10} (the volume of lung receiving more than 2.5, 5, 7, and 10 Gy of radiation, respectively) were correlated to the development of rRP ($p < 0.05$). There was only V_{10} correlated statistic significantly to the incidence of rRF, with $V_{5,}$ $V_{7,}$ and V_{10} trended towards significance. The median $V_{fibrosis}$ was 119 cm^3 with a range of 49 – 829 cm^3. The medians of the PTV and ITV were 52.6 cm^3 and 12.6 cm^3 respectively. The absolute fibrotic volume was correlated with the planning target volume (PTV), V_7 and V_{10} ($p < 0.05$). **Conclusion:** The development of rRP and rRF was associated with the volume of lung that received lower dose of radiation. The absolute fibrotic volume from SABR was correlated with PTV and the volume of lung receiving lower dose of radiation. This finding needs to be validated with more patients' data and longer follow up.

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-036 Peripheral Blood Immunophenotype Changes Following Thoracic Stereotactic Ablative Radiotherapy
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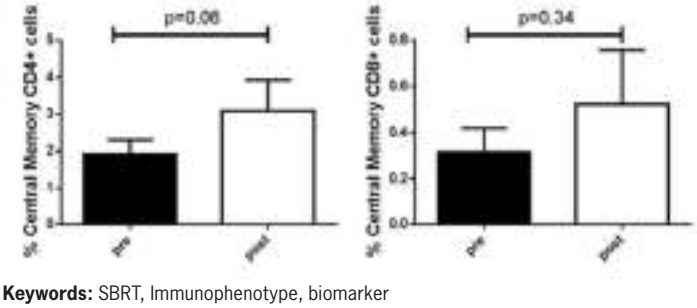
Background: Stereotactic ablative radiotherapy (SAR) is a standard therapy for early stage, medically inoperable non-small cell lung cancer (NSCLC) and select metastatic tumors. Strategies combining SAR and immune checkpoint inhibitors are of great interest in potentially augmenting anti-tumor immune response, and prospective trials evaluating SAR/immunotherapy combinations are underway. However, the systemic immune response profile following SAR is poorly defined. Better understanding of the systemic immune response following SAR should allow optimization of SAR/immunotherapy protocols. We performed pre and 1 week post-SAR immune profiling on patients undergoing lung SAR, focusing on central memory T-cells which have been implicated as important mediators of systemic anti-tumor immune responses. **Methods:** Patients are actively accruing to an IRB approved protocol examining systemic immunophenotype changes following SAR for early stage (T1-2N0) NSCLC or metastatic lesions to the lung. Patients underwent collection of 30 cc blood by venipuncture immediately prior to and at 1 week post-SAR to a median dose of 50 Gy (range: 50-54 Gy) over 5 fractions (range: 3-5 fractions). Immunophenotyping of peripheral blood mononuclear cells (pbmc's) was performed using flow cytometric analysis. Central Memory T-cells were defined as CD62L+ and CD45RA- subsets of CD4+ or CD8+ T-cells. Changes pre-treatment to post-treatment were compared across the cohort using a paired T-test. **Results:** To date eleven NSCLC patients have accrued, and evaluable pre- and post-SAR specimens are available for six, all with early stage NSCLC (T1=4, T2=2, synchronous primaries =1). At one week post-SAR increases in systemic central memory CD4+ T-cells were observed in 4/6 patients and increases in systemic central memory CD8+ T-cells were observed in 3/6 patients with substantial (up to 10-fold) increases observed in some patients. Across the cohort the percent of circulating memory CD4+ T-cells increased from 1.9% pre-SAR to 3.1% post-SAR (p=0.06, Figure 1) and the percent of circulating memory CD8+ T-cells increased from 0.3% pre-SAR to 0.5% post-SAR (p=0.34, Figure 1). **Conclusion:** Our preliminary data in a limited patient cohort suggest lung SAR may induce systemic upregulation of circulating central memory T-cells which may be important mediators of the anti-tumor immune response. As more patients accrue, additional post-treatment time points are evaluated, and further analyses including cytokine/chemokine signatures are performed, we aim to better define systemic immunophenotype changes induced by lung SAR, assess how these changes relate to treatment toxicity and efficacy, and whether they can predict which patients will most likely benefit from the addition of immunotherapy to SAR.

Figure 1. Central Memory T-cells in patient pbmc's pre- and post-SAR



Keywords: SBRT, Immunophenotype, biomarker

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-037 Thoracic Radiation-Induced Pleural Effusion and Risk Factors in Patients with Lung Cancer Jing Zhao[1], Matthew Stenmark[2], Jianyue Jin[3], Catherine Ferguson[3], Hadyn Williams[4], Leslie Quint[5], Shulian Wang[6], Martha Mastuzak[2], Randy Ten Haken[2], Regina M. Day[7], Feng-Ming (Spring) Kong[3] [1]*Georgia Regents University;Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Augusta/GA/United States of America,* [2]*Department of Radiation Oncology, University of Michigan Health System, Ann Arbor/United States of America,* [3]*Department of Radiation Oncology, Gru Cancer Center/Medical College of Georgia, Georgia Regents University, Augusta/United States of America,* [4]*Department of Radiology, Gru Cancer Center/Medical College of Georgia, Georgia Regents University, Augusta/GA/United States of America,* [5]*Department of Radiology, University of Michigan Health System, Ann Arbor/United States of America,* [6]*Department of Radiation Oncology, Georgia Regents University, Cancer Hospital and Institute, Chinese Academy of Medical Sciences and Peking Union Medical College, Augusta/GA/United States of America,* [7]*Department of Pharmacology, Uniformed Services University of the Health Sciences, Bethesda/MD/United States of America*

Background: Pleural effusion is regarded as a frequent late toxicity after thoracic radiotherapy (TRT). However, recent literature is lacking on this toxicity. This study aimed to examine the patient and dosimetric risk factors associated with radiation induced pleural effusion (RIPE) in lung cancer patients treated with TRT. **Methods:** Lung cancer patients treated with TRT having follow-up imaging, CT or PET/CT, were eligible. Pleural effusion of increased volume after TRT without evidence of tumor progression was considered to be RIPE. Parameters of lung dose-volume histogram including percent volumes irradiated with 5 to 55 Gy (V5-V55) and mean lung dose (MLD) were analyzed. Optimal dosimetric thresholds for RIPE were calculated by receiver operating characteristic (ROC) analysis. Associating clinical and treatment-related risk factors for RIPE were detected by univariate and multivariate analyses with SPSS 18.0. Data were considered statistically significant at value of $p < 0.05$. **Results:** Of 806 consecutive patients who received TRT at two institutions, 205 had post-treatment imaging available and were included in this study. The median (range) age was 63 (34-85) years; Male, Caucasian race, current smokers, stage III and squamous cell cancer accounted for 73.2%, 81.0%, 50.7%, 66.8% and 27.8%, respectively. The median follow-up duration was 14.6 (range, 0.7-80.8) months. Of 51 patients (24.9%) who developed RIPE, 40 had symptomatic RIPE including chest pain (47.1%), cough (23.5%) and short of breath or dyspnea (35.3%). The median (range) RIPE interval from end of TRT was 3.7 (0.6-18.0) months. The RIPE rates of the two institutions were 20.2% and 32.1% with a borderline significance ($p = 0.053$). Caucasian race (HR = 2.930, 95% CI: 1.197-7.172, $p = 0.019$) and histology of squamous cell lung cancer (HR = 0.645, 95% CI: 0.425-0.980, $p = 0.04$) were significantly associated with the low risk of RIPE, while age ($p = 0.378$), gender ($p = 0.071$), stage ($p = 0.148$), radiation dose ($p = 0.782$) and concurrent chemotherapy ($p = 0.173$) were not. The whole lung V5, V10, V15, V20, V25, V30, V35, V40, V45, V50 and MLD were significantly higher in patients with RIPE than in those without RIPE ($p = 0.007$, 0.022, 0.044, 0.048, 0.034, 0.016, 0.010, 0.026, 0.040 and 0.014), and only V5 was the significant predictive factor for both RIPE and symptomatic RIPE ($p = 0.007$ and 0.021) with the largest areas under ROC curve (AUC = 0.779). Using a cutpoint of 41.5% for V5, the sensitivity and specificity were 100% and 61.5%, respectively. **Conclusion:** Radiation induced pleural effusion is notable. Caucasian race and squamous cell tumor histology may be associated with lower risk of RIPE. The whole lung V5 seems to be a significant risk factor for symptomatic RIPE. **Keywords:** Thoracic radiation induced pleural effusion, risk factors, lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-038 A Comparison of Stereotactic Body Radiation Therapy vs. No Treatment for Patients with Early-Stage Non-Small Cell Lung Cancer Stefan S. Jeppesen[1], Tine Schytte[2], Carsten Brink[3], Niels Christian G. Hansen[4], Olfred Hansen[5] [1]*Institute of Clinical Research, University of Southern Denmark, Odense C/Denmark,* [2]*Department of Oncology, Odense University Hospital, Odense C/Denmark,* [3]*Laboratory of Radiation Physics, Odense University Hospital, Odense/Denmark,*[4]*Center of Thoracic Oncology, Odense University Hospital, Odense C/Denmark,* [5]*Department of Oncology, Odense University Hospital, Odense/Denmark*

Background: Scarce information is available concerning the natural history of untreated patients with early-stage Non-Small Cell Lung Cancer (NSCLC). No randomized studies have been conducted comparing Stereotactic Body Radiation Therapy (SBRT) with no treatment for patients with early-stage NSCLC. Previously, it has been suggested that SBRT increases overall survival for patients with NSCLC T1-2N0M0. In this study a national group of untreated patients with early-stage NSCLC was identified in order to compare the effect of SBRT with the natural history in a retrospective setting. **Methods:** From 2007 to 2013, 136 patients diagnosed NSCLC T1-2N0M0 with a tumor diameter up to 5 cm were treated with SBRT at Odense University Hospital. The thoracic RT consisted of 45-66 Gy/3 F delivered in 9 days. For the same period, a national group of 121 untreated patients with early-stage NSCLC was extracted from the Danish Lung Cancer Registry. Of these, 85 patients survived more than one month after the diagnosis was established and might have been candiates to SBRT. Twenty-four patients with unrecorded tumor diameter were excluded from the present analysis thus, 61 patients remained in the untreated group. Pathoanatomical diagnosis was known for all patients. Kaplan-Meier and Cox proportional hazard analyses were used for uni- and multivariable survival analyses, respectively. Overall survival (OS) was calculated from the date of diagnosis. **Results:** The mean age was 72 vs. 78 years in the SBRT and untreated group, respectively. Statistically significant ($p<0.05$) inter-group differences in patient characteristics were observed for pathological type and FEV1 (%predicted). No difference in gender, tumor size, ECOG performance status, or pack years was observed. The potential median follow-up time was 38 months in the SBRT group vs. 57 months among untreated. A log rank test showed a significant difference of overall survival (OS) between groups e.g. resulting in an OS at 5-year of 44% vs. 10% respectively and a median OS of 47.8 vs. 12.2 months for SBRT and untreated group, respectively ($p < 0.01$). Multivariate analysis indicated that age, tumor size, pack years, gender, adenocarcinoma and FEV1 (%predicted) had no significant influence on survival, while SBRT and ECOG performance status had (Table 1).

Table 1. Cox regression analysis.

	Univariate analysis			Multivariate analysis					
				Full model			Reduced model		
Covariates	HR	p-value	95% CI	HR	p-value	95% CI	HR	p-value	95% CI
Age	1.03	<0.05	1.01-1.05	1.01	0.58	0.99-1.05	-	-	-
SBRT	0.29	<0.05	0.20-0.42	0.34	<0.001	0.15-0.39	0.38	<0.001	0.19-0.42
Tumor size	1.08	0.36	0.91-1.29	1.12	0.28	0.91-1.37	-	-	-
Male gender	0.99	0.99	0.68-1.43	0.93	0.69	0.59-1.41	-	-	-
ECOG PS 1+	1.83	<0.05	1.24-2.70	2.04	0.001	1.35-3.16	2.02	<0.001	1.37-2.97
Pack years	1.00	0.93	0.99-1.01	1.00	0.74	0.99-1.01	-	-	-
Adenocarcinoma	0.94	0.67	0.64-1.33	1.16	0.49	0.76-1.77	-	-	-
FEV1 (%pred.)	1.00	0.79	0.99-1.01	1.00	0.99	0.99-1.01	-	-	-

Conclusion: In this study SBRT was associated with significantly longer OS compared to no treatment, suggesting that SBRT is a convenient treatment that increases survival for patients with early-stage NSCLC. **Keywords:** Natural history, Early-stage, NSCLC, SBRT

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.02-039 Stereotactic Radiotherapy as Salvage Treatment after Stereotactic Radiotherapy or after Operated Non-Small-Cell Lung Cancer
Charlotte Kristiansen[1], Tine Schytte[1], Stefan S. Jeppesen[2], Olfred Hansen[1] [1]*Department of Clinical Oncology, Odense University Hospital, Odense C/Denmark,* [2]*Institute of Clinical Research, University of Southern Denmark, Odense C/Denmark*

Background: Lobectomy is regarded as the standard of care for early stage non-small-cell lung cancer (NSCLC), but stereotactic radiotherapy (SBRT) is an option for patients who are not candidates for surgery. Although the curative intention treatments, a significant proportion of patients with NSCLC will develop recurrent disease. For patients previously treated with SBRT little is known of retreatment with SBRT in the recurrent setting. **Methods:** All patients with lung cancer treated at our center with SBRT have been registered prospectively. We identified the patients who had salvage SBRT after prior pulmonary surgery or SBRT. Overall survival was calculated from the day of salvage SBRT. **Results:** Between November 2008 and February 2015, 198 patients were treated with SBRT. We identified 24 patients that had received SBRT as salvage treatment for their first recurrence in the lung. Surgery was the initial treatment for 13 of the patients (OP-group) and SBRT was the initial treatment for the remaining 11 patients (RT-group). By the end of follow up, 5 patients in the OP-group had died and 3 in the RT-group. In the OP-group all the salvage SBRT was given as 66 Gy in 3 fractions. In the SB-group, 5 was treated with 56 Gy in 8 fractions, 1 with 45 Gy in 3 fraction and 1 with 45 Gy in 10 fractions when given salvage SBRT.

	Primary surgery	Primary SBRT	All
Number of patients	13	11	24
Age mean (range)	75 (62-88)	69 (53-87)	72 (53-88)
Histology Plano/Adeno/NOS	3/8/2	4/5/2	7/13/4
Time in months from primary treatment to salvage SBRT median (range)	65 (4-236)	17 (5-44)	21 (4-236)
Survival time from SBRT 1 year (%)	85	89	87
2 year (%)	62	61	60
Median follow-up months (range)	27.6 (14.3-62.8)	15.9 (1.4-32.9)	21 (1.4-62.9)
Lung function FEV1, median (range	1.4 (0.6-2.7)	1.4 (0.4-2.8)	1.4 (0.4-2.8)
ECOG Performance Status 0	4	1	5
1	5	2	7
2	3	7	10
3	1	1	2

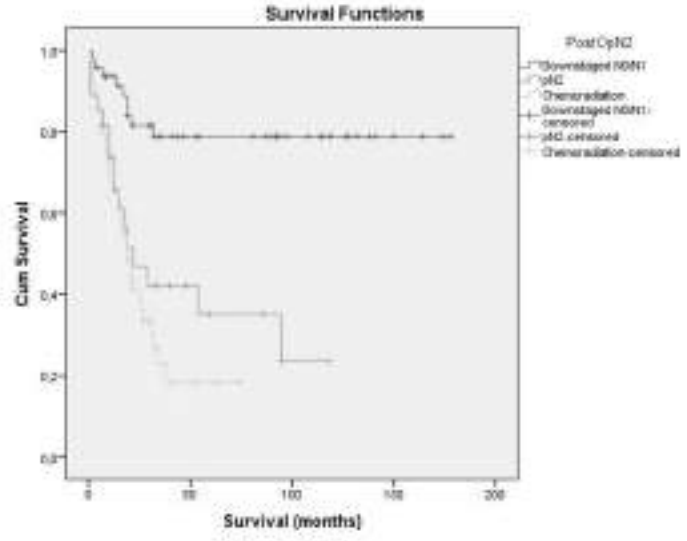
Conclusion: Although the time from primary treatment to salvage SBRT was longer if surgery was the primary treatment than if the primary treatment was SBRT, the overall survival was equal for the two groups.
Keywords: Operation, recurrence, SBRT, NSCLC

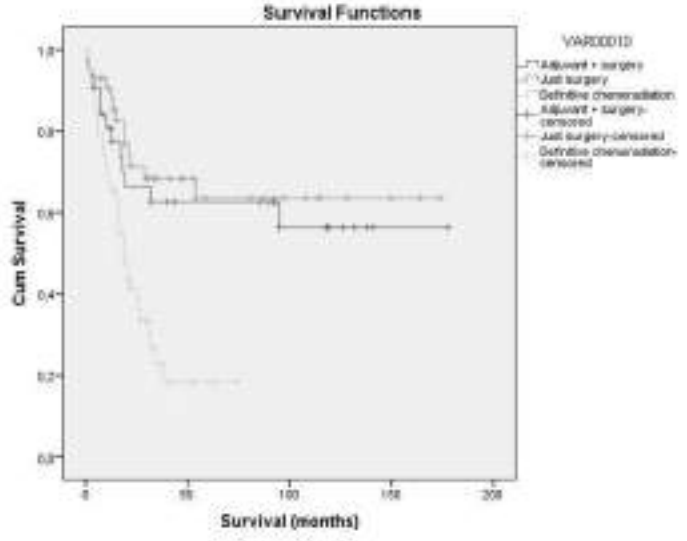
SESSION: POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC MONDAY, SEPTEMBER 7, 2015

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-001 Survival of the NSCLC Patients with Clinical Stage IIIA Disease with N2 Involvement: Case-Control Study with Emphasis on Treatment Modality
Saana Andersson, Ilkka Ilonen, Jarmo A. Salo *Department of General Thoracic Surgery, Heart and Lung Center, Helsinki University Central Hospital, Helsinki/Finland*

Background: The aim of this study was to determine the survival rate of patients with non-small cell lung cancer (NSCLC) who were preoperatively diagnosed with positive N2 lymph node and compare survival with chemo- or chemoradiotherapy treated patients to surgically operated patients, with or without preoperative chemoradiation therapy. **Methods:** Study included two patient groups. Operative patient group consisted of 74 clinical Stage IIIA patients with cN2 lymph node involment, from a 1105 patient cohort, who were operated between January 2000 and December 2014. Definitive chemoradiation group consisted of 49 Stage IIIA NSCLC patients that were treated between September 2008 and October 2014. Institutional tumour board was used to evaluate operative treatment. Routine positron emission tomography (PET) was established in 2006 at our institution. **Results:** 37 had preoperative mediastinoscopy, 66 PET-CT and 24 received both. In the operative patient group, adjuvant chemotherapy was administered 25 and chemoradiation to 7 patients. No differences were observed between patient groups in age or Charlson Co-morbidity Index. A total of 47 operated patients were downstaged to pathological N0 or N1 disease and pathological N2 disease was observed in 27 patients, of 11 patients had multi-level N2 involvement. Median survival for pN0/1 was 47 months, pN2 15 months and definitive chemoradiation 19 months. Survival for pathological N-stage is presented in Figure 1, and for preoperative therapy in Figure 2.





Conclusion: Operative treatment for clinically suspected N2 disease is feasible option if patients are downstaged to pathological N0 or N1 with means of chemoradiation therapy or pre- or intraoperative frozen sections. Surgery for pathological N2 disease has no survival advantage over definitive chemoradiation and should be discouraged.
Keywords: Staging, non-small cell lung cancer, Logoregional disease

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-002 Surgery in Subclassified Stage IIIA-N2 Lung Cancer Improves Survival
Hans-Stefan Hofmann[1], Jan Braess[2], Susanne Krause[2], Michael Allgäuer[3], Tamas Szöke[1], Michael Ried[4] [1]*Department of Thoracic Surgery, Hospital Barmherzige Brüder Regensburg, Regensburg/Germany,* [2]*Department of Oncology, Hospital Barmherzige Brüder Regensburg, Regensburg/Germany,* [3]*Department of Radiotherapy, Hospital Barmherzige Brüder Regensburg, Regensburg/Germany,* [4]*Department of Thoracic Surgery, University Medical Center Regensburg, Regensburg/Germany*

Background: Lung cancer with mediastinal lymph node involvement (N2) is a heterogeneous entity. The Robinson-classification subdivided these N2-patients in four groups ($IIIA_1$-$IIIA_4$). Objective of this analysis was to investigate the result of strict treatment strategies for N2-patients determined by the interdisciplinary tumorboard. **Methods:** Retrospective study and survival analysis of 118 consecutive patients with stage IIIA-N2 lung cancer classified according to the Robinson-classification and treated within a multimodality treatment regime between January 2009 and June 2014. All patients were evaluated and discussed in an interdisciplinary lung tumorboard and a therapy recommendation

was made based on the Interdisciplinary Guideline of the German Respiratory Society and German Cancer Society. **Results:** Robinson subgroups were: $IIIA_1$ (n= 28; mean age 60.4 years), $IIIA_3$ (n= 70; mean age 63 years) and $IIIA_4$ (n= 20; mean age 64.4 years). We have no stage $IIIA_2$, because we did not perform an intraoperative frozen section of mediastinal lymph nodes. Surgical resection with systematic lymph node dissection was performed in all patients with stage $IIIA_1$ (n= 28). After induction chemotherapy or chemo-/radiotherapy, 47% of patients in $IIIA_3$ (n= 33) and 10% of patients in $IIIA_4$ (n= 2) could be operated with curative intention. Complete tumor resection (R0) was achieved in 93% (n= 26) in stage $IIIA_1$, in 94% (n= 31) in stage $IIIA_3$ and in 100% (n= 2) in stage $IIIA_4$. Operative mortality within 30 days was 3.17%. Overall median survival was 29.8 months. The 3- and 5-year survivals were 44.9% and 28.5%, respectively, in all patients with stage IIIA-N2 disease. There were no significant differences (p= 0.477) in survival regarding the Robinson subgroups. Patients who underwent surgical tumor resection had a significant better median survival (43.6 vs. 22.8 months; p= 0.013) compared to patients treated conservatively. In addition, patients in stage $IIIA_3$ who were considered for surgery after induction therapy had a significant better median survival according to non-surgically treated patients (45.4 vs. 22.8 months; p= 0.014) and they had the good overall survival of $IIIA_1$ patients (3- and 5-year survival rates of 59.4% and 40.8%). Deviation of the interdisciplinary recommended therapy (n= 15) lead to a significant reduced median survival (12.9 vs. 31.9 months; p= 0.011) compared to implementation of the suggested treatment approach (n= 100). **Conclusion:** Stage IIIA-N2-patients should be classified according to the Robinson-classification and discussed in the tumorboard. The treatment recommendation should be respected, because enforcement of the interdisciplinary recommended therapy significantly impacts survival. Surgical resection did lead to significant better survival rates. All stage $IIIA_3$ and $IIIA_4$ patients should be reevaluated for surgery depending on their response to induction therapy. **Keywords:** lung cancer, Robinson-classification, surgery, multimodality therapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-003 A Clinicopathological Study of Resected Small-Sized Non-Small Cell Lung Cancer 2 cm or Less in Diameter with N2 Lymph Node Metastasis
Yasufumi Kato, Junichiro Ohsawa, Yoshihisa Shimada, Junichi Maeda, Koichi Yoshida, Masaru Hagiwara, Masatoshi Kakihana, Naohiro Kajiwara, Tatsuo Ohira, Norihiko Ikeda *Thoracic Surgery, Tokyo Medical University Hospital, Tokyo/Japan*

Background: The detection of small-sized (≤ 2 cm) non-small cell lung cancer (NSCLC) has increased with the development of high-resolution computed tomography. The reported 5-year survival rate of T1a (≤ 2 cm) N0M0 patients is more than 80%, and that of p-T (≤ 2 cm) N2M0 patients has also steadily improved. **Methods:** Between January 1991 and December 2011, a total of 917 patients with small-sized NSCLC underwent curative pulmonary resection with systematic lymph node dissection by open thoracotomy or video-assisted thoracic surgery at our hospital. We retrospectively evaluated their postoperative clinical outcomes and survival rates. Survival was analyzed using the Kaplan-Meier method and log-rank test. **Results:** There were 57 (6.2%) patients with mediastinal lymph node metastasis (pN2 disease). The distributions of the histological types were adenocarcinoma 41 cases, squamous cell carcinoma 11, large cell carcinoma 4, and carcinoid 1. The procedures included lobectomy in 48 cases, segmentectomy in 6, and pneumonectomy in 3. The respectively status of lymph node metastasis was single station in 36 cases and multiple station in 21. Skip lymph node metastasis (no hilum lymph node metastasis) was observed in 13 cases. In 44 cases, there was both hilum lymph node and mediastinal lymph node metastases. There were 34 cases (59.6%) that were upstaged from preoperative clinical diagnosis (cN0 or N1). The median overall survival period and 5 year survival of the 57 patients with pN2 was 43.5 months and 41%. The recurrence rate was 70% (40/57) and the median disease-free interval was 41.3 months. Of the 18 patients without recurrence, 14 (77.8%) had single station mediastinal metastasis. The 5-year overall survival rates with multiple station or single station mediastinal metastases were 34.5% and 48.9%, respectively (NS). The 5-year overall survival rates with multiple (hilum and mediastinal) station lymph node metastases and only mediastinal station lymph node metastasis were 37.7% and 64.8%, respectively. **Conclusion:** This study showed that 6.2% of small-sized NSCLC had N2 disease. Moreover, 59.6% of small-sized NSCLC was upstaged from clinical diagnosis to pathological diagnosis. Single station mediastinal metastases showed a longer overall survival rate (64.8%) than multiple station mediastinal lymph node metastases. Therefore, we recommend systematic lymph node dissection for local treatment as well as accurate diagnosis. As multiple mediastinal node metastases showed an unfavorable prognosis, surgery combined with systematic treatment is recommended. **Keywords:** recurrrence, non-small cell lung cancer, lymph node, mediastinal

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

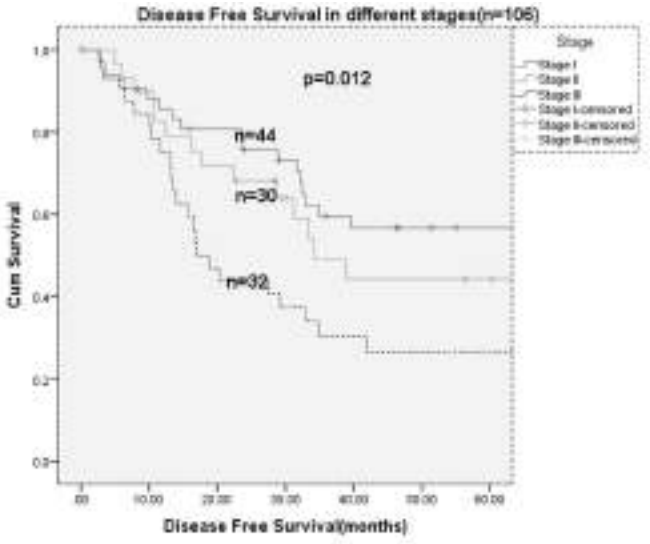
P1.03-004 Occult Primary Non-Small Cell Lung Cancer with Mediastinal Lymph Node Involvement
Paul B. Romesser[1], Andreas Rimner[2], Amanda Foster[2], Jamie E. Chaft[3], James Huang[4], David R. Jones[5], Abraham J. Wu[3] [1]*Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York/AL/United States of America,* [2]*Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [3]*Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York/United States of America,* [4]*Surgery, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [5]*Surgery, Memorial Sloan Kettering Cancer Center, New York/United States of America*

Background: Non-small cell lung cancer (NSCLC) involving mediastinal lymph nodes without an identifiable primary tumor is a rare presentation. While definitive surgery or radiotherapy with or without concurrent chemotherapy is typically recommended, little is known about the treatment outcomes. As such, we reviewed our institutional experience to determine if subsequent development of lung tumors is common and whether prognosis is comparable to stage III NSCLC in general. **Methods:** This study was an IRB-approved retrospective review of an institutional NSCLC database. Twenty-six patients with biopsy-proven NSCLC involving mediastinal lymph nodes with no identifiable lung primary lesion and no evidence of distant metastases treated with curative intent between 1995-2013 were identified. PET-CT staging was performed in 25 of 26 patients. All followup was calculated from date of diagnosis. **Results:** The median followup was 44 months. The median age at diagnosis was 60 years (range 51-81) among the 18 males (69%) and 8 females (31%). N2 and N3 disease were each present in 13 (50%) patients, respectively. Histologies included adenocarcinoma in 12 (46%), squamous cell carcinoma in 10 (38%), NSCLC not otherwise specified in 3 (12%), and large cell lung carcinoma in 1 (4%). Eleven patients underwent EGFR mutation analysis, with no sensitizing mutations identified. All patients had a smoking history (median 35 pack-years). Four (15%) patients underwent complete surgical resection, of whom 3 underwent induction chemotherapy and 1 was treated with surgery alone. One of the four patients underwent post-operative radiation therapy to 54 Gy. Twenty-two (85%) patients were treated with definitive radiation therapy including sequential chemotherapy and radiation in 8 (mean RT dose = 70 Gy), concurrent chemoradiation in 10 (mean RT dose = 60 Gy), neoadjuvant chemotherapy followed by concurrent chemoradiation in 3 (mean RT dose = 66 Gy), and radiation alone in 1 (treated to 60 Gy). The median overall survival was 78.1 months with actuarial 2- and 5-year survival rates of 78% and 67%, respectively. Five patients developed intrathoracic failure at a median of 19.8 months. One patient had an isolated lung failure at 13.6 years, but this likely represents a secondary primary and not tumor recurrence. Two patients had isolated mediastinal lymph node failures at 18.1 and 19.8 months and 2 patients initially had a mediastinal lymph node recurrence at 0.2 and 3.4 years, but subsequently failed in the lung at 8.5 and 3.6 years respectively. The actuarial 2- and 5-year intrathoracic control rates were 85.7% and 78.6%. Nine patients developed metastatic disease at a median of 16.5 months. The 2- and 5-year actuarial freedom from distant metastases was 70.9% and 59.1%. Among patients receiving definitive radiation, there was no difference between those receiving concurrent chemotherapy and those who did not. **Conclusion:** To our knowledge, this is the largest reported series of occult primary NSCLC involving mediastinal nodes. Definitive local therapy, including radiotherapy and surgery, was associated with very favorable locoregional control and survival, particularly compared with expected outcomes for stage III NSCLC. **Keywords:** non-small cell lung cancer, occult primary, chemoradiation, locally advanced disease

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-005 Bilobectomy for Lung Cancer: Postoperative Results, and Long-Term Outcomes
M Rahouma, Galal Ghaly, Mohamed Kamel, Brendon Stiles, Subroto Paul, Jeffery Port, Paul Lee, Abu Nasar, Nasser Altorki *Cardiothoracic Surgery, Weill Cornell Medical Center-Ny Presbyterian Hospital, Ny/United States of America*

Background: Bilobectomy for treatment of lung cancer is considered a high-risk procedure as it is associated with increased postoperative complication rate and the negative impact on survival. We analyzed the safety and the oncologic results of this procedure. **Methods:** We retrospectively reviewed a prospectively collected database to retrieve patients who underwent bilobectomy for lung cancer between 1991 and 2015. Age, gender, neoadjuvant treatment, bilobectomy type and indication, complications, pathology, stage, and survival were analyzed using Cox regression in univariate and multivariate analysis. Kaplan–Meier survival curves were obtained and compared by log–rank. **Results:** From our 4144 resected lung cancer cases, bilobectomy was performed on 106(2.5%) patients (55 men; mean age, 65.5 years). There were 51 upper-middle and 55 middle-lower bilobectomies (adenocarcinoma,67 (63.3%); squamous cell carcinoma,35(33%); carcinoid tumor,4(3.8%)). Indications were tumor invasion of the bronchus intermedius in 58 (54.7%), vascular invasion in 26 (24.5%), and tumor crossing the fissure in 22 (20.8%) patients. Induction therapy was performed in 24 patients (24.5%). Thirty-day mortality was 1.89% (n = 2). Overall major morbidity occurred in 13 patients (12.3%) among them 9 patients(69.2%) had pulmonary complications . Overall 3 and 5-year survivals were 64.5% and 56.2% respectively. Disease free 3 and 5-year survivals were 47.4% and 43.8% respectively. Significant decrease in 5 year survival was observed among smoker (p=0.046), higher tumor grades (Grade3 versus 1or2 (p=<0.005)), higher stages (stage I, 66.6%; stage II, 51.5%; stage III, 31.2%; p= 0.012)(see Figure) and the nodal(N) disease s (N0, 58.2%; N1and 2, 38.1%; p = 0.054) adversely influenced survival. Multivariate analysis demonstrated that a higher tumor grade (p = 0.005), a larger tumor (p=0.019), advanced N status (p=0.085) and smoking (p=0.056) adversely affecting prognosis.



Conclusion: Bilobectomy is associated with a low mortality and an acceptable morbidity. Survival relates to disease stage and N factor. Optimal prognosis is obtained in patients with early stage, low grade tumors and nonsmoker. **Keywords:** Bilobectomy, lung cancer, postoperative results, long-term survival

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-006 Survival Analysis of 121 Cases of Stage III A (N2) Non-Small Cell Lung Cancer Treated with Surgery Resection Liang Dai, Hao Fu, Ying M. Fan, Pu W. Yan, Zheng X. Kang *Thoracic Surgery, Beijing Cancer Hospital, Beijing/China*

Background: Lung cancer is the leading cause of both morbidity and mortality related to cancer worldwide. The most controversial academic strategies for the treatment of lung cancer is ⅢA-N2 non-small cell lung cancer.This study was a retrospective analysis of the clinical features of stage ⅢA-N2 patients, in order to find the factors that affecting long-term survival in the postoperative patients of stage ⅢA-N2 NSCLC. **Methods:** One thousand two houndred and ningtyLung cancer patients from a prospectively maintained database, treated by a single surgeon group between January 2000 and Jun 2013, at Beijing Cancer Hospital, Peking University, were reviewed.121 patients of stage ⅢA-N2 NSCLCs were analyzed, comparing gender, age, smoking index, perioperative chemotherapy, surgical approach, histological type, intravascular cancer emboli, pT stage and N2 lymph node status with long-term survival. **Results:** The postoperative pathological findings in this group showed that 79 patients(65.3%) were single-station N2, 42 patients (34.7%, 30 patients had 2 stations N2, 8 patients had 3 stations N2, 4 patients had 4 stations N2) were multi-stations N2; 42 patients' (34.7%) N2 status were ⅢA1/A2, and 79 patients (65.3%) N2 status were ⅢA3/A4; 54 patients (44.6%) had subcarinal lymph node metastasis. The overall 1,3,5-year survival rates of 121 patients was 91.7%, 62.2%, 43.6%, respectively, and the median survival time was 50.3 months. Univariate analysis showed that the 1,3,5-year survival rates between single-station N2 and multi-station N2 metastasis was 94.9% vs. 85.5%, 70.3% vs. 46.7%, 58.3% vs. 25.5% respectively, with a significant difference (p= 0.001); the 1,3,5-year survival rates between ⅢA1/A2 and ⅢA3/A4 was 97.6% vs. 88.5%, 78.3% vs. 53.5%, 52.7% vs. 38.4% respectively, with a significant difference (p=0.020); subcarinal lymph node metastasis was not a prognostic factor, the 1,3,5-year survival rates between metastesis and no metastasis was 92.6% vs. 91.0%, 56.0% vs. 68.4%, 37.4 vs. 49.5% respectively, with no significant difference (p=0.276). Gender, age, smoking index, perioperative chemotherapy, T stage, histological type, intravascular cancer emboli and other factors are not prognostic factors in this group. COX regression analysis showed that only single station N2 metastasis (HR=0.326, 95%CI : 0.186～0.572) and ⅢA1/A2 (HR=0.494 , 95%CI : 0.259～0.941) were the independence factors. **Conclusion:** 1. After a rigorous selection of stage ⅢA-N2 NSCLC, patients obtain good prognosis by surgery combined with multidisciplinary treatment. 2. Single-station N2 metastasis had a better survial comparing to multi-station N2 metastasis. 3. The dicovery of pathology of N2 metastasis in intraoperative or postoperative pathological findings (ⅢA1/A2) had a better survival comparing to pretreatment fingdings(ⅢA3/A4). 4. Subcarinal lymph node metastasis was not ⅢA-N2 indicator of poor prognosis in NSCLC. 5. Gender, age, surgical approach, histological type, pT staging does not affect the stage ⅢA-N2 NSCLC prognosis. **Keywords:** Non-small-cell lung cancer, N2 lymph node metastasis, survival analysis

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-007 Prognosis of Microscopic Residual Disease (R1) at Different Resection Margins and Efficacy of Adjuvant Therapy Masato Chiba *Division of Thoracic Surgery, Kinki University Faculty of Medicine, Osaka-Sayama/Japan*

Background: The aims of this study were to assess the prognosis of microscopic residual (R1) disease at different resection margins and to evaluate the prognostic impact of adjuvant therapy for R1 disease at different sites. **Methods:** We retrospectively reviewed the clinical records of 1,667 patients who underwent lung resection at the Aichi Cancer Center from 1998 to 2007. Twenty-eight patients (1.7%) were found to have R1 disease, and they were divided into three groups according to the site of residual disease. The "bronchus group" included 9 patients: 5 with cancer cells at the bronchial stump, 3 with carcinoma in situ change at the bronchial stump, and 1 with a clump of tumor cells in the parabronchial tissues (1 patient). The "lymph node group" included 5 patients with residual cancer cells in the lymph node. The "chest wall and lung tissue group" included 14 patients with cancer cells present at the following locations: the margin of chest wall invasion (9 patients), vertebral bodies (2 patients), the pericardium (1 patient) and lung tissue (2 patients). Actuarial survival curves were estimated by the Kaplan-Meier method. Statistical comparisons between survival distributions were performed using the log-rank test. A multivariate analysis was performed using the Cox proportional hazards model for overall survival analysis. A probability value of less than 0.05 was considered to be statistically significant. **Results:** This study included 24 men and 4 women with an age range of 49 to 80 years (median, 64 years). Six (21%), 18 (64%), and 4 (15%) patients had undergone pneumonectomy, lobectomy, and the other procedures, respectively. One (4%), 5 (18%), 19 (68%), and 3 (10%) patients had stage I, II, III, and IV disease, respectively. All 28 patients had non-small cell lung carcinoma. Eleven (39%), 12 (43%), and 5 (18%) patients had adenocarcinoma, squamous carcinoma, and other forms of carcinoma, respectively. The 5-year survival rate and median survival period were 30.3% and 37 months, respectively. The median recurrence-free survival time was 14.8 months. Regarding recurrence patterns, 11 (39%) patients did not experience recurrence, 4 (14%) developed only local recurrence, 5 (18%) developed only distant metastasis, 7 (25%) developed both local recurrence and distant metastasis, and 1 was lost to follow up. Sixteen patients received adjuvant therapy: 11 received radiotherapy, 3 received chemotherapy, and 2 received chemo-radiotherapy. Six patients (66%) in the bronchus group received radiotherapy. Six of the 11 patients with no recurrence were in the bronchus group. The univariate survival analysis identified the following factors that significantly influenced the 5-year overall survival rate: R1 anatomical sites (other sites vs the bronchus, p=0.0467, HR 2.775) and adjuvant therapy (no adjuvant therapy vs adjuvant therapy, p=0.0084, HR 3.509). The multivariate survival analysis identified only one factor that influenced survival: adjuvant therapy (adjuvant therapy vs no adjuvant therapy, p=0.0056, HR7.284). **Conclusion:** Patients with R1 disease generally had a poor prognosis, but this study suggested that adjuvant therapy improves the prognosis of these patients. In terms of sites of R1 disease, the bronchus group had a better prognosis than the other groups. **Keywords:** residual tumor, lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-008 Weekly Carboplatin/Gemcitabine + Concurrent Thoracic RT Followed by Consolidation Carboplatin/Gemcitabine for Inoperable Stage III NSCLC Manuel Domine, Cristina Carames, Francisco Lobo, Tatiana Hernandez Guerrero, Ana Leon, Victoria Casado, Gustavo Rubio, Irene Moreno, Jose Ignacio Martin Valades, Yann Izarzugaza, Juan Luis Arranz, Victor Moreno, Andrea Correa, Victor Zenzola, Susana Casado, Ana Ruperez, Roberto Hernandez, Jesus Garcia-Foncillas *Oncology, Hospital Universitario- Fundacion Jimenez Diaz, Madrid/Spain*

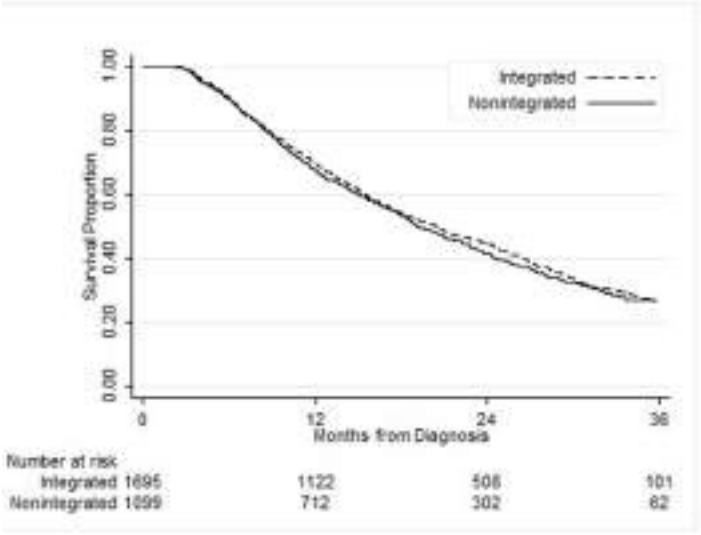
Background: Concurrent chemo and radiotherapy (CT- RT) is standard of care for inoperable stage IIIA/B non-small cell lung cancer (NSCLC). Optimal regimen and schedule of concurrent CT- RT remain undefined. This phase II trial evaluated carboplatin –gemcitabine + concurrent RT followed by consolidation carboplatin – gemcitabine **Methods:** Treatment schedule during CT-RT phase: weekly carboplatin (AUC 2) + gemcitabine (200mg/m2) for 6 weeks + concurrent RT (60 Gy). CT consolidation phase: carboplatin (AUC 3) gemcitabine (2500 mg/m2) every two weeks for 3 cycles. Primary endpoint was security and secondary response rate, time to progression (TTP) and overall survival (OS) **Results:** 24 patients were enrolled: Sex 18 male, 6 female. Histology: 12 adenocarcinoma, 8 squamous, 4 undifferentiated large cell carcinoma. Stage: IIIB: 20, IIIA: 4. ECOG 0-1: 23, ECOG 2: 1. All the patients completed concurrent CT-RT and 22 consolidation CT. **Toxicity:**CT- RT phase: No grade 4 toxicity was observed. Grade 3: Neutropenia 0, anemia 4.1%, thrombocytopenia 12.5%, esophagitis 16.6%. CT consolidation phase: Grade 3-4 toxicity: Neutropenia 16.6%, Anemia 21%, Thrombocytopenia 16.6% of the patients. 3 patients required red blood cell transfusion and 1 patient died for febrile neutropenia grade 4 during consolidation. **Efficacy**: Response Rate: 75% (Partial: 50% Complete: 22%), Stable disease 21% Progression 4%. Median TTP: 11 months (95% CI 7-17) and median OS: 18 months (95% CI 16.2- 20.5) **Conclusion:** Concurrent carboplatin – gemcitabine with thoracic RT is feasible with a favorable profile showing less hematologic toxicity and esophagitis than other CT-RT regimens. CT consolidation showed severe hematological toxicity. This regimen is active and could be a good option to combine with concurrent RT. **Keywords:** Locally advanced NSCLC, Chemo-radiotherapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-009 Integration of Chemoradiotherapy in a Single Facility: Impact on Outcomes for Locally Advanced Non-Small Cell Lung Cancer Henry S.-M. Park[1], Sanjay Aneja[1], Christopher D. Corso[1], Charles E. Rutter[1], Nataniel H. Lester-Coll[1], Roy H. Decker[1], Lynn D. Wilson[1], Anthony W. Kim[2], Cary P. Gross[3], James B. Yu[1] [1]*Therapeutic Radiology, Yale School of Medicine, New Haven/CT/United States of America,* [2]*Surgery, Yale School of Medicine, New Haven/CT/United States of America,* [3]*Internal Medicine, Yale School of Medicine, New Haven/United States of America*

Background: One of the major challenges to delivering coordinated oncologic care is multimodality management. While it has been hypothesized that providing all treatment in a single institution ("integrated") may improve access and outcomes, it is unclear whether outcomes are affected by receiving treatment at more than one facility ("nonintegrated"). Our aim was to determine whether integration of concurrent

chemoradiation therapy (CCRT) at a single center impacts outcomes for patients with locally advanced non-small cell lung cancer (NSCLC). **Methods:** Using the National Cancer Data Base, we identified adult patients with stage III NSCLC diagnosed in 2010-2011. We included non-surgical patients who underwent CCRT with thoracic radiotherapy to 59.4-74.0 Gy delivered at the reporting facility. Demographic, clinicopathologic, and healthcare system characteristics were compared among patients receiving integrated vs. nonintegrated therapy using hierarchical mixed-effects logistic regression analysis with clustering by reporting facility and bootstrapping. Overall survival was compared using Kaplan-Meier analysis, the log-rank test, and Cox proportional hazards regression analysis. Time from diagnosis to radiotherapy initiation was compared using the Wilcoxon rank-sum test given a non-normal distribution. **Results:** A total of 2,794 patients were included, among whom 1,695 (61%) received integrated therapy and 1,099 (39%) received nonintegrated therapy. Patients receiving integrated therapy were significantly more likely to have a Charlson-Deyo comorbidity score ≥1 (OR 1.67, 95% CI 1.24-2.24, p=0.001) and receive treatment at an academic center (OR 3.26, 95% CI 2.13-5.15, p<0.001) compared to those receiving nonintegrated therapy. In both unadjusted and adjusted analyses, there was no difference in overall survival among patients receiving integrated vs. nonintegrated therapy (HR 0.95, 95% CI 0.85-1.06, p=0.33). Time to radiotherapy initiation was also not significantly different among patients receiving integrated vs. nonintegrated therapy (median 35 vs. 36 days, p=0.06).



Conclusion: Our results demonstrate that administering CCRT at more than one facility may not adversely affect survival outcomes for patients with stage III NSCLC, suggesting that this approach may be reasonable based on individual patient preference and specialist availability. Further research is needed to determine the impact of integrated CCRT on tumor control and complication rates. **Keywords:** coordination, chemoradiation, survival, integration

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-010 Adjuvant Chemotherapy plus Radiotherapy is Superior to Chemotherapy in Surgically Treated IIIA N2 Non-Small-Cell Lung Cancer
Xiao-Ling Xu[1], Wei Chen[1], Weimin Mao[2], Weimin Mao[2] [1]*Zhejiang Cancer Research Institute, Hangzhou/China,* [2]*Zhejiang Cancer Hospital, Hangzhou/China*

Background: The role of addition radiotherapy for resected stage IIIA (N2) non-small cell lung cancer (NSCLC) in the setting of standard adjuvant chemotherapy remains controversial. **Methods:** A comprehensive search of PubMed, Embase, Medline database (last search updated in March 2015) for relevant studies comparing patients with stage IIIA (N2) NSCLC undergoing resection after treatment with adjuvant chemotherapy alone (POCT) or adjuvant chemoradiotherapy (POCRT) was conducted. Hazard ratios (HR) were extracted from these studies to give pooled estimates of the effect of POCRT on overall survival (OS) and disease free survival (DFS). **Results:** A total of six studies including two randomized controlled trials (RCTs) and four retrospective studies were enrolled in this meta-analysis. There were 6 studies that met criteria for analysis, including 2 RCTs and 4 retrospective reviews. The meta-analysis enrolling all studies (5172 cases) demonstrated an OS benefit to POCRT versus POCT (HR 0.87, 95% confidence interval [CI] 0.79 to 0.96, p = 0.006). DFS was investigated in four studies including 2 RCTs and 2 retrospective reviews. Unfortunately, there was no significant difference in DFS of two groups for the combined HR for PFS was 0.86 (95% CI: 0.70-1.06; p = 0.158). The sub-group analysis performed on two RCTs (n = 172 patients) demonstrated no benefit from adding radiation in neither OS (HR 0.72, 95% CI 0.49 to 1.06, p = 0.094) nor DFS (HR 1.45, 95% CI 1.00 to 2.09, p = 0.047). **Conclusion:** Compared with POCT, POCRT had a benefit for OS but not DFS in the patients with IIIA-pN2 NSCLC. Considering the relatively small sample size of most studies and only included two RCTs, caution should be taken when adopting the conclusions. Future RCT to investigate the role of POCRT after surgical resection of stage IIIA (N2) NSCLC is warranted. **Keywords:** NSCLC, N2-stage, therapy, surgery

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:3

P1.03-011 Standard Pre-Hydration May Compromise Treatment Outcome of CRT with Low-Dose Cisplatin
Else Aalbersberg[1], Linda De Wit - Van Der Veen[1], Erik Vegt[1], Maarten Smeekens[2], Michel Van Den Heuvel[2], Jose Belderbos[3], Wouter Vogel[1] [1]*Nuclear Medicine, NKI-AVL, Amsterdam/Netherlands,* [2]*Thoracic Oncology, NKI-AVL, Amsterdam/Netherlands,* [3]*Radiotherapy, NKI-AVL, Amsterdam/Netherlands*

Background: Cisplatin-based chemoradiation is the standard treatment for many types of cancer, including NSCLC. A main drawback of cisplatin is the high nephrotoxicity rate, that can be reduced by a stringent hydration regimen before, during, and/or after cisplatin administration. Standard pre-hydration with all cisplatin administrations is mandatory for high-dose cisplatin, and can be considered for low-dose cisplatin. However, it has recently been shown that pre-hydration not only reduces nephrotoxicity, but also reduces esophageal toxicity in lung cancer patients treated with concurrent daily low-dose cisplatin. This suggested that pre-hydration might systemically lower cisplatin dose in tissues, including in the tumor, and may therefore adversely affect treatment outcome. **Aim**: The aim of this study was to determine (1) if pre-hydration lowers cisplatin concentrations in tumor tissue in a mouse model, and (2) if the introduction of standard pre-hydration for low-dose cisplatin has adversely affected treatment outcome in lung cancer patients. **Methods:** Tumor-bearing Balb/c nude mice with cisplatin sensitive tumors were either pre-hydrated with saline, dehydrated, or had no intervention (control) before a single administration of cisplatin 6mg/kg or 3mg/kg. Renal function was assessed with MAG3 scintigraphy at 1, 24, 72, or 168h after treatment, and mice were subsequently sacrificed to determine tumor platinum concentrations. For the patient study, all stage III NSCLC patients who received daily concurrent low-dose cisplatin and radiotherapy in the NKI-AVL between 01-2007 and 06-2014 were evaluated for PFS. Patients treated in 2007-2010 (n=224) started pre-hydration with 1L saline only after renal function loss was detected, while patients treated in 2011-2014 (n=216) received standard pre-hydration from treatment day 1. **Results:** Pre-hydration protected mice from nephrotoxicity caused by cisplatin and dehydration worsened nephrotoxicity, confirming the validity of the mouse model. Pre-hydration significantly reduced tumor platinum concentrations (down to 50% of control mice at 1h after treatment, and comparable to mice treated with only half the dose of cisplatin), and dehydration increased tumor platinum concentrations. In patients the pre-hydration cohort demonstrated a shorter PFS (median 14 vs. 11 months, log-rank p=0.06), against the trend of gradually improving treatment outcome over the past decades. **Conclusion:** Pre-hydration reduces tumor platinum levels in mice, comparable to giving only half a dose of cisplatin. Patients treated with standard pre-hydration show a tendency to a lower PFS compared to patients with pre-hydration on indication. Further research is needed to elucidate this phenomenon. Meanwhile the application of standard pre-hydration in low-dose cisplatin regimens may be reconsidered. **Keywords:** NSCLC, Cisplatin, Prehydration

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-012 Combined Effects of SAHA and Cisplatin on Radiation Sensitivity and Cancer Cell Invasion in NSCLC
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Background: Lung cancer is a leading cause of cancer mortality worldwide. In an effort to improve local control of the disease and to increase survival, concurrent chemoradiotherapy has been explored as a therapeutic option. Of them, cisplatin-based chemoradiotherapy is currently used as first line therapy for non-small-cell lung cancer (NSCLC). However, the chemotherapeutic agents cannot be administered for most patients at full doses safely with radical doses of thoracic radiation, and thus further optimizations of chemotherapy regimen to be given with radiation are needed. **Methods:** We examined the effects of suberoylanilide hydroxamic acid (SAHA) and cisplatin on DNA damage repairs using U2OS reporter cells and in vivo end-joining assay, and determined the combination effects of SAHA and cisplatin on various cell lines, primary tumor tissues and in vivo xenograft in response to irradiation. We also investigated the potential differentiation effect of SAHA and its consequent effect on cancer cell invasion in cisplatin-treated cancer cells. **Results:** Our data demonstrated that SAHA and cisplatin compromised distinct DNA damage repair pathways. Treatment with SAHA enhanced synergistic radiosensitization effects of cisplatin in NSCLC cells, and induced prolonged persistence of γ-H2A.X nuclear foci in irradiated primary NSCLC tumor tissues treated with cisplatin. SAHA combined with cisplatin also significantly increased inhibitory effect of ionizing radiation on tumor growth in mouse xenograft model. In addition, we showed here that SAHA could induce differentiation in stem cell-like cancer cell population, reduce tumorogenesity and decrease the invasion/migration capabilities of human lung cancer H460 cells. **Conclusion:** Our results suggest a potential clinical impact for SAHA as a radiosensitizer and as a part of chemoradiotherapy regimen for NSCLC. The strategy may also benefit those patients with high risk of cancer metastasis. **Keywords:** SAHA, radiosensitivity, HDAC inhibitor, lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-013 Clinical Characteristics and Survival in Stage IIIA NSCLC Patients Treated with Neoadjuvant Chemotherapy and Surgery Narjust Duma[1], Claudia Miranda[1], Chad Glisch[1], Harry D. Harper[2], Martin Gutierrez[2] [1]*Internal Medicine, Rutgers-New Jersey Medical School, Newark/NJ/United States of America,* [2]*Medical Oncology, Hackensack University Medical Center, Hackensack/NJ/United States of America*

Background: The role of surgery in the management of stage IIIA non-small cell lung cancer (NSCLC) is controversial, with several studies reporting mixed results regarding the benefit of surgery in this group of patients. This study aimed to analyze the clinical characteristics and prognostic factors in stage IIIA patients treated with neoadjuvant chemotherapy followed by surgery. **Methods:** We reviewed the medical records of all patients diagnosed with stage IIIA NSCLC at our institution from 2000 to 2012. Tissue diagnosis and PET-Scan at our institution were required. Median follow up was 36 months. Cox regression model was used for multivariate analysis. **Results:** A total of 275 stage IIIA patients were identified, and 84 of those patients were treated with induction chemotherapy followed by surgery. Median age at diagnosis was 65 years (range: 42-82). There were more males than females (68% vs. 32%). 64% of the tumors were located in the upper, 24% lower and 12% middle lobe. Adenocarcinoma was the most prevalent histologic subtype (69%) followed by squamous cell (24%). 57% were poorly differentiated tumors. All patients received cisplatin based chemotherapy; response to induction therapy was: CR 0%, PR 55%, and SD 44%. Median time from induction chemotherapy to surgery was 80 days (range: 15-126). About surgery: 69% were lobectomies, 26% pneumonectomies and 5% wedge resections. Post-operatively, microscopic residual tumor was found in 8% of the patients. Pneumonectomies had a higher post-operatively mortality when compared with lobectomies (5% vs 2%). 50% of the patients received post-surgical radiation. Median overall survival was 19.5 months (95%CI: 14.5-26.7) and when comparing these patients with stage IIIA patients that received chemoradiation alone, a survival benefit was observed (19.5 months vs. 15.8 months). Recurrence was observed in 26% of the patients (64% had local and 36% distal recurrence). Patients that did not receive radiation had a higher risk of recurrence. Male gender (OR: 0.33, p<0.002), age>65 (OR: 2.61, p<0.03) tumor size >4cm (OR: 3.10, p<0.01) and partial response with induction therapy (OR. 0.69, p<0.005) were significant predictors of survival in this group of patients. **Conclusion:** In our cohort, we observed that patients who underwent induction chemotherapy followed by surgery had a higher overall median survival than patients treated with chemoradiation alone. Gender, age, tumor size and response to induction therapy were independent and significant predictors of survival in these patients. Adding radiation therapy to the regimen was associated with a lower recurrence rate. Further research is needed to identify the optimal management of stage IIIA NSCLC as well as the effect of other clinical characteristics on survival. **Keywords:** Stage IIIA, Predictors of Survival, Multimodality treatment

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-014 Is Concomitant Chemoradiotherapy Feasible for Patients with NSCLC Stage III A/B? Femke S. Van Der Meer[1], Franz Schramel[1], Sherif El Sharouni[2], Marco Van Vulpen[2] [1]*Department of Pulmonology, St. Antonius Hospital, Nieuwegein/ Netherlands,* [2]*Radiotherapy, University Medical Center Utrecht, Utrecht/Netherlands*

Background: In patients with NSCLC approximately 25% has locally advanced disease. For the group of patients with mediastinal lymph node metastasis the standard treatment consists of concomitant chemoradiotherapy. Concomitant chemoradiotherapy improves survival compared to sequential chemoradiotherapy in patients with locally advanced NSCLC, but has a higher toxicity. **Methods:** This is a retrospective cohort analysis of all patients with NSCLC stage IIIA/B treated in our hospital from 2008-2011. We reviewed primary treatment plans in all patients and evaluated patients primarily treated with sequential and concomitant chemoradiotherapy. Reasons to choose sequential treatment instead of concomitant treatment were reviewed. In both treatment groups completing of treatment and causes to discontinue treatment were explored. **Results:** 180 patients with NSCLC stage IIIA/B (103 stage IIIA, 77 stage IIIB) were treated in our hospital between 2008 and 2011. Surgery was the primary treatment in 28 patients (16%), chemotherapy in 22 patients (12%), radiotherapy in 16 patients (8%), best supportive care was agreed on in 32 patients (18%). In 78 (43%) patients the primary treatment was chemoradiotherapy, of who 31 were planned to receive concomitant treatment and 47 were planned to receive sequential treatment. Most frequent reasons to choose sequential instead of concomitant chemoradiotherapy were: radiation field too large (N=24) and physical condition (co-morbidity, age, poor performance score or poor lung function; N=17). Other reasons to start sequential therapy were: planning to evaluate the possibility of resection after chemotherapy (N=1), no pathological diagnosis (N=1), suspicion of second tumor (N=1) or unknown (N=3). In 20 of the 31 patients planned for concomitant chemoradiotherapy, total treatment was completed. Two patients deceased before start of therapy, five patients switched to sequential planning before start of therapy because of patients wish (N=1), radiation field too large at CT planning at radiotherapy (N=3), suspicion of cerebral tumor: (N=1) or decrease of performance score (N=1). In two patients treatment was disturbed by toxicity: one patient developed a pulmonary cavitating infection, radiotherapy was discontinued after 20Gy, the other patient switched to sequential schedule after a pulmonary infection during the first treatment cycle. In 32 of 47 patients planned for sequential therapy treatment was completed. One patient deceased before start of therapy. In one patient the radiation field was still too large after chemotherapy. Three patients developed hemoptysis and were treated primary with radiotherapy. Three patients discontinued treatment because of disease progression. Three patients discontinued during chemotherapy because of kidney failure(N=1) or other toxicity (N=2). Of one patient cause of discontinuation was not documented. One patient showed mediastinal downstaging after chemotherapy and a resection was performed. **Conclusion:** Although concomitant chemoradiotherapy is the standard of care in patients with stage IIIA/B NSCLC, more than 50% of the patients were treated otherwise. Only 17% of the patients were eligible for concomitant chemoradiotherapy. Most frequent reasons to refrain from concomitant chemoradiotherapy were the size of the radiation field and performance status of the patients (87%). **Keywords:** Chemoradiotherapy, Concomitant, Sequential, Non-small cell lungcancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-015 Safety and Effectiveness of Chemo-Radiotherapy with Weekly Nab Paclitaxel plus Carboplatin in Locally Advanced Non-Small Cell Lung Cancer Toshiyuki Sawa[1], Takaaki Hasegawa[2], Tsutomu Yoshida[1], Takashi Ishiguro[1], Akane Horiba[3], Yohei Futamura[4], Yasushi Ohno[5], Tatsuo Katoh[6], Shinya Hayashi[7] [1]*Respiratory Medicine and Oncology, Gifu Municipal Hospital, Gifu/Japan,* [2]*Gifu Municipa Hospital, Ggifu/Japan,* [3]*Gifu Municipal Hopsital, Gifu/Japan,* [4]*Gifu Municipal Hospital, Gifu/ Japan,* [5]*Respiratory Medicine, Gifu University, Gifu/Japan,*[6]*Nagara Medical Center, Gifu/ Japan,* [7]*Gifu University, Gifu/Japan*

Background: Combination therapy of carboplatin (CBDCA) and nab-PTX is a useful choice for first-line therapy of patients with advanced non-small cell lung cancer (NSCLC). The efficacy and safety of weekly albumin-bound paclitaxel (nab-PTX) and carboplatin (CBDCA) with concurrent radiotherapy for unresectable locally advanced non-small cell lung cancer was evaluated as a multicenter phase II study of Gifu thoracic oncology group. **Methods:** Patients with stage III NSCLC and an Eastern Cooperative Oncology Group performance status of 0 or 1 were eligible. Concurrent chemoradiotherapy consisted of weekly administration of nab-PTX (40 mg/m^2) plus CBDCA (area under the plasma concentration time curve (AUC) 2) and thoracic radiotherapy (60 Gy/30 fractions) for a total of 6 weeks. The primary tumor and involved nodal disease received 60 Gy in 2-Gy fractions over 6 weeks. A three dimensional treatment planning system was used in every institute. After concurrent chemoradiotherapy, patients received an additional two cycles of consolidation phase chemotherapy that consisted of 4-week cycles of nab-PTX (100 mg/m^2 on days 1, 8, and 15)/CBDCA (AUC 5 mg/ml/min on day 1). Response was evaluated in accordance with the RECIST. Progression-free and overall survival were estimated using the Kaplan Meier method. Toxicity was graded using the National Cancer Institute Common Terminology Criteria for Adverse Events. **Results:**The study became way canceled for serious adverse events, when the 10 cases were enrolled in this trial between September 2013 and January 2014 from 3 institutes. Patient characteristics are summarized as follow. The median age was 73 years. The ECOG performance status was 0 for 30% of patients and 1 for 70% of patients. Of these patients, 5 cases had squamous cell carcinoma and 5 cases had adenocarcinoma. The overall response rate was 40.0% and the median progression-free survival was 6.7 months. total of 7 patients were unable to complete the consolidation phase chemotherapy because of toxicities (pneumonitis, lung infection, or heart failure), poor PS, or patient preference. The most common grade 3/4 hematological toxicity was leukopenia (8 patients, 80%). Other grade 3/4 hematological toxicities were neutropenia (5 patients, 50%) and anemia (1 patient, 10%). Other grade 3 or worse severe toxicities were anorexia (3 patients, 30%), nausea (2 patients, 20%), diarrhea (1 patient, 10%), pneumonitis (2 patients, 20%), heart failure (2 patients, 20%), and lung infection (1 patient, 10%). Treatment-related death occurred in two patients. Grade 2 or worse severe pneumonitis was observed in all 3 patients that had volume of lung receiving at least 20 Gy (V20) >30%. **Conclusion:** The results of this study indicate that no further investigation is warranted into nab-PTX and CBDCA with concurrent thoracic radiation using three dimensional treatment planning system for stage III NSCLC with V20 >30% due to severe toxicity. **Keywords:** thoracic radiation, carboplatin, non-small cell lung cancer, nab-paclitaxel

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-016 Clinical Outcome of Hybrid-Volumetric Arc Therapy (H-VMAT) for Advanced Inoperable Non-Small Cell Lung Cancer (NSCLC) Oscar S.H. Chan, Albert W.M. Hung, Amy T.Y. Chang, Lucy L.K. Chan, Connie C.C. Chan, R M W Yeung *Department of Clinical Oncology, Pamela Youde Nethersole Eastern Hospital, Hong Kong/ Hong Kong*

Background: H-VMAT is a mix of rotational arcs and static beams. Our previous published planning study indicates that H-VMAT is superior in dosimetric outcomes: improved conformity with better sparing of lung and spinal cord, compared to VMAT alone or conformal radiotherapy (CRT). While there are many planning studies, reports on clinical outcomes in IMRT especially VMAT for NSCLC are relatively sparse. **Methods:** This retrospective study included inoperable stage IIA-IIIB NSCLC patients treated with H-VMAT or IMRT between late 2009 and 2013. Patients underwent simulation using 4D-CT. PET-CT data were fused with simulation images to enhance target delineation. H-VMAT composing of 2 hemi-arcs plus 2 static fields or 5-9 fields IMRT technique was used. Precision of treatment delivery was ensured by on-board kilovoltage imaging, mainly cone-beam CT. Survival outcomes, dosimetric data, patient characteristics and complication profiles were analysed. **Results:** A total of 71 patients were included. Patients characteristics and dosimetric parameters were tabulated in table one. The median follow-up was 2.5 years for alive subjects. The median prescribed dose was 60Gy. Three patients did not complete the planned treatment. The estimated 5-year overall survival (OS) was 19.2% (Figure 1a). Patients receiving sequential chemotherapy or chemo-radiotherapy fared much better than RT alone (Figure 1b). The 3-year disease-free survival was 12.7% in RT alone group and 17.0% in chemo-radiotherapy group. Two grade 3 esophagitis and three ≥grade 3 radiation pneumonitis were noted. Two treatment death were considered related to radiation pneumonitis, with superimposed chest infection. Compared to an unmatched historic cohort treated in 2004-08 using CRT, a trend of improvement in OS

was observed (Figure 1c). Multivariate analysis demonstrated that GTV-volume and use of chemotherapy were important predictors in OS (both p <0.01).

Patient demographics and dosimetric data (n=71)		
Age	median (range)	68 (34-89)
Gender	male: female	52: 19
Histology	Adenocarcinoma	29
	Squamous cell carcinoma	22
	Not otherwise specified	15
	Others	5
PET-CT Staging		65(91.5%)
Group Stage (7th Ed.)	IIA	3 (4.2%)
	IIB	9 (12.7%)
	IIIA	46 (64.8%)
	IIIB	13 (18.3%)
RT Technique	H-VMAT/ IMRT	60/ 11
Chemotherapy	With vs. Without	43: 28
PTV D_{mean}	median/ Gray (range)	62.2 (61.2-77.3)
GTV volume	median/ cc (range)	91.3 (12.6-312.2)
PTV volume	median/ cc (range)	359.6 (99.5-1070.5)
V20 (Lung-CTV)	median/ % (range)	22.8 (3.7-34.9)
Max Cord Dose	median/ Gray (range)	41.3 (14.8-44.8)

Conclusion: H-VMAT/ IMRT together with chemotherapy resulted in favourable OS and low incidence of esophageal and pulmonary toxicities. **Keywords:** Volumetric Arc Therapy, intensity modulated radiotherapy, advanced NSCLC, survival

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-017 Radiation Dose-Related Lymphopenia as an Outcome Predictor in Stage III NSCLC Patients Treated with Chemoradiation Nooshin Hashemi Sadraei[1], Mahender Yellu[1], Farhad Fakhrejahani[2], Arun Sendilnathan[1], Nagla Abdel-Karim[1], John Morris[1], Tahir Latif[1], Michelle Mierzwa[1], Brdaley Huth[1], Kevin Redmond[1], William Barrett[1], Patrick Ma[3], Nathan Pennell[4], Jun Ying[5], Gregory M.M. Videtic[3]
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Background: RTOG 0617 failed to show survival advantage from increased radiation dose in stage III concurrent chemo radiation-treated patients. While toxicity was not significantly different between standard and high dose radiation groups, local-regional control and survival were inferior in high dose, experimental arm. These findings have largely remained unexplained. There is increased evidence in literature suggesting survival disadvantage associated with lymphopenia in certain malignancies. We hypothesize radiation-induced lymphopenia may be dose-dependent and may carry a survival disadvantage. **Methods:** Stage III NSCLC patients treated with curative chemoradiation were retrospectively studied. Patients were categorized into those receiving standard dose and those receieiving high dose (> 66Gy). Hematologic values including absolute lymphocyte count (ALC) was evaluated at diagnosis and at regular intervals during and after treatnent. Numerical variables were summarized using median (range) and compared between groups using non parametric Wilcoxon rank sum tests. Overall survival (OS) and other time to event endpoints were assessed using Kaplan-Meier (K-M) survival curves and compared between standard and high dose groups using log rank tests. **Results:** 182 patients with stage III NSCLC were identified. 77 % male, 52% adenocarcinoma, and 41% squamous cell carcinoma. 155 patients received SD RT and 27 received HD RT. Pre-treatment ALC were not different between Standard and High dose groups [1730 /ul vs. 2065/ul (p=0.4955)]. The High dose group showed lower Nadir ALC (279/ul vs 324/ul and shorter time to Nadir (29 d vs 35 d) than the Standar group (two sided p's =0.11and 0.06, and one sided p's=0.05, 0.03 respectively). The K–M survival curves showed that Standard dose group has better OS than the High dose group (31.3 m vs 11.4 m , p<0.001). For patients whose Nadir ALC >600 (about 80% percentile level of Nadir ALC), median survival was 37.8 month as compared to 18.2 month among those Nadir ALC≤600 (p=0.192). **Conclusion:** Our study showed sutrvival among patients treated with higher dose radiation was significantly worse. Although baseline absulte lymphocyte counts were not different between the two groups, patient treated with high dose radiation reached their nadir counts more quickly and also developed a lower absolute lymphocyte count compared to patients treated with standard dose. Regardless of treatment group, there was a trend towards a worse survival among patients who developed lower lymphocyte counts subsequent to traetment. **Keywords:** lymphopenia, stage III

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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P1.03-018 International Patterns of Radiotherapy Practice for Non-Small Cell Lung Cancer Shalini K. Vinod *Cancer Therapy Centre, Liverpool Hospital, Liverpool/NSW/ Australia*

Background: Radiotherapy is an important treatment modality for Non-Small Cell Lung Cancer (NSCLC). Models of radiotherapy utilization which evaluate the proportion on NSCLC patients who have an evidence-based indication for radiotherapy estimate a utilization of 46% -68% at diagnosis and 64%-75% during the overall course of the disease. The aim of this review was to document the actual use of radiotherapy for NSCLC patients and examine reasons for any discrepancies identified. **Methods:** A literature search was conducted using Medline and Pubmed databases to identify population-based studies, published in English, which reported the use of radiotherapy between 1990 and 2014. Reference lists of the identified studies were also scrutinised for further relevant publications. **Results:** Ten studies were identified from regions including North America, Europe, United Kingdom and Australasia. Actual radiotherapy utilization varied across these regions ranging from 20%-53%. In North America, actual utilization approached model estimates, but in the other regions actual utilization was lower than model estimates. The largest differences between actual and estimated radiotherapy utilization was seen in stage III NSCLC. Some of this discrepancy is attributable to the assumptions in the models which are based on broad factors such as stage and performance status. Characteristics of the underlying lung cancer population who often have comorbidities or compromised respiratory function also impact on the ability to deliver radiotherapy safely. Sociodemographic factors such as race and income have been found to affect access to radiotherapy in certain jurisdictions. The type of clinician or medical setting the patient presents to initially has also been found to influence radiotherapy use in NSCLC. **Conclusion:** Radiotherapy utilization for NSCLC is lower than that predicted by model estimates throughout much of the world. This is partly due to characteristics of the underlying lung cancer population which may preclude guideline-based treatment including radiotherapy. Physician characteristics and referral patterns can have a significant impact on the use of radiotherapy in NSCLC. Potential solutions to overcome this include restructuring models of care to ensure all lung cancer patients are managed within a multidisciplinary team including a radiation oncologist. **Keywords:** non-small cell lung cancer, Radiotherapy, patterns of care, treatment utilization

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-019 NTCP-Models for Esophagitis with Dose-Differentiated-Radiotherapy (DART-Bid) Franz Zehentmayr[1], Matthias Söhn[2], Ann-Katrin Exeli[1], Karl Wurstbauer[1], Almut Tröller[2], Heinz Deutschmann[1], Gerd Fastner[1], Christoph Fussl[1], Philipp Steininger[3], Manfred Kranzinger[1], Claus Belka[2], Michael Studnicak[4], Felix Sedlmayer[1] [1]*Dept. of Radiation Oncology, Paracelsus Medical University, Salzburg/Austria,* [2]*Dept. of Radiation Oncology, Ludwig-Maximilians-Universität, Munich/Germany,* [3]*Institute for Research and Development of Advanced Radiation Technologies, Paracelsus Medical University, Salzburg/ Austria,* [4]*Dept. of Pneumology, Paracelsus Medical University, Salzburg/Austria*

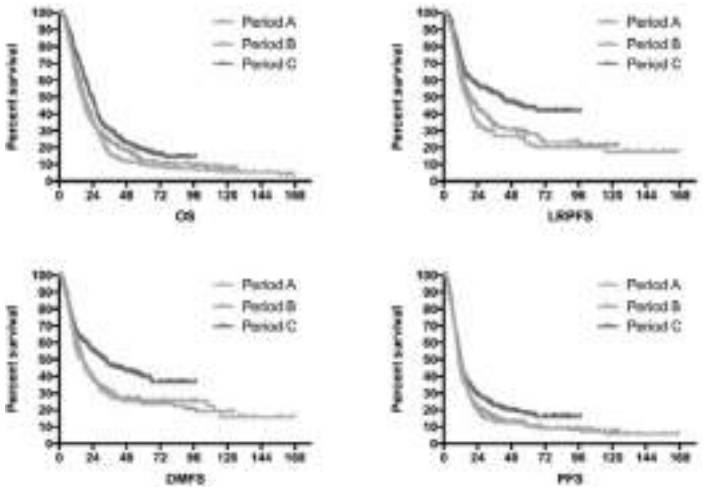
Background: The primary dose-limiting toxicity during thoracic irradiation is acute esophagitis (AE). The aim of this study is to investigate dosimetric and clinical predictors for AE grade ≥ 2 in patients treated with accelerated radiotherapy. **Methods:** 66 patients were included in the present analysis: 4 stage II, 44 stage IIIA and 18 stage IIIB. All patients received induction chemotherapy followed by dose differentiated accelerated radiotherapy (DART-bid). Depending on size (mean of three perpendicular diameters) tumors were binned in four groups: <2.5 cm 73.8 Gy, 2.5–4.5 cm 79.2 Gy, 4.5–6 cm 84.6 Gy, >6 cm 90 Gy. Patients were treated in 3D target splitting technique. In order to estimate the normal tissue complication probability (NTCP), two Lyman models and the cutoff-logistic regression model were fitted to the data with AE ≥ grade 2 as statistical endpoint. Toxicity was documented prospectively according to RTOG. **Results:** The median follow up was 686 days (range 84–2921 days), 23/66 patients (35%) experienced AE ≥ grade 2. The Lyman-MED model (D50=32.8 Gy, m=0.48) and the cutoff dose model (D_c=38 Gy) provide the most efficient fit to the current dataset. On multivariate analysis V38 was the most significant predictor of AE ≥ grade 2 (HR=1.05, CI 1.01–1.09, p=0.009). **Conclusion:** Following high-dose accelerated radiotherapy the rate of AE ≥ grade 2 is lower than reported for concomitant radio-chemotherapy with the additional benefit of markedly increased loco-regional tumor control. In the current patient cohort the most significant predictor of AE was found to be V38 (volume of the esophagus that receives 38 Gy or above, CI 28.2 – 57.3). **Keywords:** NTCP-modeling, Accelerated Radiotherapy, NSCLC

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-020 IMRT Improves Survival in Locally Advanced NSCLC (LA-NSCLC) Receiving Definitive Radiotherapy: A Population Based Time-Trend Analysis Jingbo Wang[1], Jianzhong Cao[2], Zhe Ji[2], Lipin Liu[2], Wei Jiang[2], Yu Men[2], Cai Xu[2], Luhua (Jingbo) Wang[1] [1]*Radiation Oncology, Cancer Hospital, Chinese Academy of Medical Sciences, Beijing/China,* [2]*Cancer Hospital, Chinese Academy of Medical Sciences, Beijing/ China*

Background: Currently intensity-modulated radiotherapy (IMRT) is regarded as a promising but unproven therapy for locally advanced non-small cell lung cancer (LA-NSCLC). This study aimed to evaluate the impact of introducing IMRT in LA-NSCLC based on patients receiving definitive radiotherapy (RT) throughout an 11-year span from an academic cancer center. **Methods:** Patients treated with definitive RT (≥ 50Gy) between

2000 and 2010 were divided into three eras according to availability of IMRT: 2000 to 2003 (period A, no IMRT, IMRT rate 0%), 2004 to 2006 (period B, introduction of IMRT, IMRT rate 3.5%) and 2007 to 2010 (period C, full access to IMRT, IMRT rate 85.6%). Patients' characteristics, treatment modality, survival and treatment related toxicities were compared between 3 periods. **Results:** A total of 946 patients were analyzed. Less smokers, more stage IIIA diseases and more patients receiving concurrent chemo-radiotherapy (CRT) were observed in period C. The median overall survival (OS), local-regional progression free survival (LRPFS), distant metastasis free survival (DMFS) and progression free survival (PFS) for the whole population, period A, B and C were 19.8 vs. 16.6 vs. 18.2 vs. 23.3 moths, 22.1 vs. 16.2 vs. 18.7 vs. 40.5 months, 20.7 vs. 17.1 vs. 17.0 vs. 33.1 months and 11.4 vs. 10.8 vs. 11.3 vs. 11.9 months, respectively. Accordingly, the 5-y OS, LRPFS, DMFS and PFS were 14.3% vs. 9.8% vs. 12.0% vs. 18.3%, 34.3% vs. 22.9% vs. 28.4% vs. 43.6%, 32.2% vs. 25.2% vs. 23.6% vs. 40.5% and 14.2% vs. 10.7% vs. 11.1% vs. 18.0%, respectively. All survival indexes significantly increased in period C (Figure 1). Multivariate analyses identified IMRT as the independently favorable indicators for all survival indexes. The incidence of radiation induced lung toxicity (RILT) significantly decreased in period C (32.2% vs. 24.9% vs. 12.8%, $p < 0.001$) whereas that of radiation induced esophagus toxicity (RIET) remained stable (29.4% vs. 39.0% vs. 33.1%, $p = 0.064$) throughout the overall study period.



Conclusion: IMRT was associated with improved tumor control, prolonged survival and decreased RILT, independent of treatment modality and radiation dose. **Keywords:** intensity modulated radiotherapy, time-trend analysis, survival, non small cell lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

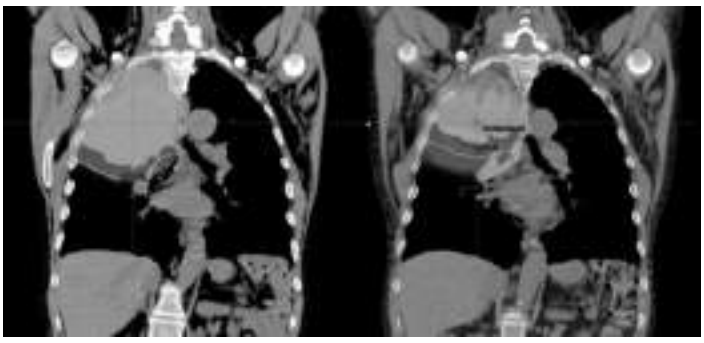
P1.03-021 Lung Damage Quantification on CT Scans Strengthens Radiation-Induced Lung Toxicity Prediction Models Gilles Defraene[1], Wouter Van Elmpt[2], Wouter Crijns[1], Pieter Slagmolen[3], Dirk De Ruysscher[1] [1]*Experimental Radiation Oncology, Ku Leuven, Leuven/Belgium,* [2]*Department of Radiation Oncology (Maastro), Grow-School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht/Netherlands,* [3]*Esat/Psi – Uz Leuven, Mirc – Iminds, Medical It Dept., Ku Leuven, Leuven/Belgium*

Background: Predictive models for radiation-induced lung toxicity have shown a lack of validation and low values of area under the curve (AUC) below 0.7, for various reasons. Radiation-induced lung tissue damage scored as density changes on CT scans proved to be a less multifactorial endpoint compared to dyspnea. Its continuous variation in the patient population is an indication that it could be an expression of patient-specific radiosensitivity variation. This study explores the advantage of incorporating patient-specific lung damage measures in the classical predictive models based on mean lung dose (MLD). **Methods:** 61 stage I-IV lung cancer patients treated with chemoradiotherapy were retrieved from two hospitals. Prescribed dose was 66 Gy in fractions of 2 Gy (concurrent) or 2.75 Gy (sequential). Baseline and follow-up dyspnea scores were retrospectively assessed according to CTCAE 4.0. Image analysis of the radiation-induced lung damage was performed by comparison of the baseline planning CT_0 and the non-rigidly registered follow-up CT_{fup}: The median Hounsfield Unit increase ($\Delta HU = HU_{fup} - HU_0$) was calculated per dose bin of 5 Gy. The local dose-ΔHU response curve was described using a sigmoidal model. This resulted in a sigmoidal parameter D_{50} (corresponding to 50% of the saturation level of ΔHU) for each patient, as an expression of the patient-specific lung tissue radiosensitivity. Logistic models predicting dyspnea increase with respect to the baseline score were then built using MLD and D_{50} as covariates. The likelihood-ratio identified significant differences between nested models. **Results:** Dyspnea score increase by 2 grades was observed in 9 patients (14,8%), while an increase by 1 grade was observed in 29 patients (47.5%). The average timepoint of CT_{fup} was 2.3 months after end of radiotherapy. For 51 patients the sigmoidal dose-ΔHU fits were acceptable (sum of squared residuals below 10 HU per datapoint on average). 10 of these patients did not show any dose response in the analysed dose range. The 41 reacting patients showed large variation in D_{50} (median: 34.8 Gy, range: 12.1 Gy-70.0 Gy) and were further analysed. Predictive models based on MLD alone had AUCs of 0.71 and 0.65 for dyspnea increase by 1 and 2 grades respectively. Incorporating the CT damage measure D_{50} as second covariate resulted in models with 0.73 and 0.83 respectively. The advantage of incorporating D_{50} was significant in the second fit ($p=0.05$). **Conclusion:** A significant improvement of predictive models for radiation-induced lung toxicity was achieved using patient-specific lung damage measured on CT scans. An early detection of the patient-specific D_{50} through dedicated per-treatment imaging optimized for the detection of lung tissue changes is crucial for the clinical implementation of the model. Future work analysing more CT features could also improve the model. **Keywords:** radiation-induced lung toxicity, lung damage, CT, radiosensitivity

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-022 The Effect of Adaptive Planning on Target and Critical Structures During Radiation Treatment for Locally Advanced Lung Cancer Hale B. Caglar, Esra Kucukmorkoc, Ayse Altinok, Nadir Kucuk, Mine Doyuran, Hilal Acar
Radiation Oncology, Medipol University Hospital, Istanbul/Turkey

Background: Many patients with lung cancer have tumor changes like shrinkage, improvement in atelectasis or mediastinal replacement during radiotherapy. The aim of this study is to determine the dosimetric effects of repeated CT scanning and adaptive planning during intensity modulated radiotherapy (IMRT) on both target volumes and critical structures. **Methods:** Patients treated with concurrent chemoradiation were included within the study. The initial IMRT planning ($IMRT_{initial}$) was done on the primary CT and 4DCT scan using the ITV technique. The dose was prescribed to 66 Gy in 33 fractions. After the initiation of the study weekly cone beam CT (CBCT) images were obtained before treatment. The volumes were evaluated by the treating physician in terms of target volume changes or mediastinal replacement. When adequate change was distinguished on the CBCT images an adaptive CT (CT_{adapt}) was obtained and the volumes were recontoured by the same physician and replanned by the same physicist ($IMRT_{adapt}$). The calculated multileaf collimator (MLC) motion on $IMRT_{initial}$ was transferred on CT_{adapt} and a recalculation was performed. The plan obtained was renamed as $IMRT_{transfer.}$ The changes occurred in critical organs such as lung, spinal cord, heart, esophagus and the target volumes were obtained and compared with $IMRT_{initial}$ using paired samples t-test. **Results:** A total of 15 patients were included in the analysis. The mean PTV volumes on initial and adaptive planning CT scans were significantly different (791 vs 498 cc; $p<0.001$). Significant changes were observed in lung doses between $IMRT_{initial}$ vs $IMRT_{transfer}$ and $IMRT_{adapt}$ vs $IMRT_{transfer}$ (mean V5, 50% vs 54%, $p=0.001$ and 40% vs 54%, $p=0.003$; mean V20, 24% vs 28% $p<0.001$ and 20% vs 28%, $p<0.001$). Spinal cord dosed also significantly changed on these 3 plans (mean Dmax on $IMRT_{initial}$ vs $IMRT_{transfer}$ and $IMRT_{adapt}$ vs $IMRT_{transfer}$ 41.4Gy vs 45.5Gy, $p=0.042$ and 37.8Gy vs 45.5Gy, $p=0.005$). The PTV coverage significantly changed in 3 patients because of replacement.



Conclusion: Repeat CT imaging and replanning during the course of IMRT for selected patients with lung cancer may help to identify dosimetric changes and to ensure safe doses to critical structures such as lung and spinal cord. With the implementation of adaptive treatments dose escalation may be possible in the future for improvements in clinical outcome without significant increase in toxicity. The anatomic changes seen throughout the treatment may increase the lung doses when replanning is not performed. **Keywords:** adaptive, Radiotherapy planning, lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-023 Changes in Pulmonary Function after Stereotactic Body Radiotherapy and after Surgery for Stage I and II Non-Small-Cell Lung Cancer Leonie Alberts[1], Sherif Y. El Sharouni[2], Frederik N. Hofman[3], Bart P. Van Putte[3], Ellen Tromp[4], Marco Van Vulpen[2], Robbert C. Van Heemst[5], Elisabeth A. Kastelijn[1], Franz M.N.H. Schramel[1] [1]*Pulmonology, St. Antonius Hospital, Nieuwegein/Netherlands,* [2]*Radiotherapy, University Medical Center Utrecht, Utrecht/Netherlands,* [3]*Cardiothoracic Surgery, St. Antonius Hospital, Nieuwegein/Netherlands,* [4]*Epidemiology and Statistics, St. Antonius Hospital, Nieuwegein/Netherlands,* [5]*Pulmonology, Deventer Ziekenhuis, Deventer/Netherlands*

Background: Although surgical resection is the standard treatment for stage I and II non-small-cell lung cancer (NSCLC), approximately 20% of these patients are not eligible for surgery. Stereotactic body radiotherapy (SBRT) is a good alternative treatment for these patients. Lung resection will lead to a decrease in pulmonary function. However, previous studies have shown that pulmonary function after SBRT remains either stable or shows a small decline post-SBRT. In this study changes in pulmonary function tests (PFTs) were evaluated at different follow-up durations, up to more than 2 years after treatment

in both groups. **Methods:** All patients diagnosed with stage I and II NSCLC and treated with SBRT or surgery between 2008 and 2011 at St. Antonius Hospital Nieuwegein, The Netherlands were included. There was no routine protocol for assessment of post-treatment PFTs. Therefore, follow-up durations were categorized in early (0-9 months), middle (10-21 months) and late (≥ 22 months). We assessed forced expiratory volume in 1 second (FEV1) and diffusion capacity to carbon monoxide corrected for the actual hemoglobin level (DLCOc) absolute and percentage of predicted values. Wilcoxon signed-rank test for paired samples was used to analyze statistical differences between baseline- and follow-up PFTs. **Results:** Among 230 patients, 123 patients had both pre- and a minimum of one post-treatment PFT. Of the 123 patients, 30 patients were treated with SBRT and 93 patients with surgery. Mean pre-treatment FEV_1 and DLCOc values were respectively 1.27 liter (54.90% of predicted) and 4.25 mL/min/mmHg (56.11% of predicted) in the SBRT group and 2.44 liter (88.38% of predicted) and 6.10 mL/min/mmHg (71.96% of predicted) in the surgery group. There were significant changes in FEV_1 and DLCOc after surgery for all follow-up durations. After SBRT, absolute FEV_1 values remained stable up to 22 months. After 22 months a statistical significant change was observed (from 1.27 liter pre-treatment to 1.11 liter (p=0.008). DLCOc was not significantly impaired after SBRT (from 4.25 mL/min/mmHg pre-treatment to 3.47 mL/min/mmHg (p=0.061)), and showed a small, non-significant, increase for the middle-follow-up term (to 5.22 mL/min/mmHg) compared to pre-treatment values. **Conclusion:** Surgery results in a decline of pulmonary function short after resection and on long-term, for stage I and II non-small-cell lungcancer. Pulmonary function after SBRT showed a non-significant decline, except for absolute FEV_1 values at long-term follow-up. Further analysis of these data must reveal if these changes are clinically significant. **Keywords:** Stereotactic body radiation, Pulmonary Function, Surgery, stage I and II non-small-cell lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-024 Comparison of Prognosis Between Patients with Solitary Lung Adenocarcinoma and With Multiple Primary Cancers Including Lung Adenocarcinoma Eunjue Yi[1], Hyun Hwak Shin[1], Hyo-Jun Jang[1], Mi Kyung Bae[2], Sukki Cho[1], Kwhanmien Kim[1], Sanghoon Jheon[1] [1]*Seoul National University Bundang Hospital, Seongnam-Si/Korea,* [2]*National Health Insurance Service Ilsan Hospital, Goyang-Si/Korea*

Background: As advances in diagnostic tools and treatment methods, patients with multiple primary cancers are expected to increase. We investigated the prognosis of multiple primary cancer patients who underwent surgical management for lung adenocarcinoma, and compared it with that of patients who suffered from lung adenocarcinoma only. **Methods:** Medical records of lung adenocarcinoma patients who underwent surgical management in our institute between 2003 and 2012 were reviewed retrospectively. Patients with multiple primary lung cancer, either synchronous or metachronous, and patients underwent neoadjuvant therapy were excluded. We categorized enrolled patients into 2 categories; (1) Group 1; patients with lung adenocarcinoma only, (2) Group 2; patients with lung adenocarcinoma and other primary cancers. Clinicopathologic characteristics were compared between two groups, and survival analysis was done. **Results:** A total of 964 patents were enrolled in this study, and 17.7% have primary cancers other than lung adenocarcinoma (Group 1; 793, and Group 2; 171). Mean follow-up periods were 55.1 months (± 29.00, ranged from 0.0 to 139.2 months), and mean age at the time of surgery were 62.0 (± 10.51, ranged from 20 to 91). There were no significant differences in gender between two groups (p=0.400), however, the mean age of Group 2 was higher in Group 2 (p=0.005). The SUVmax value and tumor sizes were higher in Group 1 (p<0.000 and p<0.000 respectively). The presence of visceral pleural invasion, EGFR mutations and p53 showed no significance between two groups (p=0.322, p=0.728 and p=0.966 respectively). N stages were higher in Group 1 than group 2 (p=0.026). Overall 3-year and 5-year survival rates in Group 1 (87.0% and 80.6%) and Group 2 (89.1% and 80.6%) showed no statistically significant differences (p=0.926), Likewise, those of disease-free survival rates in two groups (71.1% and 66.5% in Group 1, 78.0% and 74.4% in Group 2) revealed no significant differences (p=0.054). **Conclusion:** Patients of lung adenocarcinoma with multiple primary cancers showed no prognostic inferiority, and the stages of lung cancers tended to be lower. Careful inspections for finding other malignancies in multiple primary cancer patients can contribute to reduce lung cancer mortality. **Keywords:** lung adenocarcinoma, multiple primary cancers, Prognosis

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-025 Relation of Visceral Pleura Invasion with Hilar Lymph Node Involvement and Survival in Primary Lung Cancer Serhan Tanju[1], Suat Erus[2], Yusuf Bayrak[3], Nil Molinas Mandel[4], Şükrü Dilege[1] [1]*Thoracic Surgery, Koç University School of Medicine, Istanbul/Turkey,* [2]*Thoracic Surgery, Koç University Hospital, Istanbul/Turkey,* [3]*Thoracic Surgery, Vkf American Hospital, Istanbul/Turkey,* [4]*Medical Oncology, Koç University School of Medicine, Istanbul/Turkey*

Background: The aim of this study is to investigate the role of visceral pleura invasion on hilar lymph node involvement and survival in surgically treated primary lung cancer patients. **Methods:** We examined pathological data of 219 surgically treated primary non-small cell lung cancer patients operated between january 2006 & March 2012. Patients were divided into three groups. Group 1: Patients with a tumor entrapped within the thick elastic layer (PL0), Group 2: Patients with tumor crossed the elastic layer of visceral pleura (PL1), Group 3: patients with a tumor crossed the elastic layer and reached the surface of visceral pleura (PL2). Patients with parietal pleura invasion (PL3) and operative mortality (45 patients) were excluded from the study. Groups were examined in terms of tumor size, mediastinal involvement, lymphovasculary invasionand survival. **Results:** Visceral pleura invasion (PL1 and PL2) was detected in 56 of 174 surgically treated patients (32.1%). In this group, PL1 was found in 43 patients (24.7%) and PL2 was found in 13 patients (7.4%). Mean follow-up was 48.68±27.47 months (4-106). We found that visceral pleura invasion statistically significantly reduce survival independently from hilar/mediastinal lymph node involvement (N1-N2) and tumor size (mean survival 53.78±28.91 vs 37.95±20.54 months, p=0.001). Also we found that the ratio of the presence of hilar lymph node involvement with visceral pleura invasion is statistically higher than the group without visceral pleura invasion (30.9% vs 18.1% p=0.03). There were no statistically significance in terms of survival between the groups PL1 and PL2 (mean survival 39.23±20.01 vs 33.69±22.49 p=0.39). **Conclusion:** We should consider adjuvant treatment independently from tumor size and lymph node involvement for patients with visceral pleura invasion. **Keywords:** visceral pleura invasion, survival, lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-026 Prognostic Value of Pre-Treatment Neutrophil:Lymphocyte Ratio and Platelet:Lymphocyte Ratio in Stage III NSCLC Kylie H. Kang[1], Neelesh Sharma[2], Mitchell Machtay[3], Tithi Biswas[3] [1]*Radiation Oncology, Sideman Cancer Center, Case Medical Center, Cleveland/United States of America,* [2]*Medical Oncology, Sideman Cancer Center, Case Medical Center, Cleveland/United States of America,* [3]*Radiation Oncology, Sideman Cancer Center, Case Medical Center, Cleveland/OH/United States of America*

Background: Stage III locally advanced NSCLC is a challenging disease with poor outcome. The currently accepted treatment consideration is definitive chemo-radiation with the addition of surgery for selected patients. There are few if any reliable predictors for treatment outcome in these patients. Recent studies have suggested that the pre-treatment presence of systemic inflammatory response, as indicated by the neutrophil/lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR), may be useful prognostic factors. Thus, we undertook this retrospective analysis of stage III NSCLC to examine the role of pre-treatment NLR and PLR as a predictor of outcome and also to compare the value of surgery in addition to chemo and radiotherapy. **Methods:** A total of 107 patients with stage III disease were identified from our institutional lung cancer database. Patients were staged as per AJCC system, 7th edition. Patients with N0 or N1 status were excluded. The following information was collected from their electronic medical records as available: age, gender, substage, histology, grade, baseline blood work, and treatment type. NLR was defined as the ratio between neutrophil and lymphocyte count and PLR was defined as ratio between platelet and lymphocyte count, measured prior to any cytotoxic therapy. We studied both median value and NLR ≥5 in order to categorize patients as high- or low-NLR group. Median PLR was used to categorize as high- or low-PLR group. The recurrence-free (RFS) and overall (OS) cumulative probability of survival was calculated by the Kaplan-Meier method, and the difference was assessed by the log-rank test. **Results:** The median age at diagnosis was 62 years (range: 44 - 87) and 50% (n=53) were male. The median follow-up was 25 months. The most common histology was adenocarcinoma (60%, n=64) followed by squamous cell cancer (19%, n=20), large cell carcinoma (4%, n=4) while rest had NSCLC not specified. Most (54%) were of poor grade and 17% were grade 2. Only 3% had grade 1 tumor while it was not reported in 26% cases. The T stage distribution was T1 (20%, n=21), T2 (35%, n=38), T3 (17%, n=18), T4 (26%, n=28). 66 (62%) patients underwent concurrent CRT while 41 (38%) patients had surgery as a part of their treatment, with 17 (42%) underwent surgery following neoadjuvant therapy while 23 (56%) patients had upfront surgery. Surgery in any form was associated with improved RFS (p=0.013, log-rank) but not OS (p=0.074, log-rank). A higher baseline PLR ratio was associated with inferior OS (p=0.044, log-rank), but there was no significant association between NLR for either RFS or OS. **Conclusion:** This is a retrospective series of advanced NSCLC suggesting benefit in RFS but not in OS with addition of surgery as the third modality in the definitive treatment. A higher baseline PLR was associated with inferior survival, suggesting potential prognostic value but not NLR. Further analysis is underway for a multivariate model. **Keywords:** NSCLC, stage III, chemo-radiation

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-027 Factors Predicting Lymph Node Metastasis in Resected Lung Adenocarcinoma of 2cm or Smaller Jung-Jyh Hung[1], Yu-Chung Wu[2], Teh-Ying Chou[1], Wen-Hu Hsu[2] [1]*Taipei Veterans General Hospital and National Yang-Ming University, Taipei/Taiwan,* [2]*Taipei Veterans General Hospital, Taipei/Taiwan*

Background: The predictive value of the new International Association for the Study of Lung Cancer, American Thoracic Society and European Respiratory Society (IASLC/ATS/ERS) classification of lung adenocarcinoma predicting lymph node metastasis in lung adenocarcinoma has not been well demonstrated. The aim of the study is to demonstrate factors associated with lymph node metastasis in patients with resected lung adenocarcinoma of 2 cm or smaller. **Methods:** The clinicopathological characteristics of 246 patients with completely resected lung adenocarcinoma of 2cm or smaller at Taipei Veterans General Hospital between 2004 and 2012 were retrospectively reviewed. The association between clinicopathological variables and lymph node metastasis was analyzed by univariate and multivariate logistic regression. **Results:** Among the 246 patients, there were 215 (87.4%) patients with N0 status, 13 (5.3%) with N1 status, and 18 (7.3%) with N2 status. Greater tumor size (P < 0.001) and predominant pattern group (micropapillary/solid predominant) (P = 0.001) were significantly associated with higher percentage of N1 or N2 lymph node metastasis. In multivariate analysis, greater tumor size (P < 0.001), and micropapillary/solid predominant pattern (P = 0.029) were significant predictors of N1 or N2 lymph

node metastasis in tumors of 2cm or smaller. Micropapillary/solid predominant pattern ($P = 0.031$) was also a significant predictor of N2 lymph node metastasis in multivariate analysis. **Conclusion:** Tumor size and histological subtypes were significantly associated with lymph node metastasis in lung adenocarcinoma of 2cm or smaller. Micropapillary/solid predominant pattern is a significant predictor of lymph node metastasis. **Keywords:** Adenocarcinoma, lymph node metastasis, histology, predictor

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-028 Multicenter Study of the Usefulness of FDG-PET as a Predictor of the Clinicopathological Characteristics and Prognosis of Lung Cancer
Norihiko Ikeda[1], Yasufumi Kato[1], Tatsuo Ohira[1], Haruhiko Nakayama[2], Morihito Okada[3]
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Background: This multicenter study aimed to investigate the performance of standardized uptake value (SUV) on [18F]-fluoro-2-deoxy-d-glucose positron emission tomography (FDG-PET) as a predictor of the clinicopathological characteristics and prognosis of resected lung cancers. **Methods:** A total of 721 patients underwent curative resection with systematic lymph node dissection. The relationship among histological characteristics, pathological staging, prognosis, and SUV on FDG-PET was retrospectively examined. **Results:** There were 107 squamous cell carcinomas and 614 adenocarcinomas. The pathological stages of the cases were IA 408, IB 162, IIA 57, IIB 23, IIIA 65, IIIB 1, and IV 5. The SUVmax on FDG-PET/CT was significantly higher in squamous cell carcinoma than in adenocarcinoma (11.98 ± 6.81 vs 4.03 ± 4.99; p < 0.001) and this tendency was similar in all stages. Pathological N1 (n = 19), N2 (n = 9) cases showed a significantly higher SUVmax than N0 (n = 79) in squamous cell carcinoma (15.00 ± 5.42, 17.24 ± 8.10 vs 10.65 ± 6.50). This was also the case with adenocarcinoma N2 (n = 48) 8.58 ± 6.14, N1 (n = 40) 9.15 ± 7.13 vs N0 (n = 526) 3.23 ± 4.16. Cases with pathological tumor invasiveness such as lymphatic, vascular or pleural infiltration showed a significantly higher SUVmax than cases with no invasiveness in squamous cell carcinoma (13.75 ± 6.75 vs 7.21 ± 4.22; p < 0.001) and adenocarcinoma (7.39 ± 6.12 vs 1.94 ± 2.37; p < 0.001). The areas under the receiver operating characteristic curves for SUVmax used to predict the relapse-free survival were 12.3 (p = 0.058) in squamous cell carcinoma and 2.6 (p < 0.001) in adenocarcinoma. The 2-year relapse-free survival was 93%/68% (SUVmax lower/higher than 12.3) in squamous cell carcinoma and 99%/78% (SUVmax lower/higher than 2.6) in adenocarcinoma. Following multivariate analysis, pathological nodal status and SUVmax were found to be independent predictive factors for relapse-free survival. **Conclusion:** SUVmax of the primary tumor reflected the biological malignancy of lung cancers. As SUVmax tended to be higher in squamous cell carcinoma than in adenocarcinoma, this should be clinically used separately according to histology. SUVmax is also useful for predicting survival, and multimodality treatment might be indicated if the value is high. **Keywords:** Prognosis, lung cancer, FDG-PET, stage

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-029 Obesity Is Associated with Long-Term Improved Survival in Definitively Treated Locally Advanced Non-Small Cell Lung Cancer (LA-NSCLC)
Vincent K. Lam, Søren M. Bentzen, Pranshu Mohindra, Elizabeth M. Nichols, Neha Bhooshan, Melissa Vyfhuis, Steven J. Feigenberg, Martin Edelman, Josephine L. Feliciano *Greenebaum Cancer Center, University of Maryland, Baltimore/MD/United States of America*

Background: Limited studies suggest that obese patients (pts) with NSCLC paradoxically have improved survival. However, characterization of factors influencing Body Mass Index (BMI) at disease presentation and the impact that it may have on outcomes in NSCLC patients remains incomplete. We evaluated the prognostic effect of BMI in a retrospective cohort treated for LA-NSCLC (AJCC 7th edition stage III). **Methods:** From January 2000 to December 2010, 311 consecutive LA-NSCLC pts were definitively treated at our institution with chemotherapy and radiotherapy ± surgery. Radiation was most commonly administered with concurrent chemotherapy. After excluding pts for whom pre-treatment BMI was not available, we evaluated 291 pts who were stratified into four BMI groups based on World Health Organization criteria: underweight (< 18.5 kg/m2), normal weight (18.5 to < 25 kg/m2), overweight (25 to < 30 kg/m2), and obese (>= 30 kg/m2). Kaplan-Meier survival analysis was performed with log-rank test-for-trend. Cox proportional hazards modeling was used for univariate and multivariate analyses. **Results:** Baseline characteristics were similar between obese and normal weight pts (Table 1). Median survival was 17 months (mo), 19 mo, 23 mo, and 29 mo for each BMI group respectively. A trend for improved survival with increasing BMI was highly significant (P=0.009) and persisted even when underweight cases were excluded, suggesting that the survival benefit is not driven by unfavorable prognostic factors in the underweight cases. There was a sustained 31% to 58% reduction in mortality of obese relative to normal weight pts (HR 0.68±0.21, 0.61±0.19, and 0.42±0.19, for each year post-treatment respectively). Additionally, there was no correlation between BMI and smoking pack-years, even when underweight pts were excluded. (correlation coefficient 0.033 [95% CI 0.09 – 0.15, P=0.59]).

Table 1: Baseline Characteristics of Study Cohort

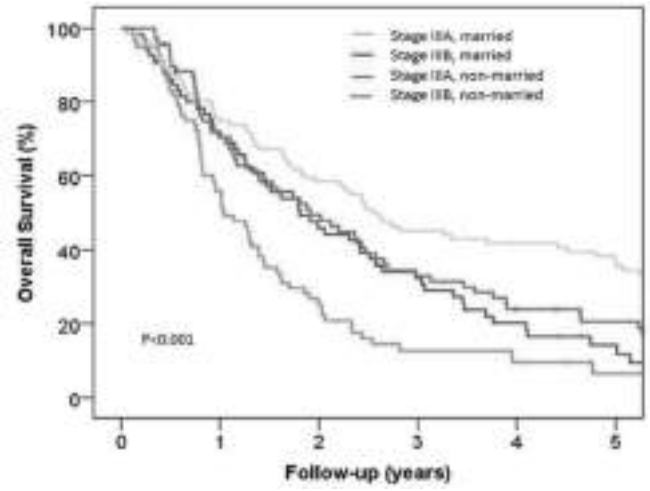
Characteristic	Underweight (N=18)	Normal (N=120)	Overweight (N=87)	Obese (N=66)	Total (N=291)
Median age (range)	56 (30-76)	60 (26-87)	62 (40-82)	63 (42-84)	61 (30-87)
Gender – no. (%)					
Male	14 (77.8)	71 (59.2)	52 (59.8)	31 (47.0)	168 (57.7)
Female	4 (22.2)	49 (40.8)	35 (40.2)	35 (53.0)	123 (42.3)
Race – no. (%)					
White	6 (33.3)	65 (54.2)	51 (58.6)	40 (60.6)	162 (55.7)
Black	12 (66.7)	52 (43.3)	33 (37.9)	25 (37.9)	122 (41.9)
Other	0 (0)	3 (2.5)	3 (2.5)	1 (1.5)	7 (2.4)
Median annual income	$33,415	$39,866	$43,723	$43,795	$41,502
PS – no. (%)					
0 – 1	17 (94.4)	111 (92.5)	76 (87.4)	57 (86.4)	261 (89.7)
2	0 (0)	6 (5.0)	6 (6.9)	7 (10.6)	19 (6.5)
3 – 4	1 (5.6)	3 (2.5)	3 (3.4)	2 (3.0)	9 (3.1)
Missing	0 (0)	0 (0)	2 (2.3)	0 (0)	2 (0.7)
Stage – no. (%)					
III-A	7 (38.9)	67 (55.8)	47 (54.0)	36 (54.5)	157 (54)
III-B	11 (61.1)	53 (44.2)	40 (46.0)	30 (45.5)	134 (46)

Conclusion: In this retrospective study of definitively treated LA-NSCLC patients, obese pts had significantly improved survival relative to normal weight pts. This favorable prognostic effect was independent of stage and was significantly more durable than previously reported in advanced NSCLC patients. Additionally, the putative relationship between BMI and smoking history was not observed in this cohort. These new findings suggest that the protective effect of obesity in NSCLC is not solely due to short-term treatment effects or decreased smoking exposure. We plan to investigate additional parameters such as histology, chemoradiation course, subsequent surgery, and metformin use to further clarify the role of obesity in survival of NSCLC pts. **Keywords:** obesity BMI NSCLC

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.03-030 Marital Status Is Strongly Prognostic and Associated with More Favorable Nutritional Status in Locally Advanced Non-Small Cell Lung Cancer
Josephine L. Feliciano, Søren M. Bentzen, Vincent K. Lam, Katherine A. Schrenk, Pranshu Mohindra, Elizabeth M. Nichols, Melissa Vyfthius, Neha Bhooshan, Steven J. Feigenberg, Martin Edelman *Greenebaum Cancer Center, University of Maryland, Baltimore/MD/United States of America*

Background: We updated our previous analysis demonstrating marital status is prognostic in stage III NSCLC. We hypothesized that married patients have more favorable nutritional or immunologic status than unmarried patients as a potential mechanism for this survival advantage. **Methods:** Between January 2000 and December 2010, 268 patients with stage III NSCLC received definitive chemotherapy and radiation therapy, with or without surgery at our institution. All had complete demographic, diagnosis, treatment, lab, and survival data. A Kaplan-Meier method estimated overall survival and we applied the log-rank test to compare mortality between groups. Multivariable analysis of prognostic factors was conducted using the Cox proportional hazards model. We tested the interaction between marital status and pre-treatment body mass index (BMI), albumin, white blood count, absolute neutrophil count, absolute lymphocyte count and calculated neutrophil-lymphocyte ratio (NLR). **Results:** More married patients presented with stage IIIA (rather than IIIB) disease (58% vs. 46%, P=0.03), had a PS 0 (57% vs. 36%, P<0.001), were white (69% vs. 43% (P<0.001) and lived in higher median income areas ($45,646 vs. $38,331, P<0.001) than non-married patients. There was no difference in tobacco history or diagnosis age between married and unmarried patients. After adjusting for stage, PS, race, and median household income, the hazard ratio for any-cause mortality in married patients was 0.59, 95% CI (0.45, 0.78), P<0.001. Median OS for married vs. unmarried patients was 28 (23, 34) vs. 16 (13, 19) months (P<0.001). Contrary to other reports, the reduction in mortality associated with being married was similar in males, 45%,and females 43%, with the test for interaction in a multivariable Cox model being non-significant (P=0.38).



We also found married status was associated with higher median, 25th, and 75th percentile BMI (26.3 vs. 23.8; 23.3 vs. 20.6, and 30.8 vs. 28.4, respectively; P=0.014) and albumin (3.7 vs. 3.6; 3.4 vs. 3.1; and 4.0 vs. 3.8, respectively; P=0.001). **Conclusion:** Marital status is an important predictor of survival in stage III NSCLC and appears to offset the disadvantage of higher stage disease. Our results suggest one mechanism for this may be married patients have more favorable nutritional status evidenced by higher BMI and albumin. We did not find an association between marital status and immunologic status in our analysis. Future studies that evaluate how social support impacts nutritional status prior to therapy may lead to interventions to target vulnerable populations. Marital status may be an important stratification factor in clinical trials. **Keywords:** marital, lung, nutrition, locally advanced

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.03-031 Concurrent Chemoradiotherapy Using Advanced Radiotherapy Technologies for Inoperable Stage III Non-Small-Cell Lung Cancer

Joseph S K Au[1], S H Chan[2], K T Yuen[3], F Lee[1], R M W Yeung[2], C C Yau[3], Y C. Li[1], C K Law[1]
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Background: Concurrent chemoradiotherapy with the standard regimen of docetaxel plus cisplatin/carboplatin for inoperable stage III non-small-cell lung cancer (NSCLC) demonstrates good synergistic activity and radiosensitizing properties but toxicities are of major concerns. This phase II noncomparative trial was conducted to determine the use of newer radiotherapy technologies including IMRT planning with PET-CT to ensure dose conformity and SPECT-CT to define functional lung volume for avoidance in reducing radiation-induced toxicity and in improving treatment outcome in patients with NSCLC. **Methods:** Patients with locally advanced, inoperable stage III NSCLC received weekly docetaxel (20mg/m2) and cisplatin/carboplatin (20mg/m^2) for 6 weeks with concurrent IMRT (66Gy/6.5 weeks over 33 fraction) followed by a resting period of two weeks before administration of 2 cycles of every 3 week adjuvant chemotherapy with docetaxel (35mg/m2) and cisplatin/carboplatin (35mg/m2) at Day 1 & 8. **Results:** A total of thirty-four patients were recruited in the study as intent-to-treat (ITT) population. Of the twenty-seven patients (as per-protocol population, PPP) evaluable for treatment response, the overall response rate was 77.8%. Median overall survival was 35.5 months (95% CI: 21.3 – 49.7 months) (Figure 1) and progression free survival was 20.8 months (95% CI: 15.3 – 26.2 months) (Figure 2). Tolerability was evaluated in the ITT population with the majority of adverse events to be predominantly grade 1 or 2. Three (8.8%) deaths occurred, two due to fulminant chest infection and one due to disease progression. Fifteen (44.1%) had emergent severe adverse events (SAE). The incidence rates of severe oesophagitis and pneumonitis were 8.8% and 5.9% respectively.

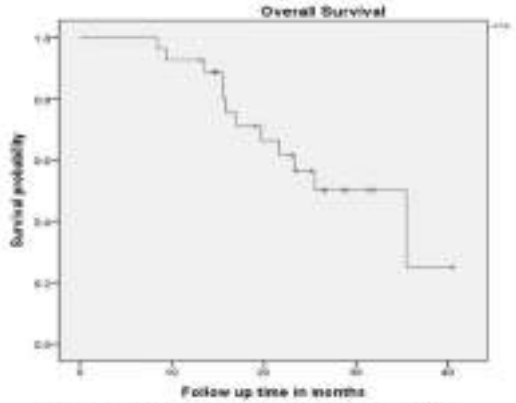


Figure 1. Overall survival in PP population. Overall survival in the PP population of a total of 27 patients. Median overall survival was 35.5 months (95% CI: 21.3 – 49.7 months). Overall survival at 1-, 2- and 3-years was 71.0% (95% CI: 52.8 – 80.3%), 50.1% (95% CI: 28.3 – 61.2 %) and 25.1% (95% CI: 0 – 43.7%)

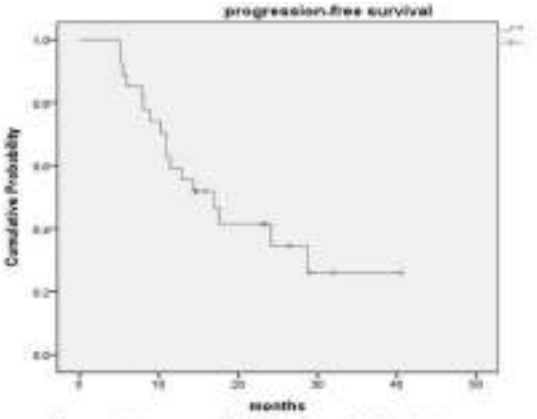


Figure 2. Progression-free survival in PP population. Progression free survival in the PP population of a total of 27 patients. Median progression free survival was 20.8 months (95% CI: 15.3 – 26.2 months). Overall progression-free survival at 1-, 2- and 3-years was 55.6% (95% CI: 36.8 – 65.2%), 25.9% (95% CI: 4.5 – 36.8 %) and not reach.

Conclusion: Concurrent chemoradiotherapy using advanced radiotherapeutic technologies and docetaxel-cisplatin followed by adjuvant chemotherapy for inoperable stage III non-small-cell lung cancer demonstrated good response rates, overall survival and progression free survival. The treatment protocol was generally safe and well tolerated. Adverse events are less common than reported in the literature. **Keywords:** lung cancer, Chemoradiotherapy, SPECT-CT, radiotherapy technologies

SESSION: POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING MONDAY, SEPTEMBER 7, 2015

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-001 MET/RON Inhibition in KRAS Mutated Non Small Cell Lung Cancer

Sravya Tumuluru[1], Rifat Hasina[2], Juan Alban[1], Aliya Husain[3], Mark Ferguson[3], Everett E. Vokes[4], Ravi Salgia[5] [1]*Bsd, Hem/Onc, University of Chicago, Chicago/IL/United States of America,* [2]*Bsd, Hem/Onc, University of Chicago, Chicago/United States of America,* [3]*University of Chicago, Chicago/AL/United States of America,* [4]*Medicine, The University of Chicago, Chicago/United States of America,* [5]*Medicine, Section of Hematology/Oncology, University of Chicago, Chicago/IL/United States of America*

Background: Molecular genetics have allowed us to categorize non-small cell lung cancer (NSCLC) based on their genetic profile. KRAS mutations occur in 25-30% of NSCLCs. KRAS regulates cellular function in response to growth factors and their receptors. When mutated, KRAS is constitutively active and is responsible for driving tumor oncogenesis. Direct inhibition of KRAS has not been a successful clinical strategy. The strategy of synthetic lethality (targeting a non-lethal defect in cancer cells combined with a second defect, that together make the cancer cell more susceptible to treatment) has gained traction in recent years. Several synthetic lethal targets have been identified with KRAS. We have previously shown that MET plays an important role in the oncogenic addiction observed in KRAS mutated NSCLC and contributes to both tumor growth and metastasis. However, the development of resistance in MET targeting due to upregulation of RON, a related receptor tyrosine kinase, is also evident. Our hypothesis is that dual targeting of MET and RON may be synthetic lethal to KRAS mutated NSCLC and studies to investigate this as a potential therapeutic strategy are warranted. **Methods:** MET- and RON-specific siRNAs (small molecule inhibitors), crizotinib, and the ligand for MET (hepatocyte growth factor), were used in *in vitro* assays. Immunoblotting, cell viability, and cell migration assays were carried out in a panel of KRAS mutated as well as KRAS wild type NSCLC cells. In addition, human bronchial epithelial cells (HBECs) that were rendered tumorigenic with sequential mutations in CDk4, hTERT, p53, and KRAS genes were also used. **Results:** Our analysis of a panel of NSCLC cells showed that most KRAS mutant cell lines express both MET and RON, and stimulation with HGF activated KRAS effector pathways such as MAPK, AKT and S6RP. When we silenced MET expression with siRNA, it led to upregulation of RON, indicating the interaction between MET and RON. Cell viability assays using crizotinib showed that KRAS mutant cell lines (A549 and H460) are three-fold more sensitive than KRAS wild type cells (H1975 and H1437), and cells with MET amplification (H1993) showed the highest response. Preliminary data with the KRAS-transformed HBECs also showed that they are more sensitive to crizotinib inhibition than the non-transformed control HBECs. Wound healing assays with these same cells showed a similar trend in MET specific inhibition of cell migration in KRAS-mutated cells compared to wild type cells. **Conclusion:** These data highlight the potential therapeutic benefit of targeting MET and RON simultaneously in a subpopulation of KRAS mutated NSCLC

patients who may have MET overexpression or amplification. Based on KRAS oncogenic addiction to MET, we propose that NSCLC cells that are MET amplified and KRAS mutated are potentially synthetic lethal and will benefit from dual MET/RON treatment
Keywords: NSCLC, KRAS

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-17:00

P1.04-002 Protein Signaling Analysis of KRAS Mutant Lung Adenocarcionomas Reveals Variable MAPK and mTOR Pathway Activation
Elisa Baldelli[1], Eric Haura[2], Lucio Crinò[3], W Douglas Cress[2], Vienna Ludovini[3], Matthew B. Schabath[4], Guido Bellezza[5], Jacopo Vannucci[6], Jianghong Deng[1], Lorenza Pistola[3], Francesca Romana Tofanetti[3], Annamaria Siggillino[3], Lance A Liotta[1], Emanuel F. Petricoin[1], Mariaelena Pierobon[1] [1]*Center for Applied Proteomics and Molecular Medicine, George Mason University, Manassas/United States of America,* [2]*Dept of Thoracic Oncology, Moffitt Cancer Center and Research Institute, Tampa/FL/United States of America,* [3]*Medical Oncology, S. Maria Della Misericordia Hospital, Perugia/Italy,* [4]*Cancer Epidemiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa/AL/United States of America,* [5]*Institute of Pathological Anatomy and Histology, University of Perugia, Perugia/Italy,* [6]*Department of Thoracic Surgery, University of Perugia, Perugia/Italy*

Background: Despite the numerous efforts made to target KRAS directly, this protein is still undruggable. A number of therapeutics that target linked KRAS pathway members have been tested, but their efficacy in KRAS mutant lung adenocarcinoma is still controversial. Understanding the biochemically linked protein signaling network associated with a KRAS mutation may lead to the identification of therapeutic targets to identify patients that may benefit from a therapeutic agent targeting KRAS downstream substrates. **Methods:** Thirty-four archived samples from surgically-treated KRAS mutant adenocarcinomas were included in this study. Samples were collected at the H.Lee Moffitt Cancer Center & Research Institute (Tampa, FL) and at the Santa Maria della Misericordia Hospital (Perugia, Italy). Pure cancer epithelial cell subpopulations were isolated using Laser Capture Microdissection. The expression/activation level of 155 proteins was then measured by Reverse Phase Protein Microarray, a high-throughput semi-quantitative platform. **Results:** The protein activation level of ERK (as measured by phosphorylation of T202/Y204**),** a direct downstream substrate of KRAS activity, was highly variable across KRAS mutant samples. While a subgroup of patients showed, as expected, high activation of ERK, approximately 2/3 of the patients had a comparable ERK activation level to the wild-type counterpart previously analyzed. The activation level of the remaining protein signaling analytes was then compared between samples with high and low ERK activation. Tumors with high levels of ERK activation showed a significant increase in the signaling network of: 1) the MAPK proliferative pathway including Ras-GRF1 S916, Mek 1/2 S217/221, MSK1 S360, p38MAPKinase T180/Y182 ($p=0.03$, $p<0.01$, $p=0.04$, $p<0.01$ respectively), 2) the AKT-mTOR pathway including Akt S473, AMPKα1 S485, ATP Citrate Lyase S454, LKB1 S428, mTOR S2448, p70S6K T389, p70S6K T412, 4E-BP1 S65 ($p<0.01$, $p<0.01$, $p<0.01$, $p<0.01$, $p<0.01$, $p=0.02$, $p=0.03$ respectively). **Conclusion:** This analysis suggests that the signaling network of KRAS mutant lung adenocarcinomas, while manifesting expected ERK activation as a group, is highly variable. In fact a majority of KRAS mutant tumors had the same range of MEK-ERK activation as KRAS WT tumors. Analysis of high and low ERK activation in the KRAS mutant tumors revealed druggable protein signaling activation of a number of important targets. If validated in a larger study set, these data may have important clinical implication for the allocation of patients toward more effective and specific targeted treatments.
Keywords: Signaling pathway analysis, KRAS mutant adenocarcinoma, Reverse phase protein microarray

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-003 Metastatic Site-Specific Variation of KRAS Status in Lung Adenocarcinoma
Zoltan Lohinai[1], Judit Moldvay[1], Katalin Fabian[2], Mihaly Cserepes[1], Anita Rozsas[3], Gyula Ostoros[4], Erzsebet Raso[2], Ilona Kovalszky[2], Gayane Badalian-Very[2], Jozsef Timar[2], Walter Klepetko[3], Balazs Dome[3], Balazs Hegedus[5] [1]*Tumor Biology, National Koranyi Institute of Pulmonology, Budapest/Hungary,* [2]*Semmelweis University, Budapest/Hungary,* [3]*Division of Thoracic Surgery, Medical University Vienna, Vienna/Austria,* [4]*8Th Dept. of Pulmonology, Koranyi National Institute of Tbc and Pulmonology, Budapest/Hungary,* [5]*Molecular Oncology Research Group, Mta-Se, Budapest/Hungary*

Background: While KRAS mutation is a negative predictive marker for EGFR tyrosine kinase inhibitor therapy, there is limited data available regarding the influence of KRAS mutation on the organ specificity of lung adenocarcinoma metastases. **Methods:** In our retrospective, single center study, 820 lung adenocarcinoma patients with KRAS mutation analyses were included. At the time of diagnosis, 462 patients had metastatic disease. These cases were analyzed for the potential association between KRAS status and metastatic site and clinical outcome. Patients with known EGFR mutations were excluded from the study. **Results:** 534 (65.3%) KRAS wild-type and 284 (34.7%) KRAS-mutant cases were identified. There was no difference in the KRAS mutation prevalence between the metastatic (35.7%) and non-metastatic cases (33.4%). The most frequent metastatic sites included bone (29%), contralateral lung (24.8%), ipsilateral lung (19.7%), brain (17.3%), adrenal gland (15.6%), pleura (12.8%) and liver (11.7%). Patients with multiple metastases tended to have inferior median overall survival (OS) compared to those with single-organ metastasis (6.3 vs. 8.2 months, respectively; $p=0.09$) and, moreover, showed a slight but non-significant increase in the prevalence of KRAS mutations (38.5%, $p=0.35$). Importantly, patients with brain (35.8%), bone (33.1%) or adrenal gland (35.2%) metastases demonstrated similar KRAS mutation frequencies. However, both ipsilateral and contralateral intrapulmonary metastatic cases demonstrated increased KRAS mutation frequency when compared to those with extrapulmonary metastases (42.2% and 42.5%, $p=0.014$). In contrast, pleural dissemination and liver metastasis were associated with decreased KRAS mutation prevalence (25.4% and 24.1%, respectively; $p=0.007$). We found no difference in the median OS between KRAS-mutant and WT cases in any metastatic site-specific analysis. **Conclusion:** Lung adenocarcinoma patients with KRAS-mutant tumors more often present with intrapulmonary metastases. KRAS mutation prevalence, however, lacks to provide prognostic information. Further studies are required to determine if KRAS status can be used to risk stratify patients for the onset of pulmonary metastasis.
Keywords: lung adenocarcinoma, KRAS, metastasis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

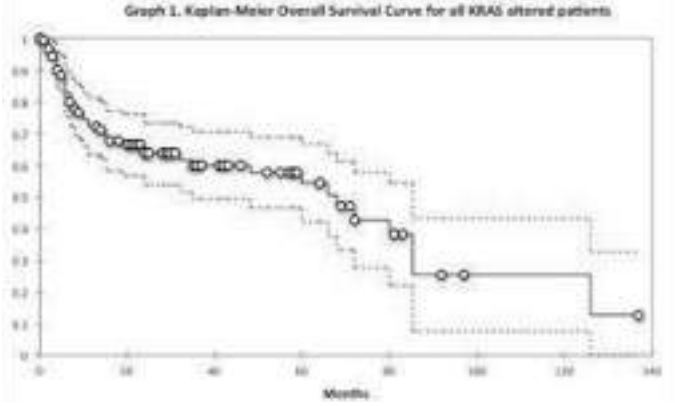
P1.04-004 Inhibition of Telomerase Activity Suppresses Kras Mutation-Induced Lung Carcinogenesis and Chemoresistance
Bin Zhang, Yuesong Yin, Hua Zhang, Bowen Shi, Jinfang Zhu, Changli Wang *Department of Lung Cancer, Tianjin Medical University Cancer Institute and Hospital, Tianjin/China*

Background: Kras mutations are one of the most common driver mutations in NSCLC, which promote lung tumorigenesis. And many patients harboring Kras mutation fail to benefit from chemotherapy. Treatment of Kras-mutant lung cancer is still a challenge. It is reported that telomere shorting inhibits tumor formation and prolongs life span in a KrasG12D mouse lung cancer model. Telomerase inhibitors show a trend toward improving survival of patients with advanced NSCLC with short telomere. However, the roles of telomerase inhibition have not been defined in Kras-mutant NSCLC. **Methods:** KrasG12D was lentivirally transduced into normal human lung cell line (BEAS-2B) and lung cancer cell lines (Calu-3 and H1299) for stable expression. The cells were transfected with TERTshRNA or treated with the telomerase inhibitor BIBR1532 to suppress the telomerase activity. Telomerase activity and telomere length were examined by the telomeric repeat amplification protocol (TRAP) assay and the Southern blot analysis of terminal restriction fragment lengths. Cell proliferation, colony formation and migration were analyzed by cell growth curves, soft agar assay and transwell migration assay. Calu-3- KrasG12D xenograft mice models were used to validate the effects of telomerase inhibition on cell growth and chemosensitivity in vivo. **Results:** We found that continuing inhibition of telomerase shorted telomere length and inhibited mutant KrasG12D-induced cell migration, colony formation, long-term proliferative capability and activation of Kras signaling pathway in both normal human lung and lung cancer cells. In addition, decreasing telomerase activity increased cells sensitivity to chemotherapeutic agents in Calu-3 and H1299 cells with KrasG12D overexpression. Notably, the effects of telomerase inhibition on Kras-mutant cells were P53 independent. In vivo experiments also confirmed treatment with telomerase inhibitor significantly enhanced tumor growth inhibition and the antitumor efficacy of chemotherapy in Calu-3-KrasG12D tumor-bearing mice. **Conclusion:** Our data suggest that Kras mutation-induced lung carcinogenesis and chemoresistance are attenuated by telomerase inhibition. Targeting telomerase/telomere may be a promising therapeutic strategy for Kras mutant NSCLC.
Keywords: non-small cell lung cancer(NSCLC), chemoresistance, telomerase, kras mutation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-005 Concurrent EGFR and ALK Mutations in KRAS-Mutant Lung Adenocarcinomas and Their Clinical Behavior
Kevin C. Wood, Thomas Hensing, Brian Won, Everett Vokes, Ravi Salgia *Medicine, Section of Hematology/Oncology, University of Chicago, Chicago/IL/United States of America*

Background: KRAS represents the most commonly mutated oncogene in non-small cell lung cancer (20-30%). Multiple studies have suggested mutations of KRAS, epidermal growth factor receptor (EGFR), and anaplastic lymphoma kinase (ALK) to be mutually exclusive[i], though there are few case studies showing coexisting EGFR and KRAS mutations[ii]. **Methods:** We reviewed clinical genotyping data from 118 patients with stage I – IV KRAS mutated NSCLC. We investigated prevalence of concomitant EGFR and ALK mutations and evaluated clinical behavior in regards to overall survival (OS) and response to tyrosine kinase inhibitor therapy. **Results:** Among these 118 samples with KRAS alterations (codon 12 =98, 13 = 8, 61 = 3, 146 = 2, 189 =1, amplification = 6), median OS was 61.97 months (Graph 1). Concomitant EGFR mutations were noted in 6 subjects (5.0%) and ALK mutations were noted in 2 subjects (1.7%). One patient was found to have mutations of KRAS, EGFR, and ALK. These patients' stage at diagnosis, response to TKI therapy (if utilized), and OS is documented in Table 1.



Stage	KRAS Mutation	EGFR Mutation	ALK Mutation	Response to TKI therapy (TTP in mo)	Overall Survival (mo)
IV	G12A	E19del	QNS	Tarceva (2)	8
IIA	Amplification	Amplification		None	15
IV	Amplification	L858R		Tarceva (15); Afatinib (3)	66
IV, recurrent	G13D	G721S subq		None	126
IV	Amplification		A585T	None	27 (Alive)
II	Amplification	Amplification		None	29 (Alive)
IIIA	G12C	L907F	T246N	Unknown	Unknown

Table 1. Patients with concomitant mutations of KRAS, EGFR, and ALK and their response to TKI therapy and overall survival. TTP = Time to progression. Mo = months. QNS = Quantity not sufficient.

Conclusion: This analysis demonstrates it is possible for KRAS mutations to occur concurrently with EGFR and ALK missense mutations (not translocation) and emphasizes that a complete molecular analysis should be performed on all NSCLC patients. Further data is needed to more firmly elucidate how these concurrent mutations affect clinical behavior. Citations [I] Gainor JF, Varghese AM, Ou SH, et al. ALK rearrangements are mutually exclusive with mutations in EGFR and KRAS in non-small cell lung cancer. Clin Cancer Res. 2013 Aug 1; 19(15): 4273-81. [II] Zhu CQ, Sants GC, Ding K, et al. Role of KRAS and EGFR as biomarkers of response to erlotinib in National Cancer Institute of Canada Clinical Trials Group study BR.21. Journal of Clinical Oncology. 2008 Sep 10; 26(26): 4268-4275.
Keywords: KRAS, NSCLC, ALK, EGFR

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-006 Prognostic and Predictive Role of KRAS-Mutations in Patients with Advanced Non-Squmous Non-Small-Cell Lung Cancer (NS-NSCLC) Mario A. Sanchez-Salinas[1], Javier Garde-Noguera[2], Jose Garcia Sanchez[1], Marisol Valera[1], Sara Marin[1], Julia Hidalgo[1], Rene Arturo Albino[1], Jose Ferrando Marco[1], Antonio Llombart Cussac[1] [1]*Hospital Arnau de Vilanova, Valencia/Spain,* [2]*Medical Oncology, Hospital Arnau de Vilanova, Valencia/Spain*

Background: KRAS is the most frequently mutated oncogene in lung adenocarcinoma patients. The prognostic rolo of mutatn-KRAS in lung adenocarcinoma is controversial, especially in non-asian populations. Studies also suggest the potencial predictive role of mutant-KRAS in the context of chemosensitivity of NSCLC. The aim of our study is to analyze the role of KRAS mutations as prognostic factor in advanced NSCLC, and their value as predictive biomarker of chemotherapy efficacy. **Methods:** Retrospective study of patients with advanced NS-NSCLC in our institution between january-2013 and december-2014. Mutation analysis for KRAS was performed an the relation with overall survival was assessed. Secondary endpoints were its relation with progression-free survival and response to chemotherapy. **Results:** A total of 42 patients met inclusion criteria. Median age was 61.5 years. Thirty-three male (78.6%), 27 ECOG-PS 0-1 (64.3%), and 40 (95.2%) adenocarcinoma. Twenty-six patients (61.9%) received chemotherapy as first line treatment, 4 (9.5%) anti-EGFR treatment and 12 supportive care. Nine patients (21.4%) harboured KRAS mutations, all of them at exon 12. There were no differences in age, performance status or smoking history between patients with KRAS mutants vs those with wild-type tumours; instead KRASmut patients presented a higher rate of brain metastases (55.5 vs 20%; p=0.05) and higher number of methastatic locations at diagnosis (77.7 vs 41.3% of patients with more than one site of metastases). Median Overall Survival was superior for patients with wild type tumours (19 vs 10 months, p =0.22). There were no differences in response rate in patients treated with platinum doblet chemotherapy (Wild-type vs KRAS mut: 44.4 vs 33.3%, p=0.5), but progression free survival and overall survival were superior for wild-type tumour patients (PFS: 3 vs 15 months, p=0.001; OS: 10 vs NR, p=0.06). **Conclusion:** With the limitation of small numbers, our data suggest that KRASmut patients are a subgroup with poorer prognostic. Moreover, they seem to benefit less from standard chemotherapy based in platinum doublets.
Keywords: KRAS mutations, lung cancer, prognostic factor, predictive factor

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTIN
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-007 KRAS Mutations in Lung Cancer: Prevalence and Outcomes Margarida Dias[1], Rita Linhas[1], José Carlos Machado[2], Luís Cirnes[2], Ana Gonçalves[1], Sérgio Campainha[1], Sara Conde[1], Ana Barroso[1] [1]*Pulmonology, Centro Hospitalar Vila Nova de Gaia Espinho, Vila Nova de Gaia/Portugal,* [2]*Ipatimup, Porto/Portugal*

Background: Non-small cell lung cancer (NSCLC) is the leading cause of cancer death worldwide. The most commonly mutated oncogene in NSCLC encodes for KRAS and its mutations are usually associated to a poor prognosis. The aim of this study was to evaluate the prevalence and the prognosis of these mutations in a Portuguese cohort of patients with NSCLC, EGFR wild-type. **Methods:** We included 201 patients diagnosed with NSCLC, EGFR wild-type, followed in a Lung Cancer Unit. KRAS mutations in exon 12 and 13 were screened. Demographic and clinical data were analyzed. Overall survival, objective response to first-line chemotherapy and time to progression was evaluated in patients staged IIIB or IV at diagnosis. **Results:** 173 (81.1%) were male, mean age 67±12 years, 40.1% smokers and 42.6% ex-smokers. At diagnosis, 9.1% were stage IA, 4.6% IB, 3% IIA, 2.5% IIB, 13.7% IIIA, 11.7% IIIB, 54.8% IV. 68.2% were adenocarcinoma and 21.4% squamous tumors. 79.5% was performance status 0-1. KRAS mutations were found in 46 (22.9%) patients and in 4.5% results were not valid. The most common mutations were G12C (41.8%) and G12V (26.1%). There was a statistically significant association between KRAS mutations and non-squamous histology (93.5% in KRAS mutated patients vs. 74.1% in KRAS wild-type patients, p=0.020) and a history of past or current smoking (93.4% vs. 78.4%, p=0.032). No statistical differences were found regarding age, gender, performance status or cancer stage at diagnosis. With respect to patients staged IIIB or IV at diagnosis, overall survival tended to be inferior in patients with KRAS mutations (median survival: 5 vs. 9 months, p=0.127). There was no statistical difference between groups regarding response to first-line chemotherapy and time to progression after first-line chemotherapy. **Conclusion:** The prevalence of KRAS mutation in this Portuguese cohort is consistent with results of similar studies in other countries (20-25%). KRAS mutations were associated to adenocarcinoma histology and smoking habits. Despite overall survival tending to be half in KRAS mutated IIIB/IV patients, this study showed little relevance as a prognostic marker. Thus, it is important to pursue the search for other molecular biomarkers that could be used in prognosis and even as therapy targets.
Keywords: non-small cell lung cancer, KRAS mutations, Prognosis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-008 Tissue Hyaluronan and Its Relationship with Angiogenesis Are Indicators of Lung Cancer Malignancy Maristela P. Rangel[1], Tabatha Prieto[2], Eloisa R. Olivieri[3], Dirce M. Carraro[3], Vera L. Capelozzi[2] [1]*Pathology, Faculty of Medicine; University of Sao Paulo, São Paulo/Brazil,* [2]*Pathology, Faculty of Medicine, University of Sao Paulo, São Paulo/Brazil,* [3]*Pathology, Ac Camargo Cancer Center, São Paulo/Brazil*

Background: Cell-extracellular matrix interactions participate in several steps required for tumor cell invasion and because of that, a group of glycosaminoglycans have been targeted as potentially useful tumor markers. Hyaluronan has shown promise, but still there is uncertainty about its localization in tumor tissue and its relationship with histological types and angiogenesis. Regarding that, we evaluated the association between HA and degree of malignancy through its expression in lung tumor tissue and association with angiogenesis. **Methods:** Forty-six lung specimens were evaluated. Hyaluronan and microvessel (CD34) quantification in situ was done in FFPE sections of nonneoplastic cells, lung cancer cells, and tumor stroma. Colocation was evaluated in tumor stroma using confocal microscopy. Cox proportional hazards model, MantelHaenszel test and Pearson's x2 were used to evaluate the hyaluronan and microvessel staining inferences and the relationship between them. **Results:** Squamous cell carcinoma showed abundant hyaluronan on the cancer cell-stroma interface coincident with prominent microvessel staining and identical colocalization at confocal microscopy. Strong hyaluronan staining associated with cancer cells was significant in 32.1% of squamous cell carcinoma compared to 17.9% of adenocarcinoma and 0.0% in large cell carcinoma (P<0.001). Adenocarcinomas revealed strong stromal hyaluronan staining in contrast with the hyaluronan-poor tumor cells. The foci of hyaluronan stromal staining was coincident with foci of microvessel and colocalization. Furthermore, adenocarcinoma more often showed a lower percentage of hyaluronan-positive cancer cells (35.7% of cases) than large cell carcinoma (14.3% of cases) or squamous cell carcinoma (0% of cases; P<0.001). For large cell carcinoma, the hyaluronan signal in tumor cells was very poor and contrasted with the foci of staining in stroma, coincident with focal microvessel density and colocalization. All these results are shown in Figure 1. A significant direct association was found between tumors with a high percentage of HA and MVD in tumor stroma (R=0.6; P=0.02). Similarly significant was the direct association between tumors at the N1 stage and high levels of hyaluronan in cancer cells (R=0.31; P=0.05). In addition, tumors in the T4 stage presented positive association with a high percentage of hyaluronan-positive cancer cells (R=0.80; P=0.01).

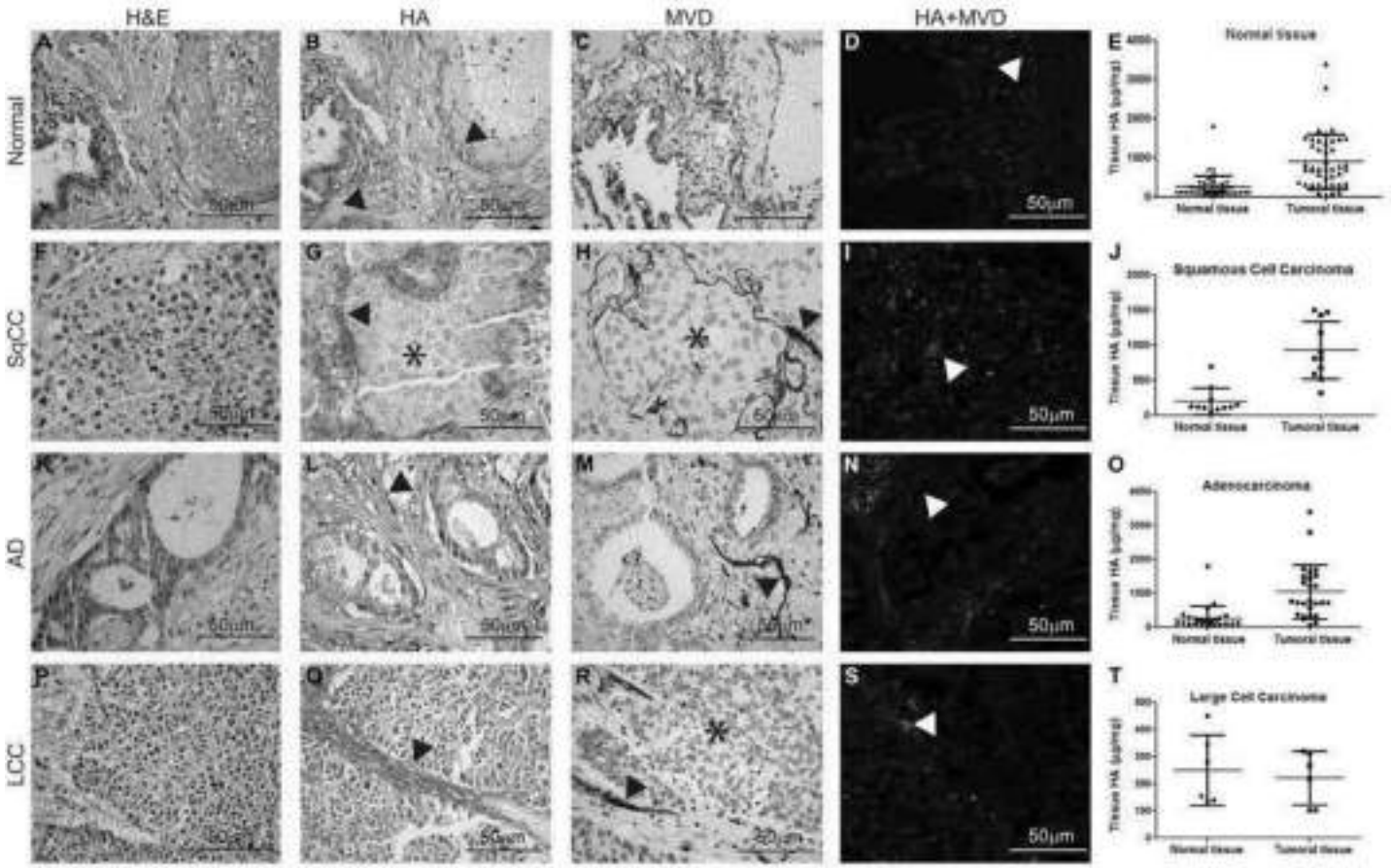


Figure 1. Strong hyaluronan (HA) signal at the epithelial cell-extracellular matrix interface (B) in normal lung (A), coincident with regular microvessels staining (C), absence of colocalization at confocal microscopy (D) and low signal when compared to tumoral tissue (E). High expression (>48%) of HA in squamous cell carcinoma (SqCC) (F) on cancer cells-stroma interface (G), coincident with high microvessel (>33%) staining foci (H), identical colocalization at confocal microscopy (I) and higher signal when compared to normal tissue (J). HA-negative in normal lung (K) and cells of adenocarcinoma (AD) (L); note the strong HA staining in tumor stroma (L), coincident with microvessels staining (M), foci of colocalization at confocal microscopy (N) and higher expression compared to normal tissue (O). Very poor signal in normal lung (P) and in large cell carcinoma (LCC) (Q); note strong HA foci staining (Q), coincident with focal microvessels density (R), focal colocalization at confocal microscopy (S) and low signal when compared to normal tissue (T). Arrowheads indicate stromal tissue; asterisks indicate carcinoma cells. H&E: hematoxylin and eosin; MVD: microvessel density.

Conclusion: Our findings showed that an elevated hyaluronan signal in tumor cells was associated with poor prognosis and its localization relationship with histological types and angiogenesis was related to malignancy of lung cancer. To realize these findings a greater larger scale study in a randomized trial will be required. **Keywords:** extracellular matrix, hyaluronan, lung cancer, angiogenesis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-009 Max Collapse and Fibrosis below 5 cm Predict the Prognosis of pT1 Lepidic Predominant Adenocarcinoma Masahito Naito[1], Masahiro Tsuboi[2], Keiju Aokage[3], Tomoyuki Hishida[4], Genichio Ishii[5], Junji Yoshida[6] *[1]Thoracic Surgery, National Cancer Center Hospital East, Kashiwa-Shi, Chiba/Japan, [2]Thoracic Surgery, National Cancer Center Hospital East, Kashiwa, Chiba/Japan, [3]Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Chiba/Japan, [4]Division of Thoracic Surgery, Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa/Japan, [5]Pathology, Resarch Center of Innovative Oncology, National Cancer Center Hospital East, Kashiwa, Chiba/Japan, [6]Thoracic Surgery, National Cancer Center Hospital East, Kashiwa/Japan*

Background: According to the International Association for the Study of Lung Cancer , American Thoracic Society, and European Respiratory Society (IASLC/ATS/ERS) classification, lepidic predominant pattern in pT1 lung adenocarcinoma is divided into adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA), and lepidic predominant invasive adenocarcinoma (LPIA) by using new diagnostic criteria. However the new criteria have many item to diagnose MIA. So we simply classified the pT1 lepidic predominant adenocarcinoma by using only collapse and fibrosis below 5cm as invasive component, and we evaluated prognosis of MIA. **Methods:** A total of 231 patients treated for pT1 lepidic predominant lung adenocarcinoma by complete resection at National cancer center hospital east, Chiba, Japan from January 2003 to December 2010 were assessed. We excluded multiple tumor and mucinous invasive adenocarcinoma from the analysis. We classified 187 patients into AIS, MIA, LPIA, according to the IASLC/ATS/ERS classification. The MIA was defined as group A. In the LPIA, we defined invasive component as collapse and fibrosis 5 cm below, and reclassified into MIA and LPIA. Reclassified MIA and LPIA were defined as Group B and C respectively. We analyzed the prognosis of these patients retrospectively. **Results:** AIS, Group A, Group B, Group C were 52 (22.5%), 29 (12.5%), 39 (16.9), 111 (48.1%) respectively. Positive lymphatic invasion and, or vascular invasion and, or pleural invasion in Group A, Group B, Group C were 0 (0%), 4 (1.2%), 24 (21.6%) respectively. There are significant difference in 5-year recurrence free survival (5y-RFS) between Group A and B (5y-RFS rate 100% versus 88.1%; p = 0.022), and Group A and C (5y-RFS rate 100% versus 88.1%: p = 0.046). **Conclusion:** Max collapse and fibrosis below 5 cm correlated with the prognosis of pT1 lepidic predominant adenocarcinoma. Max collapse and fibrosis below 5cm is more simpl and easy method to measure invasive component than the new IASLC/ATS/ERS classification. This method may have potential to diagnose MIA instead of the IASLC/ATS/ERS classification. **Keywords:** minimal invasive adenocarcinoma, collapse and fibrosis, lepidic predominant adenocarcinoma, Prognosis

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P1.04-010 Pilot Internet Survey of Interobserver Variability in Pathology Diagnoses of Multiple Tumor Nodules Wilbur A. Franklin[1], Andrew G. Nicholson[2], Kathleen Torkko[3], William D. Travis[4], Frank Detterbeck[5] *[1]Pathology, University of Colorado Health Sciences Center, Aurora/CO/United States of America, [2]Pathology, Royal Brompton and Harefield NHS Foundation Trust and National Heart and Lung Institute, London/United Kingdom, [3]Pathology, University of Colorado Health Sciences Center, Aurora/United States of America, [4]Dept of Pathology, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America, [5]Surgery, Yale U, New Haven/CT/United States of America*

Background: The distinction between separate primary lung cancers (SPLC) or intrapulmonary metastases (IM) is of great clinical importance because of the substantial staging and prognostic implications. With the broad implementation of CT screening for lung cancer, the recognition of multiple tumor nodules is increasingly common. Currently, similarities and differences in histology between two tumors provide the most definitive distinction between SPT and IM. However, the level of agreement among pathologists regarding this question has not been tested. The IASLC Pathology Committee and the Multidisciplinary SPT Working Group has addressed this issue through a pilot online survey. This study assesses the feasibility and reports preliminary results of a web-based survey to determine interobserver variation in distinguishing SPT and IM. **Methods:** A pilot study was conducted to test whether multiple observers could assess a collection

of 50 cases of multiple tumors through a digital web-based system. Five pairs of resected nodules were assembled from the University of Colorado and scanned into an image database using an Aperio AT2 slide scanner (Leica Biosystems) with a 40X objective. Reviewers were asked to review slide images, to provide a histological diagnosis according to WHO criteria, to answer questions regarding specific histological details related to each nodule and to determine whether the multiple nodules were SPT and IM. Combined results were evaluated for level of concordance on the central question of primary or metastatic status. Results were also correlated with *EGFR, KRAS, ALK and TP53* mutational status. **Results:** A total 21 pulmonary pathology subspecialists completed the survey, evaluating 10 nodules from 5 patients. Ten of the reviewers were from the US, 3 from Japan, 2 from the UK, and one each from Canada, France, Germany, the Netherlands, Korea and Sweden. On the question of SPLC vs IM, 10 reviewers agreed on all cases and these determinations were regarded the histological consensus. There was 85% overall concordance with the consensus diagnosis. Most of dissenting opinions related to a single case. In all but one instance, tumors from the same individual with different histological diagnoses were designated SPLC. However, in 30% of the cases, tumors from the same individual with identical histological diagnoses were determined to be SPLC. The histological attributes regardless of WHO diagnostic category that significantly (each p>0.0001) contributed to this conclusion included lepidic growth, cell size, nuclear pleomorphism and nucleolar prominence. The mutational status of these cases was in complete agreement with the histological consensus. Mutations that distinguished SPT included *KRAS*, *EGFR* or *TP53* mutation in only one member of a tumor pair or different *EGFR* mutations in each member of a pair. In IM, identical *KRAS* mutation was found in both members of a tumor pair. **Conclusion:** In this pilot study a high level of consensus was achieved in separating SPLC vs or IM. A large minority (30%) of tumor pairs with identical histological diagnoses were determined to be SPLC suggesting that histological features beyond those used for WHO classification are taken into account when determining SPT status. **Keywords:** Second Primary, Pathology, Internet Survey, intrapulmonary metastasis

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P1.04-011 Intraoperative Diagnosis of Lymph Node Metastasis Using a Rapid-Immunohistochemical (R-IHC) Staining Method in Non-Small Cell Lung Cancer
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Background: Nodal micrometastasis in non-small cell lung cancer (NSCLC) is associated with a poorer survival rate than node-negative disease. Furthermore, lymph node micrometastasis often cannot be detected using conventional hematoxylin and eosin staining of frozen sections; detection requires additional time-consuming immunohistochemical (IHC) analysis of paraffin-embedded tissue. We developed a novel ultrarapid immunohistochemical staining method in which an AC electric field is used to facilitate detection of tumor cells. This method allows detection of tumor cells in frozen sections in less than 20 min, and could be a useful tool for frozen diagnosis. We previously reported IHC analysis for NSCLC in detection of lymph node micrometastasis without misdiagnosis using the rapid-IHC protocol developed at our institute. This technology, which has been patented, was released in May 2014 as "Histotech-R-IHCR". The purpose of rapid-IHC analysis during surgery for NSCLC is the utility of intraoperative diagnosis of lymph node metastasis. **Methods:** Thirty-four patients with NSCLC were enrolled in the study between June 2014 and March 2015 after obtaining signed informed consent. Surgery was performed at Akita University School of Medicine and University Hospital. The patients were taken to an operating room, and the standard preparations were made for a thoracotomy and lung resection such as lobectomy with systematic/selective nodal dissection or segmentectomy. Dissected lymph nodes from each patient were used in this study. Intraoperative samples from dissected lymph nodes were sectioned, conventionally stained with HE, and immunohistochemically labeled with anti-CK (AE1/AE3) antibody using the rapid-IHC procedures, after which they were examined by a pathologist. **Results:** IHC analyses were completed within 20 min, and the diagnosis was made by the pathologist within about 30 min. Two patients were diagnosed as positive on the basis of conventional histological examination, and the same two patients were deemed positive on the basis of CK detection using rapid-IHC. There were no micrometastases in this study. All patients diagnosed as negative based on CK detection using rapid-IHC were pathologically N0. Twenty-one patients underwent lobectomy, and 13 patients received segmentectomy. Twenty-eight patients underwent lymph node dissection of hilar and mediastinal (ND2a) nodes, and six patients underwent lymph node dissection of hilar nodes only (ND1). **Conclusion:** The rapid-IHC device is useful for intraoperative diagnosis of lymph node metastasis in lung cancer surgery. We want to apply this method to the minimally invasive surgery selection such as segmentectomy and selective mediastinal lymph node dissection. Further investigation in multicenter studies will be needed to confirm the utility of this method. **Keywords:** immunohistochemical staining, Intraoperative diagnosis, lymph node metastasis, micrometastasis

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P1.04-012 Using Computed Tomography Scans to Assess the Histology of Malignant Pleural Mesothelioma
Samuel Armato[1], Fawwaz Qayyum[2], Aliya Husain[3], Christopher Straus[4], Hedy Lee Kindler[5], Wickii T. Vigneswaran[6] [1]*Department of Radiology, University of Chicago, Chicago/IL/United States of America,* [2]*University of Chicago, Chicago/United States of America,* [3]*Pathology, University of Chicago, Chicago/United States of America,* [4]*Radiology, University of Chicago, Chicago/United States of America,* [5]*Section of Hematology/Oncology, University of Chicago, Chicago/IL/United States of America,* [6]*Surgery, University of Chicago, Chicago/United States of America*

Background: The purpose of this study is to assess the histology of malignant pleural mesothelioma using computed tomography (CT) based imaging. **Methods:** 28 patients with malignant pleural mesothelioma were used (histologies: 17 epithelioid, 11 biphasic). A CT scan was acquired for each patient prior to surgical resection of the tumor. A radiologist identified and outlined the tumor boundary on each CT section that demonstrated tumor. These outlines were analyzed to determine the total volume of disease present, the mean volume of disease per outlined section, and the distribution of Hounsfield Unit (HU) values throughout the outlined tumor. These parameters were used to differentiate tumors of epithelioid and biphasic histologies. For each parameter, cutoffs were determined to maximize the extraction of biphasic cases from the entire cohort, while minimizing the extraction of epithelioid cases. **Results:** Discernable differences were extracted from the images of the two different histologies of the disease. Figure 1 shows the mean HU value, the standard deviation and skew in the distribution in the HU values, and the volume of tumor represented on each CT section demonstrating disease. With regard to HU distribution, the biphasic cases generally had a higher mean HU value. For example, 73% of the biphasic cases had a mean value greater than 30, compared to only 29% of the epithelioid cases. Biphasic cases also tend to have a more negative skew in their HU distribution; 73% of biphasic cases had a skew value less than -1, compared to 35% of epithelioid cases. It was also seen that biphasic cases also tended to have a higher volume of tumor present throughout their disease presenting CT sections. There were promising results from extracting the biphasic cases by using optimized cutoffs from gathered data. The criteria used were as follows: Cases that exhibited more than 9 mL of tumor per outlined CT section, or exhibited a mean HU value greater than 10 as well as a skew in HU values less than -1 were extracted from the cohort and identified as biphasic. Of the cases that match these criteria, 10 were actually biphasic while 6 were actually epithelioid. These results are 91% specific, missing only one biphasic case, and 65% specific, correctly excluding 11 of the 17 epithelioid cases.

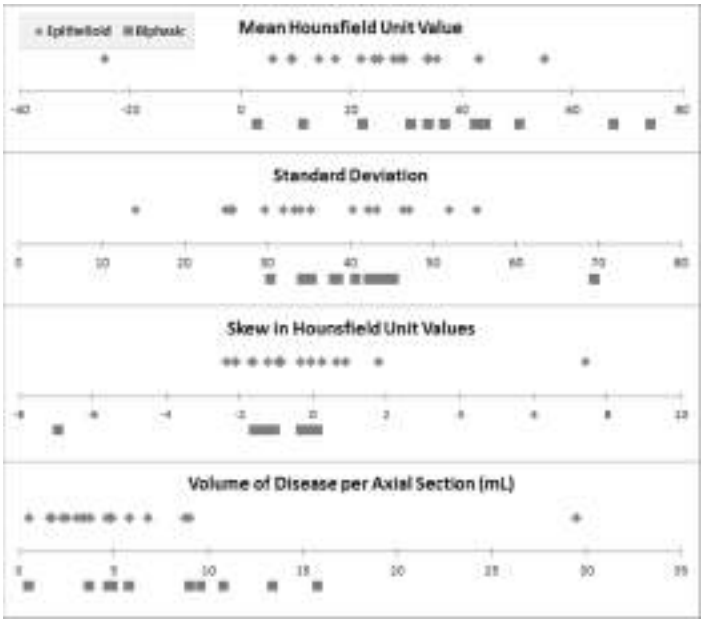

Figure 1 – Comparison of Epithlioid and Biphasic cell types. **Conclusion:** This study demonstrates that CT-based imaging may be a useful tool for the assessment of tumor histology through image analysis. **Keywords:** imaging, Mesothelioma

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P1.04-013 Clinicopathological Characteristics of Lung Cancer with Combined Pulmonary Fibrosis and Emphysema
Akihiko Yoshizawa[1], Meng Zhang[2], Shiho Asaka[3], Takayuki Shiina[4], Kazuo Yoshida[5] [1]*Department of Diagnostic Pathology, Kyoto University Hospital, Kyoto/Japan,* [2]*Dept. of Surgery 2, Shinshu University Hospital, Matsumoto/Japan,* [3]*Dept. of Laboratory Medicine, Shinshu University Hospital, Matsumoto/Japan,* [4]*Thoracic Surgery, Shinshu University Hospital, Matsumoto/Japan,* [5]*Department of Thoracic Surgery, Shinshu University School of Medicine, Matsumoto/Japan*

Background: Combined pulmonary fibrosis and emphysema (CPFE) is a clinical syndrome that is diagnosed with computed tomography (CT), sometimes in conjunction with histopathology. Mostly all patients with CPFE are smokers, and thus, they are at high risk of developing lung cancer (LC). The histological and clinical characteristics of coexisting LC and CPFE syndrome remain unclear. Therefore, we conducted a retrospective study to explore the clinicopathological characteristics of LC along with CPFE (LC-CPFE). **Methods:** We retrospectively reviewed the data of 1647 patients who underwent lung resection for pulmonary masses at Shinshu University Hospital between December 1995 and December 2013. After excluding patients without CT images, patients with metastatic tumors, and patients without sufficient clinical and histological information, the remaining patients were divided into four groups based

on chest CT findings: LC-CPFE, LC along with pulmonary fibrosis (LC-PF), LC along with emphysema (LC-Emp), and LC in normal lungs (LC-Norm). The clinicopathological characteristics of patients with LC-CPFE were compared to those of the patients in the other groups. **Results:** After excluding patients for the reasons described above, 985 patients were enrolled in this study. Of these 985 patients, there were 72, 28, 84, and 801 cases of LC-CPFE, LC-PF, LC-Emp, and LC-Norm, respectively. Patients with LC-CPFE were all smokers, with a mean Brinkman index of 1158. Compared with the other groups, patients with LC-CPFE were predominantly men (n = 67, 93.0%) and were older (a mean age of 70.5); LC-CPFE was also associated with a larger tumor size (a mean tumor size of 29.5 mm), the presence of multiple tumors (n = 13, 18.0%), higher stage, squamous cell carcinoma-predominant histology (n = 46, 63.9%), and higher tumor grade (n = 45, 62.5%). Patients with LC-CPFE showed a significantly worse outcome than did patients with LC-Emp and LC-Norm, with a 5-year disease-free survival (DFS) rate of 63.5% and a 5-year overall survival (OS) rate of 53.5%. The OS rate of patients with LC-CPFE was worse than that of patients with LC-PF, although the statistical difference was not significant (p = 0.06), whereas the DFS rates between the LC-CPFE group and the LC-PF group were not significantly different (p = 0.664). In the LC-CPFE group, the tumors were mostly found in associated fibrotic areas (n = 56, 77.7%), followed by emphysematous areas (n = 9) and normal lung areas (n = 7). The pattern of the fibrotic area was as follows: 31 unclassified, 19 UIP, and 6 NSIP. In situ carcinomatous lesions were found in fibrotic areas of more than half of the LC-CPFE cases (n = 30, 53.5%). **Conclusion:** This study indicates that LCs in patients with CPFE syndrome developed in heterogeneous tumorigenic backgrounds. However, because patients with LC-CPFE showed significantly poorer outcomes compared with the other groups, CPFE should be considered an important background disease for patients after resection of lung cancer. **Keywords:** Combined pulmonary fibrosis and emphysema, lung cancer

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P1.04-014 Clinicopathologic Significance of Epithelio-Mesenchymal Transition in Human Lung Adenocarcinoma Toshi Menju[1], Terumasa Sowa[1], Shinya Neri[1], Takao Nakanishi[1], Hiroyuki Cho[1], Kei Shikuma[1], Kyoko Hijiya[1], Hideki Motoyama[1], Akihiro Aoyama[1], Fengshi Chen[1], Makoto Sonobe[1], Toshihiko Sato[1], Mitsugu Oomasa[1], Akihiko Yoshizawa[2], Hironori Haga[2], Hiroshi Date[1] [1]*Thoracic Surgery, Kyoto University, Graduate School of Medicine, Kyoto/Japan,* [2]*Diagnostic Pathology, Kyoto University Hospital, Kyoto/Japan*

Background: Activation of Epithelial-Mesenchymal Transition (EMT) mechanisms in tumor cells is known to be associated with its invasive and metastatic properties. However, this hypothesis has not been fully elucidated from the point of detailed clinicopathological view using surgically resected clinical samples. We, hereby, examined the expression levels of EMT marker and analyzed the integrated data of clinicopathlogical information including background genetic alterations. **Methods:**Clinical samples were obtained from the 256 cases of resected lung adenocarcinoma which were consecutively operated from January 2001 to December 2007 in Kyoto University Hospital. Pathological stage distribution of the cases by TNM classification (WHO, 7th edition) was below: 1A: 132, 1B: 56, 2A: 22, 2B: 4, 3A: 26, 3B: 2, 4:14. Mean survival time of all the cases was 62 months, and 5-year survival rate was 75.3%. The distribution of predominant histlogical subtype by IASLC/ATS/ERS classification was AIS (9, 3.5 %), MIA (13, 5.1 %), lepidic (18, 7.0 %), acinar （32, 12.5 %）, papillary (122, 47.6%), solid (44, 17.2 %), micropapillary (9, 3.5 %), mucinous (8, 3.1 %), others (1, 0.4 %). We performed immunohistochemical staining for the expression of E-cadherin and Vimentin on tissue microarrays of resected samples to assess the activation level of EMT. Then, we classified the cases with positive E-cadherin expression and negative for Vimentin as “null” activation of EMT mechanisms, called ‘Group N’, whereas loss of E-cadherin and positive for Vimentin as “full” activation, ‘Group F’, and, further, either loss of E-cadherin or positive Vimentin as “partial” activation, ‘Group P’. DNA samples were extracted from frozen surgical samples and the mutations for the hot-spot exons of EGFR, ALK, K-ras, and p53 were detected by SSCP or direct sequencing methods. Statistical analyses for survival were performed by Kaplan-Meirer curve and log-rank test. Categorical data were analyzed by Pearson’s test. P-values < 0.05 were considered to be statistically significant. **Results:** Histological subtypes were significantly associated with EMT activation level. Poorly differentiated tumors mainly comprising solid, micropapillary, and mucinous adenocarcinoma possessed highly activated EMT level, and vice versa. Group F showed the highest positivity both in local lymphatic/vascular invasion and lymph-node metastasis (35.7%/ 42.9%/ 46.3%, respectively), followed by group P and group N in order. Significant difference was found in 5-year disease-free/ overall survival rate among these 3 groups: group F, 46.9%/ 50.6%; group P, 64.9%/ 73.4%; group N, 74.9%/ 85.4%. Tumors harboring wild type EGFR or mutant p53 had tendency to acquire higher EMT activation level. Interestingly, p53 mutation rate significantly correlated with EMT activation level especially in mutant EGFR tumors, whereas no correlation in wild type EGFR ones. No significant correlation was shown between EMT activation level and the proportion of K-ras mutation or ALK fusion gene. **Conclusion:** Our results revealed that the activation of EMT mechanisms in human lung adenocarcinoma is significantly associated with histological subtypes and plays important roles in the tumor progression through its lymph-vascular local involvement leading to the node-metastasis. Among human lung adenocarcinomas harboring EGFR mutation, p53 alteration deeply correlates with EMT activation. **Keywords:** lung cancer, EMT, invasion and metastasis, DNA mutation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-015 Pleomorphic Carcinoma of the Lung: A Clinicopathologic Study of 23 Resected Cases Dai Sonoda, Mototugu Ono, Yasuto Kondo, Shoko Hayashi, Masashi Mikubo, Hiroyasu Nakashima, Yoshio Matsui, Masaaki Ichinoe, Kazu Shiomi, Shi-Xu Jiang, Yoshiki Murakumo, Yukitoshi Satoh *Kitasato University School of Medicine, Sagamihara/Japan*

Background: Pleomorphic carcinoma (PC) of the lung is rare, and it is classified as a subtype of sarcomatoid carcinoma of the lung in the WHO histologic classification of lung tumors. We here demonstrated the clinicopathologic characteristics of PC surgically resected in our hospital. **Methods:** In this study, 23cases (2.3%) of PC among 968 of non-small cell lung cancer surgically resected at the Kitasato University Hospital between January 2004 and January 2015 were reviewed. The registry data of the patients with PC were analyzed, and the clinicopathologic profiles and surgical outcomes of the patients were evaluated. **Results:** There were 19 men and 4 women, and their mean age was 64 years (range: 39 to 81 y). All but two patients were smoker, and their mean smoking index was 41 pack year. In this study, the mean diameter of the tumor was 48.8 mm; tumors over 50 mm in diameter comprised 45% of all cases. The TNM pathological stages of PC were classified as: 2 (9%) cases with stage IA, 5 (22%) with stage IB, 2 (9%) with stage IIA, 8 (35%) with stage IIB, 5 (22%) with stage IIIA, and 1 (4%) with stage IIIB carcinoma. Ten tumors contained identifiable epithelial components, and the other 12 consisted of spindle cells and giant cells alone: an adenocarcinoma component was found in 11 cases, and 4 of the 11 cases had a coexisting squamous cell carcinoma component. In all the 23 patients, lymphatic infiltration and/or venous infiltration were evident. Overall follow-up ranged from 60 to 2605 days, with a median (for patients still alive) of 896 days. The overall survival rate and disease-free survival rate were 65% and 57%, respectively. Furthermore, 58% of the clinical stage I patients with PC demonstrated advance in the pathological stage. Cancer recurrence was identified in 6 patients; local or local with distant recurrence in one each and distant in 4. **Conclusion:** We concluded that PC should be considered as an aggressive disease and vascular infiltration should be usually reported and used as a factor in clinical assessments. **Keywords:** clinicopathologic study, aggressive disease, Pleomorphic carcinoma

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P1.04-016 Assessment of the Adequacy of Tissue Diagnosis by EBUS in Relation to the PET Scan and the Operator’s Experience Ahmed Mostafa[1], Nagla Abdel Karim[2], Michelle Kirshner[3], Mahmoud Mahmoud[4], Changchun Xie[5], Sadia Benzaquin[3] [1]*Pulmonary and Critical Care, The University of Cincinnati, Ohio/AL/United States of America,* [2]*Internal Medicine/Division of Hematology/Oncology, The University of Cincinnati, Ohio/OH/United States of America,* [3]*Pulmonary and Critical Care, The University of Cincinnati, Ohio/OH/United States of America,* [4]*Internal Medicine-Division of Hematology/Oncology, The University of Cincinnati, Cincinnati/United States of America,* [5]*Biostatistics, The University of Cincinnati, Ohio/OH/United States of America*

Background: Lung cancer remains the leading cause of cancer related death in USA and around the world. Multiple modalities are available for sampling lung neoplasms, mediastinal and hilar lymph nodes . Endobronchial ultrasound –guided transbronchial needle aspiration (EBUS-TBNA) has become an important diagnostic tool . Although the samples obtained by EBUS-TBNA are smaller than specimens collected by other surgical methods, the procedure has shown excellent specificity and sensitivity for the diagnosis of neoplastic diseases, is cost-effective compared to mediastinoscopy , and has become the procedure of choice for initial evaluation of patients with mediastinal and hilar lymphadenopathy . EBUS is currently performed by both interventional and general pulmonologists. Aim of the study: To assess the adequacy of tissue for diagnosis in relevance to PET scan, the diagnostic yield of the various lymph node (LN) stations and the level of experience of the operator. **Methods:** We reviewed the chart of 171 patients who underwent EBUS between the years of 2011-2013. We reviewed the pathological diagnosis, the LN stations, the PET scan results and the operator who performed the EBUS. **Results:** We included 171 patients where adequacy of tissue diagnosis was achieved by majority of patients in whom EBUS was performed (p<.0001). More tissue seemed to be positive in LN station 4 compared to the other LN stations but with no statistical significance. There was no correlation between the positivity of the PET scan and the tissue adequacy for diagnosis by EBUS (p=0.6410). PET scan showed a trend to increase in positive uptake in LN station 2 (p=0.0705). The adequacy of tissue diagnosis was achieved most significantly by Interventional Pulmonary (IP) trained operator, followed by an operator of more than 5 years’ experience followed by an operator of less than 5 years’ experience with 100% , 93.33% , 88.89% subsequently for tissue diagnosis accuracy (p=0.0019). The diagnostic tissue adequacy had a positive correlation with the PET scan when analyzed by operator, where the operator with more than five years’ experience had a closer correlation with the PET scan positive uptake. The percentage of tissue adequacy in relation to the PET scan positive uptake was of 54.64% , 76.67% and 35.56% subsequently (p=0.0009). **Conclusion:** The adequacy of tissue diagnosis was achieved by majority of patients in whom EBUS was performed. There was no correlation between the positivity of the PET scan and the tissue adequacy for diagnosis by EBUS therefore PET scan and EBUS should be used complementary to each other for the appropriate diagnosis and staging of patients. The adequacy of tissue diagnosis was achieved most significantly by (IP) trained operator, followed by an operator of more than 5 years’ experience followed by an operator of less than 5 years’ experience. **Keywords:** Tissue diagnosis, EBUS, IP, Adequacy

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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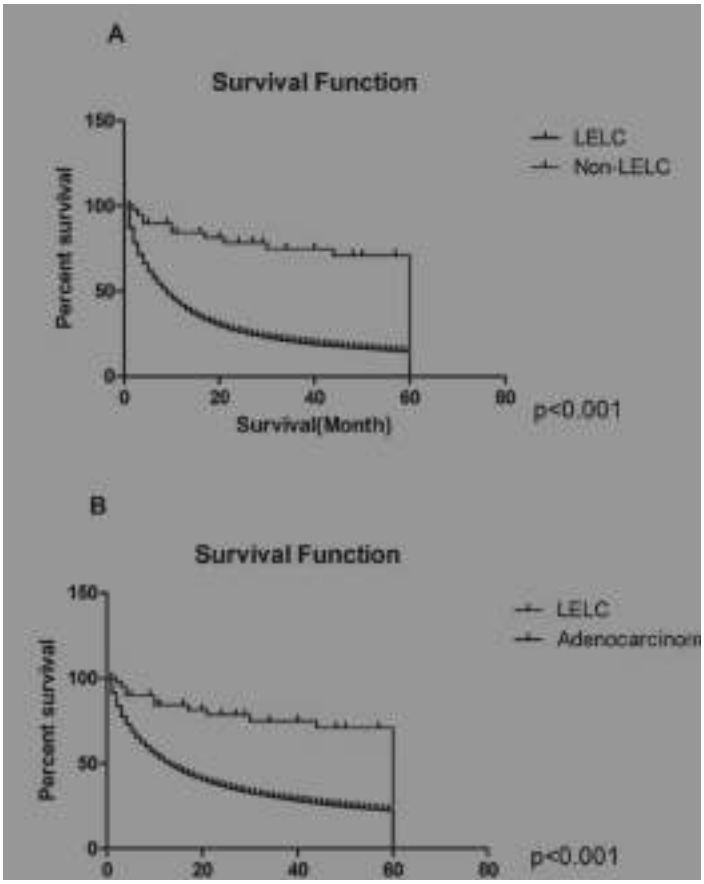
P1.04-017 Pulmonary Lymphoepithelial-Like Carcinoma: A Surveillance, Epidemiology, and End Results Database Analysis Jiaxi He, Jianfei Shen, Hui Pan, Chenglin Yang, Long Jiang, Wenhua Liang, Jianxing He *Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou/China*

Background: Pulmonary lymphoepithelial-like carcinoma (LELC) is one of the rare histological non-small cell lung cancers. Only a few case reports have been published. The knowledge of its characteristics and prognosis is limited. Based on the data of the Surveillance, Epidemiology, and End Results Database (SEER), an analysis was performed to fill the gap of our knowledge **Methods:** Characteristics, treatment and outcomes of all pulmonary LELC patients was extracted both from the SEER database with 18 registered center from 1973-2011 using SEER*Stat 8.1.5 Statistical analysis was performed using SPSS 16.0 and GraphPad Prism 5. **Results:** A total of 62 patients with pulmonary LELC are identified and recorded. Among them, Caucasian patients account for the largest proportion (64.4%). The medium age at diagnosis is 65. The 1, 3 and 5 years survival rates of LELC are 85.6%, 74.5% and 55.2%. The median survival time of all LELC patients is 34 months. Comparing to other types of lung cancer, LELC has a better survival. 14 patients have received radiation, while most of the early stage LELC patients (30/34, 88.2%) have received surgical resection as the first treatment.



Conclusion: Pulmonary LELC is a rare pathological type of lung cancer . In this cohort, male and Caucasian patients account for a large proportion of LELC patients. The mean age of pulmonary LELC patients in this study is older than the patients in Asian studies. A large amount of patients are in the early stages (localized and regional) when they are diagnosed as LELC. LELC has a better prognosis than adenocarcinoma, most early stage patients have received surgical resection. However, no prognosis factor has been identified in our study. In order to understand pulmonary LELC more thoroughly, more cases are required. **Keywords:** NSCLC, lymphoepithelial-like carcinoma, SEER, Outcomes

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-018 The Value of Histopathological Examination for Bronchoscopic Ultrasound Guided Fine-Needle Aspiration in Diagnosis of Lung Cancer Subtypes Tõnu Vanakesa[1], Ingemar Almre[1], Sirje Marran[2] [1]*Center of Cardiothoracic Surgery, North Estonia Medical Center, Tallinn/Estonia,* [2]*Department of Endoscopy, North Estonia Medical Center, Tallinn/Estonia*

Background: The role of endobronchial ultrasound (EBUS) and transesophageal bronchoscopic ultrasound (EUS-B)-guided fine-needle aspiration (FNA) of intrathoracic lymphnodes has acquired paramount importance in obtaining definitive diagnosis in malignant diseases. Recently, the diagnostic value of cell block processing of EBUS-FNA samples to obtain accurate distinction between lung cancer subtypes has been studied, but the diagnostic yield have been marginally investigated in a larger cohort of patients. **Methods:** We review tertiary hospital experience with EBUS-FNA and EUS-B-FNA in obtaining tissue diagnosis for lung cancer and evaluate, if the cell block processing method increases diagnostic accuracy in pathological lung cancer subtyping. The pathological examination was based on smear cytology (SC) and cell block preparation (CBP) routinely obtained during EBUS (EUS-B)-FNA. After cell block embedding in paraffin and sectioning at 3 micrometer hematoxylin and eosin staining and if required immunostaining was available for microscopical histopathological examination. **Results:** From January 2011 to December 2013, 608 patients, including 208 lung cancer patients with mediastinal and hilar lymphnodes pathology, underwent EBUS-FNA or simultaneous EUS-B-FNA in North Estonia Medical Center. In lung cancer patients cytological assessment was performed in all 208 cases. Formalin fixed paraffin-embedded cell block for histopathological examination was available in 196 (94.2%) cases. The overall morphological verification rate in CBP group was 85.6% (n=178) and in SC group 79.3% (n=165). The pathological diagnosis of undifferentiated type of lung cancer was provided in 43.7% (n=91) of CBP cases and in 35.6% (n=74) of SC cases. Diagnostic yield in pathological subtyping of lung cancer was significantly higher in CPB compare to SC: 81.2 % (n=169) vs. 43.7% (n=91), respectively (p<0.005). Adding CBP to SC provided an accurate subtyping of lung cancer in 102 more patients and the diagnostic efficacy was increased by 49.0% (n=102/208) (p<0.005). **Conclusion:** Cell block processing method combined with smear cytology obtained from intrathoracic lymphnodes applying EBUS (EUS-B)-FNA significantly increases diagnostic yield in pathologic lung cancer subtyping. Both tissue processing techniques should be routinely applied simultaneously whenever possible with aim to facilitate clinical decision and make impact on lung cancer patients outcome. **Keywords:** cell clock, endobronchial ultrasound, ultrasound guided fine-needle aspiration, lymphnodes

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-019 A Comparative Study of Micropapillary Pattern and Computed Tomographic Findings in the Patients with Small Lung Adenocarcinoma (≤ 2cm) Jun-Ichi Nitadori[1], Yukihiro Yoshida[1], Aya Shinozaki-Ushiku[2], Hideki Kuwano[1], Kazuhiro Nagayama[1], Masaki Anraku[1], Masaaki Sato[1], Masashi Fukayama[2], Jun Nakajima[1] [1]*Department of Thoracic Surgery, The University of Tokyo Hospital, Tokyo/ Japan,* [2]*Department of Pathology, University of Tokyo Hospital, Tokyo/Japan*

Background: We have recently demonstrated that presence of the micropapillary pattern increases the risk of local recurrence after limited resection for ≤2 cm lung adenocarcinoma (ADC). Currently, limited resection for small lung ADC has been done based on the definition of radiological non-invasive lung cancer, until histological subtype have not been examination. The purpose of this study is to investigate whether the presence of micropapillary pattern correlates with radiological non-invasive lung cancer in small lung ADC. **Methods:** All available tumor slides from patients with clinical stage IA, therapy-naive, surgically resected solitary lung ADC ≤2 cm in size (2001-2012) were reviewed. Comprehensive histologic subtyping was performed according to the IASLC/ ATS/ERS classification. Tumor diameter and solid component diameter were measured at the maximum cut surface of the tumor using high-resolution CT (HRCT). HRCT findings were classified as three groups as pure ground glass nodule (GGN), part-solid, solid based on the IASLC/ATS/ERS classification. Recurrence-free probability (RFP) was estimated using the Kaplan-Meier method. **Results:** 233 patients met inclusion criteria (50% women; median age: 67yrs; 48% never-smokers; median tumor size: 1.2cm; 68 pure GGN/ 76 part-solid/ 89 solid; 157 lobectomy; 43 AIS/ 77 MIA/113 IAD; 13 lymph node metastasis). Presence of the micropapillary pattern (≧5%) (MPP≧5) was identified in 21 cases (9%). MPP≧5 was significantly associated with tumor size, lymph node recurrence, lymphatic invasion, vascular invasion (*P* = .001, .003, .0017, .014, respectively) and was associated with increased risk of recurrence as compared to MMP<5% (5-year RFP: MIP≧5%:74.3%; MIP<5%:87.6%; *P* = .046). Twenty-one patients with MPP≧5 included 1 pure GGN / 5 part-solid / 15 solid in HRCT. The patient with pure GGN and MPP≧5 showed recurrence in lymph nodes in 10 months after surgery. In pure GGN group, MPP≧5 was associated with increased risk of recurrence as compared to MMP<5% (P=0.0001). **Conclusion:** The patient with radiological non-invasive lung cancer may be included in micropapillary pattern. It is necessary to consider lung adenocarcinoma histological subtypes for the patient with limited resection. **Keywords:** radiological non-invasive lung cancer, small lung adenocarcinoma, micropapillary, IASLC/ATS/ERS classification

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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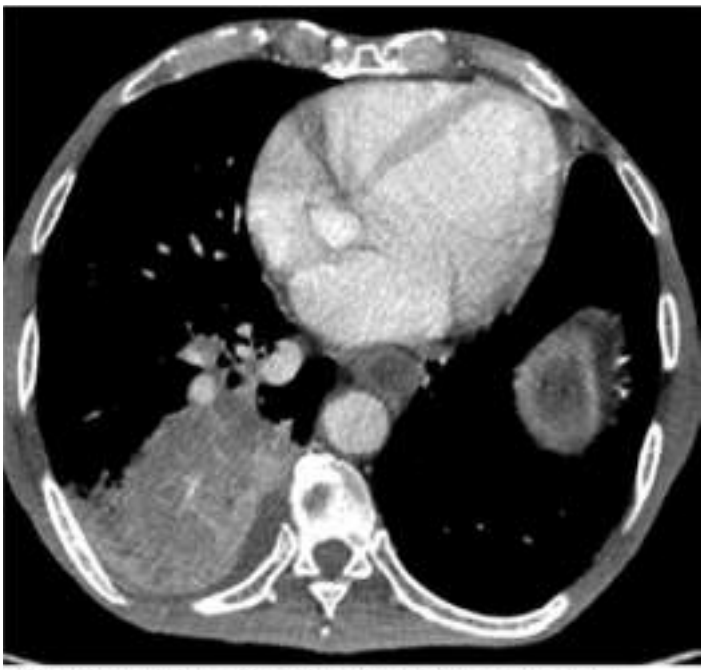
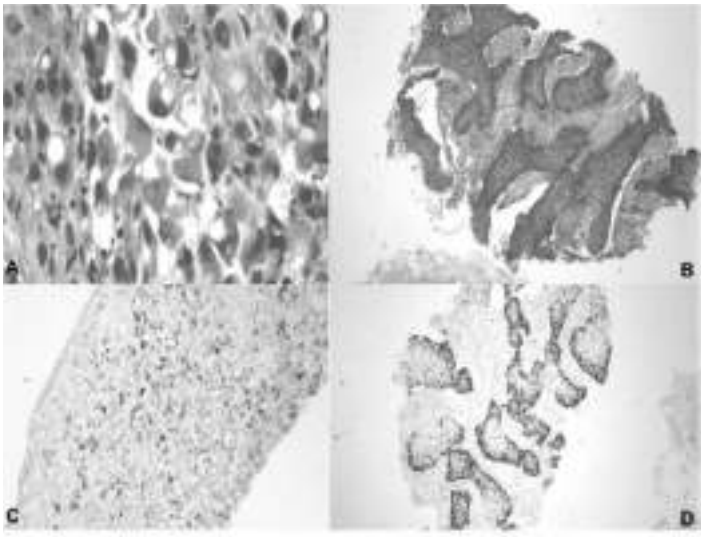
P1.04-020 Adenocarcinoma Metastatic Gastrointestinal Origin and Lung Squamous Carcinoma Associated with HIV Disease: Case Report Liliana Fernandez[1], Lina Garcia[2], Carlos A. Muñoz[3], Luz F. Sua[4] [1]*Interventional Pulmonology, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [2]*Internal Medicine Resident, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [3]*Medical Research, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [4]*Department of Pathology and Laboratory Medicine. Phd Biomedical Sciences, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia*

Background: Individuals infected with HIV have a higher predisposition to develop malignancies. The spectrum of neoplastic diseases in HIV-infected patients has changed after the introduction of antiretroviral therapy which decreased the AIDS defining malignancies such as Kaposi's sarcoma (KS) and non-Hodgkin lymphoma (NHL), but augmented other tumor types contributing to increased mortality of patients on chronic treatment. We report a patient with HIV on more than 10 years of antiretroviral treatment in whom diagnosis of a metastatic adenocarcinoma of gastrointestinal origin and a

concomitant primary lung squamous carcinoma was made. **Methods:** Clinical History Revission **Results:** A 68-year-old man with a history of HIV on antiretroviral treatment (ART) since 2004, ex-smoker with COPD, osteoporosis and chronic malnutrition, who presents with cough, dyspnea and hemoptysis. On the chest CT-scan a right paravertebral mass associated with atelectasis, a parahilar mass extending to the left upper lobe, and a mass in the pancreatic head is observed. A bronchoscopy with biopsies is performed. The morphological and inmunophenotypic expression patterns of the right lower lobe show metastatic adenocarcinoma of gastrointestinal origin while the left lower lobe biopsy shows primary squamous cell lung carcinoma and the presences of Aspergillus. The patient continued with hemoptysis, developed refractory respiratory failure and died. **Conclusion:** With the widespread use of potent ART there was a dramatic decrease in the incidence of KS and NHL and a significant increase in the incidence of several other malignancies. Although the biology of malignancy in HIV-infected people is often more aggressive than in those without HIV infection, standard treatment is generally indicated and can be associated with a favorable outcome, depending upon the tumor type, stage, and comorbidity. In this case two advanced stage tumor lesions associated with hemoptysis were documented, which finally led to the death of the patient.



Chest CT-scan a right paravertebral mass associated with atelectasis, a parahilar mass extending to the left upper lobe



A, C: H & E staining cells signet ring adenocarcinoma in RLL, positive for CK20 and CDX2 (IHC) determining a metastatic origin of the lower gastrointestinal tract. B,D: H & E staining of squamous cell tumor positive for p63 gene (IHC) in LLL

Keywords: HIV, Antiretroviral treatment, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-021 No MAML2 Gene Alteration Found in Ciliated Muconodular Papillary Tumor of Lung; Genetic Difference from Mucoepidermoid Carcinoma

Noriko Motoi[1], Hiroko Nagano[1], Hironori Ninomiya[1], Sakae Okumura[2], Yuichi Ishikawa[1]
[1]*Division of Pathology, The Cancer Institute, Japanese Foundation for Cancer Research, Tokyo/Japan,* [2]*Thoracic Surgery, The Cancer Institute Hospital of Jfcr, Tokyo/Japan*

Background: MAML2 (mastermind-like 2 (Drosophila)) gene, a transcriptional coactivator for NOTCH proteins, is known to be involved as a part of fusion gene (MECT1-MAML2) which is found in mucoepidermoid carcinoma (MEC) both of salivary gland and pulmonary origin. Ciliated muconodular papillary tumor (CMPT) is sharing morphologic features with mucoepidermoid carcinoma, at least in part, i.e. consist of mixture of mucinous and squamous epithelium. To determine whether these morphological mimics can share the molecular alterations, we evaluated MAML2 rearrangement of CMPT by FISH. **Methods:** Five cases of CMPT was recruited from pathologic diagnostic records between 2005 to 2014. Morphological assessment was done on routine HE stained slides of whole tumor specimen. Representative area was selected and submitted to FISH analysis. Fluorescence in situ hybridization (FISH) using break apart type MAML2 gene probes was performed on FFPE specimen. The break apart signal percentages on separated tumor nuclei was counted on the captured images of digital fluorescence microscope. 100 nuclei was counted in each cases. More than 30% of break apart signal is considered as positive result. **Results:** All five CMPTs were reviewed and confirmed the diagnosis on HE stained slides. These cases included 4 male, 1 female, were mean age of 71 years-old (range 60-83). There were three incidental cases which were patients with one primary lung adenosquamous carcinoma and two metastatic cancer (one colon cancer, one liposarcoma). All of five CMPT resulted negative for MAML2 break-apart FISH. **Conclusion:** These results indicated that CMPTs do not share the molecular alteration of MAML2, which is commonly detected in mucoepidermoid carcinoma of lung. In conclusion, CMPT is a distinct tumor or tumor-like lesion, does not related to MEC. Although, it is still uncertain whether CMPT is a true neoplastic lesion with multi-lineage differentiation potential or a reactive process with extensive epithelial proliferation.
Keywords: ciliated muconodular papillary tumor of lung, MAML2 (mastermind-like 2 (Drosophila), mucoepidermoid carcinoma

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-022 Prognostic Significance of Solid or Micropapillary Component in Pulmonary Invasive Adenocarcinoma Measuring ≦ 3cm

Yuki Matsuoka[1], Makoto Wakahara[1], Yohei Yurugi[1], Yuzo Takagi[1], Tomohiro Haruki[1], Ken Miwa[1], Kunio Araki[1], Yuji Taniguchi[1], Kanae Nosaka[2], Tatsushi Shiomi[2], Yoshihisa Umekita[2], Hiroshige Nakamura[1]
[1]*Department of Surgery, Division of General Thoracic Surgery, Tottori University, Faculty of Medicine, Tottori/Japan,* [2]*Department of Pathology, Tottori University, Faculty of Medicine, Tottori/Japan*

Background: According to the International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS) classification, both solid- and micropapillary-predominant pulmonary adenocarcinoma have been reported to have a poor prognosis. Although pulmonary adenocarcinoma with some solid or micropapillary component have also been reported to have a poor prognosis, the ratio of these component to be chosen as the cutoff value for a prognostic factor remains controversial. **Methods:** A total of 115 patients with pulmonary invasive adenocarcinoma measuring ≦ 3 cm who underwent curative surgery at Tottori University Hospital between January 2005 and December 2008 were included. Patients with variants of invasive adenocarcinoma were excluded from this study. The median follow-up time was 78.0 months. A total of 84, 9, and 22 patients underwent lobectomy, segmentectomy, and wedge resection, respectively, and 100, 5, and 10 patients had stages I, II, and III, respectively. The tumors were divided into subtypes according to the IASLC/ATS/ERS classification. Cases with solid component occupying ≧ 5% of the entire tumor were defined as S-positive (S+), and cases with micropapillary component occupying ≧ 1% of the entire tumor were defined as MP-positive (MP+). Of the 115 adenocarcinoma, 30 and 85 were S+ and S-, and 27 and 88 were MP+ and MP-. The clinical characteristics and pathologic data of all 115 adenocarcinoma were retrospectively evaluated. The Kaplan-Meier method was used to estimate the recurrence-free survival (RFS) and overall survival (OS) rates, and the log-rank test was used to compare the RFS and OS among the subgroups. **Results:** The 5-year OS rate of cases that were S+ and S- was 92.5% and 62.1%, respectively (log rank $P < 0.001$). The 5-year RFS rate of cases that were MP+ and MP- was 77.3% and 51.9%, respectively (log rank $P = 0.001$). On multivariate survival analysis, the presence of solid component proved to be an independent prognostic factor, and the presence of micropapillary component proved to be an independent recurrence factor. **Conclusion:** The presence of solid component occupying ≧ 5% of the entire tumor was an independent predictor of a poor prognosis in pulmonary invasive adenocarcinoma measuring ≦ 3cm. The presence of any micropapillary component, even if only in 1% of the entire tumor, was a risk factor for post-operative recurrence and it affected the prognostic value.
Keywords: pulmonary adenocarcinoma, solid, micropapillary, component

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-023 Primary Adenocarcinoma in the Lung Reclassified - Histological Subtypes and Outcome Gudrun N. Oskarsdottir[1], Tomas Gudbjartsson[2], Steinn Jonsson[1], Johannes Bjornsson[3], Helgi J. Isaksson[4] [1]*Department of Internal Medicine, Landspitali University Hospital, Reykjavik/Iceland,* [2]*Department of Thoracic Surgery, Landspitali University Hospital, Reykjavik/Iceland,* [3]*Department of Pathology, Akureyri Hospital, Akureyri/Iceland,* [4]*Department of Pathology, Landspitali University Hospital, Reykjavik/Iceland*

Background: Non-small cell lung cancer (NSCLC) comprises 85% of primary lung cancer, where adenocarcinoma, squamous cell and large cell carcinoma are the most common histological types. Recently a new classification of primary adenocarcinomas of the lung was published. The aim of this study was to review the histology of all primary lung adenocarcinomas operated on in Iceland during a 20 year period, 1991-2010, using the new criteria and assess the impact of histology on survival. **Methods:** This nationwide study included 301 patients with primary lung adenocarcinoma (mean age 65.5 yrs., 56% female) that underwent resection in Iceland between 1991-2010. Tumors were reclassified according to the current IASLC/ATS/ERS pulmonary adenocarcinoma classification system. Overall survival was estimated by the Kaplan-Meier method and multivariate Cox regression analysis used to evaluate prognostic factors of survival, including histological subtype **Results:** Acinar predominant adenocarcinoma was the most common histological subtype (45%). Solid predominant with mucin production comprised 24% of the cases, lepidic predominant 19% and papillary predominant 8%. There was one *in situ* adenocarcinoma, three minimally invasive adenocarcinomas and seven invasive mucinous adenocarcinomas. Overall survival at 1 year for all histological subtypes of adenocarcinoma was 81.1% and 42.6% at 5 years. A statistically significant difference in survival between the histological subtypes was not seen (log-rank test, p=0.43). Using multivariate analysis advanced stage and age predicted a worse outcome. Histologic subtyping did neither predict survival in uni- or multivariate analysis. **Conclusion:** Acinar and solid predominant adenocarcinoma are the most common histological subtypes for primary lung adenocarcinoma in Iceland. There was not a statistical difference in survival according to histological subtypes and the subtyping was not a prognostic factor of survival.
Keywords: survival, lung adenocarcinoma, outcome, adenocarcinoma subtypes

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-024 When Bone Starts Growing in the Lung: A Case Series of Pulmonary Ossifications Jan F. Gielis[1], Vassiliki Siozopoulou[2], Patrick Lauwers[1], Jeroen Hendriks[1], Paul Van Schil[1] [1]*Vascular & Thoracic Surgery, Antwerp University, Edegem/Belgium,* [2]*Pathology, Antwerp University, Edegem/Belgium*

Background: Pulmonary ossifications are heterotopic bone formations in the lung, previously thought to be a post-mortem finding only. Two types are described: nodular ossifications, smoothly edged, which are found in the alveoli themselves, and dendriform ossifications, branching through the alveolar septa. In this study the incidence of pulmonary ossifications was studied in a consecutive series of patients undergoing pulmonary surgery. **Methods:** From January 2008 to February 2015 19 patients with pulmonary ossifications were identified in patients undergoing thoracic surgery at Antwerp University Hospital. Diagnosis was made by the pathologist team. Neither PET nor CT was able to differentiate these ossifications from solid tumors. **Results:** 15 patients (79%) were male. 8 received lung surgery for tumoral pathology. Most ossifications (58%) were found in the lower lung lobes without predilection for either chest side. 3 patients (16%) died during follow-up due to oncologic pathology unrelated to the ossifications. Most ossifications were nodular-type (12 or 63%), 6 or 32% were dendriform and one case contained both types.

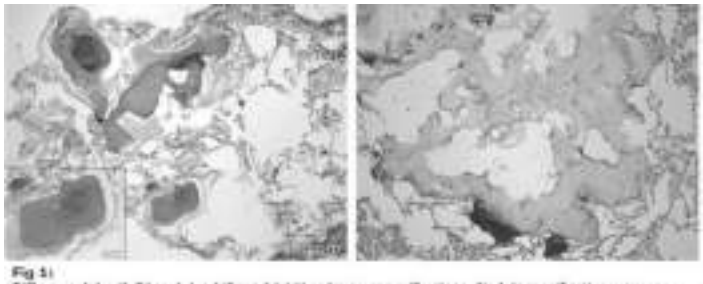

Fig 1:
Diffuse nodular (left) and dendriform (right) pulmonary ossifications. Nodular ossifications grow within the alveolar spaces, where dendriform ossifications branch through the septa and often contain fatty bone marrow. (H&E stain, 400x)

Conclusion: Pulmonary ossifications are not as seldom as previously thought. These benign lesions are not simply a post-mortem finding and could be mistaken for a malignant space-occupying process. There appears to be a predilection for the lower lung lobes in male patients, without a clear association with other pathologies. Therefore, pulmonary ossifications deserve a place in the differential diagnosis of solitary pulmonary nodules.
Keywords: Pathology, ossification, solitary pulmonary nodule

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-025 Lung Cancer Incidence by Histology, Gender, Race/Ethnicity and Socioeconomic Status Manali I. Patel[1], Meg Mckinley[2], Iona Cheng[2], Heather A. Wakelee[1], Scarlett Gomez[2] [1]*Stanford University, Stanford/United States of America,* [2]*Cpic, Fremont/United States of America*

Background: The incidence trends of lung cancer (LC) by histology, gender, race/ethnicity and neighborhood socioeconomic status (nSES, derived from US Census data) have not been reported. To examine these trends, we conducted a population-based study, using data from the California Cancer Registry across three discrete time periods to correspond with Census data on nSES: 1988-1992; 1998-2002; 2008-2011. **Methods:** Incidence data for invasive LC were abstracted for the three time periods. In each time period, male and female age adjusted incidence rates of LC and incidence rate ratios were calculated by histologic cell type and stratified by nSES. **Results:** A total of 240,307 LC cases were identified across the three time periods. Histology incidence trends by race/ethnicity are shown in Figure 1 and by nSES in Table 1 for males and females. Larger declines in incidence were seen over the 3 time periods among males than females. Among males, incidence rate declines over time were seen in all race/ethnic and nSES groups, but were largest among Blacks and Hispanics. Across all races/ethnicities among males, there was a slight increase over time in the incidence of adenocarcinoma histology. Among females, incidence rate declines were seen among Hispanics regardless of nSES, mid- and high-nSES Whites, and low- and mid-nSES Blacks; incidence trends among Asian/Pacific Islander females did not change significantly over time, regardless of nSES. Among females, there were variations in incidence trends by histology with a slight increase in the adenocarcinoma histology.

Figure 1: Histology Incidence Trends by Race/Ethnicity

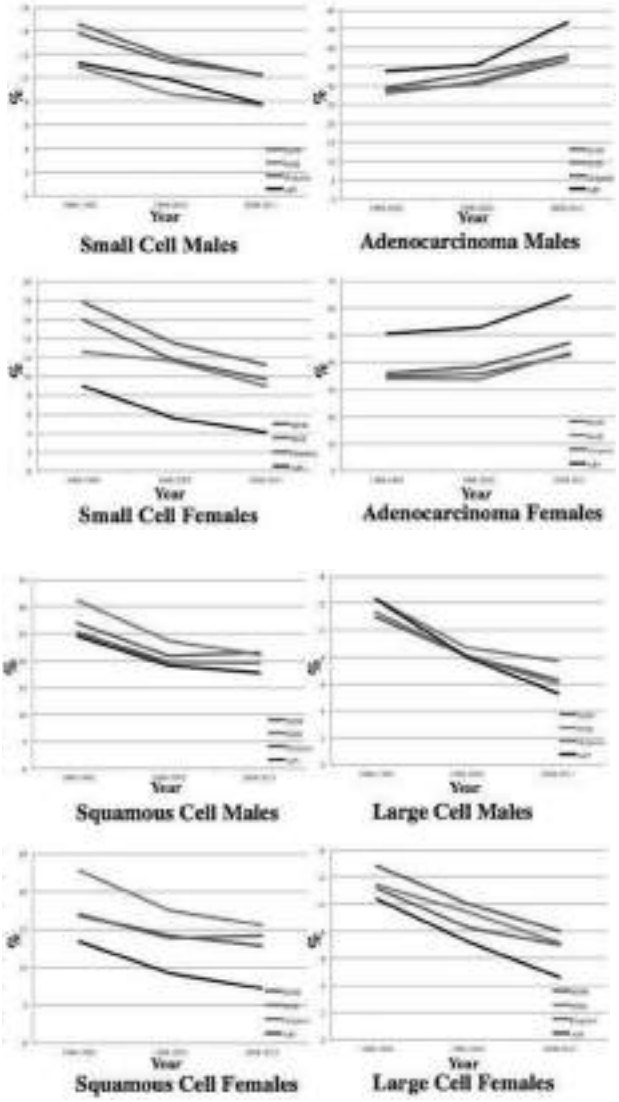
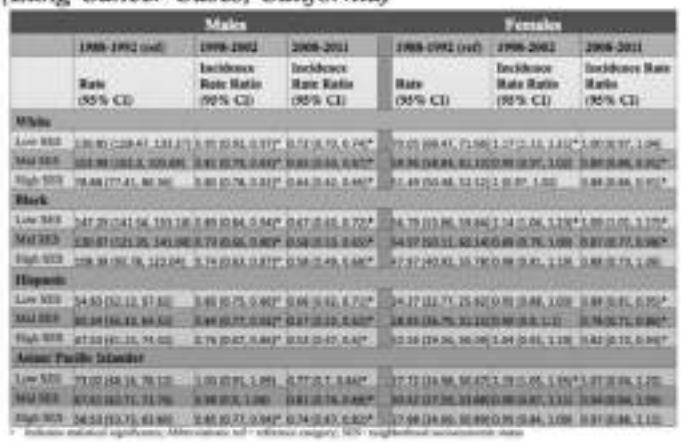


Table 1:Incidence Rate Ratios by Race/Ethnicity and Neighborhood Socioeconomic Status

(Lung Cancer Cases, California)



Conclusion: Our findings demonstrate differences in LC incidence over time by histology, gender, race/ethnicity and SES. While incidence rates consistently declined for males, there were greater declines in incidence for the high SES patient populations. For females, there were variations in trends by histology, race/ethnicity, and SES. These findings warrant further investigation. **Keywords:** incidence trends, race/ethnicity, histology, socioeconomic status

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P1.04-026 Lung Cancer Patients Who 'Relapse' After Primary Treatment May Have Different Pathology or No Malignancy Noelle O'Rourke[1], Fiona Roberts[2], Aqilah Othman[1] [1]*Clinical Oncology, Beatson West of Scotland Cancer Centre, Glasgow/ United Kingdom,* [2]*Pathology, Southern General Hospital, Glasgow/United Kingdom*

Background: In the evolving era of genetic sequencing of lung tumours and targeted agents, there is impetus to repeat biopsies of previously treated lung cancers when there is clinical and radiological evidence of relapse, justified on the basis that genetic status of the tumour may change over time. In our centre, even prior to genetic subtyping of lung cancers we have operated a policy of confirming relapse histologically and we present here the value of this strategy. This audit describes the outcome of repeat biopsies in the lung cancer population of Greater Glasgow over a five year period. **Methods:** The regional pathology database was interrogated for all patients with previous diagnosis of lung cancer who had repeat biopsy between February 2009 and March 2014. Inclusion criteria were those whose initial diagnostic biopsy was six months or more previously and included were CT guided biopsies, bronchoscopic brushings or washings, transbronchial or endobronchial guided biopsies, mediastinoscopies, surgical resections and cytology of pleural fluid. We excluded from our analysis those who were having lung biopsy due to metastasis from extra thoracic primary sites. We collated data on patient demographics, time between initial diagnosis and second biopsy, first and second pathology, stage and treatment at first presentation and again at second, whether second biopsy was a different site, and whether pathology was identical on second biopsy/similar (more or less well differentiated but same subtype of lung cancer)/ not malignant or different pathology. **Results:** 103 patients fulfilled our inclusion criteria: 41 men, 62 women; age range 35-85y with initial stage of disease: 55 I, 18 II, 25 III, 4 IV and 1 small cell. 91 had primary treatment with curative intent: 66 surgery, 25 radical radiotherapy +/- chemo. 11 had chemo alone, 1 observation only as first treatment. Time to second biopsy ranged 6-52 months (median 17). 70 patients (70%) had identical or similar pathology at second presentation. 13 had different pathology: 2 patients with initial NSCLC developed a second tumour which was SCLC, 1 previously treated SCLC developed a second tumour which was NSCLC, 1 resected carcinoid developed subsequent adenocarcinoma and one adenocarcinoma developed subsequent carcinoid. 8 patients had change of NSCLC subtype at second presentation. The remaining 20 patients had no malignancy on second biopsy: these had had prior radiotherapy or surgery all with radiological/clinical suspicion of recurrence. Of the 103 patients 42 are still alive. **Conclusion:** Although lung cancer carries a high risk of relapse following primary therapy our results demonstrate that clinical or radiological suspicion of recurrence cannot justify treatment without confirmatory biopsy. One third of our cohort either had no malignancy or a second pathology. **Keywords:** relapse, biopsy, second pathology

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-027 The Expression of Fibroblast Activation Protein (FAP) in Human Lung Cancer Tissues and Its Clinical Significance Xue Pan, Hua Shi
Department of Respiration, The Second Affiliated Hospital of Soochow University, Suzhou, China, Suzhou/China

Background: To study the expression of fibroblast activation protein (FAP) in human lung cancer tissues and its clinical significance. **Methods:** Western-blot analysis was used to explore the expression of FAP in lung cancer tissues, paraneoplatic tissues (2cm beyond the cancer margin) and distal normal lung tissues(surgical resected specimens of lung tissue near the cut end) and also the lung cancer cell lines(A549, H1299, SPCA-1). Immunohistochemistry was performed to study the expression of FAP at protein level in tissues from 41 cases of lung cancer and 6 cases of benign pulmonary lesion. **Results:** Western blot analysis showed the expression of FAP was higher than in paraneoplatic tissues as well as normal lung tissues ($P<0.05$). It was also be positive in lung cancer cell lines ($P<0.05$). Immunohisto-chemistry showed that the positive rate of FAP staining was in fibroblast cells were 75.6%(31/41), the positive rate of FAP staining was in lung cancer cells were also 90.2%(37/41), whereas the expression in benign pulmonary lesion tissues was poor plus (1/6). FAP expression was found to be significantly correlated with smoking status ($x2=5.4085$,$P=0.02$). However, there were no significant correlations between FAP and age, sex and TNM stage($P>0.05$). **Conclusion:** FAP could be over-expressed in lung cancer cells, which signifies that FAP also plays a role in the development of lung cancer and may serve as a potential biomarker in the treatment of lung cancer. **Keywords:** PD-1/PD-L1 fap

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-028 High Vimentin Expression in Micropapillary Component of Lung Adenocarcinomas Hiroyasu Nakashima, Shi-Xu Jiang, Yuichi Sato, Keika Hoshi, Toshihide Matsumoto, Ryo Nagashio, Makoto Kobayashi, Yukiko Matsuo, Kazu Shiomi, Kazushige Hayakawa, Makoto Saegusa, Yukitoshi Satoh
Kitasato University, Sagamihara City/Japan

Background: It is increasingly being recognized that adenocarcinomas (AC) of various organs with tumor cells arranged in a micropapillary pattern are more malignant than those without such a micropapillary component (MPC). However, the factors and mechanisms conferring the increased malignancy on MPC remain to be elucidated, so the exploration of such factors was the main purpose of the present study. **Methods:** We histologically reviewed the 629 radically resected lung adenocarcinomas at Kitasato University Hospital, Japan, from January 2002 to December 2012. MPC was defined as a small papillary tumor cell tuft without an obvious fibrovascular core. Tumors with ≥ 1% of their tumor cells arranged in a micropapillary pattern were diagnosed as AC with MPC (AC-MPC), while the remainder were diagnosed as conventional AC (CAC). The histological subtypes and differentiation grade of CAC as well as the background non-MPC of the AC-MPE were determined according to the 4th WHO classification. The clinicopathological features of AC-MPC and CAC were comparatively studied. The specific proteins expressed in AC-MPC were also analyzed using proteomic study based on 2-dimensional gel electrophoresis (2-DE), and the results were confirmed *in vivo* with imunohistochemistry. **Results:** One hundred and one (16.1%) of the 629 histologically reviewed lung adenocarcinomas met the criteria defined above and were thus diagnosed as AC-MPC. Compared with the CAC, the AC-MPC had worse statuses for tumor size, vascular invasion, pleural invasion, node metastasis, disease stage, postoperative up-staging, and overall survival (OS) and disease-free survival (DFS) ($p<0.0001$, respectively). On 2-DE, 19 proteins differentially expressed more than 1.5-fold in amount between lung CAC and AC-MPC; in particular, vimentin, one of the identified proteins, was most up-regulated (3.5-fold) in AC-MPC cases. Vimentin expression was detected in MPC of 95 (94.1%) AC-MPC, and when compared with the 119 control CAC, the expression scores in MPC were higher than those of well- and moderately differentiated CAC, as well as the background non-MPC of the AC-MPC ($p<0.0001$), but not significantly different from those of poorly differentiated CAC ($p=0.561$). Within the AC-MPC entity, higher vimentin expression was correlated with more frequent vascular invasion and more advanced node metastasis, and multivariate analysis showed that high vimentin expression was an independent indicator of worse prognosis (OS: $p=0.012$, DFS: $p=0.047$). **Conclusion:** Vimentin expression is prevalent and markedly up-regulated in MPC, which might reflect the biological essence of poorer differentiation or dedifferentiation of MPC, and this might have a role in the acquisition and increase of invasiveness and consequent more malignant nature of MPC. **Keywords:** micropapillary adenocarcinoma, vimentin, Immunohistochemistry, 2-dimensional gel electrophoresis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-029 Detection of Sputum Cofilin-1 Protein for Diagnosis of Human Non-Small Cell Lung Carcinomas Maristela P. Rangel[1], Milena M.P. Acencio[2], Caroline S. Faria[3], Vera L. Capelozzi[1], Cecilia A.V. Farhat[1], Leila Antonangelo[3] [1]*Pathology Department of University of Sao Paulo Medical School, Sao Paulo/Brazil,* [2]*Cardiopneumology, Pleura Laboratory, Pulmonary Division, Heart Institute (Incor) of University of Sao Paulo Medical School, Sao Paulo/Brazil,* [3]*Lim 03, Pathology Department of University of Sao Paulo Medical School, Sao Paulo/Brazil*

Background: The high incidence and mortality rates of lung cancer reflect the need for new diagnostic and prognostic markers capable to early detect the disease and also predict its recurrence. The ideal biomarker should be evaluated in biological samples obtained by minimally invasive procedures. In this context, sputum is an attractive biological sample

for these tests since it may represent the field of injury. Because cell–extracellular matrix interactions participate in several steps required for tumor cell invasion and formation of metastases, cofilin-1, hyaluronic acid (HA) and CD44 have been targeted as potential useful tumor markers. To our knowledge, cofilin-1 has never been evaluated in sputum from lung cancer patients. **Objective**: To evaluate the diagnostic and prognostic role of sputum cofilin-1 and to the relationship between this biomarker with HA and its receptor (CD44) in patients with non small cell lung cancer (NSCLC). **Methods:** Cofilin-1 and CD44 were analyzed by Elisa immunoassay and HA by "Elisa-like" fluorometric assay in the sputum of 74 NSCLC patients, 13 cancer-free patients with obstructive lung disease and 8 healthy individuals. Statistical analyses included ANOVA, ROC curves, Spearman correlation, and logistic regression. **Results:** Sputum cofilin-1 levels were increased in patients with lung cancer (1475.83 pg/ml ±145.35) when compared to cancer-free patients (662.63 pg/ml ±5.74) and volunteers (415.25 ±3.68 pg/ml). A significant association was found between cancer patients with high levels of cofilin-1 and CD44 (R=0.21; P=0.04) as well as between HA and CD44 (R=0.46; P<0.01). Cofilin-1 did not correlate with HA (P>0.4). Univariate analysis demonstrated that high expression of sputum cofilin-1 significantly correlated to T4 (P=0.01) and M stage (P=0.03), tobacco history (P=0.01) and squamous cell carcinoma histologic type (P=0.04). Logistic regression analysis controlled for tobacco history, histologic types, stage, HA and CD44 expression showed that cancer cell–associated cofilin-1 was an independent predictor of metastases [OR=5.77 (0.78-42.74)]. Patients with sputum cofilin-1 >1475.83pg/ml had a high risk for metastasis. In relating to diagnosis, sputum Cofilin-1, at a cut off value of 248.9pg/mL presented sensitivity and specificity of 0.80 and 0.67 respectively, in distinguish healthy volunteers from NSCLC patients with AUC of 0.787. Cofilin-1 was also able to distinguish cancer-free patients from cancer patients at a cut off of 802.5pg/mL with AUC of 0.693 and respective sensitivity and specificity of 0.60 and 0.54. **Conclusion:** Cofilin-1 presented moderate sensitivity as diagnostic biomarker for lung cancer in sputum. Cofilin-1 was associated with metastases, but its prognostic value was dependent on the histological type and tobacco history. The association between sputum cofilin-1 and CD44 in cancer patients suggests that during tumor development, high levels of cofilin-1 facilitate tumors growth and the penetration of capillaries into the tissue milieu. Thus, increased tumor expression of cofilin-1 seems to be more associated to primary events, while increased angiogenesis seems to be related to a secondary event. Regardless of the involved mechanism, detection of sputum cofilin-1 provides important prognostic information on cancer patients. Larger series of NSCLC patients still needs to be studied to confirm the usefulness of sputum cofilin-1 as diagnostic and/or prognostic biomarker.
Keywords: Cofilin, CD44, NSCLC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-030 Intra-Operative Pleural Lavage Cytology after Thoracotomy for Lung Cancer
Masatoshi Kakihana, Kimitoshi Nawa, Yasufumi Kato, Masaru Hagiwara, Junichi Maeda, Koichi Yoshida, Naohiro Kajiwara, Tatsuo Ohira, Norihiko Ikeda
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Background: Pleural lavage cytology (PLC) is the microscopic study of cells obtained from saline instilled into and retrieved from the chest cavity (in patients without preoperative pleural effusion) during surgery for non–small-cell lung cancer. The solution is aspirated, and cytologic analysis is performed to screen for malignant cells. Results from this procedure have been published from Japan as early as 1989,1 and internationally, an increasing number of centers have adopted this practice. **Methods:** Between 1995 and 2013, 2616 patients underwent surgical pulmonary resection for primary lung cancer without disseminated disease at our institute. Cytology of pleural lavage immediately after thoracotomy before any manipulation of the lung was examined in 1563consecutive patients with lung cancer with no pleural effusion. The macroscopic status of the pleural cavity was evaluated before any manipulation, and when no malignant findings were noted, the pleural cavity was washed with 100 ml of physiologic saline solution. **Results:** The results of the cytologic examination were **divided** into two categories, positive and negative PLC group. Papanicolaou classes I to IIIa were regarded as negative, classes IIIb, IV and V as positive. Of the 83 patients (6.8%) whose specimens were positive for PLC. Of the 83 patients in the positive PLC group, 74 (4.7%) had adenocarcinoma, with a significantly higher ratio of adenocarcinoma compared with the negative PLC group. Survival in the positive PLC group was significantly worse than in the negative PLC group ($p = 0.001$), especially in pathologic stage II ($p = 0.001$). We assume that the PLC positive cases have a T4 status. All PLC positive cases are reassigned Stage III. The result showed almost similar curves was shown between PLC negative Stage III and the adjusted PLC positive Stage III. We propose that positive PLC positive disease should be classified to pathologic T4 and managed similarly to dissemination. **Conclusion:** A positive PLC result was a strong unfavorable prognostic factor, and almost all patients with positive PLC relapsed within 5 years. PLC should be considered in all patients with early stage lung cancer suitable for resection ,especially, done when assessing the final stage in patients with adenocarcinoma of the lung. A positive result is an independent predictor of adverse survival and carries a prognosis. That suggests it may be appropriate to upstage patients by 1 T category or consider as T4 disease.
Keywords: pleural lavage cytology, NSCLC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-031 The Changing Anatomic Position of Squamous Cell Carcinoma of the Lung - A New Conundrum
William S. Krimsky[1], Manasa Vulchi[2], Daniel P. Harley[3], Pujan Patel[4], Suman B. Rao[5], Sarkar Saiyad[1], Ruth Evans[6], Joel Hammer[7]
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Background: Traditionally, squamous cell carcinoma of the lung (SqCC) is conceptualized as more of a central rather than a peripheral form of lung cancer. While there is some variability with respect to the definition in the literature of what constitutes the 'peripheral' portions of the lung, historically, rates of squamous cell carcinoma in the lung periphery are typically sited in the 15% to 30% range. More recently, and especially in light of the historical data, we increasingly observed that a significant portion of newly diagnosed peripheral lung lesions – perhaps even a majority, appeared to be squamous cell carcinomas. Therefore, a comprehensive review of the tumor data at our facility, a busy teaching hospital with a large cohort of cancer patients, was undertaken to assess whether there had been a substantive change in the traditional epidemiologic distributions of the lung cancer, specifically with respect to squamous cell carcinoma. Given the differences in cell biology and carcinogenesis of different types of cancer, a potential epidemiologic shift might suggest a change in tumor biology, etc. **Methods:** From May 12th, 2012 through May 13th of 2013, all histopathologicallly confirmed diagnoses of squamous cell carcinoma of the lung at our facility were reviewed. Again, while there is some dissonance in the literature with respect to the definition of the 'periphery', a reasonable approach given the existing data is to define the lung periphery as the lateral or outer half of the lung with respect to the position of the lesion on the axial cuts of the computed tomography scans of the chest. Each patient's lesion was then classified as peripheral or central using that definition. Furthermore, various demographic data points for each patient such as age, race, sex, smoking history, use of inhaled corticosteroids, and concomitant use of proton pump inhibitors were also collected and analyzed. In addition, a cohort of patients without a prior history of malignancy was also analyzed as a "de novo" subset. **Results:** During the evaluation period, a total of fifty-six patients were diagnosed with SqCC. Of these, 55% (31/56) had SqCC located in the lung periphery with the remaining 45% (25/56) being found in a central location. Of the 56 patients diagnosed with SqCC, 27 had a prior history of malignancy. These 27 patients were then removed from the analysis in an effort to assess whether this distribution would persist in the remaining 29 patients. This "de novo" SqCC subset was then analyzed. Of this subset of patients, 62% (18/29) had SqCC that were located in the lung periphery and 38% (11/29) had lesions that were located centrally. Other epidemiological features correlated with typical trends seen in patients with SqCC. **Conclusion:** Our findings appear to confirm our initial observation that, within our institution, there has been a substantive shift in the traditional distribution of Squamous Cell Carcinoma with the majority of these cancers now being diagnosed in the lung periphery as opposed to the more central locations. Further work will be needed to confirm these results.
Keywords: peripheral lung lesions, Squamous cell carcinoma of the lung, Distribution of SqCC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-032 Clinical and Pathological Characterization of Long-Term Survivors with Advanced Non-Small Cell Lung Cancer: A Multicenter Experience in Madrid
María Sereno Moyano[1], Rosa Alvarez[2], Maria Eugenia Olmedo[3], Javier Puente[4], Xabier Mielgo[5], Fátima Navarro[6], Francisco Zambrana[1], Juan Moreno-Rubio[1], Sagrario García[1], Enrique Casado[1], Ana Sánchez[7], Santiago Ponce[8] [1]*Medical Oncology, Infanta Sofía University Hospital, Ss de Los Reyes/Spain,* [2]*Gergorio Marañón University Hospital, Madrid/Spain,* [3]*Ramón Y Cajal Hospital, Madrid/Spain,* [4]*Hospital Clínico San Carlos, Madrid/Spain,* [5]*Fundación Alcorcón, Madrid/Spain,* [6]*Principe de Asturias University Hospital, Madrid/Spain,* [7]*Getafe University Hospital, Madrid/Spain,* [8]*Hospital 12 de Octubre, Madrid/Spain*

Background: Long-time survival is an important goal in NSCLC treatment. However, in patients (pts) with wild type EGFR and non translocated ALK (EGFRwt/ALKnt) advanced disease, median survival at diagnosis is around 9-14 months and long time survivors (LTS) constitute a very small proportion of these patients. The aim of our research was to explore the clinical-pathological characteristics of a population of EGFRwt/ALKnt LTS with an overall survival (OS) of at least 36 months, with the purpose to identify which clinical-pathological features could help to identify a better outcome in advanced NSCLC. **Methods:** We analyzed retrospectively data from patients diagnosed of EGFRwt/ALKnt advanced NSCLC with an OS of at least 36 months and treated in 8 institutions from Madrid (Spain). All these patients were selected in a period of 10 years (January 2002 to 2012). We analyzed clinical-pathological characteristics (age, sex, ECOG, stage IIIB vs IV, histology, smoking status, diabetes and vascular disease, weight loss >10%, symptoms at diagnosis and sites of metastasis), laboratory parameters (LDH and haemoglobin levels) and type of treatment administered (platinum based treatment, metasectomies, number of chemotherapy lines, maintenance, grade 4 toxicity as well as metformine intake). Finally, data from PFS and OS were also collected. **Results:** Among all patients diagnosed with EGFRwt/ALKnt NSCLC and treated in 8 institutions in 10 years, we identified 93 pts with an OS of at least 36 months. 55 pts (60%) were older 65 years, 67 pts (71%) male and 85 pts (91 %) were smokers/former smokers. Comorbidities (diabetes and vascular disease) were infrequent: 7pts (7%) and 13 pts (14%), respectively. Adenocarcinoma was most common pathological subgroup (60 pts, 65%) followed by squamous (21 pts, 22%), large cell carcinoma (7, 7%) and "other histologies" (6 pts, 6%). The majority of them, had a good PS; ECOG 0 32 pts (34%) and 1 57 pts (61%). A minority of patients had weight loss greater than 10% at presentation (12 pts, 14%). Most frequent symptoms were cough (41 pts, 44%), followed by pain (34 pts, 36%), dyspnea (25 pts, 27%) and haemoptysis (9 pts, 9%). LDH and haemoglobin leves were normal in the majority (65 pts, 70% and 72 pts, 77%, respectively). On the other hand, metformin intake was uncommon (16 pts, 17%). One or two metastatic sites at diagnosis were described in 44 pts, 47% and 29 pts, 31%, respectively and only 13 pts (14%) had

brain metastasis (mts) and 5 (5%) adrenal mts. First-line chemotherapy based in platinum was administrated in 92 pts (98%), however, maintenance therapy only in 41 pts (44%). Local treatment (metasectomies +/-RT), was done in 35 pts (38 %). Grade 4 toxicity was detected in 7 pts (7%). Finally, we estimated a median PFS of 13.4 months and median OS of 40.5 months **Conclusion:** To our knowledge, this is the largest multicenter serie reported of very long-term survivors (OS >36 months) with with EGFRwt/ALKnt advanced NSCLC. This study includes an exhaustive clinical and pathological analysis of this specific population. In this moment, we are carrying out a comprehensive molecular analysis **Keywords:** long-term survival, non small cell lung cancer, advanced disease

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-033 Case of a Patient Who Underwent Right Middle Lobectomy of Lung Adenocarcinoma with Histological Characteristics Similar to Papillary Adenoma Masato Watanabe[1], Shozo Fujino[1], Takehiro Okumura[1], Masasi Kawamoto[2], Mikiko Takahashi[2] [1]*Thoracic Surgery, Teikyo University School of Medicine Mizonokuchi Hospital, Kawasaki City/Japan,* [2]*Pathology, Teikyo University School of Medicine Mizonokuchi Hospital, Kawasaki City/Japan*

Background: Pulmonary papillary adenoma is a rare benign tumor of the lung, characterized by a histological appearance in which low-grade cuboid or single columnar cells proliferate, centering on the fibrovascular interstitium. Since diagnosis is made morphologically, genetic analysis is not used for its diagnosis in common practice. **Methods:** [Case presentation] A 60-year-old woman with no history of smoking or asbestos exposure was referred to our hospital with lung cancer suspected due to an abnormal shadow detected on a plain chest radiograph for screening. A mass lesion 3.5 cm in diameter was detected in the right middle lobe on chest computed tomography (CT). Although positron emission tomography (PET)/CT revealed fluorodeoxyglucose accumulation in the mass (SUV max 3.4), there was no other clear accumulation and there were no findings indicating lymph node metastasis or distant metastasis on enhanced CT and magnetic resonance imaging (MRI) scans. Therefore, the clinical stage was estimated as cT2aN0M0, stage IB. As a treatment strategy, we decided to use surgical biopsy because a definitive diagnosis could not be made from bronchoscopy. Thoracoscopy showed no apparent pleural dissemination or pleural effusion. Since the tumor in the middle lobe was difficult to resect, we resected the middle lobe and submitted it for intraoperative pathological examination. As a result, it was diagnosed as pulmonary papillary adenoma. Consequently, in surgery, systematic lymph node excision was not performed and samples were obtained from lymph nodes #11s and #11i. The permanent preparation showed the appearance of cuboid and low columnar-shaped cells proliferating on the fibrovascular interstitium, which was consistent with papillary adenoma. However, it also indicated a marginal region of lepidic pattern with focal low papillary projection. In immunohistological examination, both the marginal region and the body of tumor were stained with epidermal growth factor receptor (EGFR) mutation specific antibodies. Furthermore, genetic mutation was found in EGFR genetic analysis. Thus, this patient was diagnosed with invasive adenocarcinoma in papillary pattern predominant. The final pathological stage was estimated as T2aN0M0. However, adjuvant postoperative treatment was not performed. The patient was followed up in the outpatient department, and no recurrence has been observed eight months. **Results:** [Discussion] Pulmonary papillary adenoma is commonly diagnosed based on the histological forms and genetic examination is not usually used. Thus, we cannot deny the possibility that lesions with gene mutations have been present in the patients diagnosed with papillary adenoma in the past. In addition, in patients with a large primary tumor with a morphologically low grade, it is difficult to judge whether postoperative treatment should be provided and it is considered necessary to judge it by taking the clinical course into account. **Conclusion:** Pulmonary papillary adenoma is a rare tumor. To obtain the definite diagnosis with the exclusion of malignancy, it has been suggested that complete resection and genetic analysis is necessary . **Keywords:** papillary adenoma, Adenocarcinoma, EGFR mutation, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-034 A Case of Fetal Lung Interstitial Tumor (FLIT) in a Neonate Akiteru Goto[1], Toshikaki Yoshioka[2], Tomoo Ito[3], Michihiro Yano[3], Taku Hebiguchi[4], Hiroaki Yoshino[4] [1]*Department of Cellular and Organ Pathology, Akita University, Akita/Japan,* [2]*Course of Occupational Therapy, Akita University, Akita/Japan,* [3]*Pediatrics, Akita University Hospital, Akita/Japan,* [4]*Pediatric Surgery, Akita University, Akita/Japan*

Background: Fetal lung interstitial tumor (FLIT) is a newly recognized and a rare lung lesion of neonates. The entity was firstly proposed by Dishop MK, et al. in 2010. FLIT is histologically charized by unique mixture of immature interstitial mesenchyme with irregular airspace-like structures, which mimicks abnormal and incompletely developed lung.To date, only 13 cases of FLIT have been reported including 2 cases from Japan. We herein present another case of FLIT in a neonate with histopathological and immunohistochemical analyses to discuss its pathogenesis. **Methods:** not applicable **Results:** A 3 day-old boy was referred to our hospital with respiratory distress. He was born at 36 weeks of gestation, weighing 2070 g. Chest X-ray and computed tomography findings depicted a mediastinal tumor containing viscous fluid. However, the operation revealed that the tumor was developed in the left lung, and the tumor was resected. The postoperative course was uneventful and no recurrent disease was detected at his latest follow-up at 2 years after the resection. The tumor was 30x25x20mm-sized and its cut section showed a well-circumscribed solid and cystic mass. Histological examination revealed a well-circumscribed lesion with a fibrous capsule. The lesion consisted of immature airspace-like structures with widened septa containing immature mesenchymal cells, also, overlaying low cuboidal epithelium was observed. Immunohistochemically, the epithelial cells were positive for cytokeratin, EMA, and TTF-1. The interstitial cells were diffusely positive for vimentin and smooth muscle actin, and negative for desmin. Not nuclear but cytoplasmic staining of beta-catenin was observed in the epithelial cells. The tumor cells were immunohistochemically negative for ALK. The differential diagnoses of the tumor included pleulopulnmonary blastoma (PPB), and congenital cystic adenomatoid malformation/congenital pulmonary airway malformation (CCAM/CPAM) type 3. PPB is characterized by rhabdoid or blastemal cells and/or anaplastic features and CCAM/CPAM type 3 generally shows a diffuse lesion without a capsule. These histological features were not observed in the present tumor, and it was diagnosed as FLIT. Yoshida M, et al. noticed the nuclear stainig of beta-catenin in the epithelia l cells of FLIT. Its nulcear staining is also observed in the epithelai cells in fetal lung at pseudo-glandular stage, and they discussed the resembrance between FLIT and fetal lung at pseudo-glandular stage. In the present case, beta-catenin expression was observed in the cytoplasm of epithelial cells, which rahter resembled to the lung in alveolar stage. In 2014, Onoda T, et al. reported a novel chromosomal rearrangement resulting in α-2-macroglobulin (A2M) and anaplastic lymphoma kinase (ALK) gene fusion in a case of FLIT. However, the present case was negative for ALK by immunohistochemistry. Immunohistochemical findings of beta-catenin and ALK of the present case suggested the pathogenic heterogeneity of FLIT. **Conclusion:** A case of FLIT in a neonate is presented with typical histopathological findings. Pathogenic heterogeneity of FLIT was suggested by beta-catenin and ALK immunohistochemistry of the case. **Keywords:** Fetal Lung Interstitial Tumor (FLIT), Congenital lung lesions

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-035 Clinicopathologic and Biological Characteristics of Young Age Non-Small Cell Lung Cancer Tatsuo Ohira, Keishi Ohtani, Hiroaki Kataba, Sachio Maehara, Yoshihisa Shimada, Junichi Maeda, Koichi Yoshida, Yasufumi Kato, Masaru Hagiwara, Masatoshi Kakihana, Naohiro Kajiwara, Norihiko Ikeda *Surgery, Tokyo Medical University, Tokyo/Japan*

Background: The Japan Lung Cancer Society, Japanese Association for Chest Surgery, and Japanese Respiratory Society jointly established the Japanese Joint Committee for Lung Cancer Registration. The Japanese Joint Committee reported that number of resected lung cancer patients under 40 years of age in Japan was 101 cases of 11663 registered patients in 2004. Apparently there are many people on their 50s to 70s who was resected for treatment of lung cancer. Lung cancer in patients under 40 years old is rare. Young lung cancer patients should have specific characteristics. **Methods:** We performed 2835 operations for lung cancer for 15years from 2000 through 2014 in our hospital. Among 2835 patients with lung cancer, 47 patients were younger than 40. Among 47 patients 26 patients were male and 21 patients were female. We examined characteristics of young lung cancer patients by clinicopathologic and molecular biologic characteristics. **Results:**Among patients with operation, pathological stage IA, IB, IIA, IIB, IIIA, IIIB were 24, 6, 3, 2, 6, 5 cases, respectively. 36 cases were diagnosed as adenocarcinoma. Squamous cell carcinoma was only one case. 3 cases were diagnosed as large cell carcinoma. Most of young lung cancer cases were diagnosed as adenocarcinoma. 5-year survival of resected lung cancer patients was 74%. 5-year survival of inoperable cases was 23.8%. We will show the biological characteristics of young age lung cancer patients. 9cases showed EGFR sensitive mutation. 4 cases showed the transforming EML4-ALK fusion gene. **Conclusion:** Young lung cancer patients showed specific clinicopathologic and molecular biologic characteristics compared with the older age patients. **Keywords:** Adenocarcinoma, biomarker, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-036 Primary Pulmonary Melanoma: A Report of Two Cases Mototsugu Watanabe, Hiromasa Yamamoto, Hiroki Sato, Hidejiro Torigoe, Ken Suzawa, Shinsuke Hashida, Yuho Maki, Junichi Soh, Shinichi Toyooka, Shinichiro Miyoshi *Departments of Thoracic, Breast and Endocrinological Surgery, Okayama University Graduate School of Medicine, Okayama/Japan*

Background: Malignant melanoma is a refractory malignancy with a dismal prognosis. It generally arises from the skin in most cases, and cases of primary pulmonary malignant melanoma are rare and often behave aggressively. We have treated two cases of localized primary pulmonary malignant melanoma by surgical resection. Although cutaneous melanomas often carry activating mutations in the *BRAF* gene (V600E) and express programmed death ligand 1 (PD-L1), little is known about primary pulmonary malignant melanoma. **Methods:** We determined the *BRAF* mutational status (exons 11 and 15) by direct sequencing in the two tumors. Next, we performed a target sequencing analysis using the Human Lung Cancer Panel (Qiagen, Hilden, Germany), which targets 20 lung cancer-related genes including most of the exons in *BRAF*, using the same samples. We evaluated the expression of PD-L1 on the surface of the tumor cells by immunohistochemical testing in formalin-fixed, paraffin-embedded tumor specimens with the use of a rabbit monoclonal antihuman PD-L1 antibody. **Results:** No *BRAF* mutations and PD-L1 expression were detected in both of two cases. We detected a p53 mutation, which was thought to be a potential somatic mutation, in one of the two cases using a sequencing panel targeting 20 lung cancer-related genes. **Conclusion:** We encountered two cases of malignant melanoma of the lung that did not carry activating mutations in the *BRAF* gene. Further molecular analyses may uncover the characteristics of primary malignant melanoma. **Keywords:** primary pulmonary malignant melanoma, target sequencing

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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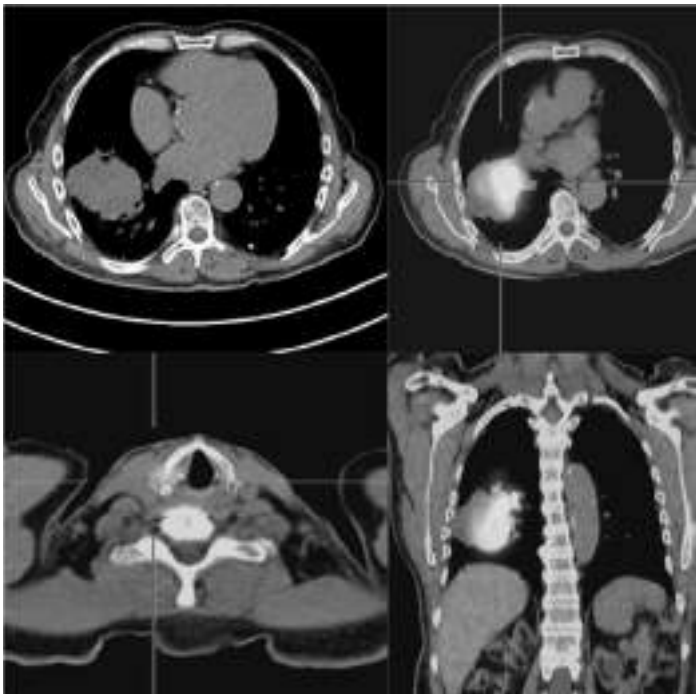
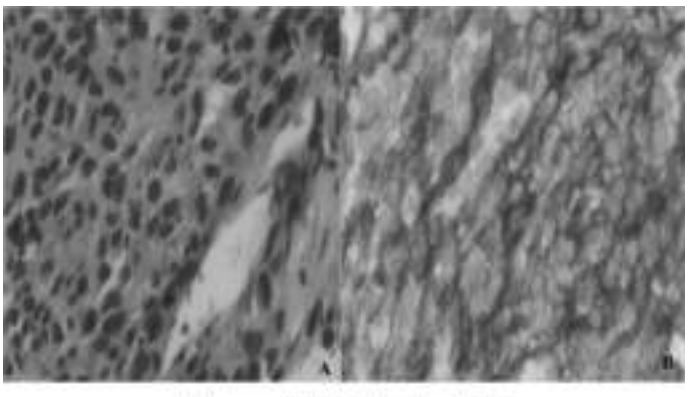
P1.04-037 Lung and Hypopharyngeal Angiosarcoma (AS) in a Renal Transplant Patient: Case Report Liliana Fernandez[1], Fernando Sanabria[2], William Martinez[2], Carlos A. Muñoz[3], Luz F. Sua[4] [1]*Interventional Pulmonology, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [2]*Clinic Pulmonology, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [3]*Medical Research, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [4]*Department of Pathology and Laboratory Medicine. Phd Biomedical Sciences, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia*

Background: (AS) are rare malignant soft tissue tumors of endothelial cell origin representing 2% of all sarcomas. Most AS develops in the absence of precursor lesions. To date, only 20 cases of (AS) have been described after renal transplantation, occurring mostly on the skin or in a dialysis fistula, their pulmonary location is very rare. We report the case of a patient with a renal transplant who presents a hypo pharyngeal and a right lower lobe (RLL) lesion where a Angiosarcoma was documented. **Methods:** Clinical History Revision **Results:** A 78 years-old patient, ex-smoker, with end-stage renal failure received a cadaveric donor renal transplant in 2000. Immunosuppressed with relatively low doses of tacrolimus and steroids, graft function remained stable with a serum creatinine in 1,2 until January 2015 when he consults with dysphonia, dysphagia, cough, and mild hemoptysis. The patient had bilateral neck lymphadenopathy, bilateral basal crackles and the rest of the physical examination within normal parameters. Pulmonology evaluated the patient finding a hypopharyngeal mass and another with round morphology in RLL that were metabolically active in PET-CT. A hypopharyngeal biopsy is taken and a CT-guided transthoracic puncture, finding a high grade undifferentiated tumor of mesenchymal origin, expressing Vimenin and CD10, with vascular marker CD31 and gene C-Myc. Gene p53 and Ki-67 in 90% of the tumor. No lymphoid or epithelial line markers are expressed. The patient is currently in chemotherapy and immunotherapy. **Conclusion:** The use of potent immunosuppressive agents has significantly reduced the rates of acute rejection after renal transplantation. However, increased cancer incidence after renal transplantation has become an important problem. Skin tumors, post-transplant lymphoproliferative diseases and organ cancers are the most common malignant tumors seen in these patients. Angiosarcoma is rarely seen in this group of patients, and location in lung and hypopharynx without evidence elsewhere of commitment affectation is very rare.





A. Angiosarcoma (H&E) B. CD31 expresión vascular (IHC)

Keywords: Angiosarcoma (AS), Renal transplant, immunosuppression

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-038 Endobronchial Ultrasound Guided Transbronchial Fine Needle Aspiration Cytology (EBUS-TBNA) for Peribronchial Mediastinal Tumor Mitsutoshi Shiba, Taiki Fujiwara, Takahide Toyoda, Tomohiko Iida *Thoracic Surgery, Kimitsu General Hospital, Kisarazu/Japan*

Background: Recently endobronchial ultrasound guided transbronchial needle aspiration system (EBUS-TBNA) was developed in Japan and probed to be an effective method to diagnose peribronchial tree lesions especially for lymphnode metastasis of lung cancer. In this time, we present our experience of EBUS-TBNA for peritracheal mediastinal tumors and discuss current advances of EBUS-TBNA for lung peri-tracheobronchial lesions. **Methods:** Between 2008 and 2014, EBUS-TBNA was performed in nine patients with peritracheal mediastinal mass to diagnose them morphologically. **Results:** Final histological type of these nine cases were, 6 malignant tumors (two malignant lymphomas, one multiple myeloma, one thyroid carcinoma, one squamous cell carcinoma, one large cell carcinoma) and 3 benign tumors (one neurogenic schwanoma, one bronchogenic cyst and one thymic cyst). Of the detected 6 malignant tumors, cytology diagnoses were positive in three cases, suspicious in two cases and inadequate in one case. Of the detected three benign tumors, cytology diagnoses were benign in two cases and inadequate in one case. Among 7 solid mediastinal tumors, histological evaluation was capable in 3 cases and insufficient in 4 cases. Combined with cytological and histological examination, morphological diagnoses were useful in 6 cases (67%) with EBUS-TBNA for peritracheal mediastinal tumors. **Conclusion:** Although histological type of peri-trachal mediastinal tumor was various, morphological diagnosis with EBUS-TBNA was useful in 67% of the lesions in this series. Analysis of atypical cells in the cytology specimen was effective to estimate the histological figures of the lesions.
Keywords: bronchoscopy, EBUS-TBNA, Mediastinal Tumor, diagnosis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-039 Ex-Vivo Artifacts and Histopathological Pitfalls in the Lung Erik Thunnissen[1], Hans J. Blaauwgeers[2], Douglas Flieder[3] [1]*Department of Pathology, VU University Medical Center,, Amsterdam/Netherlands,* [2]*Pathology, Olvg, Amsterdam/ Netherlands,* [3]*Pathology, Fox Chase Cancer Center, Philadelphia/United States of America*

Background: Surgical and pathological handling of lung physically affects lung tissue. This leads to artifacts that alter the morphological appearance of pulmonary parenchyma. **Methods:** In this study four mechanisms of ex-vivo artifacts and corresponding diagnostic pitfalls are described and illustrated. **Results:** The four patterns of artifacts are: 1) Surgical collapse, due to the removal of air and blood from pulmonary resections; 2) Ex-vivo contraction of bronchial and bronchiolar smooth muscle; 3) Clamping edema of open lung biopsies, and 4) Spreading of tissue fragments and individual cells through a knife surface. Morphologic pitfalls include diagnostic patterns of adenocarcinoma, asthma, constrictive bronchiolitis, and lymphedema. **Conclusion:** Four patterns of pulmonary ex-vivo artifacts are important to recognize, in order to avoid morphologic misinterpretations, possibly improving reproducibility in histopathological diagnosis of lung cancer
Keywords: lung*adenocarcinoma*diagnosis*artifact

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-040 Stage I Adenocarcinoma According to the 2011 IASLC/ ATS/ ERS: Case Series from Brazil André Luiz C. Trajano[1], Juliana P. Franceschini[2], Túlio Geraldo D.S. Souza[3], Tadeu L.F. Pereira[4], Mário C. Ghefter[2], Rodrigo P.C. Sapucaia[5], Ricardo S. Santos[2] [1]*Instituto Tórax, Salvador/Brazil,* [2]*Instituto Tórax, São Paulo/Brazil,* [3]*Laboratório de Anatomia Patológica E Citopatologia, Hospital Aliança, Salvador/Brazil,* [4]*Cirtorax Bahia, Salvador/Brazil,* [5]*Escola Bahiana de Medicina, Salvador/Brazil*

Background: Lung cancer is the deadliest cancer worldwide and it is of particular concern in Brazil as the second cause of cancer death in both genders. The new classification proposed by International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society Classification has proven its prognostic value with also a better clinical understanding of lung adenocarcinoma. Prior to this classification all patients diagnosed with early stage adenocarcinoma were considered to have practically the same disease. In our country, however, medical literature is still incipient on this topic. We reviewed the histopathology of a consecutive series of patients diagnosed with stage I adenocarcinoma. **Methods:** Cross-sectional study including 50 patients diagnosed with stages IA or IB adenocarcinoma undergoing surgical resection of non-small cell lung cancer. The variables: histological subtype, sex, age and tumour size. We have divided patients in two groups based on the presence of lepidic features. Statistical analysis was performed by Anova and Bonferroni multiple comparison test, to correlate tumour size among histological subtype groups. **Results:** The mean age was 63.7 (11.5) years, 50% were men. The average size of resected tumours was 1.4 (0.7) mm; 45 cases (90%) were stage IA. The predominant subtypes were histologically lepidic (n=24, 48%); the acinar subtype was found in 20 (40%) cases. Patients and tumour characteristics according to histological subtype are showed in table 1. There was statistical difference in size ($p<0.05$) when comparing lepidic tumors with acinar tumors (1.3mm versus 2.3mm respectively). Table 1: Patients and tumour characteristics according to histological subtype.

Subtypes Variables	Lepidid	Acinar	Others	p
n (%)	24 (48)	20 (40)	6 (12)	
Men n (%)	11 (45.8)	9 (45)	6 (100)	
Age mean (SD)	63 (11.6)	66.3 (10.8)	62.7 (7.7)	
Tumor size mean (SD)	1.3 (0.6)	2.3 (1.4)	1.6 (0.6)	0.02*

*Anova with Bonferroni multiple comparison test. **Conclusion:** In our brief series of lung adenocarcinoma patients, the most common subtypes were acinar and lepidic; the latter being larger in this sample. The long-term follow-up will give us important information about the prognosis of these patients treated exclusively with surgery. **Keywords:** Adenocarcinoma, Histological type, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-041 Synchronous Lung Cancers, Squamous Cell and Adenocarcinoma Coexistence, Case Report Nesrin Ocal[1], Deniz Dogan[1], Omer Deniz[1], Ali F. Cicek[2], Hayati Bilgic[1] [1]*Chest Diseases, Gulhane Military Medical Faculty, Ankara/Turkey,* [2]*Pathology, Gulhane Military Medical Faculty, Ankara/Turkey*

Background: Synchronous lung cancers are simultaneously diagnosed, physically distinct and separate lung cancers which have no common lymphatics with the primary tumor and may have same or different histology with the primary neoplasms. Although radiological imaging techniques guide in terms of initial diagnosis, histopathological evidence is required for definitive diagnosis of synchronous multiplee primary lung cancers. Early diagnosis represents the only chance to obtain a surgical cure in these patients. **Methods:** not applicable **Results:** Here, we present a case with synchronous multiplee primary lung cancers in whom both tumors are diagnosed simultaneously. A 69 year-old male patient with cough and left-sided chest pain complaints and 90 pack / year history of active smoking admitted to our clinic. Thoracic CT of the patient revealed a pleural-based mass in the right lower lobe and another mass on the left lung which is associated with the hilum and caused atelectasis in the distal airways. Diagnostic bronchoscopy was performed to the patient and separate biopsies were taken from the both lesions. Histological sections obtained from the bronchoscopic biopsy specimens revealed that there was an infiltrative tumor in both right and left lung. In right lung, the tumor composed of abortive glandular structures and single cell infiltrations within the desmoplastic stroma. The second tumor (left lung) was consist of solid islands composed of atypical squamous cells with eosinophilic cytoplasm and darkly basophilic nuclei. Histochemically, in the first tumor, neoplastic cells had intracytoplasmic vacuoles stained by mucicarmin indicating a feature of adenocarcinoma whereas there were no cells containing mucin vacuoles in the second tumor. Immunohistochemical study has supported the histological and histochemical findings. The tumor on the right side showed a diffuse immunoreactivity by CK7 which is a highly spesific marker for adenocarcinomas whereas the tumor on the left side was stained by the basal cell markers such as CK5/6 and p63 which are highly specific markers for squamous cell carcinoma. Briefly, histopathologic examination of the biopsies from left upper lobe and right lower lobe revealed squamous cell lung carcinoma and adenocarcinoma, respectively. Thereupon oncologic PET examination was performed for screening and evaluating if there is another primary tumor site for adenocarcinoma. In PET examination, FDG uptakes of extrapulmonary tissues were considered to be normal. Thus both lesions thought to be primary lung tumors. **Conclusion:** Our case is a good example of simultaneously detected synchronous primary tumors of the lung and we reported this case in order to emphasize the possibility of another primary tumor in the cases which are initially thought to be metastatic lesions and for sure the need of biopsies separately. **Keywords:** synchronous tumors, lung cancer, squamous, Adenocarcinoma

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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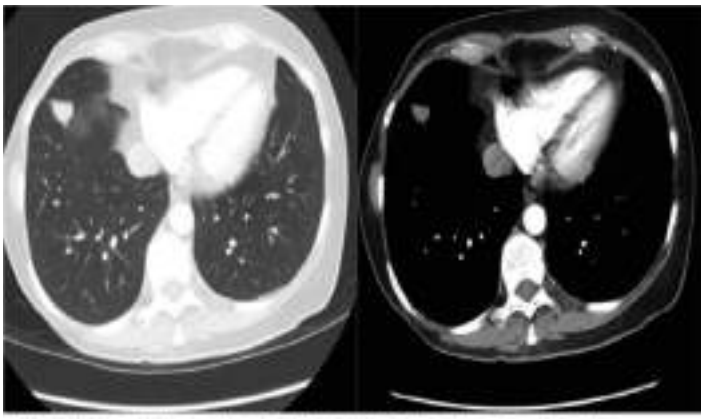
P1.04-042 Diagnostic Role of Immunocytochemistry in Malignant Pleural Mesothelioma Nguyen S. Lam *Pathology Department, Pham Ngoc Thach Hospital, Ho Chi Minh City/Viet Nam*

Background: Malignant pleural mesothelioma is a difficult diagnosis, more severe cases may not perform by pleural biopsy. With these cases, the technique of immunocytochemistry was performed proposals. **Methods:** A prospective, cross-sectional descriptive statistics with clinical series cases. **Results:** § Implementing 58 cases of malignant pleural mesothelioma by immunocytochemistry. § Technical Cytospin method has helped for immunocytochemistry have high results. § Should be done more staining with markers for the other diagnostic diseases: lung cancer and non-lung cancers that metastatic to pleura. § The results of the data: - Sensitivity: 84.06 % - Specificity: 100 % - Positive Prognostic Value: 100 % - Negative Prognostic Value: 92.25 % - Accuracy: 94.12 % **Conclusion:** The diagnosis of malignant pleural mesothelioma is always a difficult diagnosis. Needing the differential diagnosis with other types of diseases, such as lung cancer and non-lung cancers that to pleural pulmonary metastases. Staining with immunocytochemistry in cases of pleural effusion showed relatively high value. This suggests that the ability to diagnose initially screening properties of this technique is very good, especially valuable in the diagnosis of severe disease progression can not perform other diagnostic techniques. **Keywords:** Immunocytochemistry, Malignant Pleural Mesothelioma

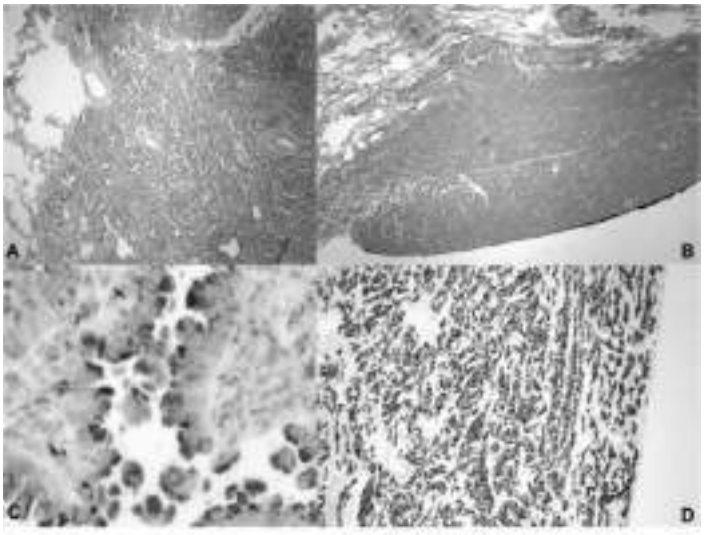
POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-043 Pulmonary Lepidic Adenocarcinoma in a Patient with Prior Diagnosis of Breast Cancer: Case Report Liliana Fernandez[1], Lina Garcia[2], Mauricio Velasquez[3], Carlos A. Muñoz[4], Luz F. Sua[5] [1]*Interventional Pulmonology, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [2]*Internal Medicine Resident, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [3]*Thoracic Surgery, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [4]*Medical Research, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [5]*Department of Pathology and Laboratory Medicine. Phd Biomedical Sciences, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia*

Background: The combined effect of improved cancer diagnosis and management has led to a marked increase in cancer survivors. Consequently, an appreciable proportion of cancer diagnoses are registered among patients who had already received a cancer diagnosis in the past, and more accurate diagnostic procedures lead to the identification of more than one cancer in a subset of patients. We present the case of a patient with breast cancer in whom a lepidic primary lung adenocarcinoma was discovered during a follow-up. **Methods:** Medical History Revission **Results:** A 68-years-old female with breast cancer EC EIII diagnosed in March / 2010, handled with lumpectomy and lymph node removal, solid mucinous ductal carcinoma Ki67 expression: 35% RH: E (+) 100%, P (-), HER 2 NEU negative, negative margins with angiolymphatic invasion 3/15. She received radiotherapy, tamoxifen and later anastrozole. In Dec / 2010 she presents tumor recurrence managed with radical mastectomy, received chemotherapy with Adriamycin and Cyclophosphamide. In April / 2013 she consults with two months of dry cough and dyspnea, normal physical examination, an unremarkable mammography, chest CT-scan with irregular right basal nodular lesion and mediastinal nodes. The patient underwent resection through thoracoscopy, pathology shows lepidic adenocarcinoma pattern with mutated EGFR exon 19 and exon 21 negative, with metastatic nodal involvement by the primary lung tumor and previous breast carcinoma. **Conclusion:** Patients that have been diagnosed with a cancer, have an increased lifetime risk for developing another de novo malignancy depending on various inherited, environmental and iatrogenic risk factors. Cancer patients could survive longer due to settling treatment modalities, and then would likely develop a new malignancy. The monitoring and evaluation procedures are especially useful for early detection of tumors associated when there's a known tumor lesion.



Chest CT-scan with irregular right basal nodular lesion and mediastinal nodes



A,C: Adenocarcinoma with lepidic pattern (H & E), positive for Napsins A and TTF-1 (IHC), positive for deletions in exon 19 of the EGFR (PCR) and negative for EML4-ALK (IHC). B,D: Subpleural metastatic tumor of ductal carcinoma of the breast (H & E), positive for estrogen and negative (Score 0) for HER2 (IHC)

Keywords: Breast cancer, Pulmonary lepidic adenocarcinoma

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-044 Local Diagnostic Practices for Advanced Non-Small-Cell Lung Cancer in Asia-Pacific and Russia: IGNITE Study Sergei Tjulandin[1], Baohui Han[2], Koichi Hagiwara[3], Nicola Normanno[4], Laksmi Wulandari[5], Konstantin Laktionov[6], Achmad Hudoyo[7], Yong He[8], Yi P. Zhang[9], Meng-Zhao Wang[10], Chien Ying Liu[11], Marianne Ratcliffe[12], Rose Mccormack[12],Martin Reck[13] [1]*Department of Clinical Pharmacology and Chemotherapy, Russian Cancer Research Center, Moscow/Russian Federation,* [2]*Department of Respiratory Medicine, Shanghai Chest Hospital, Jiao Tong University, Shanghai/ China,* [3]*Jichi Medical University, Saitama Medical Center, Saitama-Ken/Japan,* [4]*Cell Biology and Biotherapy Unit, Istituto Nazionale Tumori 'Fondazione Giovanni Pascale', Irccs, Naples/Italy,* [5]*Department of Pulmonology, Dr Soetomo General Hospital, Surabaya/ Indonesia,* [6]*Department of Clinical Biotechnology, Russian Cancer Research Center, Moscow/Russian Federation,* [7]*Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, University of Indonesia - Persahabatan, Jakarta/Indonesia,* [8]*Department of Respiratory Medicine, Daping Hospital, the Third Military Medical University, Chongqing/ China,* [9]*Department of Chemotherapy, Zhejiang Cancer Hospital and Key Laboratory Diagnosis and Treatment Technology on Thoracic Oncology, Zhejiang Province Hangzhou/ China,* [10]*Department of Respiratory Medicine, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing/China,*[11]*Division of Thoracic Medicine, Chang Gung Memorial Hospital, Chang Gung University, Taipei/ Taiwan,* [12]*Personalised Healthcare and Biomarkers, Astrazeneca, Macclesfield/United Kingdom,* [13]*Department of Thoracic Oncology, Lungen Clinic Grosshansdorf, Airway Research Center North (Arcn), Member of the German Center for Lung Research (Dzl), Grosshansdorf/ Germany*

Background: IGNITE (a large, multicentre, interventional, non-comparative diagnostic study; NCT01788163) evaluated local diagnostic practices for patients with advanced non-small-cell lung cancer (aNSCLC) in Asia-Pacific/Russia. **Methods:**Eligible patients: local/metastatic aNSCLC; chemotherapy-naïve, newly diagnosed/recurrent disease after resection; ineligible for curative treatment. We report diagnostic assessments and epidermal growth factor receptor (*EGFR*) mutation test turnaround times (secondary endpoints) associated with tissue/cytology samples from patients in Asia-Pacific/ Russia. **Results:** 3382 patients enrolled (972 Russia). Immunohistochemistry (IHC) analysis was used to confirm diagnosis in 989/2093 (47%) and 165/949 (17%) patients in Asia-Pacific and Russia, respectively (where data were available). Where IHC was used, the markers assessed were: TTF-1 (Asia-Pacific 95% and Russia 90%); p65 (3% and 5%); and p40 (17% and 4%).*EGFR* mutation tests were not performed on samples from 262 patients and tested samples from 23 patients did not yield results. The most common reason for not testing was insufficient material provided to test (Asia-Pacific 93% [100/108 responses], Russia 67% [24/36]). The percentages of neoplastic cells in samples (data available: Asia-Pacific n=1042; Russia n=187) were: <20% tumour cells: Asia-Pacific 33% vs Russia 6%; 20–50% tumour cells: 28% vs 33%; and >50% tumour cells: 40% vs 61%. Considering sampling methodologies (data available: Asia-Pacific n=2410; Russia n=972), the most common sampling sites were the lungs (Asia-Pacific 68%; Russia 80%) or lymph nodes (Asia-Pacific 14%; Russia 10%); the most common sample collection method was bronchoscopy (Asia-Pacific 22%; Russia 45%; Table 1). Median *EGFR* mutation test turnaround time was within 2 weeks for all countries except Thailand (70 days; Table 2). Mutation test success rates were high for Asia-Pacific (99.5%) and Russia (98.7%). **Conclusion:** Diagnostic assessments, sampling methodologies and EGFR mutation testing practices vary between and within Asia-Pacific and Russia; further understanding of local practices will drive improvements and enable more patients to receive appropriate personalised treatment.

Sample collection methodology; enrolled population	Asia-Pacific n/N	Asia-Pacific %	Russia n/N	Russia %
Cytology	**307/2410**	**13**	**34/972**	**3**
Cytology	177/2410	7	25/972	3
Cytology: bronchial washings	22/2410	1	1/972	<1
Cytology: fine needle aspiration	108/2410	4	8/972	1
Tissue	**1969/2410**	**82**	**914/972**	**94**
Bronchoscopic	540/2410	22	436/972	45
Core-biopsy (NOS)	223/2410	9	34/972	3
Image-guided core biopsy	351/2410	15	8/972	1
Incisional biopsy	82/2410	3	114/972	12
Lobectomy	73/2410	3	145/972	15
Localisation biopsy	21/2410	1	27/972	3
Mediastinoscopic	14/2410	1	21/972	2
Needle biopsy	463/2410	19	22/972	2
Percutaneous core biopsy	111/2410	5	16/972	2
Pneumonectomy: extra pericardial	9/2410	<1	21/972	2
Pneumonectomy: intra pericardial	0/2410	0	11/972	1
Segmental excision	14/2410	1	16/972	2
Segmentectomy	3/2410	<1	17/972	2
Sleeve	0/2410	0	0/972	0
Transbronchial	38/2410	2	6/972	1
Wedge resection	27/2410	1	20/972	2
Other				
All other combined	134/2410	6	24/972	2

NOS, not otherwise specified

Mutation test turnaround time, days; enrolled population	Overall	Asia-Pacific									Russia
		Asia-Pacific overall	China	Taiwan	South Korea	Australia	Thailand	Singapore	Malaysia	Indonesia	
Tissue/cytology samples											
N	3238	2302	1394	271	62	60	92	101	49	273	936
Mean (SD)	11 (20)	10 (17)	6 (5)	7 (12)	12 (13)	13 (8)	71 (44)	8 (5)	9 (4)	7 (2)	14 (27)
Median	7	6	5	7	9	11	70	8	8	7	9
95% CI	10, 12	9, 10	6, 7	6, 9	8, 15	11, 15	62, 80	7, 9	8, 10	6, 7	13, 16

CI, confidence interval; SD, standard deviation

Keywords: NSCLC, EGFR mutation, diagnostic practices

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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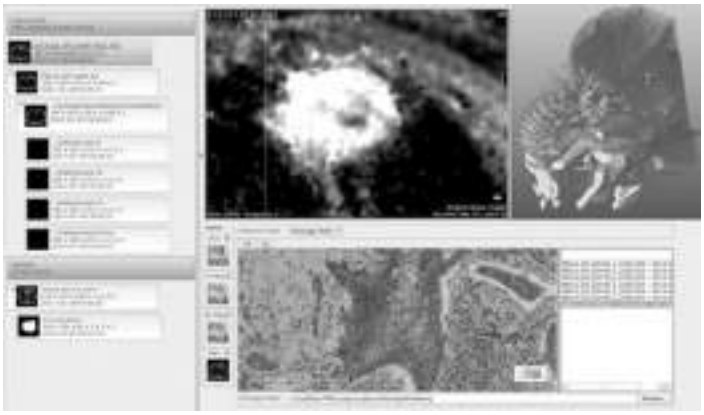
P1.04-045 Software Support for Combined Staging of Lung Cancer in CT, Functional MRI and Pathology Hendrik O.A. Laue[1], Peter Kohlmann[2], Johannes Lotz[3], Oliver Sedlaczek[4], Benedikt Müller[5], Kai Breuhahn[5], Niels Grabe[6], Arne Warth[5], Horst Hahn[1] [1]*Fraunhofer Mevis, Bremen/Germany,* [2]*Fraunhofer Mevis, Berlin/Germany,* [3]*Project Group Image Registration, Fraunhofer Mevis, Bremen/Germany,* [4]*Diagnostic and Interventional Radiology, Radiological Clinic, Heidelberg/Germany,* [5]*Institute of Pathology, University of Heidelberg, Heidelberg/Germany,* [6]*Tissue Imaging & Analysis Center, University Heidelberg, Heidelberg/Germany*

Background: Treatment and diagnosis of lung cancer is an interdisciplinary challenge. New treatment options can benefit from refined information on biological processes in the tumor. Two diagnostic disciplines, pathology and radiology, can provide oncology with valuable information allowing to select of the most appropriate treatment. Linking radiology and pathology on the imaging level requires sophisticated software. Therefore, we developed a computer tool combining quantitative functional MRI and CT with state-of-the-art whole-slide and 3D reconstructed histology. **Methods:** We selected a model lung cancer patient to investigate the requirements and possibilities for a combined software. The patient had a squamous cell carcinoma. Prior to excision, functional imaging using MRI as well as highly resolved CT and MRI volumes were acquired. These included a dynamic contrast-enhanced (DCE)- and a diffusion-weighted imaging (DWI)- MR scan. After imaging, the tumor was resected and a macroscopic slice of 5 mm thickness was resected from the center region of the tumor. This slice was further divided into 11 blocks, which were then cut into microscopic (~ 2 µm) slices. Staining was applied to these slices according to the requirements of the pathologist and then scanned by a whole-slide histological scanner (Hamamatsu, Japan). The obtained images of the microscopic slices were automatically reconstructed into histological 3D volumes by means of registration. Functional MRI and morphological CT data was imported into the software prototype. The tumor volume was determined in the CT image by a two-click automatic segmentation method. Quantitative parametric maps of the extended general kinetic model (eGKM) for vascular information and the apparent diffusion coefficient (ADC) for cell density were calculated. Afterwards, the histological blocks were aligned such that the blocks were located correctly on a photo of the macroscopic slice. They were then manually aligned to the morphologic contrast enhanced T1 image showing the best contrast for structures visible in the macroscopic slice. Finally, the pathological data were imported into the software for direct comparison of pathology and functional imaging in human lung tumors.



Results: We were able to combine histological and radiological information into a software solution which provids an integrated and improved research opportunity for pathologists, radiologists and biologists. It allows correlation of findings on molecular and cell level with findings from in-vivo functional imaging. **Conclusion:** We demonstrated that a combined evaluation of functional MRI and pathology can be facilitated. New studies will show the usage in more common lung cancers and larger numbers of patients.
Keywords: Pathology, 3D reconstruction, tumor board, functional MRI

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-046 MFN2 Regulates Lung Adenocarcinoma Cell Proliferation and Invasion Yuqing Lou[1], Rong Li[1], Jielin Liu[2], Yanwei Zhang[1], Wei Zhang[1], Xueyan Zhang[1], Hua Zhong[1], Liyan Jiang[1], Shaojun Wen[2], Baohui Han[1] [1]*Department of Pulmonary, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai/China,* [2]*Department of Hypertension Research, Beijing Anzhen Hospital, Capital Medical University and Beijing Institute of Heart Lung and Blood Vessel Diseases, Beijing/China*

Background: Mitofusin-2 gene (MFN2) encodes a mitochondrial protein which is critical for mitochondrial fusion process. MFN2 was initially identified as a hypertension-associated gene and implicated in the pathogenesis of multiple cancer types. However, roles and underlying mechanisms of MFN2 in lung adenocarcinoma development remain to be determined. **Methods:** MFN2 expression at protein level was examined in 30 pair lung adenocarcinoma/adjacent normal lung samples with immunohistochemistry staining. Then MFN2 knockdown was performed in human lung adenocarcinoma cells A549 with lentiviral-mediated shRNA strategy. The effects of MFN2 knockdown on cell proliferation, cell cycle process, cell migration and invasion was investigated in A549 cells. Then MFN2-knockdown induced gene expression changes in A549 cells was analyzed by microarray assay and then functional pathway enrichment analysis was performed to identify critical pathways involved in MFN2-mediated lung adenocarcinoma development. The expression changes of downstream factors were further determined in A549 cells by western blot. **Results:** As compared to adjacent normal lung tissues, MFN2 expression was significantly higher in lung adenocarcinoma tissues with positive MFN2 signals in 90% (27/30) lung adenocarcinoma tissues and only in 26.7% (8/30) adjacent normal tissues (Fig. 1A, B). Furthermore, MFN2 knockdown inhibited cell

proliferation (Fig. 1C), induced cell cycle arrest (Fig. 1E) and blocked invasion behavior (Fig. 1D) in A549 lung adenocarcinoma cells. Microarray analysis revealed that a lot of genes were deregulated in A549 cells with MFN2 knockdown (Fig. 1F). Then functional pathway enrichment revealed six pathways were enriched in deregulated genes including Cell cycle, DNA replication, ECM-receptor interaction, Focal adhesion, MAPK signaling pathway and Chemokine signaling pathway (Fig. 1G). Furthermore, the downregulation of RAP1A and upregulation of RALB and ITGA2 identified in MFN2-knockdown cells by microarray analysis were confirmed by western blot (Fig. 1H).

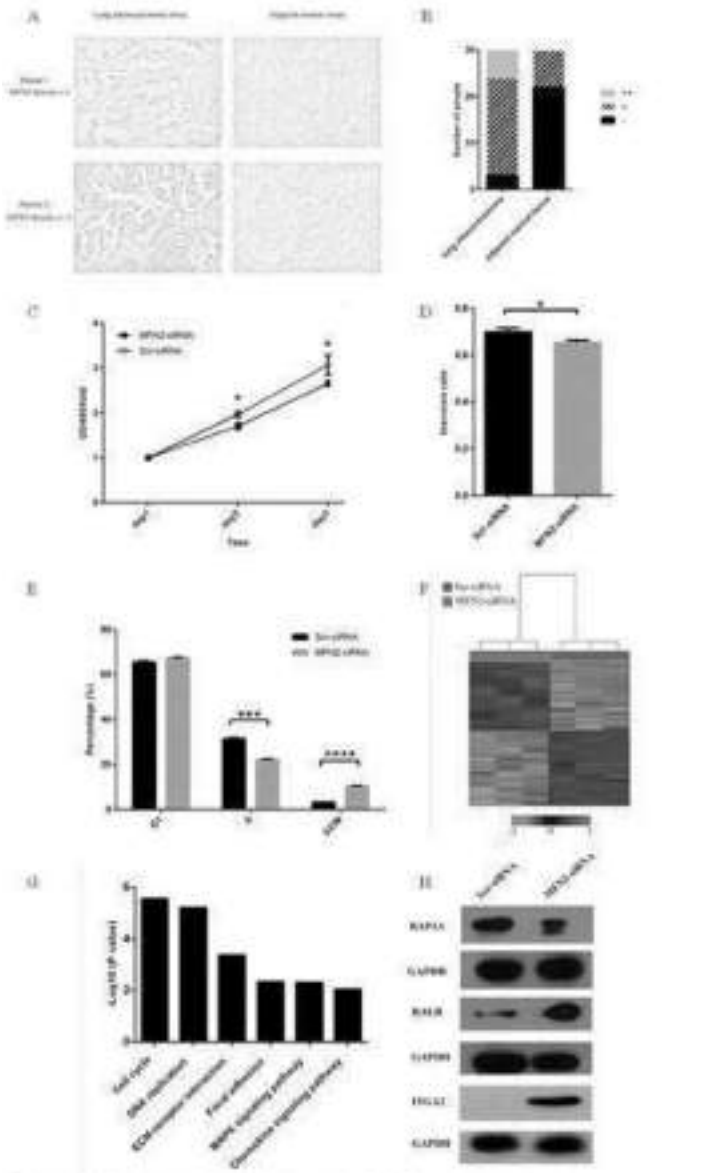

Figure 1 MFN2 regulates lung adenocarcinoma cell proliferation and invasion
(A) Representative images for MFN2 expression in lung adenocarcinoma tissues of two patients.
(B) Quantification of MFN2 expression status in lung adenocarcinoma adjacent normal tissues.
(C) Cell proliferation changes in A549 cells treated with MFN2 shRNA.
(D) Cell invasion ability in A549 cells treated with MFN2 shRNA.
(E) Cell cycle changes in A549 cells treated with MFN2 shRNA.
(F) Heatmap of gene expression profile in A549 cells treated with MFN2 shRNA.
(G) Functional pathway enrichment for deregulated genes in A549 cells treated with MFN2 shRNA.
(H) Confirmation of deregulated genes in A549 cells treated with MFN2 shRNA by western blot

Conclusion: Our results confirmed the involvement of MFN2 in the pathogenesis of lung adenocarcinoma and revealed that MFN2 was critical for cell proliferation and invasion in lung adenocarcinoma cell line A549. Furthermore, microarray analysis identified multiple pathways deregulated in MFN2-knockdown cells, providing valuable insights about the mechanisms underlying MFN2-associated lung adenocarcinoma development.
Keywords: cell proliferation, cell invasion, MFN2, lung adenocarcinoma

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P1.04-047 The Inhibitory Effects of CDK4 and MDM2 on Migration and Invasion in Human Non-Small Cell Lung Cancer Cells Soojeong Kang[1], Sachiko Takikawa[1], Alain C. Borczuk[2], Pierre P. Massion[3], Charles A. Powell[4] [1]*Icahn School of Medicine at Mount Sinai, New York/NY/United States of America,* [2]*Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York/NY/United States of America,* [3]*Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt-Ingram Cancer Center, Nashville/TN/United States of America,* [4]*Division of Pulmonary, Critical Care, and Sleep Medicine, Icahn School of Medicine at Mount Sinai, New York/United States of America*

Background: Cyclin-dependent kinase 4 (CDK4)/RB and mouse double minute 2 (MDM2)/p53 are the two main regulators of the tumor-suppressor pathways that control cellular responses to potentially oncogenic stimuli. CDK4 inhibits RB by triggering its phosphorylation, leading to releasing the G1-S restriction point. MDM2 inhibits the transcription activity of p53 by blocking the transfer of p53 from cytoplasm to nucleus and by accelerating ubiquitination of p53. Our preliminary SNP microarray analysis using lung specimens from non-invasive tumor (adenocarcinoma in situ) and invasive tumor (lepidic predominant adenocarcinoma) showed the amplification of chromosome 12q13–15, including CDK4 and MDM2 gene regions. The aim of the present study was to determine the mechanistic implications of CDK4 and MDM2 in lung adenocarcinoma migration and invasion. **Methods:** Using siRNAs specific for CDK4 and MDM2, the expressions of CDK4 and MDM2 were knocked down in the human non-small cell lung cancer cell lines A549, H460, H1299, SK-Lu-1 and H23, which harbor wild-type RB yet contain other aberrations in p53 (wild-type in A549, H460, absent in H1299, and mutated in SK-Lu-1, H23). Cell proliferation (AlamarBlue staining), mobility (scratch assay), and invasion (transwell-matrigel chamber system) were investigated. **Results:** The knockdown of CDK4 (5.5, 18.5, 2.2, 22.8 and 8.3% compared to scrambled siRNA in A549, H460, H1299, SK-Lu-1 and H23, respectively) significantly inhibited cell proliferation in H23 and SK-Lu-1, and decreased cell migration in SK-Lu-1 and H460. It also repressed cell invasion in H460, SK-Lu-1 and A549. The decreased expression of MDM2 (43.4, 69.6, 6.4, 27.3, 8.7% compared to scrambled siRNA in A549, H460, H1299, SK-Lu-1 and H23, respectively) dramatically inhibited cell proliferation in H1299, SK-Lu-1 and H23, and diminished cell migration in H23, A549 and SK-Lu-1. It also hindered cell invasion in H460 and H23. **Conclusion:** These findings suggest CDK4 and/or MDM2 pathways may play critical roles in cell proliferation, mobility and invasion, and furthermore, the targeting CDK4 and/or MDM2 may provide therapeutic benefit to lung cancer patients.
Keywords: CDK4, MDM2, siRNA, NSCLC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-048 DNA Demethylation Related Hypoxia-Induced Stem-Like Properties in Lung Cancer Hyon Soo Joo, Seung Joon Kim, Chankwon Park *Department of Internal Medicine, The Catholic University of Korea, Seoul/Korea*

Background: Tumors exhibiting extensive hypoxia have been shown to be more aggressive than corresponding tumors that are better oxygenized, which suggests that hypoxic condition induces stem-like properties. The purpose of the present study was to investigate whether hypoxic stress induces acquisition of stem-like properties, and the mechanism is involved with DNA demethylation in lung cancer. **Methods:** Normal epithelial cell line (BEAS-2B) and human lung cancer cell lines (A549, H292, H226 and H460) were incubated either in normoxic or in hypoxic (below 1% O_2) condition. The cell lines were treated with a DNA methyltransferase inhibitor (5-azacytidine, AZA) to determine whether the expression of stem cell markers (CD44, CD133, CXCR4, ABCG2, CD117, ALDH1A1, EpCAM, CD90, Oct4, Nanog, SOX2, SSEA4 and CD166) was reactivated. Methylation-specific PCR and bisulfite sequencing were used to analyze the methylation status, and real-time RT-PCR and western blotting were performed to analyze the expression of the stem cell markers. Cell migration and Matrigel invasion assay were performed for functional analysis **Results:** Among the 13 stem cell markers, CXCR4, Oct4 and Nanog were increased at least one lung cancer cell line in hypoxic condition compared with in normoxic condition. These three stem cell markers were reactivated by treatment with AZA. Methylation-specific PCR showed decreased promoter methylation of these three stem cell markers in hypoxic condition compared with in normoxic condition, which was further validated by bisulfite sequencing. Migration and invasion were increase in hypoxic condition compared with in normoxic condition **Conclusion:** These results suggest that under the hypoxic condition, reactivation of stem-like properties was related with promoter demethylation of stem cell markers. Further studies are needed to assess its value as a prognostic factor and potential therapeutic applications.
Keywords: lung cancer, DNA demethylation, hypoxic stress

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P1.04-049 The MRE11/RAD50/NBS1 Complex Was Impaired in Lung Cancer from Chromate-Exposed Workers Kazuya Kondo[1], Tomoko Kawanishi[1], Mariko Shiraishi[1], Chikako Takai[1], Yuki Morimoto[1], Tamaki Otani[1], Mitsuhiro Tsuboi[2], Koichiro Kajiura[2], Hiromitsu Takizawa[2], Gokei Kawakami[2], Hiroaki Toba[2], Shoji Sakiyama[2], Akira Tangoku[2] [1]*University Tokushima, Tokushima/Japan,* [2]*Department of Thoraci,Endocrine Surgery and Oncology, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima City/Japan*

Background: Our previous studies demonstrated that one third of lung cancers of chromate-exposed workers (chromate LC) showed high-degree microsatellite instability (MSI), most of which repressed DNA mismatch repair (MMR) hMLH1protein.

MMR-deficient tumors are characterized by widespread changes in the number of microsatellites accumulating in both coding and non-coding sequences of many human genes. The MRE11–RAD50–NBS1 complex is essential for DNA double-strand break (DSB) repair performing by homologous recombination (HR) or non-homologous end joining (NHEJ). In gastric and colorectal cancers with MSI, the mono- or biallelic deletions in the poly(T)11 within MRE11 intron 4 and the frameshift mutations in the (A)9 repeat in RAD50 exon 13 were detected and the significant reduction of both proteins were identified. **Methods:** We used formalin-fixed paraffin-embedded materials from 36 chromate LC (28 cases; all male, mean age 56.8, squamous cell ca (SQ) 35, stage I 27, BI=488, mean chromate exposure 24 years) and 28 non-chromate LC (all male, mean age 61, SQ 28, stage I 8, BI=674). DNA was extracted and amplified using nested-PCR. The fragment analysis was performed using a capillary electrophoresis and GeneScan Analysis software (Applied Biosystem, USA). **Results:** In the poly(T)11 within MRE11 intron 4, 8 (29%) of 28 non-chromate LC showed 1bp deletion or insertion and 14 (52%) of 33 chromate LC showed 1bp deletion or insertion. In the (A)9 repeat in RAD50 exon 13, none of 27 non-chromate LC showed deletion or insertion and 4 (16%) of 25 chromate LC showed deletion. 67% of chromate LC with more than 3 MSI had abnormality of MRE11 gene, and 60% of chromate LC with 2 MSI had it. While, 27% of chromate LC with less than one MSI and 28% of non-chromate LC had it. 17% of chromate LC with more than 3 MSI had abnormality of MRE11 gene, and 10% of chromate LC with 2 MSI had it. While, 25% of chromate LC with less than one MSI had it and none of non-chromate LC had it. **Conclusion:** Half of chromate LC had the abnormality of the poly(T)11 within MRE11, which was associated with the degree of MSI. Sixteen percentage of chromate LC had the abnormality of the (A)9 repeat in RAD50. The carcinogenesis of chromate LC may be involved in the abnormality of DNA repair MRE11–RAD50–NBS1 complex. **Keywords:** MRE11–RAD50–NBS1 complex, chromate-exposed workers, lung cancer, microsatellite instability

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P1.04-050 COX-2 Genetic Variants Influence Intratumoral Infiltration of Foxp-3-Positive Regulatory T Cells in Non-Small Cell Lung Cancer Masao Nakata, Takuro Yukawa, Katsuhiko Shimizu, Ai Maeda, Yuji Nojima, Sinsuke Saisho, Riki Okita
General Thoracic Surgery, Kawasaki Medical School, Kurashiki/Japan

Background: The immune microenvironment of primary tumors has been reported to be a prognostic factor. We previously reported that the tumor-infiltrating regulatory T sell (Treg) count was positively correlted with the intratumoral cyclooxygenase-2 (COX-2) expession level and was associated with a poor survival among patients with non-small cell lung cancer (NSCLC). Recently, numerous single nucleotide polymorphisms (SNPs) in the COX-2 gene have been identified, and those SNPs may contribute to differential gene expression and enzyme activity levels. However, whether COX-2 genetic variants influence the functions of COX-2 in NSCLC remains unclear. **Methods:** Eighty NSCLC patients who underwent a complete recection at our institute ware enrolled. We extracted DNA from the peripheral blood and identified five different *COX-2* SNPs. The correlations between the *COX-2* SNPs and the expression levels of COX-2, Tregs and Ki-67 were studied. The prognostic significance of the *COX-2* SNPs was also evaluated. **Results:** *COX-2* SNPs were not correlated with the expression of COX-2. However, for the *COX-2* -1195G/A polymorphism, the AA genotype group had a significantly higher Treg score. Furthermore, the AA group had a significantly higher Treg score regardless of the COX-2 expression level. The *COX-2* -1195AA genotype group tended to have a shorter disease-free survival period than the GA/GG group. **Conclusion:** In conclusion, the *COX-2* -1195G/A polymorphism influences the infiltration of Tregs into NSCLC, and the *COX-2* SNP factor may be a prognostic factor reflecting Treg infiltration in NSCLC. **Keywords:** non-small cell lung cancer, COX-2, SNP, Treg

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P1.04-051 C. Elegans, an in Vivo Model for Lung Cancer: Effect of Chronic Exposure of Nicotine on Specific Mutants Relevant to Lung Cancer Jacob J. Riehm[1], Rajani Kanteti[2], Ravi Salgia[3] [1]*Hem/Onc, University of Chicago, Chicago/IL/United States of America,* [2]*University of Chicago, Chicago/IL/United States of America,* [3]*Medicine, Section of Hematology/Oncology, University of Chicago, Chicago/IL/United States of America*

Background: There are a number of genetic abnormalities that can occur in lung cancer. We, and others, have shown that receptor tyrosine kinases (RTKs), such as EGFR, c-MET, RON, and Eph, frequently harbor gain-of-function mutations in addition to being overexpressed in lung cancer. We also have shown that the soil nematode *C. elegans* overexpressing a c-Met mutant revealed an abnormal vulval phenotype with hyperplasia. Interestingly, exposure to nicotine significantly aggravated the phenotype suggesting that *C. elegans* can be used as an *in vivo* model for rapid screening of RTK mutants as well as carcinogens. **Methods:** *C. elegans* strains *vab-1* (Eph receptor), RB2088 (MET receptor), SD551 (temperature sensitive strain expressing constitutively active form of KRAS), and three *sli-1* mutants PS2728, PS1258, and MT13032 (inactive, c-CBL) were compared to wild-type N2 worms for survival, fertility, egg-laying capacity, locomotion, and phenotypic changes in the absence or presence of nicotine. Gene expression analysis was also performed on each of the strains in the absence or presence of nicotine. **Results:** Nicotine treatment reduced the lifespan of worms for all strains (p=.0034). Nicotine treatment adversely affected egg-laying capacity of all strains, including N2 control, reducing egg production by 13% at 50μM nicotine and 31% at 500 μM nicotine. Furthermore, the fertility (the number of eggs laid/worm) was significantly reduced in SD551 mutant worms compared to N2 worms (p=.003). Overall locomotion velocity did not change with increasing concentration of nicotine except in MT13032, a c-Cbl mutant. Heat map analysis of gene expression profiling data clearly revealed that the various kinases and phosphatases in *C. elegans* that are marginally expressed in N2 worms were significantly enhanced upon chronic nicotine exposure. The expression of these genes was already elevated in SD551 and that was further increased in response to nicotine. **Conclusion:** Taken together, chronic nicotine exposure adversely affects various biological functions of *C. elegans* and these effects are exaggerated in the mutants. Interestingly, nicotine treatment also upregulates the expression of various kinases and phosphatases thereby strengthening our contention that the initial screening studies for the oncogenic mutants detected in humans can be rapidly carried out in *C. elegans*. **Keywords:** C. elegans, nicotine, vab-1, SD551

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-052 TGF-β Induced EMT and Stem-Like Characteristics in Lung Cancer Seung Joon Kim[1], Su Yeon Choi[2], Nahyeon Kang[2], Young Kyoon Kim[2] [1]*Department of Internal Medicine, The Catholic University of Korea, Seoul/Korea,* [2]*The Catholic University of Korea, Seoul/Korea*

Background: TGF-β promotes tumor invasion and metastasis by inducing an epithelial-mesenchymal transition (EMT). EMT is often associated with acquisition of stem-like characteristics. In the present study, we investigated whether EMT induced by TGF-β could acquire stem-like characteristics in lung cancer. **Methods:** Normal epithelial cell line (BEAS-2B) and lung cancer cell lines (A549, H292, H226 and H460) were used in the study. These cell lines were incubated with 10 ng/ml of TGF-β for 3 days. Western blot was performed to analyze the expression of epithelial marker (E-cadherin) and mesenchymal markers (N-cadherin, vimentin, fibronectin and alpha-smooth muscle actin). Real-time RT-PCR and western blot were performed to analyze the expression of stem cell markers (CD44, CD133, CXCR4, ABCG2, CD117, ALDH1A1, EpCAM, CD90, Oct4, Nanog, SOX2, SSEA4, and CD166). Wound-healing assay, Matrigel invasion assay and sphere formation assay were used to assess functional characteristics of EMT and stemness acquisition. **Results:** TGF-β induced EMT and stem cell markers with variable degrees according to lung cancer cell lines. Most of the stem cell markers were increased by treatment with TGF-β except H460 cell line. Increased expression of mesenchymal markers was associated with the acquisition of stem cell makers. Migration, invasion and sphere formation were increased according to the expression of stem cell markers. **Conclusion:** TGF-β induced EMT was associated with acquisition of stem-like characteristics which was different according to lung cancer cell lines. Further studies are needed to investigate the signal mechanism of EMT and stemness acquisition. **Keywords:** TGF-β, EMT, Cancer stem cell, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-053 Characterization of Invasive Cancer Cells and Potential Therapeutic Effect of Suberoylanilide Hydroxamic Acid on Human Lung Cancer Metastasis Shirong Zhang[1], Kan Wu[2], Jianguo Feng[3], Lucheng Zhu[4], Bing Wang[2], Hong Jiang[5], Zhibing Wu[4], Xufeng Chen[6], Shenglin Ma[2] [1]*Hangzhou First People'S Hospital, Hangzhou/China,* [2]*Affiliated Hangzhou First People'S Hospital of Zhejiang Chinese Medical University, Hangzhou/China,* [3]*Zhejiang Cancer Hospital, Hangzhou/China,* [4]*Department of Radiation Oncology, Affiliated Hangzhou Hospital of Nanjing Medical University, Hangzhou/China,* [5]*Affiliated Hangzhou Hospital of Nanjing Medical University, Hangzhou/China,* [6]*Department of Pathology and Laboratory Medicine, University of California at Los Angeles, California/AL/United States of America*

Background: Lung cancer is a worldwide problem andthe leading cause of death among all malignancies. Despite tremendous progresses in diagnosis and treatment, the overall treatment outcomes for lung cancer patients remain poor, and metastatic lung cancer is responsible for more than ninety percent of lung cancer related deaths. However, the details for lung cancer invasion and thereafter metastasis remain unclear. In this study, we characterized the biological features of invasive human lung cancer cells, and investigated the potential therapeutic effects of Suberoylanilide Hydroxamic Acid (SAHA) on invasive cancer cell subpopulation. **Methods:** Boyden-type cell invasion chambers were used for isolation of cancer cell subpopulations with high invasiveness (H-INV) and low invasiveness (L-INV) from human lung cancer H460 cells. The potential enrichment of stem cell-like cancer cells in H-INV cells and the resistances of H-INV cells to chemotherapy and radiation treatment were investigated. We also tested the effects of SAHA on the differentiation of cancer stem cell and its consequences on cancer cell invasion and the sensitivities to radio/chemotherapies in H-INV cells. Furthermore, microarray for message RNA was performed for identification of gene expression profiling for invasive cancer cells. **Results:** Comparing to L-INV cells, H-INV cells are with enrichments of stem cell-like cancer cells, with increased positive staining of putative stem cell markers such as CD24low/CD44+ and OCT3/4, and more tumorigenic. H-INV cells are also more resistant to treatments of chemotherapeutic agents and ionizing radiation. Treatment with SAHA can induce differentiation of stem cell-like cell in H-INV cells, causing reduced cancer cell invasion and increased sensitivity to chemo/radiotherapy in cells. With mRNA microarray assay, we identified 453 genes differentially expressed in H-INV versus L-INV, and five of these genes have been further tested for their significances in paired primary and metastatic lung tumors. **Conclusion:** Our study suggested putative roles of cancer stem cell in lung cancer invasion and migration. Study also showed that invasive lung cancer cells are resistant to most of first-line and second-line chemotherapeutic agents and radiotherapy, indicating novel therapeutic strategies are needed for the treatment of metastatic lung cancer. Of this setting, SAHA may serve as a chemotherapeutic agent for benefiting lung cancer patients. The candidate genes identified in this study may also have clinic impact as potential metastatic predictors for diagnosis and prognosis for human lung cancer. **Keywords:** lung cancer, invasion, Cancer stem cell, SAHA

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P1.04-054 Mitochondrial Status in Peripheral Blood Mononuclear Cells in Relation to Cognitive Impairment in Lung Cancer Patients Rodryg Ramlau[1], Slawomir Michalak[2], Joanna Rybacka-Mossakowska[2], Joanna Gazdulska[3], Iwona Golda-Gocka[4] [1]*Department of Oncology, Poznan University of Medical Sciences, Poznan/ Poland,* [2]*Department of Neurochemistry and Neuropathology, Poznan University of Medical Sciences, Poznan/Poland,* [3]*Oncology Center, Poznan University of Medical Sciences, Poznan/Poland,* [4]*Lung Diseases Center, Poznan University of Medical Sciences, Poznan/ Poland*

Background: Mitochondrial dysfunction is observed not only in lung cancer cel, but can develop in peripheral tissues. Peripheral blood mononuclear cells (PBMC) represent an available population of cells that can be used for the studies on remote effects of lung cancer. NADH dehydrogenase (ubiquinone) Fe-S protein 1 (Ndufs1) is located at the inner mitochondrial and transfers electrons from NADH to the respiratory system. Mitochondrially encoded cytochrome c oxidase I (MT-CO1) is involved in the coupling between O2 reduction and proton pumping. The changes in both key components of respiratory system reflect mitochodrial status. On the other hand the impairment of mitochondrial function may be crucial among pathomechanisms leading to neurological deficits. The aim of the study was evaluate mitochondrial status in PBMC in relation to the cognition in lung cancer patients. **Methods:** The study included 80 (24 females and 56 males, aged 61.5±6.7 years) consecutive lung cancer patients (5 small-cell lung cancer, 75 non-small cell lung cancer) hospitalized in Clinical Oncology with The Sub-department of Diurnal Chemotherapy Wielkopolska Center of Pulmonology and Thoracosurgery of Eugenia and Janusz Zeyland and Chair and Clinic of Oncology. PBMC were isolated by density gradient centrifugation. The expression Ndufs1 a marker of mitochondrial complex I and MTCO1 a marker of complex IV in PBMC was evaluated by means of ELISA and expressed in pg per mg of protein. Neurological examination, MiniMental State Examination (MMSE), Trail Making Test (TMT) A and B, and Hamilton scale were performed at baseline (time of lung cancer diagnosis) and after 6 months. Patients serum was tested for the presence of onconeuronal antibodies with indirect immunofluorescence as a screening and Line blot as confirmation test. **Results:** Ndufs 1 expression in PBMC was lower in patient with peripheral nervous system involvement (0.00; 0.0-3.6218 ; median; minimum-maximum) than in subjects without neurological deficit (0.0; 0.0-8.61; median; minimum-maximum; P= 0,024). Up-regulated expression of Ndufs 1 in PBMC is associated with worse TMT- A (13.61±3.13s) than in patients with down-regulated complex I marker (8.60±4.51s; P=0.003). Similarly TMT- B results were worse in patients with higher Ndufs 1 expression (162.48±46.40s) than in cases with inhibited Ndufs1 (124.78±51.77s; P<0,05). Ndufs1 expression correlated negatively with MMSE 6 months after lung cancer diagnosis (Kendall tau =-0.310; P=0.0236), and positively with Hamilton scale score after 6 months (Kendall tau=0.288; P=0.0428), TMT-A (Kendall tau=0.301; P=0.0001) and TMT-B (Kendall tau=0.199; P=0.0120) at baseline. Up-regulated expression of MTCO1 was associated with worse TMT-A results (11.05±5.81s) compared to down-regulated marker of mitochondrial complex IV (8.52±4.14s; P=0.048). MTCO1 expression correlated positively with TMT-A results (Kendall tau=0.167; P=0.0344) at baseline. In 12 patients onconeuronal antibodies were identified (Ma/Ta, Yo, Ri). No differences in Ndufs1 and MTCO1 expression were found between patients with onconeronal antibodies and seronegative subjects. **Conclusion:** Up-regulation of mitochondrial complex I and IV in PBMC of lung cancer patients is associated with cognitive decline. Stimulation of mitochondria status in PBMC may indicate cytotoxic response leading to cognitive impairement. **Keywords:** peripheral blood mononuclear cells, mitochondria, cognition, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-055 Fibroblast-Dependent Cancer Cell Invasion: Analysis of Cancer-Associated Fibroblasts That Remodel the Extracellular Matrix Shinya Neri[1], Genichio Ishii[2], Hiroshi Date[1], Atsushi Ochiai[2] [1]*Thoracic Surgery, Kyoto University, Graduate School of Medicine, Kyoto/Japan,* [2]*Pathology, Resarch Center of Innovative Oncology, National Cancer Center Hospital East, Kashiwa, Chiba/Japan*

Background: Cancer-associated fibroblasts (CAFs) communicate with cancer cells and play important roles in cancer invasion. We previously reported that local invasion of cancer cells was frequently observed in lung adenocarcinoma patients with podoplanin(PDPN)-expressing CAFs. However, the underlying mechanisms of this phenomenon have remained unclear. **Methods:** We established a novel collagen invasion assay model in which cancer cells and CAFs were co-cultured; we analyzed the mechanisms governing how cancer cell invasion was promoted by PDPN(+)CAFs. **Results:** By observing the dynamic movement of both CAFs and cancer cells in the collagen matrix, we found that PDPN(+)CAFs invaded the matrix to a greater extent, with more cancer cells invading within the "tracks" created by the CAFs, compared with control CAFs. The knockdown of PDPN in CAFs decreased the invasion of both the CAFs and the cancer cells. PDPN(+)CAFs displayed a higher RhoA activity, and treatment with a ROCK inhibitor cancelled the increased invasion ability of PDPN(+)CAFs and subsequently decreased the number of invaded cancer cells. After intravenous injection in the mouse tail vein, PDPN(+)CAFs invaded and promoted cancer cell invasion into the lung parenchyma, compared with control CAFs. Among the patients with lung adenocarcinoma, we observed some cases with PDPN(+) CAFs at the invasive front of the tumor. These cases predominantly exhibited pleural invasion of cancer cells, known as pathological invasiveness. **Conclusion:** Our results indicated that PDPN(+)CAFs were tumor-promoting CAFs that lead and enhance the local invasion of cancer cells, suggesting that the invasion activity of CAFs themselves could be rate-determining for cancer cell invasion. For analysis of fibroblast-dependent cancer cell invasion, we established single-cell derived clones from primarily cultured CAFs and conduct further investigation. **Keywords:** tumor microenvironment, cancer-associated fibroblasts, lung cancer, cancer invasion

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P1.04-056 Use of Pooled shRNA Synthetic Lethal Screens within an In Vivo Murine Model to Identify Microenvironment-Dependent Lung Cancer Genes Nathaniel R. Little[1], Joanna M. Poczobutt[2], Hannah A. Scarborough[3], Howard Li[1], Raphael Nemenoff[2], James V. Degregori[3] [1]*Division of Pulmonary Sciences and Critical Care, University of Colorado, Aurora/CO/United States of America,* [2]*Department of Medicine, University of Colorado, Aurora/CO/United States of America,* [3]*Biochemistry and Molecular Biology, University of Colorado Denver, Denver/CO/United States of America*

Background: Lung cancer remains the leading cause of cancer-related deaths worldwide. While significant knowledge has been gained regarding the characterization of mutational drivers in NSCLC, much less is known regarding interactions between tumor cells and the surrounding microenvironment that are critical for tumor progression. Additionally, a significant limitation in current understanding is the lack of knowledge regarding which tumor gene products are necessary for promoting cell survival in the context of the tumor microenvironment. We hypothesize that the use of pooled shRNA synthetic lethal screens within an in vivo murine model will allow for the elucidation of targetable microenvironment-dependent genes. **Methods:** We generated a custom murine shRNA lentiviral library targeting 250 genes implicated in the communication between cancer cells and the microenvironment, which was used to transduce two murine cell lines: Lewis Lung carcinoma (LLC) and CMT167 cells. Following puromycin selection of cells harboring incorporated shRNA's of interest, populations were expanded and designated for in vitro versus in vivo replication and growth. Selected cells were allocated to either in vitro passage vs direct in vivo injection into the lungs of 18 week-old syngeneic C57BL6 mice. After 4 weeks, cells were harvested and gDNA was isolated. Sequencing and quantitation of shRNA was performed using an Illumina deep-sequencing platform. Both raw and normalized read counts were assessed and analyzed to determine the relative representation of a particular shRNA within an in vitro or in vivo sample. Following quality control assessments which demonstrated adequate read count numbers per sample, and appropriate correlation of sample similarity per groups, direct comparisons between in vitro and in vivo samples were performed. **Results:** Multiple gene candidates were identified and largely reproducible via either rank analysis, mean, or t-test analyses. Candidate genes included multiple chemokines, and their receptors, matrix proteases, complement factors, and growth factor receptors. **Conclusion:** These results suggest a list of genes that are both intriguing and diverse, pointing toward gene products that would not have been previously predicted to influence cancer cell survival and growth through a lung cancer cell-autonomous fashion. Furthermore, these genes appear to potentially interact with multiple compartments of the tumor microenvironment including the extracellular matrix, cytokine milieu, vascular structures (complement factors), and the adaptive immune system. Validation of specific gene targets are ongoing through assessment of tumor growth comparing murine cell lines transfected with individual shRNA's of interest vs control tumor cells. Furthermore, parallel pooled shRNA synthetic lethal screens within selectively adaptive immune-deficient models are currently in progress. **Keywords:** tumor microenvironment, in vivo, synthetic lethal, murine

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P1.04-057 Wnt Signaling Regulates Cancer Stem Cell in Lung Cancer SPC-A1 Cells Xueyan Zhang[1], Yuqing Lou[1], Huiming Wang[1], Xiaoxuan Zheng[1], Qianggang Dong[2], Jiayuan Sun[1], Baohui Han[1] [1]*Shanghai Jiaotong Univ. Affiliated Shanghai Chest Hospital, Shanghai/China,* [2]*Shanghaijiaotong University, Shanghai/China*

Background: Wnt signaling is invovled in driving cancer stem cells (CSCs) activity in a variety of cancers. The aim of this study was to explore the role of Wnt signaling in the lung cancer stem cells (LCSCs). **Methods:** Sphere culture was processed by treating human lung adenocarcinoma cell line SPC-A1 with IGF, EGF and FGF-10 to obtain the LCSCs. After confirming the stemness by immunoflurescence, functional genome screening and RT-PCR were employed to perform pathway analysis. The relationship between the identified signaling pathway and stemness gene expression was explored by agnoist/antagonist assay. Moreover, the effects on sphere formation, cell viability and colony formation by different signaling molecule inhibitors were also analyzed. **Results:** The results showed that LCSCs were successfully generated and the phenotype characterization was confirmed by expressing pluripotent stem cell markers Nanog and Oct 4, and lung distal epithelial markers CCSP and SP-C. The involvement of Wnt pathway in LCSCs was confirmed by functional genome screening and verified by RT-PCR. The expression of Wnt signaling components were related with the expression of the Nanog and Oct 4. Anti-cancer effects could be exerted by using different signaling molecule inhibitors targeting Wnt signaling pathway. **Conclusion:** In conclusion, Wnt signaling pathway is involved in the stemness regulation of LCSCs and could be considered as a potential therapeutic target in the lung adenocarcinoma. **Keywords:** Lung cancer stem cells, Wnt signaling pathway, sphere culture, Functional genome screening

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P1.04-058 Inhibition of ERK1/2 Down-Regulates the Hippo/YAP Signaling Pathway in Human NSCLC Cells Bin You[1], Yi-Lin Yang[2], Zhidong Xu[2], Yuyuan Dai[2], Shu Liu[2], Jian-Hua Mao[2], Osamu Testu[3], Hui Li[1], David Jablons[2], Liang You[2] [1]*Thoracic Surgery, Beijing Chao-Yang Hospital, Beijing/China,* [2]*Surgery, UCSF, San Francisco/CA/United States of America,* [3]*UCSF, San Francisco/CA/United States of America*

Background: Alterations of the EGFR/ERK and Hippo/YAP pathway have been found in non-small cell lung cancer (NSCLC). **Methods:** Luciferase reporter and downstream

gene expression assays were used to test hippo pathway activity. **Results:** Herein, we show that ERK1 and ERK2 have an effect on the Hippo/YAP pathway in human NSCLC cells. Firstly, inhibition of ERK1/2 by siRNA or small-molecular inhibitors decreased the YAP protein level, the reporter activity of the Hippo pathway, and the mRNA levels of the Hippo downstream genes, CTGF, Gli2, and BIRC5. Secondly, degradation of YAP protein was accelerated after ERK1/2 depletion in NSCLC cell lines, in which YAP mRNA level was not decreased. Thirdly, forced over-expression of the ERK2 gene rescued the YAP protein level and Hippo reporter activity after siRNA knockdown targeting 3'UTR of the ERK2 gene in NSCLC cells. Fourthly, depletion of ERK1/2 reduced the migration and invasion of NSCLC cells. Combined depletion of ERK1/2 had a greater effect on cell migration than depletion of either one separately. Finally, the MEK1/2 inhibitor Trametinib decreased YAP protein level and transcriptional activity of the Hippo pathway in NSCLC cell lines. **Conclusion:** Our results suggest that ERK1/2 inhibition participates in reducing YAP protein level, which in turn down-regulates expression of the downstream genes of the Hippo pathway to suppress migration and invasion of NSCLC cells. **Keywords:** yes-associated protein, non-small cell lung cancer, extracellular signal regulated kinases, Hippo pathway

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P1.04-059 The Role of Histone Methyltransferases G9a/Glp in Mouse Lung Tumor Propagating Cells and Lung Stem Cells Samuel Rowbotham[1], Carla Kim[2]
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Background: Proper epigenetic control of transcription is essential for stem cell homeostasis and is frequently disrupted in cancer, but this has not been well investigated in lung biology or lung disease. We have previously demonstrated that the stem cell marker Sca-1 enriches for mouse bronchioalveolar stem cells (BASCs) and lung adenocarcinoma cells with enhanced metastatic and tumor propagation abilities (TPCs). **Methods:** I performed a small chemical library screen using a Kras; p53-flox driven mouse lung adenocarcinoma cell line, CK1750 with high expression of the stem cell markers Sca-1 and CD24. Chemically treated cels were seperated and screened by FACS analysis for changes in the surface antigens Sca-1 and CD24. I treated Sca-1 low expressing mouse lung adenocarcinoma cell lines TM1 and TnM2 with either 1 uM UNC0638 or DMSO for 4 days. 100,000 cells per mouse were injected intravenously. After 3-4 Weeks mice were sacrificed and lungs and other organs were analyzed for tumor formation. Treated cells were also plated in 3D organoid culture and grown for 14 days. After this matrigel plugs were fixed and counted for organoid formation. I isolated BASCs and AT2 cells from 6 week old mice by FACS and plated cells in 3D organoid co-culture. Cells were grown with either 250 nM UNC0638 or DMSO for 21 days. At this point plugs were fixed, sectioned and organoids were stained for lung lineage markers SPC and CC10 and organoids expressing each were scored. **Results:** A FACS screen of adenocarcinoma cell lines revealed that UNC0638, an inhibitor of H3K9me1/2 methyltransferases G9a and Glp enriches for high Sca-1 expressing, TPC-like cells. Gene expression analysis of primary adenocarcinomas shows that G9a/Glp are down-regulated in Sca-1+ metastatic TPCs. Furthermore, analysis of 400+ early stage patient lung adenocarcinomas reveals that low G9a expression and high expression of KDM3A, an H3K9me1/2 demethylase, significantly correlate with worse survival (P=0.008, P=0.002). This implies that dysregulation of H3K9me1/2 is also a significant factor in human disease. Interestingly, G9a/Glp inhibition of adenocarcinoma cells prior to transplantation increases Sca-1+ cells but does not increase recipient lung tumor burden. Instead, significantly more tumors are found in non-lung locations (58% vs. 13%, P=0.02). Whilst inhibition does not affect cell proliferation or migration, colony forming efficiency in 3D organoid culture is significantly increased (1.1% vs 0.3%, P=0.04). This suggests that altered stem-like properties such as tumor initiation may underlie the more tumorigenic phenotypes of H3K9me1/2 low, Sca-1+ TPCs. H3K9me1/2 also regulates the behavior of lung stem cells. G9a/Glp inhibition of BASCs or alveolar type 2 cells in 3D co-culture assays increases both Sca-1+ cells and undifferentiated organoids, and significantly decreases alveolar-lineage organoids (P<0.0005). BASC cultures also show increases in bronchiolar-lineage organoids (P<0.0005), implying that cell fate decisions may regulated by H3K9me1/2. **Conclusion:** These findings suggest that common mechanisms of epigenetic regulation exist between mouse lung stem cells and lung TPCs. Determining the precise mechanisms of this regulation will be important for our understanding of lung biology and disease, with potential implications for the diagnosis and treatment of human adenocarcinoma. **Keywords:** stem cells, epigenetics

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P1.04-060 Pathways Involved in Lung Adenocarcinomas, - Integrated Analyses on Methylation and mRNA Data Vilde D. Haakensen[1], Maria M. Bjaanæs[1], Liliana Gregers[2], Ann R. Halvorsen[1], Lars Jørgensen[3], Steinar Solberg[3], Alvis Brazma[2], Odd Terje Brustugun[4], Åslaug Helland[5] [1]*Institute for Cancer Research, Oslo University Hospital, Oslo/Norway,* [2]*Embl-Ebi, Hinxton/United Kingdom,* [3]*Department of Cardiothoracic Surgery, Oslo University Hospital-Rikshospitalet, Oslo/Norway,* [4]*Oncology, Oslo University Hosital,The Norwegian Radium Hospital, Oslo/Norwa, Oslo/Norway,* [5]*Department of Oncology, The Norwegian Radium Hospital, Oslo/Norwa, Oslo/Norway*

Background: Lung cancer is one of the biggest cancer killers in the world. Despite certain recent advances, mortality is still high. Targeted therapy has increased the time to death for metastastic lung cancer, but such therapy is not available for all lung cancer patients. Targeted therapy is more often available for never smokers, due to presence of druggable driver mutations. In order to search for new putative targets of therapy, we seek to identify pathways involved different subgroups of patients and in patients with early relapse. **Methods:** A total of 190 patients undergoing surgery for lung cancer were included in the study (154 EGFR positive, 23 EGFR negative, 170 smokers and 20 non-smokers). Lung cancer tissue and clinical information was available for all patients and normal lung tissue was available for 30 of the patients. Whole genome expression array analysis (Agilent) was performed using mRNA isolated from all samples and DNA-methylation was analysed for 168 tumours and 21 matched normal lung tissue samples. R was used for statistical analyses; *annHeatmap* (from *Heatplus)* for hierarchical clustering, *limma* to identify differentially expressed genes, *SPIA* for pathway analysis and canonical correlation of methylation and mRNA-expression was performed with the CCA function from the PMA package. Pathways with an FDR<0.1 were considered significant. DAVID was used for gene ontology analysis. **Results:** Based on correlation of mRNA and methylation, different pathways were identified as predominant in specific subgroups of lung adenocarcinomas. Preliminary results indicate that genes involved in the KEGG-pathways *cell cycle* are more highly expressed in EGFR positive than in EGFR negative tumours in smokers. In the EGFR-negative tumours, several pathways are up-regulated: *Oocyte meiosis*, *progesterone-mediated oocyte maturation, HTLV-1 infection, p53 signalling pathway* and *small cell lung cancer*. For non-smoking patients, four pathways were up-regulated in EGFR-positive tumours: *ECM-receptor interaction, TGF-beta signalling pathway, bile secretion* and *cocaine addiction*. There were no pathways up-regulated in EGFR-negative compared with EGFR-positive never-smokers. This may partly be due to small numbers. Similarly, pathways dominating the tumours of patients with early relapse will be identified. Genes whose expression and methylation status were correlated were identified within smokers and non-smokers separately. **Conclusion:** Based on correlation between mRNA and methylation, specific pathways were identified activated in subgroups of lung adenocarcinomas. There are significant differences between ever-smokers and never-smokers. Survival analyses are ongoing. **Keywords:** methylation, Adenocarcinoma, Pathway analysis, Gene Expression

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P1.04-061 Comparison of MET Expression in Primary and Corresponding Nodal and Distant Metastases in Non-Small Cell Lung Cancer (NSCLC) Babak Tamjid[1], Paul Mitchell[2], Thomas John[3], Simon Knight[4], Adrienne Morey[5], Carmel Murone[6], Khashayar Asadi[7] [1]*Medical Oncology, Austin Health, Heidelberg/ VIC/Australia,* [2]*Austin Health, Melbourne/ACT/Australia,* [3]*Olivia Newton-John Cancer Centre, Austin Health, Melbourne/VIC/Australia,* [4]*Surgery, Austin Health, Heidelberg/ Australia,* [5]*Pathology, St Vincents Pathology, Sydney/ACT/Australia,* [6]*Olivia Newton-John, Austin Health, Heidelberg/VIC/Australia,* [7]*Pathology, Austin Health, Heidelberg/Australia*

Background: Hepatocyte Growth Factor and its corresponding receptor MET are potential therapeutic targets for NSCLC. In NSCLC MET is over expressed, activated and mutated and is involved in resistance to tyrosine kinase inhibitors. A high proportion of primary NSCLC cases show elevated MET expression on immunohistochemistry (IHC), however, it is not clear whether expression changes during the metastatic process. We investigated paired NSCLC tumour samples to determine whether MET receptor expression differs in the primary and its corresponding lymph node and distant metastases. **Methods:** Tissue Microarrays (TMAs) were constructed using 1mm cores of primary and metastatic matched NSCLC archival paraffin tissues in triplicate. For IHC, TMAs were stained with the SP44 clone (Ventana) and an H-score calculated based on the percentage of cells stained and their intensity with a minimum of 0 and maximum of 300. The mean of values from multiple cores was calculated. Two independent scorers assessed the tissues. Discordance was defined as an H-score difference of greater than 100 between the primary tumour and its metastasis. **Results:** 61 patients with primary and matched distant metastasis were included in the main analysis with 38 (62%) male and brain the most common site of metastasis (27/61, 44%). The histology was adenocarcinoma in 26 patients, squamous cell in 21 and large cell, undifferentiated or mixed in 14. The median H-score was 100 in primary tissue and 120 in metastatic tissue. Brain secondaries showed the highest median H-score (140) compared with other metastatic sites (105). MET concordance was present in 50/61 cases (82%). MET discordance was found in 11/61 tumours including 6/26 (23%) of adenocarcinomas, 2/21 (10%) of squamous carcinomas and 3/14 (21%) of mixed or large cell tumours. Discordant elevation in metastases was present in 6/61 (10 %) and reduction in 5/61 (8%). MET FISH data was available for 54/61 of primary tissues and 60/61 of metastasis. MET was amplified only in 2/61(3%) cases, seen in both primary and secondary tissues, associated with strong positivity on IHC. An additional 75 patients had matched primary and lymph node metastasis MET IHC and FISH data available. High rate of concordance, 66/75 (88%) also was present in this nodal cohort. The median H-score was 100 in primary tissue and 117 in nodal metastatic, similar to the main primary and distant metastatic group. MET discordance between primary and nodal secondary was found only in 9/75 (12%) with discordant elevation in 4/75 (5%) and discordant reduction in 5/75 (7%). MET FISH true amplification was seen in 2 paired specimens and one primary with clonal amplification which was non-amplified in the lymph node metastasis. **Conclusion:** In this cohort of paired biopsies, increased MET expression in the primary was retained in a high proportion of distant and lymph node metastases. These data indicate that MET expression in metastases can be predicted by expression in the primary and further suggests that treatment decisions in the metastatic setting can be based on MET IHC results of archival primary or lymph node tumour. **Keywords:** NSCLC, MET expression, Lymph node and distant metastasis, Concordance

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P1.04-062 Phagocytic Behaviour in Lung Adenocarcinoma Cells: Clinical Implications and Cellular Mechanisms Hannah Mackay[1], David Moore[2], Patricia Muller[3], John Le Quesne[3] [1]*Leicester University, Leicester/United Kingdom,* [2]*University Hospitals Leicester NHS Trust, Leicester/United Kingdom,* [3]*Hodgkin Building, Mrc Toxicology Unit, Leicester/United Kingdom*

Background: Pulmonary adenocarcinoma is the commonest and the most histologically diverse form of lung cancer. 'Cell-in-cell' structures are frequently seen as incidental findings when making diagnoses of lung cancer. These structures arise when one viable tumour cell is enveloped within a vacuole within another viable tumour cell. They have been identified in a number of solid tumours including breast, lung, endometrial, pancreatic, melanoma and squamous cell carcinomas. The repeated occurrence of the phenomenon in such a range of tumour types suggests that it may represent a process that confers a selective advantage to the malignant clone (or subclone). Possible mechanisms for this include the acquisition of nutrition by the host cell, horizontal gene transfer, or simple clonal extinction of neighbouring subclones. The biological significance and mechanisms of action still all remain largely unknown. We set out to investigate these. **Methods:** 100 recent consecutive cases of lung adenocarcinoma from our surgical centre were de-archived and examined. For each, high-resolution digital images of 10 high-power field (hpf) equivalents were examined. A scoring scheme for both cell-in-cell appearances and multinucleated cells was formulated and used to score the tumours. Independently from this they were classified by histological pattern and graded for numerous architectural and cytological characteristics. Results were collated and statistical tests carried out. *In vitro* experiments using cocultures of H1299 lung cancer cells transfected to express either GFP (Green Fluorescent Protein) or RFP (Red Fluorescent Protein) were also conducted. These cells were seeded on a selection of coated surfaces including gelatin, fibronectin and collagen to mimic the extracellular matrix proteins. **Results:** Cell-in-cell structures are frequently observed in primary lung adenocarcinomas. 15% of cases have frequent occurrences (≥0.8/hpf). Cell-in-cell structure frequently is strongly associated with multinucleation (P<0.0001). In addition, there is a strong association with cytological measures of tumour grade such as mitoses (P<0.0001), necrosis (P 0.015) and solid pattern (P=0.002). In cell co-culture experiments we are able to reproduce the same appearances, and to visualize cultured lung adenocarcinoma cells engulfing one another. The process is greatly enhanced by the presence of extracellular fibronectin or collagen, but gelatin has a negative effect. This suggests integrins may be involved in the process, as collagen and fibronectin are integrin activators, while gelatin is known for its lack of integrin activation. **Conclusion:** Lung adenocarcinomas frequently contain numerous cell-in-cell structures. This is related to the solid phenotype; this implies that engulfment requires full three-dimensional movement which is impossible in two-dimensional lepidic/acinar/papillary conformations. It is associated with high cytological grade, and may be a useful component of future grading systems. The association with multinuclearity implies that cell engulfment may be the mechanism that leads to the formation of multinucleated giant cells. The same appearances can be reproduced in cell culture systems, where they appear to be dependent upon the presence of signaling from the extracellular matrix. **Keywords:** Cell-in-cell, Adenocarcinoma

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P1.04-063 Exposure to IL-1β Leads to EMT via Distinct Mechanisms in Acute and Chronic Inflammation in NSCLC Rui Li[1], Stephanie L. Ong[2], Kostyantyn Krysan[3], Tonya Walser[3], Zhe Jing[3], Steven M. Dubinett[3] [1]*Molecular and Medical Pharmacology, UCLA, Los Angeles/CA/United States of America,* [2]*Ecology and Evolutionary Biology, UCLA, Los Angeles/CA/United States of America,* [3]*Medicine, David Geffen School of Medicine at UCLA, Los Angeles/CA/United States of America*

Background: Dysregulated inflammation is associated with the development and progression of lung cancer. Pulmonary diseases characterized by increased inflammation, including emphysema and pulmonary fibrosis, are strongly related to heightened risk of lung cancer. Moreover, lung cancer patients with increased levels of inflammatory mediators or inflammatory cells have poor outcomes. It has been shown that dysregulated inflammatory cytokines in the tumor microenvironment can promote cancer metastasis. However, the mechanisms of this effect in lung cancer have not been fully understood. Interleukin 1β (IL-1β), a key pro-inflammatory cytokine, is associated with tumor aggressiveness and poor patient outcomes in NSCLC. Herein, we report that treatment of IL-1β leads to epithelial-to-mesenchymal transition (EMT) in NSCLC cell lines. Delineation of the underlying molecular pathway(s) may potentiate novel therapeutic strategies. **Methods:** We treated NSCLC cell lines with IL-1β acutely (3 days) and chronically (21 days) *in vitro* and identified EMT mediators using RNA interference and chemical inhibitors. Histone modifications and DNA methylation were analyzed with chemical inhibitors, ChIPassays and methylation-specific PCR. We utilized transwell migration, cell proliferation and anchorage-independent cell growth assays to evaluate the functional phenotypes **Results:** We found that following acute IL-1β exposure (within 7 days), the activator protein 1 (AP-1) transcription factor components, including Fra-1 and c-jun, mediate EMT. AP-1 functions downstream of ERK1/2 and JNK signaling and resides upstream of the transcription factors Slug and Zeb2. Importantly, inhibition of slug, zeb2, fra-1 or ERK1/2 and JNK signaling by RNA interference or chemical inhibitor is sufficient to abolish IL-1β-induced E-cadherin repression. This occurs concomitantly with decreased cell migration and invasion. Surprisingly, following prolonged IL-1β exposure (21 days), cells do not revert back to the epithelial state despite inhibition of these acute EMT mediators. We also found that following withdrawal of IL-1β after twenty one-day exposure, the treated cells are able to maintain their mesenchymal phenotype for more than 30 days before reverting back to an epithelial phenotype. We refer to this prolonged but reversible EMT program that persists in the absence of the original inflammatory stimulus as EMT "memory." Further studies showed that fra-1 is only required to establish but not to maintain EMT memory. Chemical inhibition of a variety of enzymes involved in histone modifications and DNA methylation indicates the repression of E-cadherin is mediated by different mechanisms depending on the duration of IL-1β exposure. H3K27Me3 and histone acetylation mediate E-cadherin repression during acute EMT but DNA methylation is responsible for the downregulation of E-cadherin in EMT memory. In fact, we have found increased CpG island methylation in the E-cadherin promoter region in EMT memory. *In vitro* functional studies further showed that EMT memory enables cancer cells to enhance their motility but gradually regain proliferative advantage. **Conclusion:** We conclude that lung cancer cells utilize distinct mechanisms for EMT in response to acute and chronic inflammation. We also demonstrate that dynamic alteration of histone modification and DNA methylation can lead to prolonged but reversible EMT, subsequently creating a time window for cancer cells to migrate to distant organs and eventually undergo mesenchymal-epithelial transition to form macro-metastases. **Keywords:** EMT memory, epigenetics, IL-1 beta, Acute and Chronic inflammation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-064 2'-Hydroxyflavanone Inhibits Lung Cancer Growth by Inhibiting Tumor Cell Proliferation and Angiogenesis David Berz[1], Sharad Singhal[2], Jotsana Singhal[3], Sushma Yadav[3], Sanjay Awasthi[1] [1]*Research/Oncology, City of Hope, Duarte/CA/United States of America,* [2]*Research, City of Hope, Duarte/AL/United States of America,* [3]*Research/Oncology, City of Hope, Duarte/United States of America*

Background: Epidemiologic studies suggest that citrus fruit consumption reduces cancer risk. We have previously shown that 2-hydroxyflavanone (2HF), a naturally occurring compound in citrus fruits, exerts antineoplastic effects in-vitro and in-vivo against renal cell carcinoma in a manner dependent on VHL function and expression of glutathione S-transferase p (GSTP). GSTP is a stress- and xenobiotic-defense protein that catalyzes the first step committed step of the mercapturic acid pathway (MPy). **Methods:** We performed mining of molecular databases, including the TCGA. Then, we conducted cytotoxicity assays, followed by signaling studies. Finally xenograft experiments, using nu/nu athymic nude mice were performed. **Results:** 2HF inhibited non-small and small cell lung cancer cell line growth *in-vitro*. Reduced CDK4 and cyclin B1 levels were correlated with G_2/M arrest. Apoptosis was accompanied by Bcl2 down-regulation and Bax upregulation. Inhibition of PI3K signaling was evident from reduction in AKT and p70S6K phosphorylation. Reduction of vimentin and fibronectin and increase in E-cadherin indicated inhibition of epithelial-mesenchymal transition. Remarkably, 2HF reduced the expression of RLIP76/RALBP1, a rate-limiting glutathione-conjugate/multidrug transporter of the MPy. 2HF also inhibited the transport activity of RLIP76. Dose-dependent 2HF cytotoxicity was enhanced by antibodies to RLIP76. Oral dosing of 2HF resulted in 3-5 mM serum concentrations and inhibited the growth of H1618 and H358 NSCLC cell line xenografts in nu/nu athymic nude mice. Residual tumors had reduced Ki67 and CD31 staining, indicating inhibited proliferation and angiogenesis. Higher MPy expression in lung cancer was evident from increased RLIP expression in human lung cancer tissues, and analyses of the TCGA database showed that RLIP76 expression was inversely correlated with survival in lung adenocarcinoma. **Conclusion:** Taken together, these studies demonstrate antineoplastic activity of 2HF against lung cancer cell lines in-vitro and in-vivo through a novel mechanism that simultaneously causes down-regulation of MaP, stress-signaling, EMT and angiogenesis. Excellent oral absorption of 2HF indicates its suitability for therapy and possibly prevention of lung cancer. **Keywords:** stress signaling, Rlip-76, lung cancer, 2-HF

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P1.04-065 Cyclin-Dependent kinase11 (CDK11) Is Crucial for Growth of Lung Cancer Cells Tomohiko Kakumu[1], Mitsuo Sato[1], Toshio Kato[1], Naoyuki Yogo[1], Tetsunari Hase[1], Masahiro Morise[1], Masashi Kondo[1], Yoshitaka Sekido[2], Yoshinori Hasegawa[1] [1]*Respiratory Medicine, Nagoya University Graduate School of Medicine, Nagoya/Japan,* [2]*Molecular Oncology, Aichi Cancer Center Research Institute, Nagoya/Japan*

Background: Cyclin dependent kinases (CDKs) are protein kinases that regulate cell growth and proliferation in cells. CDK11 belongs to transcriptional subfamilies of CDKs and has been reported to be crucial for survival of sarcoma and breast cancer cells. To examine its roles in lung cancer cells, we investigated the effect of *CDK11* knockdown on non-small cell lung cancer (NSCLC) cell lines. **Methods:** 17 NSCLC cell lines were used for expression analysis of *CDK11*. Among them, we used three lung cancer cell lines, H460, H1299 and H358 for functional analysis. Synthetic siRNAs were utilized to knockdown *CDK11*. mRNA and protein levels of CDK11 were evaluated by real-time PCR and western blotting, respectively. Changes in growth were examined by WST-1 proliferation assay and liquid and soft agar colony formation assays. Cell cycle and apoptosis were analyzed by FACS with propidium iodide staining. **Results:** Western blot analysis revealed that all of the 17 lung cancer cell lines expressed CDK11 mRNA and protein and that compared to a normal cell line, H460 expressed CDK11 at lower levels but H1299 and H358 expressed CDK11 at higher levels. *CDK11* knockdown suppressed proliferation and anchorage-dependent and independent clonal growth in H460 and H1299 cell lines but not in H358. Induction of apoptosis was seen in H460 but not in the others. **Conclusion:** *CDK11* knockdown suppressed proliferation and clonogenic growth in H460 and H1299 cells, and induced apoptosis in H460. These results suggest that inhibiting *CDK11* may be an attractive target for the treatment of NSCLC. **Keywords:** CDK11

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P1.04-066 Site-Selected Chromatin-Immunoprecipitation (ChIP) Analysis by Laser Captured Microdissection Shingo Sakashita[1], Masafumi Muratani[2], Masato Sugano[3], Tomoki Nakagawa[1], Yoshihiko Murata[1], Yoko Yano[4], Noriyuki Nakano[4], Ryota Matsuoka[4], Taiki Sato[4], Akiko Sakata[4], Yuko Minami[3], Yukio Sato[5], Masayuki Noguchi[3] [1]*Department of Pathology, Universyity of Tsukuba Hospital, Tsukuba/Japan,* [2]*Faculty of Medicine, Department of Genome Biology, Universyity of Tsukuba, Tsukuba/Japan,* [3]*Faculty of Medicine, Department of Pathology, Universyity of Tsukuba, Tsukuba/Japan,* [4]*Graduate School of Comprehensive Human Science, Department of Pathology, University of Tsukuba, Tsukuba/Japan,* [5]*Faculty of Medicine, Department of Thracic Surgery, Universyity of Tsukuba, Tsukuba/Japan*

Background: High throughput sequencing methods such as exome sequencing, RNA sequencing, Chromatin–immunoprecipitation (ChIP) sequencing are essential tools for cancer research. However, these fine and delicate analyses contain several methodological problems. For example, although tumor mass may be suitable for mutation analysis, histological heterogeneity of the tumor tissue causes insufficient results especially for epigenetic or RNA analyses. Besides, the cancer-associated stromal cells and immune cells in the tumor will also affect the results. In this study, we tried ChIP for tiny but pure tumor samples which were selected by laser captured microdissection and verified its availability for ChIP sequence analysis. **Methods:** We used a lung adenocarcinoma frozen tissue harboring EGFR L858R mutation. After formalin fixation (1%, 10min), tumor cells, stroma cells and immune cells were microdissected separately by LMD4000 (Leica) and ChIP was performed to using H3K4me3 anti-body. Then, the quality was confirmed by real-time PCR for CCR7 which is one of the tumor specific markers and CD3 which is representative T lymphocyte marker. Sanger sequence for EGFR L858R mutation was also analyzed for confirmation that each sample was dissected and extracted correctly. **Results:** Only from the sample of tumor cells, we detected EGFR L858R mutation by Sanger sequence but from stromal cells and immune cells, we did not detect EGFR mutation. The result showed that we extracted samples correctly. And H3K4me3 mark at CCR7 gene was detected only from tumor cells and was not detected from the other samples. Moreover, H3K4me3 mark at CD3 gene was detected from stroma cells and immune cells but not tumor cells. These results indicated that microdissection method is useful and necessary method for ChIP analysis. **Conclusion:** Microdissection can be applied for epigenetic analysis like ChIP method. Our results indicated that microdissection method is useful for tumor-cell-specific epigenome profiling by ChIP sequencing. **Keywords:** Chromatin–immunoprecipitation, laser micro dissection, Epigenetic

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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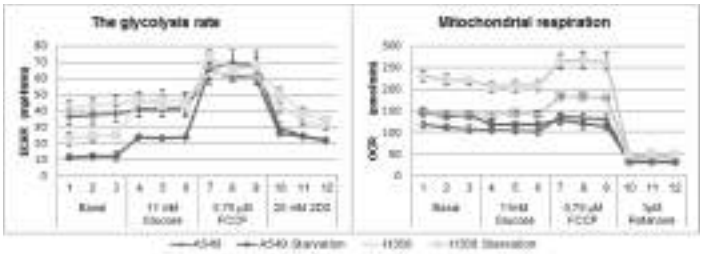
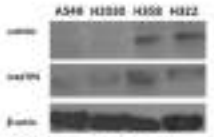
P1.04-067 Mitochondrial Respiration Capacity and Sensitivity to Glycolysis Blockade in Lung Cancer Tali Feinberg[1], Guy Lass[2], Fernanada Cerqueira[2], Dovi Shlomo[2], Maya Ilouze[3], Ronen Shavit[4], Nir Peled[5] [1]*Physiology and Pharmacology, Tel Aviv University, Tel-Aviv/Israel,* [2]*Clinical Biochemistry, Ben Gurion University, Beer Sheva/ Israel,* [3]*Thoracic Cancer Service, Davidoff Cancer Center, Rabin Medical Center, Petach Tiqwa/Israel,* [4]*Thoracic Cancer Reasearch and Detection Center, Sheba Medical Center Tel Hashomer, Ramat Gan/Israel,* [5]*Rabin Medical Center, Tel Aviv/Israel*

Background: One of the metabolic perturbations in cancer cells is the Warburg effect; glycolysis is preferred over oxidative phosphorylation (OXPHOS), even in the presence of oxygen. The precise mitochondrial alterations that underlie the increased dependence of cancer cells on aerobic glycolysis for energy generation may serve as an escape mechanism from apoptosis. Here, we aimed to profile the mitochondrial activity in different lung cancer cell lines in reference to their glycolytic activity and to their sensitivity to metabolic modifications. **Methods:** The metabolic profile of A549 and H358 cell lines were tested before and after glycolysis blockade (glucose starvation, 2DG) and mitochondrial induction (FCCP). Glycolysis inhibition and mitochondrial activity were assessed by western-blot quantification of key enzymes involved in the glycolysis pathway (e.g. Hexokinase I/II, glyceraldehyde-3-phosphate dehydrogenase, pyruvate kinase 2) and of mitochondrial coded proteins (e.g. ND1, ATP6 synthase). The oxygen consumption rates (OCR) and extra cellular acidification rate (ECAR) were measured by XFe24 extracellular flux analyzer. Further, mitochondrial index was compared to the cells' sensitivity to glycolysis inhibition. **Results:** A549 cells were highly affected by glucose inhibition/starvation accompanied by ineffective mitochondrial compensation. On the other hand, H358 cells recovered completely from glucose starvation through mitochondrial hyper-activation (Fig 1); At the basal level (when no material was applied), A549 cells that were starved had a decrease of 68% in the ECAR, as compared to non-treated cells. Their recovery was limited after glucose injection (23 vs.41 mpH/ min). In comparison, H358 cells had a 43% decrease in their glycolysis rate with a full recovery after glucose injection (44-46 mpH/min; pre & post respectively). Mitochondrial respiration was very low for A549 cells under starvation, while significantly increased in H358 cells (223 vs.143 pmol/min, *Pv<0.0001). Respectively, the expression level of mitochondrial coded proteins was higher in the cells that demonstrated higher mitochondrial capacity (Fig 2).





Conclusion: Cells with high mitochondrial capacity may tolerate glucose starvation/ blockade, while a limited mitochondrial reserve exposes the cells to higher sensitivity to glycolysis stress. This might suggest a potential therapeutic avenue with a companion predictive test. **Keywords:** mitochondria, lung cancer, glycolysis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-068 Protein Tyrosine Kinase 7 Plays a Tumor Suppressor Role by Inhibiting ERK and Akt Phosphorylation in Lung Cancer Haewon Lee[1], Junhye Kwon[2], Moonchul Kang[1], Hyungjun Yoo[3], Jae Soo Koh[4] [1]*Thoracic Surgery, Korea Cancer Center Hospital, Seoul/Korea,* [2]*Translational Research, Korea Cancer Center Hospital, Seoul/ Korea,* [3]*Radio-Oncology, Korea Cancer Center Hospital, Seoul/Korea,* [4]*Pathology, Korea Cancer Center Hospital, Seoul/Korea*

Background: Protein tyrosine kinase 7 (PTK7) is a catalytically inactive receptor tyrosine kinase that is also known as colon carcinoma kinase-4 (CCK-4). Recent reports have shown that PTK7 plays an important role in carcinogenesis, and it is known to be up-regulated in gastric cancer, colon cancer, esophageal cancer, and liposarcoma. However, we found that PTK7 expression was down-regulated at the mRNA as well as protein levels in human lung squamous cell carcinoma (SCC), unlike in other tumors. In this study, we attempted to explore the role of PTK7 in lung cancer **Methods:** We analyzed expression of PTK7 by RT-PCR and western blot analysis using tumor and normal lung tissue from 10 SCC patients. To explore the functional role of PTK7, the expression of PTK7 in SCC cells was examined using empty vector and PTK7 gene inserted vector. **Results:** We found that PTK7 expression was down-regulated at the mRNA as well as protein levels in human lung squamous cell carcinoma (SCC). Upon investigating the functional role of PTK7 in SCC, we found that overexpression of PTK7 in SCC cells resulted in inhibition of cell proliferation, invasion, and migration. Further, we confirmed that these phenotypic changes are associated with the activation of Akt and ERK. **Conclusion:** These observations may indicate a role for PTK7 in cell proliferation, wound healing and invasion via regulating Akt and Erk activation. Our findings suggest that PTK7 has different oncogenic roles in organs and target tumors. **Keywords:** biomarker, PTK7, lung cancer, Squamous cell carcinoma

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P1.04-069 LKB1 Inactivation Elicits a Redox Imbalance to Modulate Non-Small Cell Lung Cancer Plasticity and Therapeutic Response Fuming Li[1], Xiangkun Han[1], Fei Li[1], Rui Wang[2], Yuan Li[2], Kowk-Kin Wong[3], Haiquan Chen[2], Hongbin Ji[1] [1]*Shanghai Institutes for Biological Sciences, Shanghai/China,* [2]*Department of Thoracic Surgery, Fudan University Shanghai Cancer Center, Shanghai/China,* [3]*Department of Medicine, Harvard Medical School, Boston, Boston/AL/United States of America*

Background: LKB1 regulates both cell growth and energy metabolism. It remains unclear how LKB1 inactivation coordinates tumor progression with metabolic adaptation in non-small cell lung cancer (NSCLC). **Methods:** Mouse Colony, Mouse Treatment and Tumor Analyses Statistical Analysis Hematoxylin and Eosin (HE) Staining and Immunohistochemistry (IHC) Bioinformatics Analysis Cell Lines and In vitro Assays ShRNA, Plasmids, Lentivirus Production and Infection Analysis of Human Lung ADC and Ad-SCC Specimens Western Blotting Enzymatic Activity Assays and Liquid Chromatography-tandem Mass Spectrometry (LC-MS) Analysis Oil red O Staining Reverse Transcription and Quantitative PCR Analysis **Results:**Here in KRAS/LKB1 (KL) mouse model, we reveal differential reactive oxygen species (ROS) levels in lung adenocarcinoma (ADC) and squamous cell carcinoma (SCC). ROS can modulate ADC-to-SCC transdifferentiation (AST). Further, pentose phosphate pathway deregulation and impaired fatty acid oxidation collectively contribute to the redox imbalance and functionally affect AST. Similar tumor and redox heterogeneity also exist in human NSCLC with LKB1 inactivation.

In preclinical trials towards metabolic stress, certain KL ADC can develop drug resistance through squamous transdifferentiation. **Conclusion:** This study uncovers critical redox control of tumor plasticity that may affect therapeutic response in NSCLC. **Keywords:** Therapeutic response, LKB1, Plasticity, Metabolism

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-070 Silencing of Rac3 Inhibits Proliferation and Induces Apoptosis of Human Lung Cancer Cells Hongxu Liu, Tieqin Liu, Gebang Wang *Department of Thoracic Surgery, First Affiliated Hospital, China Medical University, Shenyang/China*

Background: Rac3 is a member of the Rac family of small guanosine triphosphatases (GTPases), regulates a variety of cell functions, including the organization of the cytoskeleton, cell migration, and invasion. The overexpression of Rac3 has been reported in several human cancers. However, the role of Rac3 in Lung cancer (LC) has not been determined yet. The purpose of this study is to investigate the effect of silence on Rac3 expression in human LC cells and the consequence of cell survival. **Methods:** Lentivirus small hairpin RNA (shRNA) interference techniques were utilized to knock down Rac3 gene. Gene and protein expression was quantified by quantitative Real-time polymerase chain reaction (qRT-PCR) and Western Blot. LC cell apoptosis was examined by Annexin V-APC /propidium iodide staining. **Results:** Efficient silence of of Rac3 strongly inhibited A549 cells proliferation and colony formation ability, and significantly decreased tumor growth. Moreover, flow cytometry analysis showed that knockdown of Rac3 led to G2/M phase cell cycle arrest as well as an excess accumulation of cells in the G1and S phase. **Conclusion:** Thus, functional analysis using shRNAs reveals a critical role for Rac3 in the tumor growth of LC cells. shRNAs silencing of Rac3 could provide an effective strategy to treat LC. **Keywords:** lung cancer, Rac3, proliferation, shRNAs

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-071 Inhibition of EGFR Lysosomal Degradation in Lung Adenocarcinoma by Ubiquitin-Specific Protease 8 and Stratifin Yun-Jung Kim, Aya Shiba, Masayuki Noguchi *Pathology, Tsukuba University, Tsukuba/Japan*

Background: The epidermal growth factor receptor (EGFR) is one of the best-known targets of therapy for non-small cell lung cancer (NSCLC). Our purpose was to investigate whether ubiquitin-specific protease 8 (USP8) and stratifin (14-3-3σ or SFN) inhibit or stimulate lysosomal degradation of EGFR in lung adenocarcinoma. **Methods:** Using Western blotting and immunofluorescence analysis, we examined the effect of USP8 or SFN knockdown by siRNA and overexpression of USP8. Expressions of USP8 and SFN in normal and tumorous lung tissue were examined by Western blotting and immunohistochemistry. **Results:** USP8 or SFN knockdown led to downregulation of cellular proliferation, receptor tyrosine kinases such as EGFR and proto-oncogenes (c-Met), and downstream signaling pathways such as the AKT, ERK, and STAT3 pathways, whereas it upregulated the accumulation of EGFR at lysosomes for degradation. However, overexpression of USP8 led to an increase of EGFR and downstream signaling after EGF stimulation. Moreover, USP8 and SFN expressions were increased in the tumorous lung tissue in comparison with normal lung tissue from the same patient. **Conclusion:** USP8 and SFN inhibit ubiquitination of EGFR for lysosomal degradation in lung adenocarcinoma cells, suggesting that USP8 and SFN could be potential therapeutic targets for NSCLC. **Keywords:** Epidermal growth factor receptor, ubiquitin-specific protease, stratifin, lung adenocarcinoma

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-072 Gene-Smoking Interactions in Lung Cancer Etiology Christopher I. Amos[1], Summer Han[2], Younghun Han[1], Iona Cheng[3] [1]*Biomedical Data Science, Dartmouth, Hanover/NH/United States of America,* [2]*Radiology, Stanford, Stanford/CA/United States of America,* [3]*Public Health, Cancer Prevention Institute of California, Oakland/CA/United States of America*

Background: Even among heavy smokers, the lifetime risk for developing lung cancer is between 15 and 20% which raises a question about whether there are protective factors that mitigate risk from toxic exposures in tobacco smoke. Previously we have shown significant gene-environment interaction effects between smoking and genetic loci on chromosome 15q25.1 near the nicotinic acetylcholine receptor locus contrasting minimal increases in risk for never smokers from SNPs in this region versus substantial impact on risk for smokers. Studies contrasting risk in heavy versus light smokers have not been conducted and little is known about protective factors that may reduce risk for some smokers. **Methods:** In order to identify genetic factors that might reduce lung cancer risk, we performed a genome-wide case only analysis of lung cancer risk, comparing heavy to light smokers. This approach to analysis is powerful for identifying gene-environment interactions provided there is no correlation between the genetic factor and the environment exposure. We performed a genome-wide association of heavy smokers who had a 30 packyear or more background of smoking versus 1824 lung cancer cases with less than 30 packyears of smoking exposure using data derived from studies conducted by 7 sites within the Transdisciplinary Research in Cancer of the Lung (TRICL) consortium. To improve our ability to identify genetic variants, we used imputation based on the March 2012 release of the 1000 Genomes to impute and analyze data from more than 9 million genetic variants. **Results:** This analysis identified one region showing many highly significant associations with the most significant being rs62180069 (p=5x10-8, OR = 0.76). This SNP lies between the SCHLAP1 gene encoding the SWI/SNF complex antagonist with prostate cancer 1, non protein coding, gene and the gene UBE2E3 on chromosome 2. At this locus there was no gene-smoking correlation in the controls and no evidence for heterogeneity in strength of association among the 7 contributing studies. **Conclusion:** UBE2E3 is the ubiquitin conjugating enzyme E3. This gene is overexpressed in a substantial number of lung cancers. Further studies to characterize the impact of this variant on lung cancer risk according to further variation in smoking behavior and also impacts on function are warranted. **Keywords:** genetic epidemiology, gene environment interaction, smoking behavior, population genetics

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-073 The Role of the Stress-Response to a Lung Cancer Diagnosis in Disease Progression Hronn Hardardottir[1], Steinn Jonsson[2], Tomas Gudbjartsson[3], Arna Hauksdottir[4], Kristbjorn Reynisson[5], Heiddis Valdimarsdottir[6], Magnus K. Magnusson[7], Unnur Valdimarsdottir[8] [1]*Center of Public Health Sciences, Faculty of Medicine, Reykjavik/Iceland,* [2]*Department of Internal Medicine, Landspitali University Hospital, Reykjavik/Iceland,* [3]*Department of Cardiothoracic Surgery, Landspitali University Hospital, Reykjavik/Iceland,* [4]*Center of Public Health Sciences, Faculty of Medicine, University of Iceland, Reykjavik/Iceland,* [5]*Department of Radiology, Landspitali University Hospital, Reykjavik/Iceland,* [6]*Department of Psychology, Reykjavik University, Reykjavik/Iceland,* [7]*Faculty of Medicine, University of Iceland, Reykjavik/Iceland,* [8]*Center of Public Health, Faculty of Medicine, University of Iceland, Reykjavik/Iceland*

Background: Receiving a cancer diagnosis, particularly of lung cancer, has been shown to increase psychological and biological stress responses and the immediate risks of extreme adverse health outcomes, such as suicide and cardiovascular deaths. Data are scarce on the potential influence of this diagnosis on tumor progression. Prior studies lend suggestive evidence for an association of psychobiological stress-responses on lung cancer progression. The aim of this study is to improve understanding of determinants of the stress-response to a lung cancer diagnosis and explore potential role of this response in disease progression and survival. **Methods:** We have initiated a nationwide prospective cohort study of Icelandic lung cancer patients with a comprehensive questionnaire and biomarker measures of stress, as well as detailed documentation of clinical parameters and disease course. Eligible are all individuals diagnosed with lung cancer at Landspitali University Hospital in Iceland. The aim is to recruit 300 patients over a three year period between 2015 and 2017. Patients with clinical or radigraphic changes suggestive of lung cancer are referred to our hospital. They go through a diagnostic work-up, leading to a definite lung cancer diagnosis and staging during a 24 hour diagnostic course or within few days thereafter. Assessment of psychological stress and relevant biomarkers are integrated with clinical assessments at two time points, i.e. during the diagnostic work-up and at follow-up visit 1-3 weeks later (before treatment). The study participation involves questionnaire assessment of symptoms of anxiety, depression, posttraumatic stress, sleep disturbances and quality of life. Biomarker repositories include overnight urine collection, diurnal saliva and hair sampling for analysis of cortisol and catecholamines along with ECG to determine heart rate variability. Bronchoscopic and core needle biopsies as well as surgical tumor samples will be used for assessment of apoptosis, proliferation, microvascular density and adrenoreceptors expression. Radiographic progression will be assessed at baseline and every 6 months from diagnosis along with complete documentation of clinical parameters, disease course and survival. **Results:** In 4 weeks we have recruited 8 patients (80% acceptance rate). We will characterize determinants of a severe psychological-, neuro-endocrine- and cardiovascular stress-response to a cancer diagnosis, as well as the potential relevance of these responses on tumor characteristics, radiographic progression and disease-specific survival. We expect to present preliminary results from approximately 30 patients at the conference. **Conclusion:** Significance: This research program is the first comprehensive attempt to evaluate determinants of psychobiological-induced responses to a lung cancer diagnosis and their potential impact on cancer progression. The findings might guide intervention strategies to improve quality of life, reduce morbidity and prolong survival in lung cancer patients. **Keywords:** lung cancer, Stress-response, psychobiological

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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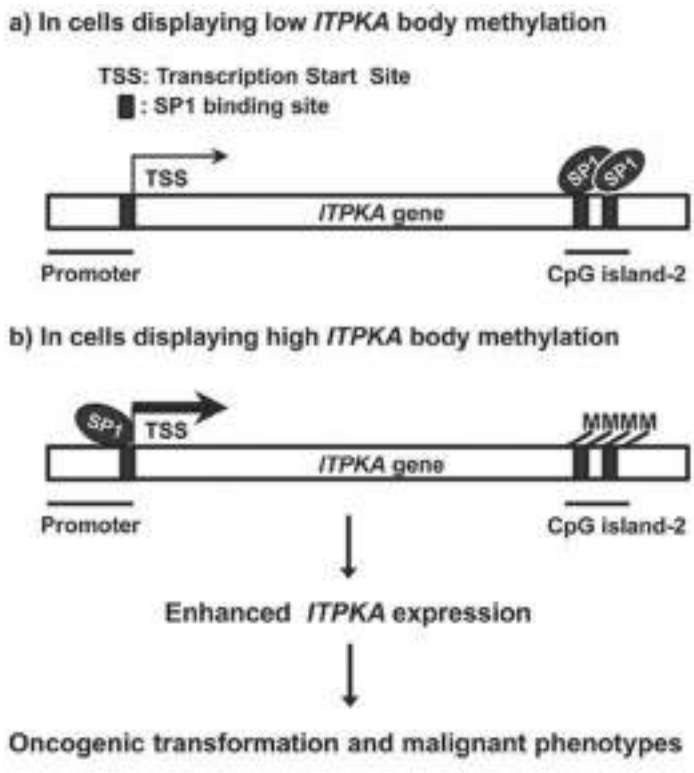
P1.04-074 ITPKA Expression in Lung and Other Cancers, Regulated via Gene Body Methylation, Functions as an Oncogene Yi-Wei Wang[1], Xiaotu Ma[2], Yu-An Zhang[3], Mei-Jung Wang[1], Yasushi Yatabe[4], Stephen Lam[5], Luc Girard[6], Jeou-Yuan Chen[1], Adi F. Gazdar[3] [1]*Institute of Biomedical Sciences, Academia Sinica, Taipei/Taiwan,* [2]*Department of Molecular and Cell Biology, University of Texas at Dallas, Richardson/TX/United States of America,* [3]*Hamon Center for Therapeutic Oncology Research, University of Texas Southwestern Medical Center, Dallas/TX/United States of America,* [4]*Department of Pathology and Molecular Diagnostics, Aichi Cancer Center, Nagoya/Japan,* [5]*British Columbia Cancer Agency, Vancouver/Canada,* [6]*Hamon Center for Therapeutic Oncology Research, University of Texas Southwestern Medical Center, Dallas/United States of America*

Background: Lung cancer is the leading cause of cancer mortality and accounts for 1.6 million deaths annually in the world. Lung cancers may be classified into non-small cell (NSCLC) and small cell (SCLC) lung cancers, which individually account for approximately 85% and 15%, respectively, of lung cancer cases. Despite recent advances in cancer therapy, the overall 5-year survival rate of lung cancer remains low. There remains an urgent need for discovery of novel approaches for early diagnosis and therapy. Inositol-trisphosphate 3-kinase A (ITPKA) regulates inositol phosphate metabolism and calcium signaling by phosphorylation of the second messenger inositol 1,4,5-trisphosphate (Ins-1,4,5-P3)

to inositol-1,3,4,5-tetrakisphosphate (Ins-1,3,4,5-P4) (1). *ITPKA* has a very limited tissue expression, mainly in brain and testis. ITPKA, previously known as a neuron-specific F-actin bundling protein, has recently been shown to be overexpressed in lung adenocarcinoma and associated with increased metastatic potential (2). However, our understanding of the role and regulation of *ITPKA* in cancers is limited. Reference: 1. Shears SB. How versatile are inositol phosphate kinases? The Biochemical journal. 2004; 377:265-80. 2. Windhorst S, Kalinina T, Schmid K, Blechner C, Kriebitzsch N, Hinsch R, et al. Functional role of inositol-1,4,5-trisphosphate-3-kinase-A for motility of malignant transformed cells. International journal of cancer Journal international du cancer. 2011;129:1300-9. **Methods:** To identify potential oncogenes that are involved in the pathogenesis of lung cancer, cDNA microarray analysis was performed to search for up-regulated genes in primary lung adenocarcinomas. Inositol-trisphosphate 3-kinase A (ITPKA) was found to be overexpressed in lung ADC. **Results:** Using gain-of-function and loss-of-function approaches, we demonstrated that ITPKA contributes to cancer development. We also showed that methylation level in the ITPKA gene body is highly tumor-specific, and is positively correlated with its expression. Furthermore, DNMT3B-mediated methylation of the CpG island in ITPKA gene body regulates its expression via modulation of the binding of transcription activator SP1 to the ITPKA promoter. ITPKA gene body methylation first appeared at the in situ carcinoma stage and progressively increased during the multistage pathogenesis of lung carcinoma.



Conclusion: Altogether, deregulation of ITPKA may promote oncogenic transformation and function as a universal or near universal hallmark of malignancy. A novel regulatory mechanism of oncogene expression was demonstrated via gene body methylation which manipulates the binding of transcriptional factor(s) to its promoter and controls gene expression. **Keywords:** SP1, biomarker, ITPKA, DNA methylation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-075 Kynurenine Pathway Activity in Peripheral Blood Mononuclear Cells and Cognitive Functions in Lung Cancer Patients Rodryg Ramlau[1], Slawomir Michalak[2], Joanna Rybacka-Mossakowska[2], Iwona Golda-Gocka[3], Joanna Gazdulska[4] [1]*Department of Oncology, Poznan University of Medical Sciences, Poznan/Poland,* [2]*Department of Neurochemistry and Neuropathology, Poznan University of Medical Sciences, Poznan/Poland,* [3]*Lung Diseases Center, Poznan University of Medical Sciences, Poznan/Poland,* [4]*Oncology Center, Poznan University of Medical Sciences, Poznan/Poland*

Background: The kynurenine pathway is crucial for tryptophan metabolism, which has been shown to be active both in macrophages and microglial cells. L-Kynurenine (L-KYN) is transported across the blood-brain barrier and serves as a source for the synthesis of all the other metabolites of the kynurenine pathway. Glial cells have the enzymatic capability for the biosynthesis of brain kynurenines as kynurenine aminotransferase (KAT). KAT converts L-KYN to kynurenic acid, which is an inhibitor of glutamate neurotransmission. The lowered KAT activity was observed in the plasma and brains of patients with neurodegenerative disorders followed by a tendency to a decrease KYNA in plasma and brains. Peripheral blood mononuclear cells (PBMC) can be considered as representative for metabolic changes in peripheral tisues during the course of lung cancer. With this background in mind we have undertaken the evaluation of translocator protein 18 kDa (TSPO), which reflects microglia activation, G Protein-coupled Receptor (GPR35), a KYNA receptor and kynurenine aminotransferase II (KAT) in PBMC and serum L-KYN concentration in relations to cognitive functions in lung cancer patients. **Methods:** We included in the study 80 consecutive lung cancer patients (5 small-cell lung cancer, 75 non-small cel lung cancer, 24 females and 56 males, aged 61.5±6.7 years) hospitalized in Clinical Oncology with The Sub-department of Diurnal Chemotherapy Wielkopolska Center of Pulmonology and Thoracosurgery of Eugenia and Janusz Zeyland and Chair and Clinic of Oncology. PBMC were isolated by density gradient centrifugation. The expression of TSPO, GPR35 KAT in PBMC was evaluated with ELISA. Serum L-KYN concentration was measured by means of spectrofotometric method. Neurological examination, MiniMental State Examination (MMSE), Trail Making Test (TMT) A and B, and Hamilton scale were performed at baseline (time of lung cancer diagnosis) and after 6 months. **Results:** Decreased TSPO expression in PBMC was associated with better results of MMSE evaluation (29.00; 28.0–29.0; median, interquartile range) than in lung cancer patients with up-regulated TPSO (28.0; 26.0–28.7; P=0.016). Also, TMT-A results were better in lung cancer patients with down-regulated TPSO (8.41±3.68s) compared to the subject with stimulated TPSO (12.92±7.30s; P=0.002). TSPO expression in PBMC negatively correlated with MMSE score (Kendall's tau = -0.182; P=0.0178) and positively with TMT-A (Kendall's tau = 0.168; P=0.0309) evaluated at baseline. The up-regulation of KAT expression in PBMC was associated with better cognitive functions measured with MMSE 6 months after baseline (28.4±0.7) comparing to lung cancer patients with inhibited KAT (27.1±1.8). KAT correlated positively with MMSE scoring 6 months after baseline (Kendall's tau= 0.308; P=0.0234).The expression of GPR35 in PBMC did not correlated with cognitive measures. Serum L-KYN concentration correlated negatively with TMT-A evaluated 6 months after baseline (Kendall's tau= -0.586; P=0.0141). Moreover, TPSO expression correlated positively with KAT (Kendall's tau= 0.253, P=0.0009) and negatively with GPR35 (Kendall's tau= -0.173, P=0.0491), but no correlation with L-KYN was found. **Conclusion:** Stimulation of kynurenine pathway in PBMC seems to be protective against cognitive decline during the course of lung cancer. Microglial activation can be independent pathomechanism leading to cognitive impairement in lung cancer patients. **Keywords:** kynurenine pathway, cognition, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-076 CDCA3 Is a Novel Cell Cycle Regulator in Lung Cancer Mark N. Adams[1], Kenneth J. O'Byrne[2], Derek Richard[3] [1]*Translational Research Institute, Institute of Health and Biomedical Innovation, Woolloongabba/QLD/Australia,* [2]*Cancer and Ageing Research Program, Queensland University of Technology, Brisbane/Australia,* [3]*Cancer and Ageing Research Program, Queensland University of Technology, Brisbane/QLD/Australia*

Background: Progression through the mammalian cell cycle relies upon coordination of a complex network of proteins. Following genomic insult, checkpoints during each stage of the cell cycle are engaged to halt cell cycle progression to allow faithful DNA repair. Failure to arrest cell cycle may lead to genomic instability and cancer development. However, the molecular basis for the loss of genome integrity during cancer development remains to be determined. Cell division cycle associated 3 (CDCA3) is a key regulator of the normal cell cycle. CDCA3 modulates this process by enabling cell entry into mitosis through degradation of the mitosis-inhibitory factor WEE1. CDCA3 itself is also degraded in G1 yet re-expressed in G2/M phase, to allow successful progression through the cell cycle. Here we describe for the first time a novel function for CDCA3 in maintaining effective cell cycle progression in lung cancer. **Methods:** To examine the role of CDCA3 in modulating the cell cycle of lung cancer cells, CDCA3 was depleted using an siRNA approach in A549, SKMES and H460 cell lines. CDCA3 depletion was assessed using Western blot analysis. Cell proliferation assays were performed on control and CDCA3 knockdown cells over a period of 96 h using the Promega CellTitre-Glo cell viability assay. Cell cycle progression was assessed on propidium iodide stained cells using a Beckman Coulter Gallios flow cytometer. To determine if CDCA3 expression is associated with lung cancer progression, a tissue microarray (TMA) with cores from 600 patients was stained with an anti-CDCA3 antibody. Correlation of CDCA3 staining with clinical data and patient prognosis is ongoing. **Results:** As a cell cycle related protein, we tested if CDCA3 is required for effective proliferation of a range of lung cancer cell lines. CDCA3 depletion reduced the proliferation of U2OS (osteosarcoma), A549, MOR (lung adenomcarcenoma) and SKMES cancer cells (squamous lung cancer). Interestingly, depletion of CDCA3 did not affect proliferation of H460 cells (large neuroendocrine lung cancer). We next tested the cell cycle progression and noted that knockdown of CDCA3 induced an increase of all cell lines in G1 arrest with the exception of H460 cells. To observe if CDCA3 expression is linked with disease progression, TMA staining of lung cancer biopsies was performed. Accordingly, elevated expression of CDCA3 was identified specifically in tumour cells. These data highlight the potential prognostic value of CDCA3 expression. **Conclusion:** Our data point to a potential role for CDCA3 in the progression of lung cancer. While the precise mechanism for CDCA3-dependent cell cycle regulation remains unknown, it is possible that elevated CDCA3 levels modulate tumour cell proliferation. Identifying the molecular basis may yield novel therapeutic avenues worth targeting during aberrant cell cycle in cancer. **Keywords:** Genome instability, proliferation, Cell cycle

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P1.04-077 KIF5B-RET Fusion Kinase Promotes Cell Invasion and Migration Which Can Be Suppressed by RET Inhibitors Jianhua Chang, Shanshan Wang, Weiwei Xie *Department of Medical Oncology, Fudan University Shanghai Cancer Center, Shanghai/China*

Background: Non-small cell lung cancer has become the leading cause of cancer-

related deaths worldwide. The subset of NSCLC can be further defined at molecular level by driver mutations that occur in multiple oncogenes, such as EGFR, KRAS and EML4/ALK alterations. The KIF5B-RET fusion gene has been established as a new oncogenic driver in NSCLC. Several studies have demonstrated that KIF5B-RET promote cell growth and tumorigenicity, however, few progress has been made further. Our study aims to investigate other characters of KIF5B-RET fusion gene and tries to explore the potential signaling pathways involved in the gene functions. **Methods:** Lentivirus (encoding KIF5B-RET) was used to transfect the lung epithelial cell line BEAS-2B and lung cancer cell line A549 to generate stable transfectant and the protein expression was analysed using western blot . To verify the oncogenic features of KIF5B-RET in vitro, we detected its expression genetically followed by CCK8 assay, colony formation assay, transwell and Annexin V-FITC/PI double staining to explore proliferation, invasion, migration and apoptosis. The mechanism by which KIF5B-RET kinase induced invasion and migration was investigated by western blot, and administration of RET and SRC inhibitions. **Results:** The stable transfected cell line expressed phosphorylation RET, examined by western blot, suggesting that KIF5B-RET could automatically activate RET protein in the absence of ligand. Firstly we detected the basic characters of KIF5B-RET, but found no significant difference in proliferation as it's reported in previous studies. To further detect the function of KIF5B-RET fusion gene, we focused on characters of invasion, migration, and apoptosis. We demonstrated that KIF5B-RET showed a significantly increased ability of invasion and migration compared with control group, suggesting that KIF5B-RET fusion gene could promote cell invasion and migration. However, no change was observed after treating the transfected cells with Cisplatin, indicating the gene may have no influence on apoptosis. As we all know, RET tyrosine kinase can activate ERK which belongs to the downstream signaling system. Our restult showed that KIF5B-RET fusion kinase can also induced activation of ERK and even SRC kinase. Finally, we found that stable cells became sensitive to the RET tyrosine kinase inhibitors Sunitinib and Apatinib. The invasion and migration could be suppressed by RET or SRC inhibitors significantly. **Conclusion:** Out data showed that KIF5B-RET fusion gene can activate ERK and SRC kinase through activating RET tyrosine kinase, and promote migration and invasion in vitro , but did not have an effort on proliferation and apoptosis. RET inhibitor Apatinib and Sunitinib and SRC inhibitor could suppress the phenomenon of invasion and migration, suggesting that KIF5B-RET promotes invasion and migration through activation of SRC kinase. Our preclinical data demonstrated the antitumor activities of Apatinib and Sunitinib against KIF5B-RET gene fusion-driven cells and indicated the therapeutic potential of tyrosine kinase inhibitors targeting RET, which may benefit this certain subpopulation of NSCLC patients.
Keywords: KIF5B-RET fusion gene, invasion, RET inhibitor, Migration

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-078 Induction of Achaete-Scute Homologue 1 (ASCL1) by Cigarette Smoke Condensate in A549 Cells Michael H. Lee, Ting-An Yie, John S. Munger, Jun-Chieh J. Tsay, William N. Rom *New York University School of Medicine, New York/NY/United States of America*

Background: About 10% of lung adenocarcinomas express neuroendocrine features, which are thought to denote a subset of adenocarcinomas with poor prognosis. Achaete-scute homologue 1 (ASCL1) is a transcription factor implicated in the neuroendocrine differentiation of lung tissue. Recently, ASCL1 was identified as a neuroendocrine marker in lung adenocarcinomas, and its expression was upregulated in lung adenocarcinomas of smokers when compared to adenocarcinomas of non-smokers and other types of lung cancers. ASCL1 expression in the peripheral airways of cancer-free smokers has not been studied. Moreover, the effect of cigarette smoke exposure on the neuroendocrine differentiation of lung cancer cells has not been examined *in vitro*. **Methods:** Distal airway brushings for epithelial cells were obtained in 8 subjects who participated in CT scan lung cancer screening at the NYU Lung Cancer Biomarker Center (part of the NCI Early Detection Research Network); never (n=1), former (n=4) and current (n=3) smokers. ASCL1 mRNA expression was measured using real time reverse transcription polymerase chain reaction (RT-PCR). A549 cell line was incubated with cigarette smoke condensate (CSC; extracted to DMSO) at 10 or 40 mcg/mL for 4, 24 or 48 hours. Following the incubation periods, ASCL1 expression levels were measured via western blot with lamin B1 as the nuclear protein loading control. Three individual experiments were performed. Statistical analyses were performed with Kruskal-Wallis test (RT-PCR) and Student's *t*-test (western blot).

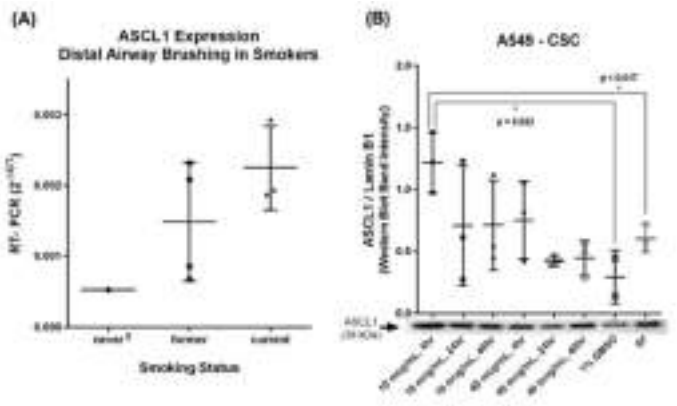

Figure 1. (A) RT-PCR of ASCL1 mRNA in the distal airways of 8 cancer-free subjects grouped according to smoking status. Difference in ASCL1 mRNA titers among the three groups did not reach statistical significance (p = 0.26). *Data available for only one never smoker (n=1). (B) Western blot band intensity (ASCL1/lamin B1) of A549 cells treated with cigarette smoke condensate (CSC), 1% DMSO or serum-free media (SF). A 4-hour exposure to 10 mcg/mL CSC led to a 4.1 fold increase in ASCL1 expression compared to 1% DMSO (p = 0.023) and a 2.0-fold increase compared to SF (p = 0.017).

Results: Real time RT-PCR data for ASCL1 in the distal airway brushing samples of the 8 subjects suggested a trend toward higher ASCL1 mRNA titers (p = 0.26) in current smokers (mean = 33 pack-years) compared to former smokers (mean = 51 pack-years), whose ASCL1 mRNA expression levels were higher than that of a never-smoker [Figure 1A]. A549 cells exposed to 10 mcg/mL of CSC for 4 hours had 4.1 fold (p = 0.023) and 2.0 fold (p = 0.017) increases in ASCL1 expression compared to those exposed to 1% DMSO and serum-free media (SF) only, respectively [Figure 1B]. No statistically significant change in ASCL1 expression was noted in the other CSC exposure groups. **Conclusion:** CSC induced ASCL1 expression in A549 cells, and the stimulatory effect of CSC was no longer observed at the higher concentration and the longer exposure times. This *in vitro* finding is in agreement with the RT-PCR data, which also suggest a trend toward increased ASCL1 expression with more recent smoking history in the distal airways of cancer-free human subjects.

Keywords: Achaete-Scute Homologue 1 (ASCL1), Cigarette Smoke Condensate, A549

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P1.04-079 RBM5-Wnt/β-Catenin Signaling in Cigarette Smoke PM 2.5 Induced Alveolar Epithelial Injury and Its Molecular Mechanism Zhang Jie, Hao Y. Qiu, Lv X. Jiao, Li J. Yao, Su Z. Zhong, Wang Chen, Bai Yue *Department of Respiratory Medicine, The Second Clinical Medical College of Jilin University, Chang Chun/China*

Background: Tobacco related death has become the first cause of death worldwide and it is estimated that approximately 1 millions patients each year died from tobacco related diseases in China ,the most common diseases from which are COPD and lung cancer. Recently,the effects of long-term exposure to PM2.5(particulate matter) on human health have drawn much attention from clinicians and researches.Cigarette smoke is one of the main sources of indoor PM2.5. At the same time, cigarette smoke also includes nearly six thousand kinds of chemical substances, most of which are harmful to the body, especially benzopyrene.It is proved that benzopyrene is a class of organic compounds with significant carcinogenic effect. However, the underlying mechanisms remain unclear. The aims of this study were to determine the involvement of RNA-binding motif protein 5 (RBM5) and Wnt/β-catenin signaling in cigarette smoke PM2.5 induced alveolar epithelial injury, as well as the interaction between both. **Methods:** A549 cells were treated with cigarette smoke extract (CSE). The MTT assay was used to assess the effects of CSE on cell viability. The levels of RBM5 and Wnt/β-catenin/GSK3β were detected by semi-quantitative reverse transcription polymerase chain reaction (RT-PCR) and western blots. A luciferase assay was used to assess the activity of β-catenin/TCF signaling **Results:** CSE inhibits the proliferation of A549 cells, with increasing CSE concentration and action time, the growth inhibition rate of A549 cells is more big, has the time and dose dependence; Cytosolic and nuclear β-catenin levels significantly increased following CSE treatment, compared with those in control cells ($P < 0.05$); The luciferase activity in CSE-exposed cells transfected with the TCF luciferase reporter wild-type plasmid (pGL3-OT) was significantly greater than that in cells without CSE exposure (33,167 ± 3085 vs. 19,978 ± 1916, respectively, $P < 0.05$);given CSE A549 cells, RBM5 mRNA increased with the increase of CSE concentration and action time prolonged expression gradually decreased, with time and dose dependence; with increasing concentrations of cigarette smoke extract, reduce the expression of RBM5 protein expression, with dose dependent(all $P < 0.05$);after pcDNA3.1-RBM5 transfection, Wnt/β-catenin signaling pathway inhibition; siRBM5 after transfection, Wnt/β-catenin signaling enhanced; give the Wnt signal pathway blocker ICG-001 blocked Wnt/β-catenin signaling pathway, the expression of RBM5 and the difference was not statistically significant. **Conclusion:** Down regulation of RBM5 and activation of Wnt/β-catenin signaling are involved in CSE PM 2.5 induced alveolar epithelial injury. RBM5 acts as an upstream molecule that negatively regulates the activity of Wnt/β-catenin signaling This study was supported by grants from the National Natural Science Foundation of China (No.81472169 and No.81241069)
Keywords: RBM5, Wnt/ β-catenin, Cigarette smoke PM2.5, Lung injury

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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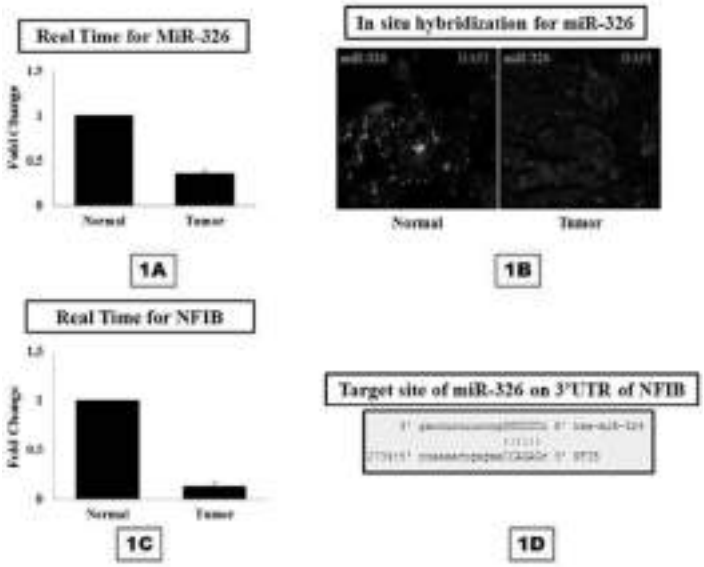
P1.04-080 miR-326 Is Down-Regulated in Non-Small Cell Lung Cancer and Targets NFIB, a Lung Developmental Gene: A Pilot Study Deepali Jain[1], Bijay Pattnaik[2], Anurag Agrawal[2], Sunil Kumar[3], Durgatosh Pandey[3], Palaniappan Ramanathan[3] [1]*Pathology, All India Institute of Medical Sciences, New Delhi/India,* [2]*Csir-Institute of Genomics and Integrative Biology, Delhi/India,* [3]*Surgical Oncology, All India Institute of Medical Sciences, New Delhi/India*

Background: Lung cancer is the leading cause of cancer mortality worldwide. Non-small cell lung cancer (NSCLC) is the most common subtype, accounting for about 80% of all lung cancers. miRNAs are small RNAs of 21-24 nucleotides in length, which play major role in cell proliferation and differentiation and their differential expression is known to be associated with various cancers including lung cancer. Role of miR-326 has been previously studied as a marker of bone metastasis in lung cancer. Moreover, we have previously shown that miR-326 plays a critical role in the epithelial to mesenchymal transition (EMT) by targeting transforming growth factor (TGF)-β1 and other members of TGF-β signaling pathway. The aim of present study is to check the expression and correlation of miR-326 and lung epithelial developmental gene nuclear factor IB (NFIB) in non-small cell lung cancer tissue samples as cancer metastasis is accompanied by EMT. **Methods:** We have examined eight pathologically confirmed non-small cell lung cancer cases. All patients were men and smokers with age ranged from 29 to 74 years (mean 54.6 years). Surgical resection was performed in all the cases which were either stage II or III. Histopathologically, 4 cases were squamous cell carcinomas, 3 were

adenocarcinomas including one case of invasive mucinous carcinoma and one case was low grade mucoepidermoid carcinoma. RNA was isolated from fresh frozen tissue to check for miR-326 and NFIB levels by real time PCR. Protein expression was checked by immunohistochemistry (NFIB; 1:200; Abcam)) and in-situ hybridization (miR-326; Exiqon). Adjoining lung tissue served as normal control in each case. **Results:** Expression of both miR-326 and NFIB was found to be down regulated in non-small cell lung cancer tissue at both RNA and protein level (Fig 1A-C). Our *in silico* experiments identified a target site of miR-326 at the 3'UTR of NFIB gene; presumably it stabilizes the transcripts of NFIB (Fig 1D).



Conclusion: Our preliminary data suggests that miR-326 stabilizes the transcripts of NFIB in normal epithelial cells and maintain epithelial cell integrity. Dysregulation of miR-326 and NFIB in non-small cell lung cancer indicate that miR-326 and NFIB work synergistically and may contribute to the development of non-small cell lung cancer. **Keywords:** miR-326, NFIB, NSCLC, epithelial to mesenchymal transition

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-081 Expression of PPAR-γ Ligand in Lung Cancer and Its Effect on the Apoptosis of Lung Cancer Qiuping Luo *Department of Pulmonary Medicine, The First Affiliated Hospital, Zhejiang University, Hangzhou/China*

Background: To explore the expression of PPAR-γ ligand in lung cancer and its effect on the apoptosis of lung cancer. **Methods:** The expression of PPAR-γ in 80 patients with lung cancer was detected using cell-culture method and its expression in the lung cancer cell lines was also determined by RT-PCR and Western blot. Additionally, TUNEL method was used to detect the apoptosis. **Results:** PPAR-γ was expressed in the lung cancer tissue and the tissue of lung benign lesions. Its optical density was the highest in the lung cancer tissue (0.1832±0.0407), then the tissue of lung benign lesions (0.1201±0.0308), and the lowest in the normal tissue (0.1185±0.0296). The total expression of PPAR-γ showed significant difference in the patients with different pathological types and differentiated degrees (P<0.05), and there was also statistical significance regarding the total expression of PPAR-γ in small cell lung cancer and non-small cell lung cancer (P<0.01). The expression of squamous cell carcinoma is the highest in non-small cell lung cancer. Significant difference was presented by comparison to the expression of PPAR-γ in poorly-differentiated and moderately, highly-differentiated lung cancer tissues (P<0.05). **Conclusion:** The expression of PPAR-γ is closely related to the pathological features of patients with lung cancer, and hence, to research PPAR-γ ligand can provide new evidences for the treatment of lung cancer. **Keywords:** apoptosis, PPAR-γ ligand; lung cancer; expression; differentiation and proliferation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-082 Anti-Neoplastic Effects of 15(S)-HETE and 13(S)-HODE in Lung Cancer George G. Chen, Ming-Yue Li, HI Yuan, Calvin S. Ng, Innes Y. Wan, Malcolm J. Underwood *Surgery, Prince of Wales Hospital, Chinese University of Hong Kong, Hong Kong/China*

Background: Previous studies have shown that the levels of 15-lipoxygenase-1(15-LOX-1),15-lipoxygenase-2(15-LOX-2) and their metabolites 13(S)-HODE and 15(S)-HETE are significantly reduced in human non-small cell lung carcinoma (NSCLC). Furthermore, animal model experiments indicate that the reduction of these molecules occurs before the establishment of lung tumor, suggesting their roles in lung tumorigenesis. However, the functions of these molecules remain unknown in NSCLC. **Methods:** We treated NSCLC cells with exogenous 13(S)-HODE and 15(S)-HETE and then examined how they affected cell functions. We also over-expressed 15-LOX-1 and 15-LOX-2 in tumor cells to restore these two enzymes to generate endogenous 13(S)-HODE and 15(S)-HETE before the cell function was assessed. **Results:** The application of exogenous 13(S)-HODE and 15(S)-HETE significantly enhanced the activity of peroxisome proliferator-activated receptor-γ(PPARγ), inhibited cell proliferation, induced apoptosis, and activated caspase-9 and caspase-3. The overexpression of 15-LOX-1 and 15-LOX-2 could obviously promote the endogenous levels of 13(S)-HODE and 15(S)-HETE, which were demonstrated to be more effective in the inhibition of NSCLC. **Conclusion:** We have demonstrated that exogenous or endogenous 13(S)-HODE and 15(S)-HETE can functionally inhibit NSCLC likely by activating PPARγ. The restoration of 15-LOXs activities to increase the production of endogenous 15(S)-HETE and 13(S)-HODE may offer a novel research direction for the molecular targeting treatment of NSCLC and avoid potential side-effects associated with the application of synthetic PPARγ ligands. **Keywords:** lung cancer, 13S-HODE, 15S-HETE, 15-lipoxygenase

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-083 The Metastasis-Related Noncoding RNA Expression Profile and LncRNA LOC101448202 Induces 95D Cell Migration and Tumor Growth Hou Yanli, Shuanying Yang, Wang Guoen *The Second Affiliated Hospital, Xi'An Jiaotong University, Xi'An/China*

Background: Metastasis of non-small cell lung cancer shortens the survival time of patients and decreases their quality of life. This unfortunate situation could be improved if the functions of long noncoding RNAs (lncRNAs) were identified in depth. **Methods:** not applicable **Results:** In the present study, a large number of lncRNAs and mRNAs with different expression patterns were verified in 95D and 95C lung cancer cell lines. The lncRNA, LOC101448202, was highly expressed in 95D cells, and lentivirus-mediated RNA interference was able to silence its expression with a silencing efficiency of 92%. LOC101448202 gene silencing led to a decrease in cell proliferation, adhesion, migration, and invasion and the number of pseudopods and microvillion the cell surface was also reduced. At the mRNA level, her-2 expression was inhibited and the expression of nm23-H1 and E-cadherin was increased. At the protein level, β-catenin and ezrin levels were decreased both*in vitro* and *in vivo*. In clinical specimens and mouse models, LOC101448202 expression was positively related to tumor growth. **Conclusion:** These data indicate that LOC101448202 expression levels are associated with 95D cell metastasis, demonstrating the tumor-promoting function of this lncRNA. **Keywords:** lncRNA, LOC101448202, 95D cells, metastasis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-084 Ubiquitin Protein Ligase E3C Promotes Growth and Metastasis of Non-Small Cell Lung Cancer Jie Gu, Di Ge *Department of Thoracic Surgery, Zhongshan Hospital Fudan University, Shanghai/China*

Background: Ubiquitin protein ligase E3C (UBE3C) has been recently proposed as a potential oncogene in hepatocellular carcinoma. However, its role and mechanism in non-small cell lung cancer remains unknown. **Methods:** Eight cases of NSCLC and matched nontumorous samples were used to analyze UBE3C expression at the level of protein. Then, we down-regulated the expression of UBE3C in NSCLC cells and assessed the biological role of UBE3C in NSCLC cell line. Finally, the prognostic role of UBE3C was examined by Immunohistochemistry (IHC) in tissue microarray (TMA) consisting of 208 cases of NSCLC. **Results:** The expression of UBE3C in NSCLC tissues was much higher than that in nontumorous samples. Downregulation of UBE3C expression suppressed the proliferation and invasion of lung cancer cells. Further analysis showed that downregulation of UBE3C expression mainly promoted cell apoptosis but without an effect on cell cycle. High levels of UBE3C expression were associated with higher tumor stage in NSCLC patients. The 5-year overall survival rate in the UBE3Chigh group was significantly lower than that in the UBE3Clow group. In multivariate analysis, UBE3C was identified as an independent prognostic factor for overall survival. **Conclusion:** Our findings indicated that UBE3C may represent a candidate therapeutic target and a novel prognostic marker of NSCLC. **Keywords:** NSCLC, Ubiquitin protein ligase E3C, invasion, Prognosis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-085 The Role and Potential Mechanisms of LncRNA-TATDN1 in the Metastasis and Invasion of 95D Cell Shuanying Yang, N Zequn *Department of Respiratory Medicine,, The Second Affiliated Hospital, Xi'An/China*

Background: The invasion and metastasis of malignant cell is generally considered as a major reason why it is always failed in the therapy of lung cancer. The mechanism in metastasis is complicated and uncertain as well. The scientific research proves that Long non-coding RNA (LncRNA) is bound up with the occurrence, development and prognoses of lung cancer. **Methods:** Application of high throughput LncRNA chip to investigate the differentially expressed LncRNA between 95D and 95C cell lines. RNA interference (RNAi) approaches were used for the analysis of the biological functions and metastasis of TATDN1. Tumor growth was studied in nude mice. **Results:** TATDN1-1 was highly expressed in 95D cells lines and NSCLC tissues. In 95D cells knockdown of TATDN1 by using small interfering RNA (siRNA) resulted in significant reduction in proliferation, adhesion, migration and invasion of these cells in vitro. 95D cells xenografts with decreased TATDN1 expression were impaired in tumor formation and growth. On genetic level, MALAT-1displays the strongest association with genes involved in cancer like cellular growth, movement, proliferation, signaling. **Conclusion:** These data indicate that TATDN1expression levels are associated with 95D cells metastasis and identify tumor-promoting functions of TATDN1.

Keywords: lncRNA, metastasis, TATDN1, 95D cell

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-086 Dopamine D2 Receptor Agonists Inhibit Lung Cancer Progression by Reducing Angiogenesis and Tumor Infiltrating Myeloid Derived Suppressor Cells Luke H. Hoeppner[1], Ying Wang[2], Anil Sharma[1], Naureen Javeed[2], Virginia P. Van Keulen[3], Enfeng Wang[2], Ping Yang[4], Anja C. Roden[5], Tobias Peikert[3], Julian Molina[6], Debabrata Mukhopadhyay[1] [1]*Biochemistry and Molecular Biology, Mayo Clinic, Rochester/MN/United States of America,* [2]*Biochemistry and Molecular Biology, Mayo Clinic, Rochester/United States of America,* [3]*Immunology, Mayo Clinic, Rochester/MN/United States of America,* [4]*Health Sciences Research, Mayo Clinic, Rochester/MN/United States of America,* [5]*Laboratory Medicine and Pathology, Mayo Clinic, Rochester/MN/United States of America,* [6]*Oncology, Mayo Clinic in Rochester, Rochester/MN/United States of America*

Background: Lung cancer remains the leading cancer related cause of death in the United States and worldwide. Non-small cell lung cancer (NSCLC), the most common subtype (85%) of lung cancer, continues to be associated with a very poor 5-year survival rate of less than 15%. Despite the recent advances in systemic lung cancer treatment due to the introduction new therapies targeting angiogenesis, epidermal growth factor receptor (EGFR), and activin receptor-like kinase-1 (ALK1) in selected patient subgroups, the overall mortality of patients with advanced stage disease remains high. The development of new biomarkers and individualized therapies is needed to overcome these challenges and make significant strides towards improving the care of lung cancer patients. Dopamine (DA) has long been used in the treatment of Parkinson's disease and acute cardiac dysfunction. Given that DA is produced by the sympathetic nerves ending in blood vessels, we originally postulated and later revealed that DA and its dopamine D2 receptor (D_2R) agonists inhibit VEGF-mediated angiogenesis and also completely block accumulation of tumor ascites and tumor growth in mice. Specifically, we demonstrated that DA stimulates endocytosis of VEGFR-2 via D_2R thereby preventing angiogenesis by inhibiting VEGF binding, receptor phosphorylation and subsequent downstream signaling. These observations define a possible link between DA and vascular biology. Subsequent studies by numerous investigators clearly demonstrate that this strategy can be successfully applied to various diseases including cancer . Correspondingly, we observed significantly more angiogenesis, tumor growth, and VEGFR-2 phosphorylation in D_2R knockout mice. We documented D_2R colocalization with VEGFR-2 and described the molecular mechanism through which D_2R/VEGFR-2 crosstalk can mediate the dephosphorylation of VEGFR-2. D_2R agonists have been shown to increase the efficacy of anti-cancer drugs in preclinical models of breast and colon cancer. Here we show that D_2R agonists inhibit tumor growth in orthotopic murine lung cancer models through inhibition of tumor angiogenesis and reduction of tumor infiltrating myeloid derived suppressor cells. **Methods:** We utilize syngeneic (LLC1) and human xenograft (A549) orthotopic murine lung cancer models as well as pathological examination of human lung cancer tissue to describe D_2R agonist-mediated inhibition of lung tumor growth. **Results:** We sought to determine whether Dopamine D2 Receptor (D_2R) agonists inhibit lung tumor progression and identify subpopulations of lung cancer patients that benefit most from D_2R agonist therapy. We demonstrate D_2R agonists abrogate lung tumor progression in syngeneic (LLC1) and human xenograft (A549) orthotopic murine models through inhibition of tumor angiogenesis and reduction of tumor infiltrating myeloid derived suppressor cells. Pathological examination of human lung cancer tissue revealed a positive correlation between endothelial D_2R expression and tumor stage. Lung cancer patients with a smoking history exhibited greater levels of D_2R in lung endothelium. **Conclusion:** Our results suggest D_2R agonists may represent a promising individualized therapy for lung cancer patients with high levels of endothelial D_2R expression and a smoking history. **Keywords:** dopamine; myeloid derived suppressor cells; VEGF, cabergoline

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-087 The Role and Mechanism of Twist1 in Non-Small Cell Lung Cancer Pathogenesis Tang F. Lv[1], Yong Song[2], Weimin Gao[3] [1]*Respiratory Medicine, Jinling Hospital, Nanjing/China,* [2]*Department of Respiratory Medicine, Jinling Hospital, Nanjing University School of Medicine, Nanjing/China,* [3]*Texas Tech University, Lubbock/United States of America*

Background: Metastasis is a multistep process and the main cause of disease failure and mortality in lung cancer patients. Twist1 is a highly conserved developmental gene involved in embryogenesis that could be reactivated in cancers promoting both malignant conversion and cancer progression through epithelial-mesenchymal transition (EMT). The aim of this study was to investigate the role and mechanism of Twist1 in the pathogenesis of lung cancer. **Methods:** We examined a series of surgical lung cancer samples from Chinese patients (n=75) and showed that Twist1 expression was linked to lymph node status ($P<0.05$). To validate that Twist1 is a driver of EMT in non-small cell lung cancer (NSCLC), we used two human lung cancer cell lines (H1650 and H1975, EGFR mutation) and demonstrated that Twist1 was associated with cell growth and mobility. **Results:** Overexpression of Twist1 increased cell growth, mobility, and a decrease of Twist1 by shRNA technology reversed the phenomenon. Twist1 promoted the tumor growth *in vivo* and induced the expression changes of many genes by tumor gene RNA array. Twist1 significantly down-regulated p4EBP1 expression in H1650 cells and up-regulated p4EBP1 in H1975 cells by qRT-PCR and western blot assay. **Conclusion:** Collectively, both our *in vivo* and *in vitro* findings support that Twist1 in promoting lung cancer by upregulation p4EBP1, which are needed to further study the role of Twist1in NSCLC **Keywords:** Twist1, p4EBP1, Metastasis,Invasion, epithelial-mesenchymal transition

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-088 Lung Cancer Cells Can Alter the Behaviour of Normal Bronchial Epithelial Cells Through Multiple Mechanisms Anne-Marie Baird[1], Martin P. Barr[2], Aaron Urquhart[1], Sarah-Louise Ryan[3], Steven G. Gray[2], Anthony Davies[3], Derek Richard[1], Kathy Gately[2], Kenneth J. O'Byrne[4] [1]*Cancer and Ageing Research Program, Queensland University of Technology, Brisbane/QLD/Australia,* [2]*Thoracic Oncology Research Group, Trinity College Dublin/St. James'S Hospital, Dublin/Ireland,* [3]*Translational Cell Imaging Queensland, Queensland University of Technology, Brisbane/QLD/Australia,* [4]*Cancer and Ageing Research Program, Princess Alexandra Hospital and Queensland University of Technology, Brisbane/Australia*

Background: Lung cancer is one of the most heterogeneous of all solid cancers. This may in part be due to hi-jacking and additional bystander affects that are exerted on the normal lung cell population by the cancer cells. A number of pathways may be stimulated through soluble factors or effector filled vesicles such as exosomes secreted by cancer cells. The aim of this project was to evaluate the effects of non-small cell lung cancer (NSCLC) cells on an immortalised normal bronchial epithelial cell line. **Methods:** A normal bronchial epithelial cell line (HBEC4) was exposed to adenocarcinoma, large cell and squamous NSCLC cell lines and a number of phenotypic and genotypic characterisations were undertaken. These included cellular proliferation (BrdU ELISA), gene (RT-PCR) and miRNA expression screening (Nanostring). The effect of cancer exosome fractions was also determined. **Results:** Exposure to various subtypes of NSCLC significantly increased the cellular proliferation rate of the immortalised cell line in a number of models. Expression of a number of miRNAs were altered in the normal cells pre- and post exposure to the cancer cells. Various stem cell factor markers (*KLF4*, *Oct*, *c-myc*) were also significantly changed at the mRNA level. In addition, exosome fractions altered the behaviour of the normal cell line, likewise stimulating cell proliferation. **Conclusion:** Lung cancer cells may influence normal cell behaviour in both a direct and indirect manner using multiple mechanisms. Normal bronchial epithelial cells with stem like features may be induced to proliferate and behave in a malignant manner. This, akin to Hodgkin's lymphoma, may contribute significantly to the composition of the tumour. Furthermore this observation may contribute to the heterogeneity of lung cancer tumours and affect treatment response. Ongoing studies are evaluating these effects in novel 2D and 3D culture systems. **Keywords:** Stem cell markers, NSCLC, miRNA, exosomes

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-089 MicroRNA miR-615-3p and let-7b Targets Multiple Key Pathways Overexpressed in Lung Adenocarcinoma Kostas Kerkentzes[1], Robin Mjelle[2], Oluf D. Røe[2] [1]*Dept. of Computer Science, University of Crete, Heraklion/Greece,* [2]*Dept. of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology, Trondheim/Norway*

Background: Lung adenocarcinoma gene expression is highly aberrant and heterogeneous and not due to mutations in all these protein-coding genes. Epigenetic regulation by microRNAs has been shown to explain some of this dysregulation. We aimed at identifying whether few microRNAs could explain multiple overexpressed genes in key pathways of lung adenocarcinoma. **Methods:** Publicly available gene expression profiling data from three different publications were included in this *in silico* analysis. In the lung adenocarcinomas (n=139/49/45) and normal lung tissue (n=17/9/65) among the common 8543 genes (based on the EntrezID), the differentially expressed and diagnostic genes were investigated. The genes with q-value under 0.01 and with concordant regulation among all three datasets were regarded as significantly differentially expressed. Diagnostic genes were identified through the performance of each differentially expressed gene as a classifier. Finally, the miRNAs with highly probable predicted (PCT>0.9 in TargetScan), miRNA targeting interactions (MTI) and/or with experimentally validated MTIs were assessed, the number of gene targets in the down- or up-regulated genes measured for each miRNA and an enrichment analysis was performed. **Results:** The common overexpressed and down-regulated genes among the three datasets were 534 and 638 respectively. Among the diagnostic genes with AUC over 0.8 were the known genes encoding recently discovered diagnostic proteins but also new unknown genes. Among the pathways in KEGG, genes of the Cell Cycle, Carbon-pool by Folate and Base Excision and Mismatch Repair were significantly overexpressed. Importantly, we identified few microRNAs ($q< 0.01$) that could target most of these genes and that are all previously shown to be down-regulated and validated in lung and/or other cancer. Among the top microRNA were the following; Mir-615-3p targets 86 highly over-expressed genes in all three datasets. This microRNA was recently shown to act as a tumor suppressor through inhibition of the AKT2 in pancreatic cancer cell lines. Let-7b targets 83 highly over-expressed genes in all three datasets. Let-7b is controlling genomic balance and is down-regulated in aggressive breast cancer and significantly reduced in serum is correlated to poor survival in resectable NSCLC. Mir-16 targets 75 of the up-regulated genes in adenocarcinoma and was verified down-regulated in NSCLC versus adjacent normal lung tissue. Mir-193b targets 65 genes and was identified as a tumor suppressor in NSCLC and hepatocellular carcinoma. Mir-320a targets 50 genes and was identified as a crucial miRNA regulating glycolysis and was verified down-regulated in NSCLC. Mir-34a targets 46 of the overexpressed genes and is a crucial miRNA down-regulated in lung cancer and already proposed as a treatment with cisplatin. **Conclusion:** By combined *in-silico* analysis of three large datasets on adenocarcinoma versus normal adjacent lung tissue we detected novel candidate diagnostic genes and important pathways that recapitulate the phenotype of this cancer. Importantly, we found microRNAs that could target and thus explain a large portion of the pathway dysregulation. One of these identified microRNAs, miR-34a, has already demonstrated a therapeutic potential in lung cancer. **Keywords:** Gene Expression, microRNA, Adenocarcinoma, multiple pathways

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-090 Roles of MLF1IP in the Proliferation of Lung Adenocarcinoma Cells
Yuqing Lou[1], Rong Li[1], Jielin Liu[2], Yanwei Zhang[1], Wei Zhang[1], Xueyan Zhang[1], Hua Zhong[1], Liyan Jiang[1], Shaojun Wen[2], Baohui Han[1] [1]*Department of Pulmonary, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai/China,* [2]*Department of Hypertension Research, Beijing Anzhen Hospital, Capital Medical University and Beijing Institute of Heart Lung and Blood Vessel Diseases, Beijing/China*

Background: MLF1IP was initially identified as a MLF1 interacting protein, which encodes a centromere protein essential for cell cycle and mitosis. It has been reported that MLF1IP depletion impaired the interaction between centromere and microtubules, finally inducing defects in cell mitosis. However, the involvement of MLF1IP in lung adenocarcinoma development and related mechanisms remain to be elucidated. **Methods:** MLF1IP expression at mRNA level in 15 pair lung adenocarcinoma/adjacent normal lung samples was examined with real-time PCR assay. Then the expression of MLF1IP in human lung adenocarcinoma cells A549 was inhibited with lentiviral-mediated shRNA strategy. Effects of MLF1IP knockdown on cell proliferation was analyzed by Cellomics cell counting method and MTT assay. Then the impact of MLF1IP knockdown on colony formation, cell cycle process and cell survival was determined in A549 cells by colonogenesis assay, PI staining and Annexin V-APC staining respectively. **Results:** MLF1IP expression was significantly increased in lung adenocarcinomas as compared to adjacent normal lung tissues (fold change=2.50, P<0.05), with higher MLF1IP expression observed in 66.7% (10/15) samples while lower expression observed in only 20% (3/15) samples (Fig. 1A). Furthermore, MLF1IP knockdown impaired cell proliferation (Fig. 1B, C), inhibited colony formation ability (Fig. 1D), induced cell cycle arrest (Fig. 1E) and promoted cell apoptosis (Fig. 1F) in A549 lung adenocarcinoma cells.

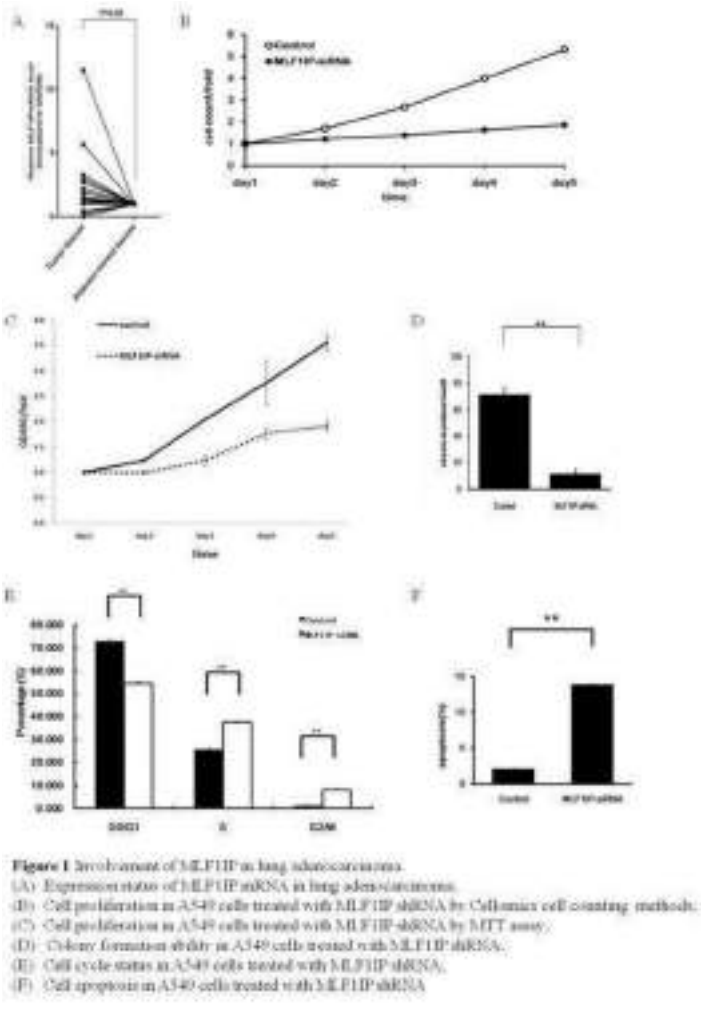

Figure 1 Involvement of MLF1IP in lung adenocarcinoma.
(A) Expression status of MLF1IP mRNA in lung adenocarcinoma.
(B) Cell proliferation in A549 cells treated with MLF1IP shRNA by Cellomics cell counting methods.
(C) Cell proliferation in A549 cells treated with MLF1IP shRNA by MTT assay.
(D) Colony formation ability in A549 cells treated with MLF1IP shRNA.
(E) Cell cycle status in A549 cells treated with MLF1IP shRNA.
(F) Cell apoptosis in A549 cells treated with MLF1IP shRNA

Conclusion: Our study showed that MLF1IP expression is correlated with lung adenocarcinoma development and MLF1IP expression is critical for cell proliferation and survival in lung adenocarcinoma cell line A549. MLF1IP represents a novel potential target for lung adenocarcinoma therapy.
Keywords: MLF1IP, lung adenocarcinoma, Cell cycle, cell proliferation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-091 Biological Significance of CHK2 Gene Expression in Lung Adenocarcinoma
Tatsuro Okamoto, Tetsuzo Tagawa, Fumihiro Shoji, Yosuke Morodomi, Mikihiro Kohno, Kensaku Ito, Yuzo Suzuki, Takatoshi Fujishita, Masakazu Katsura, Yoshihiko Maehara *Department of Surgery and Science, Kyushu University, Graduate School of Medical Sciences, Fukuoka/Japan*

Background: CHK2 is a transducer protein that is involved in DNA damage response (DDR). CHK2 phosphorylates effector proteins that play roles in DNA repair, cell cycle regulation and apoptosis. Recently, CHK2 have been found to have a critical role in the mitosis, and disruption of CHK2-BRCA pathway caused chromosomal instability in colon cancer cell lines (Stolz et al. Nat Cell Biol 2010:12; 492). The purpose of this study was to investigate the biological role of CHK2 and related factors in lung adenocarcinoma. **Methods:** We investigated 60 surgically resected lung adenocarcinomas. CHK2 and BRCA1 mRNA expression levels were evaluated by qRT-PCR. Relative mRNA expression levels of each sample were standardized to those of β-actin. EGFR mutation (exon 19 deletion and 21 point mutation) was detected by PNA-LNA PCR clamp method. KRAS mutation (exon 2, codon 12, 13) and p53 mutation (exon 5-9) were examined by direct sequencing. p27 and p21 protein expression levels were assessed by immunohistochemistry. Chromosomal aberration (CA) was examined in 20 samples with single-nucleotide polymorphism–CGH (SNP–CGH). **Results:** CHK2 mRNA levels were significantly increased in the tumor tissues compared to the normal tissues (p=0.012). CHK2 mRNA level was not correlated with patients' clinicopathological factors, EGFR mutation status or p53 mutation status. CHK2 mRNA levels were significantly correlated with BRCA1 mRNA levels (ρ = 0.569, p < 0.0001). High CHK2 mRNA expression and high p27 protein expression levels were associated with poor prognosis for recurrence free survival (P = 0.028, P = 0.048), although both expression levels were not correlated with each other. 7 samples were determined to be high CA, while 13 samples to be low CA according to SNP-CGH. CHK2 mRNA level was higher in high CA (7 samples) than in low CA samples (13 samples) (Ave. 0.326 vs. 0.185; p=0.0129). **Conclusion:** CHK2 mRNA expression level was increased in lung adenocarcinoma and was related to poor prognostic outcomes. CHK2 pathway may be important for the proliferation of lung adenocarcinoma, especially in tumors with chromosomal instability.
Keywords: chromosomal instability, lung adenocarcinoma, DNA damage response, Prognosis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-092 LKB1 Inactivation Confers Human Lung Adenocarcinoma with Strong Plasticity for Squamous Transdifferentiation
Xiangkun Han[1], Yingjiao Xue[1], Yanzhen Nie[1], Liao Kan[1], Haiquan Chen[2], Hongbin Ji[1] [1]*Shanghai Institutes for Biological Sciences, Shanghai/China,* [2]*Department of Thoracic Surgery, Fudan University Shanghai Cancer Center, Shanghai/China*

Background: Lung adenocarcinoma (ADC) and squamous cell carcinoma (SCC) are considered as two distinct subtypes of lung cancer and derived from different types of lung epithelial cells and featured with different biomarker expression. Interestingly, there exist certain lung tumors so called adenosquamous cell carcinoma (Ad-SCC) containing mixed both adenomatous and squamous pathologies; more importantly, these two different pathologies within a single tumor are consistently shown to have identical gene mutations. In consideration the fact that most tumors are derived from a single epithelial cell, it's reasonable to hypothesize that there must exist lineage transition between ADC and SCC subtypes. However, this fundamental question remains unanswered due to the difficulty of study of human clinical samples. Indeed, most studies of clinical samples can only provide indirect evidences to support this hypothesis. Taking advantage of mouse models mimicking human lung cancer, we have recently successfully shown that inactivation of a tumor suppressor LKB1 confers mouse lung ADC with strong plasticity and makes them transdifferentiate into SCC through mixed Ad-SCC as intermediates (Han XK, *et al.* **Nat Commun**, 2014). However, whether there exists a phenotypic transition from ADC to SCC in human lung cancer remains unknown. **Methods:** Immunohistochemical analyses Integrative genomic analyses Establishement of patient-derived tumor xenograft model Statistic Analyses **Results:** not applicable. **Conclusion:** We pathologically analyzed a large cohort of human NSCLC samples and carefully evaluate the prevalence of mixed pathologies in context with LKB1 genetic inactivation. Moreover, we took advantage of the established lung ADC PDX mouse models to perform serial transplantation w/o the interfere of essential signaling pathways identified from *de novo* animal model study and test if possible that human ADC with LKB1 inactivation can progress and transdifferentiate into SCC. Based on our current understanding of this type of phenotypic transition in mice as well as the resources and systems established in the lab, we here succeed in proving the transdifferentiation of human ADC to SCC.
Keywords: LKB1, Plasticity, patient-derived xenograft mouse model, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-093 CCNY2 Promotes Lung Cancer Cell Migration and Invasion via Regulating F-Actin Expression
Wentao Yue[1], Xiaoting Zhao[1], Mei Jiang[1], Weiying Li[1], Yu Teng[2], Jinjing Tan[1], Lina Zhang[1], Li Ma[2] [1]*Beijing Chest Hospital, Capital Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijng/China,* [2]*Beijing Chest Hospital, Capital Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing/China*

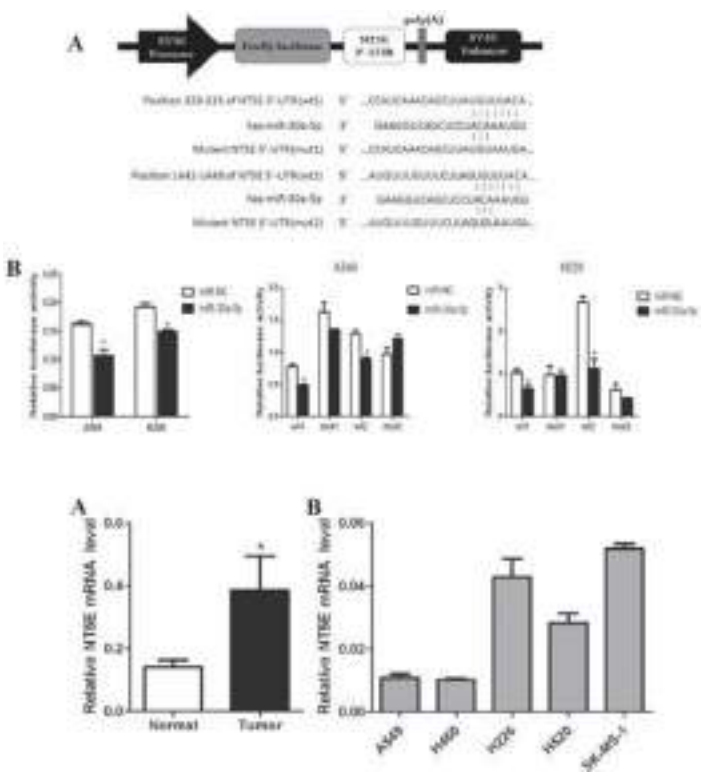
Background: Cyclin Y (CCNY) is a novel cyclin and is highly conserved in metazoan species. Cyclin Y mRNA has several transcripts and only ccny1 and ccny2 has been documented.

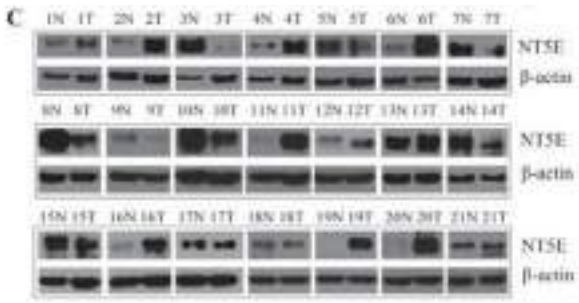
A potential CDK partner of Cyclin Y is PFTAIRE kinase (PFTK1). In hepatocellular carcinoma, cell motility and invasion was enhanced by PFTK1 expression. But the function of CCNY1 and CCNY2 on cell migration and invasiveness has not been reported yet. **Methods:** Recombined plasmids carrying CCNY1 and CCNY2 were constructed and transfected to H1299 cells to obtain CCNY up-regulation cells. A lentivirus-based RNAi delivery system was used to inhibit CCNY mRNA expression. The role of CCNY in cell motility and invasion was investigated using wound healing and transwell assay. The protein levels in lung cancer cells were determined by western-blot, immunofluorescence technique and high-content cell analysis. Mouse xenograft experiments were carried out to study the metastasis ability of CCNY1 and CCNY2 in vivo. Immunohistochemistry was used to detect the CCNY protein level of lung cancer tissues. **Results:** cell motility and invasion activity were inhibited and MET (Mesenchymal - Epithelial Transition) was caused by down-regulating of CCNY in 95D and H1299 cells. CCNY2 could enhance cell migration and invasion activity in vivo and vitro. The F-actin level was regulated by CCNY2 expression. In non-small cell lung cancer tissues, CCNY2 was highly expressed and the CCNY2 expression was associated with histological grade. **Conclusion:** CCNY2 was firstly detected in lung cancer cells and non-small cell lung cancer tissues. Our findings demonstrated CCNY2 not CCNY1 promoted cell motility and invasion by regulating the expression of F-actin and modulating intracellular cytoskeletal components. **Keywords:** CCNY, cell migration, cell invasion, actin cytoskeleton

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-094 NT5E(CD73) Is a Target of miR-30a-5p and Plays a Critical Role in Non-Small Lung Cancer Zeyi Liu[1], Jianjie Zhu[1], Yuanyuan Zeng[1], Hualong Qin[2], Jian-An Huang[1] [1]*Department of Respiratory Medicine, the First Affiliated Hospital of Soochow University, Institute of Respiratory Diseases, Suzhou/China,* [2]*Department of Cardiothoracic Surgery, the First Affiliated Hospital of Soochow University, Suzhou/China*

Background: CD73, is a glycosylphosphatidylinositol (GPI)-linked 70-kDa cell surface enzyme that catalyzes the dephosphorylation of extracellular AMP to adenosine, its dysregulation contributes to tumorigenesis and progression of a variety of malignancies, and it was suggested as a therapeutic target of cancers. But the functional relevance of CD73 and the mechanism underlying its dysregulation in lung tumorigenesis remained unclear. Here, we mainly focus on if CD73 has important functions in non-small-cell lung cancer (NSCLC) by: 1.evaluating the clinicopathologic significance of CD73 through analysing its expression in 38 human NSCLCs tissues using quantitative PCR, Western Blot; 2. determining its role in NSCLC using in vitro assays; 3. investigating the regulatory mechanism of CD73 dysregulation in NSCLS cell lines. **Methods:** Western blot analysis, real-time quantitative reverse transcriptase PCR, RNA interference microarray analysis and trans well were performed on human NSCLC tissues and cell lines. Thirty-one paired NSCLC tissues and adjacent noncancerous lung tissues were collected.





Results: CD73 was upregulated in 52.38% of the lung tumor tissues and its expression was significantly related to histology and differentiation ($P < 0.05$). Reduced CD73 expression suppressed NSCLC cell growth in vitro. miR-30a-5p was significantly downregulated in 4 paired lung cancer tissues(with > 2.0-fold change and FDR < 0.05) and was validated in the 38 independent paired tissues (63.16%, $P < 0.05$), CD73 was a novel target of miR-30a-5p predicted by TargetScan, miRanda, PicTar, MirTarget2, PITA and detected by luciferase report assay, then ectopic miR-30a-5p expression in cancer cells reduced CD73 expression. **Conclusion:** CD73 play a very important role in NSCLC, and regulated by miR-30a-5p. CD73 may provide a potential target for diagnosis and treatment for lung cancer. **Keywords:** MicroRNAs, NSCLC, CD73, miR-30a-5p

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-095 Integrin a11b1 Regulates Cancer Stromal Stiffness and Promotes Tumorigenicity and Metastasis in Non-Small Cell Lung Cancer Roya Navab[1], Elena Pasko[2], Kris S. Kim[3], Gilbert C. Walker[3], Donald Gullberg[4], Ming S. Tsao[2] [1]*Research, Princess Margaret Hospital, Mg L/ON/Canada,* [2]*Research, Princess Margaret Hospital and Ontario Cancer Institute, Mg L/ON/Canada,* [3]*Chemistry, University of Toronto, Ms H/ON/Canada,* [4]*Biomedicine, University of Bergen, Bergen/Norway*

Background: Integrin $\alpha 11\beta 1$ is a stromal cell-specific receptor for fibrillar collagens and is over-expressed in carcinoma-associated fibroblasts (CAFs) in non- small cell lung cancer (NSCLC). We have studied the direct role of stromal integrin a11 on the growth and metastasis of NSCLC cells using novel immune-compromised a11 deficient mice. **Methods:** We developed $\alpha 11$ non-expressing immune-deficient mice by back-crossing for at least 10 times the $\alpha 11$-deficient heterozygous C57BL/6J mice (+/-) to obtain a homogenous C57BL/6 background. These were subsequently bred with the BALB/c SCID mice for 7 generations, producing $\alpha 11$-deficient heterozygous (+/-) in SCID background. In vivo studies were done using subcutaneous tumorigenicity assay and orthotopic model to evaluate metastatic potential of integrin $\alpha 11$. Immunostaining were carried out using integrin $\alpha 11$, α-SMA, and cytokeratin. PisroSirius red staining was used to visualize the collagen fibers. Images were taken by polarized-light microscopy using parallel and perpendicular polarizer orientations on an Olympus BX51 microscope. Second Harmonic Generation (SHG) was used to visualize fibrillar collagen and atomic force microscopy was applied to measure the stiffness in tumor stroma. **Results:** The tumor growth of both primary human lung cancer (PHLC) and established NSCLC cells in $\alpha 11$ knockout ($\alpha 11$-/-) mice was significantly impeded compared to wild type ($\alpha 11$+/+). Orthotopic implantation of a spontaneously metastatic NCI-H460SM cell line into the lungs of $\alpha 11$-/- and $\alpha 11$+/+ mice showed significant reduction in the metastatic potential of these cells in the $\alpha 11$-/- mice. Using mouse WG-6v2 Illumina Bead Chips, we identified that alpha11 expression correlates with that of a fibrillar collagen cross-linking enzyme, LOXL1, in the xenograft stroma. Fibrillar collagen was highly disorganized and had a significantly lower elastic modulus in the alpha11 knockout xenografts compared to wildtype. The results suggest a role for $\alpha 11$ in promoting tumor growth and metastatic progression by affecting the collagen stiffness of the tumor stroma. **Conclusion:** The integrin $a11\beta 1$ signaling pathway in CAFs promotes tumor growth and metastasis of NSCLC cells. This appears closely linked to collagen cross-linking, the organization, and stiffness of fibrillar collagen matrices. **Keywords:** metastasis, non-small cell lung cancer, integrin, stroma stiffness

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-096 Second Tumors in Lung Cancer (LC) Patients. Should We Think About This Issue in Long Term Survival Setting? Martin Pitzzu[1], Norberto Olguin[1], Karina O´leary[1], Maria V. Colica[1], Ivana Fajreldine[1], Nestor Spizzamiglio[2], Miguel Galmes[2], Gustavo Jankilevich[1] [1]*Oncology Unit, Hospital Carlos Durand, Buenos Aires/ Argentina,* [2]*Thoracic Surgery, Hospital Carlos Durand, Buenos Aires/Argentina*

Background: Lung cancer (LC) is the first cause of cancer death in men and the third in women in Argentina. Multiple studies have shown that patients with LC treatment prolong their survival and thus increases the risk of second tumors. The prevalence of second tumors after lung cancer ranges from 2% to 15%, which further increases after ten years since the diagnosis was made. Reports from latinoamerica are scarce. **Methods:** We evaluated retrospectively the medical record of pts with LC from 2005 to 2014. We recorded the presence of second tumor in the follow-up. **Results:** Two hundred twelve patients were registered. Ten patients (4.56%) were recorded with second tumors. Median age was 68 years old (r. 59-80),most of them were men (80%) and smokers

(90%). Regarding primary tumor, 90% (9 pts) were non small lung cancer (NSCLC) versus 10% SCLC. The most frequent histological type was squamous carcinoma 60% (6 pts) and adenocarcinoma 30% (3 pts). The most frequent second tumor site was: lung 40% (4 pts) followed by larynx , bladder, kidney, ovary, breast and NHL. Median survival was 22 months (r. 1-160) in pts without second tumors versus 65 months (r. 22-165) in pts with second tumors (p: 0,005 – Fisher Test). The median of diagnosis time of second tumor was 22.5 months. **Conclusion:** These results show the paramount importance of a correct follow-up in these patients. In our series, one each twenty patients with lung cáncer had a second cancer during their follow-up. The most frequent site were respiratory and genitourinary tracts. There was a significant difference in the survival in pts with second tumors. **Keywords:** lung cancer, second tumors, long term survival, second tumors in lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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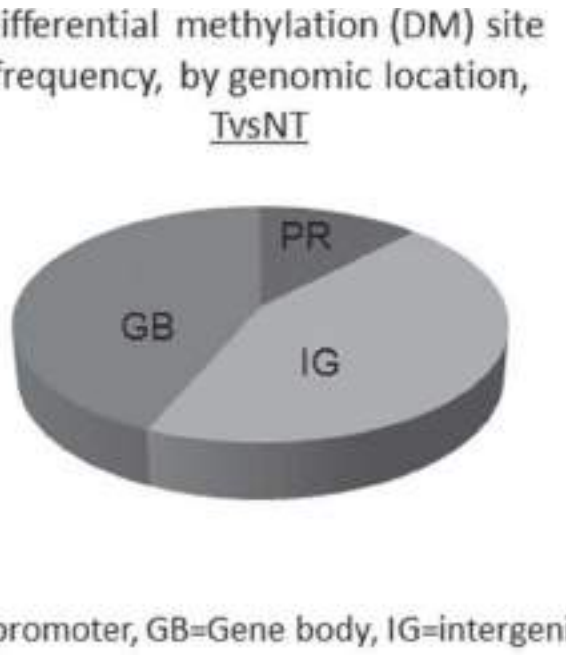
P1.04-097 Genome-Wide Methylome Alterations in Lung Cancer
Nandita Mullapudi[1], Bin Ye[2], Masako Suzuki[3], Melissa Fazzari[3], Weiguo Han[1], Miao Shi[1], Gabrielle Marquardt[1], Juan Lin[4], Tao Wang[4], Steven Keller[5], Changcheng Zhu[6], Joseph Locker[6], Simon D. Spivack[1] [1]*Medicine/Pulmonary, Albert Einstein College of Medicine, Bronx/NY/United States of America,* [2]*Bioinformatics, Albert Einstein College of Medicine, Bronx/NY/United States of America,* [3]*Genetics, Albert Einstein College of Medicine, Bronx/NY/United States of America,* [4]*Biostatistics, Albert Einstein College of Medicine, Bronx/NY/United States of America,* [5]*Thoracic Surgery, Albert Einstein College of Medicine, Bronx/NY/United States of America,* [6]*Pathology, Albert Einstein College of Medicine, Bronx/NY/United States of America*

Background: DNA cytosine methylation profiles are important features of malignancy. This study was designed to identify 5-methyl cytosines on a genome-wide scale in non-small cell lung cancers (NSCLC) relative to paired non-tumor lung which, analyzed alone or coupled to transcriptome data, could suggest methylome-deregulated loci. **Methods:** Twenty-four NSCLC tumor (T) – non-tumor (NT) pairs were interrogated for 1.2 million CCGG-bounded fragments across all genomic compartments, using a methylation-sensitive restriction enzyme based HELP-microarray assay. Expression microarrays were also employed, from specimens from the same lung resections. **Results:** We found: (i) Good correlation (r^2 =$^{0.52}$, p=$^{0.0006}$) between HELP and the reference quantitative methylation assay MassArray ®; (ii) Wide distribution of differential methylation (DM) among ^{32,037} promoters (PR, ^{26}% of array-represented loci), ^{248,721} gene bodies (GB, ^{39} %), and ^{171,996} intergenic (IG, ^{48}%) loci; (iii) In PR CpG island (CGI) hypermethylation exceeded CGI hypomethylation; (iv) DM hypermethylation in adenocarcinoma specifically was observed in many unexpected PR [*e.g., RASL*[12]*; SPTAN*[1]*, mir-*[26]*a*,] and GB [*e.g., AKAP*[13]*, ANK family, PRKCE, ROS*[1]] regions; (v) Overlay of DMxDE (differential expression) for adenocarcinoma yielded loci with canonical DM:DE patterns (*e.g.* PR hyper/hypo-methylation:mRNA down/up-regulated n=^{80}; GB hyper/hypo-methylated:mRNA up/down-regulated GB n=^{3,136}). (vi) Examples in adenocarcinoma hypermethylated PR loci with reduced expression included: *HBEGF, DPT, AGER, SPARCL*[1]*, PTPRM*; GB hypermethylated loci with upregulated expression included *FERMT*[1]*, SLC*[7]*A*[5]*, FAP, TFAP*[2]*a* genes. (vii) IPA analyses showed adenocarcinoma-specific promoter DMxDE overlay identifying familiar lung cancer nodes [*tP*[53]*, Akt*] and less familiar nodes [*HBEGF, NQO*[1]*, GRK*[5]*, VWF, HPGD, CDH*[5]*, CTNNAL*[1]*, PTPN*[13]*, DACH*[1]*, SMAD*[6]*, LAMA*[3]*, AR*].



Conclusion: Methylome sampling, alone and combined with transcriptome data, yields new loci, as well as previously recognized ones, distributed throughout the genome that are deregulated in NSCLC.

Keywords: DNA methylation, genome-wide, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-098 Mithramycin Is a Potential Therapeutic Agent for Elimination of Stem-Like Cells in Lung Cancer
Haobin Chen, Mary Zhang, Sichuan Xi, Yin Xiong, Julie A Hong, David S. Schrump *Thoracic and Gi Oncology Branch, Nci, Bethesda/United States of America*

Background: There have been several studies demonstrating existence of cancer stem-like cells in lung cancers, and resistance of such cells to conventional chemotherapy or targeted agents. As such, targeting cancer stem-like cells is a potential strategy to prevent development of drug resistance and tumor recurrence. Previously our group has demonstrated that mithramycin, a specific inhibitor of transcription factor SP1, attenuates induction of side population (a phenotype of cancer stem-like cells) by cigarette smoke condensate, and modulates expression of multiple genes regulating stem-cell related pathways in lung cancer cells. The present study was performed to further examine the effects of mithramycin on stem cell signaling pathways, and ascertain if mithramycin can eliminate stem-like cells in lung cancer following exposure to conventional chemotherapeutic or targeted agents. **Methods:** Stem-like cell populations in cultured H358 and H2228 lung adenocarcinoma cells were identified based on expression of stem cell markers, ALDH1 and CD133 using ALDEFLUORTM assay and flow cytometry, respectively. Sphere-formation assays were used to examine clonogenic growth of stem-like cells. qRT-PCR techniques were used to evaluate expression levels of stemness-related genes. Western blot techniques were utilized to assess activation of stemness-related (WNT/β-catenin and NOTCH) signaling pathways. **Results:** Small CD133+ or ALDH1+fractions were detected in untreated H2228 and H358 cells, respectively. Consistent with notion that stem-like cells are present in these two lines, H2228 and H358 cells formed pulmospheroids when cultured in stem cell media in low attachment plates; these phenotypic changes were accompanied by increased expression of stemness-related genes including Oct4, Sox2 and Nanog. Cisplatin treatment enriched CD133+ fraction in H2228 cells and ALDH+ fraction in H358 cells. Mithramycin abolished this enrichment, and mediated dose-dependent decreases in Oct4, Sox2 and Nanog expression in a dose-dependent manner. Preliminary analysis demonstrated that mithramycin decreased total as well as active forms of β-catenin, but did not affect levels of cleaved NOTCH1, suggesting that mithramycin eliminates lung cancer stem-like cells partially through suppression of WNT/β-catenin signaling. The effects of mithramycin on lung cancer stem-like cells induced by targeted agents are currently under investigation. **Conclusion:** Mithramycin suppresses stemness-related signaling, and is a potential therapeutic agent for elimination of stem-like cells emerging in lung cancers after cisplatin therapy. **Keywords:** Stem-like cell, WNT/beta-catenin, Cisplatin, Mithramycin

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P1.04-099 Wnt Blockers Inhibit the Proliferation of Lung Cancer Stem Cells
Xueyan Zhang[1], Yuqing Lou[1], Xiaoxuan Zheng[1], Huiming Wang[1], Jiayuan Sun[1], Qianggang Dong[2], Baohui Han[1] [1]*Shanghai Jiaotong Univ. Affiliated Shanghai Chest Hospital, Shanghai/China,* [2]*Shanghaijiaotong University, Shanghai/China*

Background: Previous study has confirmed that the occurrence of Wnt pathway activation is associated with risk of non-small-cell lung cancer recurrence. However, whether the pharmacologic blocking of the Wnt signaling pathway could provide therapeutic possibility remains unknown. The aim of the present study was to evaluate the therapeutic functions of the Wnt signaling pathway inhibitor pyrvinium pamoate (PP) on lung cancer stem cells (LCSCs) in vitro. **Methods:** Colony formation and sphere culture were performed to enrich LCSCs from three lung cancer cell lines: PC9, SPC-A1, and A549. After confirming stemness by immunofluorescence, PP was employed for cell viability assay by comparison with three other kinds of Wnt signaling inhibitor: salinomycin, ICG-001, and silibinin. The effect of PP on LCSCs was further verified by colony formation assay and gene expression analysis. **Results:** LCSCs were successfully generated by sphere culture from SPC-A1 and PC9 cells, but not A549 cells. Immunofluorescence assay showed that LCSCs could express pluripotent stem cell markers, including NANOG, Oct4, KLF5, and SOX2, and Wnt signaling pathway molecules β-catenin and MYC. Half-maximal inhibitory concentrations of PP on SPC-A1, PC9, and A549 were 10 nM, 0.44 nM, and 0.21 nM, respectively, which are much lower than those of salinomycin, ICG-001, and silibinin. Moreover, significantly decreased colony formation and downregulation of pluripotent stem cell signaling pathway were observed in lung cancer cells after treatment with PP. **Conclusion:** Wnt signaling inhibitor PP can inhibit proliferation of LCSCs, and the Wnt signaling pathway could be considered a promising therapeutic or interventional target in lung adenocarcinoma. **Keywords:** pyrvinium pamoate, Wnt signaling pathway, sphere culture, colony formation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-100 Combination of Pitavastatin and Erlotinib Induces Apoptosis and Growth Arrest in Non-Small Cell Lung Cancer (NSCLC)-Celllines
Christoph Minichsdorfer, Duygu Aydemr *Oncology, Medical University of Vienna, Vienna/Austria*

Background: Primary resistance against epithelial growth factor receptor (EGFR) targetet therapy is often caused by K-Ras mutations or amplification of the MET-oncogene. HMG-CoA reductase inhibitors (statins) are well tolerated drug mainly prescribed for the the primary and secondary prophylaxis of coronary artery disease. However, the majority of statins are metabolized in the liver by Cyp3A4, which may lead to interactions with Erlotinib a tyrosin kinase inhibitor (TKI) which targets the EGFR. Therefore we tested the efficacy of Erlotinib in combination with Pitavastatin, which is metabolized by Cyp3A4,

for the treatment of primary Erlotinib-resistant NSCLC celllines. **Methods:** Experiments were carried out with human NSCLC celllines A549 (K-RAS mutation), Calu-6 (K-RAS mutation, P53 mutation), HCC 827 (EGFR mutation, Erlotinib sensitive) and H1993 (MET amplification). Apoptosis was measured by the activity of caspase 3 by cleavage of specific fluorescent caspase substrates, by binding of AnnexinV by FACS analysis or by the cleavage of PARP by Western blot. Inhibition of growth was assessed by MTS assays. The effect of either drug alone or in combination on phosphorylation of AKT and ERK1/2 was evaluated by Western blot. **Results:** Inhibition of growth by erlotinib was seen in the sensitive cell line HCC 827 but not in A549, Calu6 and H1993. Pitavastatin led to growth inhibition in all 4 cell lines investigated in a dose dependant manner. However, the combination of Pitavastatin and Erlotinib was significantly more effective than either drug alone. Erlotinib and Pitavastatin did not induce apoptosis when used as single agents in A549, Calu6 or H1993. When a combination of TKI and Pitavastatin was used we observed significantly increased caspase 3 activity and a higher rate of annexin V positive cells. Moreover an increased cleavage of PARP was shown in the combination treatment. Taken together we could show increased rate of apoptosis when Erlotinib and Pitavastatin where used in combination. Importantly the activation of survival pathways mediated by phosphorylation of AKT was markedly decreased, by the combined treatment in A549, Calu6 and H1993 cells. ERK 1/2 phosphorylation was reduced in H1993 and Calu6 cells upon combined treatment. **Conclusion:** Our data indicate, that the treatment of primary EGFR-TKI resistant cells (A549, Calu6 and H1993) with Erlotinib in combination with Pitavastatin leads to growth arrest and an induced rate of apoptosis. **Keywords:** NSCLC, TKI, Statins, Erlotinib

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-101 Utility of Patient-Derived Cell Line Models Using Conditional Reprogramming for in Vitro Pharmacogenomics Platform Hyun Chang[1], Hye Ryun Kim[2], Yong-Wha Moon[2], Su Jin Heo[2], Sun Min Lim[2], Joo-Hang Kim[2], Soonmyung Paik[3], Byoung Chul Cho[2] [1]*Hematology and Medical Oncology, Catholic Kwandong University International St. Mary'S Hospital, Incheon/Korea,* [2]*Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul/Korea,* [3]*Severance Biomedical Science Institute, Yonsei University College of Medicine, Seoul/Korea*

Background: To evaluate the potential of conditional reprogrammed cells (CRCs) established from biopsy or effusion samples of advanced non-small cell lung cancer (NSCLC) for *in vitro* pharmacologic screen and identification of drug resistance mechanisms. **Methods:** A total of 48 tumor specimens obtained from 46 patients with NSCLC were cultured with irradiated fibroblast feeder cells and Rho kinase inhibitor (Y-27632) to induce tumor cells to proliferate indefinitely. The cell lines established from patients harboring *EGFR* mutation or other druggable oncogenes were subjected to genetic analyses and pharmacologic screen. Corresponding tumor cells were injected into nude mice to test for tumorigenicity and efficacy of targeted agents *in vivo*. **Results:** Twenty one male patients and twenty five female patients were assessed for establishment of CRC. Adenocarcinoma was the most frequent histologic type (84.7%). There were 21 patients (46%) who harbored an active *EGFR* mutation. There were four patients with ALK fusion and five with ROS1 fusion. Twenty-six patients experienced disease progressed while on treatment with EGFR (20), ALK (2) or ROS1 (4) tyrosine kinase inhibitors. Tumor cells came from primary or distant metastases in 48% and 52%, respectively. Thirty one (65%) samples were obtained by tumor biopsy and 17 from malignant pleural effusion. Nine CRC model were successfully established (18.7%, 9/48). The successful growth was not dependent on the clinicopathologic characteristics. Both cells from pleural effusion (4 of 17) and biopsy (5 of 31) and adenocarcinoma (8 of 41) and squamous cell carcinoma (1 of 3) were successfully cultured. For biopsy samples, the success rate of cells obtained from primary lung lesion was 21.7% (5 of 23) and cells from metastatic site outside lung was 0% (0 of 8) (P = 0.3). For effusion samples, volume of effusion required for CRC was not significant factors for establishment (success vs. failure cases: mean volume 500 ml vs. 267 ml). The genetic characteristics of patients with non-squamous cell carcinoma did not affect the success rate of CRC (EGFR mutation, 4 of 21; ALK translocation, 0 of 4; ROS1 translocation, 2 of 5; wild or unknown, 2 of 15). Two xenograft models with CRC were successfully established and passaged to maintain tumor in vivo. **Conclusion:** The CRC models derived from NSCLC patients provide useful in vitro platforms of preclinical studies evaluating novel targeted therapies and uncovering the drug resistance mechanisms. **Keywords:** Reprogrammed Cell, Lung cancer,

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-102 Ex Vivo 4D Lung Cancer Model CTCs Show Resistance to Chemotherapeutic Drugs Dhruva K. Mishra[1], Min P. Kim[2] [1]*Surgery, Houston Methodist Research Institute, Houston/TX/United States of America,* [2]*Surgery, Houston Methodist Hospital, Houston/United States of America*

Background: Metastasis is the main cause of cancer-associated mortality. We recently developed an *ex vivo* 4D lung cancer model that mimics metastasis. One of the unique features of the model is its ability to isolate tumor cells in three different phases of cancer progression: primary tumors, circulating tumor cells (CTCs), and metastatic lesions. In this study, we want to further characterize the CTCs from the model and determine whether they enter a resting cell cycle phase, and conferring them to be resistant to chemotherapeutic drugs. **Methods:** We harvested rat lung and heart block and decellularized them using 0.1% sodium dodecyl sulfate and 1% Triton-X100. Acellular lung scaffolds were set up in a customized bioreactor and seeded with 50 million cells of human lung cancer cell line H1299 that were cultured on a petri dish (2D). Culture media was replenished and CTCs were collected daily. We measured and compared the cell cycle of 2D cells and CTCs using propidium iodide. Next, we tested the CTCs and 2D cells with 5 μM vinorelbine, 50 μM gemcitabine, 0.1 μM paclitaxel, or 10 μg/ml etoposide and measured total live cells after 2 days of culture. All analysis was performed using PRISM software and Student's t-test was used to compare the significance of variance. **Results:** Cell cycle analysis of CTCs from a 4D model seeded with H1299 cells showed a significantly higher population of cells in G0/G1, resting cell cycle phase, than in respective 2D cells (65% vs 49%, $p<0.01$). Furthermore, our results showed a significant decrease in 2D cells upon treatment with all chemotherapeutic drugs. There was a significantly smaller number of 2D cells in the treatment group when treated with gemcitabine ($p<0.0001$), paclitaxel ($p=0.01$) and etoposide ($p<0.0001$) and vinorelbine ($p=0.006$) than in the control group. On the other hand, there was no significant effect of drugs on the total live CTCs from the 4D model with H1299 that were treated with all four drugs on a 96-well plate as compared to the untreated control group. For H1299 CTCs, there was no significant difference in the number of cells when treated with gemcitabine ($p=0.38$), paclitaxel ($p=0.828$), and etoposide ($p=0.162$), while there were significantly more CTCs with the vinorelbine treatment ($p=0.04$) compared to the control group. **Conclusion:** Overall, our results show that CTCs from the 4D model are different from parental 2D cells that were placed in the 4D model. These CTCs enter the G0/G1 phase, which may confer resistance to chemotherapeutic agents that are cell-cycle-dependent in efficacy. Further characterization of the CTCs from the model may provide the mechanism of the cell cycle arrest and chemotherapy resistance. **Keywords:** 4D model, Circulating tumor cells, Chemotherapy resistance, Cell cycle

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P1.04-103 Oncolytic Virus Therapy for Lung Cancers Using a Genetically Engineered Oncolytic Herpes Simplex Virus Type 1 G47Δ Yoshinori Sakata[1], Yasushi Ino[2], Tomoki Todo[2], Norihiko Ikeda[3] [1]*Thoracic Surgery, Tokyo Medical University, Tokyo/Japan,* [2]*1Division of Innovative Cancer Therapy, The Institute of Medical Science, the University of Tokyo, Tokyo/Japan,* [3]*Tokyo Medical University Hospital, Tokyo/Japan*

Background: Lung cancer is the leading cause of cancer deaths in Japan and worldwide. Despite recent advances in targeted therapy, long-term survival of patients with lung cancer remains poor. Novel treatment approaches are needed to extend survival of these patients and improve control of this disease. Oncolytic virus therapy is a promising therapy for various tumor types. A third generation oncolytic herpes simplex virus type 1 (HSV-1), G47Δ, has been tested in clinical trials in Japan for glioma, prostate cancer, and olfactory neuroblastoma. In this study, we investigated the potential of G47Δ as a new therapeutic modality for human lung cancer. **Methods:** Human lung cancer cell lines A549 (adenocarcinoma), EBC-1 (squamous cell carcinoma), LU99 (large cell carcinoma) and SBC-3 (small cell carcinoma) were used. Infectivity and cytopathic effects of G47Δ on lung cancer cell lines were assayed in vitro. Viral replication was determined by standard viral plaque assay. For in vivo studies, athymic mice harboring established subcutaneous tumors and lung tumors generated with A549 or EBC-1 were used. **Results:** All cell lines were susceptible and sensitive to G47Δ irrespective of histological types. Viral replication assay resulted in approximately a 200-fold increase in virus titer by 48 h. In subcutaneous xenograft models, intraneoplastic inoculations with G47Δ significantly inhibited the tumor growth compared with those with mock. In orthotopic xenograft models, intrapleural inoculations with G47Δ prolonged the survival time. **Conclusion:** Oncolytic HSV-1 G47Δ was effective in human lung cancer cell lines. Direct intratumoral inoculation of G47Δ induced an obvious therapeutic effect on lung cancer, suggesting G47Δ may be a potent therapeutic modality for all histological types of lung cancer. **Keywords:** herpes simplex virus, Oncolytic virus therapy

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P1.04-104 Lung Cancer Patients Derived Xenografts: Prospective Molecular Profiling and Potential Evaluation of Drug Resistance Teresa Mele[1], Silvia Novello[1], Francesca Cottino[2], Marco Busso[1], Diego Sardo[1], Francesco Guerrera[3], Enrico Ruffini[3], Elena Asteggiano[4], Luisa Delsedime[5], Luisella Righi[1], Andrea Bertotti[6], Giorgio V.V. Scagliotti[1], Livio Trusolino[6] [1]*Department of Oncology, University of Turin, Orbassano/ Italy,* [2]*Candiolo Cancer Institute – Fpo Irccs, Candiolo/Italy,* [3]*Department of Surgery, Section of Thoracic Surgery, University of Turin, Turin/Italy,* [4]*Department of Thoracic Surgery, University of Turin, Orbassano/Italy,* [5]*Department of Medical Sciences, University of Turin, Turin/Italy,* [6]*Department of Oncology, University of Turin, Candiolo/Italy*

Background: The discovery of "driver mutations" such as the Epidermal Growth Factor Receptor (EGFR) and the Anaplastic Lymphoma Kinase (ALK) has led to a remarkable improvement in the outcomes of lung adenocarcinoma, which accounts 50% of the non-small cell lung cancer (NSCLC) diagnoses. Up today, no *druggable* molecular targets have been identified for squamous carcinoma or small cell lung cancer, which are still treated with the "*one-fits-all*" therapeutic approach, as it is for a relevant percentage of adenocarcinomas too. The precise definition of molecular profile and, possibly, the description of predictive factors are research priority in the thoracic oncology field. The vast majority of preclinical data are based on *in vitro* studies, but cell lines models do not entirely reflect tumour characteristics and are hampered by genetic divergence from primary tumours. Patient derived tumour xenografts (PDTX) are a valuable alternative to closely reproduce tumour biology and to prospectively characterize *in vivo* mechanisms of cancer growth and therapeutic response. Through the generation of a cohort of lung cancer xenopatients, the project aims to confirm the reliability of such models in this disease and to prospectively characterize its biomolecular features. **Methods:** Metastatic and early stages lung cancer cases are considered for the enrolment. Written informed consent is requested from each patient. Fresh tumour tissue from lung biopsies or lung resections is collected and kept in serum free medium (4° C), embedded in 20% matrigel

and subcutaneously engrafted into NSG and NOD SCID mice, within 24 hours from sample collection. The exponentially growing tumours are passaged subcutaneously to other mice for a second passage after which they are archived for subsequent analyses (formalin fixed, snap frozen and RNA later). Each sample from surgical resection is also stored to create a DNA lung cancer bank. **Results:**Fourteen samples from TC-guided lung biopsies and sixty-six from radically resected NSCLC were engrafted in NSG and NOD SCID mice lineage in a 1:1 ratio. Due to the low engraftment rate and high morbidity observed in NGS mice in the first 73 samples, subsequent engraftments and expansions were performed in NOD SCID mice only. The overall engraftment rate in biopsy samples was 0 % in NGS and 7.14 % in NOD SCID mice as opposed to 0 % in NGS and 27,27 % in NOD SCID for surgical samples (50% adenocarcinomas, 44,45% squamous carcinomas and 5,55% sarcomatoid carcinomas). Nineteen samples underwent the second passage: of those, 10 samples have been archived after the second successful passage and will be used for further analyses. **Conclusion:** The trial is still ongoing and a longer follow-up is needed. In biopsy-derived samples, engraftment is deeply limited by the paucity of tissue. The results of this study will possibly confirm the reliability of PDTX in lung cancer and provide prospective biomolecular characterization for different histological types. **Keywords:** lung cancer mouse models, lung cancer, patient derived tumour xenografts

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P1.04-105 The Development and Assessment of Advanced Cellular Models for the Study of Non-Small Cell Lung Cancer Sarah-Louise Ryan[1], Anne-Marie Baird[2], Anthony Davies[1], Kenneth J. O'Byrne[3] [1]*Translational Cell Imaging Queensland, Queensland University of Technology, Brisbane/QLD/Australia,* [2]*Cancer Ageing and Research Program, Queensland University of Technology, Brisbane/Australia,* [3]*Cancer and Ageing Research Program, Princess Alexandra Hospital and Queensland University of Technology, Brisbane/Australia*

Background: The key mechanisms that underlie drug resistance in lung cancer have yet to be fully elucidated. A significant limiting factor is the lack of biologically relevant cellular models for basic laboratory research. To address these issues, many are now turning to three-dimensional (3D) based cellular assay systems that permit the formation of multicellular structures such as tumour spheroids. Depending on their size the internal microenvironment of these structures mimics closely that of those *in vivo*. In the majority of cases, spheroids with a diameter greater than 100µm exhibit an asymmetry in cellular proliferation and viability - proliferating tumour cells at the periphery; cell-cycle arrested cells at larger distances from the surface. Regions of necrosis associated with reduced oxygen tension and hypoxia have often been reported. This study compared drug resistant models of non-small cell lung cancer (NSCLC) in 3D culture with those in grown in two-dimensional (2D) culture. The behaviour of cells grown in these distinct geometric configurations was monitored and compared by measuring viability, proliferation and oxygen tensions. **Methods:** Happy Cell Advanced Suspension Medium™ (ASM) was chosen to culture our 3D spheroids. This polymer-based formulation was selected for its ease of use, as well as its compliance with liquid handling, high content imaging and analysis (HCSA) and high throughput screening (HTS) systems. Isogenic NSCLC cell line models of cisplatin resistance were cultured in 2D and 3D cell culture systems. Cisplatin sensitive (Pt) and isogenic cisplatin resistant (CisR) NSCLC sub-types were studied. IC50 values were calculated and a positive control was selected. All cultures were grown in a range of cisplatin concentrations for 72 hours. Subsequently, viability and hypoxia assays were conducted in order to compare the response of Pt and CisR cells in both 2D and 3D culture systems. Morphological analysis was performed via high content analysis (HCA) and confocal microscopy. **Results:** At equivalent cisplatin concentrations 3D spheroids exhibit greater resistance compared with monolayers. Imaging experiments have shown that these 3D structures have a central necrotic core, a feature of the asymmetric growth patterns associated with 3D structures. **Conclusion:** Happy Cell ASM is a novel 3D culture medium for generating multicellular tumour spheroids and has potential for HTS and HCSA. When treated with cisplatin our spheroids exhibited resistance to therapy compared to 2D monolayer cultures. These results suggest that spheroids may provide a more accurate *in vitro* model to elucidate mechanisms of drug resistance and may aid the identification of novel targets to re-sensitise patient therapy. **Keywords:** 3D Cell Culture, drug resistance, Multicellular tumour spheroids, non-small cell lung cancer

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P1.04-106 Granulocyte Colony-Stimulating Factor Enhances the Anticancer Effects of Cisplatin Against Lung Cancer by Promoting Angiogenesis Yasushi Ohno[1], Toshiyuki Sawa[2], Sayaka Toyoshi[1], Daizou Kaito[1], Koumei Yanase[1], Fumitaka Ito[1], Junki Endo[1], Megumi Morishita[1], Masahiro Asano[1], Hidenori Mori[1], Shinya Minatoguchi[1] [1]*Respirology, Gifu University, -/Japan,* [2]*Respirology, Gifu Municipal Hospital, -/Japan*

Background: G-CSF is a hematopoietic growth factor which enhances the proliferation and differentiation of neutrophil precursor cells. However the results of studies on G-CSF-induced tumor growth are controversial. Recently, some studies reported that G-CSF stimulates the growth of tumor cells such as colon cancer cells, small lung cancer cells , skin carcinoma cells and astrocytoma cells, In contrast, Brandstetter et al. reported that G-CSF does not exhibit any effect on the proliferation of ovarian carcinoma cell lines or tumor samples despite presence of the G-CSF receptor in the tested cell lines and biopsies. **Methods:** In vitro effects of G-CSF on tumor cell proliferation. Two mouse non-small lung cancer cell lines, Lewis lung cancer cell line (LL-2) and KLN-205 were grown in DMEM medium with FBS. In vivo evaluation of the effects of G-CSF on tumor growth. Seven week-old male C57BL/6 mice were purchased from CLEA Japan . LL-2 cancer cells were grown in culture, harvested and subcutaneously injected as a suspension into the C57BL/6 mice in the proximal dorsa midline. The mice were randomized into 4 groups, group 1) saline control, 2) G-CSF alone, 3) CDDP alone and 4) CDDP plus G-CSF group. The mice were injected 5 mg/kg CDDP intraperitoneally 2 hours after tumor cell transplantation and then, were given 5 mg/kg CDDP intraperitoneally each week. Two hours after CDDP or saline injection, the mice were given 30 mµg/kg G-CSF or the same volume of saline intraperitoneally each day, and 21 days after tumor cell transplantation they were sacrificed and the tumors were removed. **Results:** We found that LL-2 and KLN-205 cell proliferation was unchanged significantly in the presence of various concentrations of G-CSF. To ensure that the results were due to the absence of the G-CSF receptor,we investigated the G-CSF receptor mRNA in these two cell lines by RT-PCR.Groups of mice were intraperiotoneally given 5mg/kg CDDP or saline per week starting 2 hours after tumor cell transplantation. Then, 2 hours after CDDP or saline injection the mice were intraperitoneally given 30m µg/kg G-CSF or saline per day. Tumor growth was markedly inhibited in the CDDP and CDDP+G-CSF treatment group compared with the saline control group. Concurrent administration of G-CSF significantly enhanced the tumor suppressing effect of CDDP in early stage tumor growth. 7 days after tumor cells transplantation, the tumor volume were 6.84±9.07 for CDDP plus G-CSF treatment VS 16.34±10.29 mm3 for CDDP alone (p=0.047). **Conclusion:** In summary, our results provide evidence that G-CSF as a growth factor does not promote tumor cell proliferation. Concurrent (Combination) administration of G-CSF significantly enhances the tumor suppressing effect of CDDP in early stage tumor growth. Thus, concurrent (combination) administration of G-CSF with anticancer agents is a safe and effective method for reducing chemotherapeutic agent-induced myelosuppression. In spite of further studies are required to determine whether this effect of G-CSF is a common feature against lung cancer and the solid tumors of the other organs, in this time, our study suggested a novel importance of G-CSF treatment against cancer therapy. **Keywords:** G-CSF, lung cancer, CDDP, proliferation

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P1.04-107 Prediction of Molecular Tageting Drugs' Sensitivity Enabled by In-Vitro Drug Sensitivity Tests for Surgically Resected Lung Cancer Ryohei Miyazaki, Takashi Anayama, Kentaro Hirohashi, Hironobu Okada, Motohiko Kume, Nobutaka Kawamoto, Kazumasa Orihashi *Thoracic Surgery, Kochi Medical School, Kochi University, Kochi/Japan*

Background: The molecular target anticancer drugs such as EGFR-TKI and ALK inhibitor have dramatically changed the strategy of medical treatment for lung cancer. The investigation of each driver mutation is recommended to pick up the responder to the corresponding molecular targeting drugs. In-vitro anticancer drug sensitivity tests such as succinate dehydrogenase inhibition test (SDI) and the collagen gel-droplet embedded culture drug sensitivity test (CD-DST) are able to examine the sensitivities of the surgically resected fresh cancer tissue to multiple cytotoxic chemotherapeutic drugs at one time. We develop the method to predict the effect for multiple molecular targeting drugs for individual lung cancer patient by applying CD-DST or SDI. **Methods:** Firstly, we titrated the growth inhibitory effect of the molecular targeting drugs on cultured lung cancer cell lines (H460, A549, HCC827, H1975, H3122) using SDI and CD-DST. Secondly, we evaluated sensitivity of surgically resected cancer tissues obtained from 33 lung cancer patients to Erlotinib by using SDI or CD-DST. Finally, we compared the drug sensitivity and EGFR mutation profile. **Results:** Both Erlotinib and Crizotinib exhibited significantly stronger growth inhibitory effects on lung cancer cell lines with target gene alterations than the others without driver mutation or with T790M-mediated resistance to EGFR-TKI. In clinical study using SDI (n=21), 20µM of Erlotinib inhibited cell growth more in EGFR mutant cases (60.0 ± 9.8(%)), than in wild type EGFR cases (86.8 ± 13.9 (%)) (p = 0.0004). The area under the curve (AUC) of receiver operating characteristic (ROC) curve was 0.958 for cell viability. The ratio showed best combination of sensitivity and specificity for prediction of drug sensitivity at values >72.7 (93.3% sensitivity and 100% specificity). By using CD-DST method (n=12), the cell viabilities were 33.5 ± 21.2(%) in EGFR mutants, and 79.0 ± 18.6(%) in wild type EGFR cases (p = 0.026). The AUC of ROC was 0.963 for cell viability. The ratio showed best combination of sensitivity and specificity for prediction of drug sensitivity at values >55.9 (88.9% sensitivity and 100% specificity) **Conclusion:** The growth inhibitory effects of Erlotinib evaluated by both SDI and CD-DST were correlated with EGFR mutation profile. *In-vitro* drug sentivity tests may be able to predict the clinical effect of molecular targeted drugs. **Keywords:** molecular tageting drug, CD-DST, SDI, lung cancer

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P1.04-108 Non-Invasive Assessment of Cisplatin and Erlotinib Efficacy in Lung Cancer by Monitoring an Orthotopic SCID Mouse Model with Computed Tomography Tamaki Otani[1], Kazuya Kondo[2], Hiromitsu Takizawa[2], Koichiro Kajiura[2], Haruhiko Fujino[2], Hideki Otsuka[1] [1]*Tokushima University, Tokushima/Japan,* [2]*University Tokushima, Tokushima/Japan*

Background: Orthotopic models are likely to provide more relevant pharmacokinetic and pharmacodynamic information than subcutaneous models. We established an orthotopically implanted SCID mouse model of lung cancer without thoracotomy. This model is simple and reproducible and many transplanted mice can be produced at once. The main disadvantage of the orthotopic model is that tumor size and volume changes are difficult to continuously monitor reproducibly and can only be assessed at necropsy. In this study, we evaluated the usefulness of small-animal computed tomography (CT) to non-invasively and repeatedly monitored the inhibitory effect of cisplatin and erlotinib on lung cancer in an orthotopic SCID mouse model. Our goal was to establish a standard model to evaluate efficacy of novel treatment regimens in lung cancer. **Methods:** We

created an orthotopic lung cancer transplantation model in mice. Suspensions of 2.0 × 10^4 cancer cells were injected into the left lung of SCID mice. We tested several non-small cell lung cancer cell lines, A549, FT821 and PC9 cells—only PC9 cells have an epidermal growth factor receptor (EGFR) mutation. We treated mice with cisplatin or erlotinib. When tumor volume had reached 1–3 mm^3, mice were divided into three groups: control, cisplatin and erlotinib. After treatment had begun, tumor volumes were evaluated by CT measurement every 3 days. All mice were sacrificed for histopathological analysis on day 18 after treatment began. **Results:** Mice implanted with A549, FT821 and PC9 cells were treated beginning on day 21, 50 and 35, respectively, after implantation. In mice transplanted with PC9 cells, tumor volume in the cisplatin group measured by CT was lower than in the control group, though not achieving statistical significance. In mice with A549 cells, tumor volume in the cisplatin group was similar to that in the control group. In mice with FT821 cells, tumor volume in the cisplatin group was significantly lower than in the control group. The mice in the cisplatin group showed temporarily decreased body weights. Histopathological analysis on day 18 after treatment showed necrotic lesions in lungs of mice transplanted with PC9 and FT821 cells but not in those with A549 cells. In mice with PC9 cells, which have a deletion of exon 19 in the EGFR gene, tumor volume in the erlotinib group was significantly lower than in the control group. In mice with A549 and FT821 cells, tumor volume in the erlotinib group was similar to that in the control group. There were no body weight changes in the erlotinib group. Histopathological analysis on day 18 after treatment showed necrotic lesions in lungs of mice implanted with PC9 cells but not in those with A549 and FT821 cells. **Conclusion:** This study supports using CT to monitor, non-invasively and repeatedly, tumor progression and therapeutic response of lung cancer in an orthotopic mouse model. This model is more analogous to the clinical condition than subcutaneously transplanted tumor models. Therefore, orthotopic tumor models have potential value as fundamental tools for the design and development of new therapies for cancer treatment. **Keywords:** orthotopic mouse model, Cisplatin, Erlotinib, computed tomography

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P1.04-109 Antitumor Efficacy of Histone Deacetylase Inhibitor or in Combination with EGFR-TKI in Non-Small Cell Lung Cancer Cell Lines Xiaohong Han, Ningning Zhang, Jiarui Yao, Yuankai Shi *Department of Medical Oncology, Cancer Institute and Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing Key Laboratory of Clinical Study on Anticancer Molecular Targeted Drugs, Beijing/China*

Background: To investigate the antitumor efficacy of histone deacetylase inhibitor (HDACi) or in combination with epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) in non-small cell lung cancer (NSCLC) cell lines. **Methods:**Ten NSCLC cell lines with varying mutation status were treated with chidamide (HDACi) and icotinib (TKI) alone or in combination. MTS assay was performed to determine IC_{50} of each drug or in combination. Cell cycle was analyzed by flow cytometry. Markers of epithelial-to-mesenchymal transition (E-cadherin), apoptosis (caspase-3, PARP) were determined by western blot. **Results:** The results demonstrated that A549 (TKI-resistant, KRAS-mutated), HCC827 (TKI-sensitive, EGFR-mutated), HCC827IR (TKI-resistant, EGFR-mutated) was sensitive to chidamide, the IC_{50} of these three cell lines was less than 0.5nM and the IC_{50} of the other seven cell lines was more than 5μM. Chidamide increased the sensitivity of icotinib synergistically in EGFR and KRAS wild type cells (H292, Calu-3), KRAS mutant cells (A549, H460), and TKI resistant EGFR mutant cells (H1650, H1650GR, HCC827IR, H1975), but the synergistic effect was most meaningful in H1975 (EGFR L858R and T790M mutation). We also found that H460 and Calu-3 had no E-cadherin expression, H1975 had low level of E-cadherin expression, and the other seven cell lines had relatively high levels of E-cadherin expression. Moreover, with the increasing dosage of chidamide, E-cadherin expression was significantly increased in H1975 cell line, but was not changed in chidamide sensitive cell lines. In addition, chidamide alone or in combination with icotinib could induce H1975 cell cycle arrest at G1/S phase, and reduce the expression of casepase-3 and PARP. **Conclusion:** These results suggest that chidamide as a single agent exhibits antiproliferative effectives in NSCLC cells with EGFR and KRAS mutations. The combination of chidamide and icotinib may be a beneficial treatment strategy for NSCLC with EGFR-T790M mutation. But the role of chidamide in the antiproliferative or synergistic mechanisms should be further explored **Keywords:** Epidermal growth factor receptor tyrosine kinase inhibitor, non-small cell lung cancer, histone deacetylase inhibitor, antitumor efficacy

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P1.04-110 Use of Blood Outgrowth Endothelial Cells as a Carrier of Oncolytic Vesicular Stomatitis Virus-Interferon Beta in Treating Metastatic NSCLC Yan Ji[1], Blake Jacobson[1], Manish Patel[1], Andrea Kratzke[1], Stephen Russell[2], Robert Kratzke[1] [1]*Hematology/Oncology/Transplant, University of Minnesota, Minneapolis/MN/United States of America,* [2]*Molecular Medicine, Mayo Clinic, Rochester/AL/United States of America*

Background: Oncolytic viruses have been extensively studies in the past two decades and are promising for cancer treatment. We have shown previously that vesicular stomatitis virus expressing interferon β (VSV-IFNβ) has oncolytic activity in vitro and in vivo in an immune competent mouse model of NSCLC. However, for treatment of metastatic NSCLC, intravenous delivery of VSV-IFNβ still faces several challenges, such as rapid clearance from bloodstream due to serum complement as well as sequestration in lymphoid tissue. In order to overcome these problems, we are exploring the potential role of blood outgrowth endothelial cells (BOECs) as carrier cells to deliver VSV-IFNβ to lung tumor sites. **Methods:** Efficacy of VSV-IFNβ-infected BOECs in transferring VSV-IFNβ to co-cultured human lung cancer cell lines in presence or absence of VSV antiserum were tested in vitro. A/J mice intravenously injected with LM2 non-small cell lung cancer cells were treated with PBS, VSV-IFNβ or VSV-IFNβ-infected BOECs (3 sequential treatments 3 weeks after tumor cell injection). Tumor growth, intratumor viral titer and survival were tested. **Results:** We demonstrated that VSV-IFNβ-infected BOECs can effectively transfer VSV-IFNβ to co-cultured human lung cancer cells and result in viral oncolysis even in the presence of VSV antiserum. In mice bearing metastatic lung cancer, BOECs injected via tail vein preferentially accumulated in lung tumor tissues, and were absent in either normal lung or liver tissues. Moreover, treatment with VSV-IFNβ-BOECs had higher and more sustained intra-tumoral viral titers comparing with those treated with either PBS or naked VSV-IFNβ. Furthermore, there was a trend (p=0.09) towards reduced tumor burden in the VSV-IFNβ-BOEC treated mice (n=5). Currently, we are testing the survival benefit of VSV virus in metastatic lung cancer model. **Conclusion:** In summary, the pre-clinical data showed promise to support developing a clinical protocol in the near future to assess the safety, response and efficacy of VSV-IFNβ-infected BOECs in treatment of metastatic lung cancer. **Keywords:** blood outgrowth endothelial cells, non-small cell lung cancer, vesicular stomatitis virus

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P1.04-111 Establishing a Mouse Model for Radiation-Induced Esophagitis Kyung Su Kim[1], Sanghyuk Song[1], Young-Eun Kim[2], Seong-Uk Jeon[2], Seoyeon Bok[2], Beom-Ju Hong[2], Chan-Ju Lee[2], Moon-June Cho[3], Hong-Gyun Wu[1], G-One Ahn[2], Hak Jae Kim[1] [1]*Department of Radiation Oncology, Seoul National University College of Medicine, Seoul/Korea,* [2]*Division of Integrative Biosciences and Biotechnology, Pohang University of Science and Technology (Postech), Pohang,Gyeongbuk/Korea,*[3]*Department of Radiation Oncology, Chungnam National University Hospital & Cancer Research Institute, Daejeon/ Korea*

Background: To establish mouse models of radiation-induced esophagitis with fractionated irradiation using BALB/c or C57Bl/6 mice **Methods:** Thoracic irradiation at 0, 8, 12, or 15 Gy was given daily for 5 days by 320 kV X-ray irradiator to anesthetized, 6 week-old male BALB/c (n = 4~5 per group) or C57Bl/6 mice (n = 4 per group). Changes in the body weight and daily food intake were assessed for both strains of mice. At day 11, BALB/c esophagus was harvested and examined for the following assays: (i) histology by H&E staining; (ii) Cytokine array (R & D Systems); (iii) fluorescence-activated cell sorting (FACS) analysis by using Annexin V and propidium iodide (PI); (iv) quantitative real time-PCR (qRT-PCR) (Life Technologies) analysis. **Results:** We observed that fractionated irradiation produced a significant body weight reduction in Balb/c mice (20% by 12Gy X 5 and 30% by 15 Gy X 5). In contrast, C57Bl/6 mice seemed to be more resistant to fractionation irradiation as they exhibited little change in the body weight. As food intake in Balb/c mice was also significantly decreased at these doses compared to the control mice ($p<0.05$ for 12 Gy X 5 and $P<0.01$ for 15 Gy X 5), dose of 12Gy x 5 were selected for all assays. Histopathology of irradiated Balb/c mice showed erosive epithelium, mucosal detachment, and leukocyte infiltration. FACS analysis confirmed that irradiated esophagus had increased number of apoptotic cells, as evidenced by Annexin V and PI double positivity. We found that cytokines for C5/C5a, Timp-1 (tissue-inhibitor of metalloproteinases-1), Ccl2/Mcp-1 (monocyte chemoattractant protein-1), and Il-16 (interleukin-16) were increased in the irradiated esophagus compared to non-irradiated esophagus. qRT-PCR analyses revealed that *Timp-1* as well as other genes involved in extracellular matrix remodeling including *Pai-1* (plasminogen activator inhibitor-1), *Gm-csf* (granulocyte macrophage-colony stimulating factor), *Vegf* (vascular endothelial growth factor), and *Sdf-1* (stromal-derived factor-1) were increased whereas *Egf* (epidermal growth factor), a potent mitogen for epithelial cells, was significantly decreased in the esophagus of irradiated mice. **Conclusion:** We established that BALB/c mice were more sensitive to fractionated irradiation than C57Bl/6 mice for developing symptoms reflecting radiation-induced esophagitis. In BALB/c mice, 12 Gy X 5 regimen seem to be the best schedule producing a significant reduction in the body weight and food intake, and histopathologic features similar to human esophagitis. Increased RNA transcripts for extracellular remodeling and cytokines indicate an active dynamics of tissue remodeling in the irradiated esophagus. Decreased *Egf* expression in the irradiated esophagus suggests that EGF may be a potential therapeutic strategy to treat radiation-induced esophagitis and we are currently investigating this strategy. **Keywords:** Mouse model, EGF, Radiation esophagitis, Fractionated radiation

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P1.04-112 Rapamycin Attenuated Epithelial-Mesenchymal Transition in Lung Cancer Cells Lianjun Lin[1], Xinmin Liu[1], Nanping Wang[2] [1]*The Geriatrics Department, Peking University First Hospital, Beijing/China,* [2]*Key Laboratory of Molecular Cardiovascular Science of Ministry of Education, Peking University Health Science Center, Beijing/China*

Background: Mammalian target of rapamycin (mTOR) plays an important role in the physiological regulation of cell growth and development. Dysregulation of mTOR signaling frequently occurs in malignancies, including lung cancer. Inhibition of mTOR is a promising therapeutic strategy against lung cancer shown by clinical trials. But its mechanism remains unclear. Epithelial–mesenchymal transition (EMT) is critical in the pathogenesis of lung carcinoma. This study aimed to examine the effect of rapamycin on TGF-β1-induced EMT in lung carcinoma cells. **Methods:** Lung carcinoma cells (A549 cells) were pre-incubated with rapamycin and stimulated with TGF-β1. Morphological changes were observed under microscope. Cell phenotype markers were analyzed by western blotting and immunocytochemistry. F-actin cytoskeleton rearrangement was examined by phalloidin staining. Cell migration ability was measured by cell scratch test. The phosphorylated Smad2/3 and mTOR were measured by western

blotting. **Results:** Firstly, TGF-β1 induced EMT in lung carcinoma cells confirmed by the morphological changes, as well as the down-regulation of epithelial marker (E-cadherin) and the up-regulation of mesenchymal marker (fibronectin) and the F-actin cytoskeleton rearrangement during which the mTOR pathway was activated. Secondly, rapamycin decreased the degree of TGF-β1 induced morphological changes, attenuated the down-regulation of E-cadherin and up-regulation of fibronectin, and inhibited the F-actin cytoskeleton rearrangement. Moreover, rapamycin inhibited the migration ability of lung carcinoma cells. Further research on mechanism showed that the attenuation TGF-β1-induced-EMT by rapamycin was associated with the down-regulation of the phosphorylation of Smad2/3. **Conclusion:** Rapamycin attenuated TGF-β1- induced EMT and migration in lung carcinoma cells which was mediated, at least in part, by decrease of Smad2/3 phosphorylation.

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-113 Nonclinical Development of PF-06439535, a Potential Biosimilar to Bevacizumab Karen Rule[1], Marjorie Peraza[1], Michael Shiue[2], Gregory Finch[3], Stéphane Thibault[2], Julie A. Rosenberg[3], Michael W. Leach[1] [1]*Pfizer Inc, Andover/MA/United States of America,* [2]*Pfizer Inc, San Diego/CA/United States of America,* [3]*Pfizer Inc, Groton/CT/United States of America*

Background: Bevacizumab is a recombinant, humanized, IgG1 monoclonal antibody that binds to and inhibits the activity of vascular endothelial growth factor (VEGF), and is approved to treat a variety of advanced solid tumors. PF06439535 is under development as a potential biosimilar to bevacizumab. **Methods:** Amino acid sequences of PF06439535 and EU and USsourced bevacizumab (bevacizumabEU and bevacizumabUS, respectively) were compared by peptide mapping; post-translational modifications and biochemical properties were analyzed by N-linked oligosaccharide profiling and imaged capillary electrophoresis. Functional analysis of PF06439535, bevacizumabEU, and bevacizumabUS included an enzyme-linked immunosorbent assay to detect binding to the 4 major VEGF isoforms ($VEGF_{121}$, $VEGF_{165}$, $VEGF_{189}$, $VEGF_{206}$), and a cell growth inhibition assay in human umbilical vein endothelial cells (HUVEC). Toxicokinetics and potential toxicity of PF06439535 and bevacizumabEU were evaluated following intravenous (IV) administration (10 mg/kg twice weekly for 1 month, 9 doses total) in sexually- and skeletally-immature male cynomolgus monkeys; control animals received vehicle. **Results:** PF06439535, bevacizumabEU, and bevacizumabUS had identical primary amino acid sequences and similar levels of N-linked oligosaccharides. Predominant charge isoforms were similar; charge heterogeneity was due to variations between PF06439535 and reference products in relative proportions of species with C-terminal lysines. Target binding to each VEGF isoform showed similar dose responses between PF06439535, bevacizumabEU, and bevacizumabUS; comparable biological activity was observed by inhibition of VEGF-induced HUVEC proliferation. In cynomolgus monkeys, PF06439535 and bevacizumabEU (n=4 each) were well tolerated, with no PF06439535- or bevacizumabEU–related clinical, laboratory, or histopathology findings, except physeal dysplasia of the distal femur with similar incidence and severity for both molecules. Induction of antidrug antibodies was not observed in the PF06439535- or bevacizumabEU–dosed groups. Systemic exposure (mean area under the serum drug concentration–time curve from 0 to 72 hr ± standard deviation) was similar for PF06439535 and bevacizumabEU on Day 1 (12100 ± 876 vs 14700 ± 2260 µg·hr/mL) and Day 25 (45500 ± 5420 vs 45100 ± 3670 µg·hr/mL). **Conclusion:** Results from the analytical similarity assessments and nonclinical studies have supported the clinical development of PF06439535 as a potential biosimilar to bevacizumab. These data supported a randomized, double-blind phase I study (NCT02031991) in healthy human male volunteers in the United States, which assessed pharmacokinetics, safety, and immunogenicity of a single 5 mg/kg IV dose of PF06439535, bevacizumabEU, or bevacizumabUS. A global, randomized phase III trial (NCT02364999) comparing PF06439535 and bevacizumabEU, plus paclitaxel/carboplatin, for first-line treatment of advanced non-squamous nonsmall cell lung cancer is enrolling patients. **Keywords:** PF-06439535, bevacizumab, biosimilar, NSCLC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-114 Effect of Interleukin-2 Treatment Combined with Magnetic Fluid Hyperthermia on Lewis Lung Cancer-Bearing Mice Runlei Hu[1], Shenglin Ma[2] [1]*Department of Thoracic Surgery, Hangzhou First People'S Hospital, Hangzhou/China,* [2]*Department of Radiation Oncology, Hangzhou First People'S Hospital, Hangzhou/China*

Background: The study aimed to investigate the therapeutic effect of interleukin-2 (IL-2) treatment combined with magnetic fluid hyperthermia (MFH) on Lewis lung cancer-bearing mice. **Methods:** Magnetic fluids were prepared in vitro and directly injected into the tumors in the mice, which were subjected to an alternating magnetic field. The temperature in the tumor reached 43°C and was maintained by controlling the strength of magnetic field for 30 minutes. Twenty-four hours later, IL-2 was injected directly into the tumors. Mice were divided into four groups: group I (control), group II (MFH), group III (IL-2), and group IV (IL-2+MFH). **Results:** The tumor grew gradually in group II and group IV (both P<0.05) compared to the control group. Histological analysis showed that the tumor cells underwent apoptosis and necrosis. Immunohistochemistry results demonstrated that heat shock protein 70 (HSP70) and CD8-positive T cells were strongly expressed. **Conclusion:** The results have provided evidence that IL-2 treatment combined with MFH could improve the therapeutic effect on lung cancer-bearing mice **Keywords:** lung cancer, magnetic fluid, hyperthermia, interleukin-2

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P1.04-115 Chemoterapy and Targeted Therapy Sensitivity Testing in Malignant Pleural Effusions Safiye Aktas[1], Pınar Ercetin[1], Banu Demir[1], Ayca Pamukoglu[1], Begum Gorgulu[1], Zekiye Altun[1], Atila Akkoclu[2] [1]*Dokuz Eylul University Faculty of Medicine, Izmir/Turkey,* [2]*Dokuz Eylul University Medical Faculty, Izmir/Turkey*

Background: Clinical management of malignant pleural effusions (MPE) is a major problem in oncology with short survival. MPE is caused by various types of malignancies, especially lung, breast carcinomas, lymphomas besides ovarian carcinoma, malignant melanoma. Intrapleural chemotherapy might be a helpful treatment strategy in MPE cases. Intrapleural chemotherapy also enters systemic circulation and affects the primary tumor as well. The aim of this study is to evaluate ex vivo chemoterapy and targeted therapy sensitivity in MPE cases to project which drug might be effective. **Methods:** Effusion fluids from patients with MPE were fresh obtained. After centrifugation, the pellet was diluted in PBS and cell isolation was performed by Ficoll gradient to separate cells from erytrocytes. Cells were incubated in HITES supplemented complete RPMI medium at 37C with 5%CO2. After primary cell culture was obtained, cells were incubated to 96 well plates and agents (Bevacuzimab, Cetuximab, Rituximab, Bortozemib, Gemsitabin, Vinblastin, Bleomycin, Docetaxel, 5 Florourasil, Cisplatin, Cyclophosphamide, Doxorubicine) in different dose ranges for 24 hours. WST-1 was performed to check cell viability. **Results:** The primary tumors of nine cases in this study with MPEs are breast carcinomas, lung adenocarcinoma, small cell carcinoma and mantle cell lymphoma. Resistance were observed in most drugs. Breast carcinoma cells and lung adenocarcinoma cells were sensitive to cisplatin and/or vinsblastin. Small cell carcinoma cells were sensitive to docetaxel and/ or bleomycin. Sensitivity was not observed to targeted therapy agents at single dose during 24 hours incubation. **Conclusion:** Our results indicate that ex vivo cancer cell culture and testing cell death results of various chemotherapoetic and new targeted drugs might help managing highly agressive disease of patients with MPE. Intrapleural chemotherapy application that is found sensitive by ex vivo tests might help patients. **Keywords:** Malignant pleural effusions, Intrapleural chemoterapy and targeted therapy, ex vivo sensitivity testing

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.04-116 The Role of JAK/STAT3 Signaling Pathway on Apoptosis of Lung Adenocarcinoma Cell Line PC-9 Induced by Icotinib Yuping Zhang[1], Xia Meng[1], Hongyang Shi[1], Wei Li[1], Zongjuan Ming[1], Yujie Zhong[1], Wenjing Deng[1], Qiuhong Zhang[1], Na Fan[1], Zequn Niu[1], Guo'An Chen[2], Shuanying Yang[1] [1]*Department of Respiratory Diseases, the Second Affiliated Hospital, Medical College, Xi'An Jiaotong University, Xi'An/China, Xi'An/China,* [2]*Toracic Surgery Section, Department of Surgery,University of Michigan, Ann Arbor, Michigan/American Samoa*

Background: The aim of the study is to estimate the role of JAK/STAT3 signaling pathway on apoptosis of lung adenocarcinoma induced by icotinib. **Methods:** EGFR mutation was detected in lung adenocarcinoma cell line PC-9 by ARMS assay; The inhibitory rates of cell proliferation, at different concentrations (0 ~ 100 umol/L) of icofinib and continued incubating for 24, 48 and 72 h respectively, were evaluated by MTT assay; Apoptosis of PC-9 cells exposured to different concentrations of icotinib(0, 0.1, 1 and 10 umol/L) for 48 h were evaluated by TUNEL assay; JAK2, STAT3, Bcl-2, Bax mRNA expressions were evaluated by Real-time PCR assay; The protein levels of P-STAT3 and IL-6 were evaluated by Western-blot assay. **Results:** Human lung adenocarcinoma cell line PC-9 had an exon 19 deletion mutation in EGFR gene; Followed by treatment of icotinib, the proliferation of PC-9 cells were all inhibited significantly, especially in 48 and 72 h (P<0.01) in all concentrations; The inhibitory rates of cell proliferation in different treating time had statistical significance (P<0.01); Cell apoptosis at different concentrations were increased significantly (P<0.05); Along with the increasing concentrations, gen expression levels of JAK2, STAT3 and Bcl-2 decreased significantly (P<0.05), Bax increased significantly (P<0.05), JAK2/STAT3 ratios increased significantly (P<0.01), and Bcl-2/bax ratios decreased significantly (P<0.01); P-STAT3 and IL-6 protein levels were inhibited significantly at by higher concentration. **Conclusion:** JAK/STAT3 signaling pathway take a participate in apoptosis of PC-9 cells induced by icotinib. The most likely mechanism is icotinib inhibited the gen expression levels of JAK2, STAT3 and Bcl-2, so with the P-STAT3 and IL-6 protein levels, and mediated gene Bax overexpression. **Keywords:** icotinib, JAK/STAT3 signaling pathway, apoptosis, lung adenocarcinoma

SESSION: POSTER SESSION/ PREVENTION AND TOBACCO CONTROL MONDAY, SEPTEMBER 7, 2015

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.05-001 Rural Tobacco Smoke Pollution: Preliminary Results of a Longitudinal Study Kelly Buettner-Schmidt[1], Blake Boursaw[2], Marie L. Lobo[2] [1]*Department of Nursing, North Dakota State University, Fargo/United States of America,* [2]*University of New Mexico, Albuquerque/NM/United States of America*

Background: In 2012, North Dakota enacted a comprehensive smoke-free law. In 2014, the 3rd phase of a stratified random sample longitudinal study of tobacco smoke pollution in restaurants and bars was conducted (n = 107). Phase 1 was conducted prior to passage of the law, Phases 2 and 3 were conducted 3 and 21 months post-implementation respectively.

Methods: Tobacco smoke pollution levels were assessed by collection of particulate matter 2.5 microns aerodynamic in diameter or smaller using SidePak TM AM510 Personal Aerosol Monitors. **Results:** The geometric mean $PM_{2.5}$ was 6.9 microns/m^3. Statistically significant reduction in mean $PM_{2.5}$ occurred from Phases 1 to 3 but not from Phases 2 to 3 in all venues and for bars alone. A significant increase in indoor $PM_{2.5}$ occurred when there was outdoor smoking or ashtrays within 20 feet of the venue entrance, exit, or windows and when smoking was observed within designated outdoor smoking shelters. Multi-level linear models found that the presence of a local ordinance and venue type were predictors of $PM_{2.5}$ in Phase 1 but not in Phases 2 or 3. Significant decreases in mean $PM_{2.5}$ by rurality occurred between Phases 1 and Phase 3. In contrast with the Phase 1 study, there were no significant differences in $PM_{2.5}$ by rurality in only Phase 3. **Conclusion:** This longitudinal study is the largest rural pre and post-law rural study known globally. Passage of the comprehensive statewide smoke-free law effectively reduced $PM_{2.5}$ levels in restaurants and bars statewide. **Keywords:** compliance, pollution, Policy

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.05-002 Comparative Study regarding Perception of Japanese Tobacco-Related Disease Risk Warning Package Message Tomoyasu Uno *Health Care Center, Fukushima University, Fukushima-City/Japan*

Background: There are two types of tobacco warning messages in Japan, category A is Direct disease for smoker-themselves, category B is for other person (e.g. Nuisance around, The risk in pregnancy). Previously, we had reported that awareness of COPD is low in who visited to a certain hospital. Recognition rate is slowly increasing, however, still been not satisfactory. Assessment studies and discussions for the impact of health warnings knowledge about tobacco risks are ongoing in worldwide. However, it is insufficient since 2005. So, in this survey aimed at improvement of present condition, especially, we evaluated about the recognition of tobacco package warning messages for the smokers themselves. **Methods:** The questionnaire for our university employees[n=132, 44.6±11.6 yrs, Male(M)/Female(F)= 60.6/39.4] (Group B) and students[n=641, 20.4±1.6 yrs, M/F=53.4/46.6] (Group C) was performed. As the control subject was our previous report cases [n=335, 62.2±12.2yrs, M/F=55.6/44.0] (Group A). In particular, we evaluated about the recognition of the smokers themselves (Category A), I: Cause of lung cancer, II: Risk of cerebral stroke, III: Risk of myocardial infarction, IV: Risk of deteriorating pulmonary emphysema. **Results:**

Characteristics and Knowledge of Warning Risk Massage (*Multiple answers act)			
	A	B	C
N	335	132	641
Age(yrs±SD)	62.2±12.2	44.6±11.6	20.4±1.6
Sex[M/F] (%)	55.6/44.0	60.6/39.4	53.4/46.6
Smoking history(%)			
Current	24.3	8.3	8.4
Ex	34.3	25.0	5.6
Never	41.4	66.7	80.6
Knowledge of Warning(%)*			
I	49.2	60.3	70.5
II	17.3	27.5	41.3
III	25.6	32.1	38.4
IV	28.9	25.2	43.7

Imbalance in the warning messages recognition was observed in all groups and "Risk of Lung cancer" knowledge was significantly higher than other diseases risk warning. Knowledge of Warning(%) [Multiple answers act, I/II/III/IV] was A: 49.2/17.3/25.6/28.9, B: 60.3/27.5/32.1/25.2, C: 70.5/41.3/38.4/43.7, respectively. And also the ratio is almost same between smoker and non-smoker. Especially, disparity in identical respiratory-related emphysema (≒ COPD) risk was conspicuous. On the other hand Category B messages is almost same recognition. **Conclusion:** These results were considered that source of the text size of tobacco package warning is small and mild. In addition, smoking is harm to health, nevertheless the knowledge of package warning ratio was not unified. Furthermore it was speculated that the elderly from the young adolescents who were not exposed to anti-tobacco msg and/or were not taught about the harmful effects. Therefore we should do more educate about the risk of warning the awareness of Smoking and COPD. Awareness of tobacco risk was poor, therefore the necessity of further education about stop-smoking was indicated. Last year, the agenda debate regarding risk of pulmonary emphysema msg will be change to COPD was started in Japan. We hope the change will be widespread and raise aware COPD. **Keywords:** Education, Imbalance recognition of tobacco, Risk Warning, lung cancer

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.05-003 Dutch Government Taken to Court by 2 Chest Physicians Because of Violation WHO FCTC 5.3 Wanda D. Kanter *Chest Oncology, Netherlands Cancer Institute, Amsterdam/Netherlands*

Background: The Youth Smoking Prevention Foundation is taking the Kingdom of the Netherlands to court to end the structural and excessive influence exerted by the tobacco lobby on government anti-smoking policies. The Foundation is calling on the Dutch government to comply fully with the anti-smoking convention (WHO FCTC), which it signed and which is therefore legally binding. One of the most important articles in the convention states that every form of influence by the tobacco industry on policies to deter smoking must be avoided. In the court summons issued, the Foundation offers dozens of examples that show how the government has systematically violated this provision, and even invites the tobacco industry to clarify its position on matters of policy development. **19,000 tobacco-related deaths** More than 19,000 Dutch people, half of them younger than 65, die each year as a result of smoking. In addition, an average of 120 children under the age of 18 start smoking every day. Some 60 of them will continue to smoke for the rest of their lives, and 30 of them will die prematurely from the effects of smoking. Smoking is by far the biggest cause of death that could be avoided through prevention. However, the marketing techniques deployed by the tobacco industry are so refined that many youths cannot resist the temptation to start smoking. Moreover, cigarettes are designed to be highly addictive. Children who start smoking end up addicted within weeks. For many of them, the question of 'free will' no longer applies: they are unable to stop smoking without help. Numerous national and international laws and conventions make it a duty of the Dutch government to protect the health of its citizens from a serious cause of illness like tobacco. With as many as 19,000 tobacco deaths every year, the government has an obligation to do all in its power to combat the massive scale of premature fatalities. And it should certainly prevent minors from starting to smoke, because almost nobody starts after they turn 18. Despite all this, the Dutch government has failed to implement measures that could be very effective in achieving results: imposing much higher taxes on tobacco and greatly reducing the current number of over 60,000 points of sale. Instead, the government listens to the tobacco industry, whose effective lobbying continues to successfully obstruct measures to discourage tobacco use. **Methods:** not applicable **Results:** ongoing lawsuit. **Conclusion:** The lawsuit is ongoing. Our foundation has had a lot publicity in all national media (television ,newspapers) As a chest physician working in an oncology center mainly treating patients with lungcancer it is very powerfull to start a lawsuit against the state to prevent lung cancer. We are making progress: we are at the table of several Ministries (finance, health department) to discuss the firewall protocol against the lobby of big tobacco. We use social media and patients advocates to make our message even stronger **Keywords:** WHO FCTC 5.3 bigtobacco lobby

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.05-004 Smoking Prevention Intervention with School Classes at a University Hospital by Thoracic Surgeon and Pulmonologist Macé Schuurmans[1], Sandra Tomaszek[2], Didier Schneiter[2], Walter Weder[2], Sven Hillinger[2] [1]*Pulmonology, University Hospital Zürich, Zürich/Switzerland,* [2]*Thoracic Surgery, University Hospital Zürich, Zürich/Switzerland*

Background: Smoking prevention in schoolchildren with the aim to inform and prevent smoking initiation has been widely studied and has shown variable results. Interventions provided by physicians in a hospital setting have been rarely reported. Here we show the feasibility and gain of knowledge of our smoking prevention project in a hospital setting. **Methods:** Interventions performed from November 2009 - December 2014 were evaluated. Overall 790 children participated in our preventive intervention. A 7-item questionnaire was provided to the school classes (Grades 6 to 10) before and after a two-hour smoking prevention intervention consisting of anatomical models, oral presentations, videos, patient interviews and hands-on lung function tests. The goal was to show the anatomical and physiological basics as well as age-based information about the harms of smoking. During the intervention the children have been motivated to be actively involved. Class selection has been performed for groups of children in a highly vulnerable phase of age before smoking initiation. **Results:** The baseline questionnaire was completed by 768 children, the one after intervention by 719. The knowledge about which organs are affected by smoking increased from 7.1-99.3% to 64.5-99.5% ($p<0.01$). While only 58.9% knew that only a minority of people is able to quit smoking successfully, 96.3% answered the question correctly after intervention ($p<0.001$). Prior to the intervention only 75.6% believed that minor tobacco consumption is not damaging which increased to 87.8% after the teaching session ($p<0.05$). Smoking hookah was believed to be less harmful than cigarettes by 32.2% of children decreasing to 8.3% after the intervention ($p<0.001$). **Conclusion:** Information on health effects provided by lung specialists in the hospital leads to a statistically significant increase in knowledge as assessed by a short questionnaire. The intervention is feasible and well received. This kind of interventions might help to prevent schoolchildren from smoking in a highly vulnerable phase of age. **Keywords:** smoking prevention, Tobacco Control, school children

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.05-005 Italian Multicentric Survey on Smoking Cessation in Lung Disease Patients and the Role of Healthcare Workers in This Contest Sara Demichelis[1], Simonetta G. Rapetti[1], Domenico Galetta[2], Arianna Bruno[3], Emilio Bria[4], Sara Pilotto[4],

Giuseppe Valmadre[5], Annamaria Catino[2], Martina Gianetta[1], Stefania Vallone[6], Maria Vittoria Pacchiana[1], Silvia Novello[1] [1]*Department of Oncology, University of Turin, Turin/ Italy,* [2]*Clinical Cancer Center "Giovanni Paolo Ii",, Bari/Italy,* [3]*Pulmonology Division, Hospital of Putignano, Putignano (Ba)/Italy,* [4]*Medical Oncology, University of Verona, Verona/ Italy,* [5]*Eugenio Morelli Hospital Aovv, Sondalo/Italy,* [6]*Walce, Orbassano (To)/Italy*

Background: Smoking is a risk factor for several lung diseases. Quitting smoking provides positive outcomes and gives the best chance for the treatment in patients with pulmonary diseases, including lung cancer diagnoses. Currently few centers in Italy offer counseling for smoking cessation in cancer patients (and for patients with other lung diseases), despite the demonstrated efficacy of it. **Methods:** 408 patients with pulmonary diseases (72% with lung cancer) were prospectively and sequentially evaluated from January 2013 to February 2015. An anonymous survey was developed with the aim to understand if current or former smoker patients received information by healthcare workers about smoking cessation before or after the diagnosis, their reaction and the actions adopted for quitting smoking. The survey included the Fagerström test for assessing the intensity of addiction to nicotine and it was conducted in several Italian Thoracic Oncology Units and Pulmonology Divisions. **Results:** After a pulmonary disease diagnosis, 72% of patients state to quit smoking, 20% to smoke less or not feel the same pleasure as before and only 8% confirms to continue to smoke or smoking even more. Among former smokers (298 people), 150 patients state how long they quitted smoking and in 45% of the cases was at the time of diagnosis or even later, about 35% 10 years before the diagnosis and 8% between 5 and 10 years earlier, while 12% more recently. Most of current smokers state that they continue because smoking helps them to control the stress, others because they like it or are not able to quit and very few because is a repetitive gesture. Data show that 39% of patients did not receive information about smoking cessation by health professionals, 26% received it before the diagnosis, 12% after it and 23% received it both before and after the diagnosis. Concerning the reaction to the counseling, 53% considers positively the health care provider action, even if 28% hoped they could have helped them more quit smoking and 19% reports a warning and paternalistic attitude of them. Only 23% of patients who attempted to quit smoking considers the gradual termination as the most effective measure, more than the sudden interruption. Regarding the smoking-cessation method or specific therapy adopted, 65% disclosed they simply quitted smoking overnight and 80% confirmed it as the most effective technique, while only 16% used electronic cigarettes, 8% a nicotine replacement treatment, 7% books and 4% attending a dedicated clinic. The Fagerström Test confirms that 50% has a low to moderate dependence to nicotine, while 50% has a high dependence. **Conclusion:** The survey was distributed to 293 lung cancer patients and 115 with pulmonary disease (mainly COPD patients). The result analysis underlines that the vast majority quitted smoking after having received their diagnosis. No main differences were seen evaluating the group with malignant and non-malignant diseases. Although many of them got advice by healthcare workers, the recourse to the use of techniques, drugs or access to specific clinic is still very low, especially considering that 50% of patients result highly dependent to nicotine.
Keywords: Smoking Cessation, counseling, lung disease, pulmonary disease

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.05-006 One Cigarette Takes 12.6 Minutes of Your Life Erik Thunnissen
Department of Pathology, VU University Medical Center, Amsterdam/Netherlands

Background: Smoking is the largest cause of premature mortality. Smoking cessation is important, but is difficult to reach. A general underestimation of personal risk in smokers or a degree of misunderstanding around key risk factors for disease may be substantial. [1]The aim of this abstract is to calculate the reduction in average life expectancy per cigarette. **Methods:** Men born in 1900-1930 who smoked only cigarettes and continued smoking died on average about 10 years younger than lifelong non-smokers. Cessation at age 60, 50, 40, or 30 years gained, respectively, about 3, 6, 9, or 10 years of life expectancy.[2]Assuming that these men started at age 15 years and died at age of 72 this results on average in 57 years of smoking. Also assumed is that each day one pack of 20 cigarettes is smoked. **Results:** Smoking for 57 years 20 cigarettes per day results in a total of 416,100 cigarettes. The total number of minutes in 10 years is 5,256,000. The average decrease in life expectancy is 12.6 minutes/ cigarette or 4.2 hours /pack, equals more than a day/week. Discussion: If a smoker is aware of the reduced life expectancy then smoking of one cigarette may be looked-upon as a mini-suicide attempt. Taken also into account the passive smoking effect, the smoker may be seen as a mini-suicide-nano-terrorist. **Conclusion:** Conclusion The reduction in average life expectancy is 12.6 minutes per cigarette or 4 hours per pack. This knowledge may be of help to raise more awareness for the dangers of smoking. 1. Bethea J, Murtagh B, Wallace SE. " I don ' t mind damaging my own body " A qualitative study of the factors that motivate smokers to quit. 2015;1–9. 2. Doll R, Peto R, Hall E, Wheatley K, Gray R. Mortality in relation to consumption of alcohol: 13 years' observations on male British doctors. BMJ. 1994;309(6959):911–8.

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
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P1.05-007 One-Stop Counselling, Social Support & Stop Smoking Aids Helps Smokers Quit Emmanuel Odiase *Epidemiology, University of Ibadan, Abuja/Nigeria*

Background: It has been a normal practice for governments, not-for-profits and other platforms to provide Quitlines to help smokers quit. There has been positive results, however a recent study shows that a one-stop platform can offer more desirable outcomes. **Methods:** We conducted a 6-month study through an online survey involving 1,200 smokers who visited a revolutionary one-stop smoking cessation online platform, www.quitgate.com.

After visitors ordered a product or called the Quitline, a questionaire was emailed to them. Questions asked included year of smoking initiation, number of cigarettes smoked per day and number of quit attempts and through what means. **Results:**Interestingly, 37% of the participants reported that they were motivated to quit because when they called the Quitline and received counselling from the Tobacco Treatment Specialist, they were immediately provided without obligation, the option of getting a smoking cessation product on same platform with either some of the product free or highly discounted. Another group, 11% said they prefered the platform to quit because it was social, friendly, professional, non-judgemental and yet non-clinical. Overall, most of the participants said it was a great idea to have a one-stop platform which provided free professional counselling, smoking cessation products, tools/apps like smoking calculator, DNA (Dependence on Nicotine Assessment) low prices, free shipping and premium customer service to highly motivate smokers quit for good. **Conclusion:** It is great to note that while Quitlines are provided by several institutions to help in smoking cessation, an important area of also making smoking cessation products availble either for free or a little amount will go a long way to motivate smokers. The Centers for Disease Control and Prevention-CDC cites evidence-based counseling, behavioral cessation therapies, medication, and social support as treatments that increase the chances of tobacco cessation
Keywords: Smoking Cessation, tobacco, one-stop platform, non clinical

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.05-008 Big Tobacco and the Creation of an Epidemic of Smoking-Related Adenocarcinoma of the Lung: SEER-Based Analysis, 1973-2011 Gary Strauss[1], Alejandro Moreno-Koehler[2], Matthew Finkelman[3] [1]*Hematology/Oncology, Tufts Medical Center, Boston/MA/United States of America,* [2]*Tufts Medical Center, Boston/MA/United States of America,* [3]*Tufts University School of Dental Medicine, Boston/MA/United States of America*

Background: When epidemiologic research first demonstrated an association between cigarette smoking and lung cancer in the early 1950s, adenocarcinoma comprised about 5% of lung cancers and appeared to be unrelated to smoking. In the 1960s and 1970s, adenocarcinoma increased sharply, and became strongly related to cigarette smoking. At the 2007 IASLC-sponsored 12th World Conference in Lung Cancer in Seoul, Korea, our group reported that by 2003, adenocarcinoma of the lung had risen to comprise 47% of all lung cancers in the US. The objective of this presentation is to update and expand upon our previous analysis. **Methods:** We analyzed time trends in lung cancer histology with changes in cigarette design and Tobacco Industry actions over six decades. We utilized Surveillance-Epidemiology and End Results (SEER) data on 419,941 lung cancers diagnosed between 1973 and 2011 to analyze time trends of age-standardized incidence rates of five histologic subtypes: adenocarcinoma, squamous cell, small cell, large cell, and adenosquamous carcinoma. **Results:** Over time, the percentage of lung cancers that were adenocarcinomas increased from 29% (in 1973-1974) to 55% (in 2010-2011). During this 38-year period, the percentage of lung cancers that were squamous cell carcinomas decreased from 41% to 26%. Among all patients, adenocarcinoma incidence surpassed squamous carcinoma by 1985-1989 to become the most common histologic subtype. Adenocarcinoma surpassed squamous cell in 1990-1994 in men, while it was already most common in women by 1973-1974. Adenocarcinoma rose 77% in men from 1973-1974 to 1990-1994, while it rose 197% in women between 1973-1974 and 2005-2006. Among whites, adenocarcinoma surpassed squamous carcinoma by 1985-1989, while this occurred among blacks by 1990-1994. It was already most common among other race individuals in 1973-1974. Adenocarcinoma was already most common among patients <50 years of age by 1973-1974, while adenocarcinoma rapidly increased and surpassed squamous carcinoma in all other age groups by 1990-1994. **Conclusion:** Incidence of adenocarcinoma of the lung has continued to increase to such an extent that it comprises a clear majority of all lung cancers in the US. Indeed, our analysis demonstrated that lung adenocarcinoma currently represents 55% of US lung cancers. It is the most common histology in men and women, in whites, blacks, and other-races, and in all age groups. The question of how the actions of Big Tobacco helped to create this epidemic will be addressed in a separate presentation at this meeting.
Keywords: Big Tobacco, Adenocarcinoma, Epidemic

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.05-009 EGCG Regulated Ku70 Acetylation for Apoptosis in Human Lung

Cancer A549 Cells Min Li, Jing J. Li, Qi H. Gu, Li M. Cao, Hua P. Yang, Cheng P. Hu
Department of Respiratory Medicine, Xiangya Hospital, Central South University, Changsha/China

Background: Lung cancer is one of the malignant tumors whose global incidence and mortality are very high. The chemoprevention has become an important prevention and control means of lung cancer except for giving up smoking and early detection. Research has showed the main component in green tea (-)-epigallocatechin-3-gallate (EGCG) is a potential chemopreventive agent for various tumors, especially lung cancer. **Methods:** The cells in each group were treated with different concentrations of EGCG for a certain time in the experiment. Two gene point mutation plasmid were constructed and transfected in A549 cells. Induction of apoptosis was examined using AnnexinV/PI double staining flow cytometry. Western Blot detected the protein expressions of Bax, Bcl-xl and Caspase-3. Co-immunoprecipitation was used to detect the interaction of Ku70-Bax and acetylation status of Ku70. P<0.05 showed the difference had statistical significance. **Results:** Treatment of A549 cells with EGCG induced apoptosis with increasing expression of Bax and Caspase-3, but decreasing expression of Bcl-xl. EGCG could up-regulate K70 acetylation status of A549 cells, then down-regulate the interaction of Bax-Ku70 in the manner of concentration and time dependent. The apoptosis-promoting effect of EGCG on A549 cells was obviously weakened with the interaction of Bax-Ku70 strengthened and Caspase-3 (17KDa) expression declining after pCDNA3.1(+)-Ku70 plasmid and pCDNA3.1(+) -Ku70^{539}/^{542}R plasmid transfection. **Conclusion:** The authors induced apoptosis in human lung adenocarcinoma A549 cells after treatment with EGCG, and it was realized by interfering the interaction between Ku70 and Bax through regulating K70 acetylation. It verified that two loci K539 and K542 of Ku70 acetylation might play a crucial role in EGCG inducing apoptosis of A549 cells. **Keywords:** apoptosis, Ku70 acetylation, EGCG, lung cancer

SESSION: POSTER SESSION/ SCREENING AND EARLY DETECTION MONDAY, SEPTEMBER 7, 2015

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-001 Ultra-Low Dose-CT Accurately Detects Significant Lung Nodules with a Fraction of the Radiation of Conventional Low Dose-CT Alistair Miller[1], Dana Jackson[2], Sheetal Deshpande[1], Cathryn Hui[2], Garun Hamilton[1], Ken Lau[2] [1]*Monash Lung and Sleep, Monash Medical Centre, Clayton/VIC/Australia,* [2]*Monash Imaging, Monash Medical Centre, Clayton/VIC/Australia*

Background: Indeterminate lung nodules are a common and increasing incidental finding on CT imaging and there are widely accepted surveillance protocols. However, even when using Low Dose (LD)-CT with a total effective dose of ~1mSv, concerns exist regarding the cumulative radiation exposure of subjects under surveillance, particularly in individuals not at high risk of lung cancer. By utilizing the Model Based Iterative Reconstruction (MBIR) technique, CT images can be obtained with a radiation dose comparable to chest x-ray (0.06-0.1 mSv). At this Ultra-Low Dose (ULD), MBIR images have generally less signal to noise ratio which may prevent small nodule detection. The aim of this prospective study was to assess the efficacy of ULD-CT in detecting clinically significant lung nodules (≥4mm) as compared to LD-CT. **Methods:** Following approval from the local Human Research Ethics Committee, adult subjects undergoing CT surveillance for incidental lung nodules were recruited from a tertiary hospital. Once informed consent was obtained, both standard LD- and a ULD-CT chest were performed. Scans were performed on the GE750HD Discovery scanner. Demographic information including lung cancer risk factor evaluation was obtained by questionnaire. Patients who withdrew consent or whose images were degraded by gross movement or metallic artefacts were excluded. Images from the ULD-CT were reconstructed with MBIR prior to reading. Each of LD/ULD-CT image sets was read blindly, randomly and independently by two experienced thoracic radiologists. The number, size and location of nodules was reported and subsequently compared. **Results:** 100 subjects were recruited with a mean age of 65 years (range 32-87). Around 62% were ever smokers, with 30% smoking ≥30 pack years. Around 30% had risk factors other than smoking, but only αof these (9%) did not have a significant smoking history. Only a small proportion were high risk as evidenced by only 8 meeting Lung Cancer screening criteria (NLST criteria). A total of 200 nodules ≥4mm were detected, with all seen on both LD and ULD-CTs. In addition, there were 244 nodules <4mm seen on the LD-CT, with greater than 80% sensitivity for the ULD-CT, with minor variation between lobes. There were no false positive findings. There was a 10 fold reduction in effective radiation when comparing ULD-CT (0.09mSv) imaging with the standard LD-CT (1.11mSv). Lung nodules were subjectively better seen on the ULD-CT. **Conclusion:** ULD-CT with the advanced MBIR allows detection of all clinically significant lung nodules while achieving a radiation dose comparable to that of plain chest radiography. Particularly in low-risk populations, the use of ULD-CT for surveillance of lung nodules has the potential to significantly reduce cumulative radiation exposure. **Keywords:** Surveillance, Indeterminate nodule, Screening

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-002 Lung Cancer Screening Guidelines May Not Capture the Complete Population At-Risk April Plank[1], William Moore[1], Barbara Nemesure[2] [1]*Radiology, Stony Brook Medicine, Stony Brook/NY/United States of America,* [2]*Preventive Medicine, Stony Brook Medicine, Stony Brook/NY/United States of America*

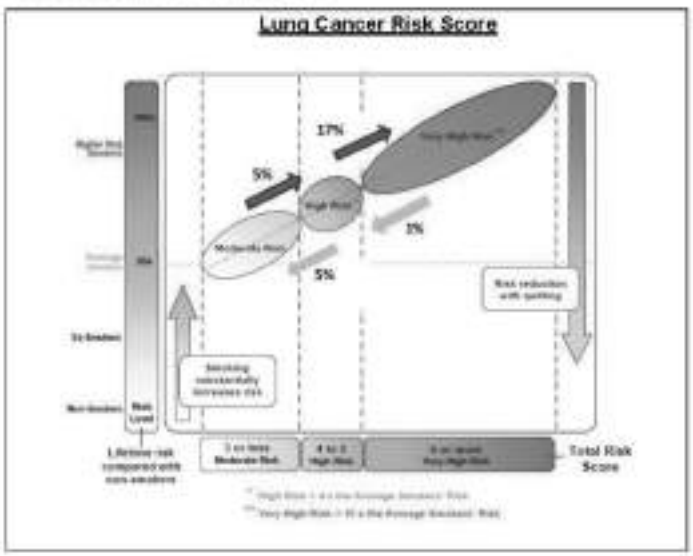
Background: In December 2013, the United States Preventive Services Task Force (USPSTF) provided a level B recommendation for the use of low-dose computed tomography (LDCT) to screen high-risk patients for lung cancer. Most recently, in February 2015, the Centers for Medicare and Medicaid Services (CMS) likewise approved coverage for at-risk patients, defined as those 55 years of age or older with a strong (30 pack-year) smoking history. The current USPSTF and CMS specified eligibility criteria for lung cancer screening are similar to those implemented by the National Lung Screening Trial and other studies which provided the evidence base that precipitated the decision to screen high risk patients, however these criteria may not adequately capture all sub-groups that comprise the complete population at risk for developing lung cancer. For example, younger patients (50+ years) who have a moderate (20 pack-year) smoking history and at least one other known lung cancer-related risk factor are considered to be at high risk by the National Comprehensive Cancer Network (NCCN). The purpose of this investigation is to investigate the prevalence of lung cancer among younger and older age groups of screening patients nationwide and to begin to provide important data that may assist with evaluating the adequacy of the eligibility criteria currently being used to define the population at-risk for developing lung cancer. **Methods:** The Center for Lung Cancer Screening and Prevention at the Stony Brook Cancer Center, recently conducted an electronic survey of all Lung Cancer Alliance Centers of Excellence for Lung Cancer Screening nationwide. The survey collected information regarding numbers and age groups of patients screened, numbers and stages of lung cancers detected, smoking history and other demographic variables. Lung cancer status (cancer detected vs. no cancer detected), stratified by age group (50-54 years vs 55-80 years) are presented here. A total of 24 Centers (among 240) provided data for the survey. Many Centers did not have available data for the younger subgroup of patients likely due to the implementation of the USPSTF criteria rather than the NCCN guidelines that recommend screening this younger, at-risk subgroup. **Results:** The survey data were cumulated over all 24 participating Centers of Excellence nationwide and included 7,252 patients. Of these, n= 697 patients were 50-54 years of age and n=6,555 were 55 years or older. Among the younger cohort, 16 patients (2.3%) were found to have lung cancer. In the older age category, lung cancer was detected in 130 patients or 2.0%. **Conclusion:** These findings suggest that this younger subgroup of at-risk patients warrant further consideration for lung cancer screening. Additionally the data suggest that this well-defined subgroup of 50-54 year old patients who have a moderate smoking history and at least one other known lung cancer-related risk factor may be at even higher risk for developing the disease than those 55+ years with a 30 pack-year smoking history. These nationwide data highlight the urgent need to re-evaluate the eligibility criteria currently being used to define the population at risk for developing lung cancer. **Keywords:** Screening, high risk, eligibility criteria, prevention

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-003 Low-Dose CT Lung Cancer Screening in the Community: A Prospective Cohort Study Incorporating a Gene-Based Lung Cancer Risk Test Robert Young[1], Raewyn J. Hopkins[1], Vincent K. Lam[2], Elwyn Cabebe[2], Mary Miller[2], Greg D. Gamble[1] [1]*University of Auckland, Auckland/New Zealand,* [2]*Genomic Institute, El Camino Hospital, Mountain View/CA/United States of America*

Background: Following the publication of the National Lung Screening Trial (NLST) results in 2011, CT screening for lung cancer is now widely recommended in the US. However concerns remain with regards to patient selection according to risk level and overdiagnosis.Moreover adherence outside screening trials is typically about 50-60% and has been shown to be highly dependent on an individual's risk perception. This feasibility study explores the relevance of gene-based data on lung cancer risk assessment and adherence to screening, in a pilot screening program. **Methods:** This feasibility study was initiated in 2010 prior to NLST results being published. Following local media-based advertising, 157 current or former smokers (>50 years old with ≥20 pack year history), volunteered for lung cancer risk assessment and CT screening (using the IELCAP protocol). Participants were followed up for a mean of 2.4 years.At baseline CT screening, participants were assigned their lung cancer risk category according to a published and prospectively validated gene-based risk algorithm. This algorithm combines clinical risk variables with risk genotypes, derived from analysis of 20 risk single nucleotide polymorphisms (SNPS), to derive a composite lung cancer risk score categorised as moderate, high or very high. **Results:** SNP genotype results contributed to overall lung cancer risk in 88% of participants compared to the contribution from age = 68%, family history of lung cancer = 29% and self reported chronic obstructive pulmonary disease =15%. The SNP genotype results were the sole basis of risk in 18% of participants and contributed to risk in a further 70% of participants (total 88%). Adding SNP scores to the clinical risk score re-assigned screening participants into different risk categories in 28% (44/157) of participants (Figure 1). Importantly, timely adherence to the CT screening protocol was two-fold greater in those with a very high risk score compared to the high and moderate risk categories (71% vs 52% vs 52% respectively, OR =2.3, P<0.05).

Figure 1. Percentage of screening participants for whom re-assignment of lung cancer risk score category occurred when their individualised SNP genotype data (genetic risk score) was added to the clinical data to derive the overall risk category.



Conclusion: In this feasibility study of a pilot community-based CT screening program we found gene-based risk assessment was of interest to all screening volunteers. As part of risk assessment, personalised SNP data made the greatest contribution to overall assignment of lung cancer risk in association with established clinical variables and significantly improved screening adherence. We conclude that gene-based risk stratification helps assign lung cancer risk and appears to improve adherence to screening. **Keywords:** Lung cancer, risk prediction, single nucleotide polymorphism, adherence to CT screening

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-004 Common Misconceptions About Lung Cancer Screening: A Nationwide Survey Alexis Cortot[1], Laurent Greillier[2], Chantal Touboul[3], François Eisinger[4], Xavier Pivot[5], Jérôme Viguier[6], Jean-Yves Blay[7], Christine Lhomel[8], Sébastien Couraud[9], Jean-François Morere[10] [1]*Hôpital Calmette, Lille/France,* [2]*Hôpital Nord, Marseille/France,* [3]*Kantarhealth, Montrouge/France,* [4]*Institut Poali Calmette, Marseille/France,* [5]*CHU de Besançon, Besançon/France,* [6]*Hôpital Bretonneau, Tours/France,* [7]*Centre Léon Bérard, Lyon/France,* [8]*Roche, Boulogne-Billancourt/France,* [9]*Hospices Civils de Lyon, Lyon/France,* [10]*Hôpital Paul Brousse, Villejuif/France*

Background: The National Lung Cancer Screening Trial has demonstrated the efficacy of lung cancer screening based on annual low-dose computed tomography (CT) scanning in both former and current smokers. Nationwide lung cancer screening programs are therefore expected to be implemented. Adhesion to these programs will depend largely on public information regarding lung cancer screening. Here, we report on widespread beliefs regarding lung cancer screening in the general population prior to any information campaigns on lung cancer screening. **Methods:** The EDIFICE French nationwide observational surveys, conducted every 3 years since 2005, set out to characterize behaviors related to cancer screening. The 4th edition, EDIFICE 4, was conducted by phone interviews of a representative sample of 1602 subjects aged between 40 and 75 years, using the quota method, from June 12 to July 10, 2014. Attitudes and opinions regarding colorectal, prostate, breast, cervical and lung cancer screening were assessed. **Results:** For 43% of the French population, lung cancer screening is more reassuring than distressing. This figure is lower than those reported for perceptions of other screening programs, including colorectal cancer screening (51%) and breast cancer screening (63% vs. 46.7% for lung cancer screening in the female population). Eleven percent of the respondents (N=162) declared having already undergone a lung cancer screening test. For the vast majority (87%, N=140), this comprised a chest X-ray and for 63%, (N=101) the chest X-ray was not associated with another type of examination. Respondent-declared reasons for not undergoing screening included absence of risk factors (36%), absence of respiratory symptoms (34%), absence of physician recommendations for screening (29%) and futility (11%). Seven percent of current smokers and 32% of former smokers did not undergo screening because they did not consider themselves at risk for lung cancer. Fear of the results pushed 9% of current smokers to avoid lung cancer screening. However, 22% of all respondents and 38% of current smokers declared their intention to undergo a lung cancer screening test in the future. **Conclusion:** The general population has many misconceptions of lung cancer screening. Implementation of nationwide lung cancer screening programs should include information for the general public regarding selection criteria, techniques used and the benefits of lung cancer screening using low-dose CT scanning. **Keywords:** lung cancer screeening, chest X-ray, risk factors

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-005 The Correlation between Visceral Pleural Invasion in T1a Non-Small Lung Cancer and Lymph Node Metastasis Mitsuhiro Tsuboi, Hiromitsu Takizawa, Daisuke Matsumoto, Naoya Kawakita, Koichiro Kajiura, Hiroaki Toba, Yukikiyo Kawakami, Syoji Sakiyama, Kazuya Kondo, Akira Tangoku *Department of Thoraci,Endocrine Surgery and Oncology, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima City/Japan*

Background: Visceral pleural invasion (VPI) of non-small cell lung cancer (NSCLC) has been recognized as a poor prognostic factor. Peripheral lung cancers often invade visceral pleura, and positive VPI upstages the T category of tumors from T1a to T2a. In addition, it is possible that peripheral lung cancers with positive VPI causes lymph nodes metastasis because of subpleural lymphovascular invasion. In this study, we statistically analyzed the correlation between VPI and lymph node metastasis. **Methods:** 129 patients with NSCLC and a tumor diameter of ≤ 2cm underwent lobectomy or segmentectomy with systematic lymph node dissection in Tokushima University Hospital between January 2008 to December 2013. Excluding 11 patients who were not examined by FDG-PET before the surgery, we reviewed the medical records of 118 patients to obtain information on age, sex, CEA, SUVmax, CT findings, pathological VPI and lymph node metastasis. **Results:** Patient characteristics were as follows: median age of 66.5 (range: 41-86); male/female: 52/66; histologic type adenocarcinoma/squamous cell carcinoma/other: 103/12/3. 13(36.1%) of 36 patients who were suspected to be with visceral pleural invasion by preoperative CT findings were diagnosed with pathological visceral pleural invasion. The mean SUVmax on FDG-PET in patients with VPI was significantly higher than that of patients without VPI(p=0.01). Pathological visceral pleural invasion was identified in 19(16.1%) of 118 patients and associated with high incidence of lymph node metastasis significantly on multivariable analyses (p=0.00). **Conclusion:** VPI is important factors of lymph node involvement in small peripheral lung cancers. It is difficult to identify VPI of peripheral lung cancers by preoperative CT findings. FDG-PET may be useful for diagnose VPI. **Keywords:** visceral pleural invasion, lymph nodes metastasis, FDG-PET

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-006 Metabolomics by NMR Facilitates the Non-Invasive Diagnosis and Staging of NSCLC Clara Pérez-Rambla[1], Leonor Puchades-Carrasco[1], Eloisa Jantus-Lewintre[2], Francisco García-García[3], Rut Lucas[2], Silvia Calabuig[2], Ana Blasco[4], J Dopazo[3], Carlos Camps[4], Antonio Pineda-Lucena[1] [1]*Structural Biochemistry Laboratory, Centro Investigación Príncipe Felipe, Valencia/Spain,* [2]*Molecular Oncology Laboratory, Fundación Investigación Hospital General Universitario, Valencia/Spain,* [3]*Computational Genomics Department, Centro Investigación Príncipe Felipe, Valencia/Spain,* [4]*Department of Medical Oncology, Consorcio Hospital General Universitario, Valencia/Spain*

Background: Lung cancer (LC) is the most common cause of cancer death worldwide. At present, the diagnosis is primarily based on symptoms and detection occurs at late stages, thus resulting in a very poor prognosis. If the diagnosis could be shifted to early stages, then the overall morbidity for this disease could be dramatically altered. Metabolomics, an analytical platform used in combination with statistical techniques, has been shown to be a very powerful approach for the understanding of biological pathways involved in the onset and progression of diseases. The objective of this study was to identify, using metabolomics by NMR, a set of specific metabolites that could be used for LC screening in the clinical context. **Methods:** Metabolic profiles corresponding to a training set of serum samples from early-stage (n = 66) and advanced-stage (n = 69) NSCLC patients were obtained using ^{1}H-NMR spectroscopy. A matched control set of 71 serum samples from healthy subjects was also included. Furthermore, NMR experiments were also performed for an external validation set consisting of 20 early-stage and 20 advanced-stage NSCLC patients, 13 healthy individuals, and 27 benign pulmonary disease patients (BPD). **Results:** Multivariate statistical modeling of the data revealed that the serum of NSCLC patients, when compared with healthy individuals, exhibit a specific serum metabolic profile (R^2 = 0.931; Q^2 = 0.873) characterized by statistically significant differences in the concentrations of a number of lipids, organic acids and amino acids. The metabolic profiles obtained for NSCLC patients and healthy individuals were also different to that obtained for BPD patients. A similar analysis performed to compare the serum metabolomic profile of NSCLC patients at early and advanced stages of the disease (R^2 = 0.779; Q^2 = 0.592) showed that disease evolution has also a reflection in the metabolic profile of patients. Furthermore, a logistic regression analysis allowed the identification of a specific combination of five metabolites (threonine, glutamine, lactate, choline and methanol) that enables the discrimination between healthy individuals and NSCLC patients with a 77,5% sensitivity and a 76,9% specificity (70% for all non-cancer samples). **Conclusion:** Our results highlight the potential of metabolomics by ^{1}H-NMR for identifying biological pathways involved in the onset and progression of NSCLC, thus providing a sensitive, specific, minimally invasive and easily implementable method in clinical practice for the early diagnosis of NSCLC and for the optimization of risk profile models. **Acknowledgements**: Spanish Ministerio de Economía y Competitividad (MINECO, SAF2011-28350), Centro de Investigación Príncipe Felipe and Fundación Mutua Madrileña for their economic support and Red de Biobancos de Valencia and Bruker BioSpin for technical contributions. This study was also supported by the ISCIII (RTICC, RD12/0036/0025). **Keywords:** Lung cancer, early detection, NMR, metabolomics, biomarker.

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-007 Plasma Circulating MicroRNA-944 and MicroRNA-3662 as Novel Histologic Type-Specific Lung Cancer Biomarkers Tomasz Powrózek[1], Pawel Krawczyk[2], Dariusz Kowalski[3], Kinga Winiarczyk[3], Marta Olszyna-Serementa[3], Marcin Nicoś[1], Maciej Krzakowski[3], Janusz Milanowski[1] [1]*Pneumonology, Oncology and Allergology, Medical University of Lublin, Lublin/Poland,* [2]*Laboratory of Immunology and Genetics, Department of Pneumonology, Oncology and Allergology, Medical University of Lublin, Lublin/Poland,* [3]*Lung and Chest Tumors, Oncology Centre - Institute M. Sklodowska-Curie in Warsaw, Warsaw/Poland*

Background: Altered expression of microRNAs is associated with development and invasion of cancers by regulating post-transcriptionally gene function. Possibility of detection of circulating miRNAs expression in patients' plasma or serum make them valuable biomarkers of different neoplasms, such as lung cancer. **Methods:** We investigated potential role of miR-944 and miR-3662 expression analysis as a novel lung cancer biomarkers and their lung tumor specificity in plasma samples of 90 lung cancer patients (40 NSCLC patients in stage IA-IIIA and 20 NSCLC patients in stage IIIB-IV; 8 SCLC patients with limited and 22 SCLC patients with extensive disease) and 85 healthy individuals using qRT-PCR analysis. **Results:**Expression of miR-944 and miR-3662 was significantly upregulated in lung cancer patients in comparison to healthy individuals. Higher stage of lung cancer correlated with higher miRNAs expression (Figure 1). Receiver operating curves (ROC) analysis have presented diagnostic power of analysis of both miRNAs expression for detection of patients with I and II stage of NSCLC with area under curve (AUC) of 0.881. Moreover, miR-944 has shown diagnostic accuracy for operable squamous cell carcinoma detection (AUC=0.982) whereas miR-3662 - for operable adenocarcinoma (AUC=0.926) (Figure 2).

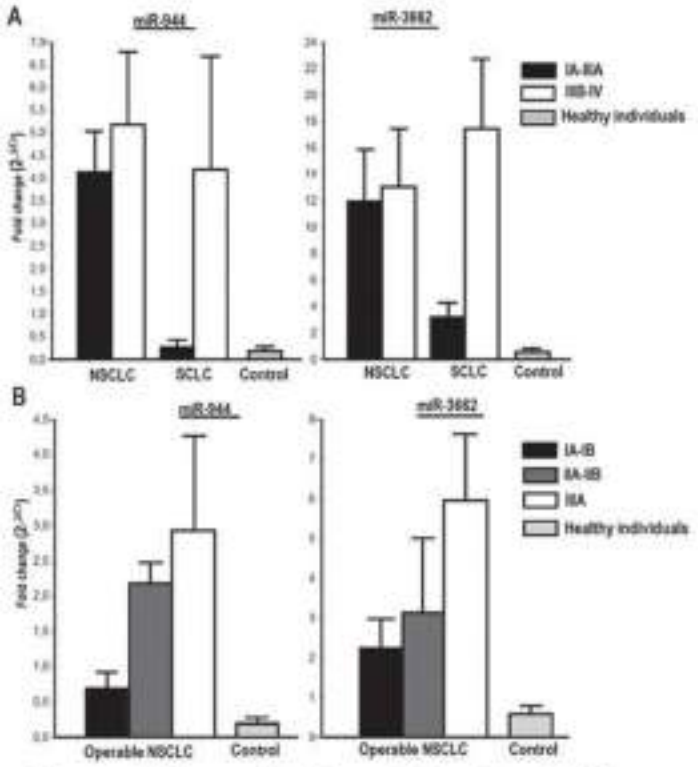

Figure 1. miRNAs expression differences. A. Comparison of miRNAs expression in patients with different stages of NSCLC and SCLC as well as in healthy individuals. B. Expression of miR-944 and miR-3662 in early stages of NSLC and in healthy control.

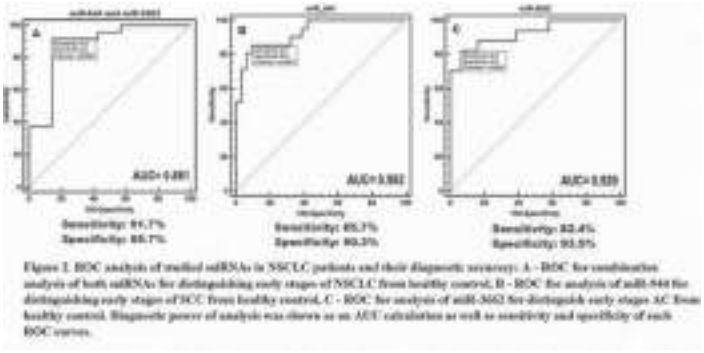

Figure 2. ROC analysis of studied miRNAs in NSCLC patients and their diagnostic accuracy. A - ROC for combination analysis of both miRNAs for distinguishing early stages of NSCLC from healthy control, B - ROC for analysis of miR-944 for distinguishing early stages of NSCC from healthy control, C - ROC for analysis of miR-3662 for distinguish early stages AC from healthy control. Diagnostic power of analysis was shown as an AUC calculation as well as sensitivity and specificity of each ROC curves.

Conclusion: Our research is a first study investigating the plasma expression of miR-944 and miR-3662 in patients with neoplasms and in healthy individuals. Moreover, this is a first study that described a miR-3662 expression. We have shown that examination of these two miRNAs may be considered as a tool for NSCLC early diagnosis as well as for non-invasive diagnosis of lung cancer late stages. Studied miRNAs have also shown high utility in detection of histological type-specific NSCLC subtypes, such as adenocarcinoma and squamous-cell carcinoma. **Keywords:** microRNA, lung cancer, biomarkers, early detection

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-008 Functional Polymorphisms in PD-L1 Gene Are Associated with the Prognosis of Patients with Early Stage Non-Small Cell Lung Cancer Deuk Kju Jung, Cheng Cheng Jin, Mi Jeong Hong, Sook Kyung Do, Jae Yong Park *Biochemistry and Cell Biology, Kyungpook National University, Daegu/Korea*

Background: This study was conducted to investigate whether polymorphisms of genes involved in immune checkpoints can predict the prognosis of patients with early stage non-small cell lung cancer (NSCLC) after surgical resection. **Methods:**Twelve single nucleotide polymorphisms (SNPs) of *PD-1*, *PD-L1*, and *CTLA-4* genes were selected and genotyped. A total of 354 patients with early stage NSCLC who underwent curative surgical resection were enrolled. The association of the SNPs with overall survival (OS) was analyzed.Twelve single nucleotide polymorphisms (SNPs) of *PD-1*, *PD-L1*, and *CTLA-4* genes were selected and genotyped. A total of 354 patients with early stage NSCLC who underwent curative surgical resection were enrolled. The association of the SNPs with overall survival (OS) was analyzed. **Results:** Among the 12 SNPs investigated, *PD-L1* SNP1C>G, SNP2G>C, and SNP3T>A were significantly associated with worse survival outcomes in multivariate analyses. When the three SNPs were combined, OS decreased in a dose-dependent manner as the number of bad genotypes increased (*P*trend = 0.0003). A higher expression of the reporter gene for the SNP2G- SNP3T haplotype was observed compared with the SNP2C- SNP3A haplotype by luciferase assay (*P* = 0.004). Patients with higher expression of *PD-L1* mRNA had a better survival compared with lower expression (P = 0.03). **Conclusion:** *PD-L1* SNP1C>G, SNP2G>C, and SNP3T>A polymorphisms may be useful for the prediction of prognosis in patients with surgically resected NSCLC. Further studies are needed to confirm our findings and to understand the role of *PD-L1* in the antitumor immunity. **Keywords:** polymorphism, lung cancer, immune checkpoint, PD-L1

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-009 Volatolomic Signatures to Assess Sensitivity to FGFR Tyrosine Kinase Inhibitors Regina Kwon[1], Orna Barash[2], Haneen Kayal[2], Leslie Rozeboom[1], Giulia Courthod[3], Ashley A. Kowalewski[1], Christopher J. Rivard[1], Brad Rikke[1], Nir Peled[4], Hossam Haick[2], Fred R. Hirsch[1] [1]*Medical Oncology, University of Colorado Denver, Aurora/ United States of America,* [2]*Technion-Israel Institute of Technology, Haifa/Israel,* [3]*Medical Oncology, University of Torino, Torino/Italy,* [4]*Rabin Medical Center, Tel Aviv/Israel*

Background: Targeted therapy is transforming the treatment of lung cancer. Such therapies are critically dependent on companion diagnostics that can predict the response to therapy. An ideal test is one that is quick, inexpensive, and non-invasive. In this regard, artificial intelligence nanosensor-based devices that profile volatolomic signatures (through volatile organic compounds (VOCs) analysis) have shown exciting potential. Numerous studies have shown cancer cells produce characteristic patterns of VOCs as a byproduct of their metabolism. These patterns can be used to diagnose patients with cancer using exhaled-breath samples. Here we asked whether the VOC patterns emanating from cancer cells could also be used to guide targeted therapy. In particular, we investigated whether lung cancer cell lines known to be sensitive to FGFR tyrosine kinase inhibitors (TKIs) can be distinguished from cell lines known to be resistant using an array of cross reactive, highly sensitive chemiresistors composed of gold nanoparticles (GNP) and carbon nanotubes (CNTs) coated with various recognition layers previously shown to be highly effective at profiling VOCs. **Methods:** Fourteen sensitive cell lines having an $IC_{50} \leq 50$ nM for Ponatinib and AZD4547 (nonspecific and specific FGFR TKIs, respectively) and 21 resistant cell lines representing small cell and non-small cell lung cancers were cultured in complete media (RPMI 1640, 10% fetal bovine serum, and penicillin/streptomycin) under standard conditions to 50% to 75% confluency. SKC Tenax® TA Adsorbent resin was used to collect the VOCs from the head space of each cell line over a period of 60 to 72 hours. Triplicate measures were collected on each sample along with biological replicates. VOCs were also collected at the same time from control plates containing media only. After thermal desorption, the VOC pattern of each sample was characterized using a chemiresistor array of 36 sensors and 4 features per sensor. A statistical pattern recognition analysis was then conducted using a discriminant function analysis (DFA) algorithm to identify the most informative sensors and features. **Results:** We found that sensitive cell lines could be distinguished from resistant cell lines using only 4 sensors and one feature from each (GNP+dodecanethiol, CNT+PAH, GNP+thiol and CNT+β dextrin). Leave-one-out cross validation indicated a sensitivity of 88% for the FGFR TKI-sensitive cell lines with 100% specificity and 92% accuracy. The area under the receiver-operating characteristic curve was 70% and Wilcoxon p-value of 0.06. **Conclusion:** Profiling the VOCs emanating from lung cancer cells shows excellent diagnostic potential as a means of gauging initial sensitivity to FGFR1 TKIs. Consequently, this study suggests that the electronic nose devices currently being developed to profile exhaled breath for cancer detection could also play an important role in predicting responses to targeted therapies. Although cell lines are useful for identifying the VOC pattern that predicts the cancer cell response to therapy, they do not necessarily reflect the complexity that occurs in vivo due to interactions

with the microenvironment. Therefore, future studies are needed to confirm if these results can be extended to project efficacy in patients assigned to FGFR TKI therapy. **Keywords:** FGFR, VOCs, inhibitor, cancer cell lines

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-010 Allelic Heterogeneity and Its Role in Identifying Non-Small Cell Lung Cancer Phenotypes Lisa M. Alley[1], Rosalind B. Penney[2], Konstantinos Arnaoutakis[3], Matthew Steliga[3], Susanne K. Jeffus[4], Mohammed S. Orloff[1] [1]*Department of Epidemiology, University of Arkansas for Medical Sciences, Little Rock/AR/United States of America,* [2]*Environmental and Occupational Health, University of Arkansas for Medical Sciences, Little Rock/AR/United States of America,*[3]*Winthrop P. Rockefeller Cancer Institute, University of Arkansas for Medical Sciences, Little Rock/AR/United States of America,* [4]*Department of Pathology, University of Arkansas for Medical Sciences, Little Rock/AR/United States of America*

Background: More people die of lung cancer (LC) annually than of prostate, colon, and breast cancers combined, making it the leading cause of cancer-related mortality in the United States. LC can be divided into two main categories: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC is the predominant LC category accounting for roughly 85% to 90% of all diagnosed LCs. NSCLC can be further subdivided into three main histological subtypes including adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Phenotypic characterization (i.e. histological features and LC subtypes) for NSCLC tissues remains a difficult task. Many studies have revealed certain genes that are associated with NSCLC; however, these genes cannot completely decipher between its varying phenotypes. *CD36* is a biologically plausible candidate gene that is significantly under-expressed in NSCLC tissues compared to normal tissues. This differential expression is not observed in NSCLC tissue subtypes; however, significant differences in *CD36* expression have been observed in NSCLC subtype-derived cell lines. Based on this previous expression data, we hypothesized that allelic heterogeneity within *CD36* exons could disparately contribute to the development of NSCLC subtypes. **Methods:** To test this hypothesis, we obtained fresh-frozen LC tissues from the UAMS tissue bank and performed mutation screenings using Sanger sequencing methods and Mutation Surveyor software. Quantitative RT-PCR was performed on tissue mRNA and *CD36* mRNA expression was normalized to *HPRT1* (a housekeeping gene that is more stable in lung tissues) expression in the same samples. Genotype-specific *CD36* expressions profiles were then identified and analyzed. **Results:** Several previously undiscovered variants were identified in Exon 4 of the *CD36* gene. Two of these variants are associated with mRNA expression differences between the variant and wild-type genotypes that identify phenotypic heterogeneity. Adenocarcinoma samples with transcript harboring the first variant genotype overexpressed *CD36* mRNA as compared to adenocarcinoma samples containing the wild-type genotype (p=0.013; N=37). In squamous cell carcinoma samples, there was no significant difference between samples with the first variant and wild-type (p=0.74; N=26). Squamous cell carcinoma samples with*CD36* transcript harboring the second variant genotype was relatively under-expressed when compared to the squamous cell carcinoma samples with the wild-type genotype, though the comparison only approached significance at p=0.053 (N=37). A similar comparison in adenocarcinoma samples yielded non-significant results (p=0.59; N=25). **Conclusion:** Identification of NSCLC phenotypes is critical to treatment, but remains difficult with current histopathological methods. Our analysis of publicly available expression data has shown that probes used in global expression microarrays cannot completely and reliably distinguish between NSCLC phenotypes at the *CD36* locus. We propose that allelic heterogeneity at the*CD36* locus may alter array probe binding properties leading to inconsistent expression results. Our data has identified two previously undiscovered *CD36* variants that may uniquely lead to altered *CD36* mRNA expressions correlating to specific NSCLC subtypes. Hence, these results suggest that we may be able to accurately quantify transcripts associated with NSCLC subtypes using allele-specific probes. **Keywords:** histologic phenotypes, expression, non-small cell lung cancer (NSCLC), allelic heterogeneity

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-011 miR-126 Is a Potential Diagnostic Marker for Malignant Pulmonary Nodules in Endobronchial Epithelial Lining Fluid Nicolas Kahn[1], Sajo Kaduthanam[2], Uwe Schirmer[2], Thomas Muley[3], Ruprecht Kuner[2], Felix Herth[1], Michael Meister[3], Holger Sültmann[2] [1]*Department of Pneumology and Critical Care Medicine, Thoraxklinik at University of Heidelberg and TLRC, Heidelberg/Germany,* [2]*Cancer Genome Research Group, German Cancer Research Center and National Center of Tumor Diseases, Heidelberg/Germany,* [3]*Translational Research Unit, Thoraxklinik at University of Heidelberg and Translational Lung Research Center (TLRC), Heidelberg/Germany*

Background: Early detection and diagnostic clarification of indeterminate pulmonary nodules by less invasive methods could contribute to better intervention strategies and to the reduction of the high mortality in lung cancer patients. Endobronchial epithelial lining fluid (EELF) might contains molecular markers with diagnostic potential. With the bronchoscopic microsampling (BMS) technique, it is possible to collect EELF in close proximity to the suspected lesion without the risk of biopsy-associated complications. We investigated whether microRNA (miRNA) in EELF collected by BMS may be useful to facilitate preoperative diagnosis of indeterminate pulmonary nodules. **Methods:** The study included 24 non–small-cell lung cancer patients with 48 EELF samples. From each patient, EELF was collected from subsegmental bronchi close to the indeterminate pulmonary nodule, which was detected by computed tomography, and from the contralateral healthy lung. Diagnosis was confirmed by transbronchial biopsy or surgery. Global miRNA expression profile analysis (754 miRNAs) was performed using quantitative real-time polymerase chain reaction (qRT-PCR) with eight sample pairs. miRNAs potentially associated with a malignant phenotype were selected for further qRT-PCR analysis in an independent validation cohort (16 sample pairs). **Results:** All patients underwent BMS without complications. miRNA profiling by qRT-PCR could be reliably applied to EELF samples and resulted in potential miRNA markers for malignant pulmonary nodules. In particular, the miRNA pair miR-126/miR-126* significantly differentiated between EELF close to the indeterminate pulmonary nodules and the sample taken from the healthy contralateral lung (p<0.0001). **Conclusion:** Our study suggests that the analysis of miR-126/miR-126* in EELF collected by BMS could be a potentially useful adjunct to other diagnostic techniques aiming at the preoperative diagnosis of indeterminate pulmonary nodules. **Keywords:** pulmonary nodules, Biomarkers, bronchoscopic microsampling

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-012 Components of Serum Peptidome Can Differentiate between Healthy Controls and Patients with Early Stage Lung Cancer Piotr Widlak[1], Monika Pietrowska[1], Joanna Polanska[2], Michal Marczyk[2], Rafal Dziadziuszko[3], Witold Rzyman[3] [1]*Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice/Poland,* [2]*Silesian University of Technologies, Gliwice/Poland,* [3]*Medical University of Gdansk, Gdansk/Poland*

Background: Screening with low-dose computed tomography of high-risk group for lung cancer development allows for early detection of malignancy in a minor proportion of subjects and leads to improved outcomes. Implementation of complementary minimally-invasive molecular markers for more efficient pre-selection of candidates for imaging tests or help to further define detected changes is a rational way to further improve efficacy of such screening. Here we aimed to identify features of serum peptidome that could be used for differentiation of individuals with early lung cancer from other participants of lung cancer screening program. **Methods:** Blood samples were collected during lung cancer screening program performed in Pomerania district (Poland). MALDI-ToF mass spectrometry was used to characterize the low-molecular-weight fraction of serum proteome in the 800-14,000 Da range (i.e. endogenous serum peptidome). The analysis was performed in a group of 100 lung cancer patients (with early stage lung cancer diagnosed without clinical symptoms during the screening program or through routine diagnostic procedures) and a matched group of 300 controls (participants of the screening without malignancy). **Results:** Components of mass spectra were detected and specific features allowing differentiation of cancer cases were identified. The first group of 50 cancer cases and 150 matched controls was used to built and test multi-component peptide signature for cancer classification; obtained classifier showed about 70% specificity and sensitivity. The signature was validated in the second group of independently analyzed samples (50 cancer cases and 150 matched controls); the classifier performed well and the total number of misclassifications was below 25%. **Conclusion:** MALDI-based profiling of serum peptidome allowed identification of components differentiating patients with early stage lung cancer from healthy individuals. Hence, biomarker based on serum peptide signature has a potential applicability for early detection of lung cancer.

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-013 Delays of Diagnosis and Treatment of Lung Cancer in a Populous Region of Brazil Fernando C. Abrão[1], Igor R.L.B.D. Abreu[1], Alessandra R. Silva[2], João H.G. Rodrigues[2], Larissa T.C. Correa[2] [1]*Thoracic Surgery, Hospital Santa Marcelina, São Paulo/Brazil,* [2]*Medicine, Faculdade Santa Marcelina, São Paulo/Brazil*

Background: This study was undertaken to measure delays of diagnosis and treatment of lung cancer in a poor region of São Paulo, Brazil, where there are four million people. In addition, the relation of delay times and survival was analyzed**Methods:** We retrospectively reviewed 509 patients with lung cancer between July 2008 and December 2014. All patients admitted with lung cancer in our institution, which is the only reference for patients with cancer in this region, were considered eligible for this study once they had not undergone any previous oncology treatment. Dates for symptoms, visits to doctors, treatment and death were recorded. The delays in the diagnosis and treatment of lung cancer were arranged in the following time intervals: -Time (months) from the first symptoms experienced by the patient (history patients - HP) to the date on which the patient was diagnosed with cancer (DX); -Time (months) from initial presentation to the first appointment (first app) with a specialist in our institution to the date on which the patient was diagnosed with cancer (DX); -Time (months) from date on which the patient was diagnosed with cancer (DX) to the starting date of treatment (TTO). Descriptive analysis of data was carried out using measures of central tendency (median). Kaplan-Meier survival estimates were used to determine 5-year lung cancer specific survival for all patient and Log-rank (Mantel-cox) and Breslow (Generalized Wilcoxon) analyses were used to compare differences between factors. Survival was calculated from the date of patient admission at our institution to the date of last follow-up or until death from any cause. Statistical analyses were performed using SPSS v 17.0 for Windows. **Results:** Demographic characteristics of the 509 lung cancer patients were analyzed. The median age of these patients was 62 years (range 26 -96 years) and more than 75 percent of these patients were smokers. For all patients, median overall survival was 7 months (95% CI: 5.7 to 8.2) with 34.5% of these patients surviving one year and 8.1% surviving five years. Patients have spent a relevant time waiting in each interval period. For instance, the median time from the history patient (HP) to the diagnosis (DX) was 3 months. From the first appointment (first app) to diagnosis (DX) was 1 month, however, 79% of patients were diagnosed up to 2 months. Finally, the median time from the diagnosis (DX) to the starting date of treatment (TTO) was 1 month, but the majority of patients (82.5%) started the treatment up to 2 months. There was no statistical relationship between

the delays and the mortality of patients. The time gap between the development of the first symptoms and the beginning of treatment was not relevant to the mortality rate of lung cancer, as shown in the survival data of the Kaplan-Meier graph. **Conclusion:** We have a relatively long time for confirmation of lung cancer and also to start treatment. Despite these data were not an independent significant factor for survival, this type of study is important to alert medical societies and government health agencies. **Keywords:** lung, Delays, Cancer, treatment

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-014 Impact of Surgery for Stage I Non-Small Cell Lung Cancer on Quality of Life Rebecca Schwartz[1], Rowena Yip[2], Ingram Olkin[3], Emanuela Taioli[1], Claudia I. Henschke[2] [1]*Occupational Medicine, Epidemiology and Prevention, Hofstra North Shore-Lij School of Medicine, Great Neck/NY/United States of America,* [2]*Radiology, Icahn School of Medicine at Mount Sinai, New York/United States of America,* [3]*Stanford University, Stanford/United States of America*

Background: The literature is mixed regarding the impact of lung cancer surgery on physical and mental health quality of life (QoL)[1-4]. Some studies have found an improvement in QoL post surgery[1] while others have indicated a decrease in various aspects of QoL[2,3]. Further, the impact on QoL is often dependent on numerous factors such as type of surgery. The current study aims to assess the impact of surgery on both physical and mental health QoL in screening-diagnosed patients with early stage lung cancer, an under-studied population. **Methods:** SF-12 QoL indicators were collected from 86 participants (40 women, 46 men) at baseline CT screening and one-year follow up post-surgery for clinical stage IA non-small cell lung cancer. 69 had lobectomy and 17 had sublobar resection. Average time of follow up was 12 months since surgery (SD: 1.5 months; range: 9-15 months post surgery). Univariate and multivariate analyses were performed to examine the difference in physical (PHC) and mental (MHC) health component scores of the SF-12 before and after surgery using the Wilcoxon signed rank and Mann Whitney tests.

SF-12 Quality of Life Scores Pre and Post Surgery

		ALL M(SD)	MALE M(SD)	FEMALE M(SD)	LIMITED RESECTION M(SD)	LOBECTOMY M(SD)
PHC	Baseline (Pre-Surgery)	49.4(6.8)	49.8(5.8)	49.0(7.8)	47.8 (7.8)	49.8(6.5)
	Post-Surgery	48.7(7.1)	48.5(7.7)	49.0(6.4)	50.3(6.3)	48.3(7.2)
	Difference (Post-Pre)	-0.7(7.6)	-1.3(7.5)	0.0(7.6)	2.5*(6.0)	-1.5(7.7)
MHC	Baseline (Pre-Surgery)	53.7(8.6)	55.5(7.6)	51.7(9.3)	52.3(13.4)	54.0(7.1)
	Post-SurgerY	55.8(8.2)	57.3(8.1)	54.1(8.2)	55.7(6.3)	55.8(8.7)
	Difference (Post-Pre)	2.0*(9.6)	1.7*(8.5)	2.4*(10.9)	2.9(10.7)	1.8(9.4)
	*p<.05					

Results: There was no significant change in PHC post-surgery (Wilcoxon signed rank test, S=-216, p=0.32), but MHC significantly improved from baseline to post-surgery (S=527, P=0.01). Mean MHC was significantly higher among males as compared to females at both baseline (Chi-square=3.95, p=.047) and post-surgery (Chi-square=4.23, p=.039) and after controlling for age, ethnicity, and education, while no differences in PHC was observed. Further, there was an improvement in PCS score post-surgery among participants who underwent limited resection while a decrease in PCS score was observed among those who underwent lobectomy. The change in PCS score was significantly different between type of surgery (t=-2.01, p=0.048). After controlling for demographics, the difference was borderline significant (F=3.62, p=0.06). **Conclusion:** Surgery for early stage lung cancer was associated with an increase in mental health QoL one year after surgery, however, physical health QoL was not affected by surgery overall, but it did marginally improve among participants who underwent limited resection as compared to lobectomy. Further, although mental health QoL improved for both males and females, females had lower mental health QoL as compared to males at both time points. Current study findings have implications for lung cancer health professionals regarding how to most effectively present the possible impacts of surgery on the QoL of this subset of patients in which disease has not yet significantly progressed. **Keywords:** early stage, epidemiology, mental health

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-015 A Population Based Study on Pulmonary Carcinoids in Iceland: Epidemiology, Diagnosis and Survival Over Sixty Years Astridur Petursdottir[1], Bjorn M. Fridriksson[1], Johanna Sigurdardottir[2], Helgi Isaksson[3], Steinn Jonsson[4], Tomas Gudbjartsson[5] [1]*Faculty of Medicine, University of Iceland, Reykjavik/Iceland,* [2]*Department of Surgery, Vasteras Hospital, Vasteras/Sweden,* [3]*Department of Pathology, Landspítali University Hospital, Reykjavik/Iceland,* [4]*Department of Pneumology, Landspítali University Hospital, Reykjavik/Iceland,* [5]*Department of Cardiothoracic Surgery, Landspítali University Hospital, Reykjavik/Iceland*

Background: Pulmonary carcinoids are usually localized to the lungs but can also metastasize to mediastinal lymph nodes or to other organs. We studied the incidence and patient outcome in a well-defined population over a 60 year period. **Methods:** A nationwide study, including all pulmonary carcinoids diagnosed in Iceland from 1955 to 2014. Histologic specimens were re-evaluated and information retrieved from medical records. The tumors were staged according to the TNM staging system (6th edition). Survival was estimated using the Kaplan-Meier method, with end of follow-up on January 1st 2015. Mean follow-up was 186 months. **Results:** 93 patients (62 females, average age of 52 years) were diagnosed during the 60 year period. Incidence increased from 0,2/100.000/year between 1955-1964 to 0,7 2005-2014. A total of 26 out of 85 patients (31%) were asymptomatic upon diagnosis and the rate of incidental detection increased from 17% in the first 30 years to 33% in the later 30 years. The most common symptoms were cough (56%), pneumonia (28%) and chest pain (11%). Mean tumor diameter was 2,7 cm (range: 0,3-6,3), 71 (84%) patients were diagnosed with typical carcinoid tumors and 14(16%) with atypical carcinoid tumors. Out of 77(91%) patients who had surgery, 65(84%) underwent a lobectomy. One patient died within 30 days of surgery. Most patients(n=67, 79%) were on stage I upon diagnosis and 4(5%) on stage II. Another 4 patients were on stage III with mediastinal lymph node metastases, all with typical histology. Out of six patients(7%) with distal metastases (stage IV), two had typical histology. Five patients(6%) had died from pulmonary carcinoids upon follow-up, but total 5-year survival was 92% for all patients and 87% for patients with typical carcinoids. **Conclusion:** The incidence of pulmonary carcinoids in Iceland has tripled over the last 6 decades, mostly due to steep increase in incidental detection on chest imaging. Most patients (>84%) are diagnosed with a localized disease, where long-term outcome is excellent.

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-016 A Novel Functional Polymorphism in CIR1 Gene Is Associated with the Risk of Lung Cancer Chengcheng Jin, Deuk Kju Jung, Jae Yong Park *Kyungpook National University, Daegu/Korea*

Background: We evaluated the associations between potentially functional variants in cancer-related genes and the risk of lung cancer to identify genetic factors responsible for lung cancer susceptibility in a Korean population. **Methods:** A total of 1,969 potentially functional single nucleotide polymorphisms (SNPs) of 1,151 genes involved in carcinogenesis were evaluated using the Affymetrix custom-made GeneChip in 610 NSCLC patients and 610 healthy controls. A replication study was performed on an independent set of 490 cases and 486 controls. **Results:** Eighty two SNPs with $P < 0.05$ for genotype distribution in the discovery set were tested in the replication study. Among the 82 SNPs, three SNPs (corepressor interacting with RBPJ 1 [*CIR1*] SNP1T>C, solute carrier family 38, member 4 [*SLC38A4*] SNP2C>T, ribonucleotide reductase M1 [*RRM1*] SNP3T>C) constantly showed significant associations with lung cancer (adjusted odds ratio [aOR] = 0.68, 95% CI = 0.59-0.84, P < 0.0001; aOR = 0.74, 95% CI = 0.63-0.88, P = 0.001; aOR = 0.72, 95% CI = 0.56-0.93, P = 0.01, respectively, under dominant model). Promoter assay demonstrated a decreased reporter gene expression for *CIR1* SNP1 C allele was observed compared with T allele ($P = 0.02$). **Conclusion:** Our results suggest that the three SNPs, particularly *CIR1* SNP1T>C, may contribute to lung cancer susceptibility in Koreans. **Keywords:** CIR1, lung cancer, polymorphism

POSTER SESSION/ SCREENING AND EARLY DETECTION
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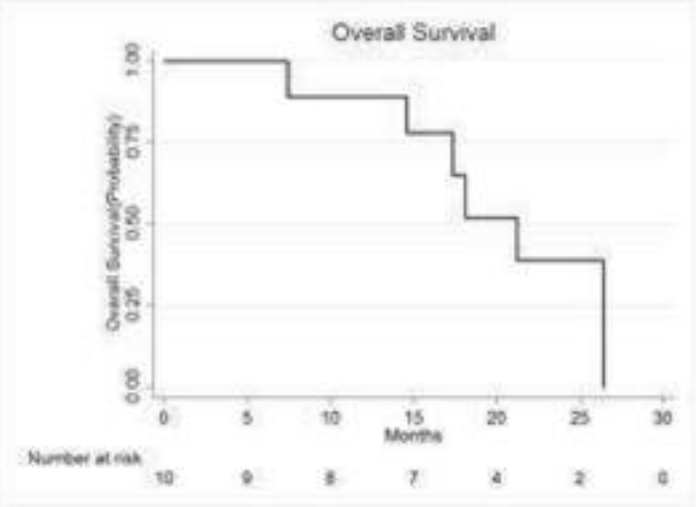
P1.06-017 Small Cell Lung Cancer in Lung Cancer Screening: Frequency and Outcome Mario Silva[1], Carlotta Galeone[2], Alfonso Marchianò[3], Giuseppina Calareso[3], Stefano Sestini[4], Carlo La Vecchia[2], Gabriella Sozzi[5], Nicola Sverzellati[1], Giuseppe Pelosi[6], Ugo Pastorino[4] [1]*Radiology, University Hospital of Parma, Parma/Italy,* [2]*Clinical Sciences and Community Health, University of Milan, Milan/Italy,* [3]*Radiology, Fondazione Irccs Istituto Nazionale Dei Tumori, Milan/Italy,* [4]*Thoracic Surgery, Fondazione Irccs Istituto Nazionale Dei Tumori, Milan/Italy,* [5]*Tumor Genomics, Fondazione Irccs Istituto Nazionale Dei Tumori, Milan/Italy,* [6]*Pathology and Laboratory Medicine, Fondazione Irccs Istituto Nazionale Dei Tumori, Milan/Italy*

Background: Only 30% of small cell lung cancers (SCLC) are diagnosed as limited stage (LS-SCLC), whereas the majority of cases show extensive stage disease (ES-SCLC). Specific frequency and outcome of SCLC within lung cancer screening trials have not been described. The purpose of this study was to describe the frequency and outcome of SCLC in lung cancer screening trials with annual or biennial LDCT controls. **Methods:** The population was selected from two lung cancer screening trials (one pilot study and one randomized controlled study) based on serial low-dose computed tomography (LDCT). Subjects with diagnosis of SCLC were selected and the stage of the disease was assessed at the time of diagnosis, as follows: a) TNM staging system; b) 2-stage staging system (e.g. LS-SCLC or ES-SCLC). Survival curves were estimated using Kaplan-Meier method and were compared by log-rank test. **Results:** 5,134 subjects were recruited

and, thereafter, followed up for a median time of 8.3 years, with 45,141 person-year of clinical follow up. Ten SCLC were reported with incidence of SCLC 22/100,000 person-year, notably, 8 in the LDCT arms with incidence of 24/100,000. SCLC was diagnosed in 3/1643 women and 7/3385 men, age at diagnosis 65 years (range 53-73), and cumulative tobacco consumption of 82 pack-years (range 30-113). The proportion of SCLC among all lung cancers diagnosed in the screening was 10/164. Six out of the 8 SCLC reported in LDCT arms were screen-detected, whereas 2 SCLC were non-screen-detected. Median standard uptake value (SUV) by ^{18}F-Fluorodeoxyglucose Positron Emission Tomography was 10 (range 5.5-14.4). According to TNM classification, all but 1 SCLC were advanced stage at the time of diagnosis, whereas according to the 2-stage system 5 LS-SCLC and 5 ES-SCLC were observed. The prevalence of LS-SCLC was 62.5% in LDCT arm, in particular, 66.7% among screen-detected and 50% non-screen-detected. The 2 SCLC reported in control group were both ES-SCLC. Six of the 10 subjects died from SCLC, with median overall survival of 21.2 months (95% CI 7.4 – nc months; Figure). Median overall survival was 12-month longer for LS-SCLC (p = 0.02). Survival at 5 years was 0%.



Conclusion: SCLC was diagnosed with higher proportion of LS-SCLC in LDCT-based screening trials, as compared to data from the literature. Median overall survival of LS-SCLC was slightly longer than ES-SCLC, allegedly related to diagnosis anticipation. None of these patients was alive at 5 years.

Keywords: small cell lung cancer, Lung Cancer Screening Trial, Early Detection, survival

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-018 Can 30-Mortality after Lung Cancer Resection Be Used as an Individual Surgeon Quality Outcome Internationally? National Data from the UK
Chiara Proli, Maria Elena Cufari, Hilgardt Raubenheimer, May Al Sahaf, Lynn Shedden, Giulia Luciano, Periklis Perikleous, Nizar Asadi, Hemangi Chavan, Miguel Meza Guzman, Michael Dusmet, Eric Lim *Department of Thoracic Surgery, Royal Brompton and Harefield NHS Trust, London/United Kingdom*

Background: Internationally, one of the most commonly reported quality outcome in surgery for lung cancer is 30 day mortality. However, is difficult to know what constitutes unacceptably high mortality or unacceptable variation between surgeons. In October 2014 national data was released from the Society for Cardiothoracic Surgery (SCTS) in the United Kingdom (UK) on hospital and individual surgeon volume performance for lung cancer resection in the UK. The implicit assumption is benchmarking of the performance. The aim of this study is to report on the impact of individual surgeon volume in relation to each death associated with the an average 30-day mortality rate of 2.2% using national data driven performance control limits (i.e. funnel plots), and determine the applicability on surgeon performance internationally. **Methods:** Data released by the SCTS were downloaded, complied and analysed. Each step change for individual mortality was calculated, and alert limits modelled using current UK national standard of the upper 99% binomial confidence limit. **Results:** Data from 29 units were published with the annual volume of 125 surgeons for 2012. Data from 6 surgeons were excluded for no lung resections performed. In the remaining 118 surgeons, the mean (SD) annual lung resection volume for cancer was 42 (27). A total of 25% of surgeons performed 18 resections (or less) per year. For 50% of surgeons undertaking 40 resections (or less) each death represents at least 2.5% (0 to 13%) of their annual work load. Using a 99% binomial confidence limit at 50 cases, the upper alert is 16%. Therefore for the majority of surgeons, a mortality rate of 15% which is 7.5 fold higher than average would not trigger the conventional national alert limits. **Conclusion:** Based on UK national data, lung cancer resection volumes for individual surgeons are low and for the majority even a single death (which could be due to chance), affects the overall mortality rate much more, carries a disproportionately high weighting and may encourage risk adverse behaviour whilst simultaneously failing to detect 7.5 fold increased mortality rates using conventional national limits. Such data driven limits would also not be applicable on an international level basis unless individual surgeon volume is higher than 100 resections per year, a level that was not achieved by most UK surgeons.

Keywords: Thoracic surgery outcomes, Lung resection for lung cancer, 30-day mortality

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-019 A Comparison of Demographic Risk Variables for Lung Cancer in New Zealand Europeans and Maori: Are Maori More Susceptible to the Effects of Smoking?
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Background: Lung Cancer is the leading cause of cancer death among New Zealand (NZ) Maori. Over the past twenty years lung cancer incidence has decreased in New Zealand for non-Maori but has increased for Maori, and is recognised to be the highest in the world of any ethnic group. Nationally, the incidence of lung cancer in Maori is 3.5 times higher than that in New Zealand Europeans, and lung cancer mortality in Maori males and females respectively, is 2.4 and 4.2 times higher than NZ Europeans. Maori have a higher incidence of lung cancer than countries with similar smoking rates. This suggests that there are additional factors other than smoking that predispose Maori to this disease. In the current study demographic and the well-established clinical risk variables for lung cancer were compared between New Zealand Maori and Europeans residing in the greater Auckland region and who were diagnosed between January 2004-January 2015. **Methods:** A retrospective review of patient clinical notes for those identified as being of NZ Maori ethnicity who were diagnosed with lung cancer (n=473) between January 2004 and January 2015 and treated within the greater Auckland region. Data extracted included histological type, smoking history, spirometry and basic demographics. This data was then compared with an established cohort of NZ European patients n= 417, with similar recruitment criteria over the period 2004-2008. **Results:**Despite comparable smoking exposure histories, NZ Maori patients were diagnosed on average 6 years younger than NZ European lung cancer patients (P<0.0001). At diagnosis, current smoking rate was 2 fold greater in NZ Maori compared to NZ Europeans (69% vs 36%, P<0.0001). Although NZ Maori patients had similar rates of COPD (≈64%), they had a trend towards less GOLD 1 (mild stage disease, P=0.08) and significantly greater airflow obstruction (worse COPD, FEV_1%predicted 64% vs 73% in NZ Europeans, P<0.001). At lower smoking exposure (≤10 pk yrs), COPD rates in Maori with lung cancer were 2 fold greater than in NZ Europeans (64% vs 32% respectively, P<0.05). NZ Maori lung cancer patients had a lower prevalence of adenocarcinoma than in NZ Europeans (32% vs 43%, P=0.002) and a higher proportion of more aggressive lung cancer subtypes (squamous, non-small cell and small cell cancers) than NZ Europeans (61% vs 52%, P<0.0007). **Conclusion:** These results show that lung cancer in NZ Maori is associated with younger age at diagnosis, worse lung function and more aggressive histological subtypes compared to NZ Europeans. These results suggest that NZ Maori may have a greater inherent susceptibility to lung cancer compared to NZ Europeans. This greater susceptibility to lung cancer in Maori, along with socio-cultural factors, may contribute to their considerably greater mortality. These results suggest that for the future management of lung cancer, prevention measures (such as smoking cessation and tobacco control), risk assessment (such as lung function testing) and early diagnostic approaches (such as computed tomography screening) should be prioritised in high risk groups, particularly those with NZ Maori ancestry.
Keywords: lung cancer, Maori, susceptibility, ethnicity

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-020 Detection of Aberrant ALK Expression from Circulating Tumor Cells for Accurate Monitoring of ALK Driven NSCLC
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Background: Insight Genetics Inc. and Biocept, Inc. have established a collaboration to develop a non-invasive work flow to enhance detection of the oncogenic Anaplastic Lymphoma Kinase (ALK) status in NSCLC patients. A barrier to detection of oncogenic transcripts in circulating tumor cells (CTCs) has been purification methods that are incompatible with downstream qPCR detection technologies. In contrast, Biocept's proprietary CTC capture technology has been shown to be benign for follow up qPCR detection using Insight Genetics proprietary qPCR-based oncogenic ALK detection assay. **Methods:** Initial studies were conducted to demonstrate cell capture on the Biocept platform with spiked ALK fusion positive H3122 cells. These studies show this to be a feasible option for non-invasive detection of ALK mRNA. A pre-amplification allele-specific approach including reference controls was incorporated. H3122 cells spiked into peripheral blood also demonstrated feasibility of the accurate detection of aberrant ALK expression using the Biocept CTC extraction methodology and Insight Genetics' qPCR detection strategy. **Results:** from these studies and the detection of aberrant ALK expression from a cohort of ALK positive patients will be presented along with the potential to use CTCs to monitor ALK inhibitor resistant mutation profiles. **Conclusion:** Together, Biocept's proprietary CTC capture technology coupled to Insight Genetics qPCR ALK detection assay appears to be a viable strategy to accurately monitor ALK status in NSCLC patient populations using a liquid biopsy.

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-021 Is Safe to Follow High-Risk Patients with Suspicious Lung Nodules without Invasive Tests?
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Background: Low dose computed tomography (LDCT) screening for lung cancer (LC) provides reduction in mortality rates among individuals at high risk. Pre-Test Probability of Malignancy (PTPM) is a common tool used during the decision process: when the probability of malignancy is moderate or high, patients should be referred for further testing or tissue sampling. However, in some cases, these statistic models may give an overestimated value, especially in countries with a high incidence of granulomatous diseases. We have calculated the PTPM in our LDCT screening program and this work explores its main results. **Methods:** Prospective cohort of current or former smokers, with a heavy smoking history. Data of the first LDCT were analyzed to calculate the PTPM. The inclusion criteria were similar to NLST. LDCT scans with indeterminate pulmonary nodules above 4mm in size were considered positive and were evaluated by a multidisciplinary team. The PTPM model used in this study was designed by Swensen et al and included patient's age, smoking history, diameter of the nodule, spiculation and upper lobe location. A PTPM > 60% was considered high and between 6 and 60% was considered moderate.

Results: From January 2013 to July 2014, 790 were included in the protocol. We found 310 positive LDCT at baseline (39%), 34 (11%) with high PTPM. Among them, 16 were followed with LDCT in 3 (56.2%), 6 (37.5%) or 12 (6.3%) months and the remaining were investigated with PET-CT and/or lung biopsy. From the patients followed by LDCT, one case showed an increase in nodule size and was investigated with lung biopsy; all others were stable in one-year follow up. LC was diagnosed in 7 patients and benign diseases in 5 patients with high PTPM, including 1 case of tuberculosis. Other 4 cases of NSCLC were found in the moderate PTPM group (n=272). Therefore, malignancy rate was 20.6% for high PTPM and 1.5% for moderate PTPM nodules. **Conclusion:** The Swensen's PTPM model overestimates the prevalence of LC in both groups of moderate and high-calculated values of PTPM. The decision making process should include other variables discussed in a multidisciplinary board, been safe to follow patients with further image tests. **Keywords:** lung cancer, Screening, Low dose computed tomography

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-022 The British Thoracic Society Guideline on the Investigation and Management of Pulmonary Nodules (2015)

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Background: British Thoracic Society (BTS) Guidelines are aimed primarily at practitioners within the UK. They are National Health Service Evidence accredited which means they must adhere to robust guideline development methodology. The evidence base for this guideline comes mostly from countries outside the UK so the recommendations will have relevance to other countries healthcare systems. **Methods:** The recommendations are based on a comprehensive review of the literature on pulmonary nodules and expert opinion. A third of the 360 references cited were from 2012 onwards, reflecting the rapid expansion of the evidence base. The new evidence has resulted in important differences from guidelines previously published by the American College of Chest Physicians and the Fleischner Society. **Results:** There are four algorithms: initial approach to solid nodules; surveillance of solid nodules; management of sub-sold nodules; and pulmonary nodule treatment. Two malignancy prediction calculators are recommended to assess the risk of malignancy; one (the Brock University model) that performs best for smaller nodules and one that has the better accuracy for larger nodules following PET-CT (the Herder model). There are recommendations based on recent evidence from screening studies, for a higher nodule size threshold for follow up (≥5mm or ≥80mm^3). This will reduce the number of follow up CTs which, in the UK at least, are not cost effective. Surveillance recommendations are also different from previous guidelines: people can be discharged after 1 year of stability if measured by semi-automated volumetry. Management is also dependent on the volume doubling time (VDT) with immediate further assessment for nodules that show a VDT of ≤400 days and either biopsy or further observation for nodules with VDTs of >400 to ≤600 days. People with nodules with a VDT >600 days have the option of discharge, if VDT is measured by volumetry. As in previous guidelines, a 3 month repaet CT is recommended for sub-solid nodules.After that, management is governed by risk assessment by the Brock tool (with the proviso that it may underestimate risk after the initial CT) and according to specific features that predict malignancy. Acknowledging the good prognosis of sub-solid nodules, there are recommendations for less aggressive options in their management. The guidelines provide more clarity in the use of further imaging, with ordinal scale reporting for PET-CT recommended to facilitate incorporation into the Herder risk model and more clarity about the place of biopsy and its influence on pre-test probability. Segmentectomy can be considered for primary diagnosis and treatment for nodules smaller than 2cm, and sub-lobar resection is recommended for pure ground glass nodules. Where fitness levels preclude surgery, non-surgical treatment with stereotactic ablative radiotherapy or radiofrequency ablation is recommended, even where biopsy is not possible, provided the probability of malignancy is high. Finally, there are evidence based recommendations about the information that people need that should be provided for them. **Conclusion:** The BTS guideline is intended to be used both as a summary in the day to day management of the person with a pulmonary nodule as well as a comprehensive reference text. **Keywords:** Guideline, pulmonary nodule

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-023 Addition of Low Dose Computed Tomography Image-Features Improves Diagnostic Accuracy for Indeterminate Pulmonary Nodules

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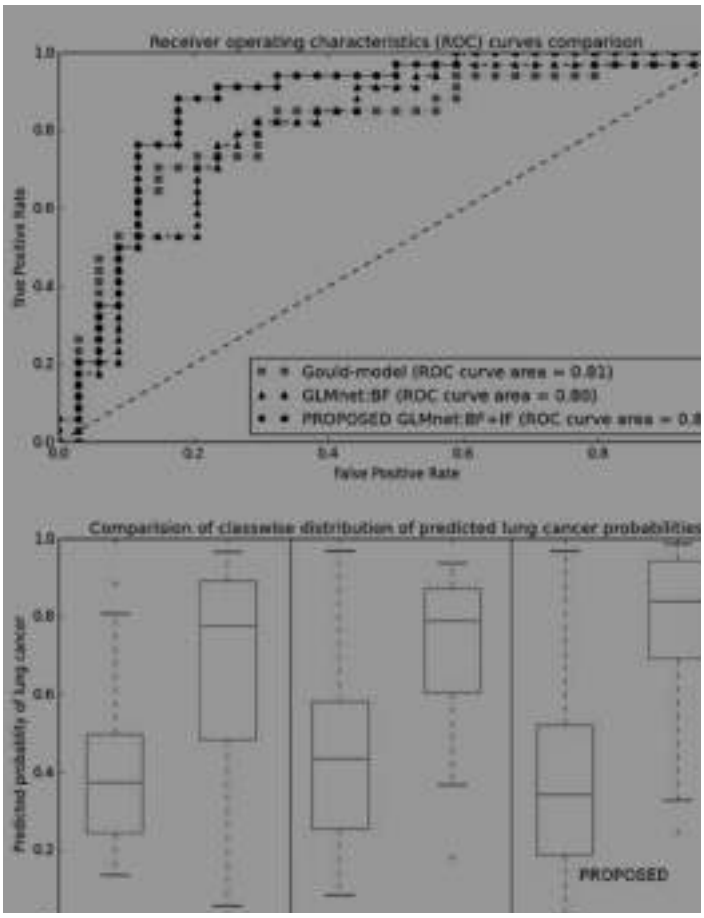
Background: Lung cancer is the leading cause of cancer related deaths world-wide. While low dose computed tomography (LDCT) screening of the high risk patient population was recently shown to decrease deaths from lung cancer by 20%, LDCT also resulted in 18% over-diagnosis [c.f. Patz-E.-F.-JAMA-2003] with a positive predictive value of only 52.9% when a suspicious LDCT finding led to a biopsy [c.f. Church-T.-NEJM-368-2003]. We tested whether combining novel image-features (IF) with routinely collected baseline-features (BF) can improve the accuracy of diagnosing suspicious findings on baseline LDCT. **Methods:** This exploratory case-control study included N=123 (66-cancer, 57-no-cancer) high risk subjects with at least one suspicious finding (nodule >= 8mm [c.f. Lung-RADS-ACR-2014]) on baseline LDCT screening at Vanderbilt University on a VCT Discovery (GE-Healthcare, UK) or a Brilliance iCT 128 SP (Philips, Amsterdam) system. The cohort was randomly divided into a separate training-set (N=55, 32-cancer, 23-no-cancer) and a test-set (N=68, 34-cancer, 34-no-cancer). All model training and leave-one-out cross-validation were strictly restricted to the training-set. Performance was evaluated on the **unseen** test-set. Definitive lung cancer or no-cancer diagnosis, smoking history and at least 6 baseline-features (BF6) viz. age, family-history, pack-smoking-years, body-mass-index, nodule-location, nodule-size were recorded for all subjects. Baseline lung cancer predictions were generated by (a) using the Gould-model [c.f. Gould,M.-Chest-2007] and (b) fitting an Elastic-Net Regularized Generalized Linear Model (GLMnet [c.f. Zou-H.-Journ-Royal-Stats-Soc-B-2005]) to BF6. The final baseline model ("GLMnet:BF") effectively utilized 4 baseline-features with the coefficients for age and body-mass-index shrunk to zero. New LDCT specific information was extracted by computing 589 intensity, shape, surface and texture features (IF589) [c.f. Aerts-H.-Nat-Comm-S2014, Way-T.-Med-Phys-2009] from a 3D volume-of-interest (VOI) encompassing a rough Graph-cuts [c.f. Li-K.-IEEE-PAMI-2006] segmentation for each suspicious nodule. A GLMnet was fit to all 595 features (BF6 and IF589) yielding a final enhanced model ("GLMnet:BF+IF"), which contained 12 features after GLMnet shrinkage: 10 IF related to VOI energy, nodule shape and surface statistics and image intensity variability and 2 BF (family-history, nodule-location). **Results:** Baseline AUC increase by 7.4% from 0.81 (Gould-model) and 0.80 (GLMnet:BF) to 0.87 (GLMnet:BF+IF). At 88% sensitivity, false positive rate reduced by 60% from 56% (Gould-model) and 44% (GLMnet:BF) to 18% (GLMnet:BF+IF); accuracy improved from 65% (Gould-model) and 71% (GLMnet:BF) to 84% (GLMnet:BF+IF). Fig.1 below shows more details:



Conclusion: This initial exploratory analysis showed that image-features extracted from suspicious LDCT findings may help reduce the number of unnecessary biopsies. Additional validation studies are warranted to determine the value of this structural imaging-based approach. **Keywords:** CT image features, Elastic-net Regularized GLM, diagnostic accuracy for indeterminate pulmonary nodules, Low dose CT lung cancer screening

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-024 Patterns of ^{18}F FDG-PET/CT Studies in Patients with Suspected or Confirmed Lung Cancer - A Johannesburg Academic Hospital Perspective
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Background: Lung cancer incidence has increased rapidly in developing countries over the last few decades. It is estimated to account for nearly one-fifth of cancer-related deaths in South Africa. Imaging plays an integral role in the evaluation of patients with lung cancer. 2-[^{18}F] fluoro-2-deoxy-d- positron emission tomography (^{18}F FDG-PET) is now an accepted part of the imaging assessment. Integrated FDG-PET/ CT imaging is recognised as being superior to PET alone and CT alone in the imaging of lung cancer especially for staging of untreated non-small cell lung cancer (NSCLC). An audit was conducted to describe the patterns of disease in our centre. **Methods:** Retrospective audit which included 89 studies performed for patients with suspected or histologically confirmed lung cancer referred to us for PET/CT from September 2008 to March 2015. PET/CT reports of the patients were retrieved together with relevant clinical information from the case files whenever necessary. Over two-third (71%) of patients were referred for diagnosis/staging, others for re-staging (19%) and response to therapy (10%). All of the studies were reported by qualified and experienced Nuclear Medicine Physicians and the CT components of these studies were also read in conjunction with qualified Radiologists. **Results:** There were 89 scans from 87 patients. Majority of the patients were males (60%) and the mean age was 61.0 ± 9.4 years. About 42% (n=37) of the studies were performed on patients with histologically confirmed lung cancer; of the remaining indications, 15% (n=13) were referred for solitary pulmonary nodule and 43% (n=39) for multiple pulmonary nodules and masses. More than two-thirds (71%) were referred for staging, about one fifth (19%) for re-staging and 10% to assess response to treatment. The vast majority (94%) of known lung cancer were NSCLC that included adenocarcinoma (40%), squamous cancer (29%) and NSCLC not otherwise specified [NOS] (26%). F-18 FDG PET/CT showed almost an equal number in the presence (37%) or absence of metastases (36%). No significant differences were noted on FDG PET uptake between the three subtypes mentioned above ($p > 0.05$, Chi square). However, there was a tendency for a difference between these histological subtypes [squamous, adenocarcinoma and NSCLC NOS] for the presence of metastases ($p<0.09$) and the sites of metastatic predilection ($p<0.08$). Just more than half (53%) of patients showed evidence of positive regional nodal involvement on PET. All SPN were visualised on PET (sensitivity 100%) with about 57% with high FDG uptake (mean SUV=7.71) and about 43% with low FDG uptake (mean SUV=1.05). Correlation with histology was available for 38% of all SPNs and FDG PET correctly identified all of them as malignant or benign (100% specificity). **Conclusion:** ^{18}F FDG-PET/CT is useful in characterising solitary pulmonary nodules (SPNs) and staging as well as monitoring treatment response in lung cancer. Although it cannot replace histological confirmation of nodal and metastatic involvement, it serves as a roadmap to identify areas for tissue diagnosis. The detection of metastases may alter the therapeutic decision of NSCLC. **Keywords:** Lung Cancer, NSCLC, SPN, PET/CT

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-025 Statistical Analysis of 18F-FDG-PET/CT Findings of Ground Glass Nodule (GGN)
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Background: 18F-FDG-PET/CT (PET/CT) is one of the most important image inspections for the diagnosis of lung cancer. However, there are often false negatives caused by small lesions such as Ground Glass Nodule (GGN). Whether PET/CT is useful for the diagnosis of GGN is unknown. Therefore, we analyzed the relationship of computed tomography (CT) findings (size, properties) and maximum standardized up-take values (SUV-max) of GGN. **Methods:** We had 69 patients with pathological-Stage IA-IB lung adenocarcinoma who underwent surgical resection and PET/CT from January 2010 to December 2014. We retrospectively examined their clinical characteristics, CT findings, and PET/CT findings. **Results:**Characteristics of 69 patients were as follows, 47 - 86 years old (median 70 years old), female/male: 39/30, pathological-Stage IA/IB: 59/10. GGN diameter: 1.1 - 41.13mm (median 19.43mm), Solid-part diameter: 0.0 - 23.23mm (median 4.55mm), Solid-part-ratio (solid-part diameter / GGN diameter): 0 - 77% (median 20%). SUV-max was insignificant to 6.8 (median 1.0). Correlation coefficient of each factor and SUV-max were as follows, GGN diameter: 0.49, Solid-part diameter: 0.54, Solid-part-ratio: 0.41 (Pearson's product-moment correlation). All pure-GGN show no significant SUV-max (<2.5), even though there are some large GGN included (max 40.0mm). GGN diameter >20mm or solid-part diameter >5mm were significant factor of FDG-uptake (Fisher's exact test). In this study, SUV-max was lower than significant level with solid-part diameter <4.55mm. **Conclusion:** There was no significant SUV-max with diagnostic value in pure-GGN. PET/CT is not useful for pure-GGN or small part-solid nodule (solid-part diameter <4.55mm). There is higher correlation in the solid-part diameter and SUV-max. We should keep in mind the limitation of PET/CT for GGN diagnosis. **Keywords:** PET/CT, GGN

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-026 18F-FDG PET/CT Evaluation of Non-Small Cell Lung Cancer - Initial Experience from Johannesburg
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Background: Lung cancer is the most common cause of cancer-related mortality, with an overall five year survival of 16.6%. It is most likely to recur in the first four years after therapy. The overall five year survival for newly diagnosed lung cancer is poor in both developed and developing countries. In South Africa, statistics show that lung cancer caused 52,217 deaths between 1995 and 2006. The 2009 data from South Africa showed that the number of male and female cases of lung cancer was 1440 and 685, respectively. ^{18}F-FDG PET/CT allows non-invasive imaging of non-small cell lung cancer (NSCLC) based on the increased glucose metabolism by the cancer cells. ^{18}F-FDG PET/CT imaging of NSCLC has been found to be useful in staging, early detection of recurrence, detection of residual disease and monitoring of treatment response. Our study was carried out to evaluate its role in histologically proven NSCLC in our center. **Methods:** We retrospectively reviewed data of 34 patients with histologically confirmed NSCLC. A total of 51 scans were reviewed, of which 17 were follow-up PET/CT scans. Eleven patients had 1 follow up (FU) scan, 5 patients had 2 FU scans and one patient had 3 FU scans. FDG-PET/CT findings were reported as positive or negative for disease. Sites for distant and nodal metastases were noted. Follow up scans were also compared with previous or base line scans to assess for treatment response, early detection of recurrence and detection of residual disease. Of the total number of patients, only 24 patients have had follow up to see how PET/CT influenced their management. **Results:** Data were analysed from 20 males (59%) and 14 females (41%) of which majority (83%) were aged between 61 to 80 years old. A total of 51 scans were done, 37 (72.5%) were positive and 14 (27.5%) were negative. Almost a quarter of PET/CT scans were referred for staging (25.3%), about half for detection of residual disease (47.1%) and the remaining for the detection of recurrence (13.8%) and assessment of treatment response (13.8%). At initial imaging, metastases were visualized in 44% of patients; two-thirds of the metastases being in the adrenal, bone and contralateral lung. Nodal disease on the initial scans was noted in 56% of patients. We compared the findings in patients with FU studies. The changes from the initial studies and the first FU showed a tendency towards a significant difference ($p=0.05$; Pearson Chi-square). When the rest of FU scans were compared, there was no significant difference ($p=0.66$ for FU1 Vs FU2) and ($p=0.71$ for FU2 Vs FU3). PET/CT correctly up staged 29.4% and down stage 5.9% of patients and at the same time falsely down staged 5.9% and upstaged 2.9% of patients. **Conclusion:** ^{18}F-FDG PET/CT is useful in staging, early detection of recurrence, detection of residual disease and monitoring of treatment response in patients with non-small cell cancer. The tendency noted in comparing the initial and FU scans is due to lower power of this study. **Keywords:** 18F-FDG PET/CT, non-small cell lung cancer, Detection of residual disease, Staging

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-027 Role of Brain MRI and PET-CT in Follow-Up after Lung Cancer Surgery
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Background: Standard follow-up method after pulmonary resection for lung cancer is not determined. While chest computed tomography (CT) is widely utilized, brain magnetic resonance imaging (MRI) and positron emission tomography (PET) are also used as follow-up examination to detect cancer recurrence recently. Object of this study is to clarify the ability of MRI and PET to detect recurrence as follow-up examination setting. **Methods:** Medical records of 281 patients with lung cancer who underwent complete pulmonary resection for lung cancer from 2009 to 2012 were retrospectively reviewed. Information regarding recurrence, such as site of recurrence, time after surgery, tumor markers, and survival, were collected. Pathological stage according to 7th version of TNM staging was IA/IB/IIA/IIB/IIIA for 143/75/23/16/24 patients, respectively. Number of the patients with adenocarcinoma/squamous cell carcinoma/large cell carcinoma/small cell carcinoma/pleomorphic carcinoma/others was 190/71/2/2/7/9, respectively. All PET images were combined with simultaneously performed CT scan. Statistical analysis was performed using Mann-Whitney test for comparing groups and log-rank test for survival analysis. P-values less than 0.05 were regarded as significance. **Results:** CT was utilized for 255(90.7%), brain MRI for 130 (46.3%), and PET for 102 (36.3%). Recurrence of lung cancer was observed in 58 patients (20.6%). Pathological stage was IA/IB/IIA/IIB/IIIA for 11/14/12/7/14 patients, respectively. Initial recurrent site was intrathorax/bone/brain/adrenal gland/liver for 34/15/5/3/1 patients, respectively. Motive to detect initial recurrence was patients' symptom/CT/MRI/PET for 16/24/3/15 patients, respectively. Brain MRI detected 3 out of 5 (60%) of brain metastasis as an initial recurrence in asymptomatic status. PET detected 8 out of 15(53.3%) of bone metastasis as an initial recurrence in asymptomatic status. In 19 of 48 (39.6%) patients, elevation of tumor markers beyond normal range was observed before detection of metastasis by diagnostic imaging examination. Time after surgery to initial recurrence was shorter in symptom-detected group than in examination-detected group (median 233 versus 404 days, $p<0.001$). Similarly, survival after initial recurrence was shorter in symptom-detected group than in examination-

detected group (median 149 versus 916 days, p<0.001). **Conclusion:** Follow up after lung cancer surgery utilizing brain MRI and PET effectively detect ansymptomatic metastasis to brain and bone. Survival benefit need be concluded by different setting. Furthermore, economic efficiency are also warranted to be analyzed. **Keywords:** Surgery, follow up, PET, MRI

POSTER SESSION/ SCREENING AND EARLY DETECTION
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.06-028 Distribution of Stage, Surgical Methods and Prognosis of Lung Adenocarcinoma According to the Initial Diagnostic Patterns Eunjue Yi[1], Hyun Hwak Shin[1], Hyo-Jun Jang[1], Mi Kyung Bae[2], Sukki Cho[1], Kwhanmien Kim[1], Sanghoon Jheon[1] [1]*Seoul National University Bundang Hospital, Seongnam-Si/Korea,* [2]*National Health Insurance Service Ilsan Hospital, Goyang-Si/Korea*

Background: Early detection of lung adenocarcinoma is important for reducing cancer mortality. We investigated how lung adenocarcinoma has been diagnosed in our institute, and evaluate the effects on the treatment and prognosis. **Methods:**Medical records of 1065 patients who had undergone lung cancer treatment including surgery in our institute between 2003 and 2012 were reviewed retrospectively. We excluded patients who lacked data for diagnostic process (3 patients) and underwent neoadjuvant therapy (38 patients). Patients were categorized into 3 groups, (1) group1; patients who were diagnosed during routine medical examination, (2) group2; patients with symptoms, and (3) group3; patients who were diagnosed during the treatment of other diseases. Surgical methods, stages and diagnostic tools were compared and survival analysis was done. **Results:** A total of 1024 patients were included. The mean follow-up periods were 55.8 months (± 29.00, range from 0.00 to 139.20). The number of sublobal resection (wedge resection and segmentectomy) in group1, 2, and 3were 85, 37 and 89 respectively. Group1 and group3 underwent significantly more limited resection than group 2 (p<0.000). The number of VATS approaches were 341 (80.6%), 148 (52.7%) and 231 (70.3%) in group1, 2, and 3 respectively. Group2 and group3 had significantly more open thoracotomy than group1 (p<0.000 for group2 and p=0.042 for group3). Early stage lung adenocarcinoma (including 0, IA and IB) was found more in group1 (318 patients, 75.2%) and in group3 (251, 78.4%) than in group 2 (150, 53.4%). Overall and disease-free survival periods of group1 (57.0 ± 27.60 and 50.4 ± 30.89) and group3 (54.6 ± 27.67 and 46.9 ± 29.57) were significantly higher (p <0.000 and p=0.002 for overall survival, P<0.000 for disease-free survival) respectively than those of group2 (55.5 ± 32.38 and 42.6 ± 34.92). Group 1 and group3 has no significant differences both in overall and disease free survival periods. Chest computed tomography was most commonly used diagnostic tool in group2 and group3 (48.4% and 35.6% respectively), on the contrary, chest roentogram in group1. **Conclusion:** Incidentally found lung adenocarcinoma during treatment for other diseases has no differences with those in regular health examinations in stages, surgical extent and prognosis. Careful inspection for those patients could contribute equally for early detection of lung adenocarcinoma as routine screening. **Keywords:** lung adenocarcinoma, diagnosis, Prognosis

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P1.06-029 Serum Glutathione Peroxidase 3 as a Biomarker of Postoperative Relapse in Patients with Lung Cancer In-Jae Oh[1], Hyun-Ju Cho[1], Chul-Kyu Park[1], Young-Chul Kim[1], Ju-Sik Yun[1], Sang-Yun Song[1], Kook-Joo Na[1], Mee Sun Yoon[1], Sung-Ja Ahn[1], Hyun-Ju Seon[1], Yoo-Duk Choi[1], Seung-Won Lee[2] [1]*Lung and Esophageal Cancer Clinic, Chonnam National University Hwasun Hospital, Jeonnam/Korea,* [2]*Department of Anatomy, Chonnam National University Medical School, Gwangju/Korea*

Background: Glutathione peroxidase 3 (GPx3) which is an extracellular secretory protein is down regulated in patients with early stage lung cancer. We examined the usefulness of serum GPx3 as a biomarker for monitoring of relapse after surgery. **Methods:** We prospectively collected serial serum samples at baseline, 3 months (3m), 6 months (6m), and 12 months (12m) after operation from the patients who underwent surgery during the year 2013. GPx3 levels were measured three times per sample using the enzyme-linked immunosorbent assay, and the mean values were analyzed by repeated measure analysis of variance. **Results:** A total of 126 (73 adenocarcinoma, 31 squamous cell carcinoma, 22 others) patients were analyzed in this study. Median age of patients was 66 years old (range, 39-80) and 19 (15.4%) out of 123 lung cancer patients were confirmed relapse during the follow-up period of 2 years. In squamous cell carcinoma, the changes of mean serum GPx3 were significantly different between relapse (baseline: 13.3 ± 1.1 μg/mL, 3m: 17.1 ± 4.6 μg/mL, 6m: 14.8 ± 2.7 μg/mL, 12m: 17.9 ± 1.7 μg/mL) and control group (baseline: 10.8 ± 2.3 μg/mL, 3m: 13.4 ± 3.4 μg/mL, 6m: 12.4 ± 2.6 μg/mL, 12m: 13.5 ± 4.7 μg/mL, p=0.043). The changes of mean serum GPx3 levels were not different between two groups in all histology (p=0.258) and adenocarcinoma (p=0.701). **Conclusion:** Postoperative serum GPx3 levels were significantly elevated only in relapsed squamous cell histology, not in adenocarcinoma. More large scaled validation studies are warranted. **Keywords:** Squamous cell carcinoma, serum, biomarker, Glutathione peroxidase 3

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P1.07-001 Preoperative Serum proGRP as a Predictor for Lung Tumor Histology Marius Lund-Iversen[1], Odd Terje Brustugun[2], Marianne N. Broughton[3], Junbai Wang[1], Nils Bolstad[3], David Warren[3], Zhenhe Sou[1] [1]*Pathology, Oslo University Hospital, Radiumhospitalet, Oslo/Norway,* [2]*Oncology, Oslo University Hospital, Radiumhospitalet, Oslo/Norway,* [3]*Medical Biochemistry, Oslo University Hospital, Radiumhospitalet, Oslo/Norway*

Background: Progastrin-releasing peptide (proGRP) is the stable precursor of gastrin-releasing peptide, a hormone secreted by neuroendocrine cells. Serum measurements of proGRP are helpful to detect relapses of small cell carcinoma during follow up, but its usefulness as a preoperative marker to distinguish between different lung tumors is unclear. **Methods:** Preoperative serum proGRP was determined in 116 patients with primary pulmonary tumors. 31% of the tumors displayed endocrine features (19 carcinoids, 8 small cell carcinoma, 9 large cell carcinomas) whilst the remainder were non-small cell carcinomas (40 adenocarcinomas and 40 squamous cell carcinomas). The presence of proGRP in tumors with possible endocrine features was evaluated by immunohistochemistry using two in-house anti-proGRP monoclonal antibodies (mAb M16 and mAb E149]. Tumors with less than 2 % positive cells were considered negative for proGRP expression. Serum levels of proGRP above 70 ng/L were considered elevated. **Results:** Mean serum proGRP (s-proGRP) was 267 ng/L (median: 96.5 ng/L, [range 25 – 2080 ng/L] for the neuroendocrine tumors, while adenocarcinomas and squamous cell carcinomas had mean values of 50 and 60 ng/L respectively [19,137] and median values 53.5 ng/L and 59.6 ng/L respectively (table 1). Among the tumors with possible endocrine features, serum levels of proGRP reflected the IHC score (Wilcoxon rank-sum test, p<0.0005). We did not find any relationship between tumor size and s-proGRP levels, but values >70 ng/L were predictive of either carcinoid tumor or small cell carcinoma. **Table 1: Tumor characteristics**

Histology	ProGRP IHC positives (n/total)	S-proGRP (median)	S-proGRP (mean)	Mean tumor size (mm)
Carcinoid	9/19	127	424	26.1
Small cell carcinoma	5/8	75.5	145	30.2
Large cell carcinoma	3/9	46	72.8	42.2
Squamous cell carcinoma	NA	59.6	60	NA
Adenocarcinma	NA	53.5	50	NA

Conclusion: The correlation between s-proGRP and IHC scores suggest that the elevated s-proGRP results from proGRP produced by the tumor. The lack of correlation between s-proGRP and tumor size might be explained by variations in number of proGRP producing cells within the different tumors and/or to the amount proGRP secreted by different tumors. For lung tumors with unclear preoperative histology or cytology, s-proGRP-levels can be helpful as an adjuvant diagnostic marker to differentiate between tumors with and without endocrine features, but the test is not robust enough for final decision making. **Keywords:** serum proGRP, immunohistochemistry proGRP, small cell carcinoma, carcinoid tumors

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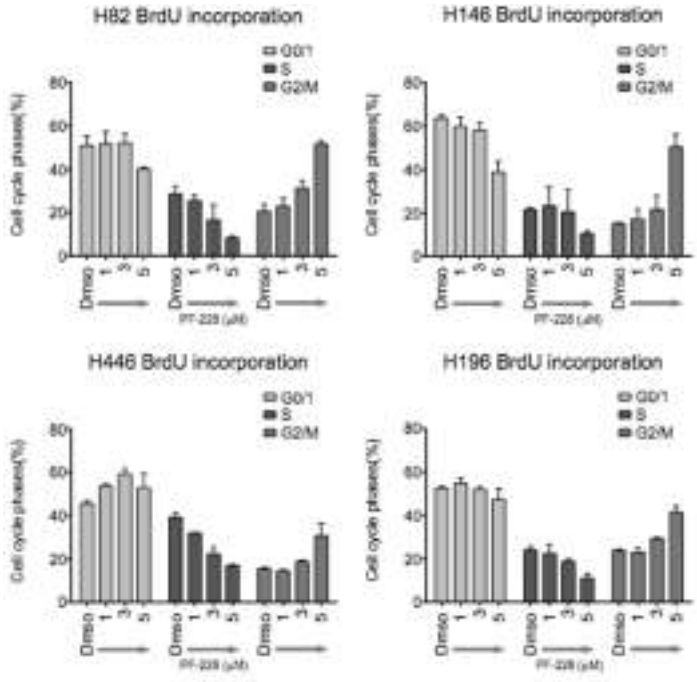
P1.07-002 FAK Inhibition by PF228 Has Anti-Tumoral Effects Associated with Inhibition of Histone 3 and Aurora Kinases A/B Phosphorylation in SCLC Frank Aboubakar Nana[1], Marylene Lecocq[1], Ladjemi Maha[1], Sebastien Dupasquier[1], Bruno Detry[1], Pierre P. Massion[2], Charles Pilette[3], Charles Pilette[1], Yves Sibille[1], Yves Sibille[4], Sebahat Ocak[4], Sebahat Ocak[1] [1]*Institut de Recherche Expérimentale Et Clinique (Irec), Pôle de Pneumologie, Orl Et Dermatologie,, Université Catholique de Louvain, Bruxelles/Belgium,* [2]*Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville/TN/United States of America,* [3]*Division of Pneumology, Cliniques Universitaires St-Luc, UCL, Bruxelles/Belgium,* [4]*Division of Pneumology, Cliniques Universitaires UCL Mont-Godinne, Yvoir/Belgium*

Background: Lung cancer is the most common cancer and the leading cause of cancer-related death worldwide. Small cell lung cancer (SCLC) accounts for 15% of all lung cancer cases and is the most aggressive histologic type, with a five-year overall survival as low as 5%. Focal Adhesion Kinase (FAK) is a non-receptor tyrosine kinase, which regulates integrin and growth factor signaling pathways involved in cell proliferation, survival, migration, and invasion. FAK is overexpressed and/or activated in many cancers,including SCLC. We hypothesized that FAK may represent a good target for therapeutic intervention in SCLC and tested the changes of cell phenotype and signaling events following FAK inhibition, by using PF-573,228 (PF-228) in SCLC cell lines. **Methods:** Two SCLC cell lines growing in suspension (NCI-H82 and NCI-H146), an adherent SCLC cell line (NCI-H196), and a mixed morphology SCLC cell line (NCI-H446) were treated with increasing concentrations of PF-228. Cell proliferation was evaluated by WST-1 assay, cell cycle by flow cytometry following propidium iodide (PI) and

bromodeoxyuridine (BrdU) staining, and apoptosis by flow cytometry after intracellular caspase 3 staining. FAK expression/activity and signaling events downstream of FAK were evaluated by Western blotting (WB). **Results:** While PF-228 did not modify total FAK expression, it decreased the phosphorylation of FAK (Tyr 397) in a dose dependent manner in all tested SCLC cell lines. Inhibition of FAK activity by PF-228 significantly decreased cell proliferation, induced cell cycle arrest in G2/M phases,decrease DNA replication and increased apoptosis in all tested cell lines proportionally to the dose. Regarding signaling events, we observed that inhibition of FAK activity induced the inhibition of phosphorylation of histone-3 (Ser 10) and Aurora Kinase A (Thr288) and B (Thr232).



Conclusion: These results show that FAK activity is required for proliferation, cell cycle progression, and survival in SCLC cell lines, suggesting that this pathway is central to SCLC biology. The antitumoral effects of PF-228 may occur through (1) the inhibition of histone-3 phosphorylation mediated by the inhibition of Aurora kinase B and leading to cell cycle arrest in G2/M phase and (2) the inhibition of Aurora kinase A leading to decreased DNA replication. **Keywords:** SCLC, lung cancer, FAK, PF-573,228 (PF-228), AURK

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P1.07-003 Role of Tumor Infiltrating Lymphocytes in Small Cell Lung Cancer
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Background: Small-cell lung cancer (SCLC), a histological subtype of lung cancers, carries a very poor prognosis. Female sex, performance status (PS), and stage are known prognostic markers for SCLC. Lymphocytes have been observed and described in SCLC biopsies from the lung. However, no information is available that defines the correlation of these lymphocytes to SCLC outcomes. To identify this correlation of TiLs to overall survival (OS) and progression free survival (PFS) in SCLC, we carried out a retrospective analysis of SCLC cases diagnosed at our hospital 2008-2013. **Methods:** 53 patients' biopsies of SCLC stained with hematoxylin and eosin were examined with light microscopy at 40X by in-house hematopathologist . Lymphocytes that were interspersed among the tumor cells were counted, and then obtained the pertinent data. Spearman rank correlation analysis was used to assess correlation. **Results:** Among the 53 patients 30 (57%) females and 23 (43%) male, age mean 62.87 years (35-89), average PS 1.53 (0-4), 99% of the patients Caucasian, TiLs mean 70 (10-400), 18 (34%) had LS-SCLC, and 35 (66%) had EX-SCLC

- Progression free survival (data available for total of 36 patient, of which 16 LS-SCLC, 20 ES-SCLC): LS-SCLC 20.84 months (95% CI; 13.76-27.92), ES-SCLC 5.7 months (95% CI; 4.17-7.23)
- OS: LS-SCLC 22.97 months (95% CI; 16.16-29.78), ES-SCLC 8.21 months (95% CI; 5.30-11.13)
- Correlation between TiLs and OS
- Spearman's rho was calculated at 0.15, p=0.28; indicating no correlation between TiLs and OS.
- Correlation when stratified by stage:
- In LS-SCLC, no correlation between OS of LS-SCLC and number TiLs's found (Spearman's rho=0.19, p=0.45 for total of 18 patients).
- In ES-SCLC, no correlation between OS of ES-SCLC and TiLs (Spearman's rho=-0.02, p=0.91).

Conclusion: Recent data in breast cancer (1) and melanoma indicate the presence of TiLs is a positive prognostic marker. However, we were not able to find a positive or negative correlation of TiLs to SCLC outcomes. It is possible that small sample size failed to show a correlation. However, the known prognostic markers for SCLC i.e. female sex, PS, and stage of disease showed correlation with OS in our sample size (data not shown). This indicates that a) our sample size is a good representation of previously studied larger samples, and b) a likely accurate assessment of this correlation. Previously, Wang et al (3) has described FOXP3+ T cell lymphocytes as negative prognostic maskers for SCLC. However, our clinical data fails to provide additional support. Taken together, these studies advocate for larger sample size evaluation. References: 1)Loi et al. Prognostic and Predictive Value of Tumor-Infiltrating Lymphocytes in a Phase III Randomized Adjuvant Breast Cancer Trial in Node-Positive Breast Cancer Comparing the Addition of Docetaxel to Doxorubicin With Doxorubicin-Based Chemotherapy: BIG 02-98. JCO September 20, 2014;32;2935-2937 2)Thomas et al. Tumor-Infiltrating Lymphocyte Grade in Primary Melanomas Is Independently Associated With Melanoma-Specific Survival in the Population-Based Genes, Environment and Melanoma Study. JCO November 20, 2013;31:4252-4259 3)Wang et al. Small cell lung cancer tumor cells induce regulatory T lymphocytes, and patient survival correlates negatively with FOXP31 cells in tumor infiltrate. IJC April 24, 2012; 131:E928–E937
Keywords: TiL, SCLC

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P1.07-004 Efficacy of Endostar Combined with Chemotherapy and Endostar Maintenance Treatment for Patients with Extensive Small-Cell Lung Cancer
Li Chen, Yongxin Wu *Department of Oncology, The First Hospital of Nanchang University, Nanchang/China*

Background: EP scheme is a standard regimen ad the first-line treatment for small cell lung cancer, with the complete remission of 10～25% and overall survival up to 10 months. However, almost all patients reoccur or progress within 1 year after first-line treatment. Endostar combined with chemotherapy had synergistic effect and slight toxic effect. **Methods:** Patient, female, was admitted in the hospital in March, 2010 because of cough and hemoptysis and diagnosed as small cell lung cancer by bronchoscopic biopsy. Patient was finally diagnosed as extensive small-cell lung cancer by pathology and imaging (CT, MRI), who was treated by EP scheme (etoposide and cisplatin) and endostar for 6 months from July, 2010—Jan. 2011. Patient was remitted completely after treated by EP scheme (etoposide and cisplatin) and endostar. However, patients had brain metastases in Jan., 2011 and received radiotherapy and endostar maintenance treatment for 4 cycles. And patient was partially remitted. The reoccurrence of lung was considered in Nov., 2011 and treated by EP plus endostar for 2 cycles and patients was remitted completely until Feb., 2012. **Results:** During the course of treatment, patient was well tolerated to chemotherapy and had no intolerant toxic effects. Performance status of patients scored 0 point. Extra-cerebral progress Free Survival (PFS) reached 13 months and the follow up on overall survival is up to 33 months. **Conclusion:**Endostar combined with chemotherapy and endostar maintenance treatment is effective and safe for the treatment of extensive small-cell lung cancer. **Keywords:** small cell lung cancer; endostar; chemotherapy; endostar maintenance treatment

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P1.07-005 Paclitaxel and Irinotecan in Platinum Refractory/Resistant Small Cell Lung Cancer: Final Analisis of One Galician Lung Cancer Group Experience
Francisco J. Afonso-Afonso[1], Natalia F. Núñez[2], María J. Villanueva Silva[3], José L. Fírvida Pérez[4], Margarita Amenedo[5], Urbano Anido Herránz[6], Laura M. De Paz Arias[1], Marta Covela Rúa[2], Gerardo Huidobro Vence[3], Maria C. Areses[4], Lorena Cadavid Vieitez[2], Nohelia Garcia Cid[3], Sergio Vzsquez-Estevez[7] [1]*Oncología Médica, Complejo Hospitalario Universitario de Ferrol, Ferrol, A Coruña/Spain,* [2]*Oncología Médica, Hospital Universitario Lucus Augusti, Lugo/Spain,* [3]*Oncología Médica, Complexo Hospitalario Universitario de Vigo, Vigo/Spain,*[4]*Complezo Hospitalario Universitario de Ourense, Ourense/Spain,* [5]*Centro Oncolóxico de Galicia, A Coruña/Spain,* [6]*Complexo Hospitalario Universitario de Santiago, Santiago de Compostela/Spain,* [7]*Oncology, Hospital Universitario Lucus Augusti, Lugo/Spain*

Background: Patients with Small Cell Lung Cancer (SCLC) whose disease progresses during or shortly after treatment with platinum, have a poor prognosis. Paclitaxel (P) and irinotecan(I) have demonstrated activity both as monotherapy as in combination regimen for this neoplasm. We have previously presented data from our experience with this agents in patients with SCLC . Here, we present a final analysis of survival and security. **Methods:** We included patients with measurable disease that had progressed during or within six months of first-line chemotherapy based on platinum, with an Eastern Cooperative Oncology Group (ECOG) performance status <2, adequate liver, renal and bone marrow function. They were treated with (P): 75 mg/m2 and (I): 50 mg/m2, both drugs administered on days 1 and 8 of a 21 day cycle. Treatment was maintained until disease progression and/or unacceptable toxicity. **Results:** We included 50 patients with a mean age of 65 years (43-77) and with metastases in two or more locations in 39 of them (78%). A median of 4 cycles of treatment was administered and eight patients (16%) received six or more cycles. The main reason for discontinuation

of chemotherapy was disease progression, observed in 22 patients (44%). Partial response was documented in 18 patients (36%), stable disease in 20 (40%) and disease progression in 7 (14%). There were five patients in whom it was not possible to evaluate response. The median progression free survival was 4.09 months (CI 95%: 2.13-6.05) and the median overall survival was 5.092 months (CI 95% 4.22 – 5.96). No treatment-related deaths were described. The clinical and hematologic toxicities most frequently observed were grade 1 and 2: asthenia (n:20; 40%), diarrhea (n:14; 28%), anorexia (n:12; 24%), alopecia (n:11; 22%), neutropenia (n:5; 10%) and anemia (n:4; 8%). There was one (2%) grade 4 and four (8%) grade 3 neutropenia. There were no cases of grade 4 clinical toxicity and there were 16 (32%) grade 3: nine of diarrhea (18%), three of asthenia (6%), one of vomiting (2%), one of hiponatremia (2%), one hepatic (2%) and one hyperglycemia (2%). **Conclusion:** This (P) and (I) regimen is an effective and well tolerated option for this subgroup of very poor prognosis patients with SCLC.Future explorations using this therapeutic regimen are warranted.
Keywords: small cell lung cancer, refractory, resistant, second-line

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P1.07-006 Final Results of Randomized Phase II Study of Carboplatin plus Irinotecan vs. Carboplatin plus Amrubicin for ED-SCLC
Yuka Fujita[1], Naoto Morikawa[2], Shunichi Sugawara[3], Makoto Maemondo[4], Toshiyuki Harada[5], Masao Harada[6], Akira Inoue[7], Terufumi Katoh[8], Hiroshi Yokouchi[9], Toshihiro Nukiwa[10] [1]*Asahikawa Medical Center, Asahikawa/Japan,* [2]*Iwate Medical University School of Medicine, Morioka/Japan,* [3]*Sendai Kousei Hospital, Sendai/Japan,* [4]*Miyagi Cancer Center, Natori/Japan,* [5]*Jcho Hokkaido Hospital, Sapporo/Japan,* [6]*Hokkaido Cancer Center, Sapporo/Japan,* [7]*Tohoku University Hospital, Sendai/Japan,* [8]*Kanagawa Cardiovascular and Respiratory Center, Yokohama/Japan,* [9]*Fukushima Medical University, Fukushima/Japan,* [10]*Japan Anti-Tuberculosis Assiciation, Tokyo/Japan*

Background: Carboplatin-based regimens, such as carboplatin plus etoposide (CE), are among the standard regimens for the management of extended disease small-cell lung cancer (ED-SCLC). However, the efficacy of carboplatin-based regimens is unsatisfactory. Carboplatin plus irinotecan (CI) and carboplatin plus amrubicin (CA) are promising new carboplatin-based regimens identified in our previous studies. Accordingly, we conducted this randomized phase II study to identify the appropriate regimen for comparison with CE in future phase III trials. **Methods:** Chemotherapy-naïve patients with ED-SCLC were randomly assigned to receive 4–6 cycles of carboplatin (area under the curve [AUC] 5.0, day 1) plus irinotecan (70 mg/m^2, days 1 and 8) every 3 weeks (CI arm) or carboplatin (AUC 4.0, day 1) plus amrubicin (35 mg/m^2, days 1–3) every 3 weeks (CA arm). The primary endpoint was the overall response rate (ORR). Secondary endpoints were progression-free survival (PFS), overall survival (OS), and toxicity. **Results:** Between December 2009 and March 2013, 71 patients were enrolled. One patient in each arm did not receive any protocol treatment owing to rapid disease progression. The characteristics of the treated patients were as follows: median age, 70 years (range 51–84 years) and proportion of males, 84%. Delivered mean dose intensities (mean actual dose/mean planned dose) were similar for both arms: carboplatin 98% and irinotecan 94% for CI arm, and carboplatin 97% and amrubicin 94% for CA arm. The ORRs were 79% and 89%, median PFS was 5.1 and 6.2 months (CA; hazard ratio [HR] = 0.59, 95% CI: 0.35–0.98, P = 0.042), and median OS was 12.2 and 15.9 months in the CI and CA arms, respectively (CA; HR, 0.77; 95% CI: 0.49–1.29; P =.318). Grade 3 or higher neutropenia (CI, 53% and CA, 89%), anemia (CI, 26% and CA, 20%), thrombocytopenia (CI, 18% and CA, 14%), and febrile neutropenia (CI, 12% and CA, 29%) were observed. No treatment-related deaths were observed. Overall, 25 patients (74%) in the CI arm and 28 patients (80%) in the CA arm received post-discontinuation therapies. **Conclusion:** CA was numerically effective than CI in chemotherapy-naïve patients with ED-SCLC, with acceptable toxicity. Therefore, CA could be selected for future phase III trials.
Keywords: ED-SCLC, carboplatin, Amrubicin, irinotecan

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P1.07-007 Prophylactic Cranial Irradiation in Extensive Stage Small Cell Lung Cancer: The Ottawa Hospital Experience
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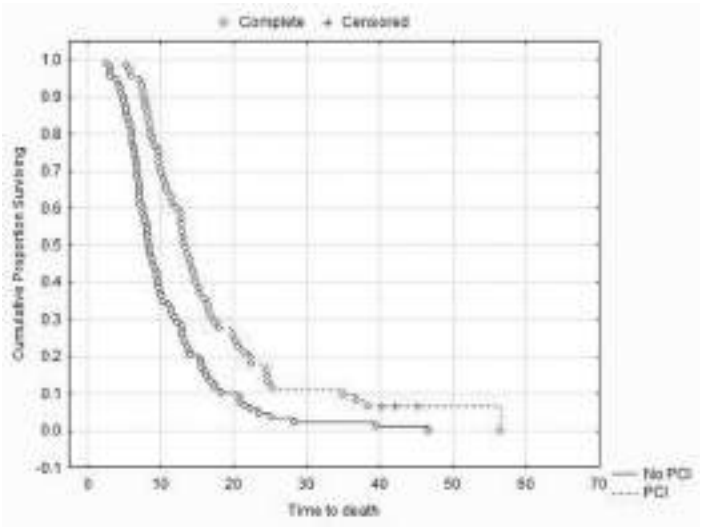
Background: The role of radiation has been investigated in extensive stage small cell lung cancer (ES-SCLC) in two-fold: prophylactic cranial irradiation (PCI) and consolidative radiotherapy. A randomized control trial was published in 2007 (Slotman) which showed benefits for PCI in median survival and decreased cumulative risk of symptomatic brain metastases. We conducted a retrospective study to evaluate the uptake of PCI at The Ottawa Hospital (TOH) for ES-SCLC and its impact on time to brain metastasis and survival. TOH is the sole provider of cancer services for a population of 1.3 million. **Methods:** The medical records of 605 patients (206 limited stage, 399 extensive stage) with small cell lung cancer between Jan. 1, 2005 and Dec. 31, 2011 were reviewed. The cumulative incidence of brain metastases and cumulative proportion surviving was estimated using the Kaplan–Meier method comparing patients receiving PCI or not. Differences between the groups with covariates including age, gender, smoking status, ECOG score, extrathoracic involvement, and response to chemotherapy were analyzed using t-test. **Results:** 158 out of 399 ES-SCLC patients (39.6%) had no brain metastases at diagnosis, received chemotherapy, and had a partial or complete response. Of the 158 patients with these criteria, 69 patients received PCI and 89 did not. 90 patients had brain metastasis on diagnosis, and 151 patients were not eligible or had no response/progression to chemotherapy. On multivariate analysis, the only statistically significant predictors of overall survival were initial performance status and use of PCI. Using t-test, only partial vs. complete response to chemotherapy was found to be significantly different between the PCI and no PCI groups. There was a statistically significant difference in survival (p= 0.0021) and time to brain metastasis curves (p = 0.00029). Median survival for PCI and non-PCI groups was 14.0 and 8.2 months respectively. Median time to brain metastasis was 18.0 and 9.0 months respectively. There was no significant difference in incidence of brain metastases (40.6% vs. 43.8%) in either group. With regards to uptake of PCI for ES-SCLC at The Ottawa Hospital, 24.2% (16/66) of patients before Jan. 1, 2008 were treated with PCI compared to 57.6% (53/92) after 2008.



Conclusion: PCI in the setting of at least partial response to chemotherapy was found to have a survival benefit and prolongation of time to brain metastasis. This has corresponded with an increased uptake of PCI at The Ottawa Hospital since publication of the EORTC 22993-08993 in 2007.
Keywords: extensive stage small cell lung cancer, prophylactic cranial irradiation, Brain metastasis, PCI

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P1.07-008 Preliminary Results from a Phase Ib/II Trial of Belotecan plus Ifosfamide in Patients with Extensive-Stage Small-Cell Lung Cancer
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Background: Belotecan is a novel camptothecin analogue, topoisomerase I inhibitor. Belotecan, alone or in combination with cisplatin, has shown activity in small cell lung cancer. The objective of the phase Ib part was to determine the maximum tolerated dose (MTD) and safety of belotecan plus ifosfamide in patients with extensive-stage small-cell lung cancer. **Methods:** Patients with age ≥ 18 years, no previous chemotherapy, measurable disease, ECOG PS 0-2, and adequate organ function were eligible. The phase Ib portion of the trial is a conventional 3+3 dose-escalation design. The following dose levels (belotecan/ifosfamide, mg/m^2) were explored: 0.5 x 4d/1200 x 2d (level 1), 0.5 x 4d/1000 x 3d (level 2, starting dose), 0.5 x 4d/1000 x 4d (level 3), 0.5 x 5d/1000 x 4d (level 4), and 0.5 x 5d/1000 x 5d (level 5) every 21 days. **Results:** Here we report the phase Ib portion of the trial. Thirteen patients were enrolled and completed at least one cycle. The median age is 68 years (range, 48-77). ECOG PS was 0/1/2:1/6/6, respectively. A total of 53 cycles (median, 5; range, 1-6) of chemotherapy were administered. The MTD was belotecan 0.5 mg/m^2 on days 1-4 in combination with ifosfamide 1000 mg/m^2 on days 1-4 (level 3). Three patients experienced dose-limiting toxicities; death from neutropenic sepsis and grade 3 fatigue at dose level 4, and febrile neutropenia at dose level 3. The most frequent grade 3-4 toxicities were myelosuppression, including neutropenia (54%), anemia (23%), and febrile neutropenia (23%). Eleven patients were evaluable for response and 9 (82%) had partial responses. **Conclusion:** The combination of bleotecan and ifosfamide is feasible and active. The recommended phase II dose is belotecan 0.5 mg/m^2 on days 1-4 and ifosfamide 1000 mg/m^2 on days 1-4 of a 21-day cycle. The phase II trial is currently ongoing. Clinical trial information:NCT01784107.
Keywords: phase Ib, small-cell lung cancer, belotecan, ifosfamide

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P1.07-009 Effect of Accurate Heart Outlining on Cardiac Dose - the CONVERT Trial Experience
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Background: RTOG 0617 showed greater one year overall survival of 81% in the 60Gy group versus 70.4% in the 74Gy group, supporting the hypothesis that cardio pulmonary effects of radiotherapy can contribute to death. It has demonstrated that the percentage of heart receiving ≥5 and ≥30Gy is correlated with survival. Hence there is a need to improve planning and delivery of radiotherapy to avoid irradiating normal lung and heart wherever possible. This current study investigates the effect on cardiac dose of inaccurate cardiac outlining (non compliant to protocol) for a selection of plans submitted as part of the CONVERT Trial quality assurance programme. **Methods:** The CONVERT Trial is a multicentre phase III study which recruited 547 patients with limited-stage small cell lung cancer from April 2008 to November 2013. Patients were randomised to receive once daily (66Gy in 33 fractions) or twice daily (45Gy in 30 fractions) radiotherapy concurrently with chemotherapy. The primary endpoint was overall survival. The spinal canal, lungs, oesophagus and heart were contoured as organs at risk for dose-volume histograms. The trial protocol specified that the heart and pericardial sac should be contoured. Outlining should extend superiorly to the inferior aspect of the aortic arch and inferiorly to the apex of the heart. An atlas was provided to each centre which included example organ at risk contours. In this current study, heart outline volumes (in cm^3) provided by participating centres have been compared to gold standard heart outlines (in cm^3) drawn according to the trial protocol for 50 patients. The impact of the change in heart volume on heart dose (V30) is also presented. The CT and structure set for each case was imported into Eclipse (Version 11), and the heart was re-outlined according to the trial protocol. The plan data were then imported into Vodca along with the dose cube provided by the centre so that DVH data could be extracted. **Results:** The mean difference in cardiac volume between the gold standard and that provided by the centre was 80.0cm^3 (range: 1.9cm^3 to 248.2cm^3). In the experimental trial arm (66Gy), an increase in calculated cardiac dose (V30/%) was seen in 22/28 cases (78.6%) by using the gold standard cardiac outline rather than that provided by the centre. The mean increase in V30 was 5.7% (range: 0.92% to 15.29%). In the control dose arm (45Gy), an increase in calculated cardiac dose (V30/%) was seen in 17/22 cases (77.3%). The mean increase in V30 was 6.9% (range: 0.93% to 14.1%). **Conclusion:** In this study we have shown that in 86% of cases reviewed the heart was not delineated according to protocol. As a result the mean heart dose was underestimated by an average of 2.3Gy. In conclusion, this study highlights the importance of collecting radiotherapy plans to check heart contours as part of a QA programme and to feedback deviations to investigators.
Keywords: heart, outlining, cardiac, Dose

POSTER SESSION/ SMALL CELL LUNG CANCER
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.07-010 Hyperfractionated Versus Hypofractionated Radiotherapy for Limited-Stage SCLC: A Retrospective Comparison of Two Prospective Studies
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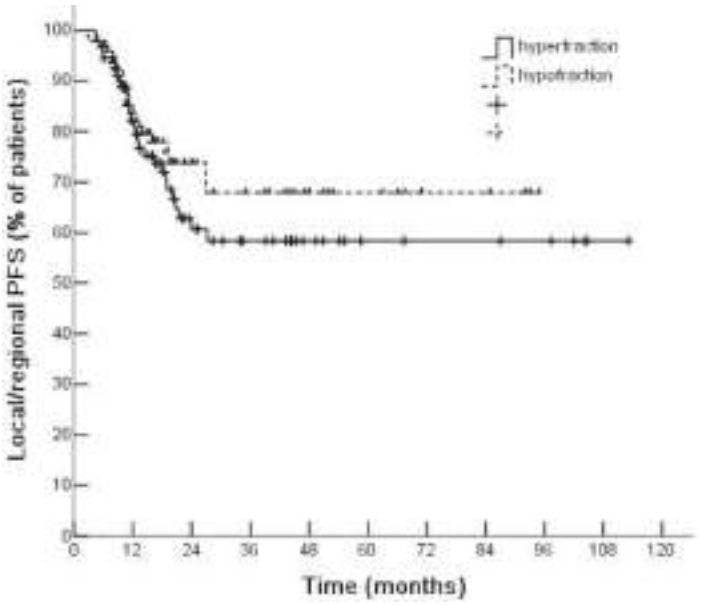
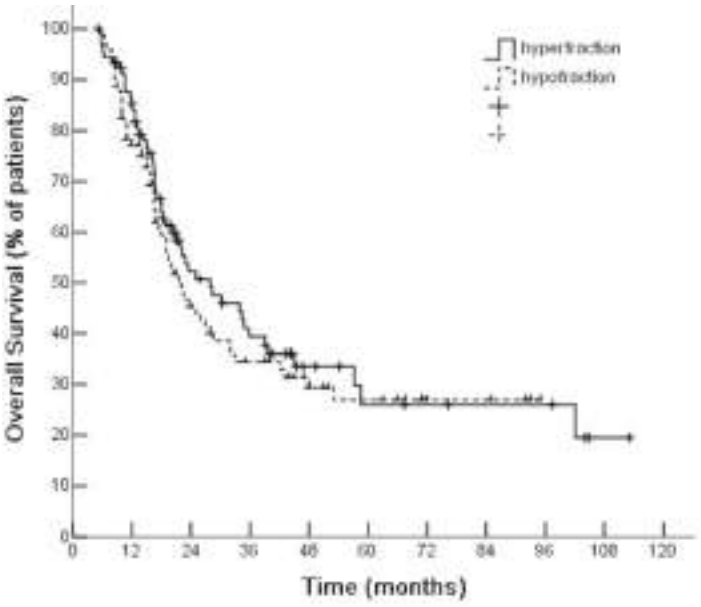
Background: The optimal thoracic radiation dose/fraction for limited-stage small cell lung cancer (SCLC) is not yet established at present. This study mainly aims to retrospectively compare the impact on local/regional control of different thoracic radiation dose/fraction schedules from two prospective trials. **Methods:** Patients received thoracic radiotherapy consisted of 1.5 Gy twice a day in 30 fractions over a 19-day period to a total of 45 Gy (hyperfractionated arm, BED=53.3 Gy) or 2.5 Gy daily in 22 fractions over a 30-day period to a total of 55 Gy (hypofractionated arm, BED=62.6 Gy) combined with concurrent chemotherapy were included into this study. A statistical software package SPSS 13.0 was applied, and Kaplan-Meier method was used to estimate survival data. Fisher's exact test was used for comparisons of categorical data. **Results:** From 2005 to 2014, nighty-two patients were accrued into to the hyperfractionated arm. From 2005 to 2012, nighty-one patients were accrued into the hypofractionated arm. The 1-year, 2-year local/regional progression free survival rates of hyperfractionated arm and hypofractionated arm were 82.1%, 60.7% and 83.8%, 67.9%, respectively (P=0.33). The median survival time (months) of hyperfractionated arm and hypofractionated arm were 27.9 (95% CI: 15.7-40.1) and 22.0 (95% CI: 16.4-27.5) respectively, while 1-year, 3-year, 5-year overall survival rates of the two arms were 85.2%, 39.4%, 26% and 77.1%, 34.4%, 26.9% respectively (P=0.48). Grade 2 and 3 acute radiation esophagitis were observed in 28.3%, 8.7% and 15.5%, 2.1% of patients in hyperfractionated arm and hypofractionated arm (P=0.009).





Conclusion: This study indicated that the use of hypofractionated radiotherapy failed to significantly improve the local regional control rate and overall survival time compared with hyperfractionated radiotherapy. However, the incidence of grade 2 and 3 acute radiation induced esophagitis was significantly more common in the hyperfractionated arm than in hypofractionated arm.
Keywords: limited-stage, thoracic radiotherapy, radiation dose, small cell lung cancer

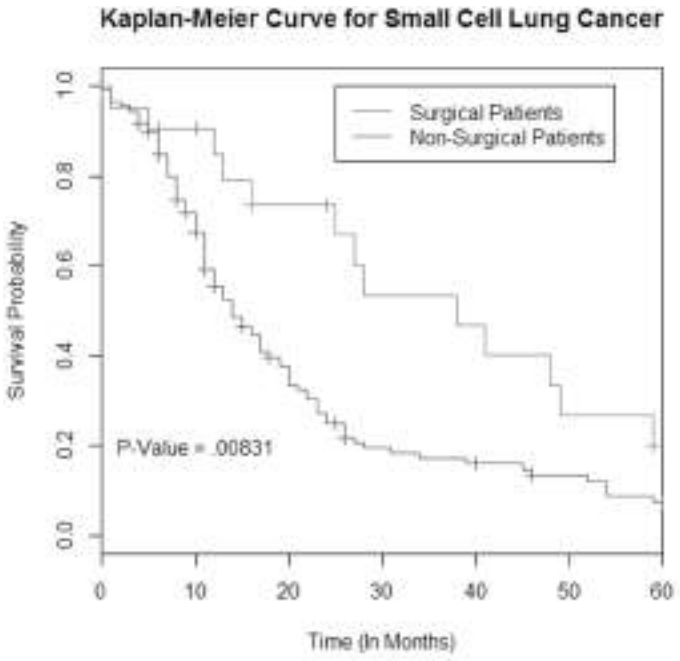
POSTER SESSION/ SMALL CELL LUNG CANCER
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.07-011 'Peripheral Limited' Small Cell Lung Cancer (SCLC). Does Surgical Resection Have a Role in Primary Management?
Lana Y. Schumacher[1], Mathew A. Vandeusen[1], Ali H. Zaidi[1], Samantha A. Martin[1], Emily J. Lloyd[1], Gene G. Finley[2], Athanasios Colonias[1], Blair A. Jobe[1], Rodney J. Landreneau[1] [1]*Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh/United States of America,* [2]*Medical Oncology, Allegheny Health Network Cancer Institute, Pittsburgh/PA/United States of America*

Background: Limited stage SCLC, even peripheral completely resectable disease, is considered by many thoracic oncologic specialists to be a systemic process with a limited role of surgery beyond diagnosis. We hypothesized that surgical resection may improve local control, and potentially enhance survival for the small subset of SCLC patients (pts) with peripheral, resectable disease. **Methods:** Retrospective review of outcomes of all pts (n=127) with "limited stage" SCLC treated at our Institution from 2004-2014. Local disease progression and distant recurrence among pts undergoing primary systemic therapy +/- radiation therapy (n=106, 83%) were compared to pts with peripheral SCLC (n=21, 17%) undergoing surgical resection as first line therapy ± adjuvant therapy. Patient demographics, surgical mortality, disease-free and overall survival outcomes were compared between the non-surgical and surgical groups. Systemic therapy was Platinum agent based. Survival was estimated using Kaplan-Meier survival analysis. Groups were

compared using a log-rank test. **Results:** Pts demographics were similar between non-surgical and surgically treated SCLC pts. Systemic therapy / radiation was utilized for 88 (83%) non-surgical pts. Systemic therapy alone was utilized for 18 (16.9%) pts, and 2 (1.8%) patients received radiotherapy alone. Local disease progression represented first site of treatment failure in 19 (17.9%), while distant metastases was first noted in 65 pts (61.3%). Of the 65 distant metastasis first site of progression, 27 (41.5%) were cerebral. First site of progression was unable to be verified 16 (26.2%) medically treated pts. Among the 21 pts having "surgical resection" of peripheral, limited SCLC, there was no perioperative (30 day) mortality. Local recurrence was noted first in 7 (33.3%) of surgical pts. Distant metastases was discovered first in 3 (14.3%), and cerebral metastasis was found in 2 of these 3 pts. Nine (42.9%) surgical pts were recurrence free (mean 43 months), while only 7 (5.7%) medically treated pts were free of recurrence (mean 31 months). The 5 year survival among medially treated pts was 8% compared to 21% among patients undergoing surgical resection of peripheral SCLC (p= 0.008).

(See figure 1. below)



Conclusion: Survival for all SCLC patients is affected by the common presence of systemic disease, despite an apparently limited, peripheral disease presentation. Surgical resection as "First line" therapy combined with adjuvant systemic ± radiation therapy for peripheral, limited small cell lung cancer may be beneficial. Cerebral metastases are important sites of first distant recurrence for all limited stage SCLC. **Keywords:** Survival, SCLC, Recurrence, Surgery

POSTER SESSION/ SMALL CELL LUNG CANCER
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.07-012 Hypo- or Conventionally Fractionated Radiotherapy in Patients with Limited Stage Small Cell Lung Cancer (LS-SCLC): A Retrospective Analysis

Jing Zhang, Min Fan, Di Liu, Yu Xin Shen, Kuai Le Zhao, Kai Liang Wu, Wei Xin Zhao, Ling Li, Xiao Long Fu, Zheng Fei Zhu *Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai/China*

Background: Previous data from our institution showed that hypofractionated thoracic radiotherapy (HypoTRT) concurrently with etoposide/platinum chemotherapy yielded favorable survival in patients with LS-SCLC. The aim of the present study was to compare the survival outcomes, failure patterns and toxicities between groups of LS-SCLC patients treated with conventionally fractionated radiotherapy (ConvTRT) or HypoTRT combined with etoposide/platinum chemotherapy. **Methods:** Medical records of LS-SCLC patients between January 2010 and December 2013 at Fudan University Shanghai Cancer Center were retrospectively reviewed. All patients treated with chemotherapy and ConvTRT (2.0 Gy per faction daily, DT≥56Gy) or HypoTRT (2.5 Gy per faction daily, DT= 55Gy) were eligible for analysis. The progression-free survival (PFS) and overall survival (OS) were generated for different populations using the Kaplan-Meier method and compared by log-rank test. The comparison of failure patterns and toxicity were analyzed with the χ^2 test. **Results:** One hundred and seventy-nine patients were indentified. All patients received 1-6 cycles of Etoposide/Platinum chemotherapy. Except for nine patients who received hyperfractionated regimen, 170 of 179 patients treated with were eligible for analysis (median age 58 years; male 85.3%). Sixty-nine patients received HypoTRT and 101 patients received ConvTRT (median 60Gy/30Fx). PCI (25Gy/10Fx) was given to patients with partial or complete remission in chest tumor. PCI was administered to 46 (66.7%) and 48 (47.5%) patients in HypoTRT and ConvTRT cohorts (p=0.014), respectively. Except for PCI, the patient- or treatment-related variables were similar between the two cohorts. With a median follow-up of 23 months, the median OS was 26.7 months (95%CI: 23.2-30.2) in the ConvTRT cohort and 30.4 months (95%CI: 25.6-35.2) in the HypoTRT cohort (p=0.221). The 2-year OS for the ConvTRT and the HypoTRT cohort were 56.0% and 62.8%, respectively. The median PFS was 19.3 months for patients received HypoTRT, which was similar to that of the ConvTRT group (13.7 months, p=0.375). Sixty-three patients(62.4%) experienced disease progression in ConvTRT cohort, compared with 41 patients(59.4%) in HypoTRT cohort. The patterns of failure (stratified by local-regional recurrence, distant metastasis or both as first relapse) were also similar between the two dose cohorts (p=0.219, p=0.466, p=0.724). The 2-year local-regional progression free survival rates for the ConvTRT and HypoTRT cohorts were 59.7% and 70.6% (p=0.128), respectively. PCI reduced the incidence of brain metastasis by 31% at 20 months. Patients who received PCI had a significant longer survival with a 2-year OS rate of 69.8%, as comparing 44.4% of those who did not (p=0.000). Concurrent chemoradiotherapy was another predictor for favorable survival. However, patients who were treated with concurrent approach tended to be younger, receive early thoracic radiotherapy, more cycles of chemotherapy and PCI. No differences in treatment-related toxicity rates were demonstrated between the two dose-prescription cohorts (p=0.815). Grade ≥3 esophagitis and pneumonitis occurred in 9.9% and 9.9% in ConvTRT cohort, whereas 11.6% and 8.6% in HypoTRT cohort, respectively. **Conclusion:** In this retrospective analysis, HypoTRT or ConvTRT combined with etoposide/platinum chemotherapy yielded statistically similar survival, treatment failure outcomes, and toxicity profiles. **Keywords:** survival, Limited-stage small cell lung cancer, Hypofractionated radiotherapy, Conventionally fractionated radiotherapy

POSTER SESSION/ SMALL CELL LUNG CANCER
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.07-013 Real-Life 2-Year Therapeutic Strategies in the Management of 525 Small-Cell Lung Cancers: The ESCAP Study Preliminary Results

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Background: In the last years, new drugs and strategies have emerged in the management of lung cancer (LC). The French College of General Hospital Respiratory Physicians therefore promoted a prospective multicenter epidemiological study: the ESCAP study. This study was aimed to describe the therapeutic strategies implemented during the first 2-year after diagnosis in patients with LC followed in French General Hospital chest departments. We report below descriptive results for small-cell lung cancer (SCLC). **Methods:** For each patient with a LC diagnosed in 2010, a standardized form was completed at diagnosis and following each change in treatment strategy up to at least 2 years after diagnosis. **Results:** 53 centers participated in the ESCAP study, and included 3,943 LC patients. Of these, 525 patients had a SCLC. Characteristics of SCLC patients at diagnosis were: mean age +/- standard deviation (SD), 65.6 +/- 10.8 years; male, 77%; never-smokers, 4.8%. The mean follow-up in SCLC patients was 10.5 months (SD: 8.8) and median number of strategies was 2 (Interquartile range: 1-3). Main strategy characteristics are summarized in the following table.

	First strategy (N=525)	Second strategy (N=309)	Third strategy (N=153)
Duration (months): mean+/- SD	5.4 +/- 4.5	3.6 +/- 3.5	2.7 +/- 2.4
Curative surgery	2%	1%	-
Radiotherapy	10%	47%	20%
Radiochemotherapy	15%	-	-
Chemotherapy	75%	55%	61%
Exclusive supportive care	8%	14%	27%
Patients died during the strategy	195 (37%)	134 (43%)	90 (59%)
Patients with a new strategy	309 (59%)	153 (50%)	54 (35%)

As regards first strategy, cisplatin (46%) and carboplatin (42%) were the most frequent used drugs associated with etoposide. As regards second strategy, the most frequently used drugs were topotecan (22%), etoposide (21%), or carboplatin (20%). Few patients received targeted therapy (< 1% in strategies 1 and 2). **Conclusion:** The ESCAP study describes the 2-year management of SCLC on real-life settings in France. Its preliminary results showed that 3 or 4 strategies were not uncommon in the management of SCLC patients. **Keywords:** therapeutic strategies, small-cell lung cancers

POSTER SESSION/ SMALL CELL LUNG CANCER
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.07-014 Predictors of Survival in Small Cell Lung Cancer (SCLC) Patients (pts) < 50 Years of Age: Results from the California Cancer Registry (CCR)
Joshua D. Lara[1], Ann Brunson[2], Jonathan W. Riess[3], Karen Kelly[3], Primo Lara Jr.[1], David R. Gandara[1] [1]*Uc Davis Comprehensive Cancer Center, Sacramento/CA/United States of America,* [2]*Uc Davis Comprehensive Cancer Center, Sacramento/United States of America,* [3]*University of California Davis Comprehensive Cancer Center, Sacramento/CA/ United States of America*

Background: SCLC is an often lethal disease that commonly occurs in older individuals with a history of heavy tobacco use. Limited epidemiologic and outcomes data are available for young SCLC pts (< 50 years of age). We analyzed the CCR to explore the clinical variables related to cause specific survival (CSS) of young pts. **Methods:** SCLC pts diagnosed between 1998-2012 were included. Primary outcome was CSS. Hazard ratios (HR) for CSS were calculated using Cox Proportional Hazards (PH) models for all ages & for pts <50 years, adjusted for baseline variables: age, gender, stage, race, year of diagnosis, treatment, socioeconomic status (SES), and location (urban vs. rural). **Results:** We identified 22,863 SCLC pts, of which 975 were <50 years of age (4.2%). Demographics for pts <50 years: Males-51%; White-71%; Stage IV-60%; Chemotherapy-79%; Urban location-92%; high SES-28%. Fewer pts < 50 years were diagnosed in later years: from 40% in '98-'02 to 24% in '08-'12. Results of multivariate Cox PH models are shown. (HR=Hazard Ratio).

Select Variables	All pts		Pts<50 years of age	
	HR	P-value	HR	P-value
Age at diagnosis (vs. ≥50yrs)	0.82	<0.0001	N/A	N/A
Female sex (vs.Male)	0.91	<0.0001	0.81	0.0045
Race (vs.White)				
Asian	0.84	<0.0001	0.57	0.0075
Year of Dx (vs.'88-'02)				
2003-'07	0.96	0.0096	0.95	0.5562
2008-'11	0.94	0.0017	0.89	0.2796
Stage (vs.I)				
Stage II	1.22	0.0111	1.20	0.7255
Stage III	1.80	<0.0001	1.81	0.0282
Stage IV	2.93	<0.0001	3.81	<0.0001
Treatment (vs.None)				
Surgery	0.43	<0.0001	0.37	0.004
Chemotherapy	0.44	<0.0001	0.49	<0.0001
Radiation	0.66	<0.0001	0.71	<0.0001
Rural (vs.Urban)	0.97	0.3042	0.75	0.0419
Low SES {vs.High SES(4,5)}	1.05	0.0011	1.04	0.6306

Conclusion: Age < 50 years was an independent predictor of improved CSS (HR 0.82, p<0.0001). In younger pts, female sex (HR 0.81, p=0.0045), Asian race (HR 0.57, p=0.0075), and rural residence (HR 0.75, p=0.042) were associated with better CSS, among other variables. Analyses for relevant interactions within subgroups will be presented.
Keywords: small cell lung cancer, epidemiology, young patients

POSTER SESSION/ SMALL CELL LUNG CANCER
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.07-015 The Prognostic Value of the Neutrophil Lymphocyte Ratio in Patients with Small Cell Lung Cancer
Harjot Kaur[1], Konstantinos Arnaoutakis[2], Andrew L. Dunn[3], Eric R. Siegel[4], Francisco A. Socola[2] [1]*Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock/AR/United States of America,* [2]*Division of Hematology and Oncology, University of Arkansas for Medical Sciences, Little Rock/AR/ United States of America,*[3]*Department of Pathology, University of Arkansas for Medical Sciences, Little Rock/AR/United States of America,* [4]*Department of Biostatistics, University of Arkansas for Medical Sciences, Little Rock/AR/United States of America*

Background: A high neutrophil to lymphocyte ratio (NLR) is reported to be a poor prognostic indicator in several malignancies and is associated with inferior survival. There is limited data exploring the prognostic role of NLR in small cell lung cancer (SCLC). The aim of the study was to evaluate the prognostic role of the NLR at the time of diagnosis in patients with SCLC. **Methods:** We retrospectively analyzed data from July 2010 to June 2013 of patients diagnosed with SCLC at a single tertiary care center. NLR ≥4 at the time of diagnosis was correlated with other prognostic variables to estimate its effect on the overall survival (OS). **Results:** There were a total of 80 eligible patients, including 33 males and 47 females. At the time of diagnosis, NLR ≥4 was seen in 36 (45%) patients. Overall, median absolute neutrophil count was 6.15 K/ uL and absolute lymphocyte count was 1.6 K/uL. Both groups were comparable for age, gender, body mass index and ECOG functional score. We found 31/36 (86.11%) patients with NLR ≥4 who had extensive stage disease. In contrast, only 24/44 (54.55%) patients with NLR <4 had extensive stage disease (P= 0.0024). All 25/25 (100%) patients with limited stage disease received chemoradiation, while 44/55 (80%) of patients with extensive stage disease received chemotherapy. The median overall survival was 8.7 versus 11.2 months for patients with NLR ≥4 versus NLR <4 (log-rank P=0.014) (Figure 1). Multivariate Cox regression detected a strong interaction (P=0.0024) between NLR and the combined status of chemotherapy and stage. In the limited stage group, NLR ≥4 patients had slightly worse OS (HR=2.13, 95% CI: 0.66-6.86; P=0.20), whereas in the extensive stage group which received chemotherapy, NLR ≥4 patients had slightly better OS (HR=0.80, 95% CI: 0.42-1.53; P=0.50). In the extensive-stage group which did not receive chemotherapy, NLR ≥4 patients had significantly worse OS (HR=12.7, 95% CI: 2.94-55.2; P=0.0007). **Conclusion:** Similar to the other studies in solid tumors, we found a prognostic value of NLR in all patients with SCLC. However, NLR was prognostically significant only among patients with extensive-stage disease who did not receive chemotherapy. Among patients of both stage groups who received chemotherapy, NLR had little prognostic value. NLR ≥4 appears to be more prevalent in patients with extensive stage disease probably reflecting an impaired immune system. Further research exploring the role of immune system and associated immune surrogate markers in SCLC is needed.

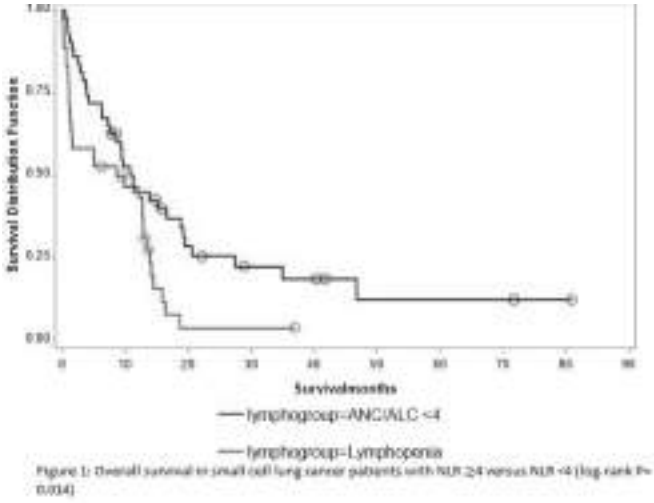

Figure 1: Overall survival in small cell lung cancer patients with NLR ≥4 versus NLR <4 (log-rank P= 0.014)

Keywords: Neutrophil lymphocyte ratio, small cell lung cancer, Prognosis

POSTER SESSION/ SMALL CELL LUNG CANCER
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.07-016 Comparison of PET/CT, 99mTc-MDP Bone Scan and Serum Alkaline Phosphatase for Detecting Bony Metastasis in Patients with Small Cell Lung Cancer
Jing Zhang, Min Fan, Di Liu, Yu Xin Shen, Xiao Long Fu, Kuai Le Zhao, Kai Liang Wu, Wei Xin Zhao, Ling Li, Zheng Fei Zhu *Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai/China*

Background: The data on the diagnostic ability of 18F-FDG positron emission tomography/computed tomography (PET/CT) compared that of 99mTc-MDP bone scan (BS) or serum alkaline phosphatase (ALP) for the detection of bone metastasis in patients with small cell lung cancer (SCLC) was sparse. The aimed of this study was to compare the diagnostic accuracy and agreement among PET/CT, BS and serum ALP for detecting bone metastasis in SCLC patients. **Methods:** The database at Fudan University Shanghai Cancer Center was retrospectively reviewed to identify all patients with SCLC who underwent both integrated whole-body PET/CT and BS between January 2010 and December 2013. In addition, serum ALP concentration of all eligible patients was recorded. The interval between PET/CT and BS was less than two weeks. Bone metastasis was confirmed if any of the following criteria were met: histology or pathology, concordance between PET/CT and BS, results of supplemental examinations (magnetic resonance imaging) or progression of bony lesions seen on follow-up studies. The sensitivity, specificity and accuracy of each modality were calculated. The overall differences were analyzed using the McNemar's paired-sample test. The comparison of sensitivity, specificity and accuracy were analyzed with the $\chi 2$ test or Fisher exact test. Agreement between PET/CT, BS and ALP was assessed by kappa statistic. The κ-value was categorized as follows: poor (< 0.30), good (0.31–0.60), and excellent (0.61–1.0). **Results:** Of 368 patients with SCLC, a total of 30 patients were enrolled in this retrospective analysis. Six (20%) of thirty eligible patients were confirmed with bone metastasis, while 24 patients (80%) were found free from bone metastasis. The corresponding sensitivity, specificity, accuracy, positive and negative predictive value of PET/CT in detecting bone metastasis were 66.7%, 100%, 93.3%, 100% and 96.2% as compared to those of BS which were 100.0%, 70.8%, 76.7%, 46.2% and 100%, respectively. PET/CT had much higher specificity than BS (p=0.009). No statistically significant differences in sensitivity and accuracy were demonstrated between PET/CT and BS (p=0.455; p=0.145). Elevated serum ALP alone has the lowest sensitivity in detecting bone metastasis (16.7%), with the specificity of 87.5% and the accuracy of 73.3%,

respectively. Combining the results of ALP and BS will significantly improve the specificity as compare to BS alone (100% vs 70.8%, p=0.009), while the sensitivity remains low (16.7%) and the accuracy remain unchanged (83.3% vs 76.7%, p=0.519). The κ-values were 0.276 between PET/CT and BS, 0.092 between PET/CT and serum ALP, and 0.099 between BS and serum ALP, indicating poor agreement among the three modalities in detecting bony metastasis. **Conclusion:** PET/CT had statistically higher specificity and numerically higher accuracy than BS in detecting bone metastasis in this group of patients with SCLC. The addition of serum ALP to BS improved the detection specificity comparing BS alone. There was still controversy involving in the use of PET/CT in SCLC. The diagnostic value of PET/CT needed to be validated in prospective and larger clinical trials.
Keywords: small cell lung cancer, bone metastasis, PET/CT, BS

SESSION: POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES MONDAY, SEPTEMBER 7, 2015

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.08-001 Rituximab for Treatment of Lymphoma Induced Marked Regression of Malignant Mesothelioma with Dynamic Changes of Serum Cytokine Profiles

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Background: Malignant mesothelioma (MM) is a highly aggressive tumor with poor prognosis. As an effective therapy remains to be established, increased attention has been given to immunotherapy in MM. **Methods:** We experienced a patient with malignant lymphoma and MM who showed marked regression of MM after the anti-CD20 monoclonal antibody rituximab therapy. Here we investigated the mechanism underlying this response by immunohistochemical staining and serum cytokine assay. **Results:** A 78-year-old man with diffuse large B-cell lymphoma and epithelioid MM was treated with rituximab for malignant lymphoma. The lymphoma responded well to rituximab, and the pleural thickening of MM regressed markedly after this treatment without therapy for mesothelioma. Immunohistochemical stainings revealed negative expression of CD20 on mesothelioma cells, indicating that rituximab did not directly attack the mesothelioma cells. The serum levels of 27 cytokines were measured 12 days before and 16, 45 and 54 days after this treatment to compare with those in 24 untreated MPM patients. The serum levels of cytokines of this patient including IL-12, INF-g, TNF-a, VEGF and IP-10 were higher than those of other mesothelioma patients before the rituximab treatment. Notably, during the treatment the level of IL-12 increased approximately 10-fold, relative to its baseline level. In addition, the levels of IL-2, Eotaxin, G-CSF, and TNF-a transiently increased several fold as compared with their baseline levels. In contrast, the levels of VEGF, PDGF, IP-10, and IL-8 which are associated with mesothelioma proliferation, decreased after the treatment. These results suggest that the mechanism of mesothelioma regression in this case involves antitumor immunity enhanced with high baseline levels of IL-12 and other Th1 cytokines and B-cell depletion by the rituximab treatment. **Conclusion:** The relationship between these cytokine profiles and the clinical outcome might provide a potential immunotherapeutic strategy for MM.
Keywords: Mesothelioma, cytokine, Immunotherapy, rituximab

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P1.08-002 Stat3 Is a Potential Target for Malignant Pleural Mesothelioma (MPM) Treatment

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Background: The prognosis of malignant pleural mesothelioma (MPM) is very poor; thus, a new drug treatment is necessary. Serum IL-6 is high in patients with MPM because of the activation of IL-6/Stat3 pathway. Thus, we investigated Stat3 as a potential target for the treatment of MPM. **Methods:** Cell viability was examined using the Cell Counting Kit-8 (CCK-8: WST-8 Dojindo). MPM cell lines (NCI-H28, NCI-H226, NCI-H2052, NCI-H2452, and MSTO-211H) were seeded onto 96-well plates. After treatment with Stattic, a Stat3 inhibitor, CCK-8 solution was added to each well and absorbance was measured using a microplate reader. Phosphorylated Stat3 levels (p-Stat3) were measured in cell lysates using the InstantOne ELISA assay (eBioscience). The expression of p-Stat3, E-cadherin, and vimentin was determined by western blot analysis. Translocated p-Stat3 was analyzed by confocal immunofluorescence microscopy. Cells were plated onto chamber slides containing medium. After the Stattic treatment, cells were fixed and cell membranes permeabilized. p-Stat3 antibody was added to chamber slides and incubated overnight at 4°C. Images were captured using a Zeiss LSM780 confocal microscopy system. Apotosis induced by Stat3 inhibitor was measured using the Caspase-GloR 3/7 assay (Promega). Cells were seeded onto 96-well plates. After the Stattic treatment, Caspase-GloR 3/7 reagent was added to each well, and the luminescence of each sample was measured in a plate-reading luminometer. For our in vivo study, H226 cells were subcutaneously injected into the flank region of nude mice. Mice were randomly assigned into two groups, with 5 mice in each group: vehicle control and Stattic (treated with10 mg/kg po 5 days per week). **Results:** Stattic inhibited viability of all MPM cell lines in a dose-dependent manner. IC50 values ranged from 3.3–106.0 μM. p-Stat3 levels decreased by 50% with 1 μM Stattic treatment in H226 cells. H226 cells were treated with 0.01 to 10 μM Stattic. Vimentin expression was stable; however, E-cadherin expression increased with 0.1, 1, and 10 μM Stattic treatment. In untreated H226 cells, p-Stat3 was observed in the cytoplasm and localized in the nucleus. In contrast, in Stattic-treated cells, decreased p-Stat3 was observed in the cytoplasm only, and it did not localize to the nucleus. Caspase 3/7 cleavage increased with Stattic treatment after 12 h and decreased after 48 h. In vivo mouse xenograft model, Stattic suppressed tumor growth (vehicle control vs.Stattic, $P < 0.05$). **Conclusion:** In this study, we have shown that Stattic inhibits proliferation of all MPM cell lines and suppresses tumor growth in a mouse model. In addition, we have demonstrated that Stattic inhibits Stat3 phosphorylation and blocks nuclear translocation. Furthermore, Stattic inhibits EMT. Thus, the STAT3 inhibitor is a promising candidate in MPM therapy.
Keywords: Mesothelioma, STAT3

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P1.08-003 Minimal Asbestos Exposure in Germline BAP1 Heterozygous Mice Is Associated with Deregulated Inflammatory Response and Increased Risk of MM

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Background: Germline *BAP1* mutations predispose to several cancers, in particular malignant mesothelioma. Mesothelioma is an aggressive malignancy generally associated to professional exposure to asbestos. However, to date we found that none of the mesothelioma patients carrying germline *BAP1* mutations were professionally exposed to asbestos. We hypothesized that germline *BAP1* mutations might influence the asbestos-induced inflammatory response that is linked to asbestos carcinogenesis, thereby increasing the risk of developing mesothelioma after even minimal exposure. **Methods:** We experimentally tested in a BAP1+/- murine model whether germline *BAP1* heterozygosity would result in alterations of the asbestos-induced inflammatory response, and whether low doses of asbestos might be sufficient to cause MM. **Results:** Germline *BAP1* heterozygosity is associated with a significantly altered peritoneal inflammatory response upon exposure to asbestos fibers and to an increased risk of MM following exposure to even minimal amounts of asbestos that rarely cause MM in wild type animals. **Conclusion:** Our findings support our hypothesis that germline *BAP1* heterozygosity increases susceptibility to the carcinogenic effects of low doses of asbestos. Based on these results, we suggest that prevention programs of MM in individuals carrying germline *BAP1* mutations should focus on reducing exposure to even minimal indoor and/or naturally occurring outdoor sources of carcinogenic fibers, levels that are within the acceptable "safe" limits for the population at large.
Keywords: macrophages, Mesothelioma, BAP1, asbestos

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P1.08-004 Aki1 as a Potential Therapeutics Target in CREB1 Signaling in Malignant Mesothelioma

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Background: Malignant pleural mesothelioma (MPM) is an aggressive tumor arising from the mesothelial cells of serosal membranes. Since current treatment options are largely ineffective, novel therapeutic strategies based on molecular mechanisms and the disease characteristics are needed to improve its prognosis. Akt kinase-interacting protein 1 (Aki1)/Freud-1/CC2D1A known as a scaffold protein of PI3K/PDK1/Akt that determines receptor signal selectivity for EGFR has been suggested as a therapeutic target in lung cancer. The aim of this study was to elucidate the role of Aki1 and its potential for treatment of MPM. **Methods:** We tested the effects of the treatment with Aki1 or CREB1 siRNAs on cell viability by MTT assay, cell cycle by FACS analysis, cell signaling by WB, and CREB transcriptional activity in 7 MPM cells and 1 mesothelial cells using in vitro experiments. We investigated the efficacy of Aki1 siRNA against growth of 211H cells in an orthotropic implantation model using SCID mice. We further examined Aki1 and p-CREB1 expressions in MPM tumors from 35 patients by TMA specimens and from 33 patients by the tissues. **Results:** Cell based assay showed that silencing of Aki1 inhibited cell viability and caused cell arrest of some of MPM cells but not mesothelial cells. Importantly, we identified that the efficacy of Aki1 is regulated by CREB1 signaling which is involved in cell viability, cell cycle, and transcriptional activity. Aki1 and phosphorylated CREB1 were frequently expressed in MPM patients (65/68 cases) (30/35 cases), respectively. Furthermore, the expression of Aki1 correlated with phosphorylation of CREB1 (Spearman rank correlations = 0.521; p = 0.002). Furthermore, direct application of Aki1 siRNA into the pleural cavity significantly inhibited growth of 211H cells compared with that of control siRNA in an orthotropic implantation model using SCID mice. **Conclusion:** Our data suggest an important role of Aki1/CREB axis in pathogenesis of MPM and provide a rationale for targeting Aki1 by intrathoracic therapy in locally advanced tumors.
Keywords: molecular target, malignant pleural mesothelioma, short interfering RNA, Aki1

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P1.08-005 Met and PI3K/mTOR as a Potential Combinatorial Therapeutic Target in Malignant Pleural Mesothelioma
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Background: There are a number of genetic alterations such as BAP1 and NF2 that can occur in malignant pleural mesothelioma (MPM). Various studies have shown that both MET and its downstream key intracellular signaling partners PI3K and mTOR are known to be overexpressed and frequently mutated in MPM. Here we have examined the therapeutic efficacy of a new generation small molecule inhibitor of MET receptor tyrosine kinase ARQ 197 and phosphatidylinositol 3-kinase and mTOR (PI3K/mTOR) inhibitors BEZ-235 and GDC-0980 in MPM. **Methods:** The mesothelioma cells were treated with ARQ 197, NVP-BEZ235, or GDC-0980 alone or in combination for 72 hours and cell proliferation was measured by using Alamar Blue assay. Synergistic efficacy was determined by isobologram and combination-index methods of Chou and Talalay. Signaling was assessed by immunoblotting. The mechanism of inhibition was further studied by using apoptosis assays and cell cycle analysis. Cell motility was studied by using scratch assays. We also examined efficacy of the combination of ARQ 197 and GDC-0980 on in vivo tumor growth by using mouse xenograft models. **Results:** MPM cell lines over-express MET and its active form p-MET, PI3K, and p-AKT and total AKT. ARQ 197, NVP-BEZ235, and GDC-0980, when used alone, significantly inhibited the cell proliferation of mesothelioma cells in a dose dependent manner. The combination of MET and PI3K/mTOR inhibitors was synergistic in suppressing MPM cell growth as compared to any single drug alone. Treatment of ARQ 197, NVP-BEZ235, and GDC-0980 alone or in combination inhibited the phosphorylation of AKT and S6 kinase in mesothelioma cells. MET and PI3K/mTOR inhibitors affect cell growth of mesothelioma cells by cell cycle inhibition (cyclin D1) and induction of apoptosis (presence of cleaved PARP, by IF/ confocal microscopy). MET inhibitor ARQ 197 alone inhibits the cell motility of mesothelioma cells in scratch assay. The combination of ARQ 197/ GDC-0980 was much more effective than each single agent alone in inhibiting the tumor growth of mesothelioma xenografts in nude mice. Compared to the control mice (2946±403 mm^3), the tumors of mice treated with ARQ 197(2262±317 mm^3) and GDC-0980 (1631±229.57mm^3) alone had a significant decrease in the tumor volume. The tumor volume of mice treated with the combination of ARQ 197 and GDC-0980 further decreased it to six fold (475±97.43 mm^3) compared to the control mice. **Conclusion:** Our results suggest that the combined use of ARQ 197/NVP-BEZ235 and ARQ 197/GDC-0980 is far more effective than single drug use in suppressing MPM cell motility and growth in vitro and tumor growth in vivo and therefore merits further translational studies. **Keywords:** BKM-120, GDC-0980, Mesothelioma,, ARQ 197

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P1.08-006 Lung Toxicity after Post-Operative Radiotherapy after EPP for Mesothelioma and Pneumonectomy for Non-Small Cell Lung Cancer
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Background: Our hypothesis is that MPM patients treated with post-operative RT after EPP are more prone to develop lung toxicity compared to non-small cell lung cancer (NCSLC) patients treated with post-operative RT after pneumonectomy, since their higher baseline inflammation status. **Methods:** We retrospectively reviewed the records of 39 consecutive patients with MPM who received post-operative RT after extrapleural pneumonectomy (EPP), and of 10 consecutive patients with non-small cell lung cancer who received post-operative RT after pneumonectomy between March 2003 and March 2012 at the University Hospitals of Leuven. For MPM patients, the planning target volume was defined as the entire hemi-thorax, chest wall incisions, drain sites, and involved nodal stations. Prescription dose was 54 Gy in 2-Gy fractions delivered to the planning target volume (PTV). For NSCLC patients, the planning target volume was defined as mediastinal nodal stations according to the pathologic nodal involvement. Prescription dose was 54-66 Gy in 2-Gy fractions delivered to the PTV. Both cohorts received induction systemic chemotherapy before surgery. Primary endpoint was lung toxicity. Dyspnea was graded using the Common Toxicity Criteria (CTC) v. 4.03 and was recorded before RT, 45 days after the completion of RT and every 3 months thereafter until the completion of the follow up. Dosimetric dose-volume parameters (lung V5, lung V20, mean lung dose [MLD], mean heart dose, heart V45) were retrieved for both cohorts. The correlation between the dosimetric parameters and the toxicity (dyspnea score) was investigated. **Results:** In MPM patients, the dyspnea score was 0-1 in 24/39 patients (61.5%), 2 in 11/39 patients (28.2%), 3 in 3/39 patients (7.7%) and 4 in 1/39 patients (2.5%). No grade 5 toxicity was recorded. In NSCLC patients, only grade 0-1 dyspnea was registered (grade 0: 4/10 patients; grade 1: 6/10 patients). Mean MLD was 7.56 Gy (range: 1.60-14.80; SD: 3.65) for the MPM group and 5.96 Gy (range: 3.2-14.5; SD: 3.57) for the NSCLC group. Univariate analysis showed a significant correlation between grade $\geq$ 2 dyspnea and MLD, lung V5 and lung V20. **Conclusion:** Post-operative radiotherapy after EPP is well-tolerated, with 10% of patients experiencing grade $\geq$ 3 dyspnea. Strict dose-constraints should be applied when radiotherapy is administered in multimodality treatment. **Keywords:** malignant pleural mesothelioma, non-small cell lung cancer, extra-pleural pneumonectomy, lung toxicity

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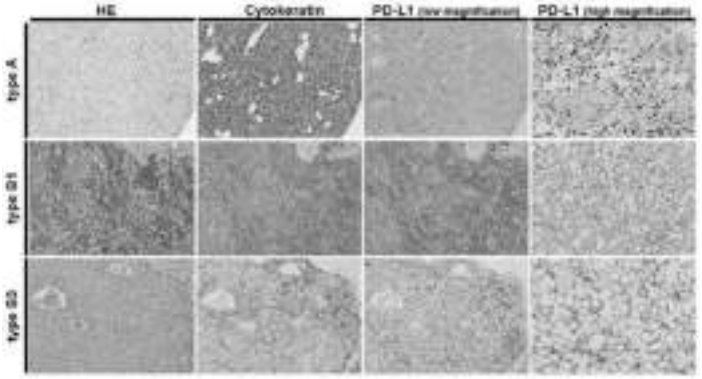
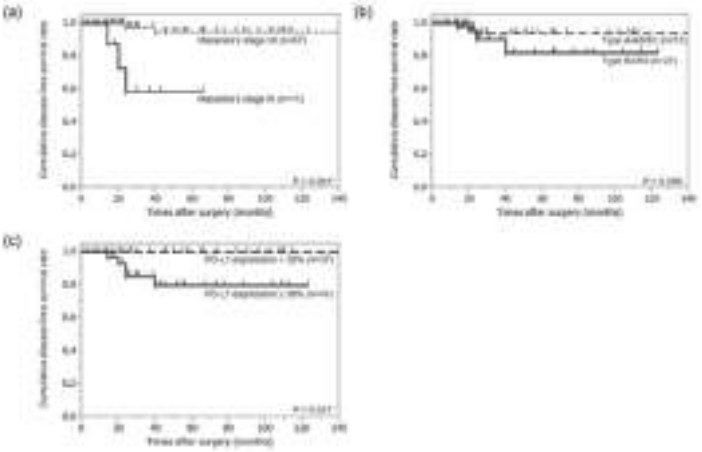
P1.08-007 Programmed Cell Death 1 Ligand 1 (PD-L1) Expression in Thymoma
Shintaro Yokoyama[1], Hiroaki Miyoshi[2], Tatsuya Nishi[1], Ryouichi Matsumoto[1], Toshihiro Hashiguchi[1], Daigo Murakami[1], Masaki Kashihara[1], Shinzo Takamori[1], Yoshito Akagi[1], Koichi Ohshima[2] [1]*Department of Surgery, Kurume University, School of Medicine, Kurume/ Japan,* [2]*Department of Pathology, Kurume University, School of Medicine, Kurume/Japan*

Background: Programmed cell death 1 ligand-1 (PD-L1) has been reported to be expressed in various malignancies, and is considered to be a prognostic factor and an immunotherapeutic target. The aim of this study was to characterize PD-L1 expression in thymoma and statistical associations between this expression and clinical features. **Methods:** We reviewed formalin-fixed paraffin-embedded tissue specimens from 82 thymoma cases at Kurume University. PD-L1 expression was evaluated by immunohistochemistry (IHC). Statistical associations between PD-L1 expression and clinicopathological features were evaluated by using chi-square test and Fisher's exact test. Disease-free survival (DFS) analysis, the end event of which is recurrence, was performed by the Kaplan-Meier method. **Results:** A total of 44 thymoma cases (54%) revealed high PD-L1 expression by IHC. No significant differences were observed between high and low PD-L1 expression with respect to sex (P = 0.938), age (P = 1.000), symptomatic myasthenia gravis (P = 0.471), anti-acetylcholine receptor antibody titer (P = 0.513), primary tumor size (P = 0.527), or curability (P = 0.620). However, high PD-L1 expression was statistically associated with Masaoka's stage III/IV disease (P = 0.043) and WHO type B2 or B3 thymoma (P = 0.044). DFS after complete resection in high PD-L1 expression cases was significantly worse than that in low PD-L1 expression cases (P = 0.021).





Conclusion: Characterization of PD-L1 expression in thymoma should enable more effective clinical approaches, including prognostic stratification of patients and use of anti-PD-L1 antibody immunotherapy. **Keywords:** Thymoma, programmed cell death 1 ligand 1, immune checkpoint, cancer immunotherapy

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P1.08-008 Efficacy of Palliative Chemotherapy in Malignant Pleural Mesothelioma from Spanish BEMME Database. The Spanish Lung Cancer Group (SLCG) Jordi Remon[1], Noemi Reguart[2], Ernest Nadal[3], Rafael López-Caastro[4], Paloma Martin Martorell[5], Eugenia Olmedo[6], José Luis González-Larriba[7], Santiago Ponce[8], Laureano Molins[2], Margarita Majem[9], Bartomeu Massuti[10], Ruth Porta[11], Maria Angeles Sala[12], Lourdes Calera[13], Pilar Diz[14], Julia Calzas[15], Belen Rubio[16], Javier Garde[17], Ana Laura Ortega[18], Elisa Galvez[19], Rafael Rosell[20] [1]*Hospital de Mataró, Mataró/ Spain,* [2]*Medical Oncology, Hospital Clinic, Barcelona/Spain,* [3]*Institut Catala D'Oncologia, L'Hospitalet, Barcelona/Spain,* [4]*Hospital Clinico Universitario de Valladolid, Valladolid/ Spain,* [5]*Hospital Clínico Universitario Valencia, Valencia/Spain,* [6]*Hospital Ramon Y Cajal, Madrid/Spain,* [7]*Hospital Clínico San Carlos, Madrid/Spain,* [8]*Hospital Universitario 12 de Octubre, Madrid/Spain,* [9]*Hopital de La Santa Creu I Sant Pau, Barcelona/Spain,* [10]*Hospital General Universitario de Alicante, Alicante/Spain,* [11]*Institut Català D'Oncologia Girona –Ico, Girona/Spain,* [12]*Hospital de Basurto, Basurto/Spain,* [13]*Hospital Universitario Miguel Servet, Zaragoza, Zaragoza/Spain,* [14]*Hospital de Leon, Leon/Spain,*[15]*Hospital Universitario de Fuenlabrada, Madrid/Spain,* [16]*Hopital Quirón de Madrid, Madrid/Spain,* [17]*Hospital Universitari Arnau de Vilanova de Lleida, Lleida/Spain,* [18]*Complejo Hospitalario de Jaén, Jaen/ Spain,* [19]*Hospital General de Elda-Virgen de La Salud, Elda/Spain,* [20]*Hospital Germans Trias I Pujol, Catalan Institute of Oncology, Barcelona/Spain*

Background: Palliative chemotherapy with cisplatin and antifolate (pemetrexed or raltitrexed) conferred a median overall survival of 12 months with a response rate of 24% to 43% in malignant pleural mesothelioma (MPM) patients. BEMME (Base Epidemiológica Mesotelioma Maligno en España) is an observational and retrospective study sponsored by the Spanish Lung Cancer Group that aimed to characterize the patient's and tumor's features as well as the treatment modalities outcomes of patients diagnosed with mesothelioma in Spain. **Methods:** Clinical records of patients with malignant pleural mesothelioma were retrospectively reviewed to collect epidemiological and survival data into an electronic and anonymous database. Thirty-five Spanish hospitals participated in the project and 538 MPM patients were included in the BEMME database. Here we present a descriptive analysis of MPM patients (stage III and IV) treated with palliative chemotherapy. **Results:** From January 2008 to December 2013, 297 of 538 patients (p) (55%) with MPM were treated with palliative chemotherapy. Most patients were males (79%), aged between 60-70y (40%), and 60% had a performance status 1 at diagnosis. No exposure to asbestos was reported in 54% of patients. Epithelioid was the most frequent histological subtype (66%), followed by sarcomatoide (12%), biphasic (9%) and not specified (14%). In stage IV, the most frequent metastatic site was lung (35%). Among patients who received chemotherapy, 55% were treated with palliative intent and reached a disease control rate (CR+PR+SD) of 62%. Platinum plus pemetrexed was the most common schedule used as a palliative treatment, without differences in ORR according to platinum-based agent used (Cisplatin: 36% *vs*. Carboplatin: 32%). A total of 61 of the 297p (21%) received maintenance treatment with an ORR of 10% and stable disease in 50% of p. The median overall survival (OS) for all patients was 12.6 months (95% CI 10.8 – 14.3). There were statistically significant differences in OS according histological subtype. The median OS for epithelioid was significantly longer (15 months, 95% CI 13.8-18) as compared with non-epithelioid (7 months 95% CI 4.3-9, $p<0.001$). There were no statistically significant differences in OS according to gender, asbestos exposure or type of platinum chemotherapy (Cisplatin 15.2 months 95% CI: 13.7-18.75; *vs*.Carboplatin 18 months 95% 12-25.3, p=0.32). **Conclusion:** In Spain, OS of MPM patients treated with platinum palliative chemotherapy exceeded the median OS reported in phase III trials. **Keywords:** Mesothelioma,, chemotherapy, Spain

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P1.08-009 Hepatocyte Growth Factor (HGF) Expression in Malignant Mesothelioma: A Potential Predictive Marker for *met*/HGF-Targeted Therapy? Morgan L. Cowan[1], Murat Yaylaoglu[2], Jocelyn Bailey[2], Susan Sa[2], Peter B. Illei[1] [1]*Pathology, Johns Hopkins University School of Medicine, Baltimore/MD/United States of America,* [2]*Pathology, Genentech, San Francisco/CA/United States of America*

Background: Malignant mesothelioma (MM) is an aggressive neoplasm predominantly involving the pleura with less than 2 years median patient survival time and limited systemic therapeutic options. The HGF-MET axis is important in cell proliferation and homeostasis. Dysregulation of the pathway has been linked to tumorigenesis. Met overexpression has been used as a predictor of response to Met-targeted therapy with limited success. HGF is the only known ligand for Met, but intratumoral HGF levels have not been studied in MM. In a preclinical glioblastoma model autocrine signaling by HGF was predictive for Met-Targeted therapy. Our aim was to evaluate HGF expression patterns and to assess the feasibility of non-isotopic bDNA in situ hybridization to reliably detect HGF expression in MM. **Methods:** We analyzed HGF expression using non-isotopic branched-DNA in situ hybridization on an automated platform in 39 samples of MM. In a subset of cases manual in situ hybridization was also performed. Immunohistochemistry for c-met using a rabbit monoclonal antibody and semiquantitative scoring system proposed for NSCLC was also available for 33 tumors. The cohort included 10 peritoneal (3 male and 7 female, age range 15-77; median 64.5) and 29 pleural tumors (24 male and 5 female, age range 24-88; median 67.4). There were 28 epithelioid, 10 biphasic and 1 sarcomatoid tumors. HGF expression was scored as none, weak, moderate or strong (normal placenta and surrounding benign tissue served as controls). **Results:** Moderate to strong HGF expression was seen in 7 cases (6 strong, 1 moderate), weak expression was noted in 10 tumors while 22 were negative. Met IHC was only available for 3 of the 6 strong HGF expressing tumors. Of the 16 met positive tumors only 1 showed strong HGF expression while the majority were HGF negative (10) or weak positive (5). Intratumoral heterogeneity and both paracrine and autocrine HGF expression were also observed. The automated and manual in situ hybridization methods showed concordant results. **Conclusion:** Non-isotopic bDNA assay can be used to reliably detect HGF mRNA in mesothelioma tissue sections. A range of HGF expression levels can be seen with a subset of cases showing moderate to strong (18%) expression. Intratumoral heterogeneity is present and both paracrine and autocrine sources of HGF can be identified. The majority of c-met positive (2+ and 3+) tumors exhibit weak or no HGF expression with only 1 of 3 HGF strongly positive tumor showing positive (2+) c-met staining. Further studies are needed to determine if HGF expression can be used as a predictive marker for c-met/HGF targeted therapy in malignant mesothelioma. **Keywords:** mesothelioma, c-met, HGF, therapy

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MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.08-010 Understanding the Genetic Landscape of Malignant Mesothelioma - A Comparison of Human and Murine Mesothelioma Cell Lines Jenette Creaney[1], Sophie Sneddon[1], Nicola Waddell[2], John Pearson[2], Sean Grimmond[3], Bruce W.S. Robinson[1] [1]*National Centre for Asbestos Related Disease, Perth/WA/Australia,* [2]*Qimr Berghofer Medical Research Institute, Brisbane/QLD/Australia,* [3]*University of Glasgow, Glasgow/United Kingdom*

Background: Malignant mesothelioma (MM) is predominantly caused by exposure to asbestos. Next generation sequencing is being used in MM to understand the nature of the genetic lesions that underlie the disease and to identify potential new therapeutic targets. MM has the unusual distinction of having a mouse homologue that largely replicates the human cancer. This provides an opportunity to use murine tumor sequence data to understand mesothelioma pathogenesis, examine asbestos mutational signatures and test potential treatment strategies predicted by the genetic landscape. We have undertaken exome sequencing of asbestos induced murine MM, and compared our findings with human MM. **Methods:** Whole exome sequencing (WES) was performed on the Ion Torrent Proton platform on 15 early passage MM cell lines developed from ascites induced following asbestos exposure and tumour development in three wild-type mouse strains (BALB/c, CBA and C57BL/6 strains). Wild type germline murine normal samples were sequenced concurrently. Somatic single nucleotide variants (SNVs) were identified using publicly available algorithms with a subset being validated using Sanger sequencing. Copy number variation was analysed using GISTIC. Mutation signatures were identified using the Somatic Signatures algorithm in R. **Results:** There were on average 760 SNV identified in mouse MM cell lines (range 212-2234) equivalent to a median of approximately 9 mutations per Mb. There were significantly more SNV detected in the BALB/c strain than the CBA and C57Bl/6 strains. As previously observed there was a tendency for chromosome deletion rather than amplification in MM. Deletions in chromosome 4 in the region of p16 were common. Non-synonymous mutations accounted for 60-80% of all exonic mutations. C>T and G>A transitions were more prevalent than other mutation types across all tumours. Mutation signature analysis showed a higher rate of C>A, C>G and C>T mutations in specific dinucleotide contexts, which was mirrored in the human MM tumours. **Conclusion:** Genetic analysis of murine models of MM enables the identification of candidate mutational changes that can help inform about changes in human tumors. These models also provide excellent opportunities for pre-clinical proof-of-principle therapeutic studies of the use of sequence information in clinical trials. **Keywords:** mouse models, Mesothelioma, sequencing

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P1.08-011 Clinical Outcome and Prognostic Factors for Advanced Malignant Mesothelioma (MM) Patients (pts) Treated on Phase I Trials Dionysis Papadatos-Pastos, Desamparados Roda, Maria Jose De Miguel Luken, Vasiliki Michalarea, Joao Lima, Nikolaos Diamantis, Marta Capelan, Awais Jalil, Shankar Bodla, Jaishree Bhosle, Rhoda Molife, Mary O'Brien, Udai Banerji, Sanjay Popat, Timothy A. Yap *Royal Marsden NHS Foundation Trust, London/United Kingdom*

Background: Relapse after approved anticancer treatments is inevitable in MM pts. Novel agents in phase I trials may benefit such pts and the development of a prognostic score can help identify those who are likely to benefit most. We review the outcome of pts with relapsed MM who have participated in phase I trials in the drug development unit (DDU) of the Royal Marsden Hospital (RMH). **Methods:** The RMH prognostic score (RPS) (albumin < 35 g/L, lactate dehydrogenase [LDH] > upper limit of normal [ULN], and > 2 sites of metastases) is an objective tool used to select pts for phase I trials. In view of the pattern of disease spread in MM, we sought to define a MM-specific RPS (m-RPS), by assessing baseline patient factors. Data from consecutive patients who participated in 33 phase I trials between 09/2003 and 12/2014 were included in this analysis. The endpoints were time to progression (TTP) overall survival (OS) and safety. Kaplan-Meier analysis using a log rank test was used to determine survival outcomes. **Results:** Data from 54 pts, M:F (36:18), median age 62 years (range, 25-76) were studied. All pts had ECOG PS 0-1. TTP was 2.5 (95% CI 1.7-3) months, OS was 7.6 (95% CI 5.3-8.4) months and the clinical benefit rate was 15%; Three (6%) pts had RECIST confirmed partial response (to PI3K pathway inhibitors [n=2] and immunotherapy [n=1]); 5 (9%) pts had RECIST stable disease ^{3}6 months. Male gender was highlighted as a factor of poor prognosis (p=0.004) in a multivariate analysis and therefore, we propose m-RPS for MM pts that now incorporates gender instead of the number of metastatic sites (Table). The good prognosis group [A] (m-RPS 0-1; n=23) had a median OS of 13.7 (95% CI 7.9-24) months and the poor prognosis group [B] (m-RPS 2-3; n=28) had a median OS of 4 (95% CI 2.8-7.5) months, $p<0.001$. 13 pts (24%) had an OS < 12 weeks: 3 (11%) pts from Group [A] and 10 (36%) pts from Group [B]. 39 (72%) pts experienced G1-G2 toxicities, ^{3}G3 toxicities were seen in 8 (15%) pts and 7 (13%) pts discontinued trial due to toxicity.

Variable	Score
LDH	
≤Upper limit of normal (ULN)	0
>ULN	1
Albumin	
³35g/L	0
<35g/L	1
Gender	
Female	0
Male	1
Table. modified RMH prognostic score (m-RPS)	

Conclusion: Experimental agents in the phase 1 setting appeared to be well tolerated with preliminary signals of benefit in selected advanced MM pts. The m-RPS should be prospectively validated as a screening tool for MM pts considered for phase I studies
Keywords: mesothelioma, phase 1, prognostic, RMH score

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P1.08-012 Immunohistochemistry as Prognostic Markers for Malignant Pleural Mesothelioma Taiichiro Otsuki[1], Nobuko Maehashi[2], Yuki Kataoka[2], Takayuki Terada[1], Kozo Kuribayashi[1], Masataka Hirabayashi[2], Ryuji Ieki[1], Takashi Nakano[1] [1]*Department of Respiratory Medicine, Hyogo College of Medicine, Nishinomiya,Hyogo/Japan,* [2]*Respiratory Medicine, Hyogo Prefectural Amagasaki Hospital, Amagasaki Hyogo/Japan*

Background: Malignant pleural mesothelioma (MPM) is a rare and aggressive malignancy of the mesothelium. Several previous studies reported the prognostic ability of immunohistochemistry markers. But there are few reports adjusted for confounding appropriately. **Methods:** A retrospective cohort study was performed using epithelial and biphasic MPM patients treated in two tertiary hospitals in Japan between 2007 and 2014. Candidate prognostic factors were as follows: age; gender; performance status; stage; treatment modality; NLR (neutrophil lymphocyte ratio); calretinin expression; D2-40 expression; WT1 (Willms' tumor 1). The primary outcome was overall survival (OS). The log-rank test and the Cox proportional hazards model were used for analyses to detect prognostic factors. We defined p<0.05 was statistically significant. **Results:** Total 371 patients comprised 309 epithelioid, 62 biphasic subtype of MPM. Median OS was 12.9 months. On univariate analysis all variables except for WT1 were associated with OS. On multivariate Cox proportional regression analysis PS (1<), Stage (II<), treatment modality, NLR (3<=), D2-40 negative expression were associated with shorter OS. **Conclusion:**Positive expression of D2-40 were associated with longer OS of epithelial and biphasic MPM. Further studies are warranted.
Keywords: Mesothelioma

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P1.08-013 Long Non-Coding RNAs Associated with Lysine Demethylases Are Overexpressed and Epigenetically Regulated in Malignant Pleural Mesothelioma Anand S. Singh[1], Leah Quinn[1], Stephen P. Finn[2], Sinead Cuffe[3], Steven G. Gray[1] [1]*Thoracic Oncology Research Group, Trinity College Dublin/St. James'S Hospital, Dublin/Ireland,* [2]*Department of Pathology, University of Dublin, Trinity College and St. James'S Hospital, Dublin/Ireland,* [3]*Hope Department, St.James'S Hospital, Dublin/Ireland*

Background: Malignant pleural mesothelioma (MPM) is an aggressive rare cancer affecting the pleura and is predominatly associated with prior exposure to asbestos. Treatment options are limited, and most patients die within 24 months of diagnosis. The current standard of care for MPM patients is a combination of cisplatin and pemetrexed (or alternatively cisplatin and raltitrexed), yet most patients die within 24 months of diagnosis. Lysine Demethylases (KDMs) containing a JmjC domain regulate gene expression by "erasing or removing" methylation on histones in chromatin. Members of this family are frequently found to have aberrant expression in cancer and currently are actively pursued as candidate pharmaceutical therapeutic targets. We have shown that various members of the JmjC family of KDMs have significantly altered expression in MPM. Long non-coding RNAs (lncRNAs) belong to a group of RNAs that are usually more than 200 nucleotides long and play important roles in different regulatory processes, including regulation of gene expression. Several lncRNAs have also been shown to play a role as oncogenic molecules in different cancer cells (one example being HOTAIR). Altered expression of lncRNAS therefore make them candidate biomarkers with diagnostic and therapeutic potential in cancer. Several such lncRNAs have now been shown to locate to the same chromosomal region as various KDMs. These are KDM4A/KDM4A-AS1, KDM5B/KDM5B-AS1 (also known as PCAT6), KDM5C/ AY927613.1 and JARID2/JARID2-AS1. We therefore examined the expression of these lncRNAs in MPM. **Methods:** A panel of MPM cell lines were screened for expression of KDM4A-AS1, KDM5B-AS1, AY927613.1 and JARID2-AS1 by RT-PCR. lncRNA transcript levels were subsequently examined by RT-PCR in a cohort of snap-frozen patient samples isolated at surgery comprising benign, epithelial, biphasic, and sarcomatoid histologies. The effects of KDM and HDAC inhibitors on their expression was also examined. **Results:** The expression of the various lncRNAs was detectable across our panel of cell lines. In primary tumours the expression of these lncRNAs were significantly elevated in malignant MPM compared to benign pleura (p<0.05), and significant differences were also observed when samples were analysed across different histological subtypes. **Conclusion:** The expression of these lncRNAs are significantly altered in MPM. We have cloned KDM4A-AS1 and PCAT6 into overexpression constructs and future studies will assess the effects of these lncRNAs overexpression on mesothelioma proliferation, cellular health and gene expression to determine their potential role in mesothelioma.
Keywords: lncRNA, Lysine Demethylase, Mesothelioma

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P1.08-014 The Small Molecule Inhibitor, LCRF004, Is Effective in Targeting the RON/MST1R Pathway in Malignant Pleural Mesothelioma Anne-Marie Baird[1], Kenneth J. O'Byrne[2], David Easty[3], Liam Shiels[4], Annette Byrne[4], Stéphane Raeppel[5], Bryan Stanfill[6], Alex Soltermann[7], Daisuke Nonaka[8], Dean A. Fennell[9], Luciano Mutti[10], Harvey I. Pass[11], Isabelle Opitz[12], Steven G. Gray[3] [1]*Cancer and Ageing Research Program, Queensland University of Technology, Brisbane/QLD/Australia,* [2]*Cancer and Ageing Research Program, Princess Alexandra Hospital and Queensland University of Technology, Brisbane/QLD/Australia,*[3]*Thoracic Oncology Research Group, Trinity College Dublin/St. James'S Hospital, Dublin/Ireland,* [4]*Royal College of Surgeons in Ireland, Dublin/Ireland,* [5]*Chemrf Laboratories Inc, Montreal/QC/Canada,* [6]*Commonwealth Scientific and Industrial Research Organisation, Brisbane/QLD/Australia,* [7]*Institute of Surgical Pathology, University Hospital Zurich, Zurich/Switzerland,* [8]*Christie Hospital NHS Foundation Trust, Manchester/United Kingdom,* [9]*Mrc Toxicology Unit, University of Leicester & Leicester University Hospitals, Leicester/United Kingdom,* [10]*Environment and Life Sciences, University of Salford, Manchester/United Kingdom,* [11]*Department of Cardiothoracic Surgery, NYU Langone Medical Center, New York/NY/United States of America,* [12]*Division of Thoracic Surgery, University Hospital Zurich, Zurich/Switzerland*

Background: Malignant pleural mesothelioma (MPM) is an aggressive inflammatory cancer. We have previously identified RON as frequently activated in MPM patient samples and cell lines. RON is a member of the MET proto-oncogene family and is bound by macrophage stimulating protein (MSP). High positivity for total RON by IHC was an independent predictor of favourable prognosis. Additionally, elevated expression levels of MSP correlated with better survival. The aim of this study was to further examine the MSP-RON signalling axis in MPM using a RON inhibitor, LCRF004. **Methods:** MPM cell lines and a normal mesothelial cell line were screened for the expression of RON and MSP at the protein (Western) and mRNA (RT-PCR) level. Downstream mediators affected by MSP stimulation and LCRF004 were identified using a proteome profiler array. The effect of LCRF004 and MSP were examined using proliferation (BrdU ELISA), viability (High Content Analysis), migration (xCELLigence), apoptosis and cell cycle (HCA) assays. A xenograft study was also completed. **Results:** Treatment with LCRF004 resulted in a significant decrease in proliferation, viability and migration *in vitro* and reduced tumour growth *in vivo* (p<0.05, compared with vehicle control). In addition, LCRF004 significantly increased apoptosis. In terms of cell cycle, drug treatment decreased cells in 2n, whilst increasing cells in the G0/G1 phase. Experiments are on going to further characterise the mechanism of action of LCRF004. **Conclusion:** The *in vivo* and *in vitro* data generated in this study, indicates that the MSP-RON signalling axis is a potential target in MPM. Targeting the RTK domain of the RON receptor with a small molecule inhibitor is an effective interventional strategy in MPM.
Keywords: LCRF004, MSP, malignant pleural mesothelioma, RON

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P1.08-015 Malignant Pleural Mesothelioma: Observational and Retrospective Analysis of Spanish Database (BEMME). The Spanish Lung Cancer Group (SLCG) Noemi Reguart[1], Jordi Remon[2], Felipe Cardenal[3], Ernest Nadal[3], Yolanda Garcia[4], M. Rosario Garcia-Campelo[5], Óscar Juan Vidal[6], J.R. Jarabo[7], Manuel Domine[8], Carlos Martinez-Barenys[9], David Cumplido[10], Sergio Bolufer[11], Delvis Rodríguez[12], Mireia Martinez-Barenys[13], Sergio Peralta[14], Isidoro Barneto[15], Pilar Lianes[2], M.P Lopez[16], Natividad Martinez[17], Ignacio Gil-Bazo[18], Nieves Martinez-Lago[19], Mariano Provencio[20] [1]*Medical Oncology, Hospital Clinic, Translational Genomics and Targeted Therapeutics in Solid Tumors, Institut D'Investigacions Biomèdiques August Pi I Sunyer (Idibaps), Barcelona/Spain,* [2]*Hospital de Mataró, Mataró/Spain,* [3]*Department of Medical Oncology, Catalan Institute of Oncology, L'Hospitalet/Spain,* [4]*Hospital de Sabadell, Sabadell/Spain,* [5]*Complejo Hospitalario Universitario A Coruña, A Coruña/Spain,* [6]*Medical Oncology, Hospital Universitari I Politècnic La Fe, Valencia/Spain,* [7]*Hospital Clínico San Carlos, Madrid/Spain,* [8]*Oncology, Hospital Universitario- Fundacion Jimenez Diaz, Madrid/Spain,* [9]*Hospital Universitari Germans Trias I Pujol, Badalona/Spain,* [10]*Hospital de Torrevieja, Alicante/Spain,*[11]*Hospital General Universitario Alicante, Alicante/Spain,* [12]*Hospital Universitario Insular de Gran Canaria, Gran Canaria/Spain,* [13]*Hospital Universitario Araba-Sede Txagorritxu, Vitoria/Spain,* [14]*Hospital Universitari Sant Joan de Reus, Reus/Spain,* [15]*Hospital Reina Sofia, Cordoba/Spain,* [16]*Centro Oncologico MD Anderson Internacional España, Madrid/Spain,* [17]*Hospital General de Elche, Elche/Spain,* [18]*Clinica Universitaria de Navarra, Pamplona/Spain,* [19]*Complexo Hospitalario Universitario de Santiago, Santiago de Compostela/Spain,* [20]*Hospital Puerta de Hierro, Madrid/Spain*

Background: Malignant Pleural Mesothelioma (MPM) is a rare but aggressive malignancy of the pleura, with a strong causal link to asbestos exposure. Although in Spain asbestos was banned in 2002, it is estimated that occupationally related deaths due to MPM will continue to occur until 2040. BEMME (Base Epidemiológica Mesotelioma Maligno en España) is an observational and retrospective study sponsored by the Spanish Lung Cancer Group that aimed to characterize the patient's and tumour's

features as well as the treatment modalities of patients diagnosed with mesothelioma in Spain. **Methods:** Clinical records of patients with malignant pleural and peritoneal mesothelioma were retrospectively reviewed to collect epidemiological data, diagnostic tests, treatment modalities and survival data into an electronic and anonymous database. Thirty-five Spanish hospitals participated in the project and 570 mesothelioma patients were included in the BEMME database. Here we present a descriptive analysis of MPM patients based upon these data. **Results:** From January 2008 to December 2013, 538 patients (p) had MPM. Most patients were males (77%) and 74% of patients were ≥ 60 years (60-70y: 33%, >70y: 41%). Most patients (49%) had a performance status 1 at diagnosis. Only 32% of patients were recorded as positive for asbestos exposure and 77% of patients were never-smokers. Dyspnoea (35%) and thoracic pain (26%) were reported as the most frequent symptoms at diagnosis. Epithelioid was the most frequent histological subtype (63%), followed by sarcomatoid (12%), biphasic (8%) and not specified (17%). Disease stages at diagnosis were: stage I, 7%; stage II, 9%; stage III, 17%; stage IV, 45%; not specified, 22%. Surgery was performed in 41p: extrapleural neumonectomy 16p, extended pleurectomy 15p and partial pleurectomy 10p. Palliative pleurodesis was performed in 22% of patients. A total of 70% of patients received chemotherapy (55% palliative, 11 neoadjuvant and 6% adjuvant). The median overall survival (OS) for all patients was 13.2 months (95% CI 12.2 – 15.2). There were no statistically significant differences in OS according to age, gender and asbestos exposure. In the univariate analysis, higher stage (III-IV *vs.* I-II, p=0.0003) and non-epithelioid subtype (non-epithelioid *vs.* epithelioid, p=0.00001) were significantly associated with shorter OS. **Conclusion:** In Spain, most MPM patients are diagnosed at advanced stages and are treated with palliative modalities: mainly chemotherapy and pleurodesis. Stage and histologic subtype were prognostic factors for survival. BEMME database is a helpful tool to describe the therapeutic strategies employed in MPM patients in Spain. **Keywords:** Epidemiology, Mesothelioma, Spain

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P1.08-016 Ponatinib Shows Promise in Malignant Pleural Mesothelioma Cells with Abl Pathway Dysregulation Yi-Wei Yang, Gavitt Woodard, Jillian Chase, Angelica Marrufo, David Jablons, Hassan Lemjabbar-Alaoui *Surgery, University of California San Francisco, San Francisco/CA/United States of America*

Background: Malignant pleural mesothelioma (MPM) remains a lethal cancer with limited treatment options. Various tyrosine kinases including c-Abl/Arg, FGFR1, Src and PDGFRa/b have been implicated in driving the growth of MPM. Ponatinib is an FDA approved potent multi-target inhibitor of cAbl/Arg, PDGFRα, VEGFR2, FGFR1, and Src. The aim of this study was to investigate the effects of ponatinib on MPM cells. **Methods:** The *in vitro* effect of ponatinib on different MPM cell lines (H2052, MSTO211H, H2452, H28) were evaluated by MTS assay and the effect on cell migration was determined using a "scratch wound" assay. Levels of phosphorylated-CrkI (pCrkI) were evaluated by western blot and double-strand DNA breaks (DSDBs) measured via the surrogate marker γ-H2AX in an ELISA assay. A xenograft MPM model was used to examine the effects of ponatinib on tumor grown *in vivo*. **Results:** High levels of pCrkI were expressed in all MPM cell lines studied indicating c-Abl/Arg pathway activation. *In vitro,* ponatinib was effective against all MPM cell lines by cytotoxicity assay, led to dramatic cell migration inhibition, significantly reduced pCrkI expression, and increased DSDBs. *In vivo*, ponatinib blunted tumor growth in a xenograft model. Reduced pCrkI levels were observed in xenograft tumor specimens following ponatinib treatment. **Conclusion:** Inhibition of Abl kinase activity with ponatinib is a potential therapeutic approach in MPM patients with Abl pathway dysregulation. pCrkI shows promise as a biomarker of increased Abl kinase activity and may be useful in identifying MPM patients most likely to benefit from ponatinib. **Keywords:** Abl, Ponatinib, DNA damage, Mesothelioma

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P1.08-017 microRNAs Expression in Malignant Pleural Mesothelioma, Asbestosis and Benign Pulmonary Disease Luca Ampollini[1], Paola Mozzoni[2], Letizia Gnetti[3], Marcello Tiseo[4], Luigi Rolli[1], Michela Solinas[1], Luigi Ventura[1], Enrico Maria Silini[3], Matteo Goldoni[2], Rossella Alinovi[2], Michele Rusca[1], Massimo Corradi[2], Paolo Carbognani[1], Antonio Mutti[2] [1]*Thoracic Surgery, University of Parma, Parma/Italy,* [2]*Department of Clinical and Experimental Medicine, University of Parma, Parma/Italy,* [3]*Pathology, University of Parma, Parma/Italy,* [4]*Medical Oncology, University Hospital of Parma, Parma/Italy*

Background: To evaluate the diagnostic potential of a panel of microRNAs in plasma samples of patients with malignant pleural mesothelioma (MPM). **Methods:** A group of patients with pathological diagnosis of MPM were randomly selected from a prospective mesothelioma database. Similarly, a group of patients with asbestosis and one with benign pulmonary disease, were chosen for comparison. A panel of miRNA including miR-16, miR-17, miR-21, miR-126 and miR-486 were evaluated. VEGF (vascular endothelial growth factor) was evaluated in plasma samples of patients with mesothelioma. Analysis of covariance (ANCOVA) followed by Bonferroni post-hoc test were used for multiple comparisons. P<0.05 was considered significant. **Results:** 14 patients with malignant pleural mesothelioma, 14 patients with asbestosis and 21 patients with benign pulmonary disease were studied. The expression of miR-16 (p=0.018), miR-17 (p=0.024) and miR-126 (p=0.019) was significantly lower in patients with MPM compared with patients with benign pulmonary disease. Interestingly, miR-486 was able to discriminate patients with MPM compared to patients with asbestosis (p=0.004). Considering patients with MPM, miR-17 (p=0.023) and miR-486 (p=0.015) were significantly more expressed in patients with epithelial type than in patients with sarcomatoid and biphasic type. Moreover, the expression of miR-16 (p<0.0001), miR-17 (p<0.0001), miR-21 (p=0.004), miR-126 (p=0.0016) and miR-486 (p=0.003) was significantly lower in patients with asbestosis compared with subjects with benign pulmonary disease. In MPM plasma samples, VEGF expression was negatively correlated to miR-126 (p=0.004). **Conclusion:** The expression of miR-16, miR-17 and miR-126 was able to distinguish patients with MPM compared with patients with benign pulmonary diseases. miR-17 and miR-486 were significantly higher in patients with epithelial mesothelioma. An immunohistochemistry analysis evaluating the expression of VEGF in MPM tissue samples is ongoing. The available data support the role of miRNAs in the aetiology of MPM, suggesting their possible use as diagnostic markers of the disease. **Keywords:** miRNA, Asbestosis, malignant pleural mesothelioma

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P1.08-018 Spontaneous Regression of Mesothelioma Gunnar N. Hillerdal, Ocar Grundberg *Pulmonary Diseases, Karolinska Hospital, Stockholm/Sweden*

Background: Malignant pleural mesothelioma is a progressive disease with a poor prognosis. However, a few cases of spontanous regression has been reported in the literature. We here report another case. **Methods:** Not applicable **Results:** A 68-year old woman was referred to the clnic because of increasing dyspnoea and changes on her chest roentgenogram. She had never smoked and had worked in an office all life and denied all exposure to asbestos or other dangerous substances. CT scan revealed an irregular pleural thickening all around the right lung, in the interlobar fissure, and some enlarged mediastinal lymph nodes on the right side. Bronchsocpy, ultrasound biopsy of the pleura, and mediastinosccopy yielded no diagnosis, and therfore the thoracic surgeons made a pleural biopsy. This showed an epitheloid tumor , and the immune staining onfirmed that it was a malignant mesothelioma. The patient was offered cytostatic treatment but refused; she wanted to try with cost changes. She excluded meat in her diet, ate broccoli, nuts etc, and at check-up 3 months later the chest X-ray and the CT scan were normal. At follow-up, however, 18 months later there was a recurrence, ans she has now been started on chemotherapy. **Conclusion:** We have in the literature managed to find only three case reports similar to this one. An immunological reaction has been postulated to be the cause. In at least two of the cases, as in this one, there was none or only slight exposure to asbestos. In one case, there was no recurrence after 7 years, in another a single local recurrence after 6 years which was surgically removed. Odd patients which have lived for many years, even decades, without any treatment have also been described. In our own experience, the longest survivor survived 20 years with minimal symptoms. It is important to realize that good otcomes not always are due to the actions of doctors. **Keywords:** Mesothelioma, survival

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P1.08-019 Pure Bronchoplasty without Lung Parenchyma Resection for Central Carcinoid Oleg Pikin[1], Andrey Ryabov[2], Victor Sokolov[3], Vladimir Glushko[1], Konstantin Kolbanov[1], Larisa Telegina[3], Ali Amiraliev[1], Vitaliy Barmin[1] [1]*Thoracic Surgery, Hertzen Research Institute of Oncology, Moscow/Russian Federation,* [2]*Thoraco-Abdominal Surgery, Hertzen Research Institute of Oncology, Moscow/Russian Federation,* [3]*Endoscopic Department, Hertzen Research Institute of Oncology, Moscow/Russian Federation*

Background: The aim of the study is to evaluate the efficacy of combined approach (endoscopic resection followed by pure bronchoplasty without any pulmonary resection) in patients with endobronchial carcinoids. **Methods:** We applied two-staged technique (endoscopic resection first followed by pure bronchoplasty) to 25 patients (males – 10) with endobronchial carcinoid. The median age was 32,4 years with a range from 19 to 64 years. The indications to this technique were pure endobronchial carcinoid without lymph node involvement. Tumour was located on the right side in 18 (72%), on the left – in 7(28%) patients. Endoscopic resection/desobliteraton of central airway was performed to all patients as the first stage procedure to resolve the obstructive pneumonia and to localize the pedicle of the tumour for proper planning of further bronchoplasty followed by endobronchial ultrasound to detect the peribronchial component. Different types of pure bronchoplasty were performed as the second stage surgery with systematic mediastinal lymph node dissection (table 1). Table 1.Types of bronchial sleeve resections in our series

type of resection	right side	left side
main stem bronchus	7	5
bronchus intermedius	7	-
main stem bronchus+upper lobe bronchus	2	2
bronchus intermedius+middle lobe bronchus	1	-
bronchus intermedius+lower lobe bronchus	1	-
Total	18(5)*	7(2)*
* polybronchial anastomosis was performed		

Results: The resection was complete (R0) in all cases. No lymph node metastases were observed, and tumours were pathologically staged as pT1aN0 in 18, pT2N0 – in 5, pT3N0 – in 2 patients and that all cases had invasive components limited to the bronchial wall. Twenty three tumours were typical and only two - atypical carcinoids. Morbidity was 33,3% (only minor complications) with no mortality. The stenosis

of bronchial anastomosis was observed in one patient treated by endoscopic intervention. Overall 5- and 10-years survival was 100,0% and 96,0% (one patient died from myocardial infarction 8 years after surgery). No recurrence of the primary tumour was observed in any case. **Conclusion:** Two-staged surgery (endoscopic resection+pure bronchoplasty without lung parenchyma resection) is an effective technique for treatment of endobronchial carcinoids with excellent oncologic outcome.
Keywords: carcinoid, bronchoplasty, endoscopic resection

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P1.08-020 Survival Impact of Adjuvant Radiation and Chemotherapy in Patients with Typical and Atypical Pulmonary Carcinoids Lindsay M. Hannan[1], Jeffrey Switchenko[2], Yuan Liu[2], Madhusmita Behera[2], Kristin A. Higgins[3], Felix Fernandez[4], Rathi N. Pillai[5], Fadlo Khuri[5], Suresh S. Ramalingam[5], Theresa W. Gillespie[2], Taofeek K. Owonikoko[5] [1]*Emory University School of Medicine, Atlanta/United States of America,* [2]*Biostatistics and Bioinformatics, Emory University Winship Cancer Institute, Atlanta/United States of America,* [3]*Radiation Oncology, Emory University Winship Cancer Institute, Atlanta/United States of America,* [4]*Thoracic Surgery, Emory University Winship Cancer Institute, Atlanta/United States of America,* [5]*Medical Oncology, Emory University Winship Cancer Institute, Atlanta/United States of America*

Background: Adjuvant chemotherapy or radiation is commonly employed after resection of primary pulmonary carcinoid especially for patients with advanced stage disease with expectation of survival benefit. The indication for adjuvant therapy is poorly defined and there are limited data in support of this clinical practice. We therefore evaluated predictors and potential benefit of adjuvant chemotherapy and radiation using the National Cancer Database (NCDB), an oncology outcomes database administered by the American College of Surgeons and the American Cancer Society **Methods:** The NCDB was queried for patients who had undergone surgical resection of pulmonary carcinoid tumors between 2003 and 2006. Patients younger than 18 years and those with incomplete survival data were excluded from this analysis. Overall survival was defined as time from date of definitive surgery to date of death or last follow-up. Univariate and multivariable models were employed to assess for association between patient survival and variables of interest. Gender, age, and race were fit in a multivariable Cox model with treatment, and backward selection criteria (alpha = 0.1) were used to determine whether education, urban/rural, tumor size, income, laterality, insurance, or comorbidity score were included in the model. The proportional hazards assumption was checked for all models. **Results:** We included 4984 eligible patients diagnosed between 2003 and 2006 in the analysis. Post resection adjuvant radiation was administered to 4.2% of the patients; 1.9% received chemotherapy while the remaining patients did not receive any adjuvant therapy. Patients treated with adjuvant chemotherapy or radiation had worse survival at 2 years post surgery (75.7% and 70.8%% respectively) in comparison to patients managed with surgical resection only (94.2%). This survival difference was still significant in multivariable Cox models after adjusting for relevant patient and prognostic factors including gender, age, race, stage, lymph node involvement, tumor size, education level and co-morbidity score (HR: 2.35, 95% CI: 1.43 - 3.85, p<0.001 and HR: 1.97, 95% CI:1.48 - 2.61, p<0.001 for adjuvant chemotherapy and radiation, respectively). Decreased survival persisted in analyses restricted to patients with lymph node involvement (HR 1.58, p 0.084 and 3.21, p<0.001 for chemotherapy and radiation, respectively), and with advanced stage cancer (HR 4.10, p <0.001 and 2.04, p=0.036 and for radiation and chemotherapy, respectively) . Results did not differ by histology **Conclusion:** We observed worse outcomes in patients with typical and atypical carcinoid treated with adjuvant chemotherapy and radiation post surgery. The poor outcome associated with adjuvant therapy may be explained in part by the fact that patients considered for adjuvant therapy are more likely to have advanced stage disease and adverse tumor characteristics. However, contribution from potential toxicities of chemotherapy and radiation cannot be entirely excluded pending additional analysis in propensity-matched cohorts of patients.
Keywords: Adjuvant therapy, Pulmonary carcinoid

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P1.08-021 Role of Surgery in Sarcomatoid Tumors of the Lung: A Multicentre Analysis Filippo Lococo[1], Cristian Rapicetta[2], Giuseppe Cardillo[3], Alessandro Stefani[4], Stefano Margaritora[5], Giovanni Leuzzi[6], Leonardo Petracca[5], Giulio Rossi[7], Uliano Morandi[4], Francesco Facciolo[6], Tommaso Ricchetti[2], Massimiliano Paci[2], Giorgio Sgarbi[2] [1]*Unit of Thoracic Surgery, Irccs_Arcispedale Santa Maria Nuova, Reggio Emilia/ Italy,* [2]*Unit of Thoracic Surgery, Irccs-Arcispedale Santa Maria Nuova, Reggio Emilia, Italy, Reggio Emilia/Italy,* [3]*Unit of Thoracic Surgery, San Camillo-Forlanini Hospital, Rome, Italy, Rome/Italy,* [4]*Unit of Thoracic Surgery, University of Modena and Reggio Emilia, Modena, Italy, Modena/Italy,* [5]*Department of General Thoracic Surgery, Catholic University, Rome, Italy, Rome/Italy,* [6]*5Department of Surgical Oncology, Thoracic Surgery Unit, Regina Elena National Cancer Institute - Ifo, Rome, Italy, Rome/Italy,* [7]*Unit of Pathology, University of Modena and Reggio Emilia, Modena, Italy, Modena/Italy*

Background: Sarcomatoid lung carcinoma (SaLC) is a very rare and aggressive subtype of non-small cell lung cancer (NSCLC). To better understand the long-term results after surgical treatment and the main prognostic factors of such rare entities, we have revisited the clinical records of patients affected by SaLC in a large multicentre surgical series. **Methods:** Among 6569 patients who underwent curative resection for NSCLC from 01/2003 to 12/2013 in 5 Institutions, 148 patients (2.2%) had sarcomatoid carcinoma. Clinical and pathological data were retrospectively reviewed. Kaplan-Meier method, log-rank test and Cox-regression analysis were used for the statistical analysis when indicated. **Results:** Mean age and male/female ratio were 66.6±9.9 yrs and 120/28, respectively. The main clinical, surgical and pathological features of the population are summarized in Table 1. Thirty-six pts (24.3%) had pathologic stage-I disease and 70 pts (47.3%) presented with mixed histological tumor (SaLC combined with NSCLC). The overall median and 5-year (LTS) survivals were 17 months and 11.3%, respectively. During follow-up, 101 patients (68.2%) experienced a relapse of disease (84 pts (57%) at distance). Log-rank analysis identified the administration of pre-op PET/CT scan (LTS: yes=17.9% vs no=5.5%; p=0.040), the surgical radicality (LTS: R0=13.2% vs R+=0%, p<0.001), the pStage (LTS: p-I=13.2%, p-II=10.6%, p-III=6.3%, p-IV=0%; p<0.001) as prognostic factors in SaLC patients. Finally, Cox regression analysis confirmed the administration of pre-op PET/CT scan (p=0.021), the surgical radicality (p<0.001) and the p-Stage (p=0.022) as independent prognostic factors in such cohort of patients. **Conclusion:** Primary SaLC presented a poor prognosis after surgical treatment (overall 5-yr survival=11.3%), even in early stages (LTS: 13.2% in pStage-I). Such results imply that the role of surgery for primary SaLC is questionable and eventually limited (after an accurate preoperative staging) to "early-stage" tumors only. In this framework, stronger efforts should be made for target therapies development for such rare entity.

Table 1. Clinical, surgical and pathological features of the sample

Features	Total sample=148
Age (Mean±SD)	66.6±9.9 yrs
Gender	
Male/ Female	120 (81%) / 28 (19%)
Side of Tumor	(64%)
Right/Left	84 (57%) / 64 (43%)
Pet/CT scan	
Yes	75 (51%)
No	73 (49%)
Pre-op Diagnosis	
Yes	76 (51%)
No	72 (49%)
Tumor-size (Mean±SD)	5.8±3.1 cm
Induction Therapy	4 (2.7%)
Surgery	
Sub-lobar Resections	5 (3.4%)
Lobectomies/bilobectomies	132 (89.2%)
Pneumonectomies	8 (5.4%)
Post-op Mortality/Complications	3 (2.0%) / 42 (28.4%)
Completeness of resection	
R0	141 (95.3%)
R+	7 (4.7%)
Pathological Staging	
I	36 (24.3%)
II	70 (47.3%)
III	32 (21.6%)
IV	10 (6.8%)
Lymph Nodal Involvement	
N0	93 (62.8%)
N1	25 (16.9%)
N2	24 (16.2%)
LFN removed (Mean±SD)	9.2±5.8
LFN involved (Mean±SD)	1.1±3.4
Histology*	
Pleomorphic	83 (56.1%)
Spindle Cell	17 (11.5%)
Giant Cell	6 (4.1%)
Blastoma	2 (1.4%)
Pathological features	
Mixed Forms (combined with NSCLC)	70 (47.3%)
Lymphatic Invasion	38 (25.7%)
Vascular Invasion	74 (50.0%)
Post-op Treatment	
CHT*	99 (66.9%)
RT*	43 (29.1%)
None	44 (29.7%)
Relapse of disease	101 (68.2%)
Local**	60 (40.5%)
Distant**	84 (56.8%)

[illegible]

Keywords: Sarcomatoid tumors, long-term survival

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P1.08-022 Intraoperative Brachytherapy for Thoracic Malignancies Resected with Close or Positive Margins Christopher Fleming[1], Andreas Rimner[1], Gilad N. Cohen[1], Kenneth Rosenzweig[2], Kaled M. Alektiar[1], Michael J. Zelefsky[1], Manjit S. Bains[1], Abraham J. Wu[1] [1]*Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York/ United States of America,* [2]*Radiation Oncology, Mount Sinai, New York/NY/United States of America*

Background: Local recurrence is a significant problem after surgical resection of

thoracic tumors, particularly when close or positive margins are anticipated. As intraoperative radiotherapy (IORT) can deliver radiation directly to the threatened margin, we used this technique in an attempt to reduce local recurrence, particularly for patients who had already received external beam radiation. We updated our experience with thoracic IORT to assess disease control and toxicity outcomes. **Methods:** We performed a retrospective review of patients undergoing permanent I-125 mesh placement or temporary Ir-192 afterloading therapy during surgical resection of primary or metastatic thoracic tumors between 2001 and 2013. In general, for I-125 brachytherapy, iodine seeds were sutured into a mesh at 1cm intervals to form a planar implant delivering 85-250Gy to the MPD, which was then sutured onto the at-risk site. For Ir-192 brachytherapy, a HAM applicator was apposed to the at-risk site, then connected to the afterloader to deliver 7.5-16Gy to a depth of 0.5cm from the applicator surface. Kaplan-Meier method was used to estimate local control and overall survival, and logrank test was used to assess the impact of various clinical or treatment factors on local control. **Results:** Fifty-nine procedures (41 permanent, 18 temporary) were performed on fifty-eight patients (median 56 years old, range 19-77). Most common tumor histologies were NSCLC (n=23), sarcoma (n=18), thymic carcinoma (n=10), and mesothelioma (n=3). Treated sites were chest wall/paraspinal (n=31), lung (n=16), and mediastinum (n=12). Thirty-four procedures were performed on patients who had previously received external beam RT (EBRT) to the area (median 53.1 Gy). Final margins were microscopically negative in 25 cases (42.4%) and positive or not assessed in the remainder. The median size of the treated area was 27cm^2 (range: 4-152cm^2). Median followup was 28.5 months. Actuarial local control at 1 and 2 years was 68.1% and 63.4% respectively. Median survival was 46.2 months. Overall survival at 1 and 2 years was 80.2% and 70.4% respectively. No perioperative deaths occurred. There was no significant difference in local control according to margin status, brachytherapy technique, use of adjuvant EBRT, or metastatic vs. primary tumor. Two patients (3.4%) experienced grade 3+ toxicities possibly related to IORT: one patient who also received preoperative EBRT developed pneumonitis; a second patient with prior EBRT for lymphoma died from complications of SVC syndrome likely induced by radiation fibrosis. An additional 8 patients had grade 3+ postsurgical complications (such as empyema, chylothorax, and pulmonary emboli) unlikely related to IORT. Four patients had grade 2 nerve injury also unlikely related to IORT. **Conclusion:** Intraoperative brachytherapy is associated with good local control after resection of thoracic tumors felt to be at very high risk for recurrence due to close or positive margins. There is a very low incidence of severe toxicity attributable to brachytherapy. Intraoperative brachytherapy should be considered in situations where the oncologic completeness of thoracic tumor resection is in doubt. **Keywords:** Thoracic, brachytherapy, Intraoperative, Radiotherapy

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P1.08-023 Induction Chemotherapy Increases the Survival of Patients with Primary Neuroectodermal Tumors of the Thorax Adalet Demir[1], Akif Turna[2], Elvin Hekimoglu[2], Alper Toker[1], Nil Molinas Mandel[3], Zeynep Hande Turna[4], Kamil Kaynak[4] [1]*Department of Thoracic Surgery, Istanbul University Istanbul Medical Faculty, Istanbul/Turkey,* [2]*Department of Thoracic Surgery, Istanbul University Cerrahpasa Medical School, Istanbul/Turkey,* [3]*Medical Oncology, Koç University School of Medicine, Istanbul/Turkey,* [4]*Department of Medical Oncology, Istanbul University Cerrahpasa Medical School, Istanbul/Turkey*

Background: Primary neuroectodermal tumors (PNETs) of the thorax are rare, small-round cell tumors with a poor prognosis despite multimodal therapy, including surgery and chemoradiotherapy. The ideal treatment was unknown since no comparative clinical series with surgical therapy had been reported. We evaluated the results of multimodal treatment in patients with PNETs located in the thoracic region. **Methods:** Between 2000 and 2013, 27 patients with PNETs in the thoracic region were treated in 3 tertiary-care hospitals. There were 15 males and 10 females with a mean age of 26.3 years (range, 6 – 60). The tumor was located in the chest wall in 21 (involving the costovertebral junction in 7), the lung in 6 patients. Thirteen patients had induction chemotherapy, whereas 22 patients underwent resectional surgery. All the patients received adjuvant chemo/radiotherapy. **Results:** There was no hospital mortality. The overall 5-year survival rate was 42% and median survival was 36±14 months in all patients. Five year survival in patients who had induction chemotherapy was 56%, whereas it was 36% in cases who did not receive induction chemotherapy (p=0.045). The 5-year survival rate of patients with and without costovertebral junction involvement was 21% and 64%respectively(p=0.076). The 5-year survival in the patients who had pulmonary involvement without vertebral or chest wall invasion had 50%. **Conclusion:** Primary thoracic PNET is an aggressive entity that often requires multimodal therapy. Induction chemotherapy seems to lead a greater complete resection rate and better survival, while involvement of the costovertebral junction indicates a slightly worse prognosis. **Keywords:** Pnet, thoracic wall, resection, neoadjuvant

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P1.08-024 Large Cell Neuroendocrine Carcinoma: How Accurate Are the WHO 2004 Classification Criteria Applied? Jules L. Derks[1], Ernst-Jan M. Speel[2], Robert Jan Van Suylen[3], Anne-Marie Dingemans[1] [1]*Department of Respiratory Diseases, Grow School for Oncology & Developmental Biology, Maastricht University Medical Center, Maastricht/Netherlands,* [2]*Department of Pathology, Grow School for Oncology & Developmental Biology, Maastricht University Medical Center, Maastricht/Netherlands,* [3]*Department of Pathology, Jeroen Bosch Hospital, 'S Hertogenbosch/Netherlands*

Background: According to the WHO 2004 (and 2015) classification, the diagnosis large cell neuroendocrine carcinoma (LCNEC) is established on presence of neuroendocrine morphology (i.e. organoid nesting/trabecular pattern, palisading cells and/or rosette formation) and neuroendocrine staining by immunohistochemical (IHC) markers. Furthermore, large cells should be present. However, diagnosis of LCNEC is restrained by the need of a resection or large biopsy specimen. Nonetheless, lung cancer is often diagnosed on small biopsies and therefore application of these WHO criteria in daily practice can be difficult. In this nationwide study we investigate on what tissue the diagnosis of LCNEC was established and to what extend the WHO 2004 criteria are reported in pathology reports established in the daily pathology practice in the Netherlands. **Methods:** Written conclusions (diagnoses) of pathology reports (2003-2012) were retrieved from the Dutch Pathology Registry (PALGA). Conclusions describing LCNEC were selected by queries on anatomic location, diagnosis and keywords (e.g. large cell + endocrine) and screened in accordance with a pathologist (JLD & RJS). Histologically diagnosed LCNEC cases were then selected and pathology centers were requested to send the report. After screening (JLD), consultation reports were excluded and the following data were extracted and compared: 1) mitotic index, 2) necrosis, 3) growth pattern (reported ≥1 feature(s) according to WHO or mentioning neuroendocrine morphology) and 4) neuroendocrine IHC marker staining. Additionally, the sampling method was recorded and retrieved diagnoses were clustered. **Results:** *N*=892 (72%) of 1235 requested reports were received (43 centers, mean 20 (range 1-67) reports). In *N*=869 pathology reports the conclusion was LCNEC including 759 original and 110 consultation reports. Most diagnoses were established on resection specimens (*N*=404, 53%) followed by needle (*N*=195, 26%) and small biopsies (*N*=160, 20%). Retrieved diagnoses could be clustered into LCNEC (N=658, 87%), combined LCNEC (*N*=41, 5%) and carcinoma favor LCNEC (*N*=60, 8%) respectively. Presence of mitoses was reported in *N*=541 (71%) yet only *N*=121 (16%) mentioned the mitotic index (≥10 mitoses 2mm^2 *N*=107). Necrosis was described in *N=466* (61%) reports, most had central/abundant necrosis *N*=317 (68%) but in *N*=84 (11%) necrosis was undefined. Neuroendocrine morphology or a feature of neuroendocrine morphology was described in *N*=452 (60%) reports and in all except *N*=13 reports a neuroendocrine IHC marker was positive. When combining the WHO criteria, only *N*=66 (9%) of reports described all criteria, this increased to *N*=253 (33%) when mitosis without description of an index was included and *N*=403 (53%) if the report described either mitosis or necrosis. Lowest reported rates were observed in reports of needle biopsy (8-27%) and biopsy (4-15%) specimens. **Conclusion:** In 91% of retrieved pathology reports the WHO criteria for the diagnosis LCNEC could not be retrieved. Although 53% of reports included descriptions of neuroendocrine growth pattern and mitosis or necrosis, these regularly were incomplete or not quantifiable. Most commonly this was observed in reports from (needle) biopsy specimens. Whether the WHO criteria could not be established or if it is due to preference of the pathologist remains unclear and requires further investigation. Nevertheless, implementation of structured pathology reporting protocols for LCNEC should be considered. **Keywords:** LCNEC, diagnosis, classification, large cell neuroendocrine carcinoma

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P1.08-025 Tumor Control of Advanced Pulmonary Neuroendocrine Tumors (Carcinoids) with Somatostatin Analogs: Experience at Gustave Roussy Ivana Sullivan[1], Eric Baudin[2], Joël Guigay[1], Jean-Yves Scoazec[3], Sophie Leboulleux[2], Amandine Berdelou[2], Caroline Caramella[4], Michel Ducreux[1], Benjamin Besse[1], David Planchard[1] [1]*Medical Oncology, Gustave Roussy, Villejuif/France,* [2]*Nuclear Medicine and Endocrine Oncology, Gustave Roussy, Villejuif/France,* [3]*Pathology, Gustave Roussy, Villejuif/France,* [4]*Radiology, Gustave Roussy, Villejuif/France*

Background: Pulmonary carcinoids are rare neuroendocrine tumors (puNETs) of the lung with no standard therapeutic option. Antitumor control benefit of somatostatin analogs (SSAs) has been demonstrated in gastroeneropancreatic (GEP)-NETs, but only a few data have been published in puNETs. **Methods:** Data from advanced puNETs patients treated with SSAs in monotherapy between 1986 and 2014 at Gustave Roussy were retrospectively collected. Demographical, clinical and tumor-related features were recorded. Patients had a tumor evaluation by CT-scan and/or MRI every 3 months. Progression-free survival (PFS) and Overall survival (OS) were estimated using Kaplan-Meier. Response rate and toxicity were assessed according to RECIST (v1.0 until 2008 and v1.1 since 2009) and NCI.CTC v4.03 criteria respectively. **Results:** Sixty-one metastatic patients with a median follow-up of 5.8 yrs (0.4-13.0 yrs) were included, with a median age of 55 yrs (13-84 yrs), 55.7% were male, 29% current or former smokers, and 95% had PS ≤1. At diagnosis, 20 patients were classified as typical carcinoids (TCs) and 41 as atypical carcinoids (ACs) according to 2004 WHO classification. Before SSAs initiation, 49 patients (80%) showed uptake at somatostatin receptor scintigraphy (SRS) (grade ≥2) and 29 (52%) showed hormone-related symptoms. The majority of patients (75.4%) presented at least two metastatic sites, liver being the most frequent one (80.3%). Forty-six (75%) patients received SSAs as first-line therapy: 32 patients (70%) for disease progression and 14 patients (30%) for symptomatic carcinoid syndrome. The median duration of SSAs was 13.7 months (3.0-155.1). Overall, median PFS (mPFS) and OS (mOS) were 17.4 [95% CI=8.7-26.0] and 58.4 months [44.2-102.7], respectively. Best response was stable disease (SD) for 43 patients (70.5%) and progression disease (PD) for 14 patients (23%). All PD were ACs. The number of events and deaths was 46 (75%) and 29 (48%), respectively. mPFS was 24.8 months [10.1-36.3] for the TCs and 12.8 months [6.2-26.0] for the ACs patients (p=0.32). mPFS was significantly longer in functional puNETs with a mPFS of 28.7 months [13.2-55.6] vs. 8.7 months [5.8-21.2] in non-functional tumors (p=0.01). The most common adverse event was grade 1 diarrhea in 43% of patients. Only one grade 3 (abdominal pain) was reported with a consequent withdrawal of treatment. **Conclusion:** In the real-world setting, SSAs are safe and potentially effective for the antitumor control of puNETs. Our results suggest that patients with typical carcinoids and functional puNETs seem to benefit most from SSAs therapy. **Keywords:** Pulmonary carcinoids tumors, advanced disease, somatostatin analogs

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P1.08-026 First Case of SMARCB1(INI1)- Deficient Squamous Cell Carcinoma of the Pleura Kazushi Yoshida[1], Yutaka Fujiwara[1], Hideaki Shiraishi[1], Keiko Goto[1], Kenjiro Tsuruoka[1], Kota Itahashi[1], Yasushi Goto[1], Hidehito Horinouchi[1], Shintaro Kanda[1], Hiroshi Nokihara[1], Noboru Yamamoto[1], Koji Tsuta[2], Yuichiro Ohe[1] [1]*Thoracic Oncology, National Cancer Center Hospital, Tokyo/Japan,* [2]*Pathology, National Cancer Center Hospital, Tokyo/Japan*

Background: SMARCB1(INI1) is a tumor-suppressor gene located at 22q11.2. It is considered an integral component of the chromatin remodeling complex SW1/SNF. Loss of SMARCB1 expression has been reported to be associated with atypical teratoid/rhabdoid tumors and malignant rhabdoid tumors of the kidney and extrarenal tissues. In addition, sinonasal basaloid carcinomas and neoplasms arising from the gastrointestinal tract, pancreas and uterus with SMARCB1 deficiency have been reported.To date, however, SMARCB1-deficient carcinoma of the pleura has not been reported. **Methods:** We report the first case of SMARCB1-deficient squamous cell carcinoma of the pleura in a patient, and describe the clinical course from initial presentation to diagnosis with pathological findings. **Results:** The case was a 33-year-old female never smoker with no previous medical or family history of malignant disease. She visited a previous hospital with a one-month history of worsening cough and dyspnea. Chest X-ray and computed tomography (CT) showed left pleural tumors with a large amount of pleural effusion. She underwent the diagnostic thoracoscopy to obtain sufficient tumor tissue from the parietal pleura. Systemic work-up including CT identified no other lesions apart from those in the left thoracic cavity. Pathological diagnosis in the previous hospital was squamous cell carcinoma of the pleura. She received six cycles of cisplatin plus gemcitabine therapy and achieved stable disease an overall best response. After progression, she transferred to our institution for expected further treatment. Although she received TS-1 therapy as second-line treatment, her disease progressed rapidly with worsening chest pain and dyspnea, and she died at 10 months after diagnosis. On pathological review of formalin-fixed, paraffin-embedded tissues of parietal pleura obtained in the previous hospital, primary tumors were composed of morphologically poorly differentiated cancer cells with characteristics of squamous cell carcinoma. Tumor cells were completely negative for INI1 protein expression by immunohistochemistry. Malignant pleural mesothelioma, thymic carcinoma and NUT midline carcinoma were ruled out. Claudin4 and MOC31 were positive, and C-kit and NUT were negative by immunohistochemistry suggesting that the tumor was primary squamous cell carcinoma of the pleura with SMARCB1 deficiency. Genome analysis using next-generation sequence data revealed no oncogene mutations, such as EGFR mutation, ALK, RET or ROS1 rearrangement. **Conclusion:** To our knowledge, this is the first report of SMARCB1-deficient squamous cell carcinoma of pleura. The tumor was highly aggressive and carried a poor prognosis with short survival. The existence of other SMARCB1- deficient tumors is likely, such as atypical teratoid/rhabdoid tumors and malignant rhabdoid tumors of the kidney and extrarenal tissues. The clinical features and treatments of this tumor are not clear, and additional cases wiii assist the establishment of treatments and improve the poor prognosis. **Keywords:** chemotherapy, SMARCB1(INI1), carcinoma of pleura

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P1.08-027 Clinicopathologic Study and Prognostic Analysis of Bronchial Mucoepidermoid Carcinoma Jian Ni[1], Zhaoying Sheng[2], Chunyan Wu[3], Likun Hou[4], Jianfang Xu[1] [1]*Department of Oncology, Shanghai Pulmonary Hospital,Tongji University School of Medicine, Shanghai/China,* [2]*Department of Radiotherapy, Shanghai Pulmonary Hospital, Shanghai/China,* [3]*Pathology, Shanghai Pulmonary Hospital, Shanghai/China,* [4]*Department of Pathology Shanghai Pulmonary Hospital, Tongji University Shcool of Medicine, Shanghai, China, Shanghai/China*

Background: Bronchial mucoepidermoid carcinoma (MEC) is a rare type of lung cancer. The present study tried to establish the clinicopathologic characteristics and prognostic factors of patients with this cancer who were treated in Shanghai Pulmonary Hospital. In addition, the common genetic changes were analyzed here. **Methods:** Sixty-four cases of bronchial MEC treated in Shanghai Pulmonary Hospital between 1995 and 2013 were collected for our study. Retrospective cohort study was performed to analyze the relationship between clinical characteristics and prognosis. The common genetic changes of non-small cell lung cancer, such as EGFR, ALK ,ROS1,BRAF, KRAS status were tested. **Results:** All 64 MECs were reconfirmed by pathologists and tumor staging of all patients were reevaluated according to AJCC 7th edition system. There were 35male patients and 29 females with median age of 40.5 years old. Cough and hemoptysis were the most common clinical manifestations. The mean time between symptom appearance and going to see doctors was 8.7months. Fibre optic bronchoscopy confirmed the presence of bronchial tumor in 48 of 64 patients, but only half of them were diagnostic of MEC by endobronchial biopsies. The pathological findings were cellular mixture consisting of mucus-secreting cells, squamous cells and mesenchymal cells. There were 52 and 4 patients who were in an early stage (stage I-II) and stage IIIA at the time of diagnosis. All those patients underwent surgical resection with lymph node sampling and dissection and 10 patients received adjuvant chemotherapy, 2 patients adjuvant radiocherapy. There were 5 and 3 patients in stage IIIB and IV. Among them, 4 were treated by chemotherapy. The median survival time for patients with stage I-II ,IIIA and IIIB-IV were 71months (10-223months), 35 months (5.3-126months) and 4 months (1-51months) respectively. Single factor analysis showed that the early TNM staging (p=0.000), no mediastinal lymph node involvement or N1 involvement (p=0.000) and surgery (p=0.001) were the positive prognostic factors for MEC patients. There was a trend that shorter disease course might benefit for survival (p=0.09). Multi-factor analysis showed that TNM staging was an independent prognostic factor for the patients suffering from bronchial MEC. Genetic testing showed that 1of 38 patient presented T790M mutation, 17 of 32 patients had KRAS positive staining and no BRAF mutation was found. Interestingly, we found 3 ALK rearrangement which accounted for 7.5% of all tested patients. **Conclusion:** TNM staging is an independent prognostic factor for bronchial MEC patients. Mediastinoscopy should be performed on patients who are clinically N2 stage to get precise stage and treatment decision. Early diagnosis and early surgery may improve patients' survival. For advanced MEC patients, ALK fusion gene may be routinely tested so as to provide patients with more therapy options. **Keywords:** Prognostic factors, Bronchial mucoepidermoid carcinoma, ALK rearrangement

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P1.08-028 PD-L1 Expression in Neuroendocrine Tumors of the Lung Kenjiro Tsuruoka, Hidehito Horinouchi, Yasushi Goto, Shintaro Kanda, Yutaka Fujiwara, Hiroshi Nokihara, Noboru Yamamoto, Shun-Ichi Watanabe, Koji Tsuta, Yuichiro Ohe *Thoracic Oncology, National Cancer Center Hospital, Tokyo/Japan*

Background: The World Health Organization (WHO) classification recognizes four major types of neuroendocrine tumors of the lung: typical carcinoid, atypical carcinoid, small cell lung cancer (SCLC), and large-cell neuroendocrine carcinoma (LCNEC). These diagnostic categories have different prognostic implications and require distinct treatment strategies. The PD-1/PD-L1 pathway is a major target of anti-tumor immunotherapy. PD-L1 expression has been reported to cause local immune suppression and is considered as a predictive marker of immune checkpoint therapeutics. In order to clarify any differences in the expression of PD-L1 according to the type of neuroendocrine tumor in the lung, we investigated the expression levels of PD-L1 by immunohistochemistry in neuroendocrine tumors of the lung. **Methods:** The subjects of this study were patients who were diagnosed as having lung neuroendocrine tumors and were treated at the National Cancer Center Hospital from 1982 to 2010. A tissue microarray (TMA) made from the surgical specimens was analyzed. After the rabbit monoclonal PD-L1 antibody was validated (clone E1L3N, Cell Signaling Technology, Danvers, MA), the TMA was stained and the tumor PD-L1 expression score was calculated by a semiquantitative method (by multiplying the intensity [0–3] by the staining area [0–100%]). To determine the PD-L1 expression, 3 (1%) was used as the cutoff score. **Results:** A total of 227 patients were included in this study. The characteristics of the entire patient population were as follows; median age, 65 years (range: 19-84 years); gender, male 168 (74.0%) / female 59 (26.0%); smoking status, smokers 191 (84.1%)/non-smokers 36 (15.9%); pStage: IA 79 (34.8%)/IB 36 (15.9%)/IIA 25 (11.0%)/IIB 29 (12.8%)/IIIA 47 (20.7%)/IIIB 6 (2.6%)/IV 5 (2.2%); histology, typical carcinoid 46 (20.3%)/atypical carcinoid 6 (2.6%)/SCLC 69 (30.4%)/LCNEC 106 (46.7%). Of the 227, samples from 15 (6.6%) showed positive staining for PD-L1. The characteristics of the patients showing positive staining for PD-L1 were as follows; median age, 71 years (range: 37-84 years); gender, males 12 (7.1%)/females 3 (5.1%); smoking status, smokers 13 (6.8%)/non-smokers 2 (5.6%); pStage, IA 3 (3.8%)/IB 2 (5.6%)/IIA 2 (8.0%)/IIB 5 (17.2%)/IIIA 2 (4.3%)/IIIB 0 (0%)/IV 1 (20.0%); histology, typical carcinoid 0 (0%)/atypical carcinoid 0 (0%)/SCLC 4 (5.8%)/LCNEC 11 (10.4%). In 31 of the 69 cases of SCLC who were treated by surgery, the disease recurred; of these 31 patients who developed disease recurrence, positive expression for PD-L1 was noted in 2 patients (6.5%). Furthermore, the disease recurred in 33 of the 106 cases of LCNEC treated by surgery; of the 33, 2 (6.1%) showed expression of PD-L1. **Conclusion:** None of the tumors in the patients with typical or atypical carcinoid in our study showed expression of PD-L1. Only the tumors in 4 of the 69 patients (5.8%) with SCLC and 11 of the 106 patients (10.4%) with LCNEC showed positive staining results for PD-L1. The data suggest that drugs directed against PD-1/PD-L1 might be potentially useful in the immunotherapy of SCLC and LCNEC. **Keywords:** carcinoid, small cell lung cancer, large-cell neuroendocrine carcinoma, PD-L1

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P1.08-029 Combination Treatment of Intrathoracic Esofageal Cancer Olga Lebedieva, Yurii Kondratsky, Roman Fridel *Tumors of Thoracic Cavity, National Cancer Institute, Ukraine, Kyiv, Kyiv/Ukraine*

Background: Introduction. Esophageal cancer (EC) is the sixth most common cause of death in cancer patients in the world. EC is classified into squamous cell carcinoma (80%) and adenocarcinoma (20%). Squamous EC is more sensitive to chemoradiotherapy (CRT) than adenocarcinoma, but long-term results of their treatment are similar. Combination therapy is used for EC treatment due to poor overall survival performance in patients who received only surgical treatment. Neoadjuvant CRT followed by surgical treatment is the most common treatment paradigm in patients with resectable EC. According to results of meta-analyses, neoadjuvant CRT in combination with surgical treatment significantly improves 3-year survival and reduces the incidence of local recurrence in comparison with surgery alone. **Objective.** To study and compare short-term results of treatment in patients with EC using intravenous and intra-arterial neoadjuvant CRT. **Methods:** using intravenous and intra-arterial neoadjuvant CRT. **Materials and methods:** 54 patients with verified squamous EC of intrathoracic esophagus (T2-3N0-1M0) were enrolled into the study and randomized into two groups. Group I patients (n = 26) received neoadjuvant CRT with intra-arterial injection, while group II patients (n = 28) - intravenous CRT. In accordance with standards, chemotherapy, radiotherapy and surgery were performed. Operation was performed 2-3 weeks after CRT. **Results:** Therapeutic pathomorphism was detected in 75% of group I patients and in 81% of group II patients. Complete tumour regression occurred in 4% and 11%, partial regression - in 73% and 68%, stabilization process - in 4% and 7%, and progression of the disease was observed in 19% and 14% of patients in groups I and II, respectively. **Conclusion:** Tumour response to neoadjuvant treatment is evident in both groups. Short-term results of treatment

demonstrate no advantages of intra-arterial chemotherapy, which is economically unjustified compared to intravenous chemotherapy. The ultimate conclusions regarding the advisability of intra-arterial neoadjuvant CRT injection of drugs in patients with intrathoracic esophageal cancer may be drawn after studying of the long-term results. **Keywords:** Chemoradiotherapy, esophageal cancer

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P1.08-030 Increasing the Interval between Neoadjuvant Chemoradiotherapy and Surgery in Esophageal Cancer. A Meta-Analysis of Published Studies
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Background: Neoadjuvant chemordiotherapy followed by surgery was the most common approach for patients with resectable esophageal cancer. Operation was performed within 2 to 8 weeks after nCRT were completed. The aim of this meta-analysis was to clarify whether a longer interval between the end of neoadjuvant chemoradiotherapy (nCRT) and surgery was associated with a better overall survival in esophageal cancer. **Methods:** We performed a systematic literature search in MEDLINE, EMBASE, Cochrane Central Register of Contralled Trials (CENTRAL/CCTR), Clinical Trials from January 2000 to December 2014. Eligible studies were prospective or retrospective studies of esophageal cancer that assessed the effects of intervals longer or shorter than 7 to 8 weeks between the end of nCRT and surgery. The primary endpoint was the overall survival (OS) and pathologic complete response (pCR). Secondary endpoints were anastomotic leak, R0 resection and postoperative mortality rate. A meta-analysis was performed to estimate odds ratios (ORs) , using the fixed- or random-effects model, with review manager 5.2. **Results:** Five studies met the eligibility requirements, including 1016 patients, with 520 in the shorter interval group (≦7~8 weeks) and 496 in the longer interval group (>7~8 weeks). The results of our meta-analysis showed that the longer interval between nCRT and surgery may be at a disadvantage in 2-year overall survival (OR =1.40 ,95% CI: 1.09–1.80, P=0.010) and R0 resection rate (OR =1.71, 95%CI:1.14-2.22, P=0.009). The pCR, anastomotic leak rate and postoperative morbidity were similar in the two groups. **Conclusion:** A longer waiting interval (more than the classical 6–8 weeks) from the end of preoperative CRT is not an increases the rate of pCR in esophageal cancer, with similar anastomotic leak rate and postoperative mortality rates. However, the longer interval between nCRT and surgery may be at a disadvantage in the long-term overall survival, thus it may be reasonable to perform surgery for patients at the esrliest opportunity after adequate recovery form nCRT, especially, who have clinical pCR. These results should be validated prospectively in a randomized trial. **Keywords:** interval, neoadjuvant therapy, esophageal cancer, Surgery

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P1.08-031 Induction of Protein Citrullination and Auto-Antibodies Production in Murine Exposed to Nickel Nanomaterials
Bashir M. Mohamed[1], Adriele Prina-Mello[2], Noreen T. Boyle[3], Anja Schinwald[4], Bruno Murer[5], Tatsiana Rakovich[1], Kieran Crosbie-Staunton[1], Omar K Mahfoud[1], Steven G. Gray[6], Yuri Volkov[2] [1]*Clinical Medicine Department, Trinity College Dublin and St James`S Hospital, Dublin/Ireland,* [2]*Clinical Medicine Department, Trinity College Dublin and Crann Institute, Dublin/Ireland,* [3]*Physiology Department, Trinity College Dublin and St James`S Hospital, Dublin/Ireland,* [4]*Centre for Inflammation Research,, Mrc/University of Edinburgh, Edinburgh/United Kingdom,* [5]*Department of Clinical Pathology, Ospedale Dell'Angelo, Venice/Italy,* [6]*Thoracic Oncology, St James'S Hospital & Trinity College Dublin, Dublin/Ireland*

Background: Citrullination, or the post-translational deimination of polypeptide-bound arginine, is involved in several pathological processes in the body, including autoimmunity and tumorigenesis. This enzymatic conversion is governed by the family of Ca^2+-dependent peptidylarginine deiminases (PAD). Citrullinated proteins are recognised as non-self-proteins, and subsequently can induce an autoimmune response. Recent studies have shown that nanomaterials of diverse origin can trigger protein citrullination, which might constitute a common pathogenic link to disease development. **Methods:** Engineered nickel nanomaterials, which can mimic environmental filamentous materials were hypothesised to trigger similar pathophysiological responses. Mice were injected intraperitoneally with either nickel nanomaterials or phosphate buffered saline. Murine sera samples for anti-CCP3 detection and tissue samples for immunohistochemical analysis were collected at day 1 and day 14. **Results:** Auto-antibody production was detected in serum of nickel nanomaterials-treated mice. Citrullination-associated phenomena and PAD levels were found to be elevated in nanomaterials -treated cell lines as well as in the spleen, kidneys and lymph nodes of mice, suggesting a systemic response to nickel nanomaterials injection, and validated in human pleural and pericardial malignant mesothelioma (MM) samples. **Conclusion:** The observed systemic responses in mice exposed to nickel nanomaterials support the evidence linking exposure to environmental factors with the development of autoimmunity responses and reinforces the need for comprehensive safety screening of nanomaterials. Furthermore, these nanomaterials induce pathological processes that mimic those observed in Pleural MM, and therefore require further investigations into their carcinogenicity. **Keywords:** Nanomaterials, nickel nanowires, protein citrullination, malignant pleural mesothelioma

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P1.08-032 Primary Pulmonary Lymphoma: Clinical Analysis of 34 Cases
Narjust Duma[1], Chad Glisch[1], Laysa Sanchez[1], Tatyana Feldman[2], Andre Goy[2], Martin Gutierrez[2] [1]*Internal Medicine, Rutgers-New Jersey Medical School, Newark/NJ/United States of America,* [2]*Medical Oncology, Hackensack University Medical Center, Hackensack/NJ/United States of America*

Background: Primary pulmonary lymphoma (PPL) accounts for only 0.5% of all primary lung cancers and 10% of all extranodal lymphomas. Though the majority are non-Hodgkin lymphomas (NHL), PPL can easily be misdiagnosed or missed due to their nonspecific clinical features and imaging findings. Our goal was to investigate the clinical characteristics, treatment and prognosis of PPL. **Methods:** We reviewed the clinical data of 34 patients diagnosed with PPL at our cancer center from 2005 to 2013. Initial diagnosis at our institution and minimum 24 month follow up were required. Kaplan-Meier method was used for survival analysis. **Results:** A total of 34 patients were identified. Median age at diagnosis was 55 years (range: 35-84), 53% were males and 47% females. 61% were current or former smokers. 14 patients (41%) had an autoimmune disorder (8 patients had Hashimoto's hypothyroidism, 4 rheumatoid arthritis and 1 DM type 1). 32% had family history of cancer and 27% of autoimmune disorders. The major clinical manifestations were: cough (53%), weight loss (41%), incidental finding on chest x-ray (29%) and only 11% presented with B symptoms. Regarding tumor characteristics, 41% of the patients were stage I, 18% stage II, 6% stage III and 35% stage IV. Marginal zone B-cell lymphoma and mucosa-associated lymphoid tissue lymphoma were the most prevalent subtypes, representing 97% of the cases. Patients were more likely to have upper lobe lesions (50%) vs. middle (29%) or lower lobe (21%) lesions. Regarding treatment, 15 patients (44%) were treated with surgery, 79% with chemotherapy (44% CHOP vs. 35% Rituximab monotherapy) and 24% with radiation (+/- chemotherapy or surgery). Overall median survival was 67.5 months (95%CI: 48.0-87.2) Factors associated with poor prognosis were: bilateral lung disease, presence of B symptoms and pleural involvement. **Conclusion:** PPL is a rare type of primary lung malignancy with an equal gender distribution. It is usually seen in middle-aged patients with history of autoimmune disorders and carries a good overall survival. The high incidence of misdiagnosis in PPL is associated with the lack of specific clinical features, making preoperative diagnosis difficult with most of the patients requiring lung tissue biopsy and immunohistochemistry studies. **Keywords:** Primary pulmonary lymphoma, Non-Hodgkin lymphomas, lung cancer

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.08-033 pRb and p16INK4 in Human Thymic Epithelial Tumors in Relation to Human Polyomavirus 7
Marlies Keijzers[1], Dorit Rennspiess[2], Sreedhar Pujari[2], Myrurgia Abdul Hamid[2], Anne-Marie Dingemans[3], Monique Hochstenbag[3], Anke Haugg[2], Marc De Baets[4], Anna Kordelia Kurz[5], Jos Maessen[1], Axel Zur Hausen[2] [1]*Cardiothoracic Surgery, Maastricht University Medical Center, Maastricht/Netherlands,* [2]*Pathology, Maastricht University Medical Center, Maastricht/Netherlands,* [3]*Pulmonology, Maastricht University Medical Center, Maastricht/Netherlands,*[4]*Neuroscience, Maastricht University, Maastricht/Netherlands,* [5]*University Hospital Aachen, Aachen/Germany*

Background: We have recently reported the presence of the Human polyomavirus 7 (HPyV7) in human thymic epithelial tumors as assessed by diverse molecular techniques. Here we report on the co-expression of p16, retinoblastoma protein (pRb) and phosphoralized retinoblastoma protein (phospho-Rb) in human thymic epithelial tumors in relation to HPyV7. **Methods:** PRB, phospho-RB and p16 expression was assessed by immunohistochemistry in 37 thymomas and 2 thymic carcinomas. 17 thymomas (46%) and 1 thymic carcinoma (50%) were recently tested positive for HPyV7. In addition, 20 follicular hyperplasias were tested. **Results:** Expression of pRb was observed in 35 thymomas (94.6%), in 16 thymomas (43.2%) the expression was strong. Phospho-Rb was observed in 31 thymomas (83.8%). 19 thymomas (51.4%) showed immunoreactivity for p16 of which 8 thymomas revealed very strong p16 expression. No p16 expression was detected in thymic carcinomas. In addition, no significant correlation between the presence of HPyV7 and pRb-, phospho-Rb- and p16-expression could be established. No correlation between pRb, phospho-Rb, p16 and WHO staging, Masaoka-Koga staging or the presence of MG was found. All 20 follicular hyperplasias showed expression of pRb and less expression of phospho-Rb. **Conclusion:** Although polyomaviruses have been shown to interact with cell cycle proteins no correlation between the presence of HPyV7 and the expression of pRb, phospho-Rb and p16 in human thymic epithelial tumors was observed. In as much HPyV7 contributes to human thymomagenesis remains to be established. Our data indicate pRb, phospho-Rb and p16 expression are rather unlikely to be involved in HPyV7 related thymomagenesis. **Keywords:** Thymic epithelial tumors, human polyomavirus 7, viral tumorigenesis

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P1.08-034 The Clinicopathological Significance of PD-L1 Expression in Thymoma
Yohei Takumi, Atsushi Osoegawa, Takafumi Hashimoto, Miyuki Abe, Shuji Suehiro, Michiyo Miyawaki, Kenji Sugio *Department of Thoracic and Breast Surgery, Oita University Faculty of Medicine, Yufu/Japan*

Background: Programmed Death Ligand 1 (PD-L1) is an immune checkpoint molecule that binds to the PD-1 receptor, thereby suppressing the activity of tumor infiltrating cytotoxic T cells. On the other hand, the immune checkpoint inhibitors (PD-L1, PD-1, CTLA-4) are notorious for causing autoimmune disorders. Ipilimab, an anti-CTLA-4 antibody, and nivolumab, an anti-PD-1 antibody, have been shown to induce myasthenia gravis (MG) in clinical trials. Although it has been hypothesized that the binding of PD-L1 to PD-1 is essential for T cell maturation, the role of PD-L1 in thymoma and autoimmune disorders remains unclear. **Methods:** We studied 52 consecutive patients who underwent resection for thymoma in our institution from 1995 to 2013. The median

age of the 52 patients was 59 years (range: 21-77), 46% were male, and 31%, 52% and 15% corresponded to the WHO types of A or AB, B1 or B2, and B3, respectively. Thirty-five percent of the patients had MG, and 23% had advanced disease (Masaoka stage IV). Formalin-fixed paraffin embedded tissue sections were stained with PD-L1 rabbit monoclonal antibody (Cell Signaling Technology). The PD-L1 staining scores were calculated by multiplying the staining intensity (0: negative to 3: strong) of the membrane / cytoplasm in the tumor cell by the proportion of stained tumor cells. The staining score, WHO classification, Masaoka stage and the coexistence of MG were compared using the Mann-Whitney *U* -test. **Results:** The mean PD-L1 score was 45 (range: 0-300). The PD-L1 scores were higher in patients with more advanced disease (Masaoka stage IV; median 60, range 10-300) than in those with localized disease (Masaoka stage I-III; median, 20; range 0-160; p=0.047). Furthermore, the score was also related with the WHO classification; it was high in WHO type B3 patients (median, 60; range, 10-300), despite the fact that it remained low among types A, AB, B1 and B2 (median 20, range 0-160, p=0.033). There was no statistically significant association between the presence of MG and a high PD-L1 score. **Conclusion:** PD-L1 was highly expressed in more aggressive and advanced stages of thymoma. No prior studies have so far reported the significance of the PD-L1 expression on thymoma. Further studies are warranted to utilize immune checkpoint targeting therapies for thymoma. **Keywords:** immune checkpoint, PD-L1, Thymoma

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P1.08-035 Pan-European Survey on Thymic Malignancies: A Collaboration of the EORTC Lung Cancer Group (LCG) with the RYTHMIC Network

Jessica Menis[1], Nicolas Girard[2], Baktiar Hasan[1], Benjamin Besse[3] [1]*Medical Department, Eortc Headquarters, Brussels/Belgium,* [2]*Respiratory Medicine, Thoracic Oncology, Louis Pradel Hospital, Hospices Civils de Lyon, Lyon/France,* [3]*Gustave Roussy Cancer Campus, Villejuif/ France*

Background: Thymic malignancies are rare tumors with an incidence of over 0.15 cases per 100.000 persons/year. Because of the indolent course and sporadic occurrence, the management of this disease has been mainly based on single-institution retrospective, observational studies. Clinical trials have been run in the recent years but no uniformly accepted guidelines are available so far. For advanced disease at diagnosis or with relapse/ progression treatment options are limited in first line and there is no standard treatment for second line treatment. The EORTC Lung Cancer Group (LCG) and French RYTHMIC network developed a survey with the aim of assessing the current treatment strategies and respective outcomes, thus providing an overview on the management of these tumors in advanced stage. **Methods:** We conducted a 25-item survey disseminated as dedicated mailing in the EORTC LCG and RYTHMIC network. Descriptive statistical analysis was applied to assess and present the preliminary replies. **Results:** At the time of the analysis, a total of 45 physicians from 11 countries participated in the study, the majority of participants were EORTC members (60.8%) and 11.1% were both EORTC and RYTHMIC members. About half of the institutions have a dedicate team for thymic malignancies (46.7%) but almost all of them have in place multidisciplinary meeting to discuss new diagnosed patients (91.1%).Diagnosis is made on surgical sample in 53.4% of the cases flowed by core needle biopsy (33.6%) and open biopsy (13%). For both thymoma and thymic carcinoma, the preferred choice for induction chemotherapy is CAP (cisplatin, doxorubicin and cyclophosphamide) (42.2% and 31.1% respectively) followed by cisplatin and etoposide (13.3% and 13.3% respectively). Also for first line chemotherapy, for both thymoma and thymic carcinoma, the preferred choice is CAP (35.6% and 28.9% respectively). For first line treatment the reported Overall Response Rate (ORR) is about 40% for thymoma and 31% for thymic carcinoma, the median Progression Free Survival (PFS) is 8 months for thymoma and 3 months for thymic carcinoma and the reported median Overall Survival (OS) is 28 months for thymoma and 18 months for thymic carcinoma. For both thymoma and thymic carcinoma, the preferred first choice for second line chemotherapy is carboplatin and paclitaxel (35.6% and 31.1% respectively) and the prefered second choice is cisplatin and etoposide (13.3 and 17.8% respectively). For second line treatment the reported ORR is about 36% for thymoma and 23% for thymic carcinoma, the median reported PFS is 8 months for thymoma and 4 months for thymic carcinoma; the median OS is 15 months for thymoma and 9 months for thymic carcinoma. No testing for c-kit or EGFR mutations is routinely performed. **Conclusion:** The survey provides a large, multi-institutional overview of the clinical practice in the management of thymic tumors in Europe, and provides relevant and updated background for the development of future collaborative trials. The survey is still ongoing and final results will be presented at the conference. **Keywords:** Thymic tumors, treatment, Survey

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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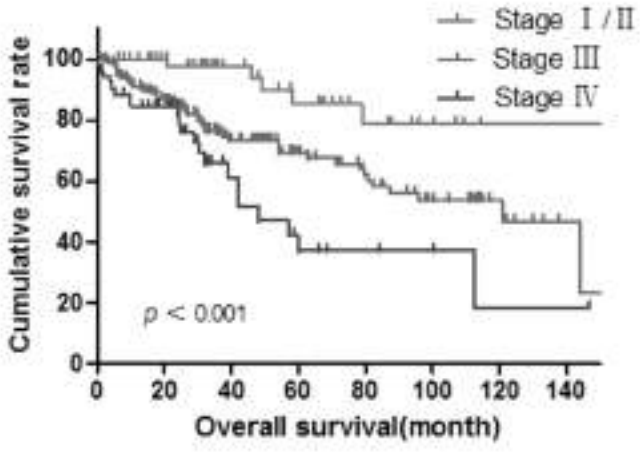
P1.08-036 Long-Term Survival after Surgical Treatment for Thymic Carcinoma

Hao Fu[1], Zhi-Tao Gu[2], Wen-Tao Fang[2], Jian-Hua Fu[3], Yi Shen[4], Yong-Tao Han[5], Yin Li[6], Zhen-Tao Yu[7], Lie-Wen Pang[8], Li-Jie Tan[9], Ke-Neng Chen[1] [1]*Beijing Cancer Hospital, Beijing/ China,* [2]*Shanghai Chest Hospital, Shanghai/China,* [3]*Sun Yat-Sen University Cancer Center, Guangzhou/China,* [4]*The Affiliated Hospital of Qingdao University, Qingdao/China,* [5]*Sichuan Cancer Hospital, Chengdu/China,* [6]*Henan Cancer Hospital, Zhengzhou/China,* [7]*Tianjin Medical University Cancer Institute and Hospital, Tianjin/China,* [8]*Huashan Hospital Affiliated To Fudan University, Shanghai/China,* [9]*Zhongshan Hospital, Shangha, Shanghai/China*

Background: Thymic carcinoma is a type of highly malignant tumor that originates from the thymic epithelium. It is rare and distinct from thymoma. Treatment methods and prognosis of thymic carcinoma remain controversial. To date, three studies with relatively large sample populations have been conducted based respectively on the Surveillance, Epidem iology and End Results database in the United States, the European Society of Thoracic Surgeons, and the Japanese multicenter database. This paper retrospectively analyzes survival data from a large-sample multicenter database in China. **Methods:** The Chinese Alliance for Research of Thymoma (ChART), established in June 2012 in China, constructed a retrospective database of patients with thymic epithelial tumors. This database enrolled 1,930 patients, including 369 with thymic carcinoma. In this study, we analyzed clinical, pathologic and treatment imformation, measured long-term survival rates, and identified relevant prognostic factors. **Results:** Among 369 thymic carcinoma underwented radical intended surgery, 211 underwent R0 resection; 34, R1 resection; and 84, R2 resection. The 3-, 5-, and 10-year survival rates were 78.3%, 67.1%, and 47.9%, respectively. The survival rates of the patients at different Masaoka-Koga stages were significantly different ($P < 0.001$). The survival rate of the patients who underwent complete resection (R0) was significantly higher than that with incomplete resection (R1/ R2) ($P < 0.001$) . Postoperative chemotherapy did not significantly affect patient survival ($P = 0.873$). Postoperative radiotherapy significantly improved the overall survival not only of the patients with R1/R2 resection but also of those with stage III/IV disease who underwent R0 resection. Multivariate analyses showed that R0 resection, Masaoka-Koga stage and postoperative radiotherapy were major prognostic factors of overall and disease-free survival.



Conclusion: Surgery remains the primary treatment for thymic carcinoma. R0 resection was the main factor of prognosis. For patients with stage III/ IV disease who had undergone R0 resection and all the patients who had undergone R1+R2 resection, postoperative radiotherapy should be administered. **Keywords:** Thymic carcinoma, Staging, Prognostic factors, Thymic tumors

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P1.08-037 PD-L1 Expression in Surgically Resected Thymic Epithelial Tumor

Su Jin Lee[1], Sang Yun Ha[2], Ingu Do[2], Joungho Han[2], Mikyong Kwak[1], Mijung Han[1], Jong-Mu Sun[1], Jin Seok Ahn[1], Jhingook Kim[3], Young Mog Shim[3], Keunchil Park[1], Myung-Ju Ahn[1] [1]*Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/Korea,* [2]*Department of Pathology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/ Korea,* [3]*Thoracic & Cardiovascular Surgery, Samsung Medical Center, Seoul/Korea*

Background: Blockade of the immune checkpoint programmed death receptor ligand-1 (PD-L1)/PD-1 pathway has recently shown clinical activity across many tumor types. PD-L1 protein expression by immunohistochemistry (IHC) is emerging as a predictive biomarker of response to these therapies. Hence, we studied PD-L1 expression in a thymic epithelial tumor (TET). **Methods:** Of the patients who previously underwent resection of TET at Samsung Medical Center between January 2000 and January 2013, 220 patients who had available tissue block for immunohistochemistry were included. Formalin-fixed paraffin embedded tumor samples were stained with murine monoclonal antibody (clone h5H1) to human PD-L1. PD-L1 staining was classified based on intensity and moderate or strong intensity in 5% or more of tumor tissues was considered as positive PD-L1 expression. **Results:** The median age was 52 years (range, 18-81), and 57.7% of patients were male. WHO histologic type was mostly B2 (N=96, 43.6%), followed by C (N=48, 21.8%), B3 (N=47, 21.4%) and neuroendocrine tumor (N=17, 7.7%). R0 resection was possible in 193 patients (87.7%). Positive PD-L1 expression was observed in 83 samples (37.7%). PD-L1 expression and histologic type was significantly correlated, with high PD-L1 expression in histologic type B2/B3/C (7.1% vs. 42.4% in type A/AB/ neuroendocrine tumor vs. type B2/B3/C; $P<0.001$). PD-L1 expression did not affect overall survival both in univariate and multivariate survival analysis. **Conclusion:** In TET, PD-L1 expression was positive in 37.7% and it was more frequently observed in aggressive histology (B2/B3/C). PD-1/PD-L1 targeting agents could be a promising therapy for TET. **Keywords:** Immunohistochemistry, Thymic epithelial tumor (TET), PD-1/PD-L1

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P1.08-038 The Effect of the WHO Histologic Classification on Thymic Specific

Survival and Overall Survival Karl Uy[1], John M. Varlotto[1], Malcolm Decamp[2], Dani Zander[3], Suhail Ali[4], Yousif Yonan[5], Geoffrey Graeber[1], Deborah Maddox[1], Syed Quadri[6], Cameron Stock[1], Fei Gu[1], James Liebmann[1], Vijay Kasturi[1], William Walsh[1], John Flickinger[7], Jonathan Glanzman[1], Aaron Yao[8] [1]*University of Massachusetts, Worcester/MA/United States of America,* [2]*Northwestern University, Chicago/IL/United States of America,* [3]*Penn State Hershey Medical Center, Hershey/AL/United States of America,* [4]*Penn State Hershey Medical Center, Hershey/PA/United States of America,* [5]*Penn State College of Medicine, Hershey/PA/United States of America,* [6]*University of Massachusetts, Worcester/United States of America,* [7]*University of Pittsburgh, Pittsburgh/AL/United States of America,* [8]*Virginia Commonwealth University, Richmond/United States of America*

Background: In 1999 the World Health Organization published a histologic classification system for thymoma that divided it into 5 categories (A, AB, B1-B3). We investigated the effect that this classification has on outcomes and determined if there was a role for radiotherapy in patients undergoing resection. **Methods:** The SEER database was used to retrospectively analyze thymomas from 2000-2011. Only those patients having first primary thymic neoplasia and undergoing resection were included in the analysis. Overall survival (OS) and thymic-specific survival(TSS) were evaluated by Kaplan-Meier Methods. Propensity Score was used to determine the role of radiotherapy. **Results:** 1047 patients had median follow-up of 53 months. In patients not receiving radiation (N=428), multivariate analysis found that worse OS was associated with older age, unmarried status, advanced stage, and partial resection. Better TSS was associated with white race and early stage. Histologic classification did not have any effect on OS or TSS. In patients with stage I and II disease (N=541), the 5-year OS and cumulative incidence rates of thymic death were 87.5% and 3.0%. In 483 stage III/IVA patients, propensity match of 153 patients treated with or without radiation demonstrated that radiation was associated with a significantly better OS (HR=0.400, p= 0.001) and TSS (HR=0.473, p=0.034), and that the effect of radiation did not depend upon histologic subtype. Selection factors for radiation included younger age and tumor size. Radiation was not associated with an increase in cardiopulmonary deaths or deaths due to second malignancies. Only 36.6% of patients had any lymph nodes explored, and 12.0% were positive. WHO Histology B3 was most likely to have involved lymph nodes (20%), while histology A (0%) and B2 (2%) were least likely. 125 (11.9%) patients have developed secondary malignancies. **Conclusion:** Radiation may be beneficial for surgically-resected advanced-stage thymoma. Neither OS or TSS was affected nodal involvement or histology. The lack of correlation of histology with outcomes may demonstrate that the current histologic system is not predictive of outcomes or that it does not translate to the broad spectrum of pathologists in SEER registry areas. **Keywords:** Thymoma, Histologic classification, radiation

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P1.08-039 Adjuvant Treatment of Thymic Carcinoma Yen-Han Tseng[1], Yuh-Min Chen[1], Yu-Chin Lee[2], Yu-Chung Wu[3], Wen-Hu Hsu[2], Sang -Hue Yen[2] [1]*Chest, Taipei Veterans General Hospital, Taipei/Taiwan,* [2]*Taipei Veterans General Hospital, Taipei/Taiwan,* [3]*Thoracic Surgery, Taipei Veterans General Hospital, Taipei/Taiwan*

Background: Thymic carcinomas are rare tumors. Surgical resection is first considered. However, data for adjuvant treatment after surgery is limited **Methods:** We retrospectively reviewed records of our thymic carcinoma patients who were treated between 2004 and 2014. Data on age, smoking or not, performance status of each patient, TNM staging, surgical margin, type of adjuvant therapy, and type of chemotherapy were collected. **Results:** Thirty-two patients received surgical resection and 49 patients did not. Both PFS and OS were significantly longer among patients who received surgical resection (26.0 months vs 7.2 months, $p<0.001$; 37.8 months vs 14.8 months, $p<0.001$). Patients with stage III thymic carcinoma had a longer overall survival when they received surgical resection. (70.1 months vs 23.9 months, $p=0.017$). Among stage IV patients, those received extended thymothymectomy had a longer PFS than did not received surgery (10.6 months vs 7.0 months,$p=0.003$). Among all 32 patients (stage I-IV) who received surgery, twenty-one patients were R0 resection, 6 patients were R1 resection, and 5 patients were R2 resection. Among 21 patients who were R0 resection, 10 received adjuvant radiotherapy and had better PFS than those received adjuvant chemotherapy (n=2) or concurrent chemo-radiotherapy after surgery (n=4) (50.3 months vs 5.9 months vs 7.5 months, $p=0.001$). **Conclusion:** Surgical resection should always be considered first whenever possible in thymic carcinoma patients. Adjuvant radiotherapy had better PFS after R0 resection. **Keywords:** Thymic carcinoma

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POSTER SESSION/ ADVOCACY
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P1.10-001 EGFR Mutation Testing Patterns and Results in Brazil and the Need for Greater Public Health Awareness of Molecular Testing Gilberto De Lima Lopes[1], Edna Prado[2] [1]*Grupo Oncoclinicas Do Brasil, São Paulo/Brazil,* [2]*Close Up International, São Paulo/Brazil*

Background: Epidermal growth factor receptor (EGFR) mutation testing allows for optimal selection of therapy with tyrosine kinase inhibitors in patients with non-small-cell lung cancer (NSCLC). Previous studies have shown a variation in EGRF genotype according to ethnic background, with scarce data about EGFR mutation status and testing patterns among Brazilian patients with NSCLC. **Methods:** Between 2011 and 2013, as part of a program sponsored by a pharmaceutical company in Brazil, tumor samples of patients with stage IIIb/IV NSCLC were submitted, at the discretion of the attending physicians, for EGFR mutation testing. All analyses were performed at 02 reference laboratories, as follows: after microdissection, DNA was isolated from serial sections of formalin-fixed, paraffin-embedded tumor tissue to obtain at least 70% tumor cells. Exons 18, 19, 20 and 21 of the EGFR gene were analysed using Sanger sequencing. EGFR mutation rate was calculated and its frequency compared between clinical subgroups using chi-square test. Data about smoking status was incomplete and thus not included in this analysis. Furthermore, a commercial database with 3,296 patients treated in Brazil in 2014 was evaluated for mutation testing patterns. **Results:** 3,364 tests out of 3,771 samples analyzed (1,799 male; 1,942 female) yielded informative results. EGFR mutation was present in 25.5% (857/3364) of informative samples. Deletions in exon 19 were the most frequent alteration detected (54%), followed by point mutations in exon 21 (28%) and exon 20 (9.7%). The most important predictors for the presence of EGFR mutations were adenocarcinoma histology ($p<0.001$), 89% of positive tests occurred in this histology; and female gender ($p<0.001$), for which 30.2% of the patients tested were positive. No differences in EGFR mutation frequency were found between age groups or regions within the country. In the commercial database of patients with NSCLC treated in the country in 2014, 1,792 patients had adenocarcinomas, 930 had squamous cancer, 71 had large cell cancer and 99 had other histologies. Overall, 34% of patients were tested for mutations (47% in the private sector and 20% in public centers); the corresponding number was 50% for patients with adenocarcinoma (62% of cases in the private and 33% in the public settings, respectively) and 10% for patients with squamous cancer. Of note fewer than 5% of patients overall were tested for ALK alterations. **Conclusion:** To the best of our knowledge, this is the largest study to assess EGFR mutation status in Latin America and in Brazil. Our findings suggest that the frequency of EGFR mutation in this cohort was lower than that found in Asia, but higher than in Caucasian populations, confirming findings seen in other Latin American countries. Despite this high prevalence, a significant number of patients, especially in the public sector, are not currently tested for mutations in the country, and further advocacy efforts are necessary to improve this situation. **Keywords:** testing pattern, EGFR, non small cell lung cancer

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P1.10-002 Lung Cancer Patients' Perspectives on Multi-Disciplinary Care in a Community Setting Orion Osborne[1], Kenneth D. Ward[2], Satish Kedia[2], Fedoria E. Rugless[1], Bianca Jackson[2], Kristi S. Roark[1], Laura Mchugh[1], Courtney Foust[1], Michael Sheean[1], Raymond U. Osarogiagbon[1] [1]*Thoracic Oncology Research Group, Multidisciplinary Thoracic Oncology Program, Baptist Cancer Center, Memphis/TN/United States of America,* [2]*School of Public Health, University of Memphis, Memphis/TN/United States of America*

Background: Lung cancer causes 27% of all cancer deaths in the United States, with very modest improvement in patient survival in the past 30 years. In addition to cancer biology, adverse patient factors such as cumulative age- and tobacco-related co-morbidities, and care-delivery factors such as the need for multiple physician involvement, contribute to the paucity of progress. The standard serial model of care, involving sequential referrals to specific care providers, if not carefully coordinated, may delay care and enable discordance between patient needs and provider priorities. The multidisciplinary model, widely touted as potentially superior, has never been rigorously evaluated. Leading up to a comparative effectiveness study of the serial and multidisciplinary care models, we closely examined patient experiences with lung cancer care delivery. **Methods:** We conducted a qualitative study, in 5 focus groups of 22 patients (10 males/12 females; 15 White/7 Black) receiving care within the previous 6 months for confirmed or suspected lung cancer at a community-based hospital, the Baptist Memorial Health Care System. Stage distribution was: 6 stage I lung cancer, 2 stage II, 3 stage III, 3 stage IV, 5 undetermined; 3 patients had a non-lung primary malignant lung lesion. A standardized script was used to ensure consistency of questions across all focus groups. Saturation of emergent themes determined the number of focus groups conducted. We used verbatim transcripts and field notes to analyze the content of each focus group, and Dedoose Software to identify recurring themes and variants. **Results:** Patients perceived that the multidisciplinary care approach enabled more timely care-delivery, better physical collaboration, improved patient-physician communication, and reduced redundant testing. Use of a nurse navigator in this model also helped decrease confusion, stress, and anxiety associated with care-coordination. There was a perception of the multidisciplinary model as providing a 'one-stop shop', a central point of contact that reduces the amount of travel and coordination required between multiple specialists. Among those patients who had prior encounters with serial care, some had experienced insensitive disclosure of diagnosis, poor physician communication, redundant testing, delays in diagnosis and treatment, misdiagnosis, and mistreatment. Patients involved in serial care were also more likely to seek a second opinion after initial diagnosis. The multidisciplinary care model was believed to provide multiple opinions in one visit. **Conclusion:** Lung cancer patients strongly preferred the multidisciplinary model of care, perceiving it to be more patient-centered and efficient than serial care. These data provide useful information on important patient-centered benchmarks that should be incorporated into rigorous comparisons of the effectiveness of these two care delivery models. Additional work is needed to examine barriers to program development through meaningful input from other key stakeholders, such as healthcare providers, institutional administrators, third party payers, and healthcare policymakers. **Keywords:** Multidisciplinary Care, One-stop shop, Lung Cancer Care, Patients' Perspectives

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P1.10-003 Lung Cancer in Ireland 2010 - 2015 - Are We Making Progress?
Aoife Mcnamara *Information Development, Irish Cancer Society, Dublin/Ireland*

Background: The burden of lung cancer: According to the National Cancer Registry in Ireland (NCRI) lung cancer was the single most common cause of cancer death during 2010-2012, with approximately 1,780 deaths annually, just over one-fifth of all cancer deaths. The lung cancer mortality rate in Ireland decreased significantly, by almost 2% annually, in males but increased by 0.5% annually in females during 1994-2012. These trends reflect smoking prevalence from decades earlier, but the contrast between males and females is striking (1). Since 2010, lung cancer detection and awareness has changed considerably in Ireland. **Health Services:** In 2010, the National Cancer Control Programme (NCCP) and Health Service Executive (HSE) distributed General Practitioner (GP) Guidelines on the management of suspected lung cancers. At the same time, rapid access clinics were established in the eight National designated cancer centres. **National Awareness:** In 2011 the Irish Cancer Society (the Society) launched a five year advertising and PR campaign to raise awareness of lung cancer in a novel and engaging way. The aim of the campaign was to avoid adding to the stigmatisation of lung cancer, but instead encourage people concerned about lung cancer and those already affected by it to contact the Society's National Cancer Helpline. **Methods:** Since 2010, substantial changes have been put in place to manage the burden of lung cancer in Ireland. An audit was performed in 2015 to measure the impact of these changes and ask if we are making progress. **Results: Health Services:** In 2013; a total of 869 primary cancers were detected by the eight NCCP rapid access lung cancer clinics. This represents a 30% detection rate (2). **National Awareness:** Behaviour & Attitudes undertook market research (commissioned by the Society) in 2011 and 2013 to evaluate the impact of the advertising and PR campaign and found just under three million adults recall some media attention on the issue of lung cancer in February (2013). This was up considerably on 2011 levels (2.1 million Vs. 2.8 million). **Conclusion:** The NCRI state that lung cancer incidence is rising and by 2040 the rate is projected to increase by 136% in females and 52% in males (3). While the burden of lung cancer increases in Ireland, **t**he changes in health services has ensured that anyone concerned about lung cancer can go to their GP and be referred to a rapid access clinic if necessary. A dedicated pathway to allow for suspect cases to be fast tracked and diagnosed on an urgent basis is now in place (2). At the same time, awareness is on the increase; by removing the link between lung cancer and grim tobacco messaging and instead communicating a message of empowerment, more people engaged with the Society's campaign and it was deemed a success. The Society continues to utilise a variety of mediums in future campaigns to support people concerned about lung cancer without stigmatising them. **Keywords:** awareness, Ireland, lung cancer, progress

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P1.10-004 Novel Survey to Identify Single Greatest Challenge for Lung Cancer Patients and Carers
Aoife Mcnamara[1], Winfield Boerckel[2], Albert Van Eijk[3]
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Background: People living with lung cancer (LC), LC survivors and carers are impacted by LC in different ways. The Global Lung Cancer Coalition (GLCC) recognises lung cancer patients' and carers' isolation and the challenges they face (GLCC, 2015). However for those affected by LC, limited data exists on the priority of their challenges, their ability to cope with these challenges and if enough relevant information and support is available. Identifiable variances between patient and carer experience and how challenges differ based on gender, age and nationality are also unknown. In 2013, The GLCC and Boehringer Ingelheim collaborated to create a global survey to identify these priorities and variances. **Methods:** A unique web-based survey was designed to isolate the single greatest challenge faced by individuals affected by LC. 200 specific and globally relevant challenges related to medical and psychosocial topics were identified by LC experts from the GLCC, grouped into categories and illustrated, with a small text descriptor. Each illustration was designed to represent a specific challenge, to be culturally sensitive and to overcome potential language barriers. At survey entry, respondents identified their greatest challenge as relevant to either daily life or medical care. Via an associated illustration, respondents chose subsequent sub-categories of challenges until one specific challenge was identified as being the most significant. Respondents answered 3 questions in relation to that challenge regarding: 1) availability of information 2) ability to cope 3) level of support required. Screening was conducted for age, gender, treatment and nationality. Respondents were asked whether they were living with LC, a LC survivor or a carer. The survey was available in 11 languages and promoted through the GLCC, LC clinicians, charities and associated support groups. **Results:** 2871 individuals visited the survey site. 725 (25%) completed the survey. 17% were from North America, 38% Europe, 31% Asia/Pacific, 7% Central/ South America, 7% Middle East / Africa. 52% were carers, 18% were LC survivors and 30% were living with LC. 64% of LC patients chose a daily life challenge as their most significant, compared to a medical care challenge (36%); 55% of carers also chose a daily life challenge, compared to a medical care challenge (45%). **Conclusion:** A unique survey to effectively isolate the single greatest challenge for individuals affected by LC and to identify current gaps in care, support and information. Bespoke illustrations, combined with a simple and easy-to-complete method, created a globally relevant tool that could produce specific, action-orientated results in order to shape global and local approaches to LC patient care and carer support; alleviate potential shortcomings and optimise patient experience. **Keywords:** Challenges, Patients, Carers, lung cancer

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P1.10-005 Immunotherapy, What Lung Cancer and Melanoma Patients ..and Physicians, Know
Enrica Capelletto[1], Silvia Novello[1], Paolo A. Ascierto[2], Maria Michiara[3], Federica Hauber[2], Raffaella Furia[2], Martina Gianetta[1], Stefania Vallone[4], Carmine Pinto[3] [1]*Department of Oncology, University of Turin, Aou San Luigi, Orbassano/ Italy,* [2]*Melanoma and Cancer Immunherapy Unit, Istituto Nazionale Tumori Fondazione Pascale, Napoli/Italy,* [3]*Medical Oncolgy Unit, University Hospital of Parma, Parma/ Italy,* [4]*Women Against Lung Cancer in Europe (Walce Onlus), Orbassano/Italy*

Background: Advances in the understanding of the role of the immune system in tumor immune-surveillance have led in the last few years to the development of a series of new drugs rapidly affirmed as new paradigm of treatment for certain cancers, like advanced melanoma. The recent re-evaluation of the immunogenicity of Non-small Cell Lung Cancer (NSCLC) has opened a new field of research, with a new attempt to apply immunotherapy also to this disease. **Methods:** A 9 question-anonymous survey has been carried out by AIOM (Associazione Italiana di Oncologia Medica) and supported by WALCE (Women Against Lung Cancer in Europe) with the purpose to investigate patients' knowledge about the immunotherapy, their expectations in terms of toxicity and efficacy, but also to evaluate how much physicians are becoming confident about the immunotherapy and their expected impact on daily clinical practice. The survey has been distributed, between 10th of November 2014 and 19th of March 2015, to 77 NSCLC patients (prevalently men and over 60 years old) and 89 melanoma patients (equally distributed for gender and age) within various Italian Oncologic Units. A similar electronic survey has been filled out by 128 and 68 physicians dealing with NSCLC and Melanoma, respectively, who reported to employ immunotherapy in their clinical practice in 55% and 74% of cases, respectively, and to have participated into clinical trials with immunotherapy in 39% and 41% of cases. **Results:** Patients' knowledge and expectations about immunotherapy resulted to be extremely heterogeneous. Only 19% of NSCLC patients, compared to 73% of melanoma patients, declared to have performed immunotherapy in their clinical history. Main results about patients' perception about immunotherapy are shown in Table 1. NSCLC and melanoma physicians globally reported a positive attitude for this new kind of treatment, postulating a general improving of their clinical practice in the next future (88% and 99% of cases, respectively). They have speculated a non-limiting toxicity profile of this drugs in 77% and 76% of cases, respectively.

Table 1: Patients' perception about immunotherapy

	NSCLC patients	Melanoma patients
Nature of the immunotherapy*		
A vaccine	6%	4%
A biological agent	10%	12%
An Antibiotic	1%	1%
A drug involving the Immune System to fight cancer	84%	80%
Not known	20%	3%
Source of information about immunotherapy*		
General Practitioner	6%	4%
Referring Physician	40%	88%
Referring Nurse	1%	1%
Other patients	3%	6%
Internet	6%	3%
Newspaper/social networks/TV	10%	1%
Other	30%	3%
Not known	10%	1%
Patients' knowledge about toxicity of the immunotherapy*		
No knowledge	61%	16%
Lower toxicity than chemotherapy	18%	30%
Equal toxicity than chemotherapy	6%	3%
Different toxicity from chemotherapy	22%	52%
Other	6%	1%
Not known	3%	6%
Patients' expectation on immunotherapy*		
I don't know	44%	6%
I don't know, but I believe in the informations received from my referral physician	19%	37%
I think immunotherapy is efficacy and better tolerated than chemotherapy	22%	29%
I don't expect more than the efficacy of other cancer treatments	0%	4%
I think the immunotherapy is efficacy	10%	22%
Other	3%	4%
No answer	4%	6%
* Possibility of multiple choices		

Conclusion: Although the role of immunotherapy for NSCLC treatment, as already happened for melanoma in the past few years, still need a confirmation by the results of the ongoing clinical trials, patients and physicians widely express great expectation on this kind of treatment, waiting for a large anti-cancer efficacy together with a low toxicity. **Keywords:** Immunotherapy, non-small cell lung cancer, Melanoma

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P1.10-006 Defining a Standard Set of Patient-Centered Outcomes for Patients with Lung Cancer
Jan P. Van Meerbeeck[1], Kimberley S. Mak[2], Annelotte C. Van Bommel[3], Caleb Stowell[4], Michael D. Peake[5], International C. Ichom[6] [1]*Thoracic Oncology, Antwerp University Hospital, Edegem/Belgium,* [2]*Radiation Oncology Program, Harvard University, Boston/MA/United States of America,* [3]*. International Consortium for Health Outcomes Measurement, Boston/MA/United States of America,* [4]*Business School, Harvard University, Boston/United States of America,* [5]*Pulmonology, University Hospital Leicester, Leicester/United Kingdom,* [6]*Lung Cancer Working Group, International Consortium for Health Outcomes Measurement, Boston/AL/United States of America*

Background: Value-based healthcare improves outcomes while controlling costs.

Registries and clinical trials frequently capture survival outcomes for lung cancer, but a unifying set of outcomes that matter to patients is lacking. Our objective was to define a Standard Set of multi-dimensional patient-centered health outcomes for measuring, comparing, and improving lung cancer treatment quality. This Set applies to all patients with newly diagnosed lung cancer, including non-small cell and small-cell lung cancer, treated with either curative or palliative intent. **Methods:** The International Consortium for Health Outcomes Measurement (ICHOM) convened an international, multi-disciplinary working group of medical oncologists, surgeons, radiation oncologists, pulmonologists, palliative care specialists, registry experts, patient representatives, and specialist nurses to review existing data and practices. Using a modified Delphi method, the group developed a consensus Set of important outcomes and case-mix variables for risk adjustment to enable meaningful benchmarking. **Results:** The outcome variables included in the Standard Set are overall survival, disease-specific mortality, cause of death, and treatment-related mortality. We recommend that complications during or within six months of treatment be collected. Patient reported outcomes should be tracked regularly using the EORTC QLQ-C30 core quality of life questionnaire and lung-cancer specific module (EORTC QLQ-LC13). Baseline demographic, clinical, and tumor information is also included in the Standard Set to improve interpretability of comparisons. **Conclusion:** We defined a Standard Set of outcomes that we believe should be measured in all patients with lung cancer. The Set provides a universal rubric for outcome comparisons, with the ultimate goal of improving the value of care. The Lung Cancer Standard Set is made possible through the generous support of the Alliance of Dedicated Cancer Centers **Keywords:** outcome indicator, lung cancer, quality performance indicator

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P1.10-007 Impact of Intensive Interprofessional Perioperative Management on Clinical Outcome in the Elderly Patients with Lung Cancer Surgery
Hidejiro Torigoe[1], Junichi Soh[1], Takako Ashiwa[2], Takeshi Kurosaki[1], Shinji Ohtani[1], Yuho Maki[1], Kentaro Miyoshi[1], Hiromasa Yamamoto[1], Seiichiro Sugimoto[1], Masaomi Yamane[1], Shinichi Toyooka[1], Takahiro Oto[1], Shinichiro Miyoshi[1] *[1]Thoracic Surgery, Okayama University Hospital, Okayama/Japan, [2]Perioperative Management Center, Okayama University Hospital, Okayama/Japan*

Background: Perioperative assessment and care, such as enhanced recovery after surgery(ERAS), are important to improve clinical outcome in the patient who receive surgery. Standard therapy for the patients with clinical stage I non-small-cell lung carcinoma (NSCLC) is radical surgery. However, the elderly patients often suffer from several comorbidities, poor performance status (PS) and/or poor respitary/motor function, causing high incidence of postoperative complication and resulting in a limited resection or other alternative therapy. In September 2008, our hospital launched a perioperative management center (PERIO) to improve perioperative management and clinical outcome of patient receiving surgery, which was organized with dedicated nurses, anesthesiologists, dentists, physiotherapists, pharmacist and nutritionist. All patients, not only elderly patients, who are scheduled to receive thoracic surgery present to PERIO center which perform intensive perioperative assessment and care with interprofessional collaboration consistently from before hospitalization until discharge after surgery. In this study, we investigated the impact of introduction of PERIO on clinical outcome in the elderly patients who received thoracic surgery due to clinical stage I NSCLC. **Methods:** Ninety-one elderly patients (over 80 years old) who received pulmonary resection were enrolled in this study. We excluded patients harboring ground glass opacity-dominant tumor in the diameter less than 2cm because of high curative rate even if it is treated with limited resection. We categorized those patients into non-PERIO group among January 2000 to August 2008 (n = 42) and PERIO group among September 2008 to November 2014 (n = 49). We compared perioperative factors between the two groups. **Results:** The median age, PS (0-1 / 2-4) and median FEV1.0 were 81.5 vs 82.0 years old, 38/4 vs 42/7, 1.9L vs 1.8L in non-PERIO and PERIO groups, respectively. The patient with comorbidity were significantly more frequent in PERIO group (75.5%) than non-PERIO group (52.4%, P =0.025). Although the radical surgery (lobectomy or segmentectomy with systemic lymph node dissection) were more frequently performed in PERIO group (75.5%) than non-PERIO group (52.4%, P =0.022), there was no significant difference in the incidence of postoperative complication (24.4% and 28.6% in non-PERIO and PERIO groups, respectively) and post-operative hospital days (median 15 days in both group) in both groups. **Conclusion:** Radical surgery was more frequently performed after introduction of PERIO without increase of postoperative complication rate and hospital days, suggesting that PERIO may play an important role to improve perioperative clinical outcome in elderly patients treated with thoracic surgery. **Keywords:** elderly, lung cancer, perioperative management, interprofessional

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P1.10-008 Stigma in Lung Cancer Patients
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Background: The burden of stigma in cancer patients is a significant problem, but it is especially emphasised problem in lung cancer patients due to their tendency to believe that their behaviour was the cause of the cancer. **Methods:** We included consecutively 39 newly hospitalised patients (58%male) with the diagnosis of lung cancer (mean age 59.3 SD 6.9 years). Stigma was assessed with 31-item Cataldo Lung Cancer Stigma Scale (mean value 45.4 SD 11.05). Each stigma item was measured using a four-point Likert-type scale ranging from 1 (strongly disagree) to 4 (strongly agree). Cronbach alpha for the scale was 0.96. Patients gave informed consent after the purpose of the study was thoroughly explained. Of the 45 patients approached, four refused to participate and two questionnaires were incomplete. **Results:** Stigma in the sample was not associated with age or gender. Contrary to expectations it was not It was not associated with current smoking status. **Conclusion:** Stigma in lung cancer patients is significant problem, but in our sample it was not associated with age gender or current smoking status. This issue needs further research. **Keywords:** stigma, lung cancer

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P1.11-001 Short Form Chronic Respiratory Questionnaire Validation in a Lung Cancer Population
Andreas Charalambous[1], Alex Molasiotis[2] *[1]Nnursing, Cyprus University of Technology, Limassol/Cyprus, [2]Nursing, The Hong Kong Polytechnic University, Hong Kong, Hong Kong/Hong Kong*

Background: The Chronic Respiratory Questionnaire short form (SF-CRQ) is frequently used in patients with obstructive pulmonary disease and it has demonstrated excellent psychometric properties. The CRQ (both in its original or short form) has not been previously used in the assessment of lung cancer patients' HRQL. Therefore this study, being part of a larger therapeutic trial, aims to evaluate the psychometric properties of the SF-CRQ in patients diagnosed with thoracic malignancies. **Methods:** Forty-six patients were assessed at two time points (with a four-week interval) using the SF-CRQ, the modified Borg Scale, five numerical rating scales related to perceived severity of breathlessness, and the Hospital Anxiety & Depression Scale. Internal consistency reliability was investigated by Cronbach's α reliability coefficient, test-retest reliability by Spearman-Brown reliability coefficient (p) and convergent validity by Pearson's correlation coefficient between the SF-CRQ, and the conceptual similar scales mentioned above and content validity was also explored. A principal component factor analysis was performed. **Results:** The internal consistency was high, indicated by an $\alpha = 0.88$ (baseline) and 0.91 (after one month). The SF-CRQ had good stability with test-retest reliability ranging from r=0.64 to r=0.78, p<0.001. Factor analysis suggests a single construct in this population showing that the items of the SF-CRQ scale are strongly correlated and represent the conceptual meaning of the underlying construct, which is the quality of life of lung cancer patients as related to breathlessness. **Conclusion:** The data analyses supported the convergent, content, and construct validity of the SF-CRQ indicating this is a valid and reliable instrument for the assessment of quality of life related to breathlessness in lung cancer patients. This study is the first study that provides initial data of the psychometric properties of the SF-CRQ in lung cancer patients, and further validation with larger sample sizes and across different settings and dyspnea severity is needed. **Keywords:** breathlessness, quality of life, lung cancer patients, Chronic Respiratory Questionnaire

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
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P1.11-002 The Impact of Gastric Acid Suppressive Therapy on Treatment Outcomes of EGFR Tyrosine Kinase Inhibitors in Non-Small Cell Lung Cancer
Nesaretnam B. Kumarakulasinghe[1], Yu Y. Soon[1], Huili Zheng[2], En Y. Loy[2], Brendan Pang[3], Ross Soo[1] *[1]National University Cancer Institute Singapore, Singapore/ Singapore, [2]National Registry of Diseases Office,Health Promotion Board, Singapore, Singapore/Singapore, [3]Cancer Science Institute, Singapore/Singapore*

Background: Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors such as gefitinib and erlotinib are dependent on gastric pH for absorption which may be affected by concomitant gastric acid suppressive therapy (AS) with proton pump inhibitors and histamine 2 antagonists. We sought to determine the effect of gastric acid suppressive therapy on overall survival (OS) in patients treated with EGFR tyrosine kinase inhibitors. **Methods:** Patients with advanced stage non-small cell lung cancer harboring *EGFR* mutations treated with EGFR tyrosine kinase inhibitors were retrospectively identified. Medical records in our single institution were reviewed from 1st January 2008 to 30th December 2013. Patient clinico-pathological characteristics,use of gastric acid suppressive therapy and the overall survival were obtained. Statistical analysis was performed using chi^2, log rank test and cox regression where indicated **Results:** We identified 191 patients. The median age of patients was 64 years (range: 30-89) ,109 (57.1%) were female, 117(61.3%) were never smokers, 91 (47.6%) harbored *EGFR* exon 19 deletion and 144 (75.4%) received EGFR tyrosine kinase inhibitors as first line treatment. 55 (28.8%) patients received gastric acid suppressive therapy The groups of patients who received gastric acid suppressive therapy and those who did not receive gastric acid suppressive therapy were similar with regards to gender, smoking status, and type of *EGFR* mutations, Charlson co-morbidity score and Kanorfsky performance status. Brain metastasis at the time of diagnosis was more frequent in the group who received gastric acid suppressive therapy compared with the group who did not receive gastric acid suppressive therapy (61.8% v 35.3% respectively, p= 0.001). The median overall survival in the total patient population was 13.1 months (95%CI 11.7-15.2 months). On multivariate analysis, presence of visceral metastasis at diagnosis was associated with a worse overall survival (HR: 1.53, 95% CI:1.10-2.13 p value: 0.012). However a Karnofsky performance score of 90-100 was associated

with an improved overall survival (HR: 0.69, 95% CI; 0.49-0.97 p value: 0.031). The median overall survival OS in patients with gastric acid suppressive therapy was 11.9 months (95%CI: 9.90-16.94 months) and 14.5 months (95%CI: 11.74-15.95 months) in the group not receiving gastric acid suppressive therapy. (HR: 0.98, 95% CI: 0.69-1.40 p value: 0.934) **Conclusion:** Although the group of patients who were treated with gastric acid suppressive therapy had a numerically poorer overall survival compared to the group who did not receive gastric acid suppressive therapy, this difference was not statistically significant. Based on the our analysis, the use of gastric acid suppressive therapy concurrent with EGFR tyrosine kinase inhibitors in patients with advanced non-small cell lung cancer harboring *EGFR* mutations did not affect overall survival. **Keywords:** EGFR TKI, NSCLC, GASTRIC ACID SUPRESSION

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P1.11-003 New Clinical and Biologic Insight Into Lung Cancer-Associated Cachexia From a Large Cohort Study Bhavani S. Gannavarapu[1], Kristen Carter[1], Chul Ahn[1], Nathan Cannon[2], Jeffrey Meyer[2], Puneeth Iyengar[2] [1]*UT Southwestern Medical Center, Dallas/TX/United States of America,* [2]*Radiation Oncology, UT Southwestern, Dallas/TX/United States of America*

Background: Cancer cachexia (CC) is a wasting syndrome without durable palliative intervention observed in 50% of all solid tumors and responsible for 20-30% of all cancer-related deaths. Knowledge of prevalence and survival outcomes for lung CC patients by clinical and pathologic parameters is scarce due to limited series. We provide the largest, most detailed evaluation of lung cancer patients for cachexia, enabling new clinical and biologic insight. **Methods:** A retrospective review of 1627 patients with non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC) treated at UT Southwestern Medical Center between 1/1/2006 and 12/31/2013 was performed. Patient demographics and tumor characteristics including histology, stage, grade, and size were collected. Each patient was assessed for CC at diagnosis, retrospectively identified by the presence of significant weight loss (>5% loss over 6 months in patients with BMI >= 20; >2% in patients with BMI <20). Overall Survival (OS) was evaluated, and clinicopathologic factors predicting for cachexia development were identified with stepwise logistic regression (SLR). **Results:** Overall, CC independently predicted reduced OS on stepwise Cox regression (1.21 OR). 419/1468 (28.5%) of all NSCLC and 57/159 (35.8%) of all SCLC patients had CC. Within NSCLC, CC was documented in 107/350 (30.6%) of squamous carcinomas and 208/761 (27.3%) of adenocarcinomas. CC significantly reduced NSCLC OS across all stages: 21.0 vs. 9.9 months (log-rank P<0.0001). However, CC did not significantly affect SCLC OS: 10.5 vs. 9.9 months (log-rank P=0.46). Prevalence of CC in NSCLC for stages 1, 2, 3, and 4 was 48/309 (15.5%), 16/124 (12.9%), 118/377 (31.3%), and 237/658 (36.0%), respectively. OS for NSCLC -/+ CC for stages 1, 2, 3, and 4 were 67.1 vs. 45.0, 35.4 vs. 37.2, 20.9 vs. 14.3, and 11.4 vs. 6.6 months, respectively (log-rank P=0.0427, =0.5803, =0.0155, <0.0001). OS for squamous histologies -/+ CC for stages 1, 2, 3, and 4 were 56.9 vs. 22.7, 19.3 vs. 19.5, 18.6 vs. 14.3, and 7.8 vs. 5.8 months, respectively. OS for adenocarcinoma histologies -/+ CC for stages 1, 2, 3, and 4 were 86.4 vs. 51.1, 43.9 vs. 23.3, 28.6 vs. 19.2, and 13.0 vs. 8.2 months, respectively. On univariate analysis, grade, stage, tumor size, and tobacco use were significant factors in the development of CC in adenocarcinomas, while stage alone was significant in squamous carcinomas. On SLR, stages 3+4 were associated with increased odds of CC development as compared to stages 1+2 (OR 2.6, P=0.0004) in squamous histologies. On SLR, tumor size >50mm was associated with increased odds of CC development when compared to 0-20 mm (OR 4.3, P<0.0001) in adenocarcinomas. **Conclusion:** Cachexia significantly impacts OS in lung cancer, primarily for NSCLC. Fundamental differences of CC prevalence and associated OS were observed for the first time between different histologies and stages. Though CC can manifest in all stages, increased stage and tumor size were independent, significant predictors for CC in squamous and adenocarcinoma populations, respectively. Understanding which clinicopathologic characteristics impact CC prevalence and OS may offer insight into the syndrome's clinical and biologic underpinnings, providing impetus for novel therapeutics and prediction methods. **Keywords:** Cachexia, non-small cell lung cancer, Weight Loss, Survival outcomes

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
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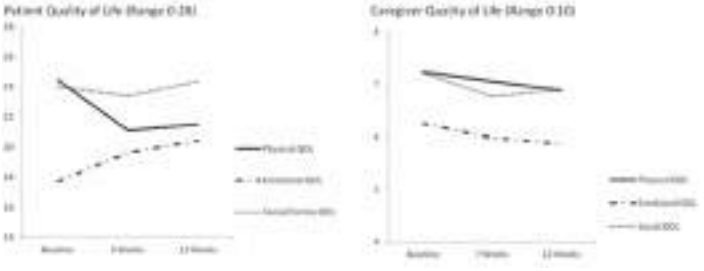
P1.11-004 Impact of Lung Cancer Surgery on Quality of Life of Family Caregivers Jae Y. Kim[1], Virginia Sun[2], Dan J. Raz[1], Anna Cathy Williams[2], Rebecca Fujinami[2], Karen Reckamp[3], Marianna Koczywas[3], Mihaela Cristea[3], Arti Hurria[3], Betty Ferrell[2] [1]*Division of Thoracic Surgery, Department of Surgery, City of Hope, Duarte/CA/United States of America,* [2]*Division of Nursing Research & Education, Department of Population Sciences, City of Hope, Duarte/CA/United States of America,* [3]*Medical Oncology and Therapeutics Research, City of Hope, Duarte/CA/United States of America*

Background: Family caregivers (FCGs) of lung cancer patients experience decreased quality of life (QOL) and psychological distress related to their caregiving role. Although there is extensive data about the significant impact of lung cancer surgery on patient QOL, little is known about the impact on FCGs. We describe QOL, psychological distress, and perceived caregiver burden outcomes among FCGs of patients undergoing lung cancer surgery. **Methods:** As part of a National Cancer Institute-supported Program Project (P01) testing the effect of a palliative care intervention in patients with non-small cell lung cancer, patients and their FCGs were sequentially enrolled into a usual care group or an intervention group, which received interdisciplinary care planning as well as a comprehensive assessment and education by an advanced practice nurse. For this subset analysis, we included only those patients who underwent surgery and their FCGs. Outcomes were assessed at baseline (pre-operatively), at 6-7 weeks, and 12 weeks after surgery. FCGs were assessed using the following validated measures: distress thermometer for psychological distress, family version of QOL scale in four domains (physical, psychological, social, and spiritual well being), and Caregiver Burden Scale. Patients were assessed using distress thermometer and FACT-L for QOL domains. **Results:** QOL data were available for 41 pairs of patients and FCGs (10 usual care and 31 intervention). Psychological distress levels were highest for patients (3.8/10) and FCGs (5.1/10) before surgery, then decreased six weeks after surgery for both groups respectively (2.9/10 and 4.2/10). Patients' distress continued to decrease at 12 weeks (2.2/10, p = .001), but FCGs did not (4.4/10, p = .0.157). Although patients had improvements in all domains between 6 and 12 weeks, FCGs did not experience similar improvements in most domains (Figure 1). Likewise, there was no significant decrease in caregiver objective burden over the 12 weeks (21.1 vs. 21.3, p = 0.942). Patients in the intervention group had improved total QOL at 12 weeks compared to usual care (Total FACT-L 116 vs. 94, p <.001). In contrast, there were no significant differences between the usual care and intervention groups in QOL of FCGs. **Conclusion:** FCGs of lung cancer patients experience significant psychological distress. FCGs continue to have decreased QOL 3 months after lung cancer surgery. The trajectory of QOL for FCGs does not mirror that of patients. FCGs play an important role in patient recovery and greater research is needed to understand how they are impacted by thoracic surgery.



Keywords: Surgery, family caregivers, quality of life, psychological distress

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
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P1.11-005 Enhancing Evaluation of Cancer Cachexia in Patients with NSCLC by Assessing Change in Skeletal Muscle Mass at the L1 Level on Routine Chest CT Jose N. Galeas[1], Alejandro Recio Boiles[1], Louise M.-W. Man[2], Ryan D. Gentzler[2], Patricia Hollen[2], Richard J. Gralla[1] [1]*Department of Medicine, Jacobi Medical Center - Albert Einstein College of Medicine, Bronx/NY/United States of America,* [2]*University of Virginia, Charlottesville/VA/United States of America*

Background: Cancer cachexia (CC) and sarcopenia occur in up to 60% of patients with lung cancer. With better knowledge of the pathophysiology leading to cancer cachexia, multiple recent therapeutic trials have been directed at these mechanisms. Additionally, it is clear that cancer cachexia is associated with several negative outcomes. Inherent in all studies for this problem, is the ability to measure components of cancer cachexia, such as skeletal muscle mass (SMM). SMM assessment by CT scanning (SD <1.2kgs) is more accurate than either Dual X ray absorptiometry (DXA, SD 3kgs) or than bioelectrical impedance (SD 9.3kgs). A single slice on CT at the third lumbar vertebra (L3) correlates highly (r=0.924) with total body SMM in healthy individuals. While CT measurement at L3 is often used in cancer cachexia trials, the problem exists that routine chest CT scans rarely extend to L3; thus routine chest CTs will not allow inclusion of most patients. Importantly, prior studies in normal subjects demonstrated high correlation (r = 0.903) of SMM measurement at L1 with L3; however, the utility and feasibility of L1 measurement of SMM has not been assessed in patients with cancer. **Methods:** We enlisted patients with NSCLC and performed SMM measurements at L1 using Slice-O-Matic software for muscle mass in the Hounsfield unit range of -29 to +150. Patients were assessed for accuracy of using the L1 level for imaging quality and the ability to use the software properly. **Results:** 56 patients with NSCLC (99 CT assessments) were enlisted at three institutions. Characteristics: 45% female; medians: age 60, KPS 80%; BMI 24.96, weight 72.38 kg, SMM index 58.89. Sarcopenia was detected in 29% of patients (58% of males <55.5 cm2/M2; 6% of females <38.5cm2/M2) with all having normal or overweight BMI. Overall, of the 99 CT images, 92.9% (95% CI = 88%-98%) included L1. 5 additional images (5%) were difficult to evaluate for SMM due to ascites or effusions; also, 1 patient was too obese for proper imaging; 2 had poor quality scans. Importantly, inclusion of L1 differed among the 3 institutions ranging from 80.6% to 97.2%. Also noted, as previously reported with assessment at L3 (r = 0.35), the correlation of BMI with SMM in this study at L1 was low (r = 0.36) as well. **Conclusion:** This study indicates that: 1) SMM assessment at L1 is achievable on routine chest CT in patients with lung cancer, with 93% of patients having images at this level, and 93% have acceptable quality for SMM evaluation; 2) although L1 is included in the majority of patients at all 3 institutions, this may vary by different radiologic protocols; 3) the low correlation and poor sensitivity of BMI to identify muscle mass loss is equally demonstrated at both L3 and L1, and 4) use of L1 enhances patient evaluation for SMM without needing additional testing or radiation exposure, and allows many more patients with NSCLC to have assessment of SMM in clinical trials and patient management. Funding in part: NIH/NCI 1 R01 CA157409-01A1 **Keywords:** skeletal muscle mass, NSCLC, sarcopenia, cancer cachexia

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P1.11-006 Association between Nutritional Status Variables and Fatigue Diagnosis in Patients with Non Small Cells Lung Cancer Julissa L. Morales, Jenny T. Chaparro, Martha De La Torre-Vallejo, Luis Fernando O. Ocaña, Oscar Arrieta Rodriguez *Thoracic Oncology Clinic, Instituto Nacional de Cancerología, Mexico City/Mexico*

Background: Cancer-related fatigue (CRF) is a common and persistent symptom experienced by patients with Non Small Cells Lung Cancer (NSCLC). It is produced by multifactorial factors including those associated to the disease itself, comorbidities, life style and/or treatment. Malnutrition is found in up to 80% of patients with advanced cancer and could be associated with the presence of CRF. Both, malnutrition and fatigue have a negative impact on many aspects of patients' Health-related quality of life, treatment compliance and prognosis. The aim of this study was to associate nutritional status variables with the occurrence of CRF in patients with advanced NSCLC. **Methods:** Patients with advance stage NSCLC under different lines of treatment were prospectively evaluated. Fatigue was assessed by the FA-13 (EORTC) test; malnutrition and anorexia were diagnosed using Subjective Global Assessment (SGA) and (S/AC-12) FAACT, respectively. Weight loss in the last six months was calculated, albumin and hemoglobin levels were used as biochemical parameters of nutrition. **Results:** 129 patients were included, 75 were female (58%), the mean age was 61.9±13.8 years, Adenocarcinoma histology was present in 92 patients (71.4%) and the rest were classified as other histology, 90 patients (69.8%) were in ≤2nd line of treatment, 106 patients (83.5%) had a functional status between 0-1 and the rest between 2-3, according to SGA 79 patients (64.8%) had any grade of malnutrition, 94 patients (75.8%) had a weight loss ≥10kg in six months, 25 patients (19.4%) were diagnosed with anorexia, albumin mean was 3.8mg/dl and 55 patients (32%) had less than that, as well as Hemoglobin level mean was 12.7 mg/dl and 61 patients (35.5%) had a valor less than it. Nutritional variables associated with CRF are shown in Table 2. Nutritional variables as Malnutrition, weight loss ≥10% and albumin were related with higher presence of physical, emotional, cognitive and daily-life fatigue. Clinical variables as histology, line of treatment and functional status were analyzed and just poor functional status was associated with higher presence of physical, emotional, cognitive and daily-life fatigue (p≤0.01).

Table 2.- Nutritional status variables related fatigue

n=129		Physic-FS	p	Emotion-al-FS	p	Cognitive-FS	p	Daily-life-FS	p	Social-FS	p
Nutritional-Status	Malnourished Wellnourished	42 25	**<0.01**	42 25	<0.01	42 25	**0.001**	33 33	**0.001**	0	0.224
Weight-loss (≥10% 6 months)	≥10 <10	50 33	**0.003**	50 33	0.001	42 25	**0.002**	67 33	**0.006**	0	0.273
Anorexia	Yes No	67 33	**<0.01**	58 33	<0.01	58 25	**<0.01**	67 33	**<0.01**	33 0	**0.02**
Albumin-(gr/dL)	<3.8 ≥3.8	42 33	**0.004**	42 25	0.003	42 25	**0.004**	33 33	**0.002**	0	0.212
Hemoglobin-(gr/dL)	<12.7 ≥12.7	42 33	0.077	42 25	0.04	42 25	**0.012**	33 33	0.227	0	**0.023**

FS: fatigue score Conclusion: Malnutrition, weight loss, anorexia, hypoalbuminemia and low hemoglobin are associated with CRF. Hence, timely nutritional evaluation should be considered in NSCLC patients. Early nutritional treatment could help to reduce treatment and disease related fatigue. Nutritional and psychological support might confer beneficial effects.
Keywords: compliance, Prognosis, nutrition, Cancer-related fatigue

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
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P1.11-007 To Determine Whether Psychosocial Factors Predict Depression among Older Indian Lung Cancer Patients Gouri Shankar Bhattacharyya[1], Purvish M. Parikh[2], Ghanashyam Biswas[3], Raja Dhar[4], Shailesh A. Bondarde[5], Hemant Malhotra[6], Amish Vora[7], K Govindbabu[8], Anantbhushan A.B. Ranade[9] [1]*Medical Oncology, Fortis Hospital, Kolkata/India,* [2]*Icon-Aro, Mumbai/India,* [3]*Sparsh Hospital and Critical Care, Bhubaneshwar/India,* [4]*Fortis Hospital, Kolkata/India,* [5]*Shatabdi Super Specialty Hospital, Nashik/India,* [6]*Medical Oncology, Sms Medical College Hospital, Jaipur/ India,* [7]*Max Healthcare, Gurgaon/India,* [8]*Kidwai Memorial Institute of Oncology, Bangalore/ India,* [9]*Deenanath Mangeshkar Hospital, Pune/India*

Background: Depression is extremely common in elderly lung cancer patients. However, it is extremely difficult to predict or develop predicting tools. There is some early studies suggesting using psychosocial factors. Unfortunately there appears to be no data from developing countries, more so from India. This is an attempt to initiate the process. **Methods:** Design: A descriptive correlational study. Setting: Multispeciality Hospitao Oncology OPD Sample: Indian Lung Cancer Patients with cancer aged 50–88 years. Methods: Fisher's exact and Wilcoxon rank-sum tests were used to evaluate differences between patients who were possibly depressed (Geriatric Depression Scale) or not.Multivariate linear regression statistics were used to identify the psychosocial factors that predicted higher depression scores. Education and gender were included as covariates. Main Research Variables: Religiosity, emotional support, collectivism, perceived stigma, and depression. **Results:** Participants (N = 67) had a mean age of 65 years (SD = 8.4), and a majority were well-educated, insured, religiously affiliated, and currently in treatment. Participants who were in the lowest income category, not married, or male had higher depression scores. The multivariable model consisting of organized religion, emotional support, collectivism, education, and gender explained 52% (adjusted R2) of the variation in depression scores. Stigma became insignificant in the multivariable model **Conclusion:** Psychosocial factors are important predictors of depression. Emotional support and organized religious activities may represent protective factors against depression, whereas collectivism may increase their risk Implications for Management: Care providers need to be particularly aware of the potential psychological strain for patients with collectivist values, experienced stigma, disruptions in church attendance, and lack of emotional support. In addition, the treatment plans for these patients should ensure that family members are knowledgeable about cancer, its treatment, and side effects so they are empowered to meet support needs. Knowledge Translation: Among Indian Lung Cancer Patients patients with cancer, emotional support and reassurance from family and friends that they will not abandon them decreases the likelihood of depressive symptoms and minimizes the impact of stigmatizing responses, but the perception that the illness is placing a strain on the family increases the likelihood of such symptoms. Emotional support likely is a stronger predictor of depressive symptoms than religious service attendance
Keywords: Psychological factors; Depression; Indian Lung Cancer Patients

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P1.11-008 What Happens to the Pleural Space Affected by Malignant Effusion after Bedside Pleurodesis? Ricardo M. Terra[1], Pedro N. Araujo[2], Thiago S. Santos[1], Rdrigo C. Chate[3], Antonio L. Paiva[3], Paulo M. Pêgo-Fernandes[1] [1]*Thoracic Surgery, Heart Institute Incor-Hcfmusp, São Paulo/Brazil,* [2]*Thoracic Surgery, Heart Institute, Incor-Hcfmusp, São Paulo/Brazil,* [3]*Radiology, Heart Institute Incor-Hcfmusp, São Paulo/Brazil*

Background: The treatment of recurrent malignant pleural effusion (RMPE) has a palliative purpose. Pleurodesis is the most used method. However, not all the procedures are effective, in part because of the lung entrapment by the visceral pleura, preventing the contact between the pleural surfaces. The behavior of the pleural cavities submitted to pleurodesis has not been studied more objectively to date. Moreover, how evolve cases with good initial lung expansion and those with poor expansion? **Methods:** Prospective study including 131 patients with recurrent malignant pleural effusion candidates for treatment with bedside pleurodesis with silver nitrate or mineral talc. Each patient underwent two chest CT scans, one right after the drainage (CT1) and another 30 days after pleurodesis (CT30). A thoracic radiologist has calculated pleural volume using the software Aquarius Intuition Viewer® (Terarecon). The evaluation of lung expansion was based on residual pleural volume on CT1 and the radiological evolution on the difference between the pleural volumes on CT30 and CT1 (Delta volume). The pleural volumes on CT1 were arbitrarily classified into small cavity after the drainage (volume <500mL) and large cavity after the drainage (volume ≥500 mL). After that, the Delta volume was classified in unchanged (≥-268.77 and ≤254,49 mL), negative (<-268.77 mL) and positive (> 254.49 mL). For such we used the average of the numerical variable and half of the standard deviation upwards and downwards. The clinical effectiveness was evaluated as the need for additional procedures to control symptoms. **Results:** We evaluated 87 patients of a total of 131 recruited. The median pleural volume on CT1 was 377 (IR: 171-722) mL and 386 (IR: 164-726) mL on CT30, and has no significant difference between them (p= 0.753). The clinical effectiveness was observed in 86.2% of patients. We found 54 patients (62.06%) in the small cavity after the drainage group and 33 (37.93%) in the large cavity group. Clinical effectiveness was 92.6% and 75.8% respectively. There was significant difference (p= 0.051), with an odds ratio of 4.00 (CI: 1.098 to 14.570) in favor of the small cavity. Among patients with small pleural cavity, 27.77% progress with a significant accumulation of fluid, 66.66% did not show significant changes and 5.55% have decreased pleural volume. Clinical effectiveness was 86.7%, 94.4% and 100% respectively with no significant difference (p= 0.552). Among patients with large pleural cavity, 21.21% progress with an even greater volume of pleural cavity, 27.27% did not show significant changes and the majority (51.51%) evolves with a decrease in the pleural volume. Clinical effectiveness was 57.1%, 77.8% and 82.4% respectively with no significant difference (p= 0.418). **Conclusion:** Almost two third of the patients with RMPE treated with pleurodesis had good lung expansion, while just over one-third had a bad one. Those with good expansion had 4 times higher chances of clinical success. Among poor lung expansion patients, more than half had significant reduction of pleural volume in 30 days, while a fifth had a significant accumulation. **Keywords:** malignant, tomography, pleural effusion, pleurodesis

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P1.11-009 Predictors of Hospital Discharge in Cancer Patients with Pericardial Effusion Who Undergo Surgical Pericardial Drainage Thamara Kazantzis, Ricardo M. Terra, Benoit J. Bibas, Leticia L. Lauricella, Pedro N. Araujo, Alberto J.M. Dela-Vega, Paulo M. Pêgo-Fernandes *Thoracic Surgery, University of São Paulo, São Paulo/Brazil*

Background: Pericardial effusion (PE) is a complication of late-stage cancer and operative pericardial drainage is its standard treatment. However, in many patients PE is an end-of-life event and some never leave the hospital despite the procedure. The main objective of this study was to identify predictors of hospital discharge in patients with cancer who coursed pericardial effusion and underwent operative pericardial drainage. We also looked at predictors of ICU discharge and overall survival and also factors that might be associated with paradoxical hemodynamic instability (PHI). **Methods:** Retrospective study carried out in a tertiary cancer center. We included all patients with known malignancy who coursed with PE and underwent surgical pericardial drainage from 2011 to 2014. Patients who underwent previous pericardial drainage or only needle pericardiocentesis were excluded from the study. **Results:** Out of the 90 patients included in this study, fifty one were discharged from hospital (56%). Renal failure and pulmonary embolism negatively influenced the chances of hospital discharge [OR 0,247; p=0,039 and OR 0,293; p=0.089, respectively]. On the other hand, patients who received recent chemotherapy were more likely to leave the hospital (OR 3,9; p=0,009). 55 patients (61%) were discharged from ICU. Renal failure was the main determinant of that (OR 0,284 (p=0,047)). Mean survival was 138.2 days (95% CI 84,48-189,90), influenced only by ECOG status (OR 1,258; p=0,047). PHI occurred in 6 patients and all of them died within 30 days after surgery. In our series, we could not identify predictors for PHI. **Conclusion:** In this study we demonstrated that almost half of cancer patients admitted with PE requiring drainage never leave the hospital. Renal failure and pulmonary embolism are strong predictors of in-hospital death. PHI remains a serious condition with causes unknown. **Keywords:** pericardial effusion, hospital discharge, survival

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P1.11-010 Therapeutic and Supportive Care Unmet Needs in Lung Cancer Patients Ronak Savla, Cornell Stamoran *Catalent Applied Drug Delivery Institute, Somerset/United States of America*

Background: The current drug evaluation model is designed at primarily optimizing therapeutic outcomes. Measures of quality of life and patient reported outcomes are often relegated as secondary endpoints. Even with excellent outcome results, there are many aspects of the patient journey that need to be addressed and improved. It is possible to improve therapeutic outcomes by addressing these other aspects of patient care. This study was concerned with elucidating these areas of unmet therapeutic and supportive needs. **Methods:** An online survey tool was used to collect lung cancer patient responses to questions about treatments, quality of life, and supportive therapies during their lung cancer treatment regimens. The various measures of outcomes, disease progression, treatments, quality of life, and side effects and their management were stratified according to lung cancer stage at diagnosis and other patient factors. **Results:** Responses from 106 lung cancer (non-small cell and small cell) patients were collected and analyzed. The study population had a significantly better 5-year survival rate compared to the national average for lung cancer patients. Only 2% of patients reported financial difficulties as a result of lung cancer. The patient population was quite homogenous (89.3% females and 90.4% white). Eighty percent of patients reported experiencing side effects from chemotherapy and of those, 86% reported that taking chemotherapy was difficult because of the side effects. Patients diagnosed at Stage II and III experienced the most side effects and received the highest average number of treatment modalities. Patients who agreed/strongly agreed that side effects affected ability to take chemotherapy experienced a significantly higher number of side effects than those patients who reported that side effects were not as bothersome. The same was seen with patients who agreed/ strongly agreed that side effects caused lifestyle disturbance. A subset of side effects negatively affected quality of life to a greater extent than other (nausea, vomiting, diarrhea, loss of appetite, and fatigue). Neuropathy and loss of appetite were the most poorly managed side effects. When asked what changes to chemotherapy administration they would like, the most common responses were oral agents or no changes. **Conclusion:** Even with excellent therapeutic outcomes, there continue to be unmet needs that can improve patient experience and quality of life. Side effects continue to be troublesome and common in cancer therapy. Side effects had negative impact on lifestyle and ability to take chemotherapy. Certain side effects are poorly managed. Better supportive care for chemotherapy-related issues can enhance patient quality of life and may further improve quality of life. **Keywords:** supportive care, quality of life, drug development, side effects

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P1.11-011 Taste Disorder in Patients with Thoracic Malignancy Who Received Chemotherapy Keisuke Azuma, Hiroshi Yokouchi, Ryuichi Togawa, Yasuhito Suzuki, Yuki Sato, Kenichiro Hirai, Manabu Uematsu, Kenichi Misa, Hiroyuki Minemura, Kenya Kanazawa, Yoshinori Tanino, Mitsuru Munakata *Department of Pulmonary Medicine, Fukushima Medical University, Fukushima/Japan*

Background: Recent development of novel cancer treatments have enabled patients to have prolonged survival; however, some patients cannot receive benefits from those effective therapies because of severe adverse effects. One of the major adverse effects that are recognized by medical staff in patients who undergo chemotherapy is taste disorder, although little is known about how to treat it. To overcome this problem, accumulating fundamental data, such as incidence rate and timing of taste disorder in cancer patients who have undergone chemotherapy, is necessary. With this in mind, we attempted to collect the data regarding taste disorder in patients with thoracic malignancy after initiation of chemotherapy as a pilot study, in order to determine the primary endpoint for subsequent intervention studies. **Methods:** All eligible patients had treatment-naive non-small-cell lung cancer (NSCLC), small-cell lung cancer (SCLC) or malignant pleural mesothelioma (MPM) with ECOG performance status (PS) 0-2, and underwent chemotherapy. Written informed consent was obtained from all participants. We prospectively investigated the incidence rate and timing of taste disorder in these patients using the following two methods: i) analysis of gustatory threshold for salty taste using a sodium-impregnated test strip (SALSAVE, Advantec Toyo Co. Ltd., Tokyo, Japan); and ii) analysis of responses of a questionnaire which asked about the patient's appetite, the timing of each taste change (sweet, salty, sour, and bitter taste), the presence of a taste in the mouth without eating any food, changes in sense of smell, tolerability against taste disorder, and the condition of the mouth and stomach after each cycle (1-4 cycles) of chemotherapy. This study was registered with the University Hospital Medical Information Network Clinical Trials Registry, identification number UMIN00007879, and approved by the Institutional Review Board of our institution. **Results:**From June 2012 to August 2014, 36 pts were enrolled. The average age was 64.5 years (range: 37-83); male/female=29/7 (81/19%); ECOG PS 0/1/2=20/12/1 (56/33/3%); NSCLC/SCLC/MPM=25/8/3 (69/22/8%), clinical stage IIIA/IIIB/IV/adjuvant of lung cancer =2/6/23/2 (6/18/70/6%), and IMIG stage III/IV of MPM=2/1. Chemotherapy regimens were as follows; cisplatin/carboplatin/pemetrexed/etoposide/ paclitaxel/ others=18/14/16/8/3/7. There was a trend of increased threshold for salty taste detected by a test strip after one or two cycles of chemotherapy (p=0.10, each). Questionnaire analysis demonstrated that patients felt changes in taste after two or three cycles of chemotherapy (p=0.04, 0.005, respectively), felt changes in their sense of smell after one to three cycles (p=0.04, 0.002, 0.001, respectively), and had a reduced sensitivity to salty tastes after three cycles (p=0.02). **Conclusion:** These results suggest that using a salt test strip may detect salty taste disorder earlier than analysis of the patient's subjective symptoms as answered in a questionnaire. The questionnaire evidently demonstrated taste disorder from various aspects in patients with thoracic malignancy receiving chemotherapy, and thus intervention using novel drugs is necessary. Further accumulation of such data is definitely warranted for further studies. **Keywords:** Adverse effects, taste disorder, chemotherapy, thoracic malignancy

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P1.11-012 Process for Developing a Rapid Tissue Donation Program in a Thoracic Program: Ethical and Logistical Considerations Gwendolyn Quinn[1], Matthew B. Schabath[1], Teresita M. Anotnia[2], Christie Pratt[2], Ivana Sehovic[3], Eric Haura[2] [1]*Cancer Epidemiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa/FL/United States of America,* [2]*Immunology, Moffitt Cancer Center and Research Institute, Tampa/United States of America,* [3]*Cancer Epidemiology, H. Lee Moffitt Cancer Center and*

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Background: Rapid tissue donation (RTD), also known as "warm autopsy," is a novel method of tissue procurement for research purposes where tissues from the primary tumor and metastatic sites are collected within 24 hours of patient death. These tissues provide tremendous research possibilities and hope for new cancer treatments. However, recruiting for RTD has ethical challenges such as diminishing patients' hope and causing distress to Next of Kin (NoK). Presently there is limited RTD education, training, or protocols for biomedical researchers and healthcare professionals (HCPs) to address the psychosocial and ethical aspects of the request for postmortem tissue donation. The purpose of this study was to: i) identify barriers and facilitators to RTD recruitment and tissue collection from key stakeholders; ii) identify the RTD processes used in other organizations and programs; and iii) establish a standardized process for RTD in a Thoracic Oncology Program at a Comprehensive Cancer Center. **Methods:** Mixed methods were used for each of the 3 purposes of the study: i) formative research (surveys and focus groups) was conducted to explore knowledge, perceptions, and barriers and facilitators to patient recruitment to RTD across key stakeholders including HCPs (n= 91), cancer patients/survivors and advocates, caregivers, physicians and clinic staff (n=42); ii) semi-structured interviews with hospice staff, morgue pathologists, funeral home directors, national organ/tissue donation programs (n= 27); and iii) conducted an extensive review of the literature regarding existing models of RTD. **Results:** Results from part 1 of the study identified several *barriers* including use of the word "autopsy"; discussing RTD during an initial appointment; approaching patients who attended visits alone; having staff discuss RTD with patients; and expecting all physicians would want to assist with recruitment. *Facilitators* included identifying enthusiastic physicians; establishing that the treating physician should identify who would be a good candidate (interest and willingness); use of the word "donation"; *only* approaching patients who have expressed interest and are coping well with their diagnosis; engaging family members in the consenting process; developing written educational materials about RTD; and allowing family members the authority to revoke consent after patient death. Results from part 2 identified the need to use a body map to indicate metastatic sites, developing a standardized operation procedure (SOP); restricting the geographic area where patients reside to facilitate quick retrieval; enlisting the help of Hospice, providing training to staff and physicians and developing a mechanism to provide study results to NoK and recognition for donors. Results from part 3 revealed that despite more than 300 publications using tissue collected via RTD, only 1 study actually described the process for obtaining the tissues and consent. Based on these results, a 12-step RTD SOP was developed. **Conclusion:** Ethical guidelines, an SOP, and training for HCPs is needed prior to initiation of an RTD program. A verbatim script is necessary for physicians' comfort level and to ensure consistent messaging. Our study provides important information about knowledge, attitudes, and logistics related to RTD from all stakeholders and guided the development of a RTD at a Comprehensive Cancer Center.

Keywords: Hospice, Rapid Tissue Donation, Ethics

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.11-013 Place and Cause of Death in Patients with Lung Cancer in the United Kingdom Emma L. O'Dowd[1], Tricia Mckeever[1], David R. Baldwin[2], Sadia Anwar[2], Richard B. Hubbard[1] [1]*Epidemiology and Public Health, University of Nottingham, Nottingham/United Kingdom,* [2]*Respiratory Medicine, Nottingham University Hospitals, Nottingham/United Kingdom*

Background: Many patients with cancer die in an acute hospital bed, which has been frequently identified as the least preferred location, with psychological and financial implications. This study aims to look at place and cause of death in patients with lung cancer to identify which factors are associated with dying in an acute hospital bed versus at home. **Methods:** We used data from the National Lung Cancer Audit (NLCA) linked to Hospital Episode Statistics (HES) and Office of National Statistics (ONS) records to determine cause and place of death in those with lung cancer overall. England was divided into 28 cancer Networks at the time these data were collected so we used these to assess geographical variation in place of death. We used multivariate logistic regression to compare demographic, co-morbid and tumour-related factors between those who died in an acute hospital versus those who died at home. **Results:** Of 143627 patients identified 40% (57678) died in an acute hospital, 29% (41957) died at home and 17% (24108) died in a hospice. Individual factors strongly associated with death in an acute hospital bed compared to home were male sex, increasing age, poor performance status, social deprivation and diagnosis via an emergency route (table 1). There was marked variation between cancer Networks in place of death. The proportion of patients dying in an acute hospital ranged from 28% to 48%, with variation most notable in provision of hospice care (9% versus 33%). Cause of death in the majority was lung cancer (86%), with other malignancies, chronic obstructive pulmonary disease (COPD) and ischaemic heart disease (IHD) comprising 9% collectively. **Conclusion:** A substantial proportion of patients with lung cancer die in acute hospital beds and this is more likely with increasing age, male sex, social deprivation and in those with poor performance status. There is marked variation between Networks, suggesting a need to improve end-of-life planning in those at greatest risk, and to review the allocation of resources to provide more hospice beds, enhanced community support and ensure equal access.

Table 1: Multivariable analysis comparing death at home versus that in an acute hospital bed.

		Death in acute hospital	
		OR	95% CI
Age at diagnosis (years)	70-74	1	
	≥ 85	1.16	1.08-1.24
Sex	Male	1.14	1.12-1.17
	Female	1	
Performance Status	0	1	
	4	1.73	1.61-1.87
Townsend quintile	0	1	
	5	1.31	1.25-1.37
Source of referral	GP referral	1	
	Emergency admission	1.45	1.39-1.51

Corrected for Charlson score, stage and histology
OR: Odds ratio, 95% CI: 95% confidence interval

Keywords: lung cancer, place of death

SESSION: POSTER SESSION/ COMMUNITY PRACTICE MONDAY, SEPTEMBER 7, 2015

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.12-001 Trends in Accuracy and Comprehensiveness of Pathology Reports of Resected Non-Small Cell Lung Cancer (NSCLC) in a High Mortality Area of the US Matthew P. Smeltzer[1], Fedoria E. Rugless[2], Nicholas Faris[2], Xinhua Yu[1], Ransome Eke[1], George Relyea[1], Carrie Fehnel[2], Nibedita Chakraborty[2], Cheryl Houston-Harris[2], Fujin Lu[2], David Spencer[3], Allen Berry[4], Elizabeth Sales[5], Clara Finch Cruz[6], Raymond U. Osarogiagbon[2] [1]*Epidemiology and Biostatistics, University of Memphis School of Public Health, Memphis/TN/United States of America,* [2]*Thoracic Oncology Research Group, Multidisciplinary Thoracic Oncology Program, Baptist Cancer Center, Memphis/TN/United States of America,* [3]*Trumbull Labs, Memphis/United States of America,* [4]*St. Francis Hospital Pathology, Memphis/TN/United States of America,* [5]*Doctors Anatomic Pathology, Jonesboro/AR/United States of America,* [6]*Va Medical Center, Memphis/United States of America*

Background: Pathologic examination of NSCLC resection specimens is vital to optimal treatment. In 2004, the College of American Pathologists (CAP) issued guidelines for NSCLC reporting, which were most recently updated in 2013. We evaluated the adoption of CAP reporting elements in a regional database. **Methods:** The Mid-South Quality of Surgical Resection (MS-QSR) database includes detailed information on 2,593 NSCLC resections in 11 institutions in 5 Dartmouth Hospital Referral Regions in Eastern Arkansas, North Mississippi and Western Tennessee from 2009-2014. In 2009, we started a multifaceted educational intervention: 1. Analyzed 2004-2008 pathology reports demonstrating the quality deficit in pathology reporting. 2. Recommended adoption of synoptic reporting of CAP checklist items. 3. Embedded a surgical intervention to improve mediastinal lymph node examination at some institutions. To allow for comparisons between eras and across the post-intervention era by intervention and type of hospital, we evaluated 4 groups: pre-intervention (pre-int), post-intervention participating hospital with surgical intervention (post-int/surg), post-intervention participating hospital without surgical intervention (post-int/non-surg), and non-participating non-surgical intervention hospital (post-int/non-part). We evaluated the inclusion of each CAP checklist item and the percent of cases with all items and 6 key items reported. We also evaluated the accuracy of T and N-stage categorization. Proportions reporting each item were compared between groups using Fisher's Exact test. **Results:** Details of the completeness of pathology reporting are shown in Table 1 by group. The percent reporting the 6 key checklist items improved significantly from 63% pre-int to 76% post-int/non-part, 86% post-int/non-surg, and 95% post-int/surg (p-value<0.0001). A similar pattern of improvement was observed for N-stage (p-value<0.0001) and T-stage (p-value<0.0001) reporting. However, we observed significant decreases in the reporting of M-stage, and therefore all key items, post-intervention (p-value<0.0001). The accuracy of N-stage reporting improved significantly from 66% pre-int to 72% post-int/non-part, 86% post-int/non-surg, and 97% post-int/surg (p-value<0.0001). A similar trend was observed for T-stage accuracy (p-Value<0.0001).

%Reporting	Pre-Int (N=1390)	Post-Int/ Non-Part (N=271)	Post-Int/ No-Surg (N=645)	Post-Int/ With-Surg (N=310)	P-Value
Specimen*	98.4	100	100	100	<0.0001
TumorSize*	97.2	99.6	98.1	99.4	0.0094
Histology*	99.8	99.6	99.5	99.7	0.59
MarginStatus*	97.1	98.5	92.6	98.7	<0.0001
T-Stage*	67.8	76.4	92.1	97.1	<0.0001
N-Stage*	66.3	76.8	89.8	97.7	<0.0001
***All Key-Items**	62.7	75.7	85.7	94.8	<0.0001
Laterality	99.8	100	99.5	100	0.56
HistologicGrade	99.9	100	99.5	100	0.18
M-Stage	75.8	31.4	25	21.6	<0.0001
VascularInvasion	28.6	10.7	25	11.9	<0.0001
All Items	10.7	4.1	6.2	3.2	<0.0001
%Accurate					
N-Stage	66.2	71.6	86.2	96.8	<0.0001
T-Stage	55.3	61.6	83	84.8	<0.0001

Conclusion: There was significant improvement in reporting of CAP checklist items and the accuracy of pT- and pN-categorization. After the introduction of synoptic reporting, we observed a secular trend of improvement, shown by our post-int/non-part external control. Direct educational intervention in 2009-2010 further improved the completeness and accuracy of reports in participating hospitals. The surgical intervention provided additional benefit. Interventions to improve the quality of reporting for NSCLC are impactful on accuracy and thoroughness of reporting, thereby improving the quality of care. **Keywords:** Pathology Reporting, non-small cell lung cancer, Accuracy, Comprehensiveness

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.12-002 International Online Tool for Therapeutic Decision Making in NSCLC (V2.0) Timothy A. Quill[1], David R. Gandara[2], Wilfried E.E. Eberhardt[3], Tony Mok[4], Nagahiro Saijo[5], Yi-Long Wu[6], Kevin Obholz[1], Andrew Bowser[1], Helen Chow[7], Giorgio V.V. Scagliotti[8] [1]*Clinical Care Options, Virginia/United States of America,* [2]*University of California Davis Cancer Center, Sacramento/CA/United States of America,* [3]*University Hospital Essen, West German Cancer Centre, Ruhrlandklinik, University Duisburg-Essen, Essen/Germany,* [4]*Princess of Wales Hospital, The Chinese University of Hong Kong, Hong Kong/Hong Kong,* [5]*Administration, Japanese Society Medical Oncology, Tokyo/ Japan,* [6]*Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhgou/China,* [7]*University of California Davis Cancer Center, Sacramento/United States of America,* [8]*Thoracic Oncology Unit, University of Turin, Turin/Italy*

Background: Practice guidelines in non-small-cell lung cancer (NSCLC) list multiple therapy choices based on levels of evidence but cannot account for variability in patient (pt)-tumor characteristics between individual patient cases. To provide oncologists with expert guidance and feedback on choice of treatment (Tx) for specific pt scenarios, we previously implemented an interactive Web-based decision support tool in 2012, in which oncologist users input specific pt characteristics and selected among treatment options, then compared their selection with that of an NSCLC expert panel for that scenario. (Chow JTO 2015). Here we report data from version 2.0 of this tool, capturing current Tx trends for advanced NSCLC and investigating the impact of this online tool on oncology practitioners. **Methods:** V2.0 was developed based on input from 6 international NSCLC experts who provided Tx recommendations for 1st-line treatment in 96 pt case variations based on histology (nonsquamous vs squamous), *EGFR* mutational status (positive [+] vs negative [-]), *ALK* rearrangement (+ vs -), age (< 70 vs ≥ 70 years), performance status (0, 1 vs 2), smoking history (never/former light vs former heavy/current), and pt primary Tx goal (response and survival vs quality of life and low adverse events). As in V1.0, oncologist users input specific pt scenarios, then were prompted for their treatment choice. Once completed, recommendations for that scenario from each of the experts were displayed, and users were prompted to indicate whether the expert recommendations changed their treatment choice. Statistical methods: as previously described (Chow JTO 2015). **Results:** V2.0 oncologist users (N = 218 unique users) contributing 314 unique cases were 87% non-USA, 13% USA. As in V1.0, experts agreed on selection of targeted therapies (TKIs) for cases with actionable EGFR mutations and ALK translocations. Choice of a specific EGFR inhibitor by experts varied depending on region and clinical factors. By comparison, among online users of V2.0, an EGFR inhibitor was selected for 67% of EGFR-mutated cases (n = 78), while an ALK inhibitor was selected for 61% of ALK cases (n = 31). For nonsquamous histology cases without actionable mutations, use of pemetrexed was more common among experts compared with oncologist users (91% vs 48% of case scenarios). In 182 cases entered by users who reported on the impact of expert recommendations, treatment choice was affected in 86% of cases (confirmed in 71%); 5.5% disagreed with expert recommendations and 8% indicated barriers to implementing the recommendations. In comparing overall results from V1.0 (2012) to V2.0 (2014), more oncologist users were likely to select TKIs in both EGFR mutation (49% vs 67%) and ALK translocation (35% vs 61%), with a corresponding decrease in use of chemotherapy. A detailed analysis of expert vs user data will be presented, comparing V1.0 (2012) and V2.0 (2014). **Conclusion:** Expert opinions were largely unchanged between V1.0 and V2.0, while oncologist users increased use of TKIs. Most oncologist users of V2.0 either confirmed or changed treatment choices based on expert recommendations. This online tool can aid decision making, serve an educational purpose, and capture practice trends. **Keywords:** online tool, first-line therapy, practice trends

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.12-003 Acquistion of and Early Clinical Results of Electromagnetic Navigational Bronchoscopy for Diagnosis of Lung Cancer in a Community Setting Alexandra Reichman[1], Jessica Parkyn[2], Jerry Birk[3], Laura De La Cruz[1], Royce Calhoun[2] [1]*Pathology, Rideout Regional Medical Center, Marysville/CA/United States of America,* [2]*Thoracic Surgical Oncology, Rideout Health, Marysville/CA/United States of America,* [3]*Administration, Rideout Regional Medical Center, Marysville/CA/United States of America*

Background: Electromagnetic Navigational Bronchoscopy (ENB) is an emerging technology to assist in obtaining a tissue diagnosis from suspicious lung nodules or masses. Despite the recognized advantages of having access to ENB technology, there are barriers to procure such expensive technology and effectively implement it. Acquiring and leveraging ENB technology is dependent on diverse considerations for community need, financial feasibility, patient / referral work flow and synergy with complimentary diagnostics and programs, proper coding and revenue cycle management and associated service development and marketing. There are many elements to implementing and achieving acceptable results which include the initial capital planning and service optimization, maximizing utilization, learning the techniques with enhanced competency and the handling and management of the specimens once obtained. Herein, we describe our approach to procuring the technology and early clinical results. **Methods:** ENB technology was purchased after partnering with the parent company (Covidien) and our health system's business development department, to perform a market analysis as well as a return on investment that integrated multiple service lines and hospital costs centers. From these data, a business plan was created and ultimately approved by the Foundation Board. All ENBs (SuperDimension®) were performed under general anesthesia by a single thoracic surgeon in the operating room, using a therapeutic bronchoscope inserted through a 9 endotracheal tube. Almost all procedures utilized fine needle aspiration, brushings, biopsies and washings. The biopsy phase of the procedure was done under fluoroscopy. Cytologic slide review via Rapid Onsite Evaluation (ROSE) was performed by a pathologist in the operating room in 100% of the cases. Results were obtained by retrospective review of a prospective database. Time period of study was 12/11/13-03/30/14. **Results:** 72 total ENB cases were performed in the time period of which 52 were for suspected malignancy. There were no pneumothoraces or bleeding complications. Two patients had to be admitted for 23 hours secondary to poor respiratory function following procedure. Of the 52 suspected malignancies, 33 (64%) were found to be a primary lung cancer, 7 were atypical and 12 benign or non-diagnostic. 5 of the patients with atypia went on to surgical resection and were found to have lung adenocarcinoma. **Conclusion:** ENB is an emerging technology with promising results for tissue diagnosis of lung nodules suspected of being malignant. Implementing new and costly technologies in smaller healthcare systems, such as a regional hospital, can be challenging. Some of the barriers to implementation are finding the capital and justification for procuring the technology, perfecting the technique and securing support from pathology, anesthesiology and operating room time. By partnering with industry and our business department, we were able to justify procurement of ENB technology. In our first 72 cases, 52 were for suspected malignancy. A diagnosis of lung cancer was achieved in 64% of lung lesions, with a low complication rate (2/72). Our results compare favorably to published results of trans thoracic needle biopsies as well as within our own health system. Initiating and implementing an ENB program in a community setting is feasible with acceptable results. **Keywords:** Community Setting, Electromagnetic Navigational Bronchoscopy, lung cancer, Thoracic Surgeon

POSTER SESSION/ COMMUNITY PRACTICE
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P1.12-004 Early Results of Endobronchial Ultrasound for Lung Cancer Mediastinal Nodal Staging in a Community Setting Alexandra Reichman[1], Jessica Parkyn[2], Laura De La Cruz[1], Royce Calhoun[2] [1]*Pathology, Rideout Regional Medical Center, Marysville/CA/United States of America,* [2]*Thoracic Surgical Oncology, Rideout Health, Marysville/CA/United States of America*

Background: Endobronchial Ultrasound (EBUS) has become an established modality for pathological mediastinal staging for lung cancer and in some centers, is used at the exclusion of mediastinoscopy, the traditional gold standard. Herein, we describe our early results of EBUS, in a community setting, for mediastinal pathologic staging for lung cancer and compare it to concomitant mediastinoscopy. **Methods:** All EBUS procedures were performed in the operating room under general anesthesia, with a Pentax scope introduced through a 9 endotracheal tube, by a single thoracic surgeon. The Pentax needle was used early in the series and the Cook needle later. Rapid Onsite Evaluation (ROSE) for immediate cytologic evaluation of specimens was performed in 100% of the cases. For lung cancer staging patients, mediastinoscopy was performed immediately after the EBUS under the same anesthetic. This was an outpatient procedure. Study

period was 04/21/14-04/13/15. Data was collected from a retrospective review of a prospective database. **Results:** There were 40 EBUS cases performed during the study period. There were no complications. 36 were performed for cancer diagnosis/staging and 21 for lung cancer staging specifically. 27 cases had EBUS and mediastinoscopy performed concomitantly under one anesthetic and thus could be directly compared. 46 total # of lymph node stations were evaulated with EBUS and 16 (35%) resulted in no lymphocytes or diagnosis. Regarding the 21 lung cancer patients who were being evaluated for pre-treatment pathologic mediastinal staging, the average # of lymph node stations was 1.1 for EBUS vs. 3.4 for mediastinoscopy. Using mediastinoscopy as the reference for pathologic staging, the sensitivity of EBUS was 80% and specificity 100%. If the EBUS stations that yielded no lymphocytes or diagnosis were eliminated from the analysis, the sensitivity was 89% and specificity 100%. **Conclusion:** EBUS has become an established technique to pathologically stage mediastinal nodes for lung cancer. In some centers, it is used at the exclusion of mediastinoscopy (the gold standard) and in others, selectively. Our early results with the adoption of this technique and comparing it to mediastinoscopy performed concommitantly, has an acceptable sensitivity and specificity. However, we experienced a relatively high rate of absence of lymphocytes/non-diagnostic (35%), compared to mediastinoscopy (0%), and fewer nodal stations biopsied per procedure (avg. 1.1) compared to mediastinoscopy (avg. 3.4). This does represent an early experience and likely not beyond the learning curve. We will continue to utilize EBUS for lung cancer staging but will be liberal to employ concomitant mediastinoscopy until we can approach the results of our mediastinoscopy with respect to yield of lymphocytes/diagnosis and # of stations biopsied per procedure. **Keywords:** Community Setting, Thoracic Surgeon, endobronchial ultrasound

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.12-005 Concomitant Electromagnetic Navigational Bronchoscopy and Endobronchial Ultrasound to Diagnose and Stage Lung Cancer in a Community Setting Jessica Parkyn[1], Alexandra Reichman[2], Laura De La Cruz[2], Royce Calhoun[1] [1]*Thoracic Surgical Oncology, Rideout Health, Marysville/CA/United States of America,* [2]*Pathology, Rideout Regional Medical Center, Marysville/CA/United States of America*

Background: Delays in lung cancer diagnosis and adequate staging can both delay and affect appropriate care. It is not uncommon to take months from the time of the first suspicion of lung cancer on imaging to diagnosis, staging and treatment. We have recently adopted both electromagnetic navigational bronchoscopy (ENB) and endobronchial ultrasound (EBUS) technologies as part of our comprehensive lung cancer program. By cultivating an early referral system, within the primary care network, of suspected lung cancer and with the understanding of which patients should have pathologic mediastinal staging, we are able to both diagnose a primary lung cancer and pathologically stage the mediastinal nodes in one setting under the same anesthetic. This combined approach by a lung cancer expert, saves many potential delays of separate serial procedures often ordered by those not as familiar with lung cancer evaluation and staging. Herein, we describe our early results with this approach. **Methods:** Criteria for patient selection was a lung nodule/mass suspicious for lung cancer and either clinically positive hilar or mediastinal lymph nodes (>1cm on short axis or > 2.5 SUV on PET) or central primary, >4 cm primary or >10 SUV of suspected primary lung cancer. All procedures were performed by a single thoracic surgeon, in the operating room with the patient under general anesthesia. The Superdimension® ENB system was utilized and the Pentax® EBUS system. Rapid Onsite Evaluation (ROSE) for immediate cytologic evaluation of specimens was performed in 100% of the cases. The study period was 04/21/14-04/13/15. Data was evaluated retrospectively from a prospective collected database. **Results:** 21 patients had a combination of ENB and EBUS and/or mediastinoscopy or both. 19 patients had lung cancer and constitute this analysis. A diagnosis of lung cancer was achieved in 16 patients (84%). EBUS/Mediastinoscopy was negative for cancer in 11 (59%) patients and positive for cancer in 8. (41%). There were no complications and all procedures were outpatient. The subsequent treatment of the patients were as follows: 5 definitive chemoradiation, 3 lobectomy followed by chemotherapy, 1 lobectomy followed by radiation to chest wall, 1 lobectomy, 2 clinical trials, 1 neoadjuvant chemotherapy followed by lobectomy (intent), 2 chemoradiation followed by lobectomy (intent), 1 radiation, 2 chemotherapy, 1 hospice. **Conclusion:** The ability to both diagnose lung cancer and pathologically stage the mediastinum under one anesthetic with utilization of ROSE, has several potential advantages. It allows an efficient and expeditious diagnosis and staging in select patients so they move expeditiously to the appropriate treatment and potentially skip several serial appointments and tests. Like most centers, we selectively pathologically stage the mediastinum for lung cancer patients and this is likely why in this series there is a relatively high percentage of pathologic N2 nodes (41%) found on pre-treatment pathologic staging and relatively high percentage of patients having adjuvant treatment after lobectomy. We believe this is an efficient approach for patients with a suspected lung cancer and meet criteria for pathologic mediastinal staging. Future studies will focus on quantifying the time savings differential between this approach and the more traditional approaches. **Keywords:** Electromagnetic Navigational Bronchoscopy, endobronchial ultrasound, Community Setting, Thoracic Surgeon

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

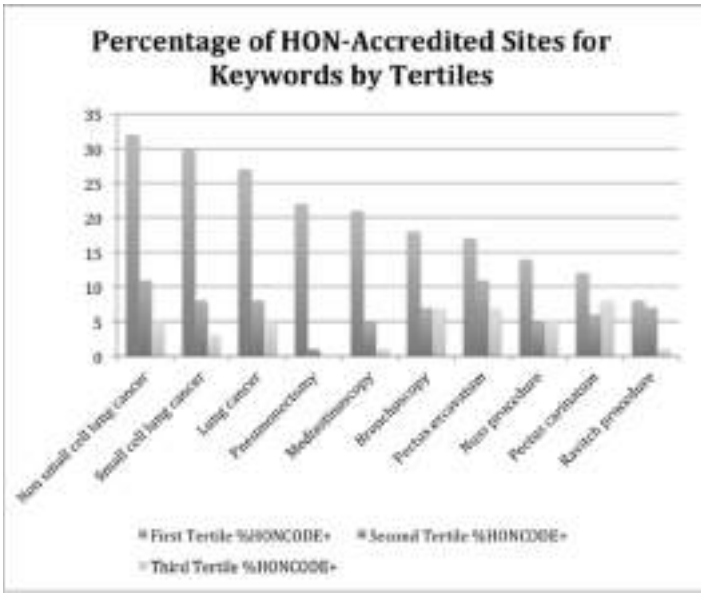
P1.12-006 Factors That Influence Tobacco Consumption Among Portuguese Adolescents Diana Silva[1], Julia A. Fernandes[2], Ana Valente[3], Claudia Dias[4], Altamiro Pereira[4], Henrique Queiroga[5], Alberto Caldas Afonso[1], António Guerra[1] [1]*Paediatric Service, Hospital São João, Porto/Portugal,* [2]*Faculty of Nutrition and Food Sciences, University of Porto[2], Porto/Portugal,* [3]*Faculty of Nutrition and Food Sciences, University of Porto, Porto/Portugal,* [4]*Department of Bioestatistics and Medical Informatics, Porto/Portugal,* [5]*Pulmonology Unit, Hospital São João, Porto/Portugal*

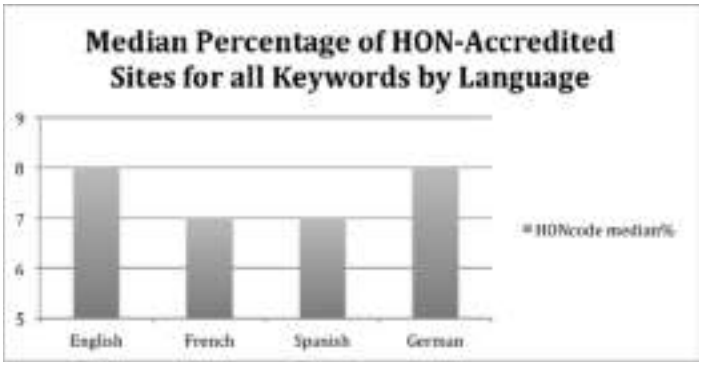
Background: The majority of smokers start smoking at a very early age. Many teenagers, who start smoking at school age, are at increased risk of becoming adult smokers. The purpose of this study was to evaluate family and social factors that might contribute to the acquisition of smoking in Portuguese adolescents. **Methods:** A cross-sectional study was conducted in 285 healthy adolescents (15–19 years old) of both sex attending 3 high schools (public and private) from northern Portugal. The smoking habits of teenagers were evaluated according to a protocol adapted from the Global Youth Survey (GYTS), Center of Disease Control and Prevention (2001). The questionnaire consisted of 34 questions related to tobacco consumption, knowledge and attitudes towards smoking, smoking cessation, school regulation and the family role in preventing smoking. Participants were classified as: 1 - never having tried smoking; 2 - have just tried smoking (not smoked in the previous month); 3 - occasional smokers (smoked at least 1 day during the previous month); 4 - current smokers (smoked at least 20 days in the previous month). The protocol was approved by the School Direction and statistical analysis was performed with SPSS ® for the entire sample and by gender. **Results:** Of the total sample (n=285), 46% were males and 54% females with an average age of 16.6±1.2 years (minimum:15; maximum:19). About 59.6% of adolescents have experienced smoking at least once, 54% of whom were female. Although the average age of tobacco onset was between 12-15 years (64%), we found that 21% of subjects experienced smoking before 11 years of age. Regarding parents tobacco use, there is a higher percentage of smoking fathers (30.2%) versus 15.2% of mothers. 38% (n=170) of smoking adolescents do it in public places, mainly in social events (65%) and with friends (91%). It is noteworthy that the major causes referred by the adolescents to smoke were: have many smoking friends [girls: OR=44,0 (9,932- 194,92)] (p<0,001); boys: OR=33,21 (6,14-179,65)] (p<0,001) and a smoking mother [girls: OR=4,39 (1,417-13,637)] (p=0,010); boys: OR=2,627 (0,824-8,378)] (p=0,103). **Conclusion:** It should be noted that in addition to early initiation, a high percentage of adolescents smoke regularly**.** Having parents and/or friends who smoke are the highest prediction factors for adolescent smoking. This study highlights the importance for an effective intervention in respect to tobacco harmful effects, with strong family involvement, in order to reduce consumption and prevent its negative health consequences, as well as the morbidity and mortality associated. **Keywords:** family, tobacco, adolescents

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.12-007 Thoracic Surgery Information on the Internet: Multilingual Quality Assessment Myles T. Davaris[1], Stephen Barnett[2], Nathan Lawrentschuk[3], Robert Abouassaly[4] [1]*University of Melbourne; Austin Hospital, Melbourne/VIC/Australia,* [2]*Austin Hospital; Peter Maccallum Cancer Institute, Melbourne/Australia,* [3]*Ludwig Institute for Cancer Research, Austin Hospital; Department of Surgery, Austin Hospital; University of Melbourne, Melbourne/VIC/Australia,* [4]*Urological Institute, University Hospitals Case Medical Centre, Case Western Reserve University, Cleveland/OH/United States of America*

Background: Previous data suggests quality of Internet information regarding surgical conditions and their treatments is variable. However, no comprehensive analysis exists for Thoracic surgery. **Methods:** World Health Organization Health on the NET (HON) principles may be applied to websites using an automated toolbar function. We used the English, French, Spanish and German Google search engines to identify 12,000 websites using keywords related to Thoracic conditions and procedures. The first 150 websites returned by each keyword in each language had HON principles examined. We compared website quality to assess for tertile (thirds) and language differences. A further evaluation of the English site types was undertaken, with a comparative analysis of website provider types. **Results:** 'Lung Cancer' returned over 150 million websites, whereas 'Ravitch Procedure' returned less than 250 thousand. Less than 10% of websites are HON accredited with differences by search term ($p<0.05$) and tertiles ($p<0.05$) of the first 150 websites but, in contrast to earlier work in other tumour streams, not between languages. Oncological keywords regarding conditions and procedures were found to return a higher percentage of HON-accreditation than cosmetic search terms. The percentage of HON-accredited sites was similar across all four languages ($p<0.05$). In general, the first tertile contained a higher percentage of HON-accredited sites for every keyword.





Conclusion: Clinicians should appreciate the lack of validation of the majority of thoracic websites, with discrepancies in quality and number of websites across conditions and procedures. These differences appear similar regardless of language. An opportunity exists for clinicians to participate in the development of informative, ethical and reliable health websites on the Internet and direct patients to them. **Keywords:** Internet, Thoracic, Tertile, Language

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.12-008 Components of Creating and Implementing a Comprehensive Lung Cancer Program in a Community Setting Jessica Parkyn[1], Alexandra Reichman[2], Laura De La Cruz[2], Jerry Birk[3], Hoa Nguyen[4], Charles M. Wilkinson[4], Russell Suey[5], Royce Calhoun[1] [1]*Thoracic Surgical Oncology, Rideout Health, Marysville/CA/United States of America,* [2]*Pathology, Rideout Regional Medical Center, Marysville/CA/United States of America,* [3]*Administration, Rideout Regional Medical Center, Marysville/CA/United States of America,* [4]*Medical Oncology, Rideout Cancer Center, Marysville/CA/United States of America,* [5]*Imaging Services, Rideout Cancer Center, Marysville/CA/United States of America*

Background: Many communities do not have a comprehensive, evidence based approach to lung cancer diagnosis, staging and treatment. This is often secondary to lack of providers in the area with expertise in lung cancer as well as lack of appropriate diagnostic and treatment modalities. Herein we describe the creation and implementation of a comprehensive lung cancer program in a community setting. **Methods:** A regional health system that serves a population with a relatively high incidence of lung cancer, recruited an experienced general thoracic surgeon, with expertise in the diagnosis, staging and treatment of lung cancer. The community had a pre-existing cardiac surgery program, a cancer center that provided chemotherapy and traditional radiation, a PET scanner and 2 CT scanners. **Results:** The study period was 9/1-2012 to 4/1/2015 which spans the time after the introduction of the general thoracic surgeon in the community to present. Under the leadership of the thoracic surgeon, the following was accomplished: **1.** An extensive outreach campaign to primary care physicians as well as directly to the community regarding lung cancer awareness, modern diagnostic, staging and treatment modalities. **2.** Establishment of a pulmonary nodule clinic to provide expertise and continuity in the evaluation of pulmonary nodules. **3**. The establishment of a lung cancer CT screening program, **4.** Evolution of the tumor board from a once a month meeting, reviewing an average of 3.1 patients retrospectively and an average attendance of 3.6 attendees to currently meeting weekly, prospectively reviewing an average of 8.6 cases per meeting (>90% lung cancer) and an average attendance of 9.3 attendees including thoracic surgery, medical and radiation oncology, pathology, social work and a rotation of surgeons, pulmonologists and primary care physicians. **5.** The procurement and implementation of Electromagnetic Navigational Bronchoscopy to the community to obtain tissue diagnosis of suspected lung lesions. 6. The procurement and implementation of Endobronchial Ultrasound for the minimally invasive pathologic staging of appropriate lung cancer patients. **7**. The procurement and participation in the Society of Thoracic Surgery (STS) General Thoracic Surgery Database for registration of patient outcomes and national comparison. **8.** The introduction of VATS lobectomies and complex open resections. **9** 400 new thoracic surgical cases to the Regional Medical Center. 10. 54 cases of multimodallity therapy for lung cancer patients compared with 4 the previous two years. **11.** The establishment of stereotactic body radiation therapy (SBRT) as a treatment alternative to surgery for medically inoperable stage I lung cancer patients. **Conclusion:** It is possible to create a de novo comprehensive lung cancer program in a community setting with the appropriate expertise and leadership. General thoracic surgeons with expertise in current lung cancer diagnostics, staging and treatment options are uniquely positioned to provide the expertise and leadership to create a comprehensive lung cancer program as they are integrally part of assessing pulmonary nodules, establishing diagnosis, rigorously staging lung cancer and treatments including surgery, radiation chemotherapy and multimodality regimens. This approach could serve as a paradigm for similar communities to bring current, evidence based lung cancer diagnostics and treatment to their region. **Keywords:** Comprehensive Lung Cancer Program, endobronchial ultrasound, Electromagnetic Navigational Bronchoscopy, Thoracic Surgeon

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.12-009 Lung Cancer in Octogenarians Nuria Cárdenas Quesada[1], Ana Laura Ortega Granados[1], Carmen Rosa-Garrido[2], Yéssica Plata Fernández[1], Tamara Díaz Redondo[1], Irene González Cebrián[1], Francisco José García Verdejo[1], Natalia Luque Caro[1], Pedro López Leiva[1], Pedro Sánchez Rovira[1] [1]*Medical Oncology, Complejo Hospitalario de Jaén, Jaen/Spain,* [2]*Fibao, Complejo Hospitalario de Jaén, Jaen/Spain*

Background: Octogenarian patients with lung cancer are underestimated in the scientific literature. Since in our institution, the median age of patients with lung cancer is 71 years old, we decide to conduct a study to get specific data of our population over 80 years **Methods:** Retrospective observational cohort study of patients with lung cancer referred to Medical Oncology at our institution, during 4 years (2010-2013) and follow-up until April 2015. Inclusion criteria were age (80 years or older) and lung cancer diagnosis. The cohort was 41 patients **Results:** Our octogenarian patients were a 6.1% of our 672 patients seen in 2010-2013 interval. Of our 41 patients, 78% were male, and the median age is 81 years (80-87). Histologies are 88% NSCLC and 12% SCLC; in the NSCLC group, squamous carcinomas are most common (50%), followed by adenocarcinoma (26.8%). 51% patients were diagnosed in stages I-III, but only 3 patients were under radical treatment (2 surgery, 1 radiation therapy). 34% patients did not receive any oncologic treatment, only palliative care. Of the patients with active cancer treatment, 92% received first-line therapy. In the first-line group, 68% were under chemotherapy, 48% platinum doublet (more used schedules were carboplatin-vinorelbine, carboplatin-pemetrexed and carboplatin-paclitaxel), and 20% monotherapy (vinorelbine, pemetrexed and carboplatin) and 24% TKi (all EGFR mutated, with gefitinib and erlotinib). 26.8% (11) of patients received second-line treatment (10 erlotinib and 1 pemetrexed), and only 2 patients received 3 or more lines (1 patient up to 7 lines). 39 of 41 patients died (95%), and most patients die at home (95%). The median survival time is 11.19 months (CI 95% 7.84-14.53) and median overall survival is 8 months (CI 95% 4.51-11.48). In male patients, median survival time expected is 9.97 months, and in female patients, 14.88 months. Depending on the stage, stage IV patients had a expected survival of 9.94 months and stage I-III patients, 11.40 months, with no statistically significant diference. Depending on smoking status, survival is 8.95 months for ever-smokers, and 18.44 months for never-smokers (p-value: 0.035). Depending on therapy, survival in active cancer treatment group is 14.56 months, and in palliative care only group is 5.28 months (p-value: 0.001) **Conclusion:** In our cohort of elderly patients, with a small number of patients (a 6% of all the patients, maybe underreferred), we found some differences with our global lung cancer patients group. The ratio SCLC-NSCLC is quite similar (12-88% in elderly vs 14-86% in all our patients), but there is a different pattern according histological subtypes, with more squamous carcinomas in this cohort (44% vs 29.6%), and more EGFR mutations (24% vs 18%). We see that survival was better in patients receiving active cancer treatment plus best supportive care vs only palliative care. Factors influencing survival are smoking status (ever vs never-smokers) and sex. Although is essential a joint management with Palliative Care, in this particular group of patients, that are believed that cancer treatment is less useful, active cancer treatment is beneficial, if we always individualize decisions in each patient. **Keywords:** elderly, octogenarians, TKI, chemotherapy

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.12-010 Bench to Bedside Detection of Actionable Genotypes by SNaPshot for Lung Cancer Panel Anuradha Choughule[1], Vaishakhi Trivedi[1], Pratik Chandrani[2], Amit Dutt[3], Kumar Prabhash[4] [1]*Medical Oncology-Molecular Laboratory, Tata Memorial Centre, Mumbai/India,* [2]*Dutt Lab, Actrec, Mumbai/India,* [3]*Dutt Laboratory, Actrec, Navimumbai/India,* [4]*Tata Memorial Centre, Mumbai/India*

Background: Conventional therapeutic solutions in NSCLC are not effective to treat the disease. Despite of all developments in understanding of the disease, mortality of lung cancer patients remains high. Recent developments of personalized therapy have given promising results in terms of improved survival of NSCLC patients. Thus, we were keen to develop a cost effective and sensitive diagnostic lung cancer panel

assay for targetable mutation detection by *using* SNaPShot PCR technique *on* FFPE samples. **Methods:** Method: Multiplexed (SNaPShot) PCR was optimized to amplify hotspot regions from 9 targetable genes followed by single base extension reaction using **fragment analysis** on **ABI 3500 Sequencer**. Gene Mapper software was used for analysis **Results:** The successfully developed mutation profiling assay was divided into 3 multiplexed reactions, covering **23 actionable genotypes** of *EGFR, KRAS, BRAF, PIK3CA, Her2, AKT1, NRAS, MEK1* and*PTEN* genes. The assay was standardized and validated on 20 blood samples, 10 cell lines and 20 FFPE samples expressing good sensitivity and specificity for wild type and mutant genotypes. **Conclusion:** This In house developed SNaPShot PCR technology is robust, economical, specific and sensitive to detect actionable mutations in FFPE Adeno as well as in Squamous Carcinoma samples. Because these variants have differing genetic, biological, and clinical properties, including response to treatment, this **Bench to Bedside** research will lead us to correct classification of lung cancer cases and will assure that lung cancer patients receive optimum management. **Keywords:** actionable genotypes, Multiplexing by SNapshot assay

POSTER SESSION/ COMMUNITY PRACTICE
MONDAY, SEPTEMBER 7, 2015 - 09:30-16:30

P1.12-011 Treatment Patterns and Overall Survival for Advanced NSCLC Following Platinum-Based Chemotherapy in US Community Oncology Clinical Practice Caroline Mckay[1], Tom Burke[2], Xiting Cao[3], Amy Abernethy[4], David P. Carbone[5] [1]*Center for Observational & Real World Evidence (Core), Merck & Co., Inc., North Wales/PA/United States of America,* [2]*Center for Observational & Real World Evidence (Core), Merck & Co., Inc., Cokesbury/NJ/United States of America,* [3]*Center for Observational & Real World Evidence (Core), Merck & Co., Inc., Cokesbury/United States of America,* [4]*Flatiron Health, Inc., New York/NY/United States of America,* [5]*Medical Oncology, The Ohio State University - James Thoracic Center, Columbus/OH/United States of America*

Background: While clinical guidelines provide clinical decision support for selection of agent, combination, and order of administration, there are few studies that provide a comprehensive description of contemporary advanced NSCLC treatment patterns in patients following platinum therapy over time; there are limited recent US data on practice patterns and outcomes for advanced NSCLC patients following chemotherapy. The purpose of this study is (1) to describe patient flow from advanced NSCLC diagnosis to anti-cancer treatment following completion of a platinum regimen, and if EGFR mutation or ALK translocation positive, an appropriate TKI; (2) to describe the characteristics of advanced NSCLC patients treated with anti-cancer therapy following platinum therapy and, if EGFR mutation or ALK translocation positive, an appropriate TKI; to describe anti-cancer treatment patterns following completion of platinum therapy and, if EGFR mutation or ALK translocation positive, an appropriate TKI. **Methods:** Retrospective EMR database cohort study using data from a cloud-based Oncology Electronic Medical Record (EMR) system with 220 cancer clinics, 700 community-based cancer treatment clinics, 1750 clinicians, and 725,000 active cancer patients, representing 17% of incident cases in the United States. The data represents lab values and physician notes from both structured and unstructured data. Variables of interest include demographic, disease-related, biomarker testing-related, anti-cancer treatment. Treatment patterns include regimens by line of therapy, agents and number of doses administered or prescribed, and distribution of dosage strengths. Analyses will be conducted by histology and EGFR/ALK status (among non-squamous cell carcinoma patients). Data will be analyzed descriptively. Overall survival, if data are available, will be estimated using a series of Kaplan Meier curves, with median OS (95% confidence interval) reported. **Results:** Approximately 1598 patients with advanced NSCLC initiating a line of therapy after completing a platinum regimen and, if EGFR mutation or ALK translocation positive, an appropriate TKI between January 1, 2013 and October 31, 2014 will be followed until April 30, 2015. Preliminary results identified 6536 patients with advanced NSCLC; of these, 5048 (77.2%) received any 1L treatment after advanced NSCLC diagnosis with 3786 (57.9%) receiving platinum-based chemotherapy as 1L treatment. Among the final cohort of patients (n=1598), the majority were men (54.0%) initially diagnosed with stage IV disease (68.5%) at age 66. The distribution of histological subtypes in the sample included non-squamous (74.4%), squamous (21.0%), and NOS (4.6%). Treatment patterns will be described according to histology and biomarker status at index date. Patient characteristics and overall survival will be reported by histology, biomarker status at index date, and regimen type. **Conclusion:** Results from this study will describe treatment patterns in the second-line setting, prior to the introduction of newer therapies, such as anti-PD1/PD-L1 inhibitors and angiogenesis inhibitors. Additionally, it will advance current understanding of the specific patterns of 2L care for patients being treated with anti-cancer therapy in the real world of community settings.

SESSION: POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC TUESDAY, SEPTEMBER 8, 2015

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-001 Dendritic Cells: Cytokine-Induced Killer Cells Therapy in Advanced Non-Small Cell Lung Cancer: A Case Report of an Aggressive Tumor Relapse Francisco Iii M. Heralde[1], Maria Teresa A. Barzaga[2], Gloria R. Cristal-Luna[3], Ana Karina De Jesus[3], Ramoncito S. Habaluyas[4], Victoria C. Idolor[5], Jose Luis J. Danguilan[6], Nelia S. Tan-Liu[2] [1]*Biochemistry and Molecular Biology, University of the Philippines - Manila, Manila/Philippines,* [2]*Pathology, Lung Center of the Philippines, Quezon/Philippines,* [3]*National Kidney and Transplant Institute, Quezon/Philippines,* [4]*Cardiology, Lung Center of the Philippines, Quezon/Philippines,* [5]*Anesthesiology, Lung Center of the Philippines, Quezon/Philippines,* [6]*Thoracic Surgery, Lung Center of the Philippines, Quezon/Philippines*

Background: Cancer has been associated with immuno-surveillance dysfunction resulting to failure in identification and removal of malignant cells, followed by subsequent proliferation. Immune cell therapy aims to restore this immuno-surveillance function and manages micro-metastasis. DC/CIK (dendritic cell/cytokine-induced killer cells) an immune-based-maintenance therapy for advanced non-small cell lung cancer has been reported to improve progression free survival in several studies. Our early study suggested limited advantage of autologous DC vaccination in advanced NSCLC, hence, we proceeded to evaluate the response of a patient with Stage IV NSCLC to DC/CIK. **Methods:** The patient, 43-year-old nonsmoker male with family history of maternal breast cancer signed an informed consent to undergo the cell therapy protocol institutionally approved by Ethics Review Board of Lung Center of the Philippines. The patient earlier diagnosed with Stage IV NSCLC in November 2013, underwent chemotherapy of two cycles of Paclitaxel and Carboplatin and subsequently Erlotinib following partial remission. Patient had no severe existing medical condition that affected protocol compliance. The patient enrolled in November 17, 2014, and underwent hematology clearance, hematopoietic stem cell (HSC) mobilization with GCSF injection and leukapheresis. HSC's recovered from the buffy coat were propagated in-vitro using standard procedures to produce dendritic cells and cytokine induced killer cells. Three DC/CIK treatments were given at three-week intervals consisting of 25-28x10^6 DC primed with mixed peptide antigens based on personalized circulating tumor cell (CTC) RT-PCR profile and 10-20x10^6 CIK. The blood IFN-Y level, CTC count, RT-PCR profile and PET-CT data were obtained. **Results:** DC/CIK treatment resulted to initial decline in IFN-Y levels relative to baseline which recovered in levels on the second and third treatment. The CTC count showed reduction in number (i.e., from 229 to 699 and down to one cell/ml) while the RT-PCR profile indicated downregulated expression of three tumor markers (MUC1, Recoverin and p53), obliteration of one marker (KRT19) and emergence of four markers (Brachury, NFYC, S100A14 and MAGE-A3). Meanwhile, the PET-CT results indicated significant regression of bilateral pulmonary nodules and masses; interval resolution of some hypermetabolic lymph nodes and interval increase in others consistent with metastatic lymphadenopathy; osseous metastasis with interval decrease in metabolic activity of bone lesions; and occurrence of patchy reticular and ground glass opacities in right upper and lower lobe with possible infectious or inflammatory nature; and right atrium and pulmonary artery thrombosis. Few days post-PET-CT, patient manifested difficulty of breathing, cough and back pain; initially managed for pneumonia and pulmonary embolism, but showed progressive deterioration. Repeat CT-scan imaging of chest with angiography revealed drastic size increase of right lung mass relative to previous PET-CT scan; while sample biopsy revealed poorly differentiated carcinoma of lung primary. In 28 days post-PET-CT, patient yielded to Acute Respiratory Distress secondary to aggressive tumor in right lung of primary origin. **Conclusion:** DC/CIK treatment can be a promising immunobiological maintenance therapy for advanced NSCLC with recognizable molecular and clinical benefit to patients. Optimization of protocol towards anticipative strategies addressing aggressive primary tumor relapse may have to be considered in order to realize its complimentary therapeutic potential.

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P2.01-002 Immunotherapy as an Effective Treatment Option in the Metastatic NSCLC in Spite of PD-1 or PDL-1 Inhibition and Line of Therapy Jesús Corral, Carlos Robles, Miriam Alonso, Maria Dolores Mediano, Maria José Flor, Marta Amérigo, Inmaculada Sánchez, María Iglesias *University Hospital Virgen Del Rocio, Seville/Spain*

Background: Lung cancer is the leading cause of cancer death globally. Important survival benefit has been recently obtained with targeted therapies against driver mutations. Immunotherapy approach under development will probably represent a new standard option of care in pretreated patients: clinical and/or pathological prognostic factors will further be needed to select the maximum benefit treated population. **Methods:** We reviewed retrospectively clinical, pathological and efficacy data from 28 patients with metastatic NSCLC treated with anti-PD1 (programmed cell death 1) and anti-PDL1 (programmed cell death-ligand 1) check-point inhibitors in our Institution between 2013 and 2015. **Results:** 28 metastatic NSCLC patients were treated: 2 (7,14%) in first line, 14 (50%) in second line and 12 (40%) patients beyond third line. 82% were males, median age was 61 years old, and 71,4% adenocarcinomas. Mutation profile was defined as 1 patient (3,5%) EGFR positive and 1 patient ROS-1 positive (3,5%). PDL-1 resulted positive by immunohistochemistry on 43% of total population. 75% of patients received anti-PDL-1 therapy versus 25% anti-PD1 check point inhibitors. With a median follow up time of 22 months, overall response rate (ORR) was 10,7% and disease control rate (DCR) was 64,3%: no differences were seen by

immunotherapy strategy. ORR, DCR, and median time for treatment (MTT) were analysed according to the line of therapy and type of immunotherapy. ORR 0%, DCR 100% and MTT 104 days at first line setting; ORR 7,14%, DCR 64,28% and MTT 98 days at second line; and finally, ORR 18,18%, DCR 63,63% and MTT 67 days at third line or beyond. Most of patients remain on treatment so survival data were not reached. The most common grade III-IV adverse events related with treatment were pneumonitis (14,3%), fatigue (3,6%), hyperamylasemia (3,6%), hypertransaminasemia (3,6%) and neurologic disorders (7%). **Conclusion:** Our retrospective and local analysis confirmed immunotherapy as a safe and effective therapy option with high rate of DCR and longer MTT than standard chemotherapy, independently PD-1 or PDL-1 inhibition or line of therapy used.
Keywords: Immunotherapy, PD-1, PD-L1, line

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-003 T-Cytotoxic Specific Immunotherapy in NSCLC with Brain Metastases NCT00104780
John Nemunaitis[1], David Mccune[2], F A. Greco[3], Francis Nugent[4], Joe Stephenson[5], Dominique Costantini[6], Alessandro Sette[7], John D. Fikes[8]
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Background: Brain metastases (BM) come with poor prognosis (median survival 3 to 6 months) and data are lacking as patients are often excluded from clinical trials. **Methods:** We present the results of a subgroup of NSCLC patients with BM treated with OSE-2101 (T-cytotoxic specific immunotherapy combining 9 epitopes targeting 5 tumor associated antigens and 1 pan-DR epitope) during a phase IIb study of OSE-2101 (1 injection per 3 week for 6 injections followed by 1 injection every 2 to 3 months) in advanced stage IIIB and IV NSCLC (Barve et al. 2008. *J Clin Oncol 26:4418-4425*). Patients were eligible whatever the number of prior chemotherapy (chemo) lines (65.5% entering 3rd line) and patients with stable BM for 2 months could be included. Six out of 64 treated patients had BM prior to inclusion and are reviewed. **Results:**

Table 1: NSCLC patients included with BM

Patient	**108**	**150**	**169**	**132**	**133**	**135**
Gender	F	M	M	M	M	M
Ethnic origin	CAU	CAU	CAU	CAU	AA	CAU
Age (years)	46	61	58	79	46	57
ECOG performance status	1	1	1	1	1	1
Previous treatment	RT 30 Gy Chemo 2 lines	WBRT 30 Gy Chemo 2 lines	RT 30 Gy Chemo 2 lines	WBRT 30 Gy Chemo 3 lines	RT 30 Gy Chemo 1 line	WBRT 30 Gy Chemo 3 lines

AA: African-American, CAU: Caucasian, Chemo: chemotherapy, F: female, Gy: Gray, M: male, RT: radiotherapy, WBRT: whole brain radiotherapy

Table 2: Response to therapy

Patient	**108**	**150**	**169**	**132**	**133**	**135**
OS	30.16 mo	41 mo*	16.5 mo	9.6 mo	11 mo	7 mo**
Time without progression	11.57 mo	24.39 mo	11.9 mo	4.53 mo	6.2 mo	2 mo*[2]
CTL response (positive epitopes out of 5 tested)	3	2	5	2	1	Not tested
HTL response	+	+	+	-	-	Not tested

* Patient still alive at the time of the last follow up, ** treatment stopped after 2 injections for progressive disease. CTL: cytotoxic T lymphocytes, HTL: helper T lymphocytes, mo: months, OS: Overall survival, The 6 BM patients present long survival (median 13 mo, range 7-41) considering the advanced stage and the poor prognosis of these heavily pretreated patients. All patients had received from 1 to 3 previous chemo lines. Evaluation of CTL responses to 5 epitopes of OSE-2101 in 5 patients shows that each patient had a CTL response to at least one and up to 5 epitopes. Surprisingly patients with positive HTL response (patient 108, 150, 169) achieve the longest OS when compared with negative HTL patients (132 and 133). **Conclusion:** Long OS has been documented in NSCLC patients with BM treated with T-specific immunotherapy following RT and 1 to 3 previous chemo lines.
Keywords: Non-small-cell lung cancer, brain metastases, T specific immunotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-004 Oncologists' Comprehension and Beliefs Surrounding Cancer Immunotherapy in Advanced NSCLC
Tara Herrmann[1], Haleh Kadkhoda[2], Sheryl L. Konrad[3], Ramaswamy Govindan[4], Daniel Morgensztern[5] [1]*Medscape Education, Fort Sam Houston/United States of America, [2]Medscape Education, New York/United States of America, [3]Society for Immunotherapy of Cancer, Milwaukee/WI/United States of America, [4]Washington University School of Medicine, St. Louis/United States of America, [5]Oncology, Washington Univresity School of Medicine in St. Louis, St. Louis/MO/United States of America*

Background: Advanced NSCLC is now recognized as an immune-modifiable disease, and with the approval of the first PD-1 inhibitor, immune checkpoint inhibitors represent a new standard of care for patients with previously treated squamous cell lung cancer. The objective of this study was to evaluate oncologists' familiarity with cancer immunotherapy in the context of advanced NSCLC and the impact of an educational curriculum on narrowing gaps in clinical practices. **Methods:** An expert panel of oncologists identified educational gaps in the area of cancer immunotherapy. A series of 9 CME online activities were developed, 2 of which centered on advanced NSCLC and are the focus of this study. Interactivity questions allowed learners to self-report their familiarity with immunotherapy concepts in the management of advanced NSCLC, while case vignette and knowledge-based questions were constructed around evidence-based medicine. Confidentiality of survey respondents was maintained and responses were de-identified and aggregated prior to all analyses. **Results:** 1368 oncologists participated in the 2 activities on advanced NSCLC. As seen in the table below participation in the education activities resulted in numerous improvements in knowledge and competence as seen in the table below. Despite improvements, several important gaps remained. Only70% of oncologists comprehend that a tumor may increase in size or new lesions appear during initial therapy with an immune checkpoint inhibitor. In addition, about half of oncologists still had difficulty grasping how immune checkpoints downregulate T cell responses. Finally, oncologists still had difficulty identifying the unique side effect profile associated with immune checkpoint inhibitors. In addition, 55% of oncologists reported they were not comfortable with managing side effects associated with these agents.

Table

	% answered correctly	**% answered correctly**
	Pre-Activity	Post-Activity
Comprehension of Basic Immunology		
Interaction of TCR with MHC-peptide complex and co-stimulatory receptors CD28/CD80 and CD86	52%	69%
Which does not represent a role of an immune checkpoint in the adaptive immune response: CTLA-4 binds to CD28, augmenting T-cell activation	50%	57%
Knowledge of Immune System's Role in Response to Cancer		
T cell infiltration and decreased risk of recurrence	69%	76%
Disease progression on an immune checkpoint inhibitor	65%	71%
Efficacy, Safety, Limitations of Immune Checkpoint Inhibitors		
Limitations PD-L1 as a biomarker	26%	70%
Durability of response	5%	30%
Unique side effect profile	41%	59%

Conclusion: The study evaluated oncologists' familiarity with cancer immunotherapy in advanced NSCLC and demonstrated the necessity of developing targeted educational interventions for improving the knowledge and practice patterns of oncologists. Additional education is needed to continue to improve clinicians' competence in the use of cancer immunotherapies in the management of NSCLC.
Keywords: Education, NSCLC, Immunotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-005 Relationship between Icotinib Exposure and Clinical Outcome in Chinese ANSCLC Jun Ni[1], Li Zhang[2] [1]*Peking Union Medical College Hosptial, Peking Union Medical College&Chinese Academy of Medical Sciences, Department of Respiratory Medicine, Beijing/China,* [2]*Department of Respiratory Medicine, Peking Union Medical College Hosptial, Peking Union Medical College&Chinese Academy of Medical Sciences, Beijing/China*

Background: The icotinib hydrochloride tablets (Conmana) is a novel orally administered EGFR-TKI agent, which is the first homegrown anticancer drug designed, synthesizedand screened by Betapharma (Zhejiang, China) . The preclinical animal experiments showed that the agent had an anticancer activity in vitro and in vivo whose mechanism is that icotinib can inhibit EGFR activity specifically and competitively through binding to the tyrosine of the EGFR. A head-to-head Phase III clinical trial (ICOGEN) comparing the roles of icotinib and gefitinib in treating NSCLC in China has suggested that icotinib has similar (and even better) efficacy with gefitinib in treating Chinese NSCLC patients, with much better safety profiles; furthermore, it is superior to gefitinib in terms of treatment cost. Recently, a retrospective study demostrated that icotinib is active in the treatment of patients with NSCLC both in first or second/third line. Up to date, Icotinib has completed phase Ⅰ、Ⅱ and Ⅲ trials, Pharmacokinetic study in Phase I clinical trial data displayde that non-linear character with saturated absorption and first-order elimination. But whether the exposure of icotinib would influence the therapeutic effects is cofused us.So Beta Pharma (China) and Peking Union Medical College Hospital (PUMCH) jointly conducted this single-center open-label Phase I clinical trial, from August 2007 to April 2009, to explore the relationship between icotinib exposure and clinical outcomes of a single dose or administration for 31 consecutive days among Chinese NSCLC patients. In this article, by analysing the clinical efficacies and pharmacokinetic characteristics of iconitib in 30 subjects, we tried to elucidate the relationship between the iconitib exposure and therapeutic effects. **Methods:** In this single-center open-label phase I clinical trial, a dose-escalation method was applied until disease progression or unacceptable toxicities. Different doses of icotinib were orally administered for 31 consecutive days in different groups until disease progression or unacceptable toxicities. Blood samples were collected in the first treatment cycle (day 1 - day 28) for the pharmacokinetic analysis. Tumor responses were assessed by using the Response Evaluation Criteria in Solid Tumors(RECIST). The plasma concentrations of icotinib were assessed by liquid chromatography–mass spectrometry (LC-MS). **Results:** Univariate analysis showed that the time to maximum (Tmax) after a single dose of icotinib was significantly correlated with the overall survival (OS) (Spearman correlation coefficient=0.441, P=0.021). Patients with higher Clast were independently associated with PFS (p=0.012). Multivariate analysis showed that the AUC0-last and AUC0-∞ after a single dose of icotinib were significantly correlated with OS (P=0.037, P=0.042, respectively). Stratification of these subjects according to smoking status indicated significant correlation between OS and AUC0-last (Spearman correlation coefficient = -0.709, P=0.015). **Conclusion:** Iconitib is a novel EGFR TKI developed by Chinese scientists. For advanced NSCLC patients who have failed prior treatment(s), the exposure of a single dose of iconitib was significantly correlated with the treatment efficacy. This finding may provide a simple and feasible clinical indicator for predicting the survivals. **Keywords:** icotinib hydrochloride, non-small cell lung cancer, pharmacokinetics, clinical outcomes

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-006 Continuing EGFR-TKI in Combination with Regional Chemotherapy Beyond RECIST PD for Patients with Advanced EGFR(+) Non-Small Cell Lung Cancer Jie Zhang, Huiwei Qi, Sen Jiang, Juan H. Ni, Caicun Zhou *Shanghai Pulmonary Hospital, Shanghai/China*

Background: Local therapy showed promising results for the patient who had an oligo-metastasis after acquired resistance of epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs).Our study is to evaluate the efficacy and safety of continuing EGFR-TKI treatment in combination with regional chemotherapy beyond RECIST progression disease (PD) of EGFR-TKI in advanced patients with EGFR mutation-positive NSCLC. **Methods:** Advanced NSCLC patients with EGFR mutation who got a locally progressed in central lung lesion after the treatment of EGFR-TKI were included.Patients received EGFR-TKI continually in combination with super-selectedsystemicarterial infusionwith docetaxel (75 mg/m2) every 21 days until disease progression again or unacceptable side effect.Response to treatment, progression-free survival (PFS) 1 (time to RECIST PD), PFS 2(time to PD if EGFR-TKI was extended beyond RECIST PD) andtreatment-related adverse effects (AEs)were analyzed. Patient-reported outcomes were evaluated inall patients who had completed a baselineassessment and at least one post-baseline assessment based on the QLQ-LC13 scales. **Results:** A total of 6 patientswere recruited. Patients had the median age of 54.17 years (range, 40-68 years).Two patients achieved partial responses and four had stable disease. Median PFS1was 11.70±8.97 months. Median PFS2 was 5.36±1.47 months.There was one death (none treatment related). OS data are immature. No unexpected side effects were found in our study.Patients reported significantly greater reductions from baseline in the symptoms of cough, hemoptysis, chest pain and dyspnea (P<0.05 for all comparisons). **Conclusion:** Continuing EGFR-TKI in combination with super-selected systemic arterial infusion chemotherapybeyond progression for advanced NSCLC patients with EGFR mutation is feasible and warrent further investigation. **Keywords:** regional chemotherapy, EGFR positive mutation, EGFR-TKI, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-007 Prognostic Factors including EGFR Status in Advanced Lung Adenocarcinoma Patients Shunsaku Hayai, Hiroyuki Taniguchi, Yasuhiro Kondoh, Tomoki Kimura, Kensuke Kataoka, Toshiaki Matsuda, Toshiki Yokoyama *Respiratory Medicine and Allergy, Tosei General Hospital, Seto, Achi/Japan*

Background: Disease stage and performance status (PS) are the most widely accepted prognostic factors of non-small cell lung carcinoma. Several other features such as sex, age, histology, and health related quality of life (HRQOL) have also been reported as prognostic factors. Adenocarcinoma, especially EGFR mutation status, influences therapeutic strategy and prognosis. However, there have been few studies evaluating prognostic factors including activating EGFR mutation status focused on lung adenocarcinoma. This study aimed to clarify prognostic factors including EGFR status in advanced lung adenocarcinoma. **Methods:** From April 2010 to December 2014, patients diagnosed with lung adenocarcinoma were identified retrospectively. Stage ⅢB, StageⅣ and recurrent post-operative patients were included. A total of 95 patients with adenocarcinoma who was measured EGFR mutation status and completed the overall health related quality of life (HRQOL) item before receiving initial cytotoxic chemotherapy were included in the analysis. We evaluated HRQOL using EORTC QOL-C30 and LC-13 (European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire). The activating EGFR mutations consist of a deletion in exon 19 and a point mutation involving the replacement of leucine with arginine at codon 858 (L858R) in exon 21. EGFR mutation status, HRQOL scales, PS, age, sex, stage, data on Charlson comorbidity index, pulmonary function testing, and serum levels of white blood cells, haemoglobin, fibrinogen, calcium, alkaline phosphatases, lactate dehydrogenase were included in univariate and multivariate Cox proportional hazard analyses. **Results:** The median age was 67 years. Sixty one patients were men. Five patients had stage ⅢB , 76 had stage Ⅳand 14 were recurrent post-operative cases. Thirty two patients had activating EGFR mutation. Median survival time was 556 days. Global health status, Physical functioning, Role functioning, Social functioning, Fatigue scales of EORTC QOL-C30, Coughing scales of LC-13, EGFR mutation status, PS, Stage and serum levels of white blood cells, fibrinogen and albumin were associated with poor prognosis in univariate analyses. On multivariate analysis, Role functioning (HR: 0.988, 95% CI: 0.979-0.997), activating EGFR mutation (HR: 2.621, 95% CI: 1.401-4.906), female sex (HR: 2.158, 95% CI: 1.118-4.163) and stage (HR: 0.213, 95% CI: 0.090-0.501) were significantly predictors of survival. **Conclusion:** EGFR mutation status, Role functioning, sex and stage are significant and independent prognostic factors for survival in patients with advanced lung adenocarcinoma. **Keywords:** advanced lung adenocarcinoma, EGFR mutation, QOL, Prognostic factors

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-008 Efficacy and Tolerability Analysis of Icotinib in EGFR Mutation-Positive and Unknown Advanced NSCLC Patients from Eastern Coastal China Chuantao Zhang, Xiaomei Xu, Xiaofei Wang, Helei Hou, Chun Yan, Wenjun Yu, Airong Tan, Congmin Liu, Xiaofeng Cheng, Zijun Yu, Junshuai Liu, Xin Liu, Xiaochun Zhang *Medical Oncology, Qingdao Municipal Hospital, Qingdao University, Qingdao/China*

Background: The phase III clinical study (ICOGEN) showed that Icotinib has a similar efficacy and tolerability in Asian patients with advanced non-small cell lung cancer (NSCLC) compared with Gefitinib. This retrospective study aims to evaluate the efficacy and tolerability of the EGFR-TKI Icotinib in first-month effective (unknown EGFR mutation type) and EGFR mutation positive (exon 19 deletion or exon 21 L858R point mutation) advanced non-small-cell lung cancer patients group from Eastern Coastal China. **Methods:** In this retrospective, observational, and multicentric study, 342 Eastern Coastal Chinese patients from 5 centers in China with histologically confirmed stage IIIB/IV non-small-cell lung cancer were treated in Qingdao, China. The patients with performance status from 0 to 3 wrote informed consent, and then received the standard dose of Icotinib (125 mg three times daily) until disease progression or unacceptable toxicity between Aug, 2012 and Dec, 2013. The patients were divided into EGFR mutation positive group and First-month effective group. First-month effective group refers to those patients whose tissue sample was difficult to obtain for EGFR measure and were responsive to Icotinib for one month trial. The primary outcome was progression-free survival among patients who received at least first dose of study treatment and the patients are still in follow-up. **Results:** The disease control rate (DCR) at 4th month was 81.6% in first-month effective group (n=170) and 89.41% in EGFR mutation positive group (n=174). The median progression-free survival (PFS) is 13.0 months (95% CI 1.0-22.8m) in first-month effective group (n=170) and 13.9 months (95% CI 1.8-24.6m) in EGFR mutation positive group (n=174), respectively (P>0.05). The 1-year survival rate of overall patients is 65.5%, 54.70% in these groups. It is impressive that PFS from first-month effective group is similar with from EGFR mutation positive group. The characteristics of non-smoker, female gender, performance status 0 or 1 are associated with a significantly better prognosis in terms of disease control rate.The median overall survival (OS) was not reached in EGFR mutation positive patients and the first-month effective group patients. The most common treatment-related adverse events are rash (n=154[45.0%]), diarrhea (n=78[22.8%]) and increase in AST and ALT (n=61[18.12%]). Most of the drug-related adverse events are mild (grade I or II) and reversible with no grade IV toxicity. **Conclusion:** Icotinib is effective and well tolerated in advanced NSCLC patients. For those patients with unknown EGFR mutation status, Icotinib first-month effective regimen may be an optical treatment rather than standard first-line chemotherapy in the future. **Keywords:** EGFR, icotinib, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-009 EGFR Mutation and Brain Metastasis in Patients with Non Small Cell Lung Cancer Eun Kyung Cho, Min Young Baek, Hee Kyung Ahn, Shin Myung Kang, Inkeun Park, Young Saing Kim, Junshik Hong, Sun Jin Sym, Jinny Park, Jae Hoon Lee, Dong Bok Shin *Hematology and Oncology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon/Korea*

Background: It has been demonstrated that lung cancer is the most common cause of brain metastases(BM). This study was designed to analyse the association of timing and survival of BM according to histology and epidermal growth factor receptor (EGFR) mutation status in patients with metastatic nonsmall cell lung cancer (NSLCL). **Methods:** We retrospectively analysed the medical records of 268 patients with NSCLC in single center in Incheon, Korea who were tested for EGFR mutation analysis from January 2010 to August 2013. We analysed the cumulative incidence of BM regard to EGFR mutation status, the time from the diagnosis to the development of BM, the time from BM to death and median survival. Survival was estimated by the Kaplan-Meier method and compared with the log-rank test. **Results:** Out of 268 patients, 74 (28%) had BM, 54(73%) patients already at the time of diagnosis. Synchronous BM was more frequent in patient with EGFR mutation than WT EGFR patient (79% vs. 69%). But patients with metachronous BM, time to BM diagnosis was not significantly different according to EGFR status. (p=0.298) Among the 67 patients with BM, 25(37%) had mutations in EGFR, including 13 exon 19 deletions and 12 L858R mutations and 40 had WT (60%). The time from diagnosis of first brain metastases to death(BM-OS) was significantly longer in patient with EGFR mutation than WT (22.28 vs. 7.55 month, p<0.005). The BM-OS in EGFR mutated patients with synchronous BM was longer than in EGFR WT patients (25.42 vs. 8.86 month, p<0.005). But the BM-OS in EGFR mutated patients with metachronous BM was not significant different from WT EGFR patients. (p=0.16). **Conclusion:** NSCLC patients with EGFR mutations were more prevalent with synchronous BM than those with EGFR WT patients. EGFR mutation was associated with significantly longer survival from BM diagnosis, especially in those with synchronous BM.

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-010 Early Radiographic Response to TKI in Non Small Cell Lung Cancer with EGFR Mutations Carmen Salvador Coloma, Óscar Niño Gómez, Encarnación Reche Santos, Dilara Akhoundova, José Gómez Codina, Sarai Palanca, Joaquin Montalar, Óscar Juan Vidal *Medical Oncology, Hospital Universitari I Politècnic La Fe, Valencia/Spain*

Background: EGFR mutations have become an important target to choose a treatment for non-small cell lung cancer (NSCLC) patients. The response to chemotherapy is evaluated after the patient completes the second-third course of treatment. The response to tyrosine Kinase Inhibitor (TKI) could be observed in few days, the time for response evaluation is not well-defined. **Methods:** From January 2009 to November 2014, EGFR mutation status was analysed in 360 NSCLC patients' samples. 55 patients (15,3%) were EGFR mutation positive. Among the 55 patients, 40 patients who were stage IIIB-IV and had received treatment with either gefitinib 250 mg, erlotinib 150 mg or afatinib 40 mg once daily were included in this analysis. The principal aim was to correlate the early radiological response (ERR) to TKI by computed tomography (TC) with progressionfree survival (PFS) and overall survival (OS) in NSCLC patients with EGFR mutations and stage IIIB-IV disease. Secondary objectives were to correlate the TKI response with different EGFR mutations and to evaluate the safety and efficacy of TKI treatment. The PFS and OS were estimated by the Kaplan–Meier method with (SPSSv.19). The logrank test was used to assess significant differences betweengroups (p<0.05). **Results:** The clinic-pathologic characteristics of the 40 eligible patients are listed in table 1. The EGFR mutations identified were mainly exon 19 deletions (12 patients) and L858R point mutations (16 patients). Twentysix patients (65%) had ERR. Four patients with a partial response (PR) on early CT achieved a complete response (CR). The median followup time was 17 months (range 2-66 months). Among the 26 patients with ERR the median PFS was 11.8 months. The median PFS for patients with stable disease (SD) and progressive disease (PD) was 7.5 months. The overall logrank test for PFS, when comparing the groups of patients (ERR vs SD and PD) showed a significant difference (p<0.034). For patients with ERR the median OS was 20.1 months. The median OS for patients with SD and PD was 11.9 months. The overall logrank test for OS, when comparing the groups showed a significant difference (p<0.017).

Table 1: The clinic-pathologic characteristics

VARIABLES	NUMBER	%
Patients	40	100
Gender Male Female	19 21	47.5 52.5
Age (years) Median (range)	62 (40-85)	
Race European Others	38 2	95 5
Smoking Yes No Former smokers	9 22 9	22.5 55 22.5
Packs-year Median (range)	35.5 (5-185)	
PS 0 1 >2	14 22 4	35 55 10
Pathology diagnosis Adenocarcinoma Squamous Others	37 2 1	82.5 5 2.5
Stage IIIB IV	2 38	5 95
Number of prior chemotherapies 0 1-2 >2	17 20 3	42.5 50 7.5
TKI Erlotinib Gefitinib Afatinib	30 8 2	75 20 5

Conclusion: The ERR to TKI could be a predictive factor of PFS and OS in NSCLC with activating EGFR mutation. Patients with SD at the first evaluation should be followed closely because of the risk of early progression. **Keywords:** TKI, NSCLC, EGFR mutation, Early Radiographic Response.

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-011 Relationship between EGFR Mutation Status and Response to Specific Chemotherapeutic Agents in Patients with Stage IV Non-Small Cell Lung Cancer Vinicius Ernani, Monica S. Chatwal, Mukesh Kumar, Chao Zhang, Zhengjia Chen, Taofeek K. Owonikoko, Suresh S. Ramalingam *Emory University, Atlanta/GA/United States of America*

Background: The purpose of this study was to investigate whether outcomes with various chemotherapy regimens were affected by the specific epidermal growth factor receptor (EGFR) mutations in patients with stage IV non-small cell lung cancer (NSCLC). **Methods:** We retrospectively analyzed the association between the different EGFR mutations (exon 19 deletion, exon 21, and 18 mutations) and their response to chemotherapy. A total of 17 patients with stage IV NSCLC treated at Winship Cancer Institute of Emory University between January 2007 and February 2015 who received chemotherapy were investigated retrospectively, and their clinical date were assessed according to EFGR mutation. **Results:** 14 (82.4%) females and 3 (17.6%) males were identified harboring EGFR mutations. Median age at the time of diagnosis was 66 years (SD 14.08). 12 patients (70.6%) were never smokers, and 5 (29.4%) were former or current smokers. EGFR exon 19 deletion was present in 7 patients (41.2%), exon 21 mutation in 8 (47.1%), and exon 18 in 2 (11.8%). 15 (88.2%) received chemotherapy, and 11 (64.7%) received pemetrexed-based treatment. Four patients had partial response (PR) as the best response to pemetrexed-based chemotherapy, and all of them harbored exon 21 mutation. Among patients that received other types of chemotherapies (paclitaxel, gemcitabine, navelbine and platinum), 6 with exon 21 mutation, and 2 with exon 19 deletion experienced PR. Progression-free survival (PFS) was not significantly different among the groups of mutation (p=0.3645) that received paclitaxel, gemcitabine, navelbine and platinum as chemotherapies, and PFS was also not different for pemetrexed-based regimen (p=0.4569). **Conclusion:** We did not find differential sensitivity to various chemotherapy agents based on mutation type in advanced NSCLC patients harboring an EGFR mutation. **Keywords:** stage IV, NSCLC, EGFR mutation, Chemotherapy response

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-012 Clinical Implications of Isolated Bone Failure without Systemic Disease Progression During EGFR-TKI Treatment Ji An Hwang[1], Eun Young Kim[1], Chang-Min Choi[2], Dae Ho Lee[3], Sang-We Kim[3], Jung-Shin Lee[3], Woo Sung Kim[2], Joon Seon Song[4], Jae Cheol Lee[3] [1]*Department of Pulmonology, Severance Hospital, Yonsei University College of Medicine, Seoul/Korea,* [2]*Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul/Korea,*[3]*Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul/Korea,* [4]*Department of Pathology, Asan Medical Center, University of Ulsan College of Medicine, Seoul/Korea*

Background: Bone metastasis and skeletal-related events (SREs) such as pathologic fracture and spinal cord compression are common in advanced lung cancer. This study was aimed to investigate the characteristics of disease progression focused on SREs during EGFR-TKI treatment. **Methods:** We retrospectively reviewed the medical records of 3,085 Korean patients with advanced non-small cell lung cancer who were treated with gefitinib or erlotinib between 2004 and 2014. SRE associated with aggravation of bone metastasis was termed 'bone failure (BF)'. BFs were classified into 2 categories according to the presence of accompanying disease progression of preexisting cancer lesions in extra-skeletal organs; isolated bone failure (IBF) versus non-IBF. **Results:** The incidence of SREs during EGFR-TKI treatment was 4.7% (146/3085). Among them, 60 patients experienced IBF without aggravation of disease in extra-skeletal organs. IBF was more

frequent in clinical benefit group (responders and stable ≥ 6 months) than in non-clinical benefit group (53.5% vs 13.3%; P < 0.001). Adenocarcinoma histology and clinical benefit from EGFR-TKI were independent risk factors for IBF (adenocarcinoma: adjusted hazard ratio [HR] 10.283; 95% confidence interval [CI] 1.148 – 92.121; P= 0.037, clinical benefit from TKI: adjusted HR 9.463; 95% CI 3.027 – 29.584; P < 0.001). The time from the start of EGFR-TKI to the occurrence of SRE was significantly longer in IBF than that in non-IBF (9.8 vs 5.2 months; P= 0.054). Moreover, patients with IBF exhibited longer survival time from the initiation of TKI (20.1 vs 7.7 months; P = 0.008) and from the occurrence of SRE (9.2 vs 1.9 months; P = 0.006). Multivariate analysis showed that IBF was one of independent prognostic factors for better survival although the statistical significance was marginal (adjusted HR 0.492; 95% CI 0.237 – 1.021; P = 0.057). **Conclusion:** IBF without systemic disease progression frequently occurs in patients with clinical benefits from EGFR-TKI treatment and shows the better survival requiring more active treatment.
Keywords: skeletal-related event, Epidermal growth factor receptor, tyrosine kinase inhibitor, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-013 Association of PK/PG with Toxicity of Gefitinib in Patients with Advanced NSCLC
Takashi Hirose[1], Ken-Ichi Fujita[2], Sojiro Kusumoto[3], Yasunari Oki[3], Yasunori Murata[3], Tomohide Sugiyama[3], Hiroo Ishida[3], Takao Shirai[3], Masanao Nakashima[3], Toshimitsu Yamaoka[2], Kentaro Okuda[3], Tohru Ohmori[2], Yasutsuna Sasaki[2], Atsuhisa Tamura[1], Ken Ohta[1] [1]*Department of Respirology, NHO Tokyo National Hospital, Tokyo/Japan,* [2]*Inst Molecular Oncology, Showa University, Tokyo/Japan,* [3]*Division of Respiratory & Allergology, Showa University School of Medicine, Tokyo/Japan*

Background: Gefitinib is a potent epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) and is a key drug for patients with advanced non-small cell lung cancer (NSCLC) harboring EGFR mutation. The orally administered gefitinib showed large interindividual variability in its pharmacokinetics. Some phase I studies have suggested there is a relationship between gefitinib plasma concentration and skin toxicity, diarrhea, and liver toxicity. The aim of this study was to evaluate the association of pharmacokinetics or pharmacogenomics with toxicity or effectiveness of gefitinib in patients with advanced NSCLC. **Methods:** The evaluation of pharmacokinetics was performed using sample obtained on day 1 at 0, 1, 3, 5, 8, 24 hour and day 8 and day 15 after start of gefitinib 250mg administration. Plasma concentration of gefitinib was analyzed by high-performance liquid chromatography. The genotypes of *ABCG2, ABCB1, ABCC2, CYP3A4, CYP3A5, CYP2D6* were analyzed by direct sequencing. **Results:** Thirty-five patients with advanced NSCLC (14 men and 21 women; median age, 72 years; range, 53 to 90 years) were enrolled. All patients were stage IV adenocarcinoma harboring EGFR mutation: 18 had exon 19 deletions, 16 had exon 21 L858R, and 1 had exon 18 G719A. The overall response rate was 82.9% (95% confidence interval 66.4-93.4%). The median survival time was 21.2 months, and the median progression-free survival time was 10 months. The common adverse events were rash or acne (68%), diarrhea (46%), and liver injury (63%). One patient died of drug induced interstitial lung disease (ILD). The median area under the plasma concentration-time curve of gefitinib estimated from 0 to 24 hour (AUC0-24) was 10.9 (1.5-31.3) μM·h. The peak plasma concentrations (Cmax) was achieved 5 hour after dosing, and the median was 0.84 (0.38-1.74) μM. There were no statistically significant association of pharmacokinetics or pharmacogenomics with response rate, survival, and toxicity, such as skin toxicity, diarrhea, liver injury, and ILD of gefitinib. However, one patient died of drug induced ILD showed the highest AUC and Cmax. **Conclusion:** The elevated gefitinib exposure could be associated with drug-induced ILD. Further studies of the association of pharmacokinetics or pharmacogenomics with toxicity of EGFR-TKI are needed.
Keywords: gefitinib, pharmacokinetics, pharmacogenomics

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-014 EGFR Tyrosine Kinase Inhibitor and Chemotherapy in EGFR Mutation-Positive Non-Small Cell Lung Cancer
Kazumi Nishino[1], Madoka Kimura[2], Takako Inoue[2], Junji Uchida[1], Toru Kumagai[1], Fumio Imamura[1] [1]*Department of Thoracic Oncology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka/Japan,* [2]*Thoracic Oncology, Osaka Medical Center for Cancer and Cardiovascular Diseses, Osaka/Japan*

Background: Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) are recommended in the first-line setting for patients with EGFR mutation-positive non-small cell lung cancer (NSCLC). However, it remains unclear whether frontline EGFR TKIs are better strategy than first-line chemotherapy in EGFR-mutant patients. Generally, EGFR-TKIs had no significant benefits in overall survival (OS) compared with chemotherapy in both first-line and second-line setting. This retrospective study compared survival benefits in patients treated with post-TKI chemotherapy and first-line chemotherapy controls. **Methods:** This retrospective study included 442 EGFR-mutant patients in our institute. We examined EGFR gene status from 2007 to 2015. The patients treated from 1999 to 2015. The study group contained 173 patients treated with first-line EGFR-TKI and the control group contained 109 patients who received EGFR-TKI after first-line chemotherapy. The overall survival (OS) was assessed. **Results:** There was no significant difference between first-line chemotherapy and EGFR-TKI in OS for patients with mutation-positive NSCLC (median OS; 43 vs. 38 months, P = 1.645). There was substantial difference in OS between patients with postoperative recurrence and those with III/IV stage disease. Among patients with III/IV stage NSCLC, median OS was 40.8 months in first-line chemotherapy group, 30.5 months in chemotherapy after frontline EGFR-TKI group and 21.1 months in only EGFR-TKI group. **Conclusion:** In EGFR-mutant patients, both EGFR-TKI and chemotherapy improve the survival. Among patients with advanced NSCLC, EGFR-TKI after first-line chemotherapy may improve survival than frontline EGFR-TKI. These findings need to be validated in further randomized trials.
Keywords: EGFR mutation, EGFR-TKI, chemotherapy, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-015 The Management of Brain Metastases in Patients with EGFR Mutated Advanced Non-Small Cell Lung Cancer
Noelle O'Rourke[1], Christine M.N. Gray[2], Aishah Coyte[3], Carolyn Featherstone[2] [1]*Clinical Oncology, Beatson Cancer Centre, Glasgow/United Kingdom,* [2]*Beatson Cancer Centre, Glasgow/United Kingdom,* [3]*Glasgow Royal Infirmary, Glasgow/United Kingdom*

Background: Brain metastases (BM) are common in non-small cell lung cancer (NSCLC). They are often associated with significant impairment of quality of life and a poor prognosis. Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) have proven superior to chemotherapy in patients with advanced NSCLC that harbour an EGFR mutation.They are now standard of care as first line treatment. Many studies, however, have excluded patients with BM. Therefore the best treatment modality for these patients remains unknown. Different treatment options include: surgery, whole brain radiotherapy (WBRT), radiosurgery, chemotherapy and TKIs. This report looks at the outcomes of patients with EGFR mutated lung cancer and BM who have undergone different treatment modalities. **Methods:** The West of Scotland Network for Lung Cancer supports over 2,000 lung cancer patients per year. We collected data on patients diagnosed with EGFR mutated lung cancer between 2012 and 2014. Patients had to have radiological evidence of BM either at time of diagnosis or subsequently. Patient demographics were recorded alongside response to different treatment modalities. Outcomes included progression free survival and overall survival. **Results:** Between 2012 and 2014, 117 patients were diagnosed with EGFR mutated lung cancer. Eleven patients had confirmed BM: 10 women, 1 man, ages 48-83 years (median 62). Nine patients had BM at presentation, one developed BM while on erlotinib and another had BM on relapse post lobectomy. The median overall survival was 28 weeks (range 10-96). Three patients remain alive at 55, 64 and 139 weeks post diagnosis. Three patients were treated with erlotinib alone. Two remain alive 64 and 55 weeks from diagnosis. The first has controlled intra and extra cranial disease, whilst the other had extracranial progression at 49 weeks. The third patient only survived 22 weeks. Three patients had WBRT, two with erlotinib. Overall survival was 19 weeks without erlotinib and 34 and 42 weeks with erlotinib. A separate patient developed BM while on erlotinib and underwent WBRT. She survived a further 13 weeks from diagnosis of BM and had an overall survival of 96 weeks. One patient achieved stable extracranial disease for 81 weeks with erlotinib. At 16 weeks, however, there was progression of an isolated BM. She underwent radiosurgery with a single 20Gy fraction and on subsequent scans has stable intracranial disease 67 weeks post radiosurgery. She remains alive 139 weeks post diagnosis. Finally, two patients received no active treatment and died at 10 and 18 weeks post diagnosis. **Conclusion:** There is currently little trial data to guide our treatment decisions in patients with EGFR mutated lung cancer and BM. In our group only 9% of patients with EGFR mutated NSCLC had BM. They underwent a variety of treatment modalities, however, numbers are too small to draw firm conclusions. Without treatment, or with WBRT alone, survival is similar to patients with advanced non EGFR mutated NSCLC. The use of a TKI either with or without radiotherapy appears to have a prolonged survival and is probably the treatment of choice. Of note, no patient in this group had a change in TKI.
Keywords: EGFR mutation, brain metastases, Tyrosine kinase inhibitors, non small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-016 BPI-7701, a Covalent Mutant-Selective EGFR Inhibitor, Inhibits the Growth of NSCLC Lines with EGFR Activating and T790M Resistance Mutations
Victoria L. Wilde, Don X. Zhang, Jirong Peng, Michael N. Greco, Michael A. Green, Michael J. Costanzo *Research & Development, Beta Pharma Usa, Inc., Princeton/NJ/United States of America*

Background: First generation EGFR TKIs, erlotinib, gefitinib and icotinib, have shown excellent clinical efficacy in non-small-cell lung cancer (NSCLC) patients with activating EGFR mutations. However, patients eventually progress due to acquired resistance in the form of a T790M point mutation. This mutation occurs in about 50-60% of EGFR TKI treated patients. Second generation, irreversible EGFR TKIs, afatinib and dacomitinib, express even higher kinase potency in the activating mutation as well as potency against the acquired resistance mutation. Clinical efficacy of these TKIs is reduced due to the dose limiting toxicities of the drugs, attributed to wild type EGFR potency of the compounds. In order to improve clinical efficacy against the activating and double mutant EGFR tumor cells, it is important to build in selectivity against wild type EGFR to avoid dose-limiting toxicities. Here, we present BPI-7701, a novel EGFR inhibitor with high potency against the activating mutant EGFR and the T790M resistance mutation with good selectivity over wild type EGFR. **Methods:** BPI-7701 was evaluated in biochemical and *in vitro* assays against mutant EGFR (L858R, del ex19, del ex19/T790M) and WT EGFR.*In vivo* anti-tumor activity was evaluated in xenografts of HCC827 (del ex19) and H1975 (del ex19/T790M) NSCLC cells. **Results:** Biochemical assays showed that BPI-7701 inhibited del ex19 and L858R mutant EGFR, as well as the T790M resistance mutation of EGFR at IC_{50} values lower than that of WT EGFR, showing an ~100-fold difference in activity. BPI-7701 showed growth inhibition of PC-9 (del ex19), HCC827 (L858R) and H1975 (del ex19/T790M) cells in vitro, with IC_{50}values of 11-160 nM. BPI-7701 showed an IC_{50} value of 1.25 μM against A431, wild type EGFR epithelial cells. *In vivo*, BPI-7701 showed greater than 90% inhibition of pEGFR at tested doses as low as 6.25 mpk in nude mice. pEGFR inhibition was dose-dependent and was maintained over

the course of 24 hours. In mouse xenograft studies, BPI-7701 induced complete tumor regression in H1975 (del ex19/T790M) and HCC827 (L858R) NSCLC cell lines after 14-day repeat dose treatment. In an H1975 xenograft model, complete tumor regression occurred after 6 days of BPI-7701 treatment (14-day regimen), with 80% of mice remaining tumor-free 35 days after the completion of BPI-7701 dosing. **Conclusion:** BPI-7701 inhibits the growth of NSCLC cells with EGFR mutations and T790M resistance mutation, both *in vitro* and *in vivo*. BPI-7701 may be an excellent option for NSCLC patients with activating EGFR mutations. Clinical trials are planned to begin Q2 2016 in Asia. **Keywords:** NSCLC, EGFR, T790M

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-017 Genetic Variations in the EGFR Gene Predicts Outcome in Advanced NSCLC Patients Treated with Erlotinib Anne Winther Larsen[1], Peter H. Nissen[1], Kristine R. Jakobsen[1], Christina Demuth[1], Boe S. Sorensen[1], Peter Meldgaard[2]
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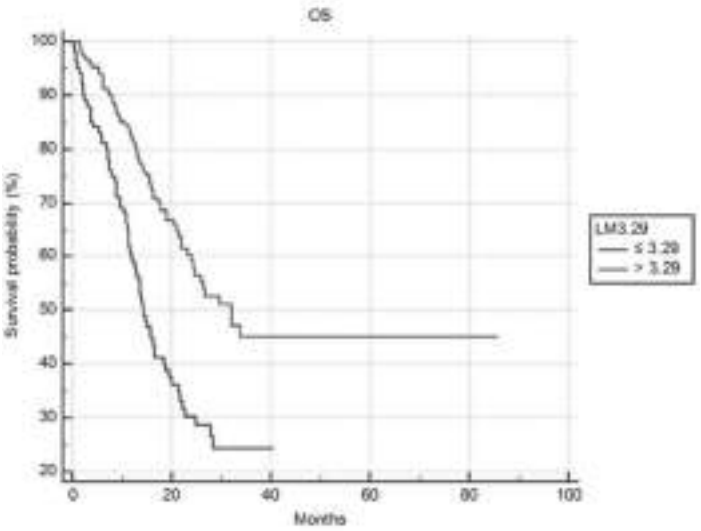
Background: Genetic variations in the epidermal growth factor receptor (EGFR) gene may alter protein expression or function and influence response to tyrosine kinase inhibitors. This study evaluates the role of genetic polymorphisms in the EGFR gene in advanced non-small cell lung cancer (NSCLC) patients treated with erlotinib. EGFR mutation status was known for all patients. **Methods:** Genotypes for -216G>T, -191C>A and 181946C>T in the EGFR gene were retrospectively evaluated by DNA sequencing and polymerase chain reaction in 354 Caucasian patients with advanced NSCLC. Hundred and seven of the patients had a somatic EGFR mutation, and all patients had been treated with erlotinib. Genotypes were correlated with clinical characteristics and outcome. A multivariate analysis was conducted adjusting for clinical relevant factors, including EGFR mutation status, using Cox proportional hazards model. A subgroup analysis was performed based on the EGFR mutation status. **Results:** Patients harboring at least one variant T allele (CT or TT) at position 181946 had a significantly longer median progression-free survival (PFS) (5.6 versus (vs.) 2.9 months; p =0.032) and overall survival (OS) (8.3 vs. 6.7 months; p=0.032) compared to patients with the CC genotype. The result remained significant in a multivariate analysis; PFS, adjusted hazard ratio (AHR)=0.73 (95% confidence interval (CI): 0.55-0.98); OS, AHR=0.72 (95%CI: 0.54-0.97). Patients carrying -216GT or TT genotypes showed a trend to a better clinical outcome compared to those with the GG genotype. The -216GT or TT and 181946CT or TT combined genotypes showed an even more pronounced association with clinical outcome compared to patients with the -216GG and 181946CC genotype (PFS, AHR=0.66 (95%CI: 0.44-0.98); OS, AHR=0.58 (95%CI: 0.38-0.87)). A subgroup analysis demonstrated that the association might be most relevant in EGFR mutation-positive patients; PFS, AHR=0.27 (95% CI: 0.11-0.68); OS, AHR=0.33 (95% CI: 0.13-0.83). **Conclusion:** A combination of 181946C>T and -216G>T polymorphisms in the EGFR gene seems to be a potential predictor of longer PFS and OS in advanced NSCLC patients treated with erlotinib; especially in EGFR mutation-positive patients. A prospective randomized study is wanted to confirm our data. **Keywords:** EGFR, TKI, genetic polymorphisms, survival

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-018 Baseline Lymphocyte-Monocyte Ratio Is a Prognostic Marker in EGFR Mutant NSCLC Patients Receiving First Line EGFR TKIs Yu-Mu Chen, Meng-Chih Lin, Wen-Feng Fang, Chien-Hao Lie, Huang-Chih Chang, Chin-Chou Wang *Pulmonary and Critical Care Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City/ Taiwan*

Background: Patients with higher lymphocyte to monocyte ratio (LMR) has shown to have favorable prognostic in early stage lung cancer, non-metastatic renal cell carcinoma, gastric cancer, colon cancer, pancreatic cancer and breast cancer. However, prognostic significance of LMR in patients with advanced stage, epidermal growth factor receptor (EGFR) mutant non-small cell lung cancer receiving first line EGFR tyrosine kinase inhibitors is not well known. We conducted a retrospective analysis to investigate the influence of baseline LMR on clinical outcomes including progression free survival (PFS) and overall survival (OS) in EGFR mutant NSCLC patients. **Methods:** This retrospective study evaluated 253 patients harboring EGFR mutation received TKIs as first line therapy for advanced NSCLC between January 2011 and October 2013. The cut- off value determined by Receiver operating characteristic (ROC) curves for LMR was 3.29. Patients were divided into high and low LMR ratio based on above cut-off level. Kaplan–Meier analysis was used for PFS and OS estimation; and the log-rank test was utilized to examine the significance of the differences of survival distributions between groups. **Results:** Among 253 patients mean age was 65.2 years, 41% were male, medium PFS was 10.3 months, medium OS was 22 months. Low baseline LMR patients had shorter PFS (low vs. high: 8.2 vs 11.6m, HR: 1.508, p=0.003), and OS (low vs. high: 14.3m vs. 32.1m HR: 2.23, p<0.001)



Conclusion: Our results suggest baseline LMR is a prognostic marker for EGFR mutant NSCLC patients receiving first line EGFR-TKIs. **Keywords:** Lymphocye to monocyte ratio, prognostic factor, Non-small-cell lung cancer, EGFR mutation

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-019 Effect of EGFR Mutation Status on Graded Prognostic Assessment for Non-Small Cell Lung Cancer and Brain Metastases Yu Yang Soon[1], Huili Zheng[2], Nesaretnam B. Kumarakulasinghe[3], Wee Yao Koh[1], Cheng Nang Leong[1], Brandon Pang[4], Atasha Asmat[5], Ross Soo[3], Ivan Tham[1] [1]*Radiation Oncology, National University Cancer Institute Singapore, Singapore/Singapore,* [2]*Health Promotion Board, Singapore/Singapore,* [3]*Medical Oncology, National University Cancer Institute Singapore, Singapore/Singapore,* [4]*Pathology, National University Hospital, Singapore/ Singapore,* [5]*Cardiothoracic Surgery, Tan Tock Seng Hospital, Singapore/Singapore*

Background: The aim of this study is to refine the existing lung cancer graded prognostic assessment (GPA) index by analysing a cohort of patients with non-small cell lung cancer (NSCLC) tested for epidermal growth factor receptor (EGFR) mutation status and newly diagnosed brain metastases. **Methods:** We used the pathology registries of two institutions to identify 259 eligible patients diagnosed with brain metastases secondary to NSCLC between 2006 and 2014. We linked the electronic medical records of these patients to the National Death Registry. Survival is defined as from date of first treatment for brain metastases or date of brain metastases diagnosis for patients on best supportive care till death. We analysed the prognostic factors significant for survival by multivariate Cox regression and recursive partitioning analysis (RPA). **Results:** Significant prognostic factors identified by multivariate Cox regression and RPA were age, Karnofsky performance status (KPS), presence of extra-cranial metastases (ECM), number of brain metastases (BM) and presence of sensitizing EGFR mutations. Patients who were age 70 years old and above (Hazard ratio (HR) 1.47, 95% confidence interval (CI) 1.07-2.01, reference (ref) age < 70 years old); with KPS score 70-80 (HR 2.37, 95%CI 1.69-3.34, ref KPS 90-100); with KPS score < 70 (HR 4.34, 95%CI 2.90-6.51, ref KPS 90-100); ECM present (HR 1.82, 95%CI 1.27-2.62, ref no ECM); having two or more BM (HR 1.40, 95%CI 1.01-1.95, ref less than two BM) and absence of sensitizing EGFR mutations (HR 1.97, 95%CI 1.49-2.61, ref sensitizing EGFR mutations present) were poor prognostic factors. There was a robust separation of survival curves between GPA score 0-1.0 (median survival (MS) 2.1 months), GPA score 1.5-2.0 (MS 6.3 months) and GPA score 2.5-3.0 (MS 14.1 months). The proposed modified GPA index is shown in below table.

Proposed modified GPA index			
Prognostic factors / score	0	0.5	1.0
Age Group	≥70 years old	<70 years old	-
KPS	<70	70-80	90-100
ECM	Present	-	Absent
No. of BM	≥2	0-1	
Sensitising EGFR mutations	Absent	-	Present

Conclusion: EGFR mutation status is a significant prognostic factor and should be considered in the design of lung-cancer GPA index. The proposed modified GPA index need to be validated with an independent dataset. **Keywords:** non-small cell lung cancer, EGFR mutation, brain metastases

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-020 Clinical Differences of EGFR Mutations in Exon 19 and 21 in Clinical Course of Non-Small Cell Lung Cancer Patients Tae Won Jang, Maanhong Jung, Chul H. Oak, Sung J. Nam *Kosin University Medical College, Pusan/Korea*

Background: In patients with non -small cell lung cancer (NSCLC), mutations in the epidermal growth factor receptor (EGFR) have been associated with sensitivity to EGRF-tyrosin kinase inhibitors (TKIs). However, clinical course of EGFR mutation subtypes are still controvertial. The aim of this study was to analyze clinical features between EGFR mutation exon 19 and 21, including treatment with EGFR-TKIs **Methods:** In patients with NSCLC, EGFR exon 19 deletion mutations and EGFR L858R point mutations were analyzed by DNA sequencing method or pyrosequencing method from paraffin blocks of tissue obtained before treatment. We reviewed clinical characteristics of the patients, retrospectively. **Results:** One hundred and sixty seven patients displayed EGFR mutations in exon 19 and exon 21 from October 2002 to December 2013. 63.6% (n=100) had EGFR 19 deletion, whereas 36.3 % (n=67) had an EGFR L858R mutation. There were no differences in sex, smoking, ECOG status, stages, blood chemistry, tumor marker, and overall survivals (OS) between two groups. Overall survival was similar in both groups. However, OS was longer in non-smoker (p=0.000), female (p=0.007), and age ≥ 65 (p=0.031) only in 19 deletion group. After treatment with gefitinib (n=74), erlotinib (n=31), and afatinib (n=2), patients with EGFR mutations had a median overall survival of 47 month. Among the patients treated with gefitinib or erlotinib, gefitinib treated patients had significantly longer progression free survival (PFS) than erlotinib treated patients in EGFR exon 19 deletions (10.3 versus 5.1 months; p=0.002), but not in exon 21 mutation. The median PFS of the patients with higher body surface area (BSA, ≥1.5 m^2) was worse than that of those with lower BSA (3.9 vs. 8.9 month; p=0.063) in exon 21 mutation group. **Conclusion:** There are different clinical course between types of *EGFR* exon 19 and 21 mutations. We need confirmation in a prospective study and have to more elucidation of the biological mechanisms of the differences between the two major EGFR mutations.
Keywords: lung cancer, Prognostic factors, Epidermal growth factor receptor

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

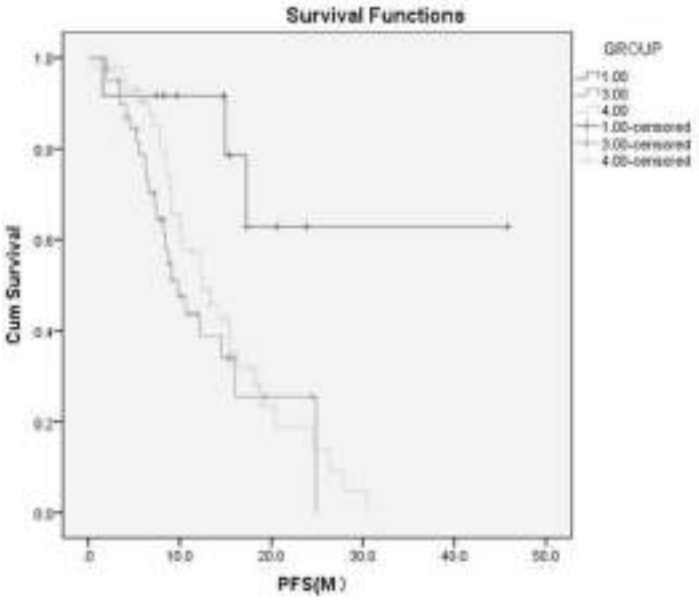
P2.01-021 Non-Inferior Progression Free Survival in NSCLC Patients Sensitive to EGFR TKI Receiving Low Dose versus Regular Dose of Gefitinib or Erlotinib Hsing-Chun Chen, Shu-Lan Hsu, Kuo-Sheng Fan, Chun-Liang Lai
Buddhist Dalin Tzu Chi Hospital, Chia-Yi/Taiwan

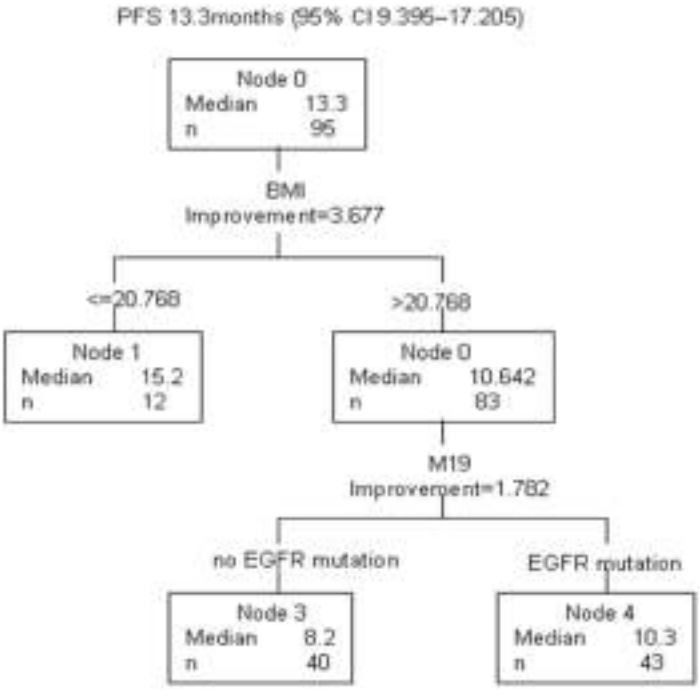
Background: Preclinical data demonstrate that the T790M clone is associated with a growth disadvantage in the absence of TKI selection. With selection stress of standard dose of TKI, T790M cells may become a dominant population. In a mathematical model, high pulse dose combined with continuous low-dose of TKI could delay the emergence of resistant clone of T790M. Clinically, some patients use lower dose of EGFR TKI due to various reasons such as toxicity. The treatment outcome in terms of PFS in this group of patients has not been reported. Whether the PFS would be impaired due to dose adjustment or unaffected and even better to support above theory may need further clarification. **Methods:** A retrospective cohort study was conducted to recruit patients with advanced NSCLC from 1997/1 to 2014/12 in a regional teaching hospital. Inclusion criteria were patients whose tumors were either tested to have sensitizing mutations of EGFR using highly sensitive methods or clinically responsive to EGFR TKI using Jackman's criteria. Patients having titrated dose of TKI to two-thirds or less for more than 6 months were assigned to low-dose (LD) group. The standard-dose (control) group includes patients receiving daily 250 mg of Gefitinib or 150 mg of Erlotinib during whole course of treatment, matched with sex and age to LD group. The primary outcome was PFS. Secondary outcome was overall survival (OS). **Results:** LD group includes 20 patients and control group 80 patients. Patients using LD treatment were mostly due to intolerable side effects with standard dose (n=18, 90%). The median PFS was 15.4 months in the LD group and 9.3 months in control (hazard ratio 0.45, 95% CI of 0.29-0.71; p=0.018). The median OS was 31.5 months in LD and 31.4 months in control (hazard ratio 0.99, 95% CI 0.49-1.98; p=0.98). In the subgroup of Gefitinib treatment, the median PFS was 17.9 months in LD and 8.1 months in control (hazard ratio 0.35, 95% CI 0.19-0.62; p=0.0037). In patients receiving Erlotinib, median PFS was 15.3 months in LD and 12.1 months in control (hazard ratio 0.67, 95% CI 0.33-1.37; p=0.2652). Median OS was similar in LD and control in either subgroup of Gefitinib or Erlotinib. **Conclusion:** This study showed that lower dose of EGFR-TKI treatment is a non-inferior strategy for patients sensitive to EGFR TKI. Better PFS in the LD group of Gefitinib-treated patients support the theory of delayed emergence of resistant clone. Since 150 mg of Erlotinib is at its maximum tolerated dose, a dose choice of no more than optimum biologic dose may be needed to gain such benefit as Gefitinib. Larger-scale studies would be needed to confirm this finding.
Keywords: gefitinib, Erlotinib, low dose, optimum biologic dose

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-022 BMI as Factor Predicting the Efficacy of Gefitinib in NSCLC with EGFR Mutation Sun Hongyan[1], Sun Xiaoteng[2], Zhai Xiaoyu[3], Guo Jingfeng[4], Liu Yutao[3], Ying Jianming[5], Wang Ziping[3] [1]*General Internal Department, Ling Nan Hospital, the Third Affiliated Hospital, Sun Yat-Sen University,, Guangzhou/China,* [2]*Department of Pathology, Rushan County People'S Hospital, Shandong/China,* [3]*Department of Medical Oncology, Cancer Institute (Hospital), Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing/China,* [4]*Hexian Affiliated Memorial Hospital of Southern Medical University, Guangzhou/China,* [5]*Department of Pathology, Cancer Institute (Hospital), Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing/China*

Background: Many randomized clinical trials have demonstrated that epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) are advantageous over standard chemotherapy either as front-line treatment or as further management of patients with EGFR mutation-positive non-small-cell lung cancer (NSCLC). But which subgroup of patients with EGFR mutation-positive advanced NSCLC could benefit more from EGFR-TKIs needs to be further explored. In the present study, we attempted to explore predictive factors in such cohorts of patients who received gefitinib by classification and regression tree (CART) analysis. **Methods:** Included in this study were 95 patients with EGFR mutation-positive advanced NSCLC who received gefitinib treatment at the Cancer Institute (Hospital) of the Chinese Academy of Medical Sciences between February 2010 and October 2013. Multivariate analysis of progression-free survival (PFS) was performed using recursive partitioning referred to as CART analysis to assess the effect of specific variables on PFS in subgroups of patients with similar clinical features. **Results:** The median PFS in patients with EGFR mutation-positive advanced NSCLC who received gefitinib treatment was 13.3 months (95% CI 9.4-17.2). CART analysis showed an initial split on body mass index (BMI), based on which three terminal subgroups were formed. The median PFS in the three subsets ranged from 8.2 months to 15.2 months, in which the subgroup with a BMI less than or equal to 20.768Kg/m2 had the longest PFS (15.2 months). In addition, PFS in EGFR exon 19 mutation group was better than that in other mutation site group (10.3 vs. 8.2 months). **Conclusion:**BMI and exon 19 mutation are predictors of PFS in patients with EGFR mutation-positive advanced NSCLC who received gefitinib treatment. Both active EGFR mutation and patient's own factors could be used to predict the therapeutic efficacy of EGFR-TKIs.





Keywords: classification and regression tree (CART), non-small-cell lung cancer (NSCLC), EGFR active mutation, body mass index (BMI)

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-023 Intercalated Therapy with Gemcitabine, Cisplatin and Erlotinib May Be Superior to TKI Alone for Patients with Advanced EGFR Mutated NSCLC

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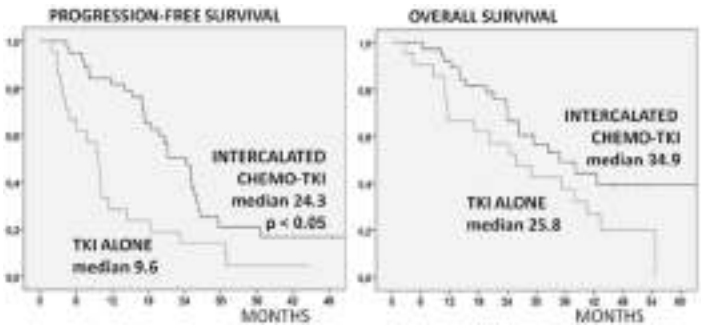
Background: The biological rationale for intercalated therapy in EGFR mutated NSCLC is to derive benefit both from cytotoxic and from targeted therapy, avoid their mutual antagonism, and prevent tumor repopulation during intervals of cytotoxic treatment. After a promising report from a single-arm trial of intercalated treatment (Zwitter et al, Radiol Oncol 2014;48:361), we here present a comparison to treatment with TKI alone on a similar population of patients. **Methods:** All patients were treatment-naive with metastatic EGFR mutated NSCLC, were in fair general condition and fulfilled the standard criteria for platin-based chemotherapy. Patients in the intercalated group joined a prospective clinical trial and signed informed consent. Treatment consisted of gemcitabine at 1250 mg/m2 on days 1 and 4, cisplatin at 75 mg/m2 on day 2 and erlotinib 150 mg on days 5 – 15 of a 3-weekly cycle for 4 to 6 cycles, followed by continuous erlotinib as maintenance. Due to reluctance of their physicians to join the intercalated trial, patients in the TKI alone group were treated with erlotinib or gefitinib as the standard treatment. **Results:** Regarding demographics and main prognostic factors, there was a slight disbalance in favor of the TKI alone group (Table). The intercalated trial recruited 38 patients. Treatment was well tolerated, with 6 cases of grade 4 toxicity. Complete or partial response was seen in 16 and 17 patients, respectively, for response rate of 87%. For 21 patients on TKI alone as standard treatment, precise evaluation of response was not feasible. Median time to progression was 24.3 months and 9.6 months ($p < 0.05$), and median survival was 34.9 and 25.8 months for the intercalated and TKI alone group, respectively.

	TKI alone 21 patients	Intercalated schedule 38 patients
Gender, Female/Male	13/8	21/17
Age, median	63	61
Age, range	42 – 70	37 – 74
Performance status, 0 - 1	18	30
Performance status, 2 – 3	3	8
Brain metastases at diagnosis	5	13



Conclusion: In advanced EGFR mutated NSCLC, intercalated schedule appears superior to TKI alone. These observations should be confirmed in a randomized trial.
Keywords: chemotherapy, NSCLC, EGFR, TKI

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-024 An ENSURE Extension Study to Evaluate 2nd Line Erlotinib and Gemcitabine/Cisplatin Cross-Over Treatment for EGFR-Mutant Chinese NSCLC Patients

Yi-Long Wu[1], Lei Chen[2], Caicun Zhou[3], Shun Lu[4], Yunzhong Zhu[5], Shukui Qin[6], Gang Wu[7], Ying Cheng[8], Baohui Han[9], Houjie Liang[10], Cheng Huang[11], Zhaoyang Zhong[12] [1]*Guangdong Lung Cancer Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou/China,* [2]*Medical College, Cancer Hospital of Shantou University, Shantou/China,* [3]*Department of Medical Oncology, Shanghai Pulmonary Hospital, Tongji University; Tongji University Medical School Pulmonary Cancer Institute, Shanghai/China,* [4]*Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China,* [5]*Oncology Department, Beijing Chest Hospital, Beijing/China,* [6]*The 81St Hospital of PLA, Nanjing/China,* [7]*Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan/China,* [8]*Thoracic Oncology, Jilin Provincial Cancer Hospital, Changchun/China,* [9]*Department of Pulmonary Medicine, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China,* [10]*10. Affiliated Xinan Hospital of Third Military Medical University, Chongqing/China,* [11]*Fujian Cancer Hospital, Fuzhou/China,* [12]*Third Affiliated Hospital of Third Military Medical University, Chongqing/China*

Background: ENSURE study shows that 1st line treatment with erlotinib provides longer PFS over gemcitabine/cisplatin (GP) for stage IIIB/IV NSCLC patients with EGFR mutations. Cross-over treatments after progression of disease (PD) was allowed in ENSURE study. However, post-study treatments might have significant impact on patient survival or other clinical benefits, which is insufficiently investigated. This trial in an extension of the ENSURE study, intended to evaluate PFS in 2nd line progression after cross-over treatments in ENSURE. **Methods:** Chinese patients who had PD after 1st line treatment in ENSURE were enrolled. Enrolled patients received cross-over treatment as 2nd line treatment after 1st line PD. The primary endpoint was PFS, defined as the time of randomization in ENSURE to disease progression or death while on 2nd line treatment. For patients who had already progressed after 2nd line therapy prior to entering this extension study, relevant information would be collected retrospectively. PFS from 1st line PD to 2nd line PD was also calculated. The study was approved by IRB and all patients signed informed consent. This study was registered in clinicalgrials.gov (NCT02000531). We also retrospectively analyzed the time to 2nd line treatment failure (TTF) defined as the time from randomization to discontinuation of 2nd line treatment for any reason. **Results:** Forty-five patients (21 from erlotinib arm and 24 from GP arm) were enrolled in the final analysis in this ENSURE extension study. Limited recruitment was mainly due to later initiation of this study (from January to December of 2014), many deaths at the beginning of this study, or unwillingness to sign informed consent by some patients. Age, sex, and ECOG at baseline in erlotinib group and GP group were balanced. Among 45 enrolled subjects, 33 (73.3%) subjects completed the study. There was no significant difference in median PFS from the date of randomization in ENSURE study to 2nd line PD for both arms 26.3 (95%CI: 19.8 , 34.0) months vs 23.4 (95%CI: 17.8, 39.0) months, HR=1.26 (95%CI: 0.61, 2.62), p=0.529). For 2nd line cross-over treatment, ORR in erlotinib and GP arms was 33.3% (7PR/21) and 66.7% (16PR/24) respectively (p=0.0377). In a retrospective analysis of 175 patients from the whole ENSURE study, 63.2% patients in erlotinib arm (n=87) received 2nd line chemotherapy and 86.4% patients in GP arm (n=88) received 2nd line targeted therapy. The median TTF in erlotinib and GP arm were 29.4 (95%CI: 24.7, 34.2) and 24.7 (95%CI: 21.9, 28.4) months respectively (HR=0.74(95%CI: 0.47, 1.17), p=0.192).The subgroup analysis (mutation type, ECOG performance status, gender) for TTF between erlotinib and GP arm showed similar trend to the primary analysis. **Conclusion:** Despite limitations, both median PFS (in prospective analysis) and TTF (in retrospective analysis) for erlotinib patients were numerically larger than that in GP arm. This first cross-over treatment ENSURE extension study further confirms benefits of erlotinib as standard 1st line treatment for EGFR mutant NSCLC. It also supports the importance of 1st and 2nd line treatment sequence of erlotinib and platinum-based chemotherapy for the treatment of EGFR mutant NSCLC.
Keywords: cross-over treatment, ENSURE study, EGFR TKI, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-025 Crizotinib in Advanced ALK-Positive NSCLC - A Retrospective Multicenter Study in the Slovak Republic

Peter Kasan[1], Peter Berzinec[2], Lukas Plank[3], Igor Andrasina[4], Robert Godal[5], Juraj Mazal[6], Andrea Cipkova[4], Maria Cerna[7], Lucia Denkova[1], Gabriela Chowaniecova[2], Iveta Kuliskova[3], Helena Kuzmova[2], Marian Martak[1], Zuzana Pribulova[4], Marian Reckova[8], Milada Vesela[1] [1]*University Hospital, Bratislava/Slovak Republic,* [2]*Specialised Hospital of St Zoerardus Zobor, Nitra/Slovak Republic,* [3]*University Hospital, Martin/Slovak Republic,* [4]*East Slovakian Cancer Institute, Kosice/Slovak Republic,* [5]*National Cancer Institute, Bratislava/Slovak Republic,* [6]*Faculty Hospital, Banska Bystrica/Slovak Republic,* [7]*Slovak Medical University, Bratislava/Slovak Republic,* [8]*Adus Polyclinic, Poprad/Slovak Republic*

Background: Crizotinib has been available in Slovakia since October 2012 for the treatment of adults with previously treated ALK-positive advanced non-small cell lung cancer (NSCLC), based on the therapeutic indication approved by the European Medicines Agency. Purpose of this study was to assess the results achieved with crizotinib in the treatment of advanced NSCLC in clinical practice in Slovakia. **Methods:** In this multicenter retrospective study, approved by the Ethical Committee of the Specialized Hospital of St Zoerardus Zobor, the data of 30 ALK-positive patients were reviewed. FISH with break-apart probes was used for the confirmation of ALK rearrangement in all cases. MedCalc® was used for the statistical analyses. **Results:** Between October 2012 and August 2014, 20 out of 30 ALK-positive patients were treated with crizotinib. Ten patients did not receive crizotinib: five due to on-going first-line chemotherapy, five due to other reasons. Characteristics of the treated patients: M/W: 6/14, age (years) median 56, range 23-77, PS (ECOG/WHO): 0/1/2/3: 1/10/4/5, Histology: 19 patients adenocarcinoma, 1 NSCLC, NOS. Treatment results: RR was evaluated in 20 patients: PR + CR: 13 (12+1), 65% (95% CI: 41-85), SD: 3, 15% (95% CI: 3-38), PD: 3, 15% (95% CI: 3-38), NS: 1, 5%, DCR: 16, 80% (95% CI: 56-94), PFS: Kaplan-Meier estimate: 13 months (95% CI: 7 -18), OS (with 60% of patients censored): 19 months (95%CI: 12 - NR), PS: significant improvement within 2 months (mean dif. –0.95, P=0.0021), toxicities grade 3/4 occurred in 11 of 20 patients (55%), hematologic: 0, non-hematologic: hepatotoxicity 3/1, pneumonitis: 1/0, diarrhea 1/0, nausea: 3/0, vomiting: 1/1, vision disorder: 1/0, peripheral edema: 1/0, QT-interval prolongation: 1/0. Crizotinib was permanently discontinued due to toxicity in only two patients. **Conclusion:** Treatment results seen in this retrospective study are encouraging and consistent with the published data from the prospective trials.
Keywords: NSCLC, crizotinib, ALK

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-026 Proactive Management of Potential Gastrointestinal Adverse Reactions with Ceritinib in Patients with Advanced ALK+ NSCLC

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Background: Anaplastic lymphoma kinase (*ALK*) gene fusions are implicated in the pathogenesis of non-small cell lung cancer (NSCLC), occurring in 3–7% of cases. Crizotinib, a first-in-class ALK inhibitor, was granted US FDA approval in 2011 to treat metastatic *ALK*-positive (*ALK+*) NSCLC. However, intrinsic and acquired resistance limits its duration of use. Ceritinib, an ALK inhibitor with activity against crizotinib-resistant NSCLC and brain metastases, was granted accelerated approval by the US FDA in 2014 for treating crizotinib-resistant *ALK+* NSCLC. Adverse events (AEs), particularly gastrointestinal (GI) AEs, are commonly experienced at the recommended dose of 750 mg/day (Shaw A *et al.* NEJM 2014;370:1189–1197) and around 60% of patients require dose interruption or reduction. This report details our experience with the use of proactive GI AE management regimens with ceritinib. **Methods:** Proactive regimens A and B were implemented in patients with metastatic *ALK+* NSCLC treated with ceritinib to manage drug-related GI AEs. Regimen A comprised ondansetron and diphenoxylate/atropine or loperamide, taken 30 minutes prior to dosage. Regimen B included dicyclomine, taken with the first ceritinib dose, ondansetron, taken 30 minutes prior to dosage for the first 7 doses, and loperamide, taken as needed with the onset of diarrhea. The proactive medications were tapered off depending on patient tolerability to ceritinib. We report a case series comprising 9 patients treated at two sites with ceritinib (750 mg/day) for whom these proactive GI AE management programs were successfully implemented. **Results:** The 9 patients presented had discontinued crizotinib due to disease progression or intolerance, and received ceritinib as their 2nd–5th line of treatment (**Table**). Rapidly starting regimens A or B before the first dose of ceritinib, or as soon as GI symptoms were encountered, prevented the need for dose reduction due to GI toxicity in 8/9 patients. One patient discontinued therapy due to GI toxicities despite prophylaxis. One patient required dose reduction to 600 mg/day due to Grade 3 transaminitis. Using these regimens, 78% of patients were able to remain on 750 mg/day fasting. Two patients have completed 16 and 12 months of therapy, and remain on ceritinib 750 and 600 mg/day, respectively.

	Patient								
	1	2	3	4	5	6	7	8	9
Age at enrollment	64	54	62	72	53	57	81	48	41
Line of therapy	3rd	2nd	4th	5th	5th	3rd	3rd	4th	3rd
Previous regimens	• Carbo/PEM • Crizotinib	• P/Carbo + RT	• Carbo/PEM • P • Crizotinib	• P/Carbo • DTX • PEM + Bev • Crizotinib	• Erlotinib • P/Carbo • PEM • Crizotinib	• Carbo/PEM + Bev • Crizotinib	• Carbo/DTX • Crizotinib	• P/Carbo + Bev • Crizotinib • P/Cis	• Cis/PEM • Crizotinib
Other previous therapies	WBRT	Chest RT	WBRT	Chest RT	None	None	Craniotomy Jul 2013; SRS Jul 2013	None	SRS Apr 2012
Reasons for discontinuation of previous therapy	PD	PD	PD	PD	PD	Intolerance	Intolerance; brain and bone lesions	Brain metastasis	PD in brain (LC)
Time on ceritinib treatment*	4 months Nov 2013–Mar 2014	5 months Oct 2012–Mar 2013	>12 months Mar 2014–present (600 mg/day)	2 weeks Nov 2013	20 months Jan 2013–Aug 2014	2 months Mar 2014–Apr 2014	>16 months Aug 2013–present	4 months Jul 2013–Oct 2013	2 months Mar 2014–Apr 2014 (compassionate use)
Reasons for discontinuation of ceritinib	New primary malignancy (sarcoma)	Comorbidity (pericarditis)	Ongoing	Abdominal cramps, diarrhea	PD	PD	Ongoing	PD in brain	PD/death
Initial regimen	Regimen A				Regimen B				
	Ondansetron and diphenoxylate/atropine	Ondansetron and loperamide	Ondansetron and diphenoxylate/atropine	Ondansetron and diphenoxylate/atropine	Ondansetron, dicyclomine, and loperamide				
Other agents added	None	Lorazepam, dicyclomine, dronabinol	None	None	Diphenoxylate/atropine for persistent diarrhea				

*Treated at current institution.
Bev, bevacizumab; Carbo, carboplatin; Cis, cisplatin; DTX, docetaxel; LC, leptomeningeal carcinomatosis; P, paclitaxel; PD, progressive disease; PEM, pemetrexed; RT, radiotherapy; SRS, stereotactic radiosurgery; WBRT, whole brain radiotherapy.

Conclusion: Although not currently recommended or implemented in clinical studies, based on the patients evaluated here, upfront or proactive treatment plans that address AEs early on can allow the majority of patients to remain on the approved 750-mg/day ceritinib dose.
Keywords: Ceritinib, ALK+ NSCLC, AE Management, Gastrointestinal

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-027 Responses to Crizotinib in Six Lung Adenocarcinoma Patients of ALK IHC-Positive and FISH-Negative Di Ma[1], Zheng Wang[2], Lin Yang[3], Xinlin Mu[4], Yan Wang[1], Xinming Zhao[1], Junling Li[1], Dongmei Lin[5] [1]*Medical Oncology, Cancer Institute and Hospital Chinese Academy of Medical Sciences Peking Union Medical College, Beijing/China,* [2]*Pathology, Beijing Hospital, Beijing/China,* [3]*Pathology, Cancer Hospital, Chinese Academy of Medical Sciences, Beijing/China,* [4]*Respiratory Disease and Critical Care Medicine, Peking University People'S Hospital, Beijing/China,* [5]*Pathology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing/China*

Background: The anaplastic large cell kinase gene (ALK)-positive is a special type of non-small cell lung carcinomas (NSCLC). Although Ventana IHC (D5F3) and FISH showed high coincidence for detecting ALK rearrangement, discordant results exist in some cases. Treatment strategy as well as efficacy of crizotinib in these cases is such an issue. We studied and reported the efficacy of crizotinib in six lung adenocarcinomas patients with ALK IHC positive and FISH negative. **Methods:** All histologic and cytologic specimens were stained by IHC with an anti-ALK monoclonal antibody (D5F3, Roche) with the OptiView DAB IHC Detection Kit (Roche) and OptiView Amplification kit (Ventana Medical Systems, Inc., Tucson, AZ). All histologic and cytologic samples were also tested by FISH, which was carried out using the Vysis ALK Break Apart FISH probe kit. Three samples [one histologic (patient 1) and two cytologic samples (patients 2 and 6), patients' numbers were listed in Table 1] were still enough to further perform for EML4-ALK fusion by qRT-PCR. Two samples [one histologic(patient 1) and one cytologic sample(patient 6)] were still enough to further perform for next generation sequencing (NGS) analysis (using modified circulating single molecule amplification and resequencing technology, cSMART). The follow up data from 6 lung adenocarcinoma patients with ALK IHC-positive and FISH-negative who received crizotinib treatment were collected. **Results:** Table 1 showed the clinicopathological characteristics and the therapeutic efficacy of crozitinib for 6 patients in the study. The patients have achieved a response rate of 66.7% (4/6). Pathologically, for patient 1, the 3 unique DNA templates with EML4->EXOC6B->ALK fusion were identified in 710 DNA copies in tumor tissue. The fusion ratio is only 0.42%. For patient 6, we detected 75 unique DNA templates in total 495 DNA copies with 15.15% fusion ration in cytologic specimen. The fusion types of patient 1 and 6 were confirmed by sanger sequencing. Some unknown mechanisms caused the 3 gene fragments fusion of patient 1, the complex fusion type and low fusion ratio cause FISH negative.

Table 1: Patient Characteristics, pathologic characteristics and molecular tests in 6 cases

Patient NO.	Gender	Age	Smoking history	ALK IHC	ALK FISH	NGS-ALK	PFS (month)	Assessment
P1	Female	31	Never smoked	+	6%	E13:EXOC6B:A20	7.46+	Partial response
P2	Male	48	Ever smoker	+	10%	-	11.96+	Stable disease
P3	Female	49	Never smoked	+	6%	-	19.94+	Partial response
P4	Male	59	Ever smoker	+	6%	-	6.60+	Partial response
P5	Male	69	Ever smoker	+	10%	-	15.08+	Partial response
P6	Female	65	Never smoked	+	12%	E13:A2	3.58	Stable disease

ALK FISH: % of split signals by FISH; NGS: Next generation sequencing; +: No progressive disease was observed at the time of analyse. **Conclusion:** Lung adenocarcinoma patients with ALK IHC-positive and FISH-negative may also response to crizotinib. Ventana IHC is another candidate method for detecting ALK. One new fusion type EML4->EXOC6B->ALK fusion was verified and the patient with this fusion type showed partial response to crozitinib. **Keywords:** Anaplastic lymphoma kinase, lung adenocarcinoma, fluorescence in situ hybridization, Immunohistochemistry

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-028 Neoadjuvant Crizotinib and Surgical Resection of Two Stage IIIA Lung Adenocarcinomas with Anaplastic Lymphoma Kinase Gene Rearrangement Shaolei Li[1], Yue Yang[2] [1]*Department of Thoracic Surgery Ⅱ, Peking University Cancer Hospital & Institute, Beijing/China,* [2]*Department of Thoracic Surgery Ii, Peking University Cancer Hospital & Institute, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Beijing/China*

Background: Neoadjuvant therapy is also known as induction therapy or preoperative therapy. For lung cancer, the neoadjuvant medication includes chemotherapy and targeted medication. Neoadjuvant chemotherapy is widely used in clinical practices, but targeted therapy is still rare in the preoperative applications. To our knowledge, this is the first report of neoadjuvant crizotinib and following surgery of pulmonary adenocarcinoma. **Methods:** Crizotinib had already been recommend as the standard treatment for advanced lung adenocarcinoma with anaplastic lymphoma kinase gene rearrangement. First-line therapy with crizotinib prolonged progression-free survival and improved qulity of life among selected patients. The possibility of using crizotinib as neoadjuvant therapy is interesting because of low toxicity of tyrosine kinase inhibitors. Here we report two cases affected by locally advanced lung adenocarcinoma, in whom one-month crizotinib treatment rendered the tumors reduction to surgical removal. **Results:** These two patients with ALK-positive stage IIIA received oral crizotinib 250mg twice daily in thirty days, and crizotinib was well tolerated with rapid, prominent responses following by surgery in a week. The sequential therapy of case 1 showed the less adverse events in crizotinib than chemotherapy, while case 2 revealed more obvious responses. **Conclusion:** For pulmonary adenocarcinoma patients with ALK rearrangement, crizotinib could achieve a higher remission rate and less adverse events as compared with the chemotherapy, suggesting that crizotinib may be better option for neoadjuvant therapy. A propositional clinical trial exploring the ability of preoperative crizotinib to achieve better results than can be obtained with chemotherapy in patients selected on the basis of ALK gene rearrangement is urgently needed. **Keywords:** neoadjuvant therapy, Surgery, lung cancer, crizotinib

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-029 Physician Decision-Making on Modifying or Discontinuing Crizotinib in *ALK*+ NSCLC: A Survey of US Physicians Annie Guerin[1], Medha Sasane[2], Jie Zhang[2], Elyse Swallow[3], Alexander R. Macalalad[3], Karen Stein[2], Andrew Kageleiry[3], Philip Galebach[3], Jacquelyn Kercheval[3], Dony Patel[4], Edmond Bendaly[5] [1]*Analysis Group, Inc., Montreal/QC/Canada,* [2]*Novartis Pharmaceuticals Corporation, East Hanover/United States of America,* [3]*Analysis Group, Inc., Boston/United States of America,* [4]*Navigant Consulting, Inc., London/United Kingdom,* [5]*Marion General Hospital, Marion/IN/United States of America*

Background: Crizotinib has been commercially available since August 2011 for the treatment of locally-advanced or metastatic *ALK*+ non-small cell lung cancer (NSCLC). In April 2014, a second-generation *ALK* inhibitor, ceritinib, was approved in the US for use after intolerance to or progression on crizotinib. Tumor progression, which varies by anatomical site and extent, is complex and evolves over time, often with insidious onset. Considering this heterogeneity, it is currently unclear at which point physicians may decide to change therapy. The objective of this study was to evaluate physicians' decision-making with regard to determining progression during crizotinib treatment of locally-advanced or metastatic *ALK*+ NSCLC. This research question is particularly relevant with the introduction of new, effective treatment options available to patients who progress on first-line *ALK* inhibitor therapy. **Methods:** In July-November 2014, US oncologists were invited to respond to a survey regarding their decision-making with regard to treatment changes following progression on crizotinib for patients with locally-advanced or metastatic *ALK*+ NSCLC. Information was also collected on the characteristics of their practice. **Results:** Of the 34 oncologists who responded to the survey, 59% were from private practice, 26% were from an academic practice, and 15% were from an institutional practice. In terms of practice size, 53% were from small/intermediate practices of 2-9 oncologists, and the rest were from larger practices. Half (50%) of physicians had their practice in an urban setting; 35% were in a suburban and 15% were in a rural setting. Responding physicians had been in practice for an average of 12 years. When asked to indicate all of the clinical scenarios for which they would modify or discontinue crizotinib therapy, 62% of the physicians indicated that they would do so following disease progression detected on scan; 53% following either new or worsening symptoms; 29% following the development of new metastases in the brain; 35% following the development of new metastases elsewhere; 29% following onset of a paraneoplastic neurological disorder; and 26% following lack of improvement of patient's symptoms. **Conclusion:** The study suggests there is substantial heterogeneity in the clinical scenarios physicians would consider for modifying or discontinuing therapy after progression on crizotinib. These findings highlight the need for further clinical guidance with regard to the early identification of progression on crizotinib, and in particular, for a better understanding of the optimal point to switch from crizotinib when patients present with different manifestations of disease progression. **Keywords:** Locally-advanced or metastatic ALK+ NSCLC, crizotinib, Physician treatment preferences, progression

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-030 Challenging Diagnosis of Adenocarcinoma of the Lung Confirmed by Molecular Analysis: A Clinical Case Robert El-Maraghi *Royal Victoria Regional Health Centre, Barrie/ON/Canada*

Background: Lung cancer is the leading cause of cancer related deaths worldwide, with approximately 1.8 million new cases diagnosed in 2012 resulting in an estimated 1.6 million deaths (Torre 2015). The basic tools of diagnosis include the assessment of clinical status (Rivera 2013), imaging to determine the size and location of tumors as well as the presence of metastases (Liam 2015), and tissue biopsies for establishing tumor histology and molecular subtype (Ofiara 2012). Correct characterization of the primary tumor can be particularly challenging when presentation includes confounding elements such as multiple lesions and/or no definite mass at the primary site. The accuracy and timing of molecular testing can play a vital role in compressing the diagnostic window for adenocarcinoma of the lung, allowing for timely treatment and a broader range of therapeutic options. **Methods:** Local research ethics board approval was obtained for this study. A standard diagnostic work up was undertaken, then supplemented by both internal and external pathological review of the available tissue sample, including EGFR and ALK mutation testing to clarify the diagnosis. **Results:** The patient, a 49 year old male smoker, initially presented with nausea, vomiting, weight loss and shortness of breath.

Imaging revealed an anterior mediastinal mass with hilar, mediastinal, bilateral neck and left supraclavicular region lymphadenopathy. Ultrasound confirmed bilateral adrenal lesions and a solid lesion in the right testicle, but no definitive lung mass was identified. Presentation characteristics were initially thought to indicate a lymphoma or germ cell tumour, however, additional analysis of tissue from a biopsy of the supraclavicular node was more consistent with a poorly differentiated carcinoma suggestive of lung adenocarcinoma, with positive staining for TTF-1 and EMA and negative staining for CK20, CK45, CK30, melanoma markers and thyroglobulin. Molecular testing for EGFR and ALK mutations was then requested, along with external pathology review. Findings from external review confirmed the aforementioned molecular profile and revealed that the tumour was also negative for CDX2, CK5, P63, PAX8, OCT3/4, SALL4 and synaptophysin expression, suggestive of thymic cancer, a teratoma, a germ cell tumour, or metastases from upper gastrointestinal origin. Molecular testing results identified an EGFR exon 21 point mutation, confirming the diagnosis of primary lung cancer. Treatment with afatinib was considered; however, due to the protracted diagnostic window, the patient was ultimately too debilitated to receive therapy. **Conclusion:** The absence of a definite lung mass and the unusual clinical and molecular presentation of this case made primary tumour site identification very challenging. The differential diagnosis was ultimately achieved through molecular testing. It is now well-established that early (reflexive testing) knowledge of EGFR and ALK mutation status, accomplished through molecular profiling, is essential for the appropriate management of patients with adenocarcinoma of the lung. However, this case also highlights the importance of this type molecular characterization in achieving a timely diagnosis. **Keywords:** ALK, lung adenocarcinoma, molecular profiling, EGFR

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-031 Characteristics of Squamous Cellular Carcinoma Patients In 'Colombian Coffee Zone' Jaime A. Echeverri F[1], Gustavo Rojas[2], Marco Kimmel[2], Paula Londno[2], Jose W. Martinez[2], German A. Moreno[2] [1]*Pulmonary Medicine, Oncologos Del Occidente, Pereira/Colombia,* [2]*Oncologos Del Occidente S.A., Pereira/Colombia*

Background: During 1998 and 2013 the "Colombian Coffee Zone" (conformed by Caldas, Quindio, and Risaralda states) had an increase of 105 mortality cases of Bronchi and lung malignant tumors, as reported in death certificates. **Methods:**This is an observational and descriptive study that was made in patients at Clinica Oncologos del Occidente in the year 2014 and the Information was taken from the Clinical History Administration System (SAHICO). Thereafter, pending data was collected, by phone calls to patients or patient's family, according to every case. Patients were interviewed to know their actual performance status and, in case of death, date and basic cause of death was asked. **Results:** SAHICO reported 178 patients with lung cancer. From these patients, 33 did not have a correct diagnosis. Basically they did not have histology report. There were 130 patients with Non-Small Cell Lung Cancer and Small Cell Lung Cancer. The frequency of lung cancer was slightly more common in men; most of the patients were from Risaralda, followed by Caldas. 50% of the patients were 60.7 to 74 years old. The median age for men was 69.1 years old, and 64.1 years old for women. These median ages differences were statistically significant (F=9,121 p value=0,003). And 90.8% of the patients were from urban areas. 85.3% of tumors treated in 2014 correspond to NSCLC, meanwhile 10% were Small Cell lung cancer. Patients who received radiation therapy had a longer survival than patients without any radiations treatment. The survival media in the radiotherapy group was 180.4 days, and 113.2 days for the group without radiation therapy. This difference was significant (Log Rank test: 4.74, p value 0.029). Only 2 patients had both surgery and radiotherapy and had the major survival time, with a media of 331 days. The mean age of the squamous cellular carcinoma patients was 69.8 years old in 64 patients. It was reported a median survival of 120 days with a confidence interval between 78 and 162 days. Only 8 patients with squamous cellular carcinoma had surgery and reported an increase in their survival time. The time median of survival for the surgical patients was 270 days. Meanwhile, this indicator decreased in the non-surgical patients to 109.9 days. **Conclusion:** In general, characteristics of lung squamous cellular carcinoma patients in the Coffee area of Colombia are similar than other regions of the world; incidence in men is only slightly greater than in women, presumably by the early age to start of smoke of the female population and the expose since childhood to others risk factors like biomass combustion smoke. Is clear that patients are detected in an advance stage of disease which has strong influence in prognosis and outcome. Highlights the importance of an integral treatment including all management alternatives and a multidisciplinary equipment of attention for modification of prognosis and survival. **Keywords:** Lung Neoplasms, Surveillance, Survival, Carcinoma Bronchogenic

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-032 Patterns of Care in Long Term Survivors (> 3 Years) in Advanced NSCLC- Retrospective Analysis of 30 Patients from a Single Institute
Indibor S. Yengkhom *Rcc, Radiation Onccology, Regional Institute of Medical Sciences, Imphal/India*

Background: Long term survivors (>3years) in advanced NSCLC is steadily increasing from 5 - 10% to 15 - 20%. It is related with the more effective and better treatment given in an individualised manner along with better understanding of the tumour biology. Many factors are also associated with the improved outcome. Our Institute's 3 years data is analysed in an attempt to find out the favourable factors. **Methods:** Data mining of Stage III & IV non small cell lung cancers treated at RCC, RIMS during 2010 to 2012 are carried out from the patient's departmental records. Only patients diagnosed and treated at RIMS who survive more than 3 years are included for analysis. Patient characteristics, disease profile & treatment pattern are analysed. **Results:** Out of 196 patients records available- Stage III & IV comprise 160 patients of these 30 patients survived more than 3 years. The analysis shows Male: Female ratio 5:4, mean age 55 years (range 36 to 90 yrs) stage III is 18(60%) stage IV 12(40%). Histologically, Squamous cell Ca. 60% Adeno ca. 24% and small cell 12% and rest others. KPS range from 60% to 90%. Treatment given: 80% received intent to cure with Chemo ± RT. And 20% palliative care only. Long survivors (>3years) 24 patients (16F + 8M) who received intent to treat chemo or chemo+ RT compared to none in supportive care only **Conclusion:** The result shows that females with Histo type adenocarcinoma who received therapy with Chemo + RT +/- targeted therapy with intent to treat are the long survivors according to this study. The study indicates that treatment should be given in a sub set of patients with advanced disease who are responders for increasing meaningful survival. **Keywords:** NSCLC long survivors, pattern of care

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-033 Patients with Advanced NSCLC Requiring Inpatient Oncology Consultation Joanna Gotfrit[1], Tinghua Zhang[2], Sylvia Zanon-Heacock[3], Paul Wheatley-Price[4] [1]*Department of Internal Medicine, University of Ottawa, Ottawa/ON/Canada,* [2]*Ottawa Hospital Research Institute, Ottawa/Canada,* [3]*The Ottawa Hospital Cancer Centre, Ottawa/ON/Canada,* [4]*Division of Medical Oncology, The Ottawa Hospital Cancer Centre, Ottawa/ON/Canada*

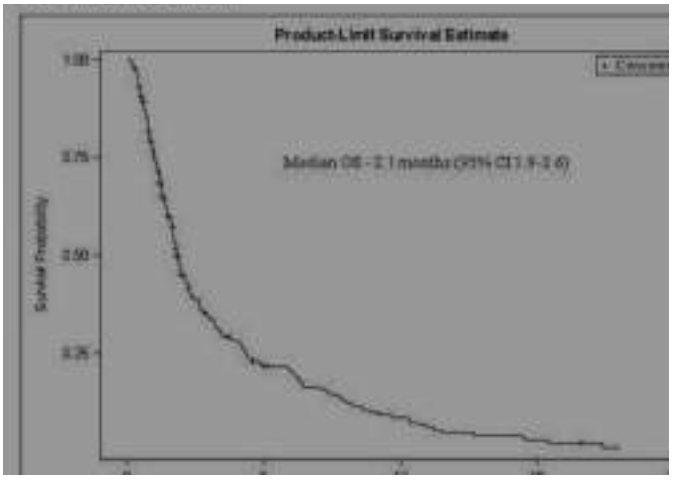
Background: Most newly diagnosed advanced lung cancer patients have an initial medical oncology consult as an outpatient. However, occasionally the initial referral occurs as an inpatient. We explored the characteristics of advanced NSCLC patients whose first medical oncology consultation occurred while hospitalized. **Methods:** With ethics approval, we performed a retrospective analysis of all advanced NSCLC patients at our institution whose initial consult occurred while hospitalized, from 2007 to 2012. Demographics, treatment and survival data were collected. This was an exploratory analysis. Multivariate survival analysis was performed using Cox regression models. **Results:** In total, 223 patients were included (baseline characteristics in Table 1). Overall, only 24% received chemotherapy while 72% received some palliative radiotherapy. Median time from diagnosis to chemotherapy was 43 days. Reasons for not receiving chemotherapy included poor performance status (PS) (72%), patient choice (9%), clinical deterioration (6%) or co-morbidities (4%). Factors associated with receiving chemotherapy were good PS (OR 11.11 [95% CI 5.56-25.00], p<0.001), no constitutional symptoms (OR 2.86 [95% CI 1.41-5.88], p=0.004), no leukocytosis (OR 2.38 [95% CI 1.23-4.55], p=0.01), fewer co-morbidities (OR 1.54 [95% CI 1.27-1.89], p<0.001) and younger age (OR 1.09 [95% CI 1.05-1.12], p<0.001). Median OS was shorter in those not receiving chemotherapy (1.7 v 7.1 months, HR 2.76 [95% CI 1.72-4.41], p-value<0.001). Figure 1 shows Kaplan-Meier survival curves. In multivariate analysis, in addition to not receiving chemotherapy, factors associated with shorter OS were PS 3-4, (HR 1.55 [CI 1.03-2.33, p=0.04]), leukocytosis (HR 2.23 [95% CI 1.51-3.28], p-value <0.001) and thrombocytosis (HR 1.52 [1.06-2.18], p=0.02). **Conclusion:** Patients whose first consultation with medical oncologists occurs while hospitalized are an inherently sick population and only a minority receive chemotherapy. The lung cancer community must advocate for earlier diagnosis and referral, so more patients have access to treatment options before a terminal functional decline.

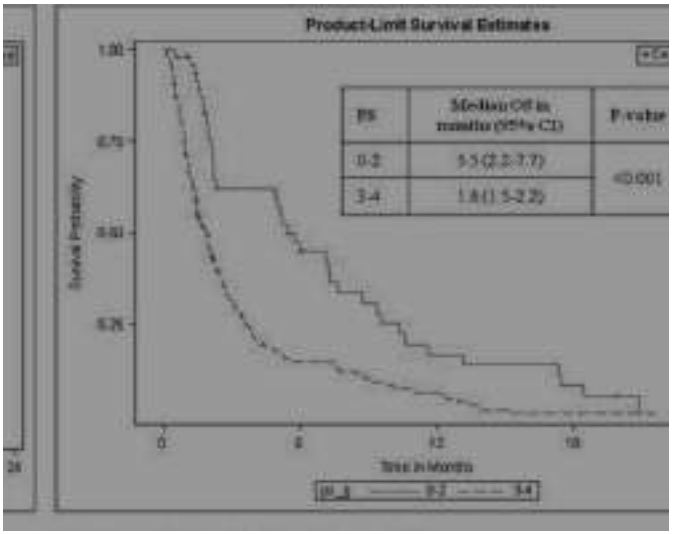
Table 1: Baseline Characteristics

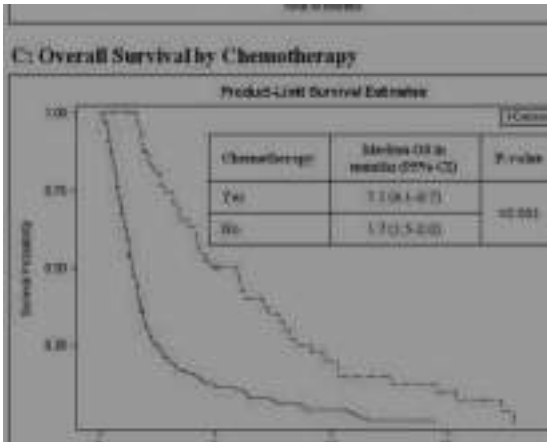
Demographic (N=223)	**%**
Age in years, median (range)	65 (23-89)
Gender	
Male	48
Female	52
Charlson Comorbidity Index total score, median (range)	10 (6-18)
Performance status	
0-2	24
3-4	69
Unknown	7
Smoking status	
Current	49
Ex	34
Never	9
Unknown	8
Stage at diagnosis	
IIIB	10
IV	89
Unknown	1
NSCLC subtype	

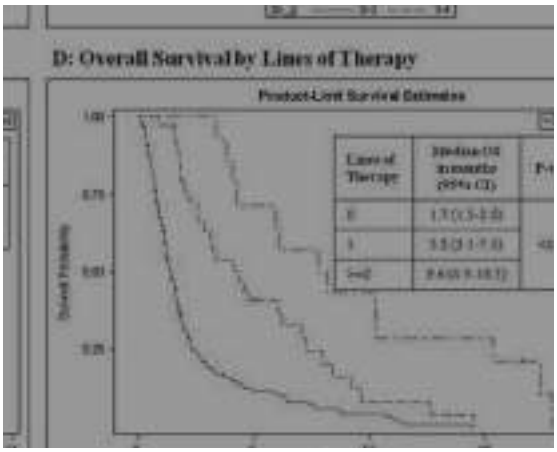
Table 1: Baseline Characteristics	
Demographic (N=223)	**%**
Adenocarcinoma	45
Squamous cell	23
Large cell	8
Other	23
Dominant presenting symptom	
Dyspnea	34
Pain	23
Constitutional symptoms	9
Pneumonia	7
Cough	5
Hemoptysis	3
Other	18
Weight loss	
<5%	22
>5%	52
Unknown	25

Figure 1: Kaplan-Meier Survival Curves









Keywords: chemotherapy, advanced NSCLC, Inpatient, Referral

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-034 Predictive Factors of Brain Metastases Development in Non-Small Cells Lung Cancer Eduardo A. Richardet, Maria E. Pacher, Matias Molina, Matias Cortes, Luciana P. Acosta, Aldo A. Riso, Pablo Companys, Eduardo Cuestas, Martin E. Richardet *Capital, Ionc (Instituto Oncologico de Cordoba), Cordoba/Argentina*

Background: Brain metastases are evidenced in 10 to 30 % of NSCLC patients sometime during the disease. The purpose of our research is to identify the clinical pathological characteristics in patients with stage IIIB-IV in relation to the development of brain metastases. **Methods:** 590 patients with lung cancer at our institution were analyzed between 2000 and 2013, of which 190 (32,3%) were stage EIIIB and 400 (67,7%) EIV. 76 (12.8%) had brain metastases. The variables included in the analysis of patients with and without brain metastases were: gender, age, histology, smoking status and ECOG. The multivariate logistic regression model was used to identify factors related to brain metastases. **Results:** 64 patients out of the total 76 had brain metastases at initial diagnosis and 11 EIIIB developed brain metastasis in relapses. The development of brain metastasis was higher in men compared to women (77.7% vs 22.2%). Over 80% of patients presented ECOG of 0-1. Regarding histology, 60.32% were adenocarcinomas; 30% squamous, and 9.5% undifferentiated. 65% of patients were under 65 years old. 66.6% of patients were former smokers. Patients under 65 years old were at increased risk of developing brain metastases than older patients (HR=0,5-IC95%= 0,6-1,16- p=0,045). Adenocarcinoma histology was associated with an increased number of brain metastases development (OR = 2.42 - 95% CI = 1.84 to 3.00 - p= 0.003). **Conclusion:** Patients who were younger than 65 years old and adenocarcinoma histology, had a statistically significant higher risk of developing brain metastases. Regarding gender, we observed an increased risk in men; however, the differences were not statistically significant.
Keywords: brain metastases nonsmall lung

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-035 The Survival Effect of Resection of Cranial Metastatic Lesions in Patients with Lung Cancer Adem Deligonul[1], Ozgur Taskapilioglu[2], Huseyin Melek[3], Ahmet Bekar[2], Gamze Cetinkaya[3], Sureyya Sarıhan[4], Ahmet Sami Bayram[3], Cengiz Gebitekin[3], Türkkan Evrensel[1] [1]*Oncology, Uludag University, Bursa/Turkey,* [2]*Uludag University, Bursa/Turkey,* [3]*Thoracic Surgery, Uludag University, Bursa/Turkey,* [4]*Radiation Oncology, Uludag University, Bursa/Turkey*

Background: The brain is one of the organs where lung cancer often metastasizes. At the time of diagnosis, the central nervous system metastases are present in approximately

10% of lung cancer cases. 80-85% of them are located supratentorially, and 10-15% of supratentorial lesions are located on cerebellar regions. Median survival is 1-2 months from the time of diagnosis without treatment. A general consensus about standard treatment could not be provided in lung cancer with a single brain metastasis; but distant metastases should necessarily be controlled with surgery or stereotactic radiation therapy. **Methods:** 74 patients (65 men and 9 women) were included in the study and evaluated retrospectively. They were followed in the department of medical oncology, school of medicine, Uludag University. All the patients had cranial operations for cranial metastases between 2004 and 2012. The ages and the first symptoms of the patients at the time of diagnosis, tumor localizations, surgical procedures, chemotherapy and radiotherapy protocols and histologic subtypes of lung cancer were analyzed. Time from diagnosis of cranial metastases to death was estimated as overall survival. **Results:**The symptoms of the patients at the time of diagnosis were as follows: 21 (28%) headache, 17 (23%) hemiparesis, 18 (24%) more than one neurologic symptoms, 8 (10%) seizure, and 8 (10%) imbalance. The distribution of histologic subtypes of patients was as follows: 42 (56%) adenocarcinoma, 17 (23%) squamous cell carcinoma, 14 (14%) small cell carcinoma, and 1 (1%) large cell carcinoma. According to surgical procedures, patients are distributed as follows: 68 (92%) total resection, 4 (5%) subtotal resection, and 2 (3%) stereotactic biopsy. 55 (74%) patients received cranial radiotherapy postoperatively. 15 (20%) patients received radiotherapy for both cranium and lung. 3 (4%) patients did not received radiotherapy. 1 patient's information about radiotherapy could not be reached. 70 (95%) patients received platinum-based chemotherapy. 4 ()patients did not receive any chemotherapy regimens. Median overall survival was 12 months (1-110 months) in patients with cranial metastases. **Conclusion:** In an article examining brain metastases that were developed postoperatively, 65 patients were evaluated. 5-year survival in this group of patients was 15%. In that study, factors that affect survival positively, were listed as: female gender, adenocarcinoma histologic subtype, presence of limited number of metastases (1-2), no other extra thoracic metastases except brain metastases, stereotactic, radiologic and/or surgical treatment for metastases. However, in the literature it was reported that three cases, whose brain metastases appeared after surgical resection of lung cancer, had overall survival over 12 years with stereotactic radiotherapy. On the other hand, it is obvious that systemic therapy is so important for metastatic patients. The benefits of the combined treatment with surgery were studied by many groups. Although the studies have not identified the prognostic factors for survival exactly and either responded which group of patients could see more benefit from aggressive treatment yet; good results have been taken by adding surgical resection of metastases to combined treatment in especially selected patients.
Keywords: lung cancer, metastases, survival

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-036 Long Term Survival of Patients with Metastatic Adenocarcinoma of the Lung in the Era of Targeted Agents
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Background: Several studies have shown that tyrosine kinase inhibitors and chemotherapy improve the short term and median survival of patients with metastatic adenocarcinoma of the lung (MAL), but the long term survival (LTS) of these patients has not been thoroughly investigated. **Methods:** We performed a univariate retrospective analysis on 174 patients with MAL diagnosed at our institution between 2009 and 2011, and with up to a 5-year follow-up. Most patients received multiple treatment modalities. Overall survival was estimated using the product-limit method and compared using the log-rank test (significant results listed in Table 1); patients alive at last follow-up were censored. **Results:** In our series, 19% (33) of all patients (174) received erlotinib as part of their treatment, and 39%(13) of those receiving erlotinib had epidermal growth factor receptor (EGFR) mutations. Although the 2-year and median survival were superior in patients receiving erlotinib and chemotherapy, neither improved the 5-year survival rate (LTS). Surprinsingly, the 60-months survival rate was higher in the no erlotinib arm (Figure 1). The only treatment modality that significantly improved LTS was surgery. For the patients treated with erlotinib and chemotherapy, regardless of EGFR mutations, all observed deaths occurred within 4 years. Factors associated with LTS were: sex, surgery, and presence of metastatic disease confined to the the lungs. **Conclusion:** In our univariate retrospective analysis, MAL patients who were treated with erlotinib and chemotherapy had improved 2-year and median survival rates compared to patients treated with chemotherapy alone, but had no improvement in LTS. Factors such as: surgery, metastases limited to the lungs only, female sex were associated with LTS in MAL patients, but larger prospective studies are needed to confirm our findings. Our study puts into question the long term survival benefit of tyrosine kinase inhibitors in MAL and suggests a prominent role of surgery in this clinical context.

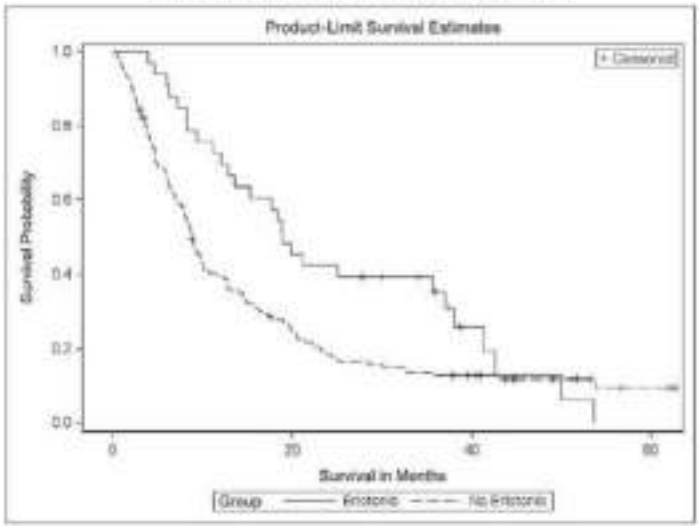
Table 1

Factor		Estimated Survival (% alive) at:		Median Survival in months (95% CI)	p-value
		24 mo	60 mo		
Treatment	Erlotinib	42.4%	0.0%	18.8 (12.9, 37.0)	0.0160
	No Erlotinib	18.8%	9.4%	8.8 (7.6, 10.1)	
	Chemotherapy	22.0%	0.0%	10.1 (8.7, 14.0)	0.7395
	No Chemotherapy	31.3%	19.6%	5.6 (2.7, 20.4)	
	Surgery	51.9%	32.6%	28.5 (8.7, *)	<0.0001
	No Surgery	17.9%	0.0%	9.3 (8.1, 11.9)	
	RT	16.7%	3.1%	8.7 (6.6, 10.1)	0.0164
	No RT	29.9%	13.3%	13.6 (9.0, 18.8)	
Sex	Male	15.2%	0.0%	7.6 (5.9, 9.7)	0.0019
	Female	29.4%	11.5%	14.0 (9.3, 18.8)	
Smoking	Never/Former	24.9%	9.0%	10.8 (8.8, 13.6)	0.2909
	Current	17.5%	0.0%	8.7 (4.8, 14.9)	
Brain Mets	Yes	27.9%	0.0%	12.7 (8.7, 19.7)	0.5319
	No	21.6%	11.7%	9.2 (8.0, 12.9)	
Bone Mets Only	Yes	11.1%	3.7%	9.0 (5.9, 9.8)	0.0681
	No	26.2%	8.3%	11.9 (8.7, 14.9)	
Lung metastases only	Yes	83.2%	28.2%	20 (8.3, 35.7)	0.0068
	No	19.3%	4%	9.4 (8.0, 12.7)	

*Could not be estimated based on the data. Statistically significant results (p<0.05) in bold.

Figure 1 Adenocarcinoma of the Lung: Survival in Months by Treatment Group

Erlotinib Treatment versus Non-Erlotinib Treatment



Keywords: metastic adenocarcinoma lung, long term survival, Tyrosine kinase inhibitors, Surgery

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-037 Genomic Alterations of KRAS, EGFR, and ALK in Patients with Non-Small Cell Lung Cancer, Single Institution Experience
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Background: This study reviews the results of extensive genetic analysis in non-small cell lung cancer (NSCLC) patients from a University of Chicago database in order to: describe how actionable mutation genes interrelate with the genes identified as variants of unknown significance; assess the percentage of patients with a potentially actionable genetic alterations; evaluate the percentage of patients who had concurrent alterations, previously considered to be mutually exclusive; and characterize the molecular subset of *KRAS*. This study reviews the results of extensive genetic analysis in non-small cell lung cancer (NSCLC) patients from a University of Chicago database in order to: describe how actionable mutation genes interrelate with the genes identified as variants of unknown significance; assess the percentage of patients with a potentially actionable genetic alterations; evaluate the percentage of patients who had concurrent alterations, previously considered to be mutually exclusive; and characterize the molecular subset of *KRAS*. **Methods:** Thoracic Oncology Research Program (TORP) Databases at the University of Chicago provided patient demographics, pathology, and results of genetic testing. Three hundred and sixty four patients included in this analysis had advanced NSCLC and underwent genotype testing by FoundationOne, Caris Molecular Intelligence, and Response Genetics. **Results:** 99.4% (159/160) of patients, whose samples were analyzed by next-generation sequencing (NGS), had genetic alterations identified with an

average of 10.8 alterations/tumor throughout different tumor types. However, mutations were not mutually exclusive. For the entire cohort 28% of patients were African Americans; adenocarcinoma was the most commonly tested tumor subtype; 91% of *KRAS* mutations were detected in smokers; 46% of *EGFR* alterations and 50% of *ALK* translocations were detected in never smokers. The majority of *ALK* translocations were detected in adenocarcinomas. **Conclusion:** Personalized medicine is a significant step forward in the realm of lung cancer treatment. In conjunction with NGS to identify and characterize tumor specific molecular abnormalities, biomarker-driven therapies have improved patients' overall survival. NGS in this study identified potentially actionable genetic alterations across various tumor histology subtypes, races and smoking status. NGS also provided additional information by uncovering targetable concurrent alterations or alterations of unknown significance at this point in time, but potentially targetable in the future. **Keywords:** next generation sequencing, gene alteration, database, non-small cell lung caancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-038 Prognostic Factors for Brain Metastasis in Non-Small Cell Lung Cancer Narjust Duma[1], Laysa Sanchez[1], Claudia Miranda[1], Chad Glisch[1], Khaleb Abu-Ihweij[1], Shijia Zhang[1], Carlos Osorio[1], Matthew Listo[1], Harry D. Harper[2], Martin Gutierrez[2]
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Background: Non-Small Cell Lung Cancer (NSCLC) patients tend to develop brain metastasis (BM) early in the course of the disease, usually within 2 years of diagnosis. BM are an important cause of morbidity and mortality, the study of prognostic factors for its development are invaluable in implementing measures to prevent or decrease the incidence of BM. The aim of this study was to evaluate the prognostic value of certain clinical characteristics in the development of BM in NSCLC patients. **Methods:** We retrospectively analyzed all patients diagnosed with NSCLC at our institution between 2000 and 2013. Demographics, tumor characteristics and metastatic patterns were studied. Median follow up was 45 months. Cox regression was used for multivariate analysis. **Results:** A total of 1062 patients were studied. Of these, 172 (16%) had BM at the time of analysis, with 61 (35%) patients having BM at diagnosis. Median age was 68 years (range, 18-91); median time from diagnosis to BM was 259 days. There were more females than males (64% vs. 36%, $p < 0.0001$). About NSCLC characteristics, patients with BM were more likely to have upper lobe tumors than all other tumor locations combined (63% vs. 37%, $p < 0.0001$). 32% of the lung tumors were 5-7cm in diameter and adenocarcinoma represented 68% of all the histologic subtypes. In regards to other distant metastases: 34% of the patients had bone metastasis, 23% adrenal and 17% hepatic. BM were most commonly located in the frontal (41%), parietal (17%) and occipital (14%) lobes. There was a significant survival difference between Stage IV patients with and without BM; patients with BM survived 6.1 months compared with 11.9 months in those without BM ($p < 0.0001$). In univariate analysis, female sex, histologic grade, upper lobe tumors and high LDH levels were associated with BM. Age < 65 years (HR: 0.60, 95%CI: 0.37-0.95, $p < 0.03$), T3-4 tumors (HR: 3.4, 95%CI: 2.04-5.64, $p < 0.0001$), adrenal metastasis (HR: 5.2 95%CI: 2.5-10.7, $p < 0.0001$) and liver metastasis (HR: 8.6, 95%CI: 4.3-17.2, $p < 0.0001$) were independent risk factors for the development BM. **Conclusion:** The results of this study pose female sex, tumor histologic grade, tumor location, and LDH levels as important prognosticators of future BM. In addition, younger age, T3-4 tumors, and the presence of adrenal/liver metastases are noted as independent risk factors for BM development. With this information, criteria for the selection of patients as suitable candidates for intra-cranial irradiation, periodic brain imaging studies, and close outpatient follow-up may aid in further prevention of BM, early identification, and timely management. **Keywords:** Brain metastasis, non-small cell lung cancer, Prognostic factors, Early Detection

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-039 Clinicopathological Factors in Non-Small Cell Lung Cancer Patients with Bone Metastases Arife Ulas[1], Ahmet Bilici[2], Ayse Durnali[3], Saadet Tokluoglu[3], Sema Akinci[4], Kamile Silay[5], Berna Oksuzoglu[3], Necati Alkis[3] [1]*Department of Medical Oncology, Ankara Ataturk Training and Research Hospital, Ankara/Turkey,* [2]*Department of Medical Oncology, Istanbul Medipol University, Medical Faculty, Istanbul/Turkey,* [3]*Department of Medical Oncology, Ankara Oncology Teaching and Research Hospital, Ankara/Turkey,* [4]*Department of Hematology, Ankara Ataturk Training and Research Hospital, Ankara/Turkey,* [5]*Department of Internal Medicine, Yildirim Beyazit University, Faculty of Medicine, Ataturk Research and Training Hospital, Ankara/Turkey*

Background: The bone is one of the most frequent sites for metastases from non-small cell lung cancer (NSCLC) and bone metastases are diagnosed in 30-40% of patients. They are resulted in skeletal-related events (SREs) that associate with an important morbidity and poor survival. In the current study, clinicopathological factors and SRE-free survival were evaluated for patients with NSCLC with bone metastases. **Methods:** Three-hundred and thirty-five NCSLC patients with bone metastases were retrospectively analyzed, between 2010 and 2013. The effect of clinicopathological factors on SRE and survival were evaluated for all patients with or without SREs. **Results:** Totally, 244 (72.8%) patients developed SREs at the diagnosis or during treatment of disease. Of these, 145 required radiotherapy to the bone or pathological fracture, 59 developed malignant hypercalcemia, 21 developed compression fracture of the vertebrae and 5 required surgical treatment of the bone. There were significant differences between the patients with respect to number of bone metastasis, the presence of palliative radiotherapy and the presence of bisphosphonate therapy. The association of histopathological subtypes and bone metastases was not detected. Patients with multiple bone metastasis had significantly increased SRE when compared to patients with single bone metastasis ($p=0.002$). Patients with single bone metastasis had a better median SRE-free survival compared with patients multiple bone metastasis (7 vs. 2 months, respectively, $p<0.0001$). Univariate analysis revealed that performance status (PS), the presence of bone metastasis at diagnosis, number of bone metastasis, SRE, the presence of palliative radiotherapy and bisphosphonate therapy were significant prognostic factors for overall survival (OS). Patients with bone metastasis at diagnosis had a shorter median OS compared with patients developed bone metastasis after diagnosis (8 vs. 18 months, respectively, $p<0.0001$). The presence of bone metastasis at diagnosis and number of bone metastasis were found to be an independent factors for predicting the occurrence of SRE ($p<0.001$ and $p<0.001$, respectively). **Conclusion:** Our results showed that the presence of multiple bone metastases was significantly associated with the development of SRE for NSCLC patients with bone metastases. In addition, bone metastasis at diagnosis is related with poor OS. The determining of additional factors affecting the occurrence of SREs may guide to best treatment for NSCLC patients with bone metastases. **Keywords:** Non-small cell lung cancer, Bone metastases, Skeletal-free events, Survival,

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-040 Survival Gains From Systemic Therapy in Advanced Non-Small Cell Lung Cancer in the U.S., 1990-2015: Progress and Opportunities Joshua A. Roth[1], Bernardo H.L. Goulart[1], Arliene Ravelo[2], Holli Dickson[2], Scott D. Ramsey[1]
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Background: Approximately 180,000 Americans are diagnosed with non-small cell lung cancer (NSCLC) annually, and more than half have advanced (Stage IIIB/IV) disease. Historically, survival for these patients has been poor. Moreover, even though standard systemic therapies (e.g. platinum-doublet chemotherapy) provide a modest survival advantage, a substantial proportion(~60%) of patients do not initiate or complete treatment. The advent of newer systemic therapies with more favorable effectiveness and toxicity profiles affords opportunities to improve NSCLC outcomes. The objectives of this study were: 1)to quantify survival gains from 1990-2015, ranging from a period when best supportive care(BSC) only was standard, to the present, where multiple cytotoxic and targeted therapies are available, and 2)to project the potential impact of increasing use of modern systemic therapies in clinically appropriate patients. **Methods:** We developed a simulation model to estimate observed and potential survival gains for patients diagnosed with advanced NSCLC in 1990 and 2015. Survival inputs were derived from Phase III clinical trials referenced in National Comprehensive Cancer Network guidelines, and extrapolated to a lifetime horizon by fitting Weibull curves. Proportions of patients receiving available therapies were derived from SEER (for % receiving BSC only) and a commercial treatment registry. Outcomes included one-year survival proportion, mean expected overall survival(OS), expected OS if the proportion receiving systemic therapy is increased by 10% ("Scenario 1") and 30% ("Scenario 2") relative to current use, and population-level estimates of total life years. Results were calibrated with SEER overall survival curves. Annual incidence of advanced NSCLC was assumed to be 92,000 in both years. **Results:** In the expected survival analysis, from 1990 to 2015, one-year survival proportion increased by 15.8% and mean per-patient survival improved by 4.3 months (33,412 population life years)(Table 1). In scenarios 1 and 2, the improvement in survival increased to 4.6 months (35,684 population life years) and 5.2 months (40,279 population life years), respectively. Considering the proportion receiving each treatment, and the size of overall survival treatment effects, the majority of the survival gains were attributable to the advent of platinum-doublet chemotherapy (49%), followed by EGFR (35%), VEGF (10%), and ALK (6%) targeted therapies.

Table 1: Advanced non-small cell lung cancer outcomes by year of diagnosis.

Diagnosis Year	Expected: One-Year Survival (%)	Expected: Mean Per-Patient Survival (Months)	Expected: Population Life Years	Scenario 1: Population Life Years with 10% Relative Increase in Proportion Treated	Scenario 2: Population Life Years with 30% Relative Increase in Proportion Treated
2015	29.3%	11.4	87,287	89,559	95,154
1990	13.5%	7.1	53,875	53,875	53,875
Difference	+15.8%	+4.3	+33,412	+35,684	+40,279

Conclusion: Though survival remains poor in advanced NSCLC relative to other common cancers, meaningful progress in per-patient and population-level outcomes has been realized over the past 25 years. These advances can be improved even further by increasing use of systemic therapies in the substantial proportion of patients who are suitable for treatment, yet currently receive BSC only. **Keywords:** Non-small cell lung cancer, Advanced, Survival, Systemic Therapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-041 MD Anderson Oncology Expert Advisor™ System (OEA™): A Cognitive Computing Recommendations Application (App) for Lung Cancer
George R. Simon[1], Daniel Gomez[2], Mara B. Antonoff[3], Quynh-Nhu Nguyen[2], Emily Roarty[4], Kathryn A. Gold[5], Sunil Patel[6], Renata Ferrarotto[1], Joshua Allen[7], Rick Stevens[8], Fernando S. Siaz[9], Mitchell Berger[10], Garrett Walsh[11], Mark Mynier[12], Rob High[13], Andy Futreal[14], Stephen Hahn[15], Stephen Swisher[16], John V. Heymach[17], Oea System Development Team[14], Lynda Chin[18] *[1]Thoracic Medical Oncology, MD Anderson Cancer Center, Houston/TX/United States of America, [2]Dept of Radiation Oncology, MD Anderson Cancer Center, Houston/TX/United States of America, [3]Thoracic and Cardiovascular Surgery, UT MD Anderson Cancer Center, Houston/TX/United States of America, [4]Thoracic, Head & Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston/TX/United States of America, [5]University of Texas MD Anderson Cancer Center, Houston/TX/United States of America, [6]1400 Holcombe Blvd, Unit#432, MD Anderson Cancer Center, Houston/TX/United States of America, [7]Watson Solutions, Ibm, Durham/NC/United States of America, [8]Ibm, Burlington/VT/United States of America, [9]Ibm, Houston/AL/United States of America, [10]Pwc, Atlanta/AL/United States of America, [11]Thoracic Surgery, MD Anderson Cancer Center, Houston/TX/United States of America, [12]Pwc, Atlanta/United States of America, [13]Ibm Watson, Austin/AL/United States of America, [14]MD Anderson Cancer Center, Houston/AL/United States of America, [15]Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston/TX/United States of America, [16]Thoracic and Cardiovascular Surgery, MD Anderson, Houston/AL/United States of America, [17]Thoracic/Head and Neck Medical Oncology, MD Anderson, Houston/TX/United States of America, [18]Instituteof Applied Cancer Sciences, MD Anderson Cancer Center, Houston/TX/United States of America*

Background: The OEATM is a clinical support system with a continuous improvement capability. Its objectives are to enable/empower evidence-based decisions/care by disseminating knowledge and expertise to physicians/users tailored to meet the clinical needs of individual patients as if consulting with an expert. Cognitive computing platforms have the potential to disseminate expert knowledge and tertiary level care to patients. This objective is made possible by making available to physicians/providers cognitive computing generated expert recommendations in diagnosis, staging and treatment. The cognitive computing software was trained by MD Anderson experts using currently available consensus guidelines and an iterative feedback process. Here we test the capability of this cognitive computing software program developed at MD Anderson to generate expert recommendations when patients with advanced-stage NSCLC have a targetable molecular aberration. **Methods:** We developed a web based prototype of MD Anderson's Oncology Expert Advisor (OEATM), a cognitive clinical decision support tool powered by IBM Watson. The Watson technology is IBM's third generation cognitive computing system based on its unique capabilities in natural language processing and deep QA (question-answer). We trained OEATM by loading historical patient cases and assessed the accuracy of targeted treatment suggestions using MD Anderson's physicians' decisions as benchmark. A false positive result was defined as a treatment recommendation rendered with high confidence that was non-correct (less optimal), whereas false negative was defined as a correct or more optimal treatment suggestion listed as a low confidence recommendation. **Results:** In our preliminary analyses, OEATM demonstrated four core capabilities: 1) Patient Evaluation through interpretation of structured and unstructured clinical data to create a dynamic case summary with longitudinal view of the pertinent events 2) Treatment and management suggestions based on patient profile weighed against consensus guidelines, relevant literature, and MD Anderson expertise, which included approved therapies, genomic based therapies as well as automated matching to appropriate clinical trials at MD Anderson, 3) Care pathway advisory that alerts the user for anticipated toxicities and its early identification and proactive management, and 4) Patient-oriented research functionalities for identification of patient cohorts and hypothesis generation for future potential clinical investigations. Detailed testing continues and the accuracy of standard-of-care (SOC) treatment recommendations of OEATM, as well as false positivity and negativity rates will be presented in detail at the meeting. **Conclusion:** OEATM is able to generate dynamic patient case summary by interpreting structured and unstructured clinical data and suggest personalized treatment options. Live system evaluation of OEATM is ongoing and the application of OEATM in clinical practice is expected to be piloted at our institution.
Keywords: Cognitive Computing, lung cancer, Targeted therapy, Oncology Expert Advisor

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-042 Cost-Effectiveness of Afatinib vs. Erlotinib in the 1st-Line Treatment of Metastatic NSCLC Patients with EGFR Exon 19 Deletion Mutations
Jonathan Graham[1], Rakesh Luthra[2], Stephanie Earnshaw[1], Rohit Borker[2] *[1]RTI Health Solutions, Research Triangle Park/NC/United States of America, [2]Boehringer Ingelheim, Ridgefield/CT/United States of America*

Background: EGFR mutation-positive (EGFR M+) NSCLC is a specific lung cancer subtype characterized by presence of EGFR mutations and sensitivity to treatment with EGFR tyrosine kinase inhibitors (TKIs). Common activating mutations (Del19, L858R) account for ~90% of EGFR M+ NSCLC cases. Afatinib, an oral, irreversible ErbB family blocker, improved progression-free survival (PFS) versus standard platinum-based chemotherapy in 1st-line EGFR M+ NSCLC. Afatinib also significantly prolonged overall survival (OS) in the EGFR Del19 mutation subgroup. Erlotinib, a reversible EGFR TKI licensed in the US has also improved PFS in EGFR Del19 mutation subgroup, but not OS. The objective of this study was to assess the cost-effectiveness of afatinib versus erlotinib in the 1st-line treatment of patients with metastatic EGFR Del19 M+ NSCLC in the US healthcare setting. **Methods:** A partitioned survival model was developed consisting of "progression-free", "progressive disease", and "death" health states. Patients entered the model in the progression-free state and advanced to progressive disease and death based on the progression-free survival and overall survival curves. The survival curves for afatinib were estimated by fitting parametric models to the empirical data from the LUX-Lung 3 clinical trial. For erlotinib the survival curves were estimated based on hazard ratios that were applied to the afatinib curves. The hazard ratios were derived via a network meta-analysis. Patients incurred treatment-specific drug costs for afatinib and erlotinib until disease progression. Costs to treat grade 3/4 adverse events were applied to each treatment. Resource use from the LUX-Lung 3 trial data and unit costs from published literature and from standard U.S. sources were used to derive the additional, monthly costs of being progression free. Monthly continuing care costs and one-time, end-of-life costs for patients with progressive disease were obtained from published literature. The utility of progression-free disease was obtained from LUX-Lung 3, and the disutility of progressive disease was obtained from the published literature. Disutilities associated with adverse events were also obtained from the literature. The model calculated patient survival (life years) and quality of life adjusted years (QALYs), and total costs per patient. Incremental cost-effectiveness ratios (ICERs) were calculated as the ratio of the difference in cost to the difference in LYs and QALYs. Costs and outcomes were calculated over a 20-year time horizon and discounted at an annual rate of 3%. **Results:** Based on the model, the patients taking afatinib accrued more life years (3.09 vs. 2.46) and QALYs (2.17 vs. 1.72) than patients taking erlotinib. Although the wholesale acquisition cost (WAC) of afatinib was lower than that of erlotinib, the incremental per patient cost was higher with afatinib ($ 32,961) owing to patients spending more time in "progression-free", and "post-progression" health states in the afatinib group. At an accepted US ICER threshold of $100,000/QALY, afatinib vs. erlotinib had an ICER/QALY gained of $74,345 and cost per LY gained was $52,401. **Conclusion:** Afatinib as a 1st-line therapy for locally advanced or metastatic NSCLC with EGFR exon 19 deletion mutations is a cost-effective alternative to erlotinib according to the commonly accepted cost-effectiveness threshold in the US.
Keywords: EGFR Del19, NSCLC, afatinib, cost effectiveness

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-043 Lung Cancer Radiotherapy - Current Patterns of Practice in Australia and New Zealand
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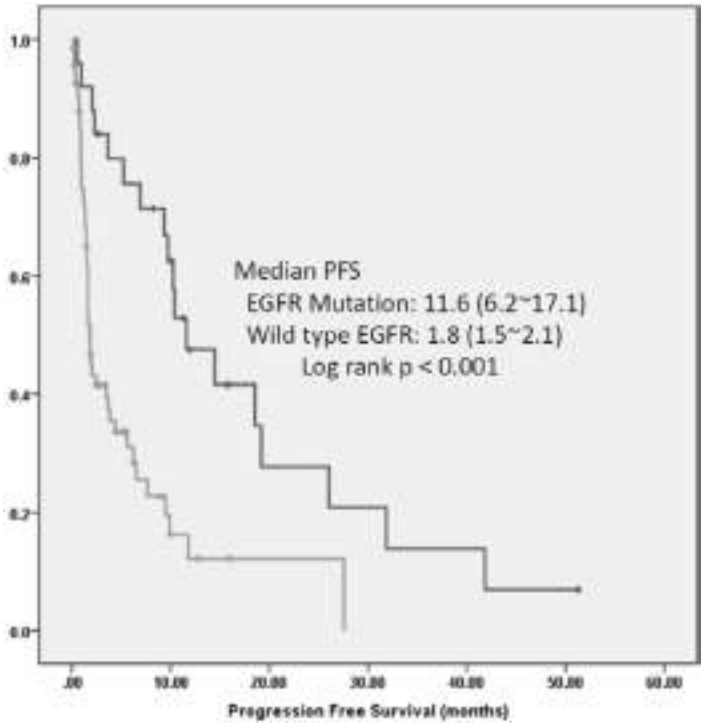
Background: The RANZCR Faculty of Radiation Oncology Lung Interest Cooperative (FROLIC) surveyed patterns of lung cancer radiotherapy practice in Australasia for both non-small cell (NSCLC)and small cell lung (SCLC) cancer to evaluate current patterns of care and define gaps in optimal care requiring improvement. **Methods:** Radiation Oncologists were surveyed at all 62 departments in Australasia using a web-based survey targeting those treating lung cancer. Questions covered current radiotherapy practice as well as measures of quality **Results:** Of 62 responses received, 57 did treat lung cancer and were eligible for analysis. All Australian states and New Zealand were represented. Sixty-two percent of respondents worked at metropolitan centres, 58% were subspecialists in lung cancer and 60% participate in lung cancer trials. Ninety-four percent discuss lung cancer patients at a tumour board, 74% peer review contours for conventional fractionation and 50% for SABR. Fifty percent used a department protocol for contouring and/or prescription, 39%, an external protocol and 11% had no protocol. For radical conventional radiotherapy, 58% use 4DCT to assess tumour motion, 44% utilise breath hold or respiratory gating, 44% use PET Fusion, 35%, free-breathing CT and 23% PET-CT simulation. In palliative settings, free-breathing CT was most common (81%). For conventional treatment, 98% use 3DCRT, 34% IMRT and 18% VMAT. Image verification was primarily with cone beam CT (86%), KV imaging (72%) and MV imaging (30%). The commonest dose fractionation regime in NSCLC was 60Gy in 30 fractions used in 95% of node-positive and 82% of node-negative disease. 66Gy in 33 fractions and 50-55Gy in 20 had been used by 32% and 30%of respondents respectively. 30Gy/10 fractions was the most frequent palliative regime that had been used (by 76%), followed by 36Gy/12 (72%) . For limited stage SCLC, the majority (61%) treated with 45-50.4Gy in 25-28 fractions while 45Gy/30 twice daily had been used by 48%. In extensive stage SCLC, consolidation chest radiotherapy was used by 63% in complete response, 48% for partial response and 24% would not treat. 46% of departments provided SABR but only half treated central tumours. For peripheral tumours, 80% used 54Gy in 3 fractions and if close to chest wall, 70% used 48Gy in 4 fractions. In fit patients with synchronous solitary brain metastasis and controlled extra-thoracic disease, 37% of respondents would treat both chest and brain definitively, 43% would do so only if chest disease was equivalent to Stage I/II, and 9% would never treat radically. If three brain metastases were present, just 46% would treat definitively. In the setting of an isolated systemic metastasis only, 35% would treat definitively while 61% do not offer definitive treatment in the setting of systemic oligo-metastases. **Conclusion:** A significant proportion of radiation oncologists did not have access to 4DCT for simulation. The majority used 3D image verification and consistently prescribed evidence-based doses. Although protocols were widely used, a significant number did not participate in peer review of contours. The treatment of synchronous oligo-metastatic disease was variable, likely due to a lack of high quality evidence and should be an area of future research.
Keywords: patterns of practice, non small cell lung cancer, small cell lung cancer, Radiotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-044 EGFR-TKIs as Second-Line Treatment of Patients with NSCLC with or without Activating EGFR Mutation as Assessed by Sensitive PNA Clamping Method Young-Chul Kim, Hayoung Choi, Cheol-Kyu Park, In-Jae Oh, Sung-Ja Ahn, Kook-Joo Na, Sang-Yun Song, Yoo-Duk Choi, Mee Sun Yoon, Ju-Sik Yun, Hyun-Ju Seon *Lung and Esophageal Cancer Clinic, Chonnam National University Hwasun Hospital, Jeonnam/ Korea*

Background: Although TAILOR phase 3 trial showed superiority of docetaxel versus erlotinib as second line treatment in NSCLC with wild type EGFR as assessed by direct sequencing, second-line treatment of patients with wild-type status is controversial and EGFR-TKIs are still used as second line treatment. **Methods:** We retrospectively analyzed the results of 2nd line treatment with EGFR-TKIs in 25 patients with activating EGFR mutations and 68 patients with wild-type EGFR as assessed by PNA clamping (Panagene®, South Korea), which is more sensitive than direct sequencing. **Results:** There was no significant difference in age, sex, smoking history and histologic subtypes of NSCLC between the two groups. Erlotinib was more frequently used in EGFR wild group (48/68, 71%), while use of gefitinib was significantly higher in EGFR mutation group (15/25, 60%, p=0.003). Progression-free survival (PFS) was significantly longer in EGFR mutation group than EGFR wild group: median PFS was 11.6 months (95% CI 6.2~17.1) in mutation group versus 1.8 months (1.5~2.1) in wild group (log rank p<0.001). PFS was numerically shorter than the 2.4 months (2.1~2.6) of TAILOR trial.



Conclusion: This results show that possibility of survival benefit using second-line EGFR-TKI is very low in patients with NSCLC with wild-type EGFR status, when tested with sensitive EGFR mutation detection technique. Thus chemotherapy should be favored for the second line treatment of patients with NSCLC with wild-type EGFR status. **Keywords:** EGFR, PNA clamping, EGFR-TKI

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-045 Clinical Experience on Treatment of Advanced Lung Adenocarcinoma With Unknown EGFR Gene Status From a Tertiary Care Center in China Long Y. Zheng[1], Chen X. Zhang[1], Li L. Chen[2], Yu C. Mao[1], Jiong Qian[1], Ping H. Jiang[1], Jing Deng[1], Ming G. Shi[1], Nong Xu[1] [1]*Medical Oncology, The First Affiliated Hospital of Zhejiang University, Hangzhou/China,* [2]*Taizhou First Hospital, Taizhou/China*

Background: Limited data are available on treatment experience in patients with advanced lung adenocarcinoma with unknown EGFR gene status (UN-EGFR-GS). We studied the demographic profile and treatment outcomes of advanced NSCLC patients with adenocarcinoma, which the EGFR gene status was unknown. **Methods:** Retrospective study of patients with UN-EGFR-GS advanced lung adenocarcinoma over a 4-year period at a tertiary care institute in China. Patients diagnosed with stage IIIb or IV were included for analysis during 2009 and 2012. **Results:** In total, 113 patients were included, females and males constituted 46.9% (n=53) and 53.1% (n=60), respectively. Among the 113 patients, 53 were non-smokers and 60 were smokers. The median age was 57.5y(35y-85y). The performance score was 2 in only 12 patients, otherwise was 0 or 1. Majority of patients had stage IV disease (95.6%). Seventy-five patients were advanced stage when diagnosed, and 38 patients were relapsed disease once received surgical resection. Nine patients received adjuvant chemotherapy, which were not relapsed in 6 months after finishing last cycle. The common regimens of first-line treatment were gemcitabine plus platinum (n=36) and pemetrexed plus platinum (n=32). Eleven patients received EGFR-TKIs as first-line treatment. Other drugs included docetaxel, paclitaxel, novelbine and etc. The commonest second-line treatment was oral EGFR-TKIs (n=44). Fifty patients received third-line treatment and 19 received fourth-line treatment. At the end of follow-up (2015-3-30), 91 patients were dead and 22 patients were alive or lost follow up. The median survival of this whole cohort was 20.0m (16.1m-24.0m, 95%CI). The overall survival was not associated with sex (p=0.441), performance status (p=0.809) and smoking (p=0.677). Those patients (29.9m, 95%CI; 18.6m-41.1m) who received surgical resection lived longer than the patients (17.8m, 95%CI; 13.8m-21.8m) who were advanced stage when diagnosed (p=0.01). The overall survival was also not associated with the chemotherapy drugs used in the first-line treatment. The patients (19.0m, 95%CI; 11.4m-26.5m) used pemetrexed plus platinum lived no longer than other regimens (20.5m, 95%CI; 13.4m-27.4m) (p=0.272). In the gemcitabine plus platinum group, the median survival was 19.9m (95%CI; 9.2m-30.6m), which was not longer than other regimens (20.0m, 95%CI; 15.4m-27.4m). The p value was 0.404. We also analyzed the influence of oral EGFR-TKIs on overall survival. Those who had a chance taken EGFR-TKIs lived numerically longer than never; the median survival was 24.8m (19.1m-30.5m, 95%CI) and 16.3m (12.7m-19.9m, 95%CI), respectively. However, the overall difference was not significant (p=0.184). **Conclusion:** The median survival of patients with advanced lung adenocarcinoma with UN-EGFR-GS was 20m. Oral EGFR-TKIs appear to be useful for this group of patients. **Keywords:** Adenocarcinoma, treatment, EGFR-TKI, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-046 Making the Diagnosis of Cardiac Tamponade in Lung Cancer Patients Pooja Ghatalia[1], Christopher Wang[2], Stefan C. Grant[3] [1]*Internal Medicine, University of Alabama at Birmingham, Birmingham/AL/United States of America,* [2]*Medical Oncology, University of Alabama at Birmingham, Birmingham/United States of America,* [3]*Medical Oncology, Wake Forest University, Winston-Salem/AL/United States of America*

Background: Malignant pericardial effusions are common in lung cancer (LC) and can produce cardiac tamponade (CT). This oncologic emergency requires a high index of suspicion for accurate, prompt diagnosis. To study how CT is diagnosed in LC, we reviewed symptoms, signs and differential diagnoses recorded, and tests obtained, at a tertiary teaching hospital. **Methods:** Records of patients hospitalized with a diagnosis of CT between April 1999 and September 2011 were reviewed, focusing on LC related CT. Extent of disease, treatment history and response, symptoms, vital signs, physical exam and EKG findings recorded by the initial and admitting physicians were recorded, together with differential diagnoses mentioned in the physician notes before radiologic testing. Finally, the radiologic tests used to make or confirm the diagnosis were recorded. **Results:** Of 770 patients with a diagnosis of CT, 57 had malignant CT and 26 had LC. Of these, 7 (27%) were newly diagnosed with cancer at the time of diagnosis of CT. The most common symptom, shortness of breath, was present in 24 (92%) cases. Physical exam findings recorded by physicians are listed in Table 1. EKG findings of low QRS voltage/electrical alternans were present in 3, absent in 3 and were not documented in 20 patients. In only 8 cases (31%) CT was included in the differential diagnosis based on the signs, symptoms and EKG findings at initial presentation. Of these, 3 had a known prior history of pericardial effusion and 3 were newly diagnosed with LC at the time of presentation. Two of these diagnoses were made by oncologists and the other 6 were made by Emergency physicians (ED)/internists. In the remaining 18 cases, the diagnosis was made serendipitously with imaging studies obtained for other reasons. Of these, 5 patients had a known history of malignant pericardial disease and 6 were newly diagnosed with LC. The physician seeing the patient initially was an oncologist in 5 cases and an ED /internist in 13 cases.

	Jugular venous distention	Distant heart sounds	Pulsus paradoxus	Tachycardia	Hypotension
Present	7 (27%)	5 (19.2%)	3 (11.5%)	22 (84.6%)	6 (23%)
Absent	10 (38.4%)	-	4 (15.3%)	4 (15.3%)	20 (77%)
Not recorded	9 (34.6%)	21 (80.7%)	19 (73%)	-	-

Conclusion: Not including CT in the differential diagnosis of LC patients presenting with dyspnea is common among physicians of all types, including oncologists, internists, and ED. Physicians should include CT in the differential diagnosis of LC patients presenting with dyspnea and tachycardia, especially those with advanced disease, and a careful physical examination will elicit the classic signs in a substantial proportion of patients. Without a high index of clinical suspicion the diagnosis may be delayed or missed. **Keywords:** lung cancer, diagnosis, physical examination, cardiac tamponade

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

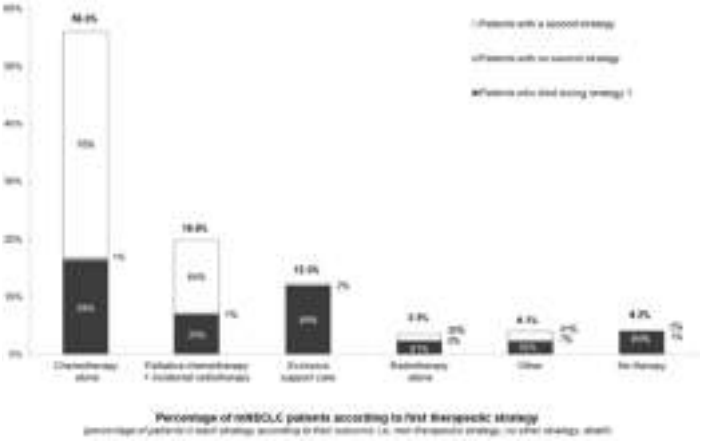
P2.01-047 Fibrobronchoscopic Cryorecanalization for Unresectable Secondary Malignant Tumors of the Trachea and Main Bronchi Qianli Ma[1], Bin Shi[2], Yanchu Tian[2], Deruo Liu[1] [1]*Thoracic Surgery, China-Japan Friendship Hospital, Beijing/China,* [2]*China-Japan Friendship Hospital, Beijing/China*

Background: Most patients with secondary malignant tracheobronchial tumors have distressing symptoms due to major airway obstruction. However, they are always too frail for curative surgical resection. We choose fibrobronchoscopic cryorecanalization to improve their life quality and analyzed the long time survival outcome.Most patients with secondary malignant tracheobronchial tumors have distressing symptoms due to major airway obstruction. However, they are always too frail for curative surgical resection. We choose fibrobronchoscopic cryorecanalization to improve their life quality and analyzed the long time survival outcome. file://localhost/Users/app/Documents/2014下半年/11122014%20JTO/冷冻/Figures/Figure%202.tif file://localhost/Users/app/Documents/2014下半年/11122014%20JTO/冷冻/Figures/Figure%201.tif file://localhost/Users/app/Documents/2014下半年/11122014%20JTO/冷冻/Figures/Figure%203.tif **Methods:** Clinical records of 14 patients were reviewed retrospectively from December 2005 to January 2013. A temperature from -50℃ to -70℃ was delivered to the central part of the tumor by cryo-probe for 4 to 6 minutes causing destruction of the tumor mass (Cryo-melt method). Subsequently, the edge of tumor was froze for 0.5 to 2 minutes and then tore the lesion piece by piece immediately with the advantage of concretion between the frozen probe tip and the tumor tissue (Cryo-resection method). file://localhost/Users/app/Documents/2014下半年/11122014%20JTO/冷冻/Figures/Figure%204.tif **Results:** The rates of dramatic and partial symptomatic alleviation were 57.1% and 28.6% respectively. There were no intraoperative deaths. The median survival was 16.0 months. Overall survival was 64.3% at half year, and 50.0% at 2 years. 2-year survival was significantly correlated to age (less than 60 years 22.2% versus more than 60 years 100%, p=0.011), tumor location (main bronchi 0% versus trachea 77.8%, p=0.003), and cryorecanalization times (one time 33.3% versus two or more times 80.0%, p=0.037). file://localhost/Users/app/Documents/2014下半年/11122014%20JTO/冷冻/Figures/Figure%205.tif file://localhost/Users/app/Documents/2014下半年/11122014%20JTO/冷冻/Figures/Figure%206.tif file://localhost/Users/app/Documents/2014下半年/11122014%20JTO/冷冻/Figures/Figure%207.tif **Conclusion:** Fibrobronchoscopic cryorecanalization is a safe, easily repeatable and effective minimally invasive choice for releasing the airway obstructive symptoms. In addition to high local-regional control rates, a rewarding result of prolonged survive time can also be obtained. **Keywords:** secondary tracheobronchial tumors, Airway obstruction, cryosurgery, bronchoscopy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-048 Real-Life 2-Year Therapeutic Strategies in the Management of Metastatic Non-Small-Cell Lung Cancers: The ESCAP Study Didier Debieuvre[1], François Goupil[2], Bertrand Lemaire[3], Dominique Herman[4], Lionel Falchero[5], Patrick-Aldo Renault[6], Antoine Lévy[7], Patrick Dumont[8], Nadine Paillot[9], Philippe Masson[10], Jean-Renaud Barrière[11], Yannick Duval[12], Bernard Asselain[13], François Blanchon[14], Françis Martin[15], Michel Grivaux[14] [1]*Emile Muller General Hospital, Mulhouse/France,* [2]*Centre Hospitalier Du Mans, Le Mans/France,* [3]*Centre Hospitalier D'Orléans, Orléans/France,* [4]*Hopital Pierre Beregovoy, Nevers/France,* [5]*Centre Hospitalier de Villefranche-Sur-Saône, Villefranche-Sur-Saône/France,* [6]*Centre Hospitalier Général de Pau, Pau/France,* [7]*Centre Hospitalier Jacques Coeur, Bourges/France,* [8]*Centre Hospitalier de Chauny, Chauny/France,* [9]*Hôpital Notre Dame de Bon Secours, Metz/France,* [10]*Centre Hospitalier de Cholet, Cholet/France,* [11]*Centre Hospitalier Général Draguignan, Draguignan/France,* [12]*Centre Hospitalier Cannes, Cannes/France,* [13]*Institut Curie, Paris/France,* [14]*Centre Hospitalier de Meaux, Meaux/France,* [15]*Centre Hospitalier Général de Compiègne, Compiegne/France*

Background: In the last years, new drugs and strategies have emerged in the management of lung cancer (LC). The French College of General Hospital Respiratory Physicians therefore promoted a prospective multicenter epidemiological study: the ESCAP study. This study was aimed to describe the therapeutic strategies implemented during the first 2-year after diagnosis in patients with LC followed in French General Hospital chest departments. We report below descriptive results for metastatic non-small-cell lung cancer (mNSCLC). **Methods:** For each patient with a LC diagnosed in 2010, a standardized form was completed at diagnosis and following each change in treatment strategy up to at least 2 years after diagnosis. **Results:** 53 centers participated in the ESCAP study and included 3,943 patients. Among them, 3,418 patients had a NSCLC. NSCLC was metastatic in 2,003 patients. In patients with mNSCLC, the first therapeutic strategy was chemotherapy alone (56%) followed by palliative chemotherapy plus incidental radiotherapy (35%); 4% of patients died without any implemented therapeutic strategy (see figure). 29% of patients with chemotherapy alone as first strategy died without undergoing any other strategy and 70% had a second strategy (72% chemotherapy alone). 35% of patients with radiochemotherapy died without undergoing any other strategy and 64% had a 2nd strategy (73% chemotherapy alone).



The most frequent chemotherapy during the first strategy was platinum salts doublet with pemetrexed (39%), followed by platinum salts doublet with paclitaxel (15%). Chemotherapy during the second strategy was second line chemotherapy (67%) or maintenance therapy (25%). EGFR-TKi (34%) and docetaxel (26%) alone were the most frequently prescribed drugs for second line chemotherapy, and pemetrexed (44%) and EGFR-TKi (26%) alone for maintenance therapy. **Conclusion:** The ESCAP study describes the 2-year management of metastatic NSCLC on real-life settings in France. Its preliminary results are consistent with the guidelines of the French National Cancer Institute. **Keywords:** therapeutic strategies, Metastatic NSCLC, New drugs

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-049 Surgical Treatment Results of T4 Lung Cancer Invading Mediastinum Masayuki Tanahashi, Hiroshi Niwa, Haruhiro Yukiue, Eriko Suzuki, Naoko Yoshii, Masayuki Shitara, Toshio Fujino *Division of Thoracic Surgery, Respiratory Disease Center, Seirei Mikatahara General Hospital, Hamamatsu, Shizuoka/Japan*

Background: Inoperable cases are common in T4 lung cancer patients, and their prognoses are mostly poor. Nevertheless, among those who undergo resection, some can achieve long-term survival. We reviewed the validity of surgical treatment for T4 lung cancer at our department. **Methods:** Fifty-six cases of pathologically confirmed T4 lung cancer resection between January 1989 and December 2013 were selected for this study. Cases of nodules in different lobes of the same lung were ineligible. The relationships among the number of infiltrated organs, pN factor, presence or absence of preoperative treatment, histological effect (Ef), and surgical curative rate and prognosis were assessed using statistical techniques. **Results:**The subjects consisted of 53 males and 3 females with an average age of 62.2 years. Depending on the histological types, they were classified as squamous cell cancer (29 cases), adenocarcinoma (16 cases), adenosquamous cancer (7 cases), large cell cancer (1 case), and other cancers (2 cases). Also, there were 37 single and 19 multiple organ infiltration cases, which were classified by infiltrated organ as 16 in the trachea and tracheal bifurcation, 11 in the vertebral body, 10 in the aorta, 10 in the superior vena cava, 9 in the mediastinum, 6 in the left atrium, 6 in the pulmonary artery, 5 in the esophagus, and 2 in the subclavian artery, including duplicated cases. Preoperative treatment was carried out in 22 cases (chemoradiotherapy, 14; chemotherapy, 8), whose histological effect was Ef0-1 in 13 and Ef2-3 in 9. The surgical curative rate was complete resection in 27 and incomplete resection in 29; complete resection was common in those receiving preoperative treatment. There were no death cases within 30 days after the surgery. In all cases, the five-year survival rate was 21.7% and median survival time (MST) was 16.5 months. The five-year survival rate was 27.5% in single organ infiltration compared with 15.8% in multiple organ infiltration (P = 0.08), 27.5% in n0-1 versus 13.8% in n2-3 (P = 0.30), 36.8% with preoperative treatment in contrast to 11.2% without preoperative treatment (P = 0.06), 9.4% in Ef0-1 as opposed to 76.2% in Ef2-3 (P = 0.05), and 37.7% in complete resection in comparison with 7.8% in incomplete resection (P = 0.003). Long-term survival over 5 years was noted in 7 cases (12.5%), 4 of which involved single organ infiltration, n0-1, preoperative treatment, and Ef2-3. **Conclusion:** Single organ infiltration and n0-1 are good surgical indications for T4 lung cancer, and a favorable prognosis can be expected if preoperative treatment and complete resection are performed. **Keywords:** T4 NSCLC, Surgical treatment, Induction treatment

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-050 Influence of Maintenance Therapy on Incidence of 2nd Line Therapy and OS in NSCLC IV Anne C. Lueers[1], Nicole Neemann[2], Regina Prenzel[1], Douglas Scriba[1], Michael Hoheisel[1], Katrin Wedeken[1], Kay Wilborn[1], Frank Griesinger[1] [1]*Pius-Hospital, Oldenburg/Germany,* [2]*University of Oldenburg, Oldenburg/Germany*

Background: One of the strongest rationale for maintenance therapy in NSCLC is the fact that exposure to 2nd line therapy is only 40-60% in clinical trials in specialized treatment centers. Even with follow-up intervals of 6 weeks, the 2nd line treatment rate does not seem to increase. We analyzed the exposure of 2nd line therapy as well as OS and PFS in patients with stage IV NSCLC in the subgroups no 2nd line, 2nd line after maintenance and

2nd line without maintenance therapy. **Methods:** All primary lung cancer cases stage IV in the lung cancer center were analyzed based on the documentation files between 2009 and 2013. Patients were followed-up between 1st and 2nd line therapy every 6-8 weeks according to S3 guidelines. Patients with EGFR+, ALK+ or ROS1+ were excluded from the analysis. **Results:** 221 patients were diagnosed with NSCLC IV (UICC7), or had systemic relapse of localized disease and were treated with 1st line therapy for metastatic disease. Of these, 160 (72%) received 1st line combination therapy with Carboplatin, 50 (23%) with Cisplatin and 11 (5%) with platin-free single agent therapy. 45 (19%) of all patients received maintenance therapy, most of them with bevacizumab. Of 221 patients, 203 (92%) progressed after 1st line therapy or 1st line and maintenance therapy. 106/163 (65%) of non-maintenance therapy patients received 2nd line therapy, 57 patients (36%) did not. Of 40 patients receiving maintenance therapy and requiring 2nd line therapy, 31 (78%) received 2nd line therapy. Reasons for not obtaining 2nd line therapy were captured and were manifold. Survival analyses showed significant differences regarding overall survival (median survival 21 (maintenance and 2nd line) vs. 13 (1st and 2nd line) months) but no relevant differences regarding progression free survival on 2nd line (median 2 months). **Conclusion:** In a certified lung cancer center and stringent follow-up every 6 to 8 weeks, 1/3 of patients do not receive 2nd line therapy because of various reasons. The application of maintenance therapy raises the chances of receiving 2nd line therapy and increases overall survival whereas progression free survival is not affected. **Keywords:** second line therapy, maintenance therapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-051 Determinants of Sequential versus Concurrent Chemoradiotherapy in Stage III Non-Small Cell Lung Cancer Patients Iris Walraven[1], M Ten Berge[2], Ronald Damhuis[3], C. Tissing-Tan[4], E. Troost[5], B. Reymen[5], J. Widder[6], F. Koppe[7], A. Van Der Wel[8], E. Vonk[9], I. Coremans[10], J. Bussink[11], K. De Jaeger[12], N. Van Der Voort Van Zyp[13], Sherif El Sharouni[14], H. Knol[15], D. Woutersen[16], Jose Belderbos[1]
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Background: Concurrent chemoradiotherapy (CCRT) is considered the standard treatment regimen in patients with inoperable stage III non-small cell lung cancer (NSCLC). Sequential chemoradiotherapy (SCRT) is recommended in patients who are deemed unfit to receive CCRT. As this selection criterion is not very explicit, the 'personalized' choice for either CCRT or SCRT is mainly dependent on the multidisciplinary team and treating physician's judgment. Consequently, this may result in a variation of treatment policies across hospitals/radiotherapy (RT) departments. In this study, we investigated the ratio CCRT/SCRT in eight RT departments in the Netherlands. Furthermore, we explored which patient and disease characteristics determined the choice for SCRT compared to CCRT. **Methods:** Data were derived from the Dutch Lung Radiotherapy Audit (DLRA). Within the DLRA, lung cancer patients undergoing a curative intent treatment are prospectively registered with respect to patient and disease characteristics, diagnostics and treatment. For this study, from eight out of 21 Dutch RT departments, patients with stage III NSCLC undergoing chemoradiotherapy in 2014 were selected. CCRT was defined as ≤ 50 days between the start of chemotherapy and the start of radiotherapy. Furthermore, RT had to start before the end of the last chemotherapy in CCRT. Patients with < 150 days between treatments were scored as undergoing SCRT. Differences in patient and disease characteristics between CCRT and SCRT were tested with independent samples t-tests (for continuous variables) and with chi-square tests (for categorical variables). A multivariate logistic regression model was constructed to determine patient and disease characteristics associated with the choice for SCRT, using a backward selection procedure. Odds ratios (OR) with 95% confidence intervals (CI) are reported. **Results:** In total, 453 stage III NSCLC patients (mean age 65.4 years, 56.5% male) were registered. Of those, 351 (77.5%) patients underwent CCRT and 102 (22.5%) patients received SCRT. The proportion of patients treated with CCRT ranged from 51% to 89% across RT departments. Gender, smoking, gross target volume (GTV), performance score (PS), lung function, Charlson comorbidity index and tumor location were not significantly associated with SCRT in the multivariate model. Conversely, older age (OR 1.05 [95%CI 1.03-1.09]), histology (large cell carcinoma vs adenocarcinoma [OR 0.42 CI 0.19 to 0.97]) and cN-stage (N3 vs N0-1 [OR 5.71 {95%CI 2.10-15.50}]) were significantly associated with SCRT. **Conclusion:** In this selected group of registered NSCLC patients, a large variation was observed in the proportion of stage III NSCLC patients treated with CCRT, ranging from 51% to 89% across RT departments. Surprisingly, PS and comorbidity index (as indicators of a patients' physical fitness) were not significantly different in CCRT or SCRT patients while age and cN-stage were. Based on the analyzed patient and disease characteristics, it is currently unclear why patients treated with SCRT were not eligible for CCRT. **Keywords:** sequential chemoradiotherapy, non-small cell lung cancer, concurrent chemoradiotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-052 Augmentation of NAD+ by NQO1 Activation Attenuates Cisplatin-Mediated Hearing Impairment Seihoon Yang[1], Sun-Rock Moon[2], Kang-Beom Kwon[2], Hong-Seob So[2], Sam-Youn Lee[2] [1]*Internal Medicine, Wonkwang University Hospital, Iksan/ Korea,* [2]*Wonkwang Universit Hospital, Iksan/Korea*

Background: Cisplatin [cis-diaminedichloroplatinum-II] is an extensively used chemotherapeutic agent, and one of its most adverse effects is ototoxicity. A number of studies have demonstrated that these effects are related to oxidative stress and DNA damage. However, the precise mechanism underlying cisplatin-associated ototoxicity is still unclear. The cofactor nicotinamide adenine dinucleotide (NAD+) has emerged as a key regulator of cellular energy metabolism and homeostasis. Although a link between NAD+-dependent molecular events and cellular metabolism is evident, it remains unclear whether modulation of NAD+ levels has an impact on cisplatin-induced hearing impairment. **Methods:** To investigate whether augmentation of NAD+ by NQO1 activation using b-Lapachone (b-Lap) attenuates cisplatin-mediated hearing impairment, male C57BL/6 mice and NQO1 knockout mice on a C57BL/6 background were used. For analysis of the auditory threshold, auditory brainstem response (ABR) was recorded. For biochemical analysis, we measured the enzymatic activity of SIRT1, PARP1, ROS production, NAD+/NADH ratio, mRNA levels of miR-34a and pro-inflammatory cytokines. Immunohistochemistry and western blot analysis were also performed. **Results:** We have demonstrated for the first time that both the protein expression level and the activity of SIRT1 were suppressed by the reduction of intracellular NAD+ levels in cisplatin-treated cochlear tissue. We also found that the decrease in SIRT1 protein expression and its activity after cisplatin exposure were mediated by the increase in transcriptional activity of p53 for miR-34a expression and PARP-1 activation causing NAD+-depletion, respectively. However, the increase in cellular NAD+ levels by NQO1 activation using b-Lap prevented mice from cisplatin-induced cochlear damage and hearing impairment through the modulation of PARP-1, SIRT1, p53, and NF-kB. **Conclusion:** Considering that b-Lap itself did not attenuate the tumoricidal effect of cisplatin, these results suggest that the direct modulation of the cellular NAD+ level by pharmacological agents could be a promising therapeutic strategy for enhancing the efficacy of cisplatin chemotherapy without its adverse effects. **Keywords:** cisplatin, ototoxicity, Lapachone, NAD+

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-053 The Role of Systemic Therapy in Sarcomatoid Carcinoma of the Lung Nagla Abdel Karim, Jiang Wang, Tariq Namad, Ehsan Malek, Changchun Xie, John Morris *The University of Cincinnati, Ohio/OH/United States of America*

Background: Primary sarcomatoid carcinoma (PSC) accounts for 2% to 3% of all lung cancers. Stage-for-stage, PSC carries a poorer prognosis compared to the more common types of lung cancer. It typically occurs in older heavy smoking men and has a predilection for upper lobe involvement. PSC of the lung was initially described by Virchow in 1865 as a "biphasic" lesion of adenocarcinomatous or squamous cell components along with spindle cell or giant cell elements forming at least 10% of the tumor mass. This description fulfills the current WHO criteria for the diagnosis of PSC. Mutational analysis has revealed a common origin of both elements and it is thought that epithelial-mesenchymal transition (EMT) is the mechanism of that gives rise to this tumor, with the epithelial elements (adenocarcinoma or squamous component) that has undergone a transition to a poorly-differentiated mesenchymal type (sarcomatoid) with the expression of mesenchymal proteins such as vimentin. Efforts to study PSC has been hindered by the rarity of this variant. Aim of the study: To assess the impact of surgery and various systemic therapies on patients with PSC of the lung at the University of Cincinnati Medical Center (UCMC). **Methods:** This retrospective study included all patients identified with a pathologically confirmed diagnosis of PSC of the lung treated at UCMC between the years 2000-2014. Death was considered as the study endpoint. Kaplan-Meier analysis was used to calculate median overall survival (OS) and 95% confidence intervals (CI). Cox model was used to test the chemotherapy effect adjusted for age, sex and surgery, and determine hazard ratios (HR). Data was analyzed using SAS® Version 9.4. **Results:** We identified 21 patients with a diagnosis of PSC of the lung that were eligible for chart review and analysis. The 14 men and 7 women had a median age of 59 (range, 31-84 years). Treatment with systemic chemotherapy showed a trend in improvement in outcome among all stages of disease (p=0.08 and HR 0.04) but chemotherapy was most often used in advanced stages. Female gender demonstrated a trend for improved OS (p=0.1), and older patients demonstrated a better OS (HR=0.849; p=0.041) by a one-year increase in age. The median OS of the patients with PSC treated with systemic chemotherapy was 375 days (95% CI 114-600 days). Patients with early stage disease who were eligible for surgical resection, with or without the addition of systemic chemotherapy had a median survival of 457.5 days (95% CI 206.-1187 days), only slightly different from patients with advanced disease that received systemic chemotherapy. Patients who did not receive systemic chemotherapy had a lower median OS of 256 days (95% CI 98-999 days). Two patients demonstrated EML-4/ALK translocations. The patient with the longest OS of about three years was treated with systemic therapies including cisplatin, gemcitabine, docetaxel and crizotinib. **Conclusion:** Patients with PSC of the lung may benefit from systemic therapy. Larger prospective studies are needed to confirm this benefit especially if used as an adjuvant therapy in early stage disease. **Keywords:** Sarcomatoid Carcinoma of the lung, Systemic therapy, chemotherapy, Primary Sarcomatoid Carcinoma

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-054 Continuation Maintenance Therapy of Pemetrexed and Renal Toxicities Teppei Yamaguchi, Kazuyoshi Imaizumi, Toru Nakanishi, Masamichi Hayashi, Yasuhiro Goto, Sumito Isogai, Atsushi Kato *Department of Respiratory Medicine, Fujita Health University, Toyoake/Japan*

Background: Pemetrexed is a multitargeted antifolate agent approved for use in the treatment of pleural mesothelioma and non-small cell lung cancer. A recent phase III PARAMOUNT trial has shown that pemetrexed continuation maintenance therapy reduced the risk of disease progression and death compared with a placebo. However, renal toxicities of maintenance therapy of pemetrexed has not been clarified. **Methods:** We retrospectively evaluated a total of 30 patients who had received 4 cycles of induction therapy with pemetrexed with platinum (cisplatin or carboplatin) regimens with or without bevacizumab followed by more than 4 cycles of pemetrexed (± bevacizumab) maintenance therapy. Estimated creatinine clearance at three different time points (before the induction therapy, after the induction therapy, and after the 4 cycles of maintenance therapy) were analyzed. We also investigated factors significantly associated with deterioration in renal function during pemetrexed maintenance therapy using univariate and multivariate logistic regression analyses. **Results:** Significant decrease in the mean value of eCcr could be observed during pemetrexed maintenance therapy in both cisplatin and carboplatin groups. Multivariate analysis *revealed* that cisplatin administration and poor performance status (PS ≥1) were risk factors significantly associated with eCcr decrease. **Conclusion:** Continuance maintenance therapy of pemetrexed generally could cause renal dysfunction. More attention should be paid to the patients receiving a cisplatin based induction therapy and patients with poor performance status. **Keywords:** non-small cell lung cancer, pemetrexed, maintenance therapy, renal toxicity

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-055 Prospective Study of UGT1A1*27 Gene Polymorphism for Irinotecan Therapy: Result of Lung Oncology Group in Kyushu (LOGiK1004B) Minoru Fukuda[1], Takayuki Suetsugu[2], Midori Shimada[3], Takeshi Kitazaki[3], Kohji Hashiguchi[3], Junji Kishimoto[4], Noriyuki Ebi[5], Koichi Takayama[6], Kenji Sugio[7], Hiroshi Semba[8], Yoichi Nakanishi[4], Yukito Ichinose[9] [1]*Clinical Oncology Center, Nagasaki University Hospital, Nagasaki/Japan,* [2]*Respiratory Medicine, Sendai Medical Association Hospital, Kagoshima/ Japan,* [3]*Department of Medicine, Japanese Red Cross Nagasaki Genbaku Hospital, Nagasaki/ Japan,* [4]*Center for Clinical and Translational Research (Ccrt), Kyusyu University Hospital, Fukuoka/Japan,* [5]*Department of Respiratory Oncology Medicine, Iizuka Hospital, Fukuoka/ Japan,* [6]*Research Institute for Disease of the Chest, Graduate School of Medical Sciences, Kyusyu University, Fukuoka/Japan,* [7]*Department of Thoracic and Breast Surgery, Oita University Faculty of Medicine, Oita/Japan,* [8]*Department of Respiratory Medicine, Kumamoto Regional Medical Center, Kumamoto/Japan,* [9]*Department of Thoracic Oncology, National Hospital Organization Kyusyu Cancer Center, Fukuoka/Japan*

Background: *UGT1A1*27* is known that exist together with *UGT1A1*28* as linkage disequilibrium and impair the effect of UDP-glucuronosyltransferase (UGT) in basic research, however, poor clinical investigation because of the rare frequency. The aim of this study is to evaluate the effect of *UGT1A1*27* gene polymorphism for safety and efficacy in irinotecan therapy. **Methods:** Eligibility criteria were: lung cancer patients; scheduled the dose of irinotecan therapy as single ≥ 80 mg/m^2, combination ≥ 50 mg/m^2, radiation with single ≥ 50 mg/m^2, radiation with combination ≥ 40 mg/ m^2; age ≥ 20 years; performance status 0-2. After informed consents, patients were enrolled and collected the blood to examine *UGT1A1*28* and*UGT1A1*6* polymorphism and received irinotecan therapy. Examination of *UGT1A1*27* were added when founding *UGT1A1*28* polymorphism. We planned 111 enrollment for an accrual of 10 patients with *UGT1A1*27* gene polymorphism. **Results:** Fifty patients were enrolled in this trial between October 2011 and December 2013. Two patients judged protocol violation. Remaining 48 were evaluated. *UGT1A1* gene polymorphisms *28/*28, *6/*6, *28/*6, *28/-, *6/-, -/- observed 0, 1, 1, 7, 17 and 22, respectively. *UGT1A1*27* were analyzed in 9 patients including ineligible one patients with *28/*28, however, no *UGT1A1*27* gene polymorphism was found and the study was stopped. A total of 153 times of irinotecan therapy were administered with a median of 3 times per one patient: 1 time in 7 patients (15%), 2 times in 9 (19%), 3 in 19 (40%), 4 in 3 (6%), 5 in 1 (2%), and 6 in 9 (19%). Irinotecan were used as combination chemotherapy in 32 (67%) patients, with cisplatin in 12 (25%), carboplatin in 10 (21%), gemcitabine in 9 (19%), paclitaxel in 1 (2%). In remaining 16 patients (33%), only irinotecan single therapy were administered. Radiotherapies were administered concurrently in 23 (48%) patients with median 60 (range 40-61.4) Gy. Febrile neutropenia were observed higher tendency in patients with *UGT1A1*6* (32%) and *UGT1A1*28* (25%) gene polymorphism compare with wild type (14%) but had no significant difference. Grade 3/ 4 leukopenia and neutropenia were observed in 6 out of 8 patients with *UGT1A1*28* gene polymorphism and significant higher compare with wild type (75% vs. 32%, p=0.049; 75% vs. 36%, p=0.039, respectively). The other toxicities have no difference between*UGT1A1* gene polymorphism and wild type. There was no pneumonitis and treatment-related death. Tumor response was not evaluated because not included endpoints. Median PFS of 48 patients was 6.8 months and the 1- and 2-year survival rates were 20.8%. Median PFS separated by UGT1A1 gene polymorphisms were 10.1 months in *UGT1A1*28* heterozygous, 8.5 months in *UGT1A1*6* heterozygous, and 6.8 months in both wild type, respectively. Median OS of 48 patients was 15.7 months and the 1- and 2-year survival rates were 57.7% and 40.3%, respectively. Median OS separated by UGT1A1 gene polymorphisms were not reached in in *UGT1A1*28* heterozygous, 16.4 months in *UGT1A1*6* heterozygous, and 12.3 months in wild type, respectively. **Conclusion:** *UGT1A1*27* gene polymorphism was not found in our methods. Further investigation might be warranted in patients with *UGT1A1*28* wild type. **Keywords:** irinotecan, UGT1A1, gene polymorphism, lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-056 Thyroid Transcription Factor 1 (TTF1) as a Possible Predictive Biomarker for Pemetrexed-Based Chemotherapy in Non-Squamous NSCLC Xabier Mielgo Rubio[1], Alejandro Velastegui[1], Ruth Martínez Cabañes[2], Adriana Rosero[1], Leticia Ruiz-Giménez[1], Maria Garcia Ferron[1], Jorge Silva[1], Cristina Aguayo[1], Clara Olier[1], Carlos Jara[1] [1]*Medical Oncology, Hospital Universitario Fundación Alcorcón, Alcorcón/ Spain,* [2]*Medical Oncology Research Unit, Hospital Universitario Fundación Alcorcón, Alcorcón/Spain*

Background: There are no demonstrated predictive molecular markers for pemetrexed. The aim of this study is to explore and evaluate whether thyroid transcription factor 1 (TTF1) protein expression can be a predictive biomarker of clinical activity for pemetrexed-based chemotherapy in patients with nonsquamous non-small cell lung cancer (NSCLC). **Methods:** 123 patients with advanced nonsquamous NSCLC treated with pemetrexed-based chemotherapy as first-line, maintenance, second or later-line therapy were retrospectively reviewed. Then we chosen patients who had undergone assay of immunohistochemical expression of TTF1 in their tumor tissue sample, and we analyzed for their clinicopathological features, expression of TTF1 and clinical outcomes. Analysis of TTF1 expression was done according to the routine clinical practice of our center. **Results:** Immunohistochemical analysis of TTF1 expression was only performed in 51 of the 123 patients reviewed. Of these 51 patients, 36 were men and 15 women, 7 (13,7%) had never smoked and 44 (86,3%) were former or current smokers. Median age was 65 (range 39-79). Performance status (PS) distribution: 0 (25,4%), 1 (62,7%), 2 (7,8%), 3 (3,9%). Predominant histology type was adenocarcinoma (78,4%), followed by large cell carcinoma (13,7%) and not otherwhise specified-NOS (7,8%). 36 patientes had TTF1-positive tumors (70,5%), and 15 TTF1-negative ones (29,5%). The types of tumor tissue sample in which TTF1 assay was undergone were the following: endobronquial biopsy (43,1%), percutaneous biopsy (33,3%), fine needle aspiration puncture (17,6%), citology (0,5%). TTF1 positive tumors shown a higher disease control rate (DCR) for pemetrexed-based chemotherapy (60,5% vs 39,5%, p=0,05). Median progresión free survival (PFS) and overall survival (OS) in the whole group was 5,55 and 23,95 months respectively. TTF1-positive tumors had significant longer PFS (6,96 vs 3,64 months; p=0,0156) and a nonsignificant trend of longer OS (24,27 vs 13,66 months; p=0,581) to pemetrexed-based chemotherapy than patients with TTF1-negative tumors. **Conclusion:** TTF1 protein expression was associated with better clinical outcomes. TTF1 positive tumors shown a significant association with better PFS and a nonsignificant trend of better DCR and OS in nonsquamous NSCLC patients who were treated with pemetrexed-based chemotherapy. The predictive role of TTF1 expression should be further studied. **Keywords:** pemetrexed, TTF1, biomarker, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-057 Serum Mass-Spectrometry Test in First-Line Advanced Non-Small Cell Lung Cancer Patients Treated with Standard Chemotherapy Regimens Francesco Grossi[1], Carlo Genova[1], Erika Rijavec[1], Maria Giovanna Dal Bello[1], Giulia Barletta[1], Federica Biello[1], Claudia Maggioni[1], Julia Grigorieva[2], Krista Meyer[2], Heinrich Roder[3] [1]*Lung Cancer Unit, Irccs Aou San Martino - Ist, Genova/Italy,* [2]*Biodesix Inc., Boulder/ CO/United States of America,* [3]*Biodesix Inc., Boulder/United States of America*

Background: The mass-spectrometry based serum test VeriStrat® (VS) was developed using samples from non-small cell lung cancer (NSCLC) patients (pts) treated with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs); VS was shown to be prognostic in several tumors and predictive of differential overall survival (OS) benefit for erlotinib vs. chemotherapy (CT) in 2nd line for NSCLC. We investigated the role of VS in pts receiving Cisplatin (CDDP) or Carboplatin (CBDCA) plus Pemetrexed (P) as 1st line for advanced, non-squamous NSCLC. **Methods:** VeriStrat classification was available for 55 eligible pts, who were classified as VS Good (VSG) or VS Poor (VSP); VS testing was done blinded to clinical data. Progression-free survival (PFS) and OS were analyzed by Kaplan-Meier method and compared using log-rank p-values; Cox models were used in multivariate analysis. Association with categorical variables was analyzed by Fisher's exact test. **Results:** 36 (65%) pts were classified as VSG and 19 (35%) as VSP. In the overall population, median PFS was 6.1 months (mo) for VSG vs.1.3 mo for VSP (hazard ratio (HR) 0.39 [0.21-0.70], p=0.001); adjusted HR (AHR) 0.43 [0.21-0.91], p=0.026). Median OS was 10.6 mo for VSG vs. 3.1 mo for VSP (HR 0.26 [0.14-0.50], p<0.001; AHR 0.20 [0.09-0.47], p<0.001). A similar relationship was found in both treatments: In CBDCA-P median PFS in VSG and VSP was 3.9 mo and 1.6 mo respectively (HR 0.34 [0.14-0.81], p=0.011); median OS was 10.0 mo in VSG and 2.0 mo in VSP (HR 0.26 [0.11-0.61], p=0.001). In CDDP-P median PFS was 6.6 mo in VSG and 1.2 mo in VSP (HR 0.52 [0.20-1.33], p=0.161), median OS was 12.3 mo in VSG, 3.5 mo in VSP (HR 0.25 [0.09-0.70], p=0.005).When compared within VS groups, no statistically significant differences between CBDCA-P and CDDP-P was found either for PFS (VSG: p=0.471, VSP: p=0.493) or OS (VSG: p=0.319, VSP: p=0.429). VS was significantly associated with disease control rate (p=0.003) and objective response (p=0.021).

Population (N°)	Median PFS (months)		Hazard ratio, p	Median OS (months)		Hazard ratio, p
	VSG	VSP		VSG	VSP	
Overall (55)	6.1	1.3	0.39 [0.21-0.70] p=0.001	10.6	3.1	0.26 [0.14-0.50] p<0.001
CBDCA-P (30)	3.9	1.6	0.34 [0.14-0.84] p=0.011	10.0	2.0	0.26 [0.11-0.61] p=0.001
CDDP-P (25)	6.6	1.2	0.52 [0.20-1.33] p=0.161	12.3	3.5	0.25 [0.09-0.70] p=0.005

Conclusion: VeriStrat has prognostic significance in platinum-based CT: overall, VSP pts have significantly shorter PFS and OS than VSG pts. In each VS group, CDDP-P and CBDCA-P showed similar behavior. Further research is needed to find alternative treatments to improve outcomes for VSP pts. ClinicalTrials.gov Identifier: NCT02055144.
Keywords: prognostic factor, non-small cell lung cancer, VeriStrat, chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-058 Factors Predicting Long Duration of Pemetrexed Maintenance Therapy: A Retrospective Cohort of 65 Patients Clara Fontaine-Delaruelle[1], Virginie Avrillon[2], Jérôme Fayette[2], Maurice Pérol[2] [1]*Service de Pneumologie, Centre Hospitaliser Lyon Sud, Pierre Bénite/France,* [2]*Groupe Thoracique Et Orl, Centre Léon Bérard, Lyon/France*

Background: BACKGROUND: The Paramount trial demonstrated a significant survival benefit with pemetrexed continuation maintenance therapy for non-squamous NSCLC. This retrospective work aims to study predictive factors for a long duration of maintenance therapy and its toxicities. **Methods:** METHOD: All patients who received pemetrexed maintenance between 1st January 2009 and 1st July 2013 in Centre Léon Bérard (France) were included. Patients were classified in two groups: "long maintenance" if they received ≥ 5 cycles of maintenance with pemetrexed and "short maintenance" if they received ≤ 4 cycles. We retrospectively collected data about patients (age, gender, smoking status, PS), histological subtype, number of metastatic sites, number of induction and maintenance cycles, response to induction chemotherapy, bevacizumab use, reason for discontinuation, and toxicities. Proportions of patients or disease characteristics in each group were compared with univariate test (Fisher exact and Wilcoxon). **Results:** RESULTS: 65 patients were included, 33 in "short maintenance" group and 32 in "long maintenance" group, with 60% male and a mean age of 61.13 (±7,78). 55% of patients had ≥ 2 metastatic sites with PS 0, 1 or 2 in 21%, 67%, and 13% out of patients, respectively. Induction cycles were initiated with cisplatin in 71% and carboplatin in 29% of patients; median number of induction cycles was 4 [3-6]. 39% of patients achieved partial response to induction chemotherapy and 61% stable disease. Median number of maintenance cycles was 4 [1-28]. 19 patients (29%) received bevacizumab in combination to pemetrexed during induction and maintenance therapy. Maintenance discontinuation was due to progressive disease in 61%, toxicity in 19% and local treatment in 16% of patients, respectively. Significant predictive factors of a long duration of maintenance therapy were female gender (27% vs 53%; p=0.044) and ≥ 2 metastatic sites (42% vs 70%; p=0,046). Age, smoking status, histological subtype, response to induction therapy, bevacizumab use, and PS were not significantly related to maintenance duration. Grade 3-5 adverse events occurred in 20 patients (31%) including 5 treatment-related deaths (8%) (including 4 infectious-related deaths). There was a similar rate of grade 3-5 toxicities in both groups. Toxicities were mainly infectious (n= 13; 65%) including 4 febrile neutropenia. Predictive factors of grade 3-5 toxicities were age > 70 years (35% vs 9%; p=0.026) and carboplatin use (50% vs 20%; p=0,020). At the end of the study, maintenance therapy was ongoing in 3 patients. Among the 62 other patients, 81% received subsequent systemic therapy with a similar duration of treatment between "short" and "long" maintenance groups. **Conclusion:** CONCLUSION: Univariate analysis identified female gender and ≥2 metastatic sites as only predictive factors for a long duration of pemetrexed maintenance therapy. Patients with single metastasis frequently stopped maintenance treatment for administration of local therapy. Predictive factors for severe toxicities were age > 70 years and carboplatin use whereas addition of bevacizumab to pemetrexed did not result in an increase of toxicity.
Keywords: pemetrexed, maintenance therapy, lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-059 Does Pemetrexed/Platinum Fit All Patients with Non-Squamous Non-Small Cell Lung Cancer? A Retrospective Study of Clinical Factors and Outcomes Junichi Shimizu[1], Yuko Oya[1], Kosuke Tanaka[1], Tatsuya Yoshida[1], Yoshitsugu Horio[1], Yasushi Yatabe[2], Toyoaki Hida[1] [1]*Thoracic Oncology, Aichi Cancer Center, Nagoya/Japan,* [2]*Pathology and Molecular Diagnostics, Aichi Cancer Center, Nagoya/Japan*

Background: Pemetrexed/platinum is one of the standard treatment regimens for patients with advanced non-squamous non-small cell lung cancer(NSCLC). The aim of this study was to examine the association between survival of lung cancer patients treated with pemetrexed/platinum and clinical factors. **Methods:** The medical records of advanced or relapsed non-squamous NSCLC patients treated with pemetrexed/platinum at our hospital between January 2010 and December 2013 were reviewed. Basic characteristics, histological subtypes of NSCLC, driver mutation status, TTF1 staining status and status of treatment with taxane were evaluated for association with the survival from pemetrexed/platinum started day to deaths. **Results:** Two hundreds nine records were reviewed. The median age was 62 (28-79), 60% were male, 40% were never smoker, 89% had an ECOG PS0-1 and 11% had a PS 2-3. The median value of CEA and CYFRA were 10.5 ng/ml and 3.0 ng/ml, respectively. 93% were diagnosed as adenocarcinoma and 7% were diagnosed as other subtypes (large, adenosquamous, sarcomatoid and not otherwise specified). 79% (81/102) had a positive TTF1 staining. 26% had EGFR mutation, 7% had ALK fusion and 11% had KRAS mutation. 36% of patients were received bevacizumab with pemetrexed/platinum. 35% of patients were treated with cisplatin. The response rate of pemetrexed/platinum was 34.8%. Median overall survival was 537days. 65% of patients were treated with taxane and the response rate was 15.0%. In multivariate analysis, poor PS(HR 1.33; p=0.027), others in histological subtypes (HR2.00; p=0.047) and K-RAS mutation(HR 2.74; p=0.021) correlated significantly with a shorter overall survival and low CYFRA(≤3.0ng/ml, HR 0.55; p=0.002) correlated significantly with a longer overall survival. **Conclusion:** High CYFRA, KRAS mutation and others in histological subtypes may be associated with shorter overall survival treated with pemetrexed/platinum in non-squamous NSCLC. The development of effective treatment regimens for such patients is needed to improve their outcomes.
Keywords: pemetrexed, NSCLC, CYFRA, histology

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-060 Biweekly Irinotecan/Bevacizumab in Heavily Treated Advanced NSCLC and Survival According to TIMP1 and EGFR Expression Andrés F. Cardona[1], Leonardo Rojas[2], Carlos A. Vargas[1], Hernan Carranza[1], Jorge M. Otero[1], Claudio Martin[3], Luis Corrales[4], Mauricio Cuello[5], Guillermo Bramuglia[6], Pilar Archila[1], Oscar Arrieta Rodriguez[7] [1]*Clinical and Translational Oncology Group, Foundation for Clinical and Applied Cancer Research - Ficmac, Bogotá/Colombia,* [2]*Centro Javeriano de Oncología, Hospital Universitario San Ignacio, Bogotá/Colombia,* [3]*Clinical Oncology, Instituto Fleming, Buenos Aires/Argentina,* [4]*Clinical Oncology, Hospital San Juan de Dios, San José/Costa Rica,* [5]*Clinical Oncology, Hospital de Clínicas - Udelar, Montevideo/Uruguay,* [6]*Argenomics, Buenos Aires/Argentina,* [7]*Unidad Funcional de Oncología Torácica Y Laboratorio de Medicina Personalizada, National Cancer Institute, Mexico City/Mexico*

Background: Irinotecan and bevacizumab are effective against non-small cell lung cancer (NSCLC) and synergism with non-cross-resistance has been demonstrated in preclinical studies. Tissue inhibitor of metalloproteinases 1 (TIMP1) and EGFR regulates extracellular matrix catabolism and promotion of cell growth and anti-apoptotic activity in NSCLC. **Methods:** Forty nine patients with heavily treated metastatic NSCLC were enrolled from March 2011 to November 2014. Thirty-three (67%) had never been exposed to bevacizumab and 16 had received antiangiogenic therapy as part of their first-line (all had achieved a previous response for more than 6 months). Treatment consisted of a 90-min intravenous infusion of 125 mg/m^2 irinotecan on day 1 and 8 plus 7.5 mg/kg bevacizumab on day 1 (treatment was repeated every 3 weeks). In all patients the mutational status of KRAS and EGFR, as well as TIMP1 and EGFR expression was evaluated. **Results:** The median age was 60 years (range, 44-78 years), 57% was male and 75% had ECOG 0-1. The median follow-up was 13.2 months and twenty-three patients had received >3 prior lines. The ORR was 32% (95%CI 22% to 39%) and thirteen patients (26%) achieve stable disease. Median progression-free survival (PFS) rate was 4.4 months (95%CI 2.8-8.3) and median overall survival (OS) rate was 18.0 months (95%CI 16.2-30.7). Nine patients harbouring EGFR mutations had a long-lasting, partial response (>5 months after at least 4 prior lines). Major toxicity was myelosuppression (grade 3 neutropenia occurred in 32% of patients and thrombocytopenia in 8.3%). Three patients experienced febrile neutropenia, one patient suffered grade 4 diarrhoea, and non-haematological toxicity was usually mild. Shorter OS was found in patients with a higher expression of TIMP1 mRNA (P=0.0001) but not according to the expression of EGFR (P=0.14). **Conclusion:** Irinotecan plus bevacizumab resulted in favourable activity and manageable toxicity profiles as third or fourth line for patients with advanced NSCLC. Our results suggested that such regimen can represent a reasonable chemotherapeutic option, especially for subjects having EGFR mutations and low expression of TIMP1.
Keywords: irinotecan, TIMP1, Heavily treated, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-061 COX-2 Expression Does Not Predict Outcome of Celecoxib in Addition to Standard Chemotherapy in Advanced Non-Small Cell Lung Cancer Miklós Gulyás[1], Johanna S.M. Mattsson[2], Andrea Lindgren[3], Christer Sederholm[4], Lars Ek[5], Kristina Lamberg[6], Annelie Behndig[7], Erik Holmberg[8], Patrick Micke[2], Bengt Bergman[9] [1]*Academic Hospital, Clinical Pathology, Uppsala/Sweden,* [2]*Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala/Sweden,* [3]*Inst for Medicine and Health, Linkoping University, Linkoping/Sweden,* [4]*Pulmonary Medicin, Linkoping University Hospital, Linkoping/Sweden,* [5]*Pulmonary Medicine, Skane University Hospital, Lund/Sweden,* [6]*Pulmonary Medicine, Akademiska Hospital, Uppsala/Sweden,* [7]*Pulmonary Medicine, Norrland University Hospital, Umeå/Sweden,* [8]*Dept of Oncology, Inst of Clinical Sciences, Sahlgrensk Academy at University of Gothenburg, Gothenburg/Sweden,* [9]*Dept of Pulmonary Medicine, Sahlgrenska University Hospital, Gothenburg/Sweden*

Background: Increased expression of cyclooxygenase-2 (COX-2) is common in non-small cell lung cancer (NSCLC), and is therefore a potential target for treatment. However, phase III trials have failed to demonstrate beneficial survival effects of adding COX-2 inhibitors to standard chemotherapy. We investigated whether COX-2 expression in tumor and stromal cells had any predictive impact on the effects of celecoxib, a selective COX-2 inhibitor. **Methods:** In a previously published multicenter phase III trial, 316 patients with NSCLC stage IIIB or IV and WHO performance status 0-2 were randomized to receive celecoxib 400 mg b.i.d. or placebo up to one year in addition to a two-drug platinum-

based chemotherapy regimen. In a subset of 122 patients, archive tumor tissue was available for further analyses. Immune stainings for COX-2 expression were undertaken. Intensity and extent of positively stained cells in tumor and stroma cells were scored on a 0 to 3 scale, and the product of these scores was used as a co-variable in the predictive analysis. **Results:** An updated analysis of all 316 patients included in the original trial, and of the 122 patients with available tumor tissue showed no survival differences between the celecoxib or placebo arms (HR 0.99; 95% CI 0.79-1.24 and HR 0.89; 95% CI 0.62-1.28, respectively). Similarly, in patients with high COX-2 expression in tumor cells (n=71) or stroma cells (n=55), survival did not differ significantly between patients who received celecoxib or placebo (HR 0.96; 95% CI 0.60-1.54 and HR 0.66; 95% CI 0.38-1.16). The p-value for interaction effect between COX-2 score in tumor or stroma cells and celecoxib effect on survival was 0.48 and 0.25, respectively. **Conclusion:** In this subgroup analysis of patients with advanced NSCLC treated in a randomized trial, we could not detect any significant interaction between COX-2 expression in tumor or stroma cells and outcome of celecoxib treatment in addition to standard chemotherapy. **Keywords:** non-small cell lung cancer, COX-2 expression, chemotherapy, celecoxib

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-062 Efficacy and Safety of Weekly Albumin-Bound Paclitaxel for Non-Small-Cell Lung Cancer Patients Who Have Failed ≥ 2 Prior Systemic Regimens

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Background: To evaluate the efficacy and safety of weekly intravenous Nanoparticle albumin-bound paclitaxel (NAB-paclitaxel) for the patients with advanced non-small-cell lung cancer (NSCLC) who have failed prior multilines treatments, and to investigate the association of status of secreted protein, acidic and rich in cysteine (SPARC) expression and clinipathological factors with clinical outcome. **Methods:** We retrospectively analyzed the efficacy and toxicities of NAB-paclitaxel monotherapy in treating 84 patients who had progression disease after at least two lines standard chemotherapy from May 1, 2011 to June 31, 2014. All patients were treated with NAB-paclitaxel 130mg/m2 on days 1 and 8 of a 21-day cycle. Radiologic tumor assessment was performed every 6 weeks or when the patient's symptoms deteriorated obviously. We also detected the SPARC status expression (by immunohistochemistry) in 35 patients who had tumor tissue available. 76 of 84 patients had EGFR mutation status. The date of last follow-up was March 31, 2015. **Results:** Of these 84 patients, 76 patients had complete follow-up data, 5 patients lost of follow-up for overall survival, and 3 patients couldn't tolerate the continuous NAB-paclitaxel therapy due to serious adverse events and had only the evaluation of safety data. EGFR mutation were found in 22 of 76 patients and their median PFS and OS were 4.4 months and 11.5months. The median treatment line of weekly NAB-paclitaxel therapy was 4 line (range: 2~7 line). The median follow-up interval time was 11.2 months. The objective response rate (ORR) and disease control rate (DCR) (N=81) were 14.8% (12/81) and 67.9% (55/81), respectively. The median progression-free survival (PFS) and overall survival (OS) were 3.9 months (95% CI: 2.8~5.0 months) and 11.0 months (95%CI: 7.6~14.4 months), respectively. Pearson's correlation analysis showed that previous treatment with Solvent-based Paclitaxel or Docetaxel didn't affect the response to NAB-paclitaxel. However, the patients who reached disease control after previous Solvent-based Paclitaxel or Docetaxel presented better DCR than the patients who failed to previous Solvent-based Paclitaxel or Docetaxel (DCR: 77.1% vs 47.6%, p=0.040) (by Fisher's Exact Test). Cox regression analysis showed that ORR was related with both PFS and OS. The common adverse events (N=84) included leukopenia (36.1%), neutropenia (29.2%), peripheral neurotoxicity (23.6%), et al. The main grade 3/4 toxicities included neutropenia (9.7%) and leukopenia (6.9%). 3 patients had discontinued chemotherapy due to drug induced lung injury, serious fatigue and serious anorexia, separately. In this study, no association between SPARC expression and efficacy was observed. **Conclusion:** Advanced NSCLC patients who have experienced multiline chemotherapy with disease progression could benefit from weekly NAB-paclitaxel therapy with good safety and clinical outcome. It seemed that SPARC expression could not predict efficacy to NAB-paclitaxel. **Keywords:** nab-paclitaxel, Advanced Non-Small Cell Lung Cancer, SPARC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-063 Dynamic Change of Fatigue for East-Asian Patients in the JMEN Trial

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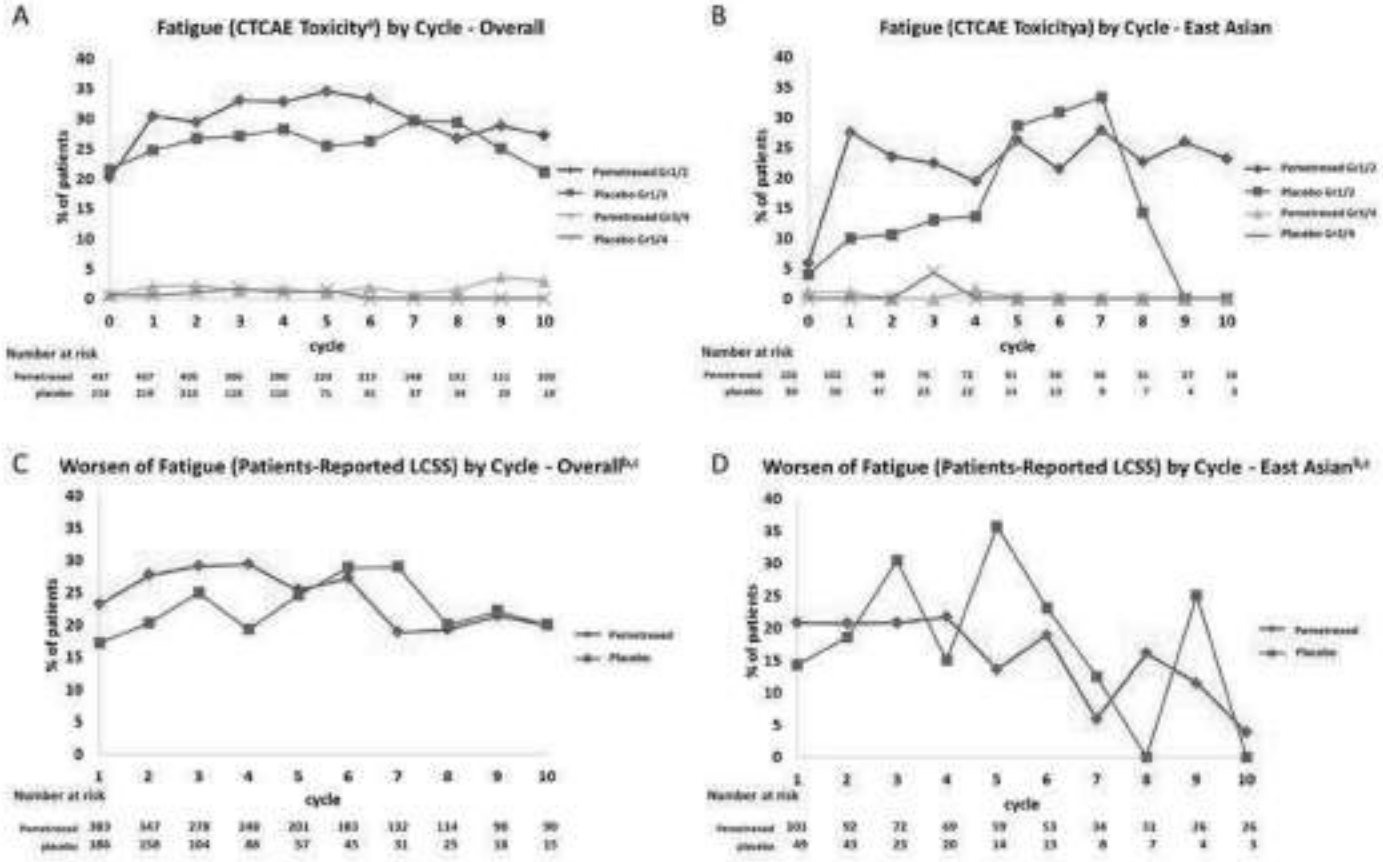
Background: In the JMEN trial (Ciuleanu et al., Lancet 374:1432-1440, 2009), patients with advanced non-squamous non-small cell lung cancer (NSCLC) derived a benefit from pemetrexed maintenance therapy after platinum-based initial therapy by extending survival, delaying disease progression, and maintaining overall quality of life (QoL). However, fatigue was the most common physician-reported toxic effect in the pemetrexed treated group. We conducted a post-hoc analysis to investigate the dynamic change of fatigue in overall population and East-Asian (EA) patients treated on the JMEN trial. **Methods:** This analysis was performed in the overall safety population (N=656) and the EA subgroup safety population (N=152) mainly from China, Taiwan, and Korea including squamous and non-squamous NSCLC patients. The Common Terminology Criteria for Adverse Events (version 3.0) was used for summary of the AE incidence rates by cycle and AE severity reported by investigator. The Lung Cancer Symptom Scale (LCSS) was used to evaluate patients' QoL. Worsening of fatigue was defined as an increase of 15 mm or more from baseline on a 100 mm scale in LCSS reported by the patients. The percentage of patients with worsening fatigue was also summarized by cycle. The time to worsening of fatigue symptom was analyzed using Kaplan-Meier method and Cox proportional model. **Results:** In the EA population drug-related fatigue (grade 1-4) occurred more frequently in pemetrexed arm compared with placebo arm (30.4% vs 16.0%, p=0.075). The grade 3/4 drug-related fatigue was rare in both arms (1 event reported in each arm). For both overall and EA populations, the fatigue incidence by cycle during the maintenance treatment with pemetrexed did not increase during subsequent cycles (Figure 1A, B). The percentage of patients who experienced worsening of fatigue based on the patients-reported LCSS scores was also comparable between the two arms in the overall and EA populations (Figure 1C, D). EA Patients in the pemetrexed arm experienced a numerically longer median time to worsening of fatigue compared to EA patients in the placebo arm, although the difference is not statistically significant (5.95 months vs. 3.91 months, HR= 0.84, 95% confidence interval [CI]: 0.51-1.37, p= 0.471).

(See next page for figure.)

Figure 1. **Fatigue Incidence and Worsen of Fatigue by Maintenance Cycle.** Incidence of CTCAE grade 1/2 and grade 3/4 fatigue for overall (A) and East-Asian (B) patients in the pemetrexed and placebo treatment arms for maintenance cycles 1 through 10. Worsening of fatigue based on the patients-reported LCSS scores for overall (C) and East-Asian (D) patients in the pemetrexed and placebo treatment arms for maintenance cycles 1 through 10.



[a] The CTCAE (version 3.0) was used for summary of the AE incidence by cycle and AE severity.
[b] The LCSS was used to evaluate patients' quality of life. Worsening of fatigue symptom was defined as an increase of 15 mm or more from baseline on a 100 mm scale for the fatigue item in LCSS.
[c] Fisher exact test was used to compare the two treatment arms at each cycle and all the p-values > 0.05.
Abbreviations : CTCAE = Common Terminology Criteria for Adverse Events, LCSS = Lung Cancer Symptom Scale, CI = confidence interval, HR = hazard ratio, Gr = grade..

Conclusion: These analyses suggest that despite a higher incidence of grade 1/2 drug-related fatigue compared with placebo, pemetrexed maintenance treatment for EA patients with advanced NSCLC will not impair patient-reported QoL.
Keywords: Dynamic change, fatigue, Quality of life, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-064 A Randomized Phase II Trial of ERCC1 and RRM1 Expression-Based Chemotherapy versus Docetaxel/Carboplatin in Advanced Non-Small Cell Lung Cancer Su Jin Heo[1], Hye Ryun Kim[1], Inkyung Jung[2], Jaeheon Jeong[3], Sun Min Lim[1], Yong Wha Moon[1], Joo-Hang Kim[1], Byoung Chul Cho[1] [1]*Medical Oncology, Yonsei University College of Medicine, Seoul/Korea,* [2]*Biostatistics and Informatics, Yonsei University College of Medicine, Seoul/Korea,* [3]*Kyung Hee University, Seoul/Korea*

Background: Platinum-based doublet chemotherapy is still mainstay in treatment of advanced non-small-cell lung cancer (NSCLC). There was no molecular determinant for guiding platinum-based chemotherapy. Excision repair cross-complementing group 1 gene (ERCC1) is important for platinum-induced DNA adduct repair and ribonucleotide reductase subunit 1 (RRM1) is crucial for nucleotide metabolism and has been known for the dominant molecular determinant of gemcitabine efficacy. We assessed whether selection of first-line chemotherapy based on ERCC1 and RRM1 mRNA expression levels would improve clinical outcomes in patients with advanced NSCLC. **Methods:** Eligible patients were randomly assigned 1:1 to experimental arm and control arm. The experimental arm consisted of gemcitabine/carboplatin (GC) if ERCC1 and RRM1 were low, gemcitabine/vinorelbine (GV) if ERCC1 was high and RRM1 was low, docetaxel/carboplatin (DC) if ERCC1 was low and RRM1 was high, and docetaxel/vinorelbine (DV) if both were high. In the control arm, patients received docetaxel/carboplatin (DC). All chemotherapy regimens were to be continued for maximum 4 cycles every 3 weeks or unacceptable toxicity. ERCC1 and RRM1 mRNA expression were measured by quantitative real-time PCR in formalin-fixed paraffin-embedded (FFPE) tissue. The trial was powered for an 80% improvement in overall response rate (ORR, P0=0.25, P1=0.45, α=0.1). Secondary endpoints included progression-free survival (PFS), overall survival (OS), and safety. The study was prematurely terminated after the futility analysis of 42 PFS events, which showed a low conditional probability (conditional power=0.14) of a statistically significant outcome. **Results:** A total of 56 patients (n=26 in experimental arm, n=30 in control arm) were evaluable for efficacy and toxicity. Patient characteristics were well balanced in both groups. Majority of patients had adenocarcinoma histology (64.3%) and ECOG performance status 0 to 1 (96.4%). *EGFR* mutation was documented in 8 patients (4 in experimental arm, 4 in control arm). Among 26 patients in the experimental arm, mRNA expression of ERCC1 and RRM1 ranged from 0.18 to 2.81 (median, 0.69) and 0.22 to 16.65 (median, 0.66), respectively. Based on mRNA expression levels, 19 (73.1%) patients were assigned to GC, 0 (0.0%) to GV, 4 (15.4%) to DC, and 3 (11.5%) to VD. The median number of chemotherapy cycles delivered was 3.7 in experimental arm and 3.5 in control arm. The ORRs were 26.9% in experimental arm and 40.0% in control arm, which were not statistically significant (*P*=0.58). With a median follow-up of 30.1 months, median PFS was 4.6 months in experimental arm and 5.1 months in control arm (hazard ratio [HR] 1.27; 95% CI 0.69-2.31; *P*=0.43). Median OS was 18.2 months in experimental arm and was 12.6 months in control arm (HR 0.71; 95% CI 0.32-1.53; *P*=0.38). The occurrence of grade 3 or higher neutropenia (69.2% vs. 93.4%, *P*=0.02) and febrile neutropenia (3.8% vs. 23.3%, *P*=0.04) was significantly more common in control arm. There was no treatment-related death. **Conclusion:** ERCC1 and RRM1 expression-based chemotherapy did not improve clinical outcomes in advanced NSCLC (NCT01648517). **Keywords:** advanced NSCLC, ERCC1, RRM1, chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-065 ***nab*-Paclitaxel + Carboplatin in Advanced NSCLC: Analysis of Age and Renal Function** Eric Bernicker[1], Corey J. Langer[2], Amy Ko[3], Teng Jin Ong[3], Mark A. Socinski[4], Mary E.R. O'Brien[5] [1]*Houston Methodist Cancer Center, Houston/United States of America,* [2]*Abramson Cancer Center, University of Pennsylvania, Philadelphia/PA/United States of America,* [3]*Celgene Corporation, Summit/NJ/United States of America,* [4]*University of Pittsburgh, Pittsburgh/PA/United States of America,* [5]*Royal Marsden Hospital, London/United Kingdom*

Background: Renal impairment increases with age and can impact treatment decisions. In a phase III trial, first-line treatment with *nab*-paclitaxel plus carboplatin (*nab*-P/C) significantly improved the overall response rate (ORR; primary endpoint) compared with solvent-based paclitaxel plus C (sb-P/C) in patients with advanced NSCLC (Socinski et al. *J Clin Oncol.* 2012;30:2055-2062). In a subgroup analysis of this phase III trial, *nab*-P/C demonstrated promising efficacy and was well tolerated in patients with or without renal impairment (Langer et al. *Clin Lung Cancer.* 2015;16:112-120). This analysis examined outcomes of patients in the phase III trial stratified by age and renal function. **Methods:** Patients with histologically or cytologically confirmed stage IIIB/IV NSCLC and no prior chemotherapy for metastatic disease received either *nab*-P 100 mg/m^2 on days 1, 8, and 15 or sb-P 200 mg/m^2 on day 1 in combination with C AUC 6 on day 1 every 21 days (randomized 1:1). Treatment continued until disease progression. Baseline renal function (creatinine clearance [CrCl]) was assessed in a central lab. ORR and progression-free survival (PFS) were assessed by blinded, centralized review. *P* values for ORR were based on the chi-square test, and those for overall survival (OS) and PFS were based on the log-rank test. **Results:** Treatment with *nab*-P/C resulted in improved outcomes compared with sb-P/C in patients with mild renal impairment, regardless of age (Table). *nab*-P/C also consistently demonstrated greater treatment effect compared with sb-P/C for ORR and similar or better PFS and OS in patients ≥ 60 years, regardless of renal function. In patients with either mild renal impairment or normal renal function, the toxicity profiles in each treatment arm were similar to those of the intent-to-treat population. **Conclusion:** These results suggest that, in general, clinical outcomes in patients with advanced NSCLC and mild renal impairment are better with *nab*-P/C vs sb-P/C, regardless of age. It should be noted that these were small subset analyses and results should be interpreted with caution.

Outcome by Age Group	CrCl > 50 to ≤ 80 mL/min Mild Renal Impairment		CrCl > 80 mL/min Normal Renal Function	
	nab-P/C	sb-P/C	nab-P/C	sb-P/C
< 60 years	n = 74	n = 66	n = 177	n = 179
ORR, %	32	21	31	26
RRR	1.53		1.28	
P value	0.136		0.172	
Median PFS, mo	8.2	5.6	5.6	6.7
HR	0.80		1.09	
P value	0.383		0.559	
Median OS, mo	10.1	9.1	11.4	12.6
HR	1.06		1.15	
P value	0.790		0.271	
≥ 60 to < 70 years	n = 66	n = 94	n = 90	n = 92
ORR, %	40	30	30	25
RRR	1.33		1.20	
P value	0.169		0.450	
Median PFS, mo	7.3	5.7	5.6	5.6
HR	0.69		1.00	
P value	0.070		0.999	
Median OS, mo	15.7	13.6	11.4	11.1
HR	0.74		0.93	
P value	0.124		0.671	
≥ 70 years	n = 38	n = 46	n = 22	n = 20
ORR, %	32	28	45	25
RRR	1.12		1.82	
P value	0.741		0.167	
Median PFS, mo	10.0	8.2	7.0	7.0
HR	0.60		0.93	
P value	0.196		0.888	
Median OS, mo	18.3	13.6	22.3	8.4
HR	0.73		0.34	
P value	0.274		0.017	

HR, hazard ratio; RRR, response rate ratio

Keywords: nab-paclitaxel, carboplatin, NSCLC, renal function

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-066 A Prospective, Randomized, Multicenter, Phase III Study, Comparing rhTPO with rhIL-11 Treating CIT - An Interim Analysis (NCT02344979) Shun Lu[1], Xia Song[2], Fang M. Du[3], Li Liu[4], Yun H. Xu[1], Zhi Y. Ma[5], Qiong Zhao[6], Yi P. Zhang[7], Hai Y. Liu[8] [1]*Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China,* [2]*Respiratory Medicine, Shanxi Cancer Hospital, Taiyuan/China,* [3]*Medical Oncology, Dongyang People'S Hospital, Dongyang/China,*[4]*Cancer Center, Wuhan Union Hospital, Wuhan/China,* [5]*Medical Oncology, Henan Cancer Hospital, Zhengzhou/China,* [6]*Medical Oncology, The First Hospital of Zhejiang Province, Hangzhou/China,* [7]*Thoracic Medical Oncology, Zhejiiang Cancer Hospital, Hangzhou/China,* [8]*Medical Oncology and Hematology, Jilin Oil Field General Hospital, Songyuan/China*

Background: Chemotherapy-induced thrombocytopenia (CIT) has seriously hindered the application of anti-cancer drugs. Thrombopoietic factors such as recombinant human interleukin-11(rhIL-11), thrombopoietin and its derivative(recombinant human thrombopoietin, rhTPO) are routinely administrated for CIT. But there is no randomized study to compare rhTPO with rhIL-11 on efficacy and safety of thrombocytopenia prophylactic treatment before. This is the first randomized, open-label, multicenter, phase Ⅲ study to compare them in China. We tried to investigate the efficacy and safety of prophylactic administration with rhTPO or rhIL-11 to prevent CIT in advanced non-small-cell lung cancer(NSCLC) patients. **Methods:** From June 2009 to February 2015, 71 patients with advanced NSCLC who were receiving the first-line platinum-based chemotherapy suffered severe thrombocytopenia(the nadir of platelet counts<50×10^9/L, confirmed by two times of blood routine in different days) during prior chemotherapy cycle. They were randomized to rhTPO arm or rhIL-11 arm in the following chemotherapy cycle, and the chemotherapy regimens and drug doses were consistent in the prior and following cycle (GC Gemcitabine 1000-1250 mg/m^2, D1 and D8; Carboplatin dosing by AUC value=5, D1; Q3W) or GP (Gemcitabine 1000-1250 mg/m^2, D1 and D8; Cisplatin 75 mg/m^2, D1; Q3W). 49 patients (34 males, 15 females) were enrolled rhTPO arm and 22 patients (14 males, 8 females) were enrolled rhIL-11 arm. There were no statistical difference between two arms in terms of gender[34 males(69.4%) *vs.*14 males(63.6%),P>0.05], age(58.5±9.3 yrs *vs.* 60.3±7.5 yrs, P>0.05), and the nadir of platelet counts during prior chemotherapy cycle(31.4±13.1×10^9/L *vs.* 28.6±12.8×10^9/L, P>0.05). rhTPO (15000U/d) was injected subcutaneously on the 2nd, 4th, 6th, 9th Day after the initiation of chemotherapy, and IL-11(3mg/d) was injected subcutaneously per day from Day 9 to Day15 after the initiation of chemotherapy. Blood routines were conducted to test before chemotherapy initiation and the 3th, 5th, 7th, 9th, 11th, 13th, 15th, 17th, and 21th day after chemotherapy. Toxicity and efficacy were monitored. **Results:** In the following chemotherapy cycle there were no statistical difference between rhTPO arm and rhIL-11 arm on the following indexes: the nadir of platelet counts(66.6±43.1×10^9/L *vs.* 53.8±40.6×10^9/L, P>0.05) , the maximum platelet counts (219±132×10^9/L *vs.* 240±151×10^9/L, P>0.05) , duration of platelet counts less than 50×10^9/L[Median (95%CI): 4.0(3.0-5.0) days *vs.* 4.5(3.0-6.0) days, P>0.05], time of platelet count recovered to 75×10^9/L [Median(95%CI): 2(2-3) days *vs.* 3(0-4) days, P>0.05] and to 100×10^9/L[median(95%CI): 4(3-6) days *vs.* 4.5(3-8) days, P>0.05]. Drug-related adverse events in rhTPO arm were less than that of rhIL-11 arm (5 cases(10.2%) in rhTPO arm, 7 cases(31.8%) in rhIL-11 arm, P<0.05). **Conclusion:** Although there is no statistical difference on efficacies, prophylactic administration of rhTPO is safer and more convenient than that of rhIL-11 in advanced NSCLC patients. This is an interim analysis. More data is still waiting.

Keywords: recombinant human thrombopoietin, prophylactic use, Non-small-cell lung cancer, chemotherapy-induced thrombocytopenia

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-067 Quality in Lung Cancer Care: The Victorian Lung Cancer Registry Pilot Initial Report

Rob Stirling[1], Sue Evans[1], Meera Senthuren[1], Peta Mclaughlin[1], Sara Mclaughlin-Barrett[2], Jeremy Millar[3], Julian Gooi[3], Jennifer Phillip[4], Louis Irving[5], Paul Mitchell[6], Andrew Haydon[3], Jeremy Ruben[3], Matthew Conron[4], Neil Watkins[7], John Mcneil[1] [1]*Epidemiology and Preventative Medicine, Monash University, Melbourne/VIC/Australia,* [2]*Epworth Healthcare, Richmond/VIC/Australia,* [3]*Alfred Health, Melbourne/Australia,* [4]*St Vincents Hospital, Fitzroy/VIC/Australia,* [5]*Royal Melbourne Hospital, Melbourne/ACT/Australia,* [6]*Austin Health, Melbourne/ACT/Australia,* [7]*Garvan Institute, Sydney/NSW/Australia*

Background: The Victorian Lung Cancer Registry is a clinical quality registry designed with the aim of improving the quality of care delivered to Victorians with lung cancer by collecting and assessing management, treatment and outcome data on all new cases of lung cancer. **Methods:** The establishment of the Victorian Lung Cancer Registry Pilot Project commenced with the appointment of a Steering Committee to provide project governance. Review of current literature and evidence-based national and international clinical practice guidelines was undertaken by an expert working group. Included data items were epidemiologically sound, reproducible and valid. The data set enables the capture of identified quality indicators designed to describe the structural quality, process quality and indicators of outcome in lung cancer management. Case ascertainment is derived from institutional ICD-10 coding and participant consent occurs via an "opt-off" system. Follow up and outcome measures are collected at baseline, 6 and 12 months after diagnosis capturing survival, treatment and quality of life. Institutional recruitment was designed to sample from metropolitan public, metropolitan private and regional hospitals. **Results:** Data was collected on 690 patients from 1 July 2012 to 31 June 2013 from 8 Victorian Hospitals (3 public and 3 private metropolitan and 2 regional). Evidence of distress screening was available for 27% of subjects. Diagnosis was confirmed < 28 days from referral in 66% of cases across institutions. A statement of ECOG status was available in 45% of cases and clinical TNM staging in 49% prior to treatment. A record of multidisciplinary team meeting presentation was available in 59% of cases. First treatment was initiated < 42 days from diagnosis in 76% of cases. Curative surgery was provided for 28% of subjects, curative chemotherapy <5% and curative radiotherapy < 5%. **Conclusion:** The evaluation of registry outcomes at governance, administrative and clinical levels may identify targets for quality and service improvement and further define safety measures. The comparison of performance outcomes across institutions and sectors may drive competitive recruitment to improve measures on a longitudinal basis.

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-068 Androgen Deprivation Therapy for Prostate Cancer Associated with Improved Survival in Non Small Cell Lung Cancer: A SEER-MEDICARE Analysis

Mukesh Kumar[1], Camille Ragin[2], Chao Zhang[3], Zhengjia Chen[3], Erica J. Han[3], Vinicius Ernani[3], Madhusmita Behera[3], Conor Steuer[3], Nabil Saba[3], Dong Shin[3], Chandra P. Belani[2], Fadlo Khuri[3], Suresh S. Ramalingam[3], Taofeek K. Owonikoko[1] [1]*Hematology/Oncology, Emory University, Atlanta/GA/United States of America,* [2]*Penn State Milton S. Hershey Medical Center, Hershey/PA/United States of America,* [3]*Hematology/Oncology, Emory University, Atlanta/United States of America*

Background: Cancer of the prostate and lung are most commonly diagnosed in the elderly. Aberrant female sex hormone signaling has been well-described in NSCLC. The impact of androgen deprivation therapy (ADT) on non-small cell lung cancer (NSCLC) outcome has, however, not been well studied. **Methods:** We employed the linked SEER-MEDICARE database to assess the potential impact of ADT on NSCLC. We analyzed data from patients diagnosed with NSCLC between 1985 and 2005 and registered in the SEER-MEDICARE database. Patients were categorized into three groups: prostate cancer diagnosis followed by NSCLC (PL), NSCLC followed by prostate cancer (LP) and NSCLC only (L). Demographic and survival outcomes were compared between these groups. The impact of sequence of cancer diagnosis and ADT on survival post NSCLC diagnosis was assessed within the PL group using logistic regression model. Cox proportional hazards models were employed to estimate the effect of ADT and stage of prostate cancer on survival with adjustment for significant prognostic factors. **Results:** A total of 417630 patients were included in this analysis; male/female (56.4%/43.6%); Race: White (84.0%), Black (9.0%), Asian (2.1%), Hispanic (1.0%), others (3.0%); Stage: I (17.4%), II (2.9%), III (33.6%) and IV (46.1%). The majority of the patients were in the L group (96.3%), followed by PL (2.9%) and LP (0.8%). Patients in the LP group had the best 12-month survival rates (84.5%), followed by L (44.4%) and PL (40.1%). Analysis within the PL group showed an inverse correlation between stage of prostate cancer diagnosis and interval of time to NSCLC diagnosis: 54.8, 54.1, 62.1 and 59.3 months for stage I, II, III and IV prostate cancer, respectively. Prostate cancer patients exposed to ADT had a shorter interval to lung cancer diagnosis (48.3 vs. 52.7 months; p < 0.001). On multivariate analysis, patients exposed to ADT had a higher median survival (10 months vs. 9 months; p < 0.001) and reduced risk of death (HR:1.11; 95%CI:1.05-1.18), p <0.001). **Conclusion:** ADT therapy for prostate cancer was associated with improved survival for subsequent NSCLC diagnosis. Our result supports systematic exploration of ADT as a treatment strategy for NSCLC. **Keywords:** Androgen Deprivation Therapy (ADT), NSCLC, Androgen Receptor

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-069 Design and Stratification for Phase III Trials in First-Line Non-Small Cell Lung Cancer

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Background: Metastatic non-small cell lung cancer (NSCLC) remains an incurable disease. Sacher et al reviewed phase III studies in first-line advanced/metastatic NSCLC conducted from 1981 to 2010. Although trends in study outcomes were assessed, design and stratification factors have never been analyzed. **Methods:** The recently published list of phase III trials by Sacher et al (JCO 2014;32:1407-11) was reviewed thoroughly. Eligible trials for this study must have been published in the English literature between 1981 and 2010. Trials that included a substantial number of previously treated NSCLC patients were excluded. Maintenance studies after first-line chemotherapy were also excluded. Characteristics in each decade were determined for sample size, number of trials, region, rate of meeting accrual goal, primary endpoint, type of phase III, interim analysis, allocation method, and stratification factors (SFs). Any p-value of less than 0.05 was considered significant for statistical analysis. **Results:** A total of 162 studies were considered to meet the criteria. The number of studies and median sample size increased from 29 and 133 in 1980s to 46 and 181 in 1990s to 87 and 407 in 2000s, respectively. Primary endpoint was reported more frequently in recent decades; 24% of studies in 1980s, 83% in 1990s, 99% in 2000s. Non-overall survival endpoints were frequently chosen in European and Asian studies. Interim analysis was planned for 3% in 1980s, 20% in 1990s, 33% in 2000s. Allocation method was rarely reported throughout the three decades (0% in 1980s, 22% in 1990s, 28% in 2000s). The median number of SFs increased significantly from one in 1980s to three in 2000s (see Table). Performance status (PS), stage, and institution have been most frequently selected, and at least one of the three factors was used in most of the studies (84%) in 2000s. There are many other SFs that were used infrequently. More details will be presented. Table: SFs in first-line phase III NSCLC trials. All others; stratification factors other than PS, stage, and institution. The median number of SFs increased significantly (one way ANOVA, p=0.003).

	1981-1990	1991-2000	2001-2010	Total
No. of studies	29	46	87	162
Median no. of SFs	1	2	3	2
PS	14(48%)	21(46)	48(55)	83(51)
Stage	2(7)	22(48)	63(72)	86(53)
Institution	2(7)	17(37)	37(43)	56(35)
PS or Stage	15(52)	29(63)	6(7)	113(70)
PS, Stage, or Institution	16(55)	32(70)	73(84)	121(75)
Not reported or None	12(41)	13(28)	13(15)	38(23)
All others	1(3)	1(2)	1(1)	3(2)

Conclusion: This study reports extensive details in design of phase III trials for first-line NSCLC that have been published over three decades. We found increases in sample size and reporting primary endpoint, whereas allocation method remains underreported. Although PS, stage, and institution are the most frequently selected, choice of SFs remains inconsistent across studies. Our report provides researchers with valuable information for future studies. **Keywords:** meta-analysis, phase III, non-small cell lung cancer, first-line

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P2.01-070 Serum Albumin in Patients with Advanced-Stage NSCLC Treated with Erlotinib

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Background: Molecular targeted therapy based on tyrozine kinase inhibitors (TKI), directed at epidermal growth factor receptor (EGFR) is one of the novel effective agents in management of advanced-stage NSCLC. However several candidate predictors have been extensively studied, apart from activating *EGFR* gene mutations, no reliable biochemical or molecular predictors of response to erlotinib have been validated. The aim of our retrospective study was to evaluate the association of baseline serum albumin with outcomes in a large cohort of patients with advanced-stage NSCLC treated with erlotinib. **Methods:** Clinical data of 457 patients with locally-advanced (IIIB) or

metastatic stage (IV) NSCLC treated with erlotinib were analysed. Serum samples were collected and the measurement was performed one day before the initiation of erlotinib treatment. **Results:** Before the treatment initiation, low albumin was (<35 g/l) measured in 37 (8.1%) patients and normal albumin (≥ 35 g/l) was measured in 420 (91.9%). The median PFS and OS for patients with low serum albumin was 0.9 and 1.9 months compared to 1.9 and 11.4 months for patients with normal serum albumin (p=0.001 and p<0.001). The multivariate Cox proportional hazards model revealed that *EGFR* mutation status (HR=2.50; CI: 1.59-3.92; p<0.001) and pretreatment serum albumin (HR=1.73; CI: 1.21-2.47; p=0.003) were significant independent predictive factors for PFS, whereas *EGFR* mutation status (HR=3.14; CI: 1.70-5.81; p<0.001), stage (HR=1.48; CI: 1.09-2.02; p=0.013), ECOG PS (HR=1.77; CI: 1.37-2.29; p<0.001) and pretreatment serum albumin (HR=4.60; CI: 2.98-7.10; p<0.001) were significant independent predictive factors for OS. **Conclusion:** The results of the present retrospective study indicate that pretreatment hypoalbuminemia is associated with poor outcome of NSCLC patients treated with erlotinib. Based on the present study results, measuement of serum albumin is an objective laboratory method feasible for estimation of prognosis of patients with advanced-stage NSCLC. *This study is supported by Ministry of Health, Czech Republic - conceptual development of research organization Faculty Hospital in Pilsen - FNPl, 00669806 and by the project CZ.1.05/2.1.00/03.0076 from European Regional Development Fund.*
Keywords: NSCLC, albumin, Erlotinib, biomarker

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-071 TULUNG REGISTRY: Data Analysis of Patients with Non-Squamous NSCLC Treated with Bevacizumab in the Czech Republic Libor Havel[1], Jana Krejci[1], Karel Hejduk[2], Jana Skrickova[3], Marcela Tomiskova[4], Helena Coupkova[5], František Salajka[6], Michal Hrnciarik[6], Vitezslav Kolek[7], Ivona Grygarkova[8], Jaromir Roubec[9], Milos Pesek[10], Milada Zemanova[11], Leona Koubkova[12], Marketa Cernovska[13]
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Background: We conducted a systematic review of data from patients reported in the TULUNG registry (data cut-off 26-Jan-15). The TULUNG registry is Czech national oncology registry which prospectively collects data from all NSCLC patients treated with new targeted therapies in Czech Republic since 2008. **Methods:** Analysis was performed on a group of patients with non-squamous NSCLC with good performance status (PS 0-2), treated with bevacizumab. Since 2008 bevacizumab has been used for treatment in 193 patients (full record criteria met). 10 patients with incomplete records were not included to the review **Results:** In this group of patients 35.8% were female; the median age at bevacizumab treatment initiation was 60 years (range 29-83). The majority of patients were smokers and ex-smokers (37.8% and 34.7% respectively) and 91.7% of tumors were adenocarcinomas by histology. 91.7% patients were at the metastatic stage at the initiation of bevacizumab treatment, 6.2% of patients were in stage IIIb and only 2.1% of patients in stage IIIa (UICC6). The performance status was distributed between ECOG PS0 and PS1 mainly (40.9% PS0 and 58% PS1)at the initiation of the bevacizumab treatment. Majority of patients received bevacizumab treatment in the first line (96.4%). Two main chemotherapy regimens were used; carboplatin+paclitaxel (68.4%) and cisplatin+gemcitabine (9.8%). In this group of 193 patients analyzed, bevacizumab therapy was terminated in 152 (78.8%) patients at data cut-off. The most frequent reasons for termination were disease progression, in 55.9%, termination of treatment according to plan in 8.6% and death, in 7.9% of patients. Treatment with bevacizumab is ongoing in 41 (21.2%) patients. In 152 of patients with terminated treatment, the median duration of treatment was 15.6 weeks (95% CI 0.3 – 51.3). Response assessment showed CR in 0.7%, PR in 40.8% and SD in 35.5% of patients. Median progression free survival was 6.9 months (95% CI 5.8 – 8.1), median overall survival 16.7 months (95% CI 11.7 – 21.7). 1-year survival from bevacizumab treatment initiation was 67.9%. Adverse events were reported in 9.8% of patients, the most frequently reported adverse events were thromboembolic events (5.2%) and neutropenia (1.6%). Tromboembolic events were observed in 10 patients, none of these was fatal. We didn´t observe any severe episode of bleeding event. **Conclusion:** Therapy with bevacizumab in non-squamous NSCLC was active and very well tolerated. In eligible patients, only 7 patients (4.6%) had to discontinue bevacizumab therapy due to safety reasons. In patients with completed bevacizumab therapy 77.0% disease control rate was reached with a median survival of approximately 16.7 months from initiation of first line therapy with bevacizumab. **Keywords:** non-squamous, bevacizumab, advanced NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P2.01-072 A Phase II Study of Carboplatin/Pemetrexed/Bevacizumab Followed by Bevacizumab/Erlotinib Maintenance for NonSq-NSCLC with Wild-Type EGFR Hiroshi Yokouchi[1], Taichi Takashina[2], Hajime Asahina[2], Noriyuki Yamada[3], Masao Harada[4], Kosuke Nakano[4], Kenya Kanazawa[1], Kei Takamura[5], Takahiro Ogi[5], Toshiyuki Harada[6], Osamu Honjo[7], Naoto Morikawa[8], Ichiro Kinoshita[9], Ryoichi Honda[10], Toraji Amano[11], Hirotoshi Dosaka-Akita[9], Hiroshi Isobe[12], Masaharu Nishimura[2]
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Background: Maintenance therapy (MT) after platinum doublet chemotherapy has been shown to improve progression-free survival (PFS) and overall survival (OS) in advanced non-small-cell lung cancer (NSCLC), whereas optimal strategies for MT, such as continuation or switch maintenance, have yet to be determined. ATLAS trial adopted a combination maintenance strategy design in which both EGFR-positive and -negative NSCLC patients received platinum doublet chemotherapy at the choice of investigators plus bevacizumab (Bev) followed by Bev with either erlotinib (Erl) or a placebo as a maintenance therapy. The trial demonstrated that Erl plus Bev was favorable for PFS, but not for either OS or toxicity, when compared with placebo plus Bev. The aim of this phase II study was to clarify the effects and safety of a fixed induction regimen: carboplatin (Cb)/pemetrexed (PEM)/Bev followed by Bev plus Erl as a maintenance therapy in non-squamous (nonSq)-NSCLC patients with wild-type (WT) EGFR. **Methods:** All eligible patients (pts) had treatment-naive nonSq-NSCLC (stage IIIB, IV, or postoperative recurrent) with WT EGFR. Cb (AUC 5), PEM (500 mg/m^2) and Bev (15mg/kg) were administered on Day 1 every three weeks for four-to-six cycles and maintenance therapy with Bev (15mg/kg) once every three weeks plus continuous Erl (150mg/body) was administered until occurrence of either disease progression or unacceptable toxicity. The primary endpoint was PFS at 6 months (mo). The secondary endpoints included OS, tumor response, toxicity, and quality of life (QOL). **Results:** From September 2011 to June 2014, 51 pts were enrolled. Fifty pts were evaluated for the efficacy and safety of the treatment. The median follow-up duration was 14.3 months (range: 1.1-30.7). The median age was 64 years (range: 36-74); male/female=27/23 (54/46%); ECOG PS 0/1=28/22 (56/44%); Stage IIIB/IV/recurrent=5/41/4 (10/82/8%); adenocarcinoma/NSCLC=48/2 (96/4%). The median cycles of the induction/maintenance therapy were 4 (range: 1-6)/4 (range: 1-20). Twenty-nine pts (58%) received the MT. Overall response rate was 48.0% (95% CI: 34.8-61.5%), and disease control rate was 86% (95% CI: 73.8-93.0%). Six-month PFS rate was 59.5% (95% CI: 45.0-72.6%). Median OS and PFS were 18.4 mo (95% CI: 11.9-24.9 mo) and 6.5 mo (95% CI: 5.8-7.2 mo), respectively. CTCAE Grade (Gr) 3/4 hematological toxicities were neutropenia (48%/3.4%), anemia (18%/3.4%) and thrombocytopenia (22%/0%). The most frequent Gr 3/4 non-hematological toxicities were anorexia (14%/3.4%), hypertension (10%/3.4%), malaise (6%/3.4%), nausea (6%/0%) and rash (0%/10%). There were two interstitial lung diseases (Gr1), one gastrointestinal perforation (Gr4), and one treatment-related death due to ventricular fibrillation. QOL results are still under analysis. **Conclusion:** Cb/PEM/Bev followed by maintenance Bev/Erl was effective and well tolerated in NS-NSCLC pts with WT EGFR. **Keywords:** Non-small-cell lung cancer, phase II trial, maintenance, wild type EGFR

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P2.01-073 Impact of Prophylactic Doxycycline (Doxy) on Maintaining Planned Dosing of Dacomitinib (D) an Irreversible panHER Inhibitor Mario E. Lacouture[1], Dorothy Keefe[2], Stephen T. Sonis[3], Nagdeep Giri[4], Tao Wang[5], Arlene Reisman[6], Eric Sbar[7], Diana Gernhardt[5], Aminah Jatoi[8] [1]*Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York/NY/United States of America,* [2]*Royal Adelaide Hospital, Adelaide/ ACT/Australia,* [3]*Brigham and Women'S Hospital, Dana-Farber Cancer Institute, Boston/ United States of America,* [4]*Pfizer Oncology, La Jolla/CA/United States of America,* [5]*Pfizer Oncology, Groton/CT/United States of America,* [6]*Pfizer Oncology, New York/NY/United States of America,* [7]*Pfizer Oncology, Collegeville/PA/United States of America,*[8]*Mayo Clinic, Rochester/MN/United States of America*

Background: ARCHER 1042 (NCT01465802) was a randomized patient (pt) blinded trial that explored prophylactic interventions to minimize select dermatologic adverse events of interest (SDAEI) and diarrhea associated with D, an irreversible small molecule PanHER inhibitor. **Methods:** In Cohorts I (CI) and II (CII) pts with advanced NSCLC, ≥1 prior chemo, ECOG 0–2, were randomized (pt blinded) in CI to (a) D 45 mg daily (QD) plus placebo (pbo) (D+pbo) or (b) D 45 mg QD plus doxy 100 mg twice daily x 4 wks (D+doxy) and in CII assigned to D 45 mg QD plus probiotic (prob) and topical alclometasone (alclo) (D+prob+alclo). Primary endpoints in first 8 wks included: all grade (G) and G≥2 SDAEI and PRO (Skindex-16) (CI, CII) and CII G and G≥2 diarrhea and PRO (modified Mucositis Daily Questionnaire). Plasma samples were collected to confirm that exposure of D is not altered with doxy treatment. **Results:** As of August 25, 2014, 112 pts randomized to Cohort I D+pbo vs. D+doxy (median age 66 years, 53% male) and 59 pts to CII D+prob+alclo (median age 66 years, 66% male) were evaluable (>6 wks treatment).

Median relative dose intensity (RDI) of D in the first 8 wks was 82.74% for D+doxy compared with 79.76% for D+pbo and 75.00% for D+prob+alclo.

Table 1: All G and G≥2 SDAE Incidence, Diarrhea Burden Index and Adverse Events Discontinuations (Evaluable, Data First 8 Wks)

	G SDAE† %, 95% CI	SDAE† ≥G2 %, 95% CI	Diarrhea Burden Index* Mean	D Discontinuations for AE%
Placebo N=56	82.1 69.6,91.1	48.2 34.7,62.0	2.4	8.9
Doxy N=58	70.6 63.6,87.0 vs. Pbo P=0.640	25.0 14.4,38.8 vs. Pbo P=0.019‡	1.8 vs. Pbo P=134	5.4
Alclometasone+g robiotic N=59	79.7 67.2,89.0 vs. Pbo P=0.920 vs. Doxy P=0.883	35.6 23.6,49.1 vs. Pbo P=0.237 vs. Doxy P=0.392	2.4 vs. Pbo P=0.943 vs. Doxy P=2.140	3.4

† All P-values based on risk difference. ‡CI2 SDAE for Doxy statistically significantly lower than Pbo
* Diarrhea burden index factors both duration and grade for all episodes in first 8 weeks.

PRO Skindex scores improved with prophylactic doxy, but not alclo; prophylactic probiotic was not associated with improved CTCAE or PRO. Plasma exposure of D was similar when administered either with pbo or doxy. **Conclusion:** These preliminary data suggest prophylactic doxy improves ≥G2 Select Dermatologic AEs with improved D RDI and less need for dose discontinuations. The prophylactic effect observed with doxy cannot be attributed to altered exposure of D. In contrast, prophylactic topical corticosteroids had no effect on rash or diarrhea. **Keywords:** Dacomitinib, dermatologic toxicity, doxycycline prophylaxis

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-074 Phase II Trial of Erlotinib Monotherapy for Pretreated Elderly Patients with Advanced EGFR Wild-Type Non-Small-Cell Lung Cancer
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Background: In industrialized countries, the age of approximately 50% of patients at diagnosis of non-small cell lung cancer (NSCLC) is >70 years old. Exploration of an optimal treatment strategy for elderly patients with NSCLC as either a first-line or second-line therapy is required. Erlotinib is an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor that is an effective treatment for patients with NSCLC, especially those harboring activating EGFR mutations. A previous phase III trial suggested that patients with EGFR wild-type (EGFR-wt) NSCLC or elderly patients with disease progression after cytotoxic chemotherapy might benefit from erlotinib monotherapy. However, few studies have prospectively evaluated the efficacy and safety of second or third-line erlotinib monotherapy in elderly patients with EGFR-wt advanced or recurrent NSCLC. **Methods:** Eligibility criteria included: patients aged ≥70 years with pathologically or cytologically proven NSCLC; measurable tumor sites according to the Response Evaluation Criteria in Solid Tumors (RECIST) guideline version 1.1; an Eastern Cooperative Oncology Group performance status of 0–2; no activating EGFR gene mutations (exon 18, 19, 20 and 21); history of 1–2 regimens of systemic chemotherapy; stage IIIB or IV NSCLC, or postoperative recurrence; treatment naïve to EGFR-TKI; and appropriate organ function. EGFR gene mutation analysis was performed by using invasive signal amplification reaction with a structure-specific 5′ nuclease and a polymerase chain reaction (PCR) product (PCR-invader). Patients received oral erlotinib at a dose of 150 mg/day until disease progression. Primary outcome was the objective response rate (ORR). Secondary end points included the disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and toxicity profile. **Results:** This study was terminated early because of the results from a Japanese phase III trial (DELTA trial). Sixteen patients were enrolled between April 2010 and May 2013. The median age was 78 years (range, 70–84 years), and six patients were female. Five patients had an Eastern Cooperative Oncology Group performance status of 0, and 11 (69%) patients had adenocarcinoma. Fifteen (94%) patients were treated with erlotinib as a second-line therapy. The ORR was 0% (95% confidence interval [CI]: 0–17.1) and DCR was 56.3% (95% CI: 33.2–76.9). The median PFS and OS were 1.7 months (95% CI: 1.3–2.2) and 7.2 months (95% CI: 5.6-8.7), respectively. The most commonly occurring adverse events included acneiform eruption (31.3%) and skin rash (25.0%). One patient developed grade 3 interstitial lung disease, which was improved by following steroid therapy. **Conclusion:** In pretreated elderly patients with advanced or recurrent EGFR-wt NSCLC, daily oral erlotinib was well tolerated; however, administration of the drug should not be considered as a second-line therapy. **Keywords:** elderly, Non-small-cell lung cancer, Erlotinib, EGFR wild-type

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-075 Bevacizumab with Docetaxel or S-1 in Non-Squamous NSCLC (HANSHIN 0110)
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Background: This multicenter, randomized phase II trial investigated the efficacy and safety of docetaxel plus bevacizumab and S-1 plus bevacizumab in the second-line treatment of non-squamous (non-Sq) non-small-cell lung cancer (NSCLC). **Methods:** Patients with non-Sq NSCLC who experienced disease progression after prior platinum-based chemotherapy with or without bevacizumab were randomly assigned (1:1) to receive docetaxel 60 mg/m^2 plus bevacizumab 15 mg/kg (DB) once every 3 weeks or S-1 40 mg/m^2 orally twice daily on days 1–14 plus bevacizumab 15 mg/kg (SB) on day 1 every 3 weeks until disease progression. The primary endpoint was progression-free survival (PFS). **Results:** Ninety patients were randomized. The median PFS was 3.9 months (95% confidence interval [CI] = 3.0–6.5) in the DB arm and 3.5 months (95% CI = 2.9–5.9) in the SB arm. The objective response rate was significantly higher in the DB arm than in the SB arm (22.2%*vs.* 2.2%; $P = 0.004$), whereas the disease control rates of the arms were identical (62.2% *vs.* 62.2%; $P = 1.00$). Patients receiving DB were more likely to have ≥grade 3 neutropenia (93.4% *vs.* 4.4%) and febrile neutropenia (33.3% *vs.* 0%) than SB-treated patients. In the DB arm, PFS and overall survival were significantly longer among bevacizumab-naïve patients than among bevacizumab-experienced patients (median PFS: 7.4 months *vs.* 2.8 months; $P < 0.001$; and median OS: 27.4 months *vs.* 11.7 months; $P = 0.002$). **Conclusion:** DB and SB produced modest PFS benefits in the second-line treatment of patients with advanced non-Sq NSCLC. Because of the toxicity of DB and the low response rate of SB, neither regimen warrants further investigation, excluding DB in bevacizumab-naïve patients with advanced non-Sq NSCLC. **Keywords:** Non-squamous non-small-cell lung cancer, bevacizumab, docetaxel, S-1

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-076 Clinical Study of Anti-Angiogenesis Therapy Combined with Neo-Adjuvant Chemotherapy on NSCLC Patients in Phase IIIa (N2)
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Tianjin Medical University Cancer Institute & Hospital, Tianjin/China

Background: This study aimed to explore the safety and effectiveness of anti-angiogenesis agent Endostar combined with neo-adjuvant chemotherapeutic therapy in the treatment of non-small cell lung cancer (NSCLC) patients in phase ⅢA (N2). **Methods:** From April, 2011 to December, 2013, a total of 30 patients diagnosed as NSCLC in phase ⅢA (N2) by pathology or assistant examinations were selected in the randomized, control and open clinical study treated with NP combined with Endostar or single NP neo-adjuvant chemotherapeutic therapy. Control group was treated with neo-adjuvant NP chemotherapy for 2 weeks, on which basis trial group was added with Endostar for 2 weeks. Clinical efficacy was evaluated 3 weeks and surgery was performed within 4 weeks after 2-cycle treatment. The primary end points were response rate (RR), clinical benefit rate (CBR) and tumor regression rate (TRR) as well as peri-operative clinical indexes and safety. The secondary end points included disease-free survival time (DFS) and overall survival time (OS). **Results:** In the 26 patients with evaluable efficacy, trial group and control group were 50.0% and 40.0% in RR (P=1.0), 87.5% and 64.0% in CBR (P=0.76), 19.7% and 7.1% in TRR (P=0.036), 12.0 months and 10.0 months in total DFS (P=0.44) and 16.0 months and 14.0 months in OS (P=0.39), respectively. however, there was no significant difference between two groups in all clinical indexes and hematological and non-hematological toxicities in all degrees (P>0.05). **Conclusion:** Endostar combined with NP chemotherapy are markedly higher than single NP neo-adjuvant chemotherapy in RR, CBR, TRR, DFS and OS without increasing the therapeutic toxicities. In addition, there is no significant difference between two groups in peri-operative clinical indexes, indicating that Endostar combined with NP chemotherapy are safe and effective in treating patients with NSCLC in ⅢA (N2). **Keywords:** Recombinant human endostatin; NP protocol; Randomized; Control; Non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-077 A Phase 1b Trial of the Combination of Capecitabine and Erlotinib in Advanced Lung Cancer
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Background: Erlotinib is active in tumors with an *EGFR* mutation. Capecitabine, a thymidylate synthetase inhibitor, has shown some activity in advanced lung cancer (ALC). The combination of erlotinib and capecitabine has not been studied in ALC. **Methods:** We conducted a phase 1b trial, using a standard 3+3 dose escalation design to define the maximum tolerated dose (MTD) and safety of the combination of erlotinib and capecitabine, given on a 3-weekly cycle in 2nd line patients unselected for *EGFR* status. DLT was any grade≥2 toxicity. After MTD was defined in the 2nd line patients, we planned expansion of the trial to 1st line patients for further dose escalation. Dosing levels are listed in Table 1. Toxicity was assessed using CTCAE v3.0, response rate was assessed using RECIST 1.1, and survival assessed using Kaplan-Meier method. **Results:** We recruited 40 patients with adenocarcinoma. 55% were male, with median age of 67 years (range 38-84). 65% were ex-smokers and 28% were current smokers. Performance status was ECOG 1 in 65% and 2 in 35% of patients. 85% of patients had received platinum-

doublet chemotherapy for 1st line ALC, with 10% having maintenance pemetrexed. One patient had an *EGFR* mutation. Dose escalation stopped at level 3 in 2nd line patients with expansion to 6 patients due to dose limiting toxicities (DLTs) of grade (G) 2 creatinine rise, G2 anemia, G3 atrial fibrillation, and G3 pneumonia in 2/6 patients. The MTD was thus at level 2 that was also expanded to 6 patients, confirming safety. First line patients were then recruited at MTD but resulted in DLTs in 3/4 patients with G3 troponin rise, G2 rash, and G2 bilirubin rise in 2 patients. Hence the 1st line approach was abandoned. The MTD in 2nd line patients was further expanded for toxicity and activity. The overall response rate was 3% with a disease control rate of 34%. A partial response was seen in 1 patient with *EGFR* mutation of 11.3 months duration. The median progressive free survival was 1.6 months (95%CI 1.4 – 3.5) and the median overall survival was 6.1 months (95%CI 5.1 – 12.5). **Conclusion:** The MTD for capecitabine is 750mg/m^2 bd days 1–14 and erlotinib 100mg od on a 3-weekly cycle. The addition of capecitabine does not improve the efficacy of erlotinib in unselected ALC. This combination could be explored further in ALC selected for *EGFR* mutation. Table 1: Patient disposition.

Dose escalation	No. of pts	No. of pts with DLTs
Level 1 - Erlotinib 100mg od, Capecitabine 500mg/m^2, bd, days 1-14	3	
Level 2 - Erlotinib 100mg od, Capecitabine 750mg/m^2, bd, days 1-14	3 + 3	
Level 3 - Erlotinib 100mg, od, Capecitabine 1000mg/m^2 bd, days 1-14	3 + 3	2
1st line ALC at level 2	4	3
Dose Expansion		
2nd line ALC	21	

Keywords: Erlotinib, Capecitabine, Non-small-cell lung cancer, Phase 1

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-078 Concurrent Thoracic Radiotherapy and Tyrosine Kinase Inhibitors for Wild-Type EGFR Patients with Locally Advanced Non-Small Cell Lung Cancer

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Background: Concurrent chemoradiotheray is the standard of care for patients with locally advanced non-small cell lung cancer (NSCLC), but often accompanying with high toxicities and poor tolerability. Radiosensitization of EGFR tyrosine kinase inhibitors (TKI) has been proved in preclinical studies, and the safety of TKI combined with thoracic radiotherapy has also been evaluated in several phase II trials. **Methods:** Patients with previously untreated, non-metastasis NSCLC, EGFR wild-type, Easter Cooperative Oncology Group performance status of 0-2 and acceptable organ function were eligible. The prescribed radiation dose was 60-70Gy, and both three dimensional conformal and intensity-modulated radiation therapies were allowed. TKI was administrated concurrently with thoracic radiotherapy. The primary endpoint was local-regional control; second endpoints included progression-free survival, overall survival and treatment-related toxicities. **Results:** Between 2012.1 and 2015.3, 12 eligible patients were recruited into this study, with an median age of 65 years (range 47 ~ 82 years). 1 female and 11 males. One of them was stage Ⅳ, two of them were stage Ⅱ and nine of them were stage Ⅲ. During the process of treatment, 2 (16.7%) of patients developed grade Ⅱ radiation pneumonitis and 9 (75.0%) developed level Ⅰ~Ⅱ hematological toxicity. Patients were followed up with a median follow-up time of 13 months (6~35months) and the last follow-up time was 2015.3. The results showed that 1-year and 2-year overall survival rates were 76.2% and 57.1%, respectively. 1-year and 2-year local recurrence-free survival rates (LRFS) were 62.2% and 62.2%, respectively. 1-year and 2-years PFS rates were 55.0% and 55.0% (see table), respectively. **Conclusion:** The preliminary results showed that concurrent thoracic radiotherapy and EGFR-TKI were safe and effective in NSCLC patients with wild-type EGFR. This trial is on going. **Keywords:** EGFR-TKI, NSCLC, Concurrent thoracic radiotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-079 A Phase I Study Comparing PF-06439535 (A Potential Biosimilar) with Bevacizumab

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Background: PF-06439535, a potential biosimilar to bevacizumab, is a humanized monoclonal IgG1 antibody that targets the vascular endothelial growth factor. This study (B7391001) compared the pharmacokinetics (PK) of PF-06439535 to bevacizumab sourced from the US (bevacizumab-US) and EU (bevacizumab–EU), and the PK of bevacizumab-EU to bevacizumab–US in healthy male volunteers. **Methods:** In this double-blind study, 102 healthy males, aged 21-55 years, were randomized 1:1:1 to receive a single 5 mg/kg intravenous dose of PF-06439535, bevacizumab-US, or bevacizumab-EU. One subject discontinued before dosing. Assessments for PK were conducted for 71 days, with extended safety and immunogenicity assessments up to 100 days postdose. PK similarity was achieved if 90% confidence intervals (CIs) for the test-to-reference ratios of the maximum concentration (C_{max}), the area under the concentration-time curve (AUC) from time 0 to the last quantifiable time point (AUC_T), and AUC from time 0 extrapolated to infinity ($AUC_{0-\infty}$) were within 80.00%–125.00%. **Results:** Ninety-seven subjects were eligible and included in the PK analysis. The demographics of the PK eligible subjects were comparable among the 3 treatment groups. The 3 study drugs exhibited similar PK parameters (**Table 1**). For the comparisons of PF-06439535 to bevacizumab-EU or bevacizumab-US, and of bevacizumab-EU to bevacizumab-US, the 90% CIs for the ratios of C_{max}, AUC_T, and $AUC_{0-\infty}$ were all within 80.00%–125.00% (**Table 2**). Treatment-related adverse events were reported in 15.2%, 25.7%, and 18.2% of subjects in the PF-06439535, bevacizumab-EU, and bevacizumab-US treatment arms, respectively. **Table 1**: Mean (±SD) PK Parameter Estimates

Parameters (units)	PF-06439535	Bevacizumab-EU	Bevacizumab-US
N	32	33	32
C_{max} (µg/mL)	142.9 ± 20.3	137.0 ± 20.5	130.0 ± 18.2
AUC_T (µg•hr/mL)a	40840 ± 6411	41010 ± 6711	38920 ± 4566
$AUC_{0-\infty}$ (µg•hr/mL)	43080 ± 7103	43830 ± 8326	41450 ± 5350

aAUC_T was ≥80% of the corresponding $AUC_{0-\infty}$ in all 97 PK eligible subjects. **Table 2: Comparisons of Pharmacokinetic Exposure Parameters between Test and Reference Products**

Comparison (Test to Reference)	Parameters, units	Testa	Referencea	Test/Reference Ratio (%)	90% CI for Ratio
PF-06439535 to bevacizumab-EU	C_{max}, µg/mL	141.5	135.5	104.42	98.36–110.84
	AUC_T, µg•hr/mL	40330	40490	99.62	93.69–105.93
	$AUC_{0-\infty}$, µg•hr/mL	42490	43100	98.58	92.16–105.44
PF-06439535 to bevacizumab-US	C_{max}, µg/mL	141.5	128.9	109.79	103.38–116.60
	AUC_T, µg•hr/mL	40330	38660	104.32	98.06–110.97
	$AUC_{0-\infty}$, µg•hr/mL	42490	41120	103.33	96.55–110.58
Bevacizumab-EU to bevacizumab-US	C_{max}, µg/mL	135.5	128.9	105.15	99.05–111.62
	AUC_T, µg•hr/mL	40490	38660	104.71	98.48–111.34
	$AUC_{0-\infty}$, µg•hr/mL	43100	41120	104.82	98.00–112.12

aAdjusted geometric means **Conclusion:** This study demonstrates PK similarity of PF-06439535 to both bevacizumab-US and bevacizumab-EU, and of bevacizumab-EU to bevacizumab-US. The safety profile was similar in the 3 treatment groups with no significant safety findings reported. **Keywords:** biosimilar, NSCLC, PF-06439535, bevacizumab

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-080 Pemetrexed, Carboplatin and Bevacizumab in Patients with Non-Squamous NSCLC without or with Activating EGFR Mutation (CJLSG0909/0910)

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Background: Treatment strategies for advanced non-squamous (sq) non-small cell lung

cancer (NSCLC) are divided by EGFR mutations. However, there has been no previous report about efficacy of cytotoxic agents separated by EGFR mutations. In addition, the influence of the EGFR mutations on the maintenance therapy with pemetrexed (Pem) or bevacizumab (Bev) has not been elucidated. We planned two studies designed to evaluate the efficacy and safety of combination therapy with Pem, carboplatin (Cb) and Bev followed by Pem and Bev maintenance therapy for non-sq NSCLC patients without or with activating EGFR mutation. **Methods:** We undertook two multicenter, open-label, single-arm, phase II studies. Patients with wild type EGFR or with EGFR mutation (exon 19 deletions or exon 21 point mutation) entered CJLSG0909 or 0910, respectively. Patients received Pem 500mg/m^2, Cb AUC 6, and Bev 15mg/kg day1, every 3 weeks, 4 to 6 cycles (induction therapy). Patients who had achieved disease control received Pem+Bev maintenance therapy until progressive disease or unacceptable adverse event. Key inclusion criteria were stage IIIB, IV, or recurrent disease after surgery, no prior chemotherapy, age 20 to 74. The primary endpoint was the objective response rate (ORR), and the secondary endpoints were the disease control rate (DCR), progression free survival (PFS), overall survival (OS) and safety. (Unique trial Number; UMIN000003736/UMIN000003737) **Results:** In CJLSG0909, 50 patients received induction treatment. They had a median age of 64 years and were predominantly men (40 [80%]) with adenocarcinoma (47 [94%]), stage IV (40 [80%]), and a performance status (PS) of 1 (40 [80%]). The median of induction therapy was 5 cycles. Thirty-five (70%) patients received maintenance therapy, and the median of maintenance therapy was 5 cycles. Partial response was observed in 25 patients with a ORR of 50.0% (95% confidence interval, 33.7–62.6%). Stable disease was observed in 21 patients and the DCR was 92%. Median PFS was 6.8 months and median OS was 19.4 months. Grade 3/4 toxicities during induction therapy included neutropenia (40 [80%]), thrombocytopenia (12 [24%]), anemia (8 [16%]), nausea (4 [8%]), anorexia (3 [6%]), ALT elevation (3 [6%]), AST elevation (2 [4%]), vomiting, periodontal, hemoptysis, thrombosis and proteinuria (1 [2%]) respectively. In CJLSG0910, 30 patients received induction treatment. They had a median age of 65.5 years and were predominantly women (17 [57%]) with adenocarcinoma (29 [97%]), stage IV (27 [90%]), and a PS of 0 (23 [77%]). The median of induction therapy was 6 cycles. Twenty-five (83%) patients received maintenance therapy, and the median of maintenance therapy was 8.5 cycles. Partial response was observed in 15 patients with a ORR of 50.0% (95% confidence interval, 33.9–66.1%). Stable disease was observed in 15 patients and the DCR was 100%. Median PFS was 10.0 months and median OS was 41.4 months. Grade 3/4 toxicities during induction therapy included neutropenia (14 [47%]), thrombocytopenia (6 [20%]), anemia (6 [20%]), diarrhea (2 [7%]), nausea, anorexia, amylase elevation (1 [3%]) respectively. **Conclusion:** These studies suggested that chemotherapy with Pem+Cb+Bev, including Pem+Bev maintenance therapy is candidate for first line therapy in non-sq NSCLC patients regardless of the activating EGFR mutations. **Keywords:** non-squamous NSCLC, activating EGFR mutation, pemetrexed, bevacizumab

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-081 Case Series of HER2 Mutated Metastatic Lung Adenocarcinoma and Response to HER2 Targeted Therapies Jody Chuang[1], Joel W. Neal[2], Heather A. Wakelee[3] [1]*Hematology and Oncology, Stanford Hospial & Clinics, Stanford/AL/United States of America,* [2]*Medicine (Oncology), Stanford Cancer Intitute/Stanford University, Stanford/CA/United States of America,* [3]*Stanford University, Stanford/United States of America*

Background: HER2 has long been recognized as an oncogenic driver in some breast and gastro-esophageal cancers. More recently, somatic mutations in HER2 have been reported in 1-2% of patients with lung adenocarcinoma, and the promise of HER2 as a treatment target in lung cancer has been suggested using anti-HER2 small molecules and antibodies. **Methods:** Here we report the outcomes of three patients with metastatic lung adenocarcinoma with HER2 mutations being treated with HER2 targeted therapies at a single institution. **Results:** The first patient is a 65yo Caucasian woman, minimal smoking history, with stage IIIA lung adenocarcinoma who then developed recurrent metastatic disease mainly in the liver after completing definitive chemoradiotherapy. She progressed through three lines of chemotherapies, with near replacement of liver with tumor. At that time she was found to have HER2 exon 20 insertion mutation (A775_G776 insSVMA) and was started on vinorelbine and trastuzumab. The main side effect was fatigue, which was tolerable. She achieved radiographic stable disease with 13% reduction of her liver metastasis as her best response by RECIST v1.1 for 6 months and significant clinical improvement before progression of disease in all sites. The second patient is a 60yo Caucasian woman, former smoker, diagnosed with stage IV lung adenocarcinoma with HER2 exon 20 insertion mutation (unknown exact sequence) with extensive bony disease. She was treated with carboplatin, paclitaxel, bevacizumab, and an investigational anti-Met therapy with initial mild decrease in lung mass and nodules after one month, then mild progression for 14 months. She was taken off trial then and started on vinorelbine and trastuzumab, and so far shows no measurable growth after 5 months on therapy. The third patient is a 35yo Asian woman, non-smoker, diagnosed with stage IV lung adenocarcinoma with HER2 exon 20 insertion mutation (unknown exact sequence) with malignant pleural effusions, bilateral lung and brain lesions, and extensive lymph node involvement. She was treated with carboplatin, pemetrexed, and bevacizumab first followed by pemetrexed and bevacizumab maintenance, with initial mild improvement then progression after 4.5 months. She was then treated with erlotinib with rapid progression within 1 month. She was then treated with afatinib 40mg daily based on the HER2 mutation, improved disease after 2 months with best response 21% reduction, then progression after 3 more months (5 months total of clinical benefit). She was then started on vinorelbine and trastuzumab. Treatment was interrupted due to one new brain lesion requiring stereotactic radiation treatment. She has shown partial response with best response of 31% on the latest imaging done 4 months after starting therapy. **Conclusion:** From our single institution experience, HER2 targeted therapy can provide disease control for patients with metastatic HER-2 mutated NSCLC that has progressed on previous therapies. Our results are consistent with the study by Mazières *et al*. Vinorelbine was dosed as 25 mg/m2 and trastuzumab as 2 mg/kg every 1 week (with 4mg/kg first loading dose) or 6 mg/kg every 3 weeks. All three patients were able to tolerate therapies well with no significant toxicities nor cardiac toxicity. **Keywords:** trastuzumab, NSCLC, HER2

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-082 Pathological Response with Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blocker Use in Advanced Non-Small Cell Lung Cancer Jalal Hyder[1], Neha Bhooshan[1], Josephine L. Feliciano[2], Melissa Vyfhuis[1], Vincent K. Lam[2], Mohan Suntharalingam[1], Whitney Burrows[3], Elizabeth M. Nichols[1], Martin Edelman[2], Steven J. Feigenberg[1], Eric P. Cohen[4], Zeljko Vujaskovic[1],Pranshu Mohindra[1] [1]*Radiation Oncology, Univeristy of Maryland, Baltimore/United States of America,* [2]*Department of Medicine, University of Maryland, Baltimore/United States of America,* [3]*Department of Surgery, University of Maryland, Baltimore/MD/United States of America,* [4]*Medical College of Wisconsin, Milwaukee/WI/United States of America*

Background: Angiotensin converting enzyme inhibitor (ACEi) and angiotensin receptor blocker (ARB) are among the most common medications in the treatment of hypertension and diabetes. These drugs are under evaluation as a means to mitigate radiation pneumonitis/fibrosis likely mediated by anti-inflammatory and endothelial effects. Their collateral impact on oncological outcomes is unknown. We retrospectively evaluate the effect of ACEi and ARB usage on pathological response during preoperative platinum-based concurrent chemoradiotherapy (CCRT) with high-dose radiotherapy (≥59.4 Gy) in a cohort of patients with stage III non-small cell lung cancer (NSCLC). **Methods:** Between June 2000 and December 2009, 79 patients with stage III NSCLC (AJCC 7th ed.) were treated with preoperative CCRT at our institution. Data on ACEi/ARB usage during CCRT and pathological response was available for 72 patients. The primary end-point was pathological complete response (pCR), in both the primary site and involved lymph nodes. X^2 analysis was to assess distribution of categorical variables, Kaplan-Meier survival analysis with log rank test for univariate and Cox regression multivariate (age, gender, race, stage, RT dose and chemotherapy regimen) analysis of overall survival (OS) and freedom-from recurrence (FFR) was performed. **Results:** The median age at diagnosis was 56 years (range, 38-78) with 56% males, 74% Caucasians and 96% smokers. Stage distribution was IIIA (72%), IIIB (28%), T1/2 (54%), T3/4 (46%), N0/1 (14%) and N2/3 (86%). The median radiation dose was 66.6 Gy (range 59.4-69.6 Gy) with the most common CCRT regimen being carboplatin-paclitaxel (54%). At a median follow up of 3.8 years for all patients and 6.8 years for surviving patients, the median OS and FFR of the entire cohort were 4.9 years (95% Confidence Interval (CI): 3.5-6.5) and 3.1 years (95% CI: 1.3-4.9), respectively with overall pCR rate of 44%. During CCRT, 11 patients (15%) were taking ACEi/ARB and 61 patients (85%) were not taking ACEi/ARB. No statistical differences were seen in the distribution of baseline variables between the two cohorts. None of the patients developed acute radiation pneumonitis in the time interval between radiotherapy completion and surgery (median 55 days; range, 33-105 days). The pCR rate without and with ACEi/ARB was 46% vs 36% (p=0.56). The median FFR without and with concurrent ACEi/ARB use was 3.1 years vs. not reached, p = 0.35, while the corresponding median OS values were 4.8 years and 5.5 years, p = 0.59, respectively. On multivariate analysis, an improved OS was associated with younger age (HR: 0.39, 95%CI: 0.2-0.8, p<0.01), an improved FFR was associated with lower stage (HR: 0.3, 95%CI: 0.15-0.76, p<0.01) and Caucasian race (HR=0.37, 95% CI: 0.15-0.88, p=0.02), with no impact of ACEi/ARB use on either outcome. **Conclusion:** The use of ACEi/ARB did not have any apparent influence the rates of pCR in this small cohort of advanced stage NSCLC patients treated with trimodality therapy following preoperative platinum-based CCRT with high-dose radiotherapy. As the role of these drugs in mitigating radiation pneumonitis continues to be evaluated, simultaneous assessment of lack of a negative impact on disease outcomes needs to be validated in larger, prospective analyses. **Keywords:** Angiotensin converting enzyme inhibitor, radiation toxicities mitigators, trimodality therapy, locally advanced NSCLS

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-083 Prognostic Significance of CK19mRNA Positive Cells in the Peripheral Blood of Patients with Advanced Non Small Cell Lung Cancer (NSCLC) Ippokratis Messaritakis[1], Stella Apostolaki[1], Georgia Milaki[2], Filippos Koinis[3], Lefteris Manouras[1], Maria Perraki[1], Vassilis Georgoulias[1], Athanasios Kotsakis[3] [1]*University of Crete,Laboratory Tumor Cell Biology, Heraklion/Greece,* [2]*Venizeleio Hospital, Heraklion/Greece,* [3]*Medical Oncology, University Hospital of Heraklion, Heraklion/Greece*

Background: Circulating Tumor Cells (CTCs) have been shown to be a useful prognostic tool in several cancers. Non-small-cell-lung cancer (NSCLC) lacks validated prognostic biomarkers and, thus, this study aimed to explore the sensitivity and clinical significance of the detection of *CK19*mRNA (+) CTCs in NSCLC patients. **Methods:** Peripheral blood was obtained from 642 patients with previously untreated stage IIIB/IV NSCLC and from 455 patients after the completion of 1st line chemotherapy. RNA extracted from the Calu-3 and ARH-77 cell lines was used as positive and negative controls, respectively. The detection of *CK19*mRNA-positive cells was performed using an RT-qPCR assay. **Results:** The analytical detection limit of the method was found to correspond to 0.42 Calu-3 cell equivalents/5μg RNA. One hundred and sixty seven (26.0%) patients had detectable *CK19*mRNA (+) CTCs at baseline; the detection of *CK19*mRNA (+) CTCs post chemotherapy was associated with significantly decreased PFS and OS (PFS: 2.6 vs 3.8 months, p=0.008; OS: 5.7 vs 10.0 months, p=0.006). Multivariate analysis revealed that gender, performance status and the detection of *CK19*mRNA (+) CTCs post chemotherapy emerged as independent factors associated with reduced PFS (HR=1.350, p=0.010) and

OS (HR=1.608; p=0.001). **Conclusion:** Detection of peripheral blood CK19mRNA (+) CTCs post chemotherapy is an adverse prognostic factor correlated with poor clinical outcome in patients with stage IIIB/IV NSCLC.

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-084 Post-Market Clinical Trial of Dianhydrogalactitol in the Treatment of Relapsed or Refractory Non-Small Cell Lung Cancer Anne Steino[1], Guangan He[2], Jeffrey A. Bacha[1], Sarath Kanekal[1], Dennis M. Brown[1], Nancy D. Santos[3], Ming Chen[4], Zahid Siddik[2], Lu Shun[5] [1]*Delmar Pharmaceuticals, Vancouver/BC/Canada,* [2]*University of Texas MD Anderson Cancer Center, Houston/AL/United States of America,* [3]*BC Cancer Agency, Vancouver/BC/Canada,* [4]*Guangxi Wuzhou Pharmaceutical (Group) Co. Ltd., Guangxi/China,* [5]*Shanghai Lung Cancer Center, Shanghai/China*

Background: The median overall survival time for patients with stage IV non-small cell lung cancer (NSCLC) is 4 months, and 1- and 5-year survival is less than 16% and 2%, respectively. NSCLC is usually treated with surgery followed by radiation and treatment with platinum-based regimens or in some cases Tyrosine Kinase Inhibitors (TKIs). Unfortunately, long-term prognosis with platinum-based therapies is poor, and TKI resistance has emerged as a significant unmet medical need. Dianhydrogalactitol (VAL-083) is a structurally unique bi-functional alkylating agent mediating interstrand DNA crosslinks at N^7 of guanine. It has previously demonstrated activity against NSCLC in NCI-sponsored preclinical and clinical trials and is approved for treatment of lung cancer in China *(Approval No. Guoyao Zhunzi H45021133)*; however, it is currently not widely known or used for the treatment of NSCLC. **Methods:** not applicable **Results:** Recent preclinical data suggest that VAL-083 may be a therapeutic option for drug-resistant NSCLC. VAL-083 has superior activity to cisplatin in both *in vitro* and *in vivo* models of NSCLC, including TKI-resistant NSCLC. When combined with either cisplatin or oxaliplatin *in vitro*, VAL-083 demonstrates significant superadditivity ($p<0.05$) and synergism (CI < 1) for both combinations in NSCLC cell lines A549, H1975 and H460. When tested in a standard syngeneic mouse fibrosarcoma model (RIF-1 cell-line in C3H mice), VAL-083 (10 mg/kg) was superior to cisplatin (4 mg/kg) in tumor growth delay. Mice were treated with a single IP injection of either cisplatin, VAL-083 or VAL-083 followed immediately by cisplatin. Combination treatment of with cisplatin produced a more than additive effect by delaying growth 8.65 days. In another *in vivo* model using NSCLC cell-line A549 in Rag2mice, VAL-083 was given as part of a combination treatment with cisplatin. Tumour growth delays of 11, 18 and 25 days were observed for 2 mg/kg cisplatin in combination with 2, 2.5 or 3 mg/kg VAL-083, respectively, while no significant tumour growth delay was observed between untreated and Cisplatin (2 mg/kg). The median survival time was increased by 2 days for cisplatin alone, while the combination of VAL-083 (2 mg/kg, 2.5 mg/kg and 3 mg/kg) with cisplatin (2 mg/kg) increased survival by 17 days, 17 days, and 14 days, respectively. **Conclusion:** The preclinical data strongly suggest VAL-083 as a potential treatment for drug-resistant NSCLC. A planned open-label phase IV (post market) clinical trial will investigate the activity of VAL-083 in relapsed or refractory NSCLC assessed by objective response rates, complete and partial response rates and stable disease. VAL-083 will be dosed in accordance with the approved label (40 mg/day) and the results will provide guidance to treating physicians under the context of VAL-083's current approval in China, as well as serve as proof of concept for expanded development in the rest of the world. **Keywords:** VAL-083, NSCLC, Cisplatin, combination-treatment

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-085 Abemaciclib in Combination with Single Agent Options in Stage IV NSCLC, a Phase 1b Study Karen Kelly[1], Jonathan W. Goldman[2], Pilar Garrido[3], Shadia Jalal[4], Daruka Mahadevan[5], Martin Gutierrez[6], Luis Paz-Ares[7], Mariano Provencio[8], Eric Schaefer[9], Monte Shaheen[10], Erica L. Johnston[11], Na Cai[11], William J. John[11], Edward S. Kim[12] [1]*University of California Davis Comprehensive Cancer Center, Sacramento/CA/United States of America,* [2]*University of California at Los Angeles, Santa Monica/CA/United States of America,* [3]*Hospital Universitario Ramón Y Cajal, Madrid/Spain,*[4]*Indiana University School of Medicine, Indianapolis/IN/United States of America,* [5]*West Cancer Center, Memphis/TN/United States of America,* [6]*Medical Oncology, Hackensack University Medical Center, Hackensack/NJ/United States of America,*[7]*7Servicio de Oncología Médica, University Hospital Virgen Del Rocio, Seville/Spain,* [8]*Servicio de Oncología Médica, Hospital Puerta de Hierro, Madrid/Spain,* [9]*Highlands Oncology Group, Fayetteville/AR/United States of America,* [10]*Division of Hematology-Oncology, Dept of Internal Medicine, and the Cancer Center, University of New Mexico, Albuquerque/NM/United States of America,* [11]*Eli Lilly and Company, Indianapolis/IN/United States of America,* [12]*Levine Cancer Institute, Carolinas Healthcare System, Charlotte/NC/United States of America*

Background: Abemaciclib, a cell cycle inhibitor selective for CDK4/6, demonstrated acceptable safety and early clinical activity in metastatic NSCLC, given orally as monotherapy on a continuous schedule. Combinations of abemaciclib showed greater activity compared with monotherapy in KRAS-mutant NSCLC preclinical models. Primary aim of study NCT02079636 was safety/tolerability of combination therapy with abemaciclib; secondary aims included pharmacokinetics and antitumor activity. **Methods:** In this open-label 3+3 dose-escalation study with expansion cohorts, eligibility included stage IV NSCLC, measurable or nonmeasurable disease (RECISTv1.1), ECOG PS ≤1, and 1-3 prior therapies. Abemaciclib was combined with pemetrexed (Part A, nonsquamous, 500 mg/m^2 IV day 1), gemcitabine (Part B, 1250 mg/m^2 IV days 1 and 8), ramucirumab (Part C, 10 mg/kg IV day 1, or 8 or 10 mg/kg IV days 1 and 8) (Q21), or LY3023414 (dual PI3K-mTOR inhibitor) (Part D, 100 mg, 150 mg or 200 mg orally Q12H). In escalation, patients were dosed continuously until progression with abemaciclib at 100 mg (Part D), 150 mg or 200 mg orally Q12H. **Results:** As of February 27, 2015, 70 patients (Parts A-C) received ≥1 dose; 15 patients at 150 mg and 55 patients (including all 39 patients in expansion) at 200 mg Q12H abemaciclib. The MTD was established at 200 mg Q12H abemaciclib for Parts A-C. See Table 1 for treatment-emergent adverse events (TEAEs). Stable disease was observed in 13/23 patients in Part A; 7 unknown, 4/24 patients in Part B; 10 unknown, and 7/23 patients in Part C; 12 unknown. In Parts A-C, 18/70 (26%) patients started ≥4 cycles (Part A=9, Part B=3, Part C=6). Three confirmed PRs were observed: Part B, 1 patient with squamous histology (unknown mutation status), Part C, 1 patient with nonsquamous histology (KRAS mutation positive; EGFR mutation negative), and 1 patient with squamous histology (unknown mutation status). Updated analyses will be presented including Part D and longer term follow-up for Parts A-C through approximately June 2015. Table 1. TEAEs related to treatment (≥20% in ≥1 part)

% All grades (% Gr3/4)	Part A (n=23)	Part B (n=24)	Part C (n=23)
Diarrhea	65 (4)	50 (17)	52 (9)
Fatigue	57 (9)	63 (8)	17 (4)
Nausea	35 (0)	50 (4)	48 (9)
Neutropenia	61 (61)	50 (33)	17 (4)
Anemia	57 (26)	33 (17)	9 (0)
Thrombocytopenia	39 (9)	38 (8)	17 (13)
Decreased appetite	30 (0)	25 (0)	22 (0)
Vomiting	9 (0)	21 (0)	35 (0)
Blood creatinine increased	30 (0)	8 (0)	17 (4)
Leukopenia	30 (22)	17 (8)	9 (4)

Conclusion: Abemaciclib combined with single-agents with acceptable toxicity. Safety findings observed in Parts A and B are consistent with AEs expected when combining myelosuppressive compounds with abemaciclib, resulting in an increased myelosuppressive effect. In Part C, safety findings are consistent with those of single-agents. Tumor responses were observed in Parts B and C. **Keywords:** NSCLC, CDK4, CDK6, Cell cycle

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-086 Ceritinib in ALK+ NSCLC Metastatic to Brain and/or Leptomeninges: The ASCEND-7 Study Laura Q. Chow[1], Fabrice Barlesi[2], Erin M. Bertino[3], Dong-Wan Kim[4], Martin J. Van Den Bent[5], Heather A. Wakelee[6], Patrick Y. Wen[7], Pilar Cazorla Arratia[8], Junwu Shen[8], Fabrice Branle[9] [1]*Department of Medicine, Division of Medical Oncology, University of Washington, Seattle/WA/United States of America,* [2]*Aix Marseille University, Assistance Publique Hôpitaux de Marseille, Multidisciplinary Oncology and Therapeutic Innovations, Marseille/France,* [3]*The Ohio State University, Columbus/OH/United States of America,* [4]*Seoul National University Hospital, Seoul/Korea,* [5]*Erasmus Mc, Rotterdam/Netherlands,* [6]*Department of Medicine, Division of Oncology, Stanford University, Stanford/CA/United States of America,* [7]*Center for Neuro-Oncology, Department of Medical Oncology, Dana Farber Cancer Institute, Boston/MA/United States of America,* [8]*Novartis Pharma, East Hanover/NJ/United States of America,* [9]*Novartis Pharma Ag, Basel/Switzerland*

Background: Although the anaplastic lymphoma kinase inhibitor (ALKi), crizotinib achieves high responses in patients with ALK-rearranged (ALK+) non–small cell lung cancer (NSCLC), disease progression within 1 year can occur, with the brain/central nervous system (CNS) as a common site of progression and relapse. Ceritinib is a novel oral ALKi with 20-fold greater potency than crizotinib in enzymatic assays and crosses the blood-brain barrier with good CNS penetration in preclinical studies. In the pivotal phase 1 study (NCT01283516), ceritinib was highly active in ALK+ NSCLC patients (regardless of prior crizotinib exposure) and achieved intracranial responses in 7 of 14 patients with measurable baseline brain lesions. The adverse events profile in these patients was similar to that of the full study population. **Methods:** This international, prospective, phase 2, open-label study is designed to evaluate the antitumor activity of ceritinib in patients with ALK+ NSCLC metastatic to the brain or leptomeninges (ASCEND-7; CLDK378A2205). Eligible patients must have ALK+ (centrally assessed) NSCLC metastatic to the brain and ≥ 1 extracranial measurable lesion using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Patients must be neurologically stable ≥ 1 week prior to study drug administration and will be allocated to 1 of 5 arms depending on prior treatment:

Arms 1-4 (patients with active* brain metastases, without leptomeningeal carcinomatosis [LC])	Prior ALKi treatment	No prior ALKi treatment
Prior whole brain radiotherapy (WBRT)	Arm 1	Arm 3
No prior WBRT	Arm 2	Arm 4
Arm 5: patients with LC with or without evidence of active lesion at baseline		

*Lesion free of local treatment (stereotactic or WBRT) or lesions in unequivocal progression after radiotherapy. Oral ceritinib 750 mg/d will be dosed on a continuous schedule and study assessments are consistent across arms. The primary and key secondary objectives are to evaluate overall response rate and disease control rate, respectively. Other secondary objectives include assessment of intracranial and extracranial responses for all patients and for each of arms 1–4; overall survival and safety for all patients and for each of arms 1–5; and ceritinib pharmacokinetics in all patients. Enrollment is ongoing. **Results:** This study is in the activation phase. **Conclusion:**This study will demonstrate the efficacy of ceritinib in ALK+ NSCLC brain metastases and leptomeningeal metastases, in both WBRT-naive patients and prior irradiated patients. **Keywords:** Ceritinib, ALK, NSCLC, brain metastases

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-087 A Phase 1 Trial Combining Plinabulin and Nivolumab for Metastatic Squamous NSCLC Shihfan Yeh[1], Lyudmila Bazhenova[1], Gloria Lee[2], Lan Huang[2]
[1]*University of California, San Diego, San Diego/CA/United States of America,* [2]*Beyondspring Pharmaceuticals, Inc, New York/NY/United States of America*

Background: Plinabulin (P) is a microtubule-depolymerizing agent that inhibits tumor growth by targeting both angiogenesis and tumor vasculature as well as directly by inducing apoptosis via the Ras-JNK pathway. It also could activate anti-tumor immunity via inducing maturation of dendritic cells. Pinabulin at 30 mg/m2 given on days 1 and 8 was studied in a randomized phase 2 study in combination with docetaxel 75 mg/m2. Despite the fact that ITT overall survival (OS) was not statistically different between both arms, duration of response was notably longer in DP compared to D, 12.7 months vs 1.5 month in the 30 cohort (p=0.049). Nivolumab (Nivo) is the first PD-1 inhibitor approved by the FDA in metastatic squamous NSCLC, based on results of a phase III trial showing that patients receiving Nivo lived, on average, 3.2 months longer than patients receiving standard ChRx. Microtubule-depolymerizing agents are known to induce dendritic cell maturation and synergize with immune checkpoint inhibitors in immune competent cancer models. Therefore we hypothesize that combining plinabulin with nivolumab will enhance the immune response which will in turn lead to a higher response rate (RR) and longer OS in patients with metastatic squamous NSCLC. **Methods:** This is a phase I open-label, dose escalation study of plinabulin in combination with nivolumab (PNivo) in patients with metastatic squamous NSCLC that have progressed through one line of platinum-containing ChRx. The primary objectives are safety and tolerability of combination therapy to define the maximum tolerated dose (MTD), dose limiting toxicities (DLT) and/or RP2D for PNivo. The secondary objective is the efficacy of PNivo in terms of RR, progression free survival and OS in the expanded cohort. Plinabulin will be escalated from the biologically active dose of 13.5 mg/m2 using a "3+3" design. At the MTD or highest dose level in this study, the cohort will be expanded as applicable to ensure a total of 9 subjects are treated at the RP2D. Correlative studies to investigate pharmacodynamical effects will be performed. Main inclusion criteria are histologically documented metastatic squamous NSCLC with measurable disease, EGFR/ALK and ROS-1 negativity, ECOG status 0 to 2, preserved organ and marrow function. Main exclusion criteria are untreated brain metastases, concurrent radiation and systemic therapy within 21 days of the first dose of study drug. **Results:** not applicable **Conclusion:** not applicable **Keywords:** plinabulin, Nivolumab, squamous NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-088 *nab*-Paclitaxel + Carboplatin for Elderly Patients with Advanced NSCLC (ABOUND.70+) Corey J. Langer[1], Katayoun I. Amiri[2], Morton Coleman[3], Daniel Haggstrom[4], Katrik Konduri[5], Alexandra Sanford[2], William Skinner[6], David Smith[7], Matei Socoteanu[5], Nataliya Trunova[2], Jared Weiss[8], Edgardo Santos[9] [1]*Abramson Cancer Center, University of Pennsylvania, Philadelphia/PA/United States of America,* [2]*Celgene Corporation, Summit/NJ/United States of America,* [3]*New York Presbyterian, Weill Cornell, New York City/NY/United States of America,*[4]*Levine Cancer Institute; Carolinas Healthcare System, Charlotte/NC/United States of America,* [5]*Usoncology Research, Houston/TX/United States of America,* [6]*Paducah Cancer and Blood Center, Paducah/KY/United States of America,* [7]*Compass Oncology, Vancouver/WA/United States of America,* [8]*Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill/NC/United States of America,* [9]*Thoracic and Head and Neck Cancer Programs, Eugene M. & Christine E. Lynn Cancer Institute, Florida Atlantic University, Boca Raton, Fl, Boca Raton/FL/United States of America*

Background: Treatment of elderly patients with non-small cell lung cancer (NSCLC) is challenging due to comorbidities and reduced tolerability; as a result, these patients often receive suboptimal treatment. In addition, 5-year survival rates are lower in elderly than in younger patients with NSCLC. In a multicenter phase III trial, first-line treatment with *nab*-paclitaxel plus carboplatin (*nab*-P/C) significantly increased median overall survival (OS) vs solvent-based paclitaxel plus C in a subset of patients ≥ 70 years of age with advanced NSCLC (19.9 vs 10.4 months; HR 0.583; $P = 0.009$; Socinski et al. *Ann Oncol*. 2013;24:314-321). However, 55% of elderly patients treated with *nab*-P/C required dose reductions and 84% had dose delays, primarily due to adverse events, including myelosuppression. In the open-label, multicenter phase IV ABOUND.70+ trial, the safety and efficacy of 2 different schedules of first-line *nab*-P/C treatment will be evaluated prospectively in elderly patients with advanced NSCLC. **Methods:** Approximately 284 patients with NSCLC ≥ 70 years of age who are not candidates for curative surgery or radiation therapy will be randomized 1:1 to *nab*-P 100 mg/m^2 intravenously (IV; 30-minute infusion) on days 1, 8, and 15 plus C AUC 6 on day 1 every 21 days or the same *nab*-P/C dose every 21 days followed by a 1-week break. Key eligibility criteria include histologically/cytologically confirmed locally advanced or metastatic NSCLC, no prior chemotherapy for metastatic disease, ECOG performance status ≤ 1, adequate organ function, no active brain metastases, and absence of preexisting peripheral neuropathy (PN) grade > 2. Patients will be stratified by ECOG performance status (0 vs 1) and histology (squamous vs nonsquamous). ClinicalTrials.gov identifier NCT02151149.

Key Endpoints	
Primary	• Percentage of patients developing either PN grade ≥ 2 or myelosuppression grade ≥ 3
Secondary	• Safety • Progression-free survival • OS • Overall response rate
Exploratorya	• Healthcare resource utilization throughout the study • Changes in quality of life

a Additional exploratory endpoints may be defined in the statistical analysis plan if applicable. **Results:** TPS Abstract Section NA **Conclusion:** TPS Abstract Section NA **Keywords:** elderly, nab-Paclitaxel,, carboplatin, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-089 A Phase 1b/2 Randomized Study of PEGPH20 in Combination with Docetaxel in Hyaluronan High NSCLC Patients Treated with Platinum Chemotherapy Chandra P. Belani[1], Steve Shuey[2], Deborah Carson[2], Xionghua Wu[2], Athena Countouriotis[2] [1]*Penn State Milton S. Hershey Medical Center, Hershey/PA/United States of America,* [2]*Halozyme Therapeutics, San Diego/CA/United States of America*

Background: Patients with advanced non-small cell lung cancer (NSCLC) progressing after 1st line platinum containing doublet chemotherapy +/- targeted therapy for EGFR mutations and EML4-ALK fusion genes have limited therapeutic options. Extracellular components such as hyaluronan (HA) make up the tumor microenvironment (TME) and may limit access of chemotherapeutic agents to the cell as a result of increased interstitial pressure and decreased blood flow. PEGPH20 (PEG) decreases HA and restores blood flow. In animal models of NSCLC, PEG + docetaxel (Doc) significantly prolonged survival compared to Doc alone. These results are consistent with results in previous studies in pancreatic adenocarcinoma (PDA). In a Phase 1b trial of the combination of PEG + gemcitabine in Stage IV pts with PDA whose tumors were HA-high pts had higher ORR, PFS and OS compared to pts with HA-low tumors. **Methods:** This is an ongoing Phase 1b/2 open-label, randomized study of the addition of PEG to docetaxel (PDoc) compared to docetaxel (Doc) in pts with Stage IIIB/IV NSCLC having been treated with at least 1st line platinum containing chemotherapy. The Phase 1b portion of the study will determine the maximum tolerated dose (MTD), dose limiting toxicity and recommended Phase 2 dose for two schedules of PEG; one given every 21 days with Doc and the second dosed 2X per week with Doc. Up to 40 subjects are expected to be enrolled in the Phase 1b dose escalation. Once MTDs are determined the second portion of the Phase 1b will accrue approximately 10 patients whose tumors are HA-high to determine which schedule will go forward in Phase 2. The Phase 2 will randomize 188 patients in a 1:1 fashion to receive PDoc or Doc stratified by histology and prior targeted therapy. The primary endpoint of the Phase 2 portion is PFS. This is the first clinical trial evaluating PEGPH20 in NSCLC. The trial is currently accruing to the dose finding portion of the Phase 1b. ClinicalTrials.gov Identifier: NCT02346370 **Results:** not applicable **Conclusion:** not applicable **Keywords:** NSCLC, PEGPH20, hyaluronan, TME

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-090 A Phase 2, Single Arm Study of Lucitanib in Patients with Advanced/Metastatic Lung Cancer and FGF, VEGF, or PDGF-Related Genetic Changes David R. Spigel[1], Enriqueta Felip[2], Silvia Novello[3], Marina C. Garassino[4], Melanie Collins[5], Jason B. Litten[5], Andrew R. Allen[5], Roberta Cereda[6], Taofeek K. Owonikoko[7], Mark A. Socinski[8], Ross Camidge[9], Benjamin Besse[10] [1]*Sarah Cannon Research Institute/Tennessee Oncology, Pllc, Nashville/TN/United States of America,* [2]*Vall D'Hebron University Hospital and Vall D'Hebron Institute of Oncology (Vhio), Barcelona/Spain,* [3]*Department of Oncology, University of Turin, Aou San Luigi, Orbassano/Italy,* [4]*Fondazione Irccs Istituto Nazionale Dei Tumori, Milano/Italy,* [5]*Clovis Oncology, San Francisco/CA/United States of America,* [6]*Clovis Oncology, Milano/Italy,* [7]*Winship Cancer Institute of Emory University, Atlanta/United States of America,* [8]*University of Pittsburgh Cancer Insitute, Pittsburgh/PA/United States*

of America, [9]Medical Oncology, University of Colorado, Denver/CO/United States of America, [10]Institut Gustave Roussy, Villejuif/France

Background: Lucitanib is a potent, oral inhibitor of the tyrosine kinase activity of Fibroblast Growth Factor Receptors 1-3 (FGFR1-3), Vascular Endothelial Growth Factor Receptors 1-3 (VEGFR1-3) and Platelet-Derived Growth Factor Receptors A/B (PDGFRA/B). Clinical activity was observed in a phase 1/2 study of lucitanib monotherapy in cancer patients with tumor amplification of FGF-related genes or in tumors with predicted sensitivity to VEGF inhibitors. Genomic evidence of FGF, VEGF or PDGF axis aberrancy is seen in up to 15% of patients with lung cancer, which provides a strong rationale to assess lucitanib in this setting. **Methods:** The current study evaluates daily oral lucitanib monotherapy in 40 patients with amplification or activating mutations in FGF, VEGF or PDGF-related genes. This is an international, multicenter, open-label, single-arm study. The primary endpoint is objective response rate (ORR; RECIST 1.1) with secondary endpoints of response duration, clinical benefit rate, progression-free survival, and safety. Exploratory objectives include volumetric assessment of tumor growth kinetics, serial circulating tumor DNA measurement, and identification of additional biomarkers of lucitanib activity. Key inclusion criteria include: patients with advanced/metastatic non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC) or large cell lung cancer and tumor tissue evidence of relevant genomic aberrancies. Patients must have measurable disease and at least one previous treatment for advanced disease. Key exclusion criteria include: carcinoid histology, symptomatic CNS metastases, anti-cancer treatment for lung cancer within 28 days or 5 half-lives before first dose of lucitanib. This study is enrolling patients in the United States and Europe at centers skilled in the identification of patients with relatively uncommon genetic tumor alterations. **Results:** not applicable **Conclusion:** not applicable
Keywords: SCLC, FGFR1, VEGF, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-091 Multicenter, Randomized, Double-Blind Study of Erlotinib plus Ramucirumab or Placebo in Patients with EGFR Mutation-Positive Metastatic NSCLC Edward B. Garon[1], Martin Reck[2], Oscar J. Vidal[3], Ernest Nadal[4], Pablo Lee[5], Rita Dalal[5], Jingyi Liu[6], Shuang He[6], Joseph Treat[6], Kazuhiko Nakagawa[7] [1]*UCLA Medical Center, Santa Monica/CA/United States of America, [2]Lungen Clinic Grosshansdorf, Grosshansdorf/Germany, [3]Hospital Universitario La Fe, Valencia/Spain, [4]Institut Catala D'Oncologia, L'Hospitalet, Barcelona/Spain, [5]Eli Lilly and Company, Bridgewater/NJ/United States of America, [6]Eli Lilly and Company, Indianapolis/IN/United States of America, [7]Kinki University School of Medicine, Osaka/Japan*

Background: Ramucirumab, a human IgG1 monoclonal antibody, binds to Vascular Endothelial Growth Factor (VEGF) Receptor 2, preventing binding of VEGF-A, C and D. Ramucirumab in combination with docetaxel has demonstrated improvement in overall survival, progression free survival (PFS), objective response rate and disease control rate in 2nd line treatment of NSCLC patients in the phase III REVEL study, which included non-squamous and squamous cell carcinoma patients. Although erlotinib is recognized as one of the standard of care options in the frontline treatment of patients whose tumors harbor an Epidermal Growth Factor Receptor (EGFR) mutation, it is hypothesized that the duration of disease control would be greater when an antiangiogenic agent such as ramucirumab is added to erlotinib. This global phase Ib/III trial will assess safety, tolerability and efficacy (phase III) of the combination of ramucirumab with erlotinib in previously untreated stage IV NSCLC patients harboring activating EGFR mutations. The trial is planned to be conducted in ~120 sites in the Americas, Europe, and Asia and is currently open for enrollment. (RELAY, NCT02411448) **Methods:** In part A (phase Ib) approximately 12 patients (6 Japan + 6 US/EU) will receive ramucirumab (10mg/kg on day 1) every two weeks + erlotinib (150 mg/day). DLT assessment will be performed after patients complete four weeks of treatment. In part B (phase III), approximately 450 patients will be randomized in a 1:1 ratio to receive ramucirumab or placebo every two weeks with erlotinib until disease progression, unacceptable toxicity, or other withdrawal criteria are met. The primary endpoint is PFS. There are 3 planned interim analyses that will evaluate safety, futility and efficacy, respectively. Other secondary endpoints include overall survival, objective response rate, disease control rate, duration of response, safety and quality of life. **Results:** Not applicable **Conclusion:** Not applicable
Keywords: treatment, EGFR, antiangiogenic, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-092 A Phase IB Dose-Escalation Study of Pemetrexed and AUY922 in Previously Treated Metastatic Non-Squamous, Non-Small Cell Lung Cancer Edward B. Garon[1], James Sanchez[2], Brian A. Dicarlo[3], John L. Barstis[1], Mark Hancock[4], Eddie H.-L. Hu[1], Fairooz F. Kabbinavar[1], Brad Adams[1], Diego A. Martinez[1], Naeimeh Kamranpour[1], Kevin Chau[1], Phillip Abarca[1], Mary Han[1], Marshall L. Spiegel[1], Brian Wolf[1], Isett Laux[1], Meghan B. Brennan[1], Jonathan W. Goldman[5] [1]*David Geffen School of Medicine at University of California, Los Angeles/Translational Research in Oncology-Us Network, Santa Monica/CA/United States of America, [2]Comp Cancer Ctrs of Nevada, Las Vegas/NV/United States of America,[3]Coastal Integrative Cancer Care, San Luis Obispo/CA/United States of America, [4]St. Mary'S Hospital & Regional Medical Center, Grand Junction/CO/United States of America, [5]School of Medicine of California, Los Angeles/AL/United States of America*

Background: Despite advances in targeted therapy, treatment options for metastatic NSCLC progressing after initial therapy remains limited. HSP90 is an ATP-dependent molecular chaperone that plays a vital role in protein stabilization. Some HSP90 client proteins are key regulators in cell proliferation and survival. Many mutant oncoproteins are more dependent on HSP90 for proper folding and stability compared to their wildtype counterparts. AUY922 potently inhibits HSP90, showing preclinical activity in a wide range of cancer cell lines, including NSCLC (1). Phase I clinical trials established 70 mg/m^2 as the dose for further development (2). A single agent phase II trial demonstrated clinical activity of AUY922 in NSCLC, particularly molecular subsets with driver mutations in the known HSP90 client proteins, epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) (3). Pemetrexed is a folate antimetabolite chemotherapeutic approved for use in advanced non-squamous, NSCLC. In pre-clinical models, mRNA for dihydrofolate reductase (DHFR), a target of pemetrexed, reliably decreased in response to AUY922 exposure (1). These findings suggest that the combination of AUY922 and premetrexed in NSCLC is worthy of investigation. **Methods:** Adult patients with previously treated stage IV non-squamous, NSCLC, measureable disease per RECIST 1.1, ECOG performance status $\leq$ 2, and life expectancy > 3 months are eligible for this open label phase Ib clinical trial (NCT01784640). A standard 3 x 3 design will evaluate 3 cohorts, all with pemetrexed at the standard 500 mg/m^2 dose, plus: AUY922 40 mg/m^2, 55 mg/m^2, and 70 mg/m^2 qwk. Enrollment of the 70 mg/m^2 qwk cohort has been open since November 2014 and is currently ongoing. After the optimal dose for further evaluation is determined, an additional 20 patients will be enrolled at that dose. This expansion phase will focus on patients with EGFR mutations and ALK gene rearrangements. The primary endpoint is safety and tolerability of AUY922 combined with pemetrexed in patients with previously treated non-squamous NSCLC. [Funding by Novartis, K23CA149079, Wolfen Family, One Ball Matt Memorial Golf Tournament]. **References** 1) Garon EB et. al. Mol Cancer Ther. 2013 2) Sessa C et. al. Clin Cancer Res. 2013 3) Garon EB et. al. ASCO 2012 **Results:** Not applicable **Conclusion:** Not applicable
Keywords: NSCLC, AUY922, HSP90, pemetrexed

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-093 A Phase III Study of Radiosurgery with TTFields for 1-10 Brain Metastases from NSCLC Minesh P. Mehta[1], Vinai Gondi[2], Paul D. Brown[3] [1]*University of Maryland Medical Center, Baltimore/MD/United States of America, [2]Cadence Health Brain Tumor Center and Cadence Health Proton Center, Chicago/United States of America, [3]MD Anderson Cancer Center, Huston/TX/United States of America*

Background: Tumor Treating Fields (TTFields) are a novel, non-invasive regional anti-mitotic treatment modality, based on low intensity alternating electric fields. Efficacy of TTFields in non-small cell lung cancer (NSCLC) has been demonstrated in multiple *in vitro* and *in vivo* models, and in a phase I/II clinical study. TTFields treatment to the brain was shown to be safe and effective in glioblastoma patients. Local treatment options for patient with brain metastases (BM) are limited to neuro-surgery (NS), stereotactic radiosurgery (SRS) or whole brain radiotherapy (WBRT) or a combination thereof. In patients treated with NS or SRS, intracranial recurrence remains high, since the rest of the brain is not treated. The addition of WBRT, can improve intracranial control either alone or when added to SRS but at the risk of severe neurocognitive and other complications. Thus, new therapeutic options are needed, particularly ones that allow for greater intracranial control while minimizing the risk of neurocognitive and other adverse events. **Methods: The METIS Clinical Trial** 240 patients with 1-10 BM from NSCLC will be randomized in a ratio of 1:1 to receive SRS followed by either TTFields or supportive care alone. Patients are followed-up bimonthly until 2nd intracerebral progression. Patients in the control arm may cross over to receive TTFields at the time of 1st intracerebral progression. **Objectives** To test the efficacy, safety and neurocognitive outcomes of TTFields in this patient population. **Endpoints** Time to intracerebral progression (primary); time to first/second intracerebral progression for patients with 1-4 and 5-10 BM; 2, 4, 6, 8, 10, 12-month first/second intracerebral progression rate; intracerebral progression free survival; overall survival; time to neurocognitive failure; rate of decline in cognitive function; neurocognitive failure-free survival; radiological response; safety (secondary). **Treatment** Continuous TTFields at 150 kHz will be applied to the brain using the NovoTTF-100M System within 7 days of SRS. The System is a portable medical device allowing normal daily life activities. The device delivers alternating electric fields to the brain using 4 Transducer Arrays, which may be covered by a wig or a hat for cosmetic reasons. Patients will receive the best standard of care for their systemic disease. **Statistical Considerations** This is a prospective, randomized, multicenter study for 240 patients. The trial is designed to detect an increase in the time to intracerebral progression from 7.7 to 13.4 months (hazard ratio 0.57). This sample size assessment takes into consideration a competing risk (death prior to intracerebral progression) of 0.08252 per month in both treatment arms. The competing risk is based on a predicted median overall survival of 8.4 months mainly due to systemic disease progression. The trial has 80% power at a two sided alpha of 0.05. The sample size was calculated using a log-rank test (based on Lakatos 1988 and 2002) with the competing risk taken as loss to follow up (patients will be censored at time of death if it occurs prior to intracerebral progression). **Results:** not applicable **Conclusion:** not applicable
Keywords: Tumor Treating Fields, brain metastases, Stereotactic Radiosurgery, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-094 Phase II Trial of Tepotinib/Gefitinib vs Cisplatin/Pemetrexed in T790M-/c-Met+ NSCLC Yi-Long Wu[1], Keunchil Park[2], Dong-Wan Kim[3], Ross Soo[4], Uz Stammberger[5], Huiiling Xiong[6], Christian Ihling[5], James Chih-Hsin Yang[7] [1]*Guangdong Lung Cancer Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou/China, [2]Innovative Cancer Medicine Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/Korea, [3]Department of Internal Medicine, Seoul National University Hospital, Seoul/Korea, [4]National University Cancer Institute Singapore, National University Health System, Singapore/Singapore, [5]Merck Kgaa, Darmstadt/Germany,[6]Merck Serono Pharmaceutical R&D Co., Ltd, Beijing/China, [7]National Taiwan University, Graduate Institute of Oncology, Taipei/Taiwan*

Background: The recommended phase II dose of the highly selective c-Met inhibitor tepotinib (MSC2156119J) for use in combination with gefitinib was confirmed as 500 mg/day in the phase Ib part of the current trial, in which patients with gefitinib-resistant locally advanced/metastatic c-Met-positive NSCLC were treated with tepotinib plus gefitinib. This trial demonstrated that the combination regimen is well tolerated and has evidence of antitumor activity that may be associated with c-Met-positive tumor status. These observations suggest that c-Met inhibition may have a role in EGFR tyrosine kinase inhibitor-resistant NSCLC and that a phase II trial is warranted. **Methods:** The design of the phase II part of a phase Ib/II trial (NCT01982955) is described. Asian adults with histologically or cytologically confirmed, gefitinib-resistant locally advanced/metastatic NSCLC other than predominantly squamous histology and ECOG PS 0/1 are eligible. Patients must have tumors with documented activating mutations of EGFR. Tumor tissue obtained between documentation of acquired resistance to gefitinib and enrollment must be available. Tumors must be confirmed as being c-Met positive (2+/3+ c-Met protein overexpression by immunohistochemistry using CONFIRM anti-total c-MET [SP44] rabbit MAb [Ventana] or c-Met gene amplification on IQ FISH [Dako] [c-Met:CEP7 ratio ≥2 or <2.0 with >15 c-Met signals/cell in >10% of cells or clusters in >10% of tumor cell nuclei]). EGFR mutation status will be assessed centrally using the therascreen® EGFR RGQ PCR Kit (QIAGEN). Patients will be enrolled into different parts of the trial based on tumor T790M status. Patients with c-Met-positive, T790M-negative NSCLC (n=136) will be randomized to tepotinib 500 mg/day p.o. + gefitinib 250 mg/day q3w or cisplatin 75 mg/m^2 + pemetrexed 500 mg/m^2 q3w for up to 6 cycles. Patients with c-Met-positive, T790M-positive NSCLC (n=15) will be treated with tepotinib 500 mg/day p.o. + gefitinib 250 mg/day q3w. The primary objective is to determine whether progression-free survival (PFS) in patients treated with second-line tepotinib combined with gefitinib is superior to that of pemetrexed + cisplatin in patients with c-Met-positive, T790M-negative advanced NSCLC and acquired resistance to first-line gefitinib. The two T790M subgroups will be analyzed separately. An interim analysis of the randomized part of the study is planned when 50% of PFS events have occurred in both arms. Secondary objectives are to evaluate: the safety and tolerability tepotinib combined with gefitinib; the efficacy of tepotinib combined with gefitinib; the antitumor activity of tepotinib combined with gefitinib in patients with c-Met-positive, T790M-positive tumors; and patient-reported outcomes. **Results:** not applicable **Conclusion:** This randomized phase II trial will provide the first evidence regarding whether tepotinib has a role in the treatment of Asian patients with gefitinib-resistant, c-Met-positive, T790M-negative NSCLC. **Keywords:** MSC2156119J, phase II, c-Met, tepotinib

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-095 *nab*-Paclitaxel/Carboplatin Followed By *nab*-Paclitaxel for NSCLC PS 2 (ABOUND.PS2) Ajeet Gajra[1], Mark A. Socinski[2], Haythem Ali[3], Katayoun I. Amiri[4], Nagla Abdel Karim[5], Eric Kim[6], Marc R. Matrana[7], Alexandra Sanford[4], Nataliya Trunova[4], David R. Spigel[8] [1]*Upstate Medical University, Upstate Cancer Center, Syracuse/NY/United States of America,* [2]*University of Pittsburgh, Pittsburgh/PA/United States of America,* [3]*Henry Ford Health System, Detroit/MI/United States of America,* [4]*Celgene Corporation, Summit/NJ/United States of America,* [5]*Medicine-Division of Hematology/Oncology, The University of Cincinnati, Oh/OH/United States of America,* [6]*University of Rochester Medical Center, Wilmott Cancer Institute, Rochester/NY/United States of America,* [7]*Ochsner Medical Center, New Orleans/NY/United States of America,* [8]*Sarah Cannon Research Institute/Tennessee Oncology, Pllc, Nashville/TN/United States of America*

Background: Many patients with advanced non-small cell lung cancer (NSCLC) often present with poor performance status (PS), and there is no clear consensus on how best to treat these patients. Despite an increased risk of toxicity resulting from standard chemotherapy, patients with NSCLC and a poor PS can clinically benefit from platinum-doublet therapy. In a multicenter phase III trial, first-line treatment with *nab*-paclitaxel plus carboplatin (*nab*-P/C) in patients with NSCLC and an ECOG PS 0-1 significantly improved the overall response rate (ORR) compared with solvent-based paclitaxel plus C (33% vs 25%; *P* = 0.005; Socinski et al. *J Clin Oncol*. 2012;30:2055-2062). In the single-arm, open-label, multicenter phase II ABOUND.PS2 study, the safety and efficacy of first-line *nab*-P/C followed by *nab*-P monotherapy will be evaluated in patients with locally advanced/metastatic NSCLC and an ECOG PS of 2. **Methods:** During the induction part of the study, approximately 50 patients will be treated with 4 cycles of *nab*-P 100 mg/m^2 intravenously (IV; 30-minute infusion) on days 1 and 8 plus C AUC 5 IV on day 1 every 21 days. Patients without disease progression may proceed to the monotherapy part of the study in which they will continue to receive *nab*-P 100 mg/m^2 IV (30-minute infusion) on days 1 and 8 every 21 days until progression or unacceptable toxicity. Key eligibility criteria include histologically/cytologically confirmed stage IIIB/IV NSCLC, no prior chemotherapy for metastatic disease, ECOG PS of 2, adequate organ function, no active brain metastases, and preexisting peripheral neuropathy grade < 2. ClinicalTrials.gov number NCT02289456.

Key Endpoints	
Primary	• The percentage of patients who discontinue treatment during the induction part due to treatment-emergent adverse events
Secondary	• Safety • Progression-free survival • Disease control rate • Overall survival • ORR
Exploratory	• Healthcare resource utilization throughout the study • Changes in physician-reported ECOG PS and patient-reported quality of life • Summary of Charlson Co-Morbidity Index at baseline • Correlation between patient- and physician-reported ECOG PS during treatment • Correlation between patient- and physician-reported Karnofsky PS at baseline

Results: This is a TPS abstract Results = NA **Conclusion:** This is a TPS abstract Results = NA **Keywords:** PS2, nab-paclitaxel, NSCLC, carboplatin

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-096 Randomized, Double-Blind, Placebo-Controlled Trial of Evofosfamide (TH-302) in Combination with Pemetrexed in Advanced ns-NSCLC Jonathan W. Goldman[1], Charles Bennett[2], Corey Carter[3], Tudor Ciuleanu[4], Morton Coleman[5], Tibor Csoszi[6], Filippo De Marinis[7], Ramon Garcia Gomez[8], Maciej Krakowski[9], Julian Molina[10], Silvia Novello[11], Sergei Orlov[12], Gyula Ostoros[13], Robert Palmer[2], Francisco Robert[14], Philip Stella[15], Joachim Von Pawel[16], Tillman Pearce[17], Stew Kroll[17], Chandra P. Belani[18] [1]*Oncology, UCLA Hematology/Oncology-Santa Monica, Santa Monica/CA/United States of America,* [2]*Oncology, Wm Jennings Bryan Dorn Va Med Ctr, Columbia/SC/United States of America,* [3]*Oncology, Walter Reed National Military Med Ctr, Bethesda/MD/United States of America,* [4]*Radiotherapy, "Prof. Dr. Ion Chiricuta" Institute of Oncology, Cluj-Napoca/Romania,* [5]*Oncology, Clinical Research Alliance, Inc., New York/AL/United States of America,* [6]*Department of Oncology, Hetenyi G Korhaz, Onkologiai Kozpont, Szolnok/Hungary,* [7]*European Institute of Oncology, Milan/Italy,* [8]*Department of Oncology, General University Hospital Gregorio Maranon, Madrid/Spain,* [9]*Oncology, Maria Sklodowska-Curie Institute of Oncology, Warsaw/Poland,* [10]*Oncology, Mayo Clinic in Rochester, Rochester/MN/United States of America,* [11]*Department of Oncology, University of Turin, Aou San Luigi (Orbassano), Italy, Orbassano/Italy,* [12]*Oncology, First Pavlov State Medical University of St. Peterburg, St. Petersburg/Russian Federation,* [13]*8Th Dept. of Pulmonology, Koranyi National Institute of Tbc and Pulmonology, Budapest/Hungary,* [14]*Oncology, U. Alabama-Birmingham, Birmingham/AL/United States of America,* [15]*Oncology, St. Joseph Mercy Ann Arbor Hospital, Ann Arbor/MI/United States of America,* [16]*Asklepios Fachkliniken München-Gauting, Gauting/Germany,* [17]*Clinical, Threshold Pharmaceutical, Inc., South San Francisco/CA/United States of America,* [18]*Penn State Hershey Cancer Institute, Hershey/PA/United States of America*

Background: Tumor hypoxia is associated with chemo- and radioresistance and is a prevalent characteristic in tumors of patients with non-small cell lung cancer (NSCLC). Evofosfamide (previously known as TH-302) is a hypoxia-activated prodrug designed to release the bis-alkylating DNA crosslinker bromo-isophosphoramide mustard (Br-IPM) when reduced in severe hypoxia. In a Phase 1/2 study (NCT00743379) that included a single arm evofosfamide in combination with pemetrexed in 18 patients with relapsed/refractory non-squamous NSCLC, median PFS was 7.0 months and median OS was 14.9 months. Response in 15 evaluable patients: 6 partial responses (4 confirmed), 6 stable disease and 3 progressive disease. The most common adverse events were fatigue, anemia, stomatitis and nausea. **Methods:** An international, multicenter, randomized, double-blind, placebo-controlled trial was initiated to evaluate evofosfamide in combination with pemetrexed versus placebo and pemetrexed as a potential second-line treatment for patients with non-squamous NSCLC (NCT02093962). Approximately 440 patients will be enrolled with histologically confirmed stage IIIB or IV NSCLC with non-squamous histology, measurable disease according to RECIST 1.1, and ECOG performance status 0-1. Eligible patients have recurrent or progressive disease after one prior platinum-based non-pemetrexed chemotherapy treatment for advanced disease with or without maintenance. EGFR-activating and ALK rearrangements status must be known, and if identified, patients must have received a targeted kinase inhibitor. Evofosfamide (400 mg/m^2) or matched placebo is administered by IV infusion over 30 - 60 minutes on Day 1 and Day 8 of a 21-day cycle. Pemetrexed (500 mg/m^2) is administered by IV infusion 2 to 4 hours after evofosfamide administration on Day 1. Overall survival (OS) is the primary endpoint; secondary endpoints include safety, progression-free survival and RECIST response rate. The study design has 85% power to detect a 40% improvement in OS with a one-sided alpha of 0.025. The first patient was enrolled in June 2014; recruitment is ongoing. **Results:** not applicable **Conclusion:** not applicable **Keywords:** Phase 2/3, Hypoxia, microenvironment

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-097 Phase 3 Study of Pembrolizumab vs Platinum-Based Chemotherapy for PD-L1+ NSCLC Tony Mok[1], Yi-Long Wu[2], Sara Sadowski[3], Jin Zhang[3], Reshma Rangwala[3], Gilberto De Lima Lopes[4] [1]*Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong/Hong Kong,* [2]*Guangdong Lung Cancer Institute, Guangdong General Hospital, Guagnzhou/China,* [3]*Merck & Co., Inc., Kenilworth/NJ/United States of America,*[4]*Centro Paulista de Oncologia E Hcor Onco, Members of the Oncoclínicas Do Brasil Group, São Paulo/Brazil*

Background: Platinum-based chemotherapy with or without maintenance therapy is the standard of care for treatment-naive non-small cell lung carcinoma (NSCLC) that lacks *EGFR* sensitizing mutations and *ALK* translocations. The PD-1 pathway is frequently used by tumors to evade an immune response. Pembrolizumab (MK-3475), an anti–PD-1 monoclonal antibody, has demonstrated manageable toxicity and promising antitumor activity in patients with treatment-naive NSCLC enrolled in the phase 1b KEYNOTE-001 study. In this study, a relationship between increased tumor PD-L1 expression and improved pembrolizumab antitumor activity was observed. KEYNOTE-042 (ClinicalTrials.gov identifier NCT02220894) is a randomized, open-label, international, phase 3 study designed to compare the efficacy and safety of pembrolizumab with those of platinum-doublet chemotherapy as first-line therapy for PD-L1–positive advanced NSCLC. **Methods:** Eligibility criteria include age ≥18 years, advanced NSCLC without *EGFR* sensitizing mutations or *ALK* translocation, no prior systemic chemotherapy, PD-L1 expression in ≥1% of tumor cells, and Eastern Cooperative Oncology Group performance status (ECOG PS) 0-1. Patients are randomly assigned in a 1:1 ratio to a 200-mg fixed dose of pembrolizumab every 3 weeks (Q3W) or investigator's choice of carboplatin AUC 5 or 6 plus paclitaxel 200 mg/m^2 Q3W or carboplatin AUC 5 or 6 plus pemetrexed 500 mg/m^2 Q3W. Randomization is stratified by ECOG PS (0 vs 1), histology (squamous vs nonsquamous), region (East Asia vs non-East Asia), and PD-L1 expression (strong [staining in ≥50% of tumor cells] vs weak [staining in 1%-49% of tumor cells], as assessed by immunohistochemistry at a central laboratory). Pembrolizumab will be continued for 35 cycles or until disease progression, intolerable toxicity, or investigator decision; treatment may be continued beyond initial radiographic disease progression in eligible patients. Discontinuation of pembrolizumab is permitted for patients who experience a complete response confirmed on a follow-up scan performed ≥4 weeks after initial observation. Chemotherapy will be given for a maximum of 6 cycles and may be followed by optional pemetrexed 500 mg/m^2 Q3W maintenance therapy in patients with nonsquamous histology. Adverse events will be collected throughout the study and for 30 days (90 days for serious adverse events) thereafter and graded per NCI CTCAE v4.0. Response will be assessed every 9 weeks per RECIST v1.1 by independent central review. Patients will be followed for survival every 2 months. Primary end point is overall survival in the PD-L1–strong-positive stratum; secondary end points are progression-free survival in the strong-positive stratum and progression-free and overall survival in all patients. Enrollment is ongoing and will continue until approximately 1240 patients have been allocated to study treatment. **Results:** Not applicable. **Conclusion:** Not applicable. **Keywords:** pembrolizumab

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-098 Addition of Custirsen, a Clusterin Inhibitor, to Docetaxel in Stage IV Non-Small Cell Lung Cancer (NSCLC): The ENSPIRIT™ Phase 3 Trial Joachim Von Pawel[1], Kirsten Anderson[2], Cindy Jacobs[3] [1]*Pneumology, Asklepios Fachkliniken, Gauting/Germany,* [2]*Clinical Operations, Oncogenex Pharmaceuticals, Inc., Bothell/WA/United States of America,* [3]*Clinical Development, Oncogenex Pharmaceuticals, Inc., Bothell/WA/United States of America*

Background: Treatments that improve overall survival (OS) in advanced NSCLC are urgently needed. Docetaxel (DOC) is recommended as 2nd-line chemotherapy for advanced NSCLC, with a median OS of 7-8 months. The chaperone protein clusterin (CLU) is upregulated in NSCLC and other cancers in response to anticancer therapies. Custirsen (OGX-011) is a second-generation antisense oligonucleotide that inhibits CLU expression, enhances chemotherapeutic activity, and in vivo has reversed DOC resistance. In early phase studies in metastatic castration resistant prostate cancer (mCRPC), custirsen plus DOC was well tolerated and showed encouraging results. In a phase 3 mCRPC study (SYNERGY), 50% of patients defined as poor prognosis had survival benefit from custirsen when added to 1st-line DOC. **Methods:** ENSPIRIT was initiated September 2012. Eligible patients in this phase 3, multinational, open-label trial have failed 1 prior line of platinum (PT)-based therapy, have an ECOG of 0-1, and adequate bone marrow, renal, and liver function. Randomization is 1:1, with stratification by gender, NSCLC histology, best response to 1st-line PT therapy (response/stable disease vs progression), and ECOG score. Patients receive 21-day cycles of DOC (75 mg/m^2 IV day 1) or DOC plus custirsen (640 mg IV/wk, preceded by 3 doses during a 9-day loading period) until progressive disease, unacceptable toxicity, or withdrawal. The primary efficacy measure is OS. Two interim analyses are planned for stopping the trial based on inadequate evidence of clinical benefit or futility; the first futility analysis was completed in August 2014. A recent amendment changed the hypothesized hazard ratio for the primary analysis from 0.80 to 0.75 (power remains at 90%), resulting in a required sample size of 700 patients (instead of original 1100). In addition, the second futility has a more rigorous criterion for stopping due to survival futility and is to occur earlier than originally planned. The study will not be stopped early for efficacy. The aim of the ENSPIRIT amendment is to assess for a more clinically relevant survival benefit when adding custirsen to 2nd-line DOC or terminate the trial early for survival futility. **Results:** Not applicable. **Conclusion:** Not applicable. **Keywords:** custirsen, clusterin, docetaxel, survival

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-099 nab-Paclitaxel as Maintenance Therapy in Patients with Squamous Cell NSCLC (ABOUND.sqm) David R. Spigel[1], Cesare Gridelli[2], Robert Jotte[3], Edward S. Kim[4], Amy Ko[5], Teng Jin Ong[5], Robert Pirker[6], Michael Thomas[7], Nataliya Trunova[5], Howard West[8], Craig H. Reynolds[9] [1]*Sarah Cannon Research Institute, Nashville/TN/United States of America,* [2]*S.G. Moscati Hospital, Avellino/Italy,* [3]*Rocky Mountain Cancer Centers, Denver/CO/United States of America,* [4]*Levine Cancer Institute--Morehead, Carolinas Healthcare System, Charlotte/NC/United States of America,* [5]*Celgene Corporation, Summit/NJ/United States of America,* [6]*Department of Medicine I, Medical University of Vienna, Vienna/Austria,* [7]*Thoraxklinik at Heidelberg University, Heidelberg/Germany,*[8]*Swedish Cancer Institute, Seattle/WA/United States of America,* [9]*Ocala Oncology Center, Ocala/FL/United States of America*

Background: Patients with squamous cell (SCC) non-small cell lung cancer (NSCLC) may be at risk of poorer outcomes and have fewer treatment options than those with other histologies. Furthermore, no randomized studies have demonstrated the benefit of maintenance therapy in these patients. In a phase III trial, first-line treatment with *nab*-paclitaxel plus carboplatin (*nab*-P/C) demonstrated a 68% improvement in the overall response rate (ORR; 41% vs 24%; $P < 0.001$) and a trend toward improved overall survival (OS; median, 10.7 vs 9.5 months; HR 0.890; $P = 0.310$) compared with solvent-based paclitaxel plus C in a subset of patients with advanced SCC NSCLC (Socinski et al. *Ann Oncol.* 2013;24:2390-2396). An exploratory analysis of the phase III trial demonstrated that therapy with *nab*-P/C beyond 4 cycles of first-line treatment was effective in the subset of patients with SCC NSCLC who did not progress (from the time of randomization, median progression-free survival [PFS] and OS were 6.8 and 13.8 months, respectively), and no new safety signals were noted (Socinski et al. IASLC 2013 [abstract 3438]). In the open-label, multicenter phase III ABOUND.sqm trial, the efficacy and safety of *nab*-P maintenance therapy after *nab*-P/C induction therapy will be evaluated in patients with advanced SCC NSCLC. **Methods:** During the induction part of the study, approximately 540 patients will be treated with 4 cycles of *nab*-P 100 mg/m^{2}intravenously (IV; 30-minute infusion) on days 1, 8, and 15 plus IV C AUC 6 on day 1 every 21 days. Patients with a complete response (CR), a partial response (PR), or stable disease (SD) will be eligible for maintenance. In the maintenance part of the study, approximately 260 patients will be randomized 2:1 to *nab*-P 100 mg/m^2 on days 1 and 8 every 21 days plus best supportive care (BSC) or BSC alone until disease progression. Patients will be stratified by disease stage (IIIB vs IV), response to induction therapy (CR/PR vs SD), and ECOG performance status at the end of induction (0 vs 1). Key eligibility criteria include histologically or cytologically confirmed stage IIIB/IV SCC NSCLC, no prior chemotherapy for metastatic disease, ECOG performance status ≤ 1, adequate organ function, no active brain metastases, and preexisting peripheral neuropathy grade < 2. ClinicalTrials.gov identifier NCT02027428.

Key Endpoints	
Primary	• PFS from randomization into the maintenance part of the study
Secondary	• Safety • OS from randomization into the maintenance part of the study • ORR during the induction and maintenance parts of the study
Exploratory	• Correlation between pretreatment tumor characteristics and response to treatment • Association between changes in tumor characteristics and acquisition of resistance to therapy at the time of treatment failure during maintenance • Correlation between genetic polymorphisms and treatment efficacy and/or toxicity • Healthcare resource utilization during the maintenance part of the study • Changes in quality of life

Results: Not applicable. **Conclusion:** Not applicable. **Keywords:** nab-paclitaxel, maintenance, squamous cell, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-100 Phase Ib Trial of Afatinib and BI 836845 in Advanced Non-Small Cell Lung Cancer (NSCLC) Keunchil Park[1], Chia-Chi Lin[2], Dennis Chin-Lun Huang[3], Heather Hye-Jung Shin[4], Thomas Bogenrieder[5], Daniel S.-W. Tan[6] [1]*Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/Korea,* [2]*Department of Oncology, National Taiwan University Hospital, Taipei/Taiwan,* [3]*Boehringer Ingelheim Taiwan Limited, Taipei/Taiwan,* [4]*Boehringer Ingelheim Korea, Seoul/Korea,* [5]*Boehringer Ingelheim Rcv, Vienna/Austria,* [6]*Department of Medical Oncology, National Cancer Center, Singapore/Singapore*

Background: Patients harboring epidermal growth factor receptor (*EGFR*)-mutated NSCLC treated with EGFR tyrosine kinase inhibitors (TKIs) invariably develop acquired resistance (AR). The mechanisms of AR are unknown in 30–40% of patients. In pre-clinical studies, insulin-like growth factor (IGF) signaling has been implicated in AR to EGFR TKIs in the absence of other known mechanisms including T790M mutation. It is hypothesized that an EGFR TKI combined with an IGF inhibitor can overcome this resistance. BI 836845

is a fully human, affinity-optimized, IGF ligand-neutralizing antibody. BI 836845 binds to IGF-1 and IGF-2 and neutralizes growth-promoting signaling. Preliminary results from two Phase I studies have shown a tolerable safety profile. This trial was designed to evaluate the safety and anti-tumor activity of BI 836845 combined with afatinib in patients with *EGFR*-mutated NSCLC progressing following prior treatment with reversible or irreversible EGFR TKIs. **Methods:** This is an open-label, dose-escalation trial in Korea, Taiwan and Singapore (NCT02191891; Study 1280.16) consisting of a dose confirmation part (Part A) followed by an expansion part (Part B). Eligible patients are aged ≥18 years with advanced and/or metastatic NSCLC progressing during continuous treatment with single-agent EGFR TKI ≤30 days immediately prior to study treatment, with documented presence of an activating *EGFR* mutation and lacking an *EGFR* T790M mutation (confirmed by central testing in Part B). Patients with prior afatinib treatment at a dose below the assigned dose level (Part A only) or <30 mg/day (Parts A and B), or disease progression on an insufficient dose of EGFR TKI immediately prior to study in the investigator's opinion, or >2 (Part A) or >1 (Part B) prior EGFR TKI treatment regimens for relapsed or metastatic NSCLC are excluded. Part A follows a 3+3 design to determine the MTD and/or recommended Phase 2 dose (RP2D) of BI 836845 combined with afatinib (starting dose: BI 836845 1000 mg/week intravenous infusion over 60 minutes plus oral afatinib 30 mg/day administered in 4-week courses). Patients receive continuous treatment until disease progression, intolerable adverse events (AEs), consent withdrawal or non-compliance with the study protocol. Patients are entered sequentially into escalating/de-escalating dose tiers to determine the MTD based on the occurrence of dose-limiting toxicities (DLTs) during Course 1 (3–6 patients per cohort); 6 additional patients will be enrolled in an extension cohort at the R2PD. Part B consists of two separate expansion cohorts of patients previously treated with irreversible EGFR TKIs (e.g. afatinib, dacomitinib; Cohort 1) and those previously treated with reversible EGFR TKIs (gefitinib or erlotinib; Cohort 2). In each cohort, 18 patients will be treated with the RP2D determined in Part A. Primary endpoints are the MTD and DLTs during Course 1 (Part A) and the objective response assessed using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 (Part B). Secondary endpoints include disease control, time to objective response, duration of objective response, and pharmacokinetic parameters. AEs are evaluated according to Common Terminology Criteria for AEs (CTCAE) v4.03. All analyses will be descriptive and exploratory. **Results:** Not applicable. **Conclusion:** Not applicable. **Keywords:** Monoclonal antibody, IGF, Phase 1, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-101 Randomized Phase 3 Trial of Docetaxel+Plinabulin Compared to Docetaxel in Advanced Non-Small Cell Lung Cancer with at Least 1 Large Lung Lesion Lyudmila Bazhenova[1], Gloria Lee[2], William Mikrut[3], Lan Huang[2] [1]*Moores Cancer Center, University of California San Diego, La Jolla/United States of America,* [2]*Beyondspring Pharmaceuticals, New York/United States of America,* [3]*Currently Vantage Data Designs, San Diego/CA/United States of America*

Background: Plinabulin (BPI-2358) is a marine derived tubulin binding agent, which inhibits existing tumor vasculature and directly induces cancer cell apoptosis via the Ras-JNK pathway. Additional effect of inducing dendritic cell maturation is also observed. Phase 1/2 randomized clinical trial of Docetaxel + Plinabulin (DP) compared to Docetaxel (D) alone failed to show improvement in OS in an ITT analysis. The median OS was 8.6 months in DP, and 7.5 months in D arm. (HR 0.97, P=0.90). However, *post hoc* subset analysis showed improvement in OS in patient with pulmonary tumors >3 cm regardless of number of prior therapy for metastatic disease. In this population, OS was 11.47 (7.13, 16.73) months vs. 7.10 (4.06, 10.60) in DP vs D arm (HR 0.76 and P=0.36). Mechanistically it is postulated that those patients are more dependent on angiogenesis. This phase 3 protocol is designed to test the hypothesis generated from the subset analysis. **Methods:** This is a randomized phase 3, open label clinical trial comparing DP at 75 mg/m2 of D on day1 and 30 mg/m2 of P on days 1 and 8 to D alone at 75 mg/m2 on day 1 in a 21-day cycle. Randomization stratified by ECOG performance status and region. Study population: patients with metastatic with non small cell lung cancer (NSCLC), who has failed one line of chemotherapy and have at least one lung lesion larger than 3 cm. Primary endpoint of the study is to compare overall survival (OS) between two arms. Secondary endpoints are Progression free survival (PFS), overall response rate (ORR), duration of response (DOR), and adverse event profile. Planned number of subjects 550 (440 from China and 110 from the US). Primary outcome analysis is planned after 434 death events which will provide a 0.85 power to detect a statistically significant treatment effect using a two-sided log-rank test at a significance level of $\alpha = 0.05$. **Results:** Not applicable, trial in progress. **Conclusion:**not applicable **Keywords:** metastatic, lung cancer, trial in progress

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.01-102 Phase I Study of Inhaled 5-Azacytidine in Patients with Advanced NSCLC Emrullah Yilmaz[1], Haiying Cheng[1], Bilal Piperdi[2], Chirag D. Shah[3], Simon D. Spivack[3], Rasim A. Gucalp[1], Steven M. Keller[4], Roman Perez-Soler[1] [1]*Oncology, Montefiore Medical Center, Bronx/NY/United States of America,* [2]*Merck Research Laboratories, Rahway/NJ/United States of America,* [3]*Pulmonary Medicine, Montefiore Medical Center, Bronx/NY/United States of America,*[4]*Cardiovascular and Thoracic Surgery, Montefiore Medical Center, Bronx/NY/United States of America*

Background: Epigenetic changes due to promoter hypermethylation have been shown to cause loss of tumor suppressor gene (TSG) function in NSCLC. Significant toxicity and lack of tumor selectivity have been the main limitations of systemic demethylating agents. We previously showed that aerosolized 5-Azacytidine (Aza) was superior to systemic administration in prolonging the survival of mice with carcinogen-induced lung cancer. These results suggest that inhaled Aza could inhibit lung cancer initiation and progression in subjects with chronic airborne carcinogen exposure. Thus, we designed the first phase I study of aerosolized Aza to determine the minimum effective dose of inhaled Aza required to induce relevant TSG re-expression in the bronchial epithelium of patients with advanced NSCLC. **Methods:** This is a phase I study following a 6+6 dose escalation and de-escalation design. Patients with advanced NSCLC, who have received at least one prior standard chemotherapy or targeted therapy, with ECOG PS 0-1, and adequate baseline bone marrow reserve, pulmonary reserve, and organ function are eligible. This study has received IRB and FDA approval as of 01/2015. Patients will be treated with inhaled Aza daily (20-minute inhalation) x 5 days per week once every 2 weeks. Based on our toxicity studies in mice, the recommended starting dose is 15 mg/m^2 . Dose escalation will proceed if <33% subjects in a given cohort experience pre-defined dose limiting toxicity (DLT) defined as grade 2 or higher pulmonary toxicity, grade 4 anemia, neutropenia, thrombocytopenia or any grade 3 or higher non-hematologic toxicity. The primary objective of the study is to determine the minimum effective dose of inhaled Aza required to induce re-expression of 5 relevant candidate TSGs (p16, H-Cad, OPCML, SFRP-1, and RASSF1A) that are silenced in the bronchial tissue of 20-50% heavy smokers with lung cancer. This will be determined in the bronchial epithelium of patients with advanced NSCLC in pre and post treatment biopsies. Secondary objectives include determining changes in global methylation patterns in the bronchial epithelium, and changes in methylation patterns in the exhaled breath. Clinical trial information: NCT02009436. Supported by NIH CA154755 **Results:** not applicable **Conclusion:** not applicable **Keywords:** lung cancer, 5-azacytidine

SESSION: POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC TUESDAY, SEPTEMBER 8, 2015

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.02-001 Predictors of Occult Nodal Metastasis in Clinical Stage I NSCLC Staged by FDG-PET/CT Kaoru Kaseda[1], Ken-Ichi Watanabe[1], Keisuke Asakura[1], Akio Kazama[2] [1]*Department of Thoracic Surgery, Sagamihara Kyodo Hospital, Kanagawa/Japan,* [2]*Department of Pathology, Sagamihara Kyodo Hospital, Kanagawa/Japan*

Background: Integrated 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) is widely used for lymph node staging in patients with non-small cell lung cancer (NSCLC). However, FDG-PET/CT has certain limitations. If N0 cases staged by FDG-PET/CT were reliable, anatomy resection and systematic lymph node dissection might be avoided. And prediction of occult nodal metastasis could allow selection of candidates for preoperative cervical mediastinoscopy or endobronchial ultrasound-guided transbronchial needle aspiration. This study defined risk factors for occult nodal metastasis in patients with NSCLC patients who were diagnosed as clinical stage I by preoperative integrated FDG-PET/CT. **Methods:** We retrospectively reviewed the records of 423 NSCLC patients who underwent surgical resection from April 2007 to March 2015 at the department of Thoracic Surgery, Sagamihara Kyodo Hospital. No preoperative mediastinoscopy was carried out in this group and all underwent curative intent surgical resection. The following patients were excluded from the present study: those who were diagnosed as clinical stage IIA/IIB/IIIA by preoperative integrated FDG-PET/CT (n = 101), patients who underwent limited resection (wide-wedge resection or segmentectomy; n = 62), patients who received neo-adjuvant chemotherapy or radiotherapy (n = 1), and patients with preoperative integrated FDG-PET/CT was not performed (n = 20). The remaining 239 patients who were diagnosed as clinical stage I NSCLC were identified. They underwent surgical resection with systematic lymph node dissection. The prevalence of occult nodal metastasis in patients as clinical stage I was analyzed according to clinicopathological factors such as gender, age, smoking status, history of lung disease, serum carcinoembryonic antigen (CEA) level, concurrent diabetes, histopathological type, grade, tumor side, tumor localization, primary tumor location (central, non-central), tumor size (cm), pleural invasion, standardized uptake value (SUV) max of primary tumor. Risk factors for occult nodal metastasis were defined by univariate and multivariate analysis. **Results:** Occult nodal metastasis was detected in 12.5% (30/239) of the patients. N1 involvement was identified in 5.0% (12/239) of the patients and N2 disease was identified in 7.5% (18/239). An optimal cut-off value of primary tumor SUVmax for occult nodal metastasis was identified as 3.0 by the receiver operator characteristic (ROC) curve, the sensitivity and specificity were 90.0% and 42.1% respectively. In univariate analysis, the following were significant predictors of occult nodal metastasis: adenocarcinoma (P = 0.023), tumor size >3cm (P = 0.002), pleural invasion (P = 0.034) and SUVmax of primary tumor >3.0 (P = 0.018). In multivariate analysis, the following were independent predictors of occult nodal metastasis: adenocarcinoma (P = 0.006), tumor size >3cm (P = 0.013), and SUVmax of primary tumor >3.0 (P = 0.033). **Conclusion:** The present study demonstrated that adenocarcinoma, tumor size >3 cm, and SUVmax of primary tumor > 3.0 are risk factors for occult nodal metastasis in patients with NSCLC who were diagnosed as clinical stage I by preoperative integrated FDG-PET/CT.This study may provide some aids to pre-therapy evaluation and decision-making. **Keywords:** Positron emission tomography / computed tomography, lymph node staging, occult nodal metastasis

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-002 Impact of Multiple Cancer Treatment History on Outcome in Patients with Surgically Resected Non-Small Cell Lung Cancer Masaki Anraku[1], Kazuhiro Nagayama[1], Jun-Ichi Nitadori[1], Tomohiro Murakawa[2], Jun Nakajima[1] [1]*General Thoracic Surgery, The University of Tokyo, Tokyo/Japan,* [2]*Kansai Medical University, Hirakata, Osaka/Japan*

Background: It has been common that patients with previous cancer treatment history undergo curative resection of non-small cell lung cancer (NSCLC); however, the impact of multiple cancer history on outcome after surgery remains unclear. **Methods:** We conducted a retrospective study by using data from patients who underwent curative surgical resection for NSCLC between 1998 and 2011 at our institution. Data recorded for analyses were: age, gender, clinical and pathological stages of NSCLC, mode of surgical resection, comorbidities, pre-treatment serum CEA level, smoking history, and previous cancer history (organ, histologic type, number of cancer treated). The chi-square test and Wilcoxon test were used to analyze the factors between groups (ie, cases with previous cancer history versus those without cancer history). The Kaplan-Meier method was used to estimate survival rates. The log-rank test was applied to compare the survival rates between the groups. A p value less than 0.05 was considered as statistically significant. **Results:** In the study, 229 out of 923 cases (24.8%) had previous cancer treatment history. In the 229 cases, 194 had single cancer treatment history, 30 had double cancer treatment history, and 5 had triple cancer treatment history. Types of cancer treated were: colorectal cancer (n=51), lung cancer (n=30), hepatocellular carcinoma (n=25), breast cancer (n=16), esophageal cancer (n=15), renal cell cancer (n=12), cancers of head and neck (n=11), and others (n=56). There were significantly increased rate of having cancer treatment history in the later study period (2005-2011) compared to a rate in the earlier study period (1998-2004)(30% versus 15%, p<0.01). When comparing to patients without previous cancer history, those with previous cancer history were significantly older (69.1 versus 66.4 years, p<0.01), and had higher smoking history rate (75.1% versus 64.7%, p<0.01). On the other hand, the proportion of stage I NSCLC was significantly higher in cases with previous cancer history than those without previous cancer history (95.2% versus 74.4%, p<0.01). All cases with triple cancer treatment history had clinical and pathological stage I NSCLCs. The survival outcome after surgical resection was significantly better in cases without previous cancer treatment history than those with cancer treatment history (5-year survival rates; 79% versus 75%). In those with cancer treatment history, cases with 2 or more cancers treated had worse outcome than those with only one cancer treated before lung cancer resection (5-year survival rates; 69% versus 76%). **Conclusion:** Although the previous cancer treatment history and the number of cancers treated affected the outcome of patients who underwent curative lung cancer resection, the 5-year survival rate of 75% was achieved in the population. In those with previous cancer history, lung cancer tends to be found in early stage because of the periodical check-up for previous cancers. Therefore, surgical resection of newly detected NSCLC can be a viable option, if the previously treated cancer(s) are well controlled and the new lung cancer is deemed resectable. **Keywords:** cancer history, Surgery, NCSLC

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-003 Blood Loss Volume During Surgery Is a Significant Adverse Prognostic Factor in Patients with Stage I to IIIA Resected NSCLC Wenhua Liang[1], Gening Jiang[2], Qun Wang[3], Lunxu Liu[4], Deruo Liu[5], Zheng Wang[6], Zhihua Zhu[7], Jianxing He[1] [1]*The First Affiliated Hospital of Guangzhou Medical University, Guangzhou/China,* [2]*Shanghai Pulmonary Hospital of Tongji University, Shanghai/China,* [3]*Shanghai Zhongshan Hospital of Fudan University, Shanghai/China,* [4]*West China Hospital, Chengdu/China,* [5]*China and Japan Friendship Hospital, Beijing/China,* [6]*Shenzhen People'S Hospital, Shenzhen/China,* [7]*Cancer Center of Sun Yat-Sen University, Guangzhou/China*

Background: There is little evidence reagrding the impact of blood loss volume during operation on long term survival. Using a large-scale multicenter database for NSCLC, we sought to investigate the prognostic value of blood loss volume. **Methods:** We collected a cohort of resected NSCLC patients from a multi-institutional registry in China (7 centers, 2001-2008) to examine the relationship between blood loss volume and overall survival (OS). According to clinical significance and expertise, blood loss volume was divided into two groups, <200 or ≥200. OS was calculated with the Kaplan-Meier method and univariate comparison between groups was performed using the log-rank test. Cox regression served as a multivariate technique. **Results:** A total of 5,762 cases were available. The mean blood loss volume was 218.4±197.2 mL, median value was 200 mL (0-5000mL). Patients who had less than 200mL blood loss during the operation had more favorable prognosis than those with blood loss of 200mL or more (median OS, 98.8 vs. 76.0 months; HR 0.756, 95% CI 0.691 to 0.829). After adjusting for sex, age, histology, T stage, N stage and operation type (complete VATS, assisted VATS and thoracotomy), blood loss volume remained an independent prognostic factor (HR 0.791, 95% CI 0.716 to 0.874). The volume of blood loss directly correlated with operation time (r=0.21, P<0.001), drainage days (r=0.17, P<0.001), days of ICU stay (r=0.11, P<0.001), drainage volume (r=0.05, P=0.04), and potentially the number of stations examined (r=0.03, P=0.06). **Conclusion:** We revealed that blood loss volume during surgery is a significant adverse prognostic factor for long-term survival. Patients with blood loss volume greater than 200mL require more attention on the recovery strategy. In addition, blood loss volume might be a comprehensive reflection of surgical trauma, and might serve as a marker for evaluating the adequacy of patient's physical condition for receiving adjuvant chemotherapy. **Keywords:** survival, NSCLC, Surgery, Blood Loss Volume

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-004 Clinicopathological Features and Outcomes of AAH, AIS and MIA in Resected Lung Adenocarcinoma Hironori Ishida[1], Hirozo Sakaguchi[1], Nobuhiro Yamazaki[1], Hiroyuki Nitanda[1], Ryo Taguchi[1], Soichiro Suzuki[1], Akitoshi Yanagihara[1], Koichi Kaneko[1], Masanori Yasuda[2], Yoshihiko Shimizu[3] [1]*General Thoracic Surgery, Saitama Medical University International Medical Center, Saitama/Japan,* [2]*Pathology, Saitama Medical University International Medical Center, Saitama/Japan,* [3]*Pathology, Saitama Cardiovascular and Respiratory Center, Saitama/Japan*

Background: After proposal of a new histologic classification of lung adenocarcinoma from the IASLC/ATS/ERS in 2011, the 2015 WHO classification of lung cancer new defines the new subtypes of adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA). The former shows a lepidic growth pattern without invasion (BAC) and the latter a lepidic growth pattern with <= 5mm invasion. Atypical adenomatous hyperplasia (AAH) and AIS (previously, bronchioloalveolar carcinoma) are categorized as preinvasive lesions of adenocarcinoma. Recent studies have shown that patients with AIS and MIA had nearly 100% disease-free survival (DFS), if complete resection was achieved, though the details of the surgical procedures were not mentioned. **Methods:** We reviewed 93 patients with AAH, AIS or MIA, enrolled from among 629 lung adenocarcinoma patients who underwent resection at our hospital from 2007 to 2014. We retrospectively investigated clinical features, pathological findings and the presence of epidermal growth factor (EGFR) mutations, as well as the surgical procedures of wedge resection, segmentectomy and lobectomy. The results were compared with clinical outcomes. **Results:** The patients ranged in age from 40 to 82 years (median 66) and included 40 males and 53 females. Synchronous or metachronous multiple primary lung carcinomas were documented in 15 (16%) patients, who had undergone resections of one to four lesions. Seven of 15 patients had combined lesions of AAH, AIS and MIA, and 8 of 15 had invasive adenocarcinoma combined with AIS or MIA. The total numbers of resected lesions were 7 AAHs, 28 AISs, and 70 MIAs. The diameters of the AAH, AIS and MIA were 4 to 10 mm (median 7), 5 to 20 mm (median 8) and 4 to 23 mm (median 11), respectively. In gene analysis for each lesion, the EGFR mutations were detected in one of five AAH lesions (20%), in eight of 28 AIS lesions (28%) and in 34 of 67 MIA lesions (50%). It was confirmed that both tumor size and the frequency of EGFR mutations gradually increased in the direction from AAH to MIA. As for surgical procedures, we performed 1) wedge resection for 5 AAH lesions, 12 AIS lesions and 22 MIA lesions, 2) segmentectomy with N1 lymph node sampling for 1 AAH, 6 AIS and 15 MIA and 3) lobectomy with N2 lymph node dissection for 1 AAH, 10 AIS and 33 MIA. None of the cases had lymph node metastasis pathologically and all were p-Stage IA. The median follow-up duration from the date of surgery was 31 months (1.7-86 months). Two patients with MIA died 22 and 29 months after surgery due to other malignancies, but none of the patients experienced recurrence and the 5-year DFS rate was 100%. Of 70 MIA lesions, 37 (53%) were removed by wedge resection or segmentectomy. **Conclusion:** AAH/AIS/MIA lesions were related to multiple primary lung carcinomas. Gradual malignant progression from AAH to AIS to MIA was verified. Although accumulation of further cases and long-term follow-up are needed, a subset of these lesions might be treated by wedge resection or segmentectomy. **Keywords:** adenocarcinoma in situ, minimally invasive adenocarcinoma, segmentectomy, wedge resection

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-005 Precise Prediction of 5-Year Survival of Lung Cancer Patients after Radical Surgery Oleg Kshivets *Surgery, Kaluga Cancer Clinical Center, Kaluga/Russian Federation*

Background: This study aimed to determine homeostasis and tumor factors for 5-year survival (5YS) of non-small cell lung cancer (LC) patients (LCP) (T1-4N0-2M0) after complete en block (R0) lobectomies/pneumonectomies (LP). **Methods:** We analyzed data of 665 consecutive LCP (age=57.5±8.3 years; tumor size=4.4±2.4 cm) radically operated and monitored in 1985-2015 (m=575, f=90; lobectomies=423, pneumonectomies=242, combined LP with resection of trachea, carina, atrium, aorta, VCS, vena azygos, pericardium, liver, diaphragm, ribs, esophagus=180; only surgery-S=524, adjuvant chemoimmunoradiotherapy-AT=141: CAV/gemzar + cisplatin + thymalin/taktivin + radiotherapy 45-50Gy; T1=237, T2=248, T3=125, T4=55; N0=419, N1=130, N2=116, M0=665; G1=163, G2=199, G3=303; squamous=377, adenocarcinoma=243, large cell=45; early LC=132, invasive LC=533. Multivariate Cox modeling, clustering, SEPATH, Monte Carlo, bootstrap and neural networks computing were used to determine any significant dependence. **Results:** Overall life span (LS) was 2114.8±1685 days and cumulative 5YS reached 69.6%, 10 years – 61.2%, 20 years – 43.1%. 415 LCP lived more than 5 years without cancer (LS=3041.4±1472.5 days). 194 LCP died because of LC (LS=559.6±373.5 days). AT significantly improved 5YS (65.1% vs. 34.3%) (P=0.00001 by log-rank test) only for LCP with N1-2. Cox modeling displayed (Chi2=290.78, df=13, P=0.000) that 5YS of LCP significantly depended on: phase transition (PT)"early-invasive LC" in terms of synergetics, PT N0-N12, histology, G, blood cell subpopulations, cell ratio factors (ratio between blood cells subpopulations and cancer cells-CC), prothrombin index, heparin tolerance, recalcification time, glucose, AT (P=0.000-0.035). Neural networks, genetic algorithm selection and bootstrap simulation revealed relationships between 5YS and PT N0-N12 (rank=1), PT "early-invasive LC" (rank=2), lymphocytes (3), segmented neutrophils (4), tumor size (5), AT (6), T1-4 (7), ESS (8), prothrombin index (9), glucose (10), thrombocytes/CC (11), healthy cells/CC (12), lymphocytes/CC (13), erythrocytes/CC (14). Correct prediction of 5YS was 100% by neural networks computing (error=0.000; area under ROC curve=1.0). **Conclusion:** 5YS of LCP after radical procedures significantly depended on: tumor characteristics, blood cell circuit, cell ratio factors, hemostasis system and AT.

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-006 Development of the New Photodynamic Therapy for Peripheral Type Lung Cancer Keishi Ohtani, Sachio Maehara, Yujin Kudo, Shotaro Ono, Junichiro Osawa, Masatoshi Kakihana, Naohiro Kajiwara, Tatsuo Ohira, Norihiko Ikeda *Department of Surgery, Tokyo Medical University, Tokyo/Japan*

Background: In Japan, photodynamic therapy (PDT) has been recommended for the treatment of centrally located early lung cancers (CLELC). With recent advances in the diagnosis lung cancer, we continually attempt to expand the indications of PDT, not only for CLELC but also for peripheral type lung cancer. PDT for peripheral lung cancer could be one of the desirable treatment options for patients without surgical indication such as poor pulmonary function. To perform PDT for peripheral lung nodules, it is necessary to use a thin and flexible laser fiber that can sufficiently reach the peripheral lung parenchyma. In this study, we evaluated the feasibility and efficacy of a plastic laser fiber for peripheral PDT. **Methods:** A plastic fiber (cylindrical light diffuser Model RD [Medlight, Switzerland]) was used as a laser fiber for peripheral PDT. The laser output and the light irradiation distribution of the RD cylindrical light diffuser were measured and compared with those of the Panasonic cylindrical probe currently used for PDT. NPe6-PDT was performed for peripheral pig lung. One week after PDT, the pigs were dissected and the lung was removed. The efficacy of NPe6-PDT was evaluated by the pathological findings. **Results:** The mean difference in laser output and the laser source output was 17.7±1.6% for the Panasonic cylindrical fiber and 11.6±3.1% for the RD cylindrical light diffuser. For the light irradiation distribution, the RD cylindrical light diffuser was able to produce more uniform irradiation than the Panasonic cylindrical fiber. The pathological findings showed necrotic tissue and infiltration of lymphoid cells at the laser irradiation area. Around the necrotic tissue, thickening of the alveolar walls and obstruction of the vessels due to thickening of the vascular endothelium were observed. **Conclusion:** The cylindrical light diffuser Model RD showed comparable laser irradiation to the Panasonic cylindrical fiber. The animal experiment showed the effect of PDT in peripheral lung. We conclude that PDT for peripheral lung using the new fiber is feasible and could become one treatment option for peripheral lung cancer. **Keywords:** Photodynamic therapy, peripheral lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.02-007 Correlation Between Histological Invasiveness and CT Value in Pure GGNs Akihiko Kitami, Fumitoshi Sano, Shoko Hayashi, Kosuke Suzuki, Shugo Uematsu, Takashi Suzuki *Respiratory Disease Center, Showa University Northern Yokohama Hospital, Yokohama/Japan*

Background: The purpose of this study is to evaluate the correlation between histological invasiveness and computed tomography (CT) value and size in pure ground glass nodules (GGNs) to determine optimal "follow-up or resection" strategies. **Methods:** Between 2001 and 2014, 78 resected pure GGNs were evaluated retrospectively. Maximum diameter and CT value of pure GGNs were measured using a computer graphics support system. **Results:** All GGN with a maximum diameter ≦10mm and CT value ≦-600 Hounsfield units (HU) were noninvasive lesions, while 21 of 26 (81%) with a maximum diameter >10 mm and CT value >-600 HU were invasive lesions. With respect to a correlation between each histological type and pure GGN with a maximum diameter ≦10 mm and CT value ≦-600 HU, the specificity was 90% and the sensitivity and negative predictive value were both 100% in atypical adenomatous hyperplasia (AAH), while the specificity was 58% and the sensitivity and positive predictive value were 0% in minimally invasive and invasive adenocarcinoma. **Conclusion:** In establishing follow-up criteria for pure GGNs at a maximum diameter of ≦10mm and CT value of ≦-600HU, unnecessary surgery for AAH and therapeutic delay for invasive adenocarcinoma can be avoided. **Keywords:** lung cancer, diagnosis, Surgery, computed tomography

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-008 Planning the Optimal Patient Pathway in the Diagnosis and Staging of Suspected Lung Cancer; What Infrastructure Is Needed? Matthew Evison, Stuart Britton, Haider Al-Najjar, Philip Crosbie, Richard Booton *Manchester Thoracic Oncology Centre, University Hospital of South Manchester, Manchester/United Kingdom*

Background: Lung cancer is the commonest cause of cancer death in the world. Recent research has suggested reducing the length of the diagnostic and staging pathway from 30 to 14 days may improve survival. University Hospital of South Manchester (UHSM) is a regional cancer centre in Manchester Cancer, a large cancer network in the North of the United Kingdom. Manchester Cancer diagnoses over 2000 lung cancers every year and UHSM is responsible for the diagnostic and staging pathways for over 200 lung cancer patients per year locally. We anticipate that an efficient patient journey will involve an "investigation day" where patients undergo the majority of the necessary investigations in a single visit/overnight stay. The results of this work may assist in planning the infrastructure required. **Methods:** Prospective data was collected on all patients referred to the rapid access chest clinic (suspected lung cancer) at UHSM from November 2014 to February 2015. Specifically, the investigations each patient underwent in their pathway, both for diagnosis/staging and physiological tests to determine appropriate treatment were recorded. **Results:** Results are presented in table 1.

	n (%)
Total number of patients	264
Number with lung cancer	73 (28%)
PET-CT	67 (25%)
Bronchoscopy	45 (17%)
Diagnostic EBUS	29 (15%)
Staging EBUS	29 (15%)
Mediastinoscopy	0 (0%)
Percutaneous CT-guided lung biopsy	25 (9%)
Neck USS & biopsy	6 (2%)
Liver biopsy	1 (1%)
MR (brain, spine, adrenal, liver)	10 (4%)
Bone biopsy	1 (1%)
Bone scan	2 (1%)
Spirometry	109 (41%)
Diffusion studies	69 (26%)
Differential perfusion scan	6 (2%)
Shuttle walk	41 (16%)
CPET	17 (6%)
Echocardiogram	29 (11%)

Conclusion: Approximately one-third of new referrals to this lung cancer clinic are subsequently diagnosed with lung cancer. Reliable and rapid access to PET-CT, specialist bronchoscopy services and cardiorespiratory physiology testing is paramount for streamlining patient pathways. To realise our aspirations of an "investigation day" we estimate a need for 4 PET-CT slots, 4 lung function slots (with capability of spirometry, diffusion studies and shuttle walk), 8 bronchoscopy / EBUS slots and 2 CT-guided biopsy slots per week to serve our lung cancer population. **Keywords:** Lung Cancer diagnosis and staging

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-009 Expected Variability of C-Reactive Protein after Pulmonary Resections: Which Factors Are Associated with Their Normal Variation? Diogo G. Augusto, Hugo V. Sampaio-Fonseca, Ricardo M. Terra, Benoit J. Bibas, Leandro R. Iuamoto, Pedro N. Araujo, Alessandro W. Mariani, Paulo M. Pêgo-Fernandes *Thoracic Surgery, University of São Paulo, São Paulo/Brazil*

Background: In patients undergoing lung resection, infectious complications are diagnosed when clinical and radiological evidences are observed. Therefore, early detection of complications may benefit patients and could lead cost reduction. C-reactive protein (CRP) measurements persistently high may indicate complications after surgical resection. Our aim is to define the expected variability of CRP after pulmonary resections which have not progressed to clinical or surgical complications. **Methods:** Retrospective Cohort of patients with neoplastic lung disease treated by anatomic pulmonary resection, between January-2010 and June-2014, which had not developed postoperative complications. A CRP curve was built with data until the fifth postoperative day (POD). Surgical and clinical data was collected to look for predictors of CRP values. Statistical analysis was made with median and confidence interval, T-test for median comparison and logistic regression for predictors. **Results:** We analyzed 220 medical records, 100 patients were excluded because lack of data and 50 due to complication development. Seventy patients were included. The median age was 65 years (from 14 to 89). Forty-one were male (58%). Ten patients (14,8%) had Diabetes, 1 (1,42%) hepatopathy and 1 (1,42%) renal failure. Sixty-one patients (87,14%) underwent lobectomy, 8 (11,42%) pneumonectomy and 1 (1,42%) segmentectomy. There were 48 (68,57%) open thoracotomy and 22 (31,42%) video assisted thoracotomy. The histologic type of tumor was 33 (47,14%) adenocarcinoma, 14 (20%) spinocellular carcinoma, 3 (4,28%) benign diseases and 20 (28,57%) others. The median CRP were 12,85 mg/dl (CI-5,44) preoperative; 76,82 mg/dl (CI-8,49) first day, 156,36 mg/dl (CI-17,91) second , 132,35 mg/dl (CI-17,62) third, 103,24 mg/dl (CI-16,29) forth and 94,11 mg/dl (CI-14,32) fifth. Logistic regression pointed that patients operated by videothoracoscopy (VATS) approach are associated with are associated with lower increase of CRP levels (p=0,002). Other studied factors as age, sex, type of surgery, comorbidities and histology fail to predict CRP level. **Conclusion:** It was observed that CRP peak occurs in the second POD. From the third to the fifth POD, there was a drop of CRP levels, however, it does not returne to the preoperative baseline. The VATS approach induces smaller increases in CRP **Keywords:** C-reactive protein, lobectomy, complications

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

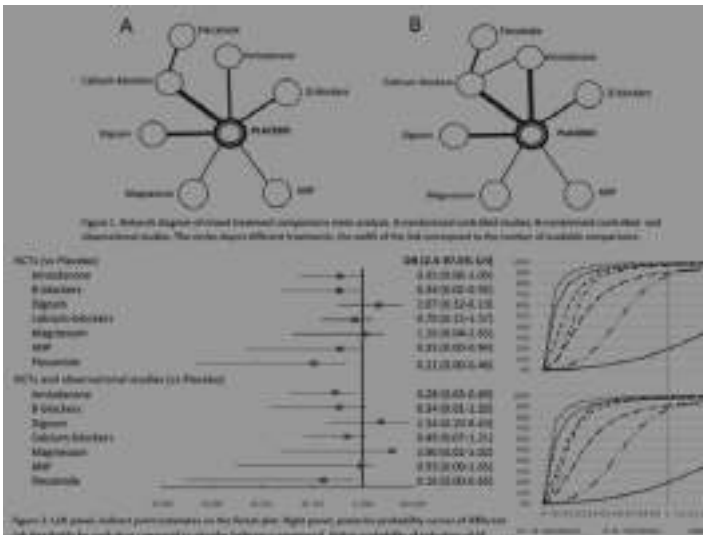
P2.02-010 Pathological Examination of Primary Lung Adenocarcinoma Cases That Were Positive for Intraoperative Pleural Effusion (E1(+), M1a) Shunta Ishihara[1], Masanori Shimomura[2] [1]*General of Thoracic Surgery, Ayabe City Hospital, Ayabe, Kyoto/ Japan,* [2]*Department of General Thoracic Surgery, Ayabe City Hospital, Ayabe, Kyoto/Japan*

Background: Malignant pleural effusion or dissemination is not an indication for surgery or poor prognosis. However, cases that are positive for intraoperative pleural effusion may have better prognosis. We retrospectively examined cases that were positive for intraoperative pleural effusion. **Methods:** We retrospectively investigated the data of 96 patients with primary lung adenocarcinoma who underwent surgery between 2010 and 2013 at the Department of Thoracic Surgery of the Ayabe City Hospital. A total of 11 patients (11.5%) were positive for intraoperative pleural effusion. We compared the data between these patients and the patients who were negative for intraoperative pleural effusion. **Results:** The mean patient age was 72 years (range, 57–83 years); 4 patients were men and 7 were women. The median time from diagnosis to surgery was 89 days (range, 39–1610 days). The median tumor size was 42 mm (range, 15–90 mm). All cases were clinical N0 tumors. Regarding the surgical technique, 2 patients underwent exploratory thoracotomy, 4 underwent wedge resection, and 5 underwent lobectomy. The following pathological findings were obtained. Pleural invasion was pl1 in 1 patient, pl2 in 6, and pl3 in 2. Five patients showed lymphatic vessel invasion (Ly+), 4 patients showed vascular invasion (V+), and 3 patients showed the presence of micropapillary patterns (MPPs). One patient was positive for an *EGFR* mutation. Five patients had received adjuvant chemotherapy. The overall 4-year survival rate was 72.7%. The patients with E(+) showed a significantly higher extent of Ly+, pleural invasion (pl2), and MPPs ($P < 0.05$ for all). **Conclusion:** Primary lung adenocarcinoma with intraoperative findings of malignant pleural effusion tend to show Ly+, vascular invasion, and MPPs. **Keywords:** intraoperative pleural effusion, lung cancer, lung adenocarcinoma

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-011 Optimal Strategy to Prevent Atrial Fibrillation in Patients Undergoing Pulmonary Resection for Lung Cancer. Network Meta-Analysis Mariusz Kowalewski[1], Marzena A. Lewandowska[2], Lukasz Zolna[1], Aleksandra Chrzastek[1], Paweł Wnuk[1], Maciej Dancewicz[1], Mariusz Bella[1], Przemysław Bławat[1], Tomasz Szczęsny[1], Janusz Kowalewski[3] [1]*Department of Thoracic Surgery and Tumours, Oncology Centre – Prof. Lukaszczyk Memorial Hospital in Bydgoszcz, Department of Thoracic Surgery and Tumours, Bydgoszcz, Poland;, Bydgoszcz/Poland,* [2]*Molecular Oncology and Genetics Departament, The Inovative Medical Forum, the Franciszek Lukaszczyk Oncology Center, Bydgoszcz/Poland,* [3]*Department of Thoracic Surgery and Tumors, Collegium Medicum, Nicoalus Copernicus University in Torun, Bydgoszcz/Poland*

Background: Atrial fibrillation (AF) after pulmonary resections for lung cancer, although transient in most cases, occurs in up to 30% following lobectomy and up to 65% after pneumonectomy and might, in turn, lead to serious adverse events including stroke, myocardial infarction and death. Different preventive measures have been investigated, however because of paucity of evidence from randomized studies, straightforward recommendations are still uncertain. We aimed to perform a Bayesian-framework mixed treatments comparison (network) meta-analysis of both randomized controlled- (RCTs) and observational studies, to investigate the net-relative benefit of diverse drugs in prevention of atrial fibrillation following pulmonary resections for lung cancer. **Methods:** We screened Medline, Google Scholar, EMBASE and Cochrane CENTRAL registries for randomized and observational studies comparing drugs to each other and/or to placebo. Studies with post-operative AF as prespecified end-point were retrieved for detailed abstraction. Primary outcome was assessed at longest available follow-up. **Results:** Overall 15 studies (13 RCTs) were identified, enrolling N=1753 patients. Beta-blockers, Atrial Natriuretic Peptide and Flecainide were associated with significant relative reduction in odds of postoperative AF, OR (2.5-97.5% CrI) of 0.34 (0.02-0.92); 0.35 (0.00-0.94) and 0.11 (0.00-0.46) respectively; Digoxin was found to increase these odds. Addition of observational data allowed for identification of Amiodarone as another potentially preventive treatment OR (2.5-97.5% CrI) 0.28 (0.03-0.69). Bayesian posterior probability curves revealed the ranking among treatments with Flecainide, beta-blockers, ANP and Amiodarone being associated with the highest probability to reduce the odds of AF, magnesium and calcium blockers with virtually no effect and digoxin found inferior to placebo.



Conclusion: Beta-blockers and Flecainide are effective in reducing the incidence of postoperative AF in patients after pulmonary resections which is not the case with digoxin; data on remaining treatments are sparse and preclude drawing definite conclusions. **Keywords:** non-small cell lung cancer, meta-analysis, postoperative atrial fibrillation, pulmonary resection

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-012 Prediction of Postoperative Pulmonary Function Using CT Volumetry Masayuki Hashimoto[1], Jun Hanaoka[1], Koji Teramoto[2], Tomoyuki Igarashi[3] [1]*Division of General Thoracic Surgery, Department of Surgery, Shiga University of Medical Science, Seta-Tsukinowa, Otsu, Shiga/Japan,* [2]*Department of Medical Oncology, Shiga University of Medical Science, Otsu/Japan,* [3]*Department of Surgery, Shiga University of Medical Science, Otsu/Japan*

Background: According to some guidelines, prediction of postoperative pulmonary function is important in preoperative assessment for the lung cancer resection. Generally, it used to be calculated the function by Segmental method (S method) or Subsegmental method (SS method). But, the volume of pulmonary (sub) segments varies between individuals. The purpose of this study is to evaluate the efficacy of the prediction of postoperative pulmonary function using CT volumetry. **Methods:**This study included 29 cases who were performed segmentectomy or (bi) lobectomy for primary lung cancer from August 2013 to June 2014. Actual pulmonary function obtained at 6 months postoperation (VC, %VC, FVC, %FVC, FEV1.0, %FEV1.0, DLco', % DLco', DLco'/ Na', %DLco'/Na') was compared with the predicted pulmonary function calculated by S method, SS method and CT volumetry method (CTV method), respectively. CTV method was calculated by Image analysis software (Synapse Vincent; Fuji Film, Japan) which used the preoperative chest CT scan data (mediastinum conditions, 0.5mm thickness). **Results:** The median age of patient was 69 years old, ranging 47 to 83 years old. Seven patients underwent thoracotomy and 22 underwent VATS. Upper lobectomy or upper and middle bilobectomy / upper segmentectomy / middle or lower lobectomy / lower segmentectomy were 12/3/10/4 cases, respectively. These 3 methods were found to have a good correlation with actual pulmonary function. In particular, the CTV method's function was better correlated with actual VC, %VC, FVC, %FVC, FEV1.0, %FEV1.0(r = 0.909, 0.839, 0.913, 0.849, 0.935, 0.875, respectively). On the other hand, SS method's function has better correlated with actual DLco', DLco'/Na', %DLco'/Na' (r=0.916, 0.817, 0.789, respectively). The cases of upper lobectomy or upper segmentectomy (U group) were found to overestimate on DLco'/Na', %DLco'/Na' (t =4.714, 4.634). The other cases (non-U group) were found to overestimate on FVC, FEV1.0, %FEV1.0 (t=2.446, 3.797, 5.657) . **Conclusion:** CTV method may be better correlated evaluation of the ventilation ability than conventional methods, but the evaluation of the diffusion ability is not. Therefore, in the poor pulmonary function case, it is necessary to selectively use these methods in order to make more accurate predictions. And, you should take care that there is pulmonary function to be overestimated or underestimated by the location. **Keywords:** CT volumetry, Pulmonary Function, lung cancer

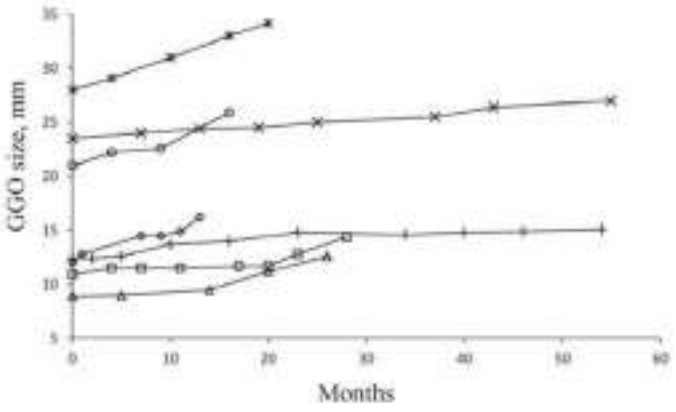
POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-013 Strategy of Management for Synchronous Pure GGOs Detected in Patients Undergoing Resection for Primary NSCLC Chenyang Dai[1], Yijiu Ren[1], Huikang Xie[2], Sen Jiang[3], Ke Fei[1], Gening Jiang[1], Chang Chen[1] [1]*Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/ China,* [2]*Department of Pathology, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China,*[3]*Department of Radiology, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

Background: It is quite common to discover some synchronous pure ground-glass

opacity (GGO) nodules in other lobes beside the operable primary tumor on initial CT scans, while the appropriate surgical strategy for these pure GGOs remains controversial. **Methods:** We included patients with primary tumor lesion and pure GGOs in different lobes between June 2010 and December 2013. The radiographic manifestations of all GGOs, pathologic features of resected GGOs and follow-up outcomes of unresected GGOs were analyzed to make clear which GGOs should be resected concomitantly with the primary tumor**. Results:** A total of 59 patients with 72 pure GGOs were included, of which, 29 were resected at the primary surgery and 43 were left behind and followed up. In the resection group, 8 (27.6%) were invasive or minimally invasive lesions, 12 (41.4%) were preinvasive lesions and 9 (31%) were benign lesions. In the follow-up group, 7 nodules grew, and the growth rate was 16.3% (7 of 43) on a per-nodule basis, and 19.4% (7 of 36) on per-person basis. In all, concomitant resection at the primary surgery was considered for 15 of 72 GGOs (8 malignant lesions and 7 growth lesions). Multivariate analysis showed that the initial size was an independent risk factor for these GGOs (*P*=0.011), and a cut-off value was calculated as 9.9 mm by receiver operating curve (ROC) curve analysis. Tabel Predictors for synchronous GGO nodules which need concomitant resection

	Univariate analysis		Multivariate analysis	
	P value	OR	*P* value	OR
Age at operation	0.056	1.075	0.872	1.01
Sex	0.279	0.527		
Smoking	0.136	2.667		
Size	<0.001	18.733	0.011	10.922
Location				
LUL		Reference		
LLL	0.345	0.333		
RUL	0.217	0.381		
RML	0.577	1.778		
RLL	0.886	0.889		
Location of primary lesion				
Ipsilateral		Reference		
Contralateral	0.334	1.8		
Shape				
Round		Reference		
Oral	0.584	1.625		
Irregular	0.349	2.275		
Margin				
Smooth		Reference		
Lobulated	0.629	1.4		
Spiculated	0.125	3.111		
Air bronchogram	0.001	8	0.355	2.199
Bubble lucency	0.024	6.545	0.274	3.356
Pleural tag	0.006	6.933	0.175	3.724



Conclusion: About 20% of synchronous pure GGO nodules should need surgical treatment at the time of primary operation, and a lesion size of more than 9.9 mm is an effective discriminator of these GGOs. As to the unresected GGOs, a close follow-up is always indispensible.
Keywords: lung adenocarcinoma, follow-up,, ground-glass opacity, limited surgery

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-014 Cross-Sectional Study on Surgical Treatment Patterns of 1927 Stage I-IIIa NSCLC Patients from 11 Medical Centers in China in 2013 Jian Zhou, Fan Yang, Xun Wang, Tian Guan, Jun Wang *Thoracic Surgery, Peking University People'S Hospital, Beijing/China*

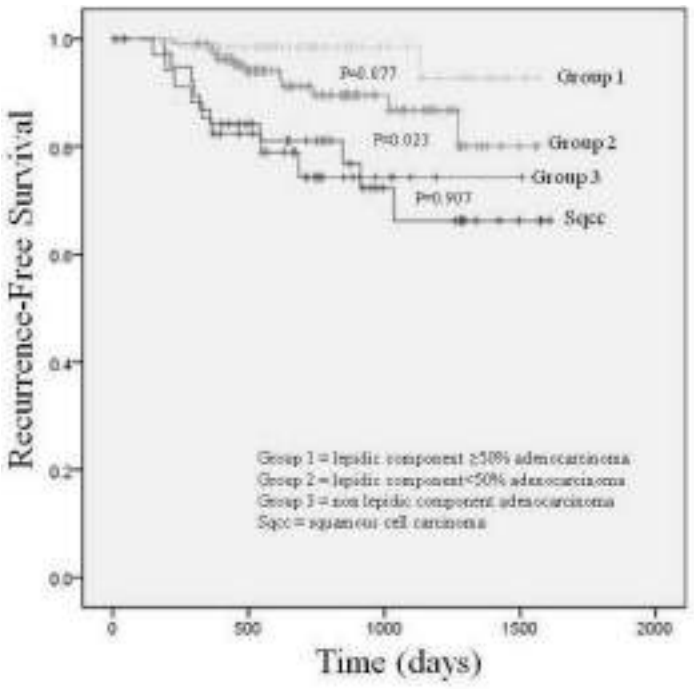
Background: Video- assisted thoracoscopic surgery (VATS) was introduced into China in 1992. Over the past two decades, VATS has experienced dramatic development in China. However, the development is imbalanced. This cross-sectional study aimed to assess the ulitility of VATS in lung cancer patients in China **Methods:** Data of non-small cell lung cancer (NSCLC) patients who received curative-intent resections during the year 2013 were obtained from the national lung cancer registry , which included 1927 patients from 11 tertiary hospitals nationwide. Surgery patterns, stations of lymph nodes dissected, operation time were analyzed. **Results:** Among the 1927 patients, the mean age was 60.0 years old, and 1228 were male. The numbers of patients in final pathologic stages 0, Ia, Ib, IIa, IIb, IIIa were 13, 571,414,243,171,495. Sublobar resection/ lobectomy/ sleeve lobectomy/ pneumonectomy number was 112/1643/57/111. The overall VATS rate is 45.0%, 71.9%, 52.2%,19.3%,6.3% in lobectomies, wedge resection, segmentectomy, sleeve lobectomy, pneumonectomy respectively . In different centers, the median number of lymph nodes stations dissected in VATS single lobectomy is 6 (ranging from 0 to 11) in different centers, while 6.5 (ranging from 0 to 11) in thoracotomy . The average VATS lobectomy surgery time is 184.0 minutes. VATS rates of lobectomy in different centers ranged from 4.4% to 90.2% respectively . VATS rates of Ia,Ib,IIa,IIb,IIIa lobectomy is 65.4%, 41.7%, 31.3%, 24.2%, 38.5% respectively. **Conclusion:** The difference of VATS rate is quite significant between different centers in China . Some centers perform 90-100% VATS in early stage patients and more VATS than thoracotomy in II and III patients. While some centers still perform over 80% thoracotomy surgeries even in stage I patients.
Keywords: cross-sectional study, lung cancer, registry, VATS

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-015 Prognostic Significance of Histologic Subtype in Stage I Non-Small Cell Lung Cancer Youngkyu Moon, Jae Kil Park, Sook Whan Sung *Thoracic and Cardiovascular Surgery, Seoul St. Mary'S Hospital, Seoul/Korea*

Background: Non-small cell lung cancer consist of several histologic types. Among them, pulmonary adenocarcinoma has histologic heterogeneity. Current staging system relied on anatomical involvement of lung cancer. Histologic subtype has not been reflected in the TNM stage of lung cancer although there is some positive reports on prognostic factor. This study aimed to evaluate histologic difference as prognostic factor in stage I lung cancer. **Methods:** We retrospectively reviewed 269 patients with stage I adenocarcinoma and squamous cell carcinoma after curative pulmonary resection at single institute in Korea from August 2010 to December 2013. Adenocarcinoma was divided into 3 groups according to lepidic component; group 1(lepidic component ≥50%), group 2(lepidic component <50%), and group 3(no lepidic component). We compared these three groups with squamous cell carcinoma. **Results:** Mean tumor size of squamous cell carcinoma was larger than other three groups(2.8cm vs 1.9cm, 2.3cm, 1.9cm, p<0.001). There was no difference between group 3 and squamous cell carcinoma in the presence of pleural invasion(p=0.386) or vascular invasion(p=0.930), but lymphatic invasion was more frequent in squamous cell carcinoma(p=0.018)(Table 1). Three-year recurrence free survival of group 1, group 2, group 3 and squamous cell carcinoma were 98.5%, 86.8%, 74.3%, and 66.3%, respectively. (group 1 vs group 2, p=0.077; group 2 vs group 3, p=0.023; group 3 vs squamous cell carcinoma, p=0.907)(figure). Multivariate analysis showed that these 4 grouping was the statistically significant risk factor for the recurrence (HR 1.719, 95% confidence interval 1.051-2.811, p=0.031) Table 1. Clinicopathologic characteristics

	Group 1(n=74)	Group 2(n=119)	Group 3(n=36)	Sqc-c(n=40)	p value
Age	61.2(±9.2)	65.0(±10.0)	65.3(±10.0)	67.3(±1.7)	0.009
Female	45.9%	69.7%	25.0%	12.5%	<0.001
Smoking history(pack years)	7.8(±14.7)	5.2 (±11.8)	20.8 (±22.9)	35.4 (±26.2)	<0.001
Procedures Standard resection Limited resection	86.5% 13.5%	86.6% 13.4%	83.3% 16.7%	75.0% 25.0%	0.337
SUVmax	1.9 (±1.7)	3.8 (±3.3)	4.7 (±3.8)	10.0(±5.8)	<0.001
Tumor size	1.9 (±0.8)	2.3 (±0.9)	1.9 (±0.6)	2.8(±1.0)	<0.001
Number of dissected lymph nodes	12.7 (±7.6)	14.6 (±9.9)	11.1 (±8.1)	14.0 (±10.1)	0.181
Pleural invasion	6.8%	27.7%	25.7%	15.4%	0.003
Lymphatic invasion	13.5%	32.8%	25.7%	53.8%	<0.001
Vascular invasion	1.4%	10.9%	14.3%	15.0%	0.037



Conclusion: Among stage I adenocarcinoma, the prognosis of non lepidic component adenocarcinoma was poorer than lepidic adenocarcinoma. Although the malignant potential of squamous cell carcinoma was higher than adenocarcinoma in this study, the prognosis was not different between non lepidic component adenocarcinoma and squamous cell carcinoma. We expect these histologic prognosis factor will be considered in the new staging system. **Keywords:** Prognosis, histologic component, Squamous cell carcinoma, Adenocarcinoma

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-016 A New Strategy for Preoperative-Management of Patients with Lung Cancer with Chronic Obstructive Pulmonary Disease (COPD) Jitsuo Usuda
Nippon Medical School, Tokyo/Japan

Background: Recently, it has been reported that the prognosis for patients with lung cancer with Chronic obstructive lung disease (COPD) was worse than that of patients with lung cancer without COPD. Therefore, long-term respiratory management not only perioperative care is also important. For lung cancer patients with COPD, the frequency of the postoperative complications should be reduced. **Methods:** In lung cancer patients with COPD, it was examined whether it is possible to reduce the frequency of post-operative complications after surgical resection of the lungs by smoking cessation not only the introduction of inhaled long-acting anticholinergic (LAMA) or long-acting β2-agonists (LABA). Patients who quit smoking more than 6 months before the operation were defined as former smokers and those who were smoking at the time of the operation or quit within 6 months before the operation were defined as current smokers. COPD was defined as FEV1/FVC< 0.7 (FEV1; forced expiratory volume in one second, FVC, forced vital capacity) with a smoking history. Among 260 patients who underwent surgical resection for lung cancer from January 2013 to February 2015 in our hospital, COPD patients 77, non-COPD 183. We analyzed retrospectively the relationship between the introduction of inhaled LABA or LAMA and the frequency of the postoperative complications in lung cancer patients with COPD. **Results:** In COPD patients 77 cases, male 62 cases, female 15 cases, age 60-85 years old (mean: 74). Smoking history 15~150 pack-years (mean 57), current smokers were 39 cases, and former-smokers were 38 cases. The average of FEV1/FVC is 59.6% (26.6~69.5%). Lung resection, partial resection 11 cases, segmental resection 1 case, lobectomy 64 cases, pneumonectomy 1 case. There was no mortality. There were 17 postoperative complications in COPD (22.1%), prolonged air leak (more than 7 days) 9 cases, pneumonia 3 cases, arrhythmia 2 cases, chylothorax 2 cases, wound infection 1 case. In particular, the frequency of postoperative pulmonary complications such as prolonged air leakage and pneumonia, showed a significant high in COPD (12 cases, 15.6%) compared with non COPD (9 cases, 4.9%).Inhaled bronchodilators such as LAMA or LABA were prescribed to 22 cases in COPD, not to 50 cases. The pulmonary complications were significant lower in LAMA or LABA users (2 cases, 9.1%) than in no users (10 cases, 18.2%). Among current smoker 38 cases, which were preoperatively treated with smoking cessation and chest physiotherapy for more than one month, the inhalants with LABA or LAMA were prescribed before pulmonary resection in 18 cases, not prescribed in 20 cases. The frequency of the pulmonary complications was 2 cases (11.1%) in the inhalant users, respectively 4 cases (20%) in the inhalant-no-users. **Conclusion:** For lung cancer patients with COPD, preoperative management using the inhalants with LABA or LAMA, and smoking cessation can reduce the frequency of the postoperative pulmonary complications after surgical lung resection. The inhalants with LAMA or LABA may be adapted for the management of not only perioperative care but also long-term survival of COPD patients after surgery, and the hypothesis should be examined in the future. **Keywords:** morbidity, LABA, lung cancer, copd

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-017 Video-Assisted Mediastinoscopic Lymphadenectomy Decreases the Need for Lymph Node Dissection during Lobectomy in Lung Cancer Patients
Akif Turna[1], Elvin Hekimoglu[2], Ezel Ersen[1], Kamil Kaynak[3] *[1]Department of Thoracic Surgery, Istanbul University, Cerrahpasa Medical Faculty, Istanbul/Turkey, [2]Department of Thoracic Surgery, Istanbul University Cerrahpasa Medical School, Istanbul/Turkey, [3]Department of Medical Oncology, Istanbul University Cerrahpasa Medical School, Istanbul/Turkey*

Background: Mediastinoscopy has been accepted as a gold standard in preoperative staging of patients with cT1-3N1-3M0 non-small cell lung cancer. However, video-assisted mediastinoscopic lymphadenectomy (VAMLA) has been shown to provide higher negative predictive value. We aimed to investigate the role of VAMLA on the need and time for lymph node dissection following anatomical resection in these patients. **Methods:** Between May 2005 and March 2014, 299 patients who have undergone lobectomy following mediastinoscopy or VAMLA were analyzed.One-hundred-four patients (34.8%) underwent VAMLA, wehereas 195 patients (65.2%) had standard mediastinoscopy. 245 patients (81.9%) underwent open lobectomy while 54 (8.1%) had videothoracoscopic lobectomy. The median and mean numbers of resected lymph node stations were 5 and 4.9 in the VAMLA group and 4 and 4.2 in the mediastinoscopy group. **Results:** The mean number of lymph nodes per biopsy specimen using standard mediastinoscopy was 11.0 (ranging 2 to 33), whereas it was 29.7(Ranging 16-110) using VAMLA (p<0.001). ,The negative predictive value, sensitivity, false-negative value, and accuracy of VAMLA were statistically higher in the VAMLA groups compared with those of standard mediastinoscopy. In the VAMLA group, lymph node dissection of stations 2R, 2L, 4R, 4L, 7, and 8 was achieved in 90 (86.5%), 61 (59.6%), 90 (86.5%), 88 (84.6%), 101 (97.1%), and 30 (28.8%) of the patients, respectively. In the standard mediastinoscopy group, 2R, 2L, 4R, 4L, 7, and 8 underwent biopsy in 101 (52.0%), 46 (23.7%), 145 (74.7%), 91 (46.9%), 157 (80.9%), and 0 of the patients, respectively. The difference was statistically significant (p < 0.001). The mean number of dissected mediastinal lymph nodes following pulmonary resection was 9.4 (ranging 0 to 32) or 4.4 (ranging, 0-11) in patients who underwent standard mediastinoscopy or VAMLA, respectively (p<0.001). A statistical difference was found when analyzing the VATS lobectomy patients (mean 8.6 vs 3.1 lymph nodes)(p<0.001). The time for lymph node dissection was also found to be shorter(p=0.02). **Conclusion:** VAMLA provides bilateral lymph node dissection before resectional surgery and it decreases the necessity of lymph node dissection and alleviates it during VATS and open lobectomies performed in non-small cell lung cancer patients. **Keywords:** VAMLA, mediastinoscopy, resection, lymph node dissection

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-018 Evaluation of Invasiveness among 3 Methods of Thoracoscopic Lobectomy in Patients with NSCLC: A Favorable Result for Uniportal VATS
Qihang Zhu, Haiping Xiao, Ming Liao, Yong Tang, Yiwen Xuan, Kai Su, Zhe He, Xiufan Peng, Zhuohua Zhang, Yan Liu, Guibin Qiao *Department of Thoracic Surgery, General Hospital of Guangzhou Military Command of P.L.A, Guangzhou/China*

Background: Video-assisted thoracoscopic surgery (VATS) lobectomy includes 3 main methods: assisted VATS (a-VATS), multiport complete VATS (m-VATS), and uniportal VATS (u-VATS). However, the comparison of invasiveness among 3 methods remains unclear. **Methods:** 74 consecutive patients with early stage NSCLC undertaken VATS lobectomies at a single unit during Jan 2014 to Aug 2014 were analyzed. According to the surgical approach, patients were divided into a-VATS group (n=31), m-VATS group (n=21), and u-VATS group (n=22). Certain perioperative parameters, VAS scores, WBC and CRP levels were analyzed. **Results:** Age, gender, pathological type, TNM stage, operative time, postoperative drainage time, volume of drain, postoperative hospital stays and hospitalization cost were no statistical difference among 3 groups. Intraoperative blood loss of u-VATS was less than c-VATS, and c-VATS was less than a-VATS (Kruskal-Wallis test, p<0.01).VAS scores on the postoperative 3rd day and 1 month of a-VATS were higher than u-VATS (p<0.05). WBC level on postoperative 5th day of a-VATS was higher than u-VATS (p<0.05). CRP levels of u-VATS on the postoperative 1st, 3rd and 5th day (p<0.01) were all significantly difference compared to a-VATS. **Conclusion:** Uniportal VATS lobectomy causes less surgical damage than assisted VATS method. Further researches are needed to clarify whether uniportal VATS lobectomy is better than multiport complete VATS in surgical damage. **Keywords:** Thoracic Surgery, Video-assisted thoracic surgery, non-small cell lung cancer, Thoracoscopy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-019 Role of Sentinel Node Biopsy in Stage IA NSCLC Surgery Nenad Ilic[1], Josko Juricic[2], Vinko Markovic[2], Dragan Krnic[2], Nives Frleta Ilic[2], Duje Orsulic[2], Darko Ilic[2], Ivan Simundza[2] *[1]Thoracic Surgery Dept., University Surgical Hospital, Split/Croatia, [2]Thoracic Surhery Dept., University Surgical Hospital, Split/Croatia*

Background: Systematic mediastinal lymphadenectomy is still essential for an adequate intraoperative staging and adjuvant therapy of NSCLC. We tried to investigate still controversial role of sentinel node biopsy (SNB) in early stage non small cell

lung cancer (NSCLC) surgery. **Methods:** A total of 72 patients with clinical T1N0M0 NSCLC underwent SN navigation lobectomy using Tc-99 labeled tin colloid followed by systematic mediastinal lymphadenectomy (SML) in three years time period (2010-2013). Mapping of the mediastinal lymph nodes by their number and station followed by hystopathological evaluation was performed. Patients data were statistically analyzed. **Results:** Intraoperative SN was identified in 62 (87%) of these patients with 92% of accuracy. We found lobe specific skip nodal metastases in 7 (10%) patients resulting in upstaging. The incidence of ML metastases seemed to be more often in adenocarcinoma patients ($p<0.05$), but skip nodal metastases showed higher rate in squamous cell carcinoma patients. Intraoperative frozen section was not confirmed accurate for detecting micrometastases in two (4%) patients. Operative time was prolonged for 10 (8-25) minutes showing no difference in complication rate. **Conclusion:** Procedure showed absolute safety and high accuracy. Our results indicated that SN identification could replace mediastinal lymph node dissection in early stage NSCLC. Further clinical studies should be carried out in order to prove that minimally invasive mediastinal surgical procedures could be curative for T1N0M0 NSCLC. **Keywords:** Surgery, Sentinel node biopsy, Mediastinal lymphadenectomy, NSCLC

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-020 Determining the Location of Early-Stage Lung Cancer Using an Endoscopic Ultrasound Device during VATS Procedure Takashi Inoue, Ikuo Wakamatsu, Osamu Araki, Yoko Karube, Norio Seki, Satoru Kobayashi, Tetsu Sado, Takeshi Oyaidu, Masayuki Chida *Department of General Thoracic Surgery, Dokkyo Medical University, Mibu Tochigi/Japan*

Background: Recently, it is possible to detect early-stage lung adenocarcinoma by using computed tomography. However, during video-assisted thoracic surgery (VATS), it is difficult to determine the location of early-stage lung adenocarcinoma without pleural indentation. In this study, we used an endoscopic ultrasound device to identify the location of early stage lung adenocarcinoma during VATS. **Methods:** We enrolled patients with a pure ground-glass-opacity (GGO) lesion (considered adenocarcinoma in situ) of less than 2 cm, which was considered undetectable during VATS because it was located inside the lungs, and was not adjacent to the visceral pleura. After single lung ventilation, we inserted the endoscopic ultrasound device (UST-5536-7.5, Hitachi Aloka Medical, Tokyo, Japan) through a 12-mm thoracoport . **Results:** Three patients (age range: 49–69 years) were enrolled. The diameter of the three lesions was 7 mm, 10 mm, and 12 mm, respectively. These lesions could not be observed through the visceral pleura and could not be palpated. The endoscopic ultrasound device detected each lesions as an area with high-signal intensity. The location of each lesion was determined on the basis of the intersection of the device when inserted from two different thoracoports;,the tumors were then resected. Pathological examination revealed adenocarcinomas in situ in 2 patients and an atypical adenomatous hyperplasia in 1. Local recurrence after surgery was not observed in any of the patients. **Conclusion:** Detecting a GGO lesion by using an endoscopic ultrasound device is an easy and effective method during the VATS procedure to determine the location of early-stage lung adenocarcinoma. **Keywords:** Early-stage lung cancer, Ultrasound, video-assisted thoracic surgery (VATS), Endoscopy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-021 Robotic Pulmonary Resection for Lung Cancer: Analysis of the Learning Curve in a Novel Surgical Program Wael C. Hanna[1], Christine Fahim[2], Priya Patel[3], Yaron Shargall[1], Thomas K. Waddell[3], Kazuhiro Yasufuku[3] [1]*Division of Thoracic Surgery, St. Joseph'S Healthcare Hamilton, Hamilton/ON/Canada,* [2]*St. Joseph'S Healthcare Hamilton, Hamilton/Canada,* [3]*University Health Network, Toronto/ON/Canada*

Background: We present the first Canadian series of robotic pulmonary resection for lung cancer, examining the effects of learning curves associated with new technology on perioperative outcomes. **Methods:** Prospective databases at two institutions were queried for patients who underwent robotic pulmonary resection for lung cancer between October 2011 and February 2015. Data was collected on demographics, comorbidities, perioperative variables and complications. Results are presented as median (range). The learning curve effect was evaluated in temporal tertiles, stratified by surgeon. Differences in perioperative outcomes were evaluated using the Mantel-Cox Log-Rank test. **Results:** Of 116 patients included, 48% were males and median age was 67 (28-88). The majority (88%, 102/116) underwent a robotic lobectomy, 9% (11/116) a segmentectomy, and 3% (3/116) a wedge resection. Five patients (4%) were converted to thoracotomy. Median operative time was 281 minutes (134-650) and length of stay was 4 days (1-19). Total operative time decreased significantly ($p<0.01$) over the learning curve; tertile 1 (326 min (290-362)), tertile 2 (275 min (261-289)) and tertile 3 (235 min (210-260)). Median time spent on the robotic console also decreased significantly ($p<0.01$) over tertiles- 195 (144-246), 148 (136-160), and 116 (100-132) minutes, respectively. Across tertiles, there were no differences in the median number of lymph node stations harvested (6, 5, 6; $p=0.33$), length of stay (4, 4, 4; $p=0.25$, or the rate of major complications (Clavien-Dindo Class >= III; 5, 1, 4, respectively; $p=0.26$). There were no mortalities. **Conclusion:** The early Canadian experience with robotic lung cancer resection demonstrates excellent results that are comparable to those of experienced centers in operative times, length of stay and conversion rates. Further improvement was demonstrated by the learning curve effect. A prospective study to examine the outcomes and cost of robotic pulmonary resection compared to video-assisted thoracoscopic surgery should be done in the context of the Canadian healthcare system. **Keywords:** robotic pulmonary resection, Robotic surgery, Canadian, case series

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P2.02-022 Short and Long-Term Outcomes of Pneumonectomy for Lung Cancer: 15-Years Experience Syed S.A. Qadri[1], Mubarak Chaudhry[2], Alex Cale[1], Michael Cowen[1], Mahmoud Loubani[1] [1]*Cardiothoracic Surgery, Castle Hill Hospitall, Hull/United Kingdom,* [2]*Castle Hill Hospital, Hull/United Kingdom*

Background: Surgery is the most important therapeutic modality for the treatment of lung cancer. Surgical outcomes are normally reported as 30-day or 90-day mortality or 5-year survival. However, 10-years survival is rarely mentioned in the national data or international studies. **Methods:** Patients included who underwent penumonectomy from January1998 to February2013, and analysed their short and long-term outcome till september2014. Thoracoscore was used to calculate the risk of hospital mortality **Results:** 306-patients underwent pneumonectomy mainly for lung cancer. 79% were male, median age was 64-years(22-82years) and 24% were ≥ 70-years. Operative mortality was 4.5% while predicted mortality was 8%. However, operative mortality for cancer patients was 3.3% while reported national mortality for lung cancer is 6.5%. Only 2-patients died in hospital after pneumonectomy in the last 5 years. Half of the patients, who died in hospital, were ≥70-years while 29%(4-patients) died after urgent operation for non-malignant-disease. Overall 5 and 10-year survival rates were 32% and 20%. Median and mean survival was 26 and 57-months respectively. Long-term survival was better in female, patients with age <70 years, in left pneumonectomy and for squamous-cell-lung-cancer patients. **Conclusion:** This retrospective single institutional review have shown that our mortality for pneumonectomy is 50% less than national mortality and significantly lower than that predicted by Thoracoscore for lung cancer. This confirms that pneumonectomy is still an effective modality in the treatment of lung cancer with low operative mortality and good long-term survival especially in younger patients. It can be done safely with good short and long-term outcome by trained experienced surgeons. **Keywords:** Pneumonectomy, Lung Cancer, survival, mortality

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P2.02-023 Robotic Thoracic Surgery for Elderly Patients with Non-Small Cell Lung Cancer Ryan T. Hughes[1], Vanessa M. Dipasquale[1], Stefan C. Grant[2], Brian E. Lally[3], William J. Petty[2], Alfred Proto[4], Leonard J. Wudel[4] [1]*Wake Forest School of Medicine, Winston-Salem/NC/United States of America,* [2]*Medical Oncology, Wake Forest Baptist Medical Center, Winston-Salem/NC/United States of America,* [3]*Radiation Oncology, Wake Forest Baptist Medical Center, Winston-Salem/NC/United States of America,* [4]*Cardiothoracic Surgery, Wake Forest Baptist Medical Center, Winston-Salem/NC/United States of America*

Background: The evidence supporting robotic pulmonary resection for the management of early stage NSCLC continues to grow. Limited data exist describing the results of elderly patients undergoing these procedures. We compared the outcomes of patients ≥70 years old versus patients <70 years old undergoing robotic-assisted thoracic surgery. **Methods:** We retrospectively reviewed the medical records of patients treated with robotic-assisted pulmonary resection with lymph node dissection for NSCLC at our institution from March 2013 to the present. Clinical, pathologic, and treatment-related factors were analyzed with regard to perioperative complication rates, hospitalization duration, and clinical outcomes in patients ≥70 versus <70 years old. Categorical and continuous data were compared between age groups using the Chi-square and t-test, respectively. Survival data were described using the Kaplan-Meier method and compared between age groups using the log-rank test. **Results:** This analysis included 101 consecutively treated patients, 40 of whom were over the age of 70 at diagnosis. The cohort was predominantly female (64%), clinical stage I (80%), with an ECOG performance status of 0-1 (97%). Lobectomy (92.5%), wedge resection (13%) and bilobectomy (3%) were performed involving the upper (48.5%), middle (16.8%) and lower (47.5%) lobes. The majority (80%) were right sided due to institutional policies. Open conversion was required in only 3 (3%) patients. The above data did not differ significantly between the two age cohorts. The median chest tube duration (4 days) and length of stay (5 days) were equal in both groups. The median length of epidural anesthesia was 3 days in patients <70 and 2 days in the patients ≥70 years of age. The most common complications for younger vs. older patients included persistent air leak (18% v. 12.5%), atrial fibrillation (8.2% v. 17.5%), urinary retention (3.3% v. 12.5%), and pneumonia (3.3% v. 10%); none of these differences reached statistical significance. Major perioperative complications included one non-fatal myocardial infarction and 2 inpatient deaths secondary to septic shock (one in each age group). The 1-month readmission rate was 4.9% vs. 2.5% for patients younger vs. older than 70 years ($p=0.54$). The 1-year overall survival was 90% and 89% for younger and older patients, respectively ($p=0.35$). **Conclusion:** Robotic-assisted thoracic surgery is an appropriate surgical approach for patients older than 70 years of age with early stage NSCLC. Although some complication rates were increased in older patients, these differences did not reach statistical significance and do not appear to be related to the particular surgical procedure performed. Elderly patients with good performance status tolerate minimally-invasive robotic pulmonary resection extremely well and should be considered candidates for this surgical procedure when clinically appropriate. **Keywords:** Robotic surgery, NSCLC, elderly

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P2.02-024 Simplified Comorbidity Score for Elderly Patients with Primary Lung Cancer Treated by Video-Assisted Thoracoscopic Surgery Yohei Yurugi, Tomohiro Haruki, Yuki Matsuoka, Ken Miwa, Kunio Araki, Yuji Taniguchi, Hiroshige Nakamura
General Thoracic Surgery, Tottori University Hospital, Yonago/Japan

Background: Especially for elderly lung cancer patients, it would be important to evaluate the risks for postoperative complication and prognostic implication accurately. The aim of this study is to investigate whether Simplified Comorbidity Score (SCS) is useful for prediction of postoperative complication and prognosis. **Methods:** We reviewed 216 elderly lung cancer patients aged 75 years and older who underwent pulmonary resection by video-assisted thoracoscopic surgery (VATS) between January 2005 and December 2012. The SCS, which is one of the weighting and scoring system for patients' comorbidities, summarized the following variables: tabacco consumption, diabetes mellitus and renal insufficiency (respective weightings = 7, 5 and 4), respiratory, neoplastic and cardiovascular comorbidities and alcoholism (weighting = 1 for each item). Patients were divided into high and low groups according to calculated SCS (cut-off valued = 9), and we analyzed the differences of perioperative factors and prognosis between these groups. **Results:** There were 154 patients with low SCS and 62 with high SCS. Limited resection was performed more frequently in high SCS group than in low SCS group (58% and 40%, respectively; $p = 0.02$). Postoperative complications were occurred more frequently in high SCS group than in low SCS group (15% and 45%, respectively; $p < 0.01$). High SCS was a significant predictive factor of postoperative complications by logistic regression analysis (Odds ratio: 2.7; $p = 0.02$). The five year overall survival was 74% for low SCS group and 49% for high SCS group, respectively, with a significant difference ($p < 0.01$). **Conclusion:** SCS could provide useful information about postoperative complications and prognosis in elderly lung cancer patients with VATS treatment. **Keywords:** non-small cell lung cancer, Elderly patients, Video-assisted thoracoscopic surgery, Simplified comorbidity score

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P2.02-025 The Equivalent Efficacy of Multiple Operations for MPLC and a Single Operation for SPLC Keneng Chen[1], Liang Dai[1], Hao Fu[2] [1]*Thoracic Surgery, Peking University Cancer Hospital, Peking/China*, [2]*Beijing Cancer Hospital, Beijing/China*

Background: The incidence of synchronous and metachronous multiple primary lung cancers (MPLCs) has been increasing recently. The new multidisciplinary classification of lung adenocarcinoma and TNM Classification of Lung Cancer (7thedition, 2009), have improved the understanding of MPLC. Most researchers recommend that surgical therapy be actively pursued if the patient's physical condition and lung function permit it and if a complete cure can be achieved. However, few studies have reported the long-term efficacy of surgical treatment for MPLC, which we explored in this study. **Methods:** One thousand two houndred and ningty Lung cancer patients from a prospectively maintained database, treated by a single surgeon group between January 2000 and July 2013, at Beijing Cancer Hospital, Peking University, were reviewed. We retrospectively analyzed the clinical data of 31 patients diagnosed with MPLC out of 1290 lung cancer patients, focusing on long-term survival. **Results:** MPLC patients accounted for 2.4% (31/1290) of the patient cohort: 27 had synchronous MPLC (87.1%) and 4 had metachronous MPLC (12.9%). The 1- and 3-year postoperative survival rates were 100% and 73.5%, respectively. On stratification according to TNM stage, the 1- and 3-year survival rates of patients with stage I cancer (20 patients) were 100% and 77.8%, respectively, not statistically significant with those for the entire cohort (1290 patients; 95.4% and 80.5%, respectively, $p=0.876$). **Conclusion:** When the patient's physical condition and tumor-related factors permit it, surgery should be the first choice of treatment for MPLC; it is associated with an equivalent efficacy to that of surgery for single primary lung cancer. **Keywords:** multiple primary lung cancer, Surgery, survival

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-026 Mediastainal Lymph Node Metasatsis Pattern from Left Upper Lobe Cancer: Results of Bilateral Superior Mediastinal Nodal Dissection Toshiya Yokota, Shingo Ikeda *Thoracic Surgery, Misui Memorial Hospiral, Tokyo/Japan*

Background: The accurate assessment of lymph node involvement is an important part of the management of lung cancer. However, due to anatomical limitations imposed by arch of aorta, it is difficult to perform complete dissection of superior mediastinal lymph nodes through the left thoracotomy in the left lung cancer. The aim of this study is to evaluate the location, frequency of metastatic lymph nodes in the mediastinum among patients with left upper lung cancer who underwent complete dissection of the bilateral superior mediastinal lymph node through a median sternotomy (Hata's method, ND3 operation). **Methods:** 202 patients with left upper lobe cancer underwent extended radical mediastinal lymph node dissection. We retrospectively studied clinical data of these patients [202 male and 87 female, mean ages 60.2 years (range, 38-75)], underwent ND3 operation due to NSCLC, from January 1988 till December 2014. Mediastinal nodal status was assessed according to the systems of IASLC lymph node map 2009. The superior mediastinal lymph nodes which cannot be dissected through a left thoracotomy (bilateral #1,#2 and #4, right #3a according to IASLC lymph node map 2009 were defined as extra-superior mediastinal nodes for left lung cancer . **Results:** N1 disease was identified in 28 patients,N2 was in 39 patients, N3α disease was in 18, N3γ disease was in 10. 67 patients (33.2%) had one or more metastases to mediastinal lymph nodes . Among them the most common metastatic station was the aortic nodes (AP Zone). 34 cases (50.7%) had metastasis to #5 or #6 (19 cases(29.2%) to #5 and 15 cases (22.4%) to #6). Mediastinal lymph nodes metastasis occurred 34 cases in absence of N1 metastasis. Among the 48 cases with aortic nodes metastasis, 45.8%(22 cases) had Upper Zone (superior mediastinal nodes) metastasis. The next common metastatic station was #4L nodes (24 cases(35.8%)). Metastasis to the Upper Zone lymph nodes occurred in 32 cases of the 202 cases (15.8%), representing 47.8% rate of occurrence (32/67) among those with mediastinal nodal involvement. Furthermore, Upper Zone metastasis was rare 5.0% in the absence of aortic node metastasis. **Conclusion:** The aortic lymph node is the most common site of metastasis from left upper lobe cancer. Based upon the rates of metastasis in our study, dissection of aortic nodes and left tracheobronchial nodes may be important for patients with left upper lobe cancer. We conclude our procedure (Hata's method, ND3 operation) improve pTNM staging in left upper lobe lung cancer,whether Upper Zone dissection has a beneficial effect on prognosis remains controversial. **Keywords:** non small cell lung cancer, Hata's operation, lymph node disseciton, ND3 opration

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P2.02-027 A Study of Segmentectomy for Primary Lung Cancer Kotaro Mizuno, Risa Oda, Takuya Matsui, Takeshi Yamada *Kariya Toyota General Hospital, Kariya/Japan*

Background: Lung segmentectomy has been developed to reduce the invasion for patients. We have performed segmentectomy for primary lung cancer as much as possible. We have analyzed the usefulness of segmentectomy, especially by focusing on the recurrent cases. **Methods:** A total of 639 patients underwent operation for primary lung cancer in the period of January 2006 to August 2014 in our hospital. We performed an analysis of 144 patients (22.5%) who accepted segmentectomy. To compare the clinical data, we divided 144 patients into four groups depending on the size. Group A means ≤1.0cm, B means >1.0cm and ≤2.0cm, C means >2.0 cm and ≤3.0cm, D means >3.0cm. The overall survival rates were calculated using Kaplan-Meier test. **Results:** Group A are 40 (27.8%), B are 72 (50.0%), C are 20 (13.9%), D are 12 (8.3%). The pathological stage was 0/1=3/37 in Group A, 0/1A/1B(pl1)/2A(n1)/2B(pl3)=1/63/5/2/1 in B, 1A/1B/2A/3A/4=11/6/1/1/1 in C, 1A/1B/2A/3A=1/8/1/2 in D. The 5-year survival rate was 89.6% in 144, 100% in A, 90.1% in B, 68.1% in C, 83.3% in D, respectively. There were 8 recurrent cases (5.6%) for all 144 cases, pulmonary metastasis (same lobe) = 1 in A, carcinomatous pleuritis / pulmonary metastasis (same lobe) / pulmonary and liver metastasis = 2/1/1 in B, brain metastasis = 1 in C, pulmonary metastasis (contralateral) / chest wall metastasis = 1/1 in D. **Conclusion:** This study revealed segmentectomy could contribute to long-term survival for group A and B. In recurrent cases of A and B, two of carcinomatous pleuritis and pulmonary and liver metastasis were showed pl1 or pl3. These cases would not be able to prevent recurrence even if they were performed lobectomy. However, two cases of pulmonary metastasis possibly could not occur recurrence if they were enforced lobectomy. **Keywords:** primary lung cancer, survival, lung segmentectomy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P2.02-028 Diagnostic and Therapeutic Benefits of Thoracoscopic Surgery in Pulmonary Mucosa-Associated Lymphoid Tissue Lymphoma Hirohisa Kato, Hiroyuki Oizumi, Makoto Endoh, Jun Suzuki, Hikaru Watarai, Mitsuaki Sadahiro *Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata/Japan*

Background: Only a few reports have been published on pulmonary mucosa-associated lymphoid tissue lymphoma, a relatively rare disease. However, diagnostic and therapeutic surgery for this disease has increased recently due to the greater number of cases with indeterminate tumors detected by CT. We elucidated the characteristics of pulmonary mucosa-associated lymphoid tissue lymphoma and evaluated the role of thoracoscopic surgery. **Methods:** From March 2005 to March 2015, 13 patients underwent surgery for pulmonary mucosa-associated lymphoid tissue lymphoma diagnosed post-operatively. Three-dimensional CT simulation provides useful information for thoracoscopic surgery. We performed thoracoscopic lobectomy, anatomic segmentectomy, and subsegmentectomy for almost of these patients using the three-dimensional CT simulation. We evaluated patient characteristics, CT and FDG-PET findings, diagnostic methods, surgical procedures, operative time and bleeding, and prognosis. **Results:** The median age of the patients at surgery was 64 yr (range, 38–78 yr). All the tumors were solid nodules, with 11 patients having a single tumor and 2 patients multiple tumours. Median tumor size was 2.5 cm (range, 1.5-10 cm). FDG-PET showed SUV was 3.89-5.54 (range, 1.86-18.02). Only two patients were diagnosed preoperatively with mucosa-associated lymphoid tissue lymphoma by trans-bronchoscopic biopsies, while 11 patients were assumed preoperatively to have lung cancer and were diagnosed finally with the frozen section using a surgical approach. Ten of the 13 patients underwent resections with thoracoscopic surgery and 3 patients underwent resection with thoracotomy. The procedures were 6 lobectomies, 5 segmentectomies, and 2 wedge resections. The most recent case had a thoracoscopic lobectomy combined with a segmentectomy and subsegmentectomy. The mean surgical time and median bleed were 194 min and 9 mL and 215 min and 200 mL in the thoracoscopic and thoracotomy groups, respectively. These operative parameters were showing a tendency to reduce in the thoracoscopic group. No complications or recurrences occurred during the follow-up period (range 4- 120 mth, mean, 45.8 mth). **Conclusion:** Three-dimensional CT simulation was very useful and safely enabled reliable thoracoscopic segmentecomy and subsegmentectomy. Thoracoscopic surgery for pulmonary mucosa-associated lymphoid tissue lymphoma in which preoperative diagnosis is difficult can be performed safely and is beneficial for diagnosis and curative treatment. **Keywords:** Thoracoscopic surgery, MALT lymphoma

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P2.02-029 Pre-Operative Pulmonary Function Tests (PFT) and Outcomes from Stage I and II Non-Small Cell Lung Cancer (NSCLC) Treated with Surgery
Nabin Khanal[1], Daniel Almquist[2], Lynette Smith[3], Apar K. Ganti[4] [1]*Internal Medicine, Creighton University Medical Center, Omaha/NE/United States of America,* [2]*Internal Medicine, University of Nebraska Medical Center, Omaha/NE/United States of America,* [3]*University of Nebraska Medical Center, Omaha/NE/United States of America,* [4]*Internal Medicine/Oncology-Hematology, Veteran'S Affairs Nebraska-Western Iowa Health Care System, University of Nebraska Medical Center, Omaha/NE/United States of America*

Background: Pre-operative PFTs predict operative morbidity and mortality after resection in lung cancer. However, the impact of pre-operative PFT on overall survival (OS) in surgically resected stage I and II NSCLC is relatively less studied. **Methods:** This is a retrospective study of 149 patients who underwent surgical resection as first-line treatment for stage I and II NSCLC at a single center between 2003 and 2014. PFTs (FEV1, DLCO, both absolute values and percentage of predicted values were categorized into quartiles The Kaplan-Meier method and Cox regression analysis were used to determine whether PFTs predicted for OS. The t-test was used to compare the risk of post-op complications and length of stay greater than 10 days based on the results of PFTs and multivariate logistic regression was used for predictive modeling. P-value<0.05 was considered statistically significant. **Results:** The median age of the cohort was 68 years. The cohort was predominantly male (98.6%), current or ex-smokers (98%), with stage I NSCLC (82.76%). The majority of patients underwent a lobectomy (n=121, 81.21%). The predominant tumor histology was adenocarcinoma (n=70, 47%) followed by squamous cell carcinoma (n=61, 41%). The median follow-up of surviving patients was 53.2 months. Although DLCO was found to be a significant predictor of OS (HR: 0.93, 95% CI, 0.87-0.99; p=0.03), this was no longer significant on multivariate analysis. While PFTs did not predict for post-operative complications, worse PFTS were significant predictors of length of stay >10 days. **Table 1. PFTs and Outcome:**

Multivariate model for of LOS > 10 days	Odds Ratio(95% CI, p-value)
FEV1	0.34(0.16-0.76,p=0.0087)
FEV1 (percentage predicted)	0.96(0.94-0.99,p=0.0033)
DLCO	0.78(0.68-0.90,p=0.0004)
DLCO (percentage predicted)	0.96(0.94-0.99,p=0.0060)

OS=Overall Survival, LOS= Length of stay, ULN= Upper Limit of Normal *PFT as continuous variables **Conclusion:** Preoperative PFTs did not predict for survival from resected early stage NSCLC, but did predict for longer hospital stays following surgery.
Keywords: NSCLC, Surgical treatment, Pulmonary Function test, Survival

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-030 Bronchoscopic Therapy for Centrally-Located Early Lung Cancers
Taichiro Ishizumi, Jitsuo Usuda, Tatsuya Inoue, Takayuki Ibi, Akira Sato *Thoracic Surgery, Nippon Medical School Hospital, Tokyo/Japan*

Background: Photodynamic therapy (PDT) is recommended as a treatment option for centrally-located early lung cancers (CLELCs). Although PDT using Photofrin has not been recommended for large tumors or deeply invasive tumors, in the past, if their mass is reduced by electrocautery, PDT with the NPe6 second-generation photosensitizer has been found to be capable of destroying the residual cancer lesion. NPe6 is a second-generation photosensitizer, and since it has a longer absorption band (664 nm) than Photofrin (630 nm), we hypothesized that NPe6-PDT would exert a strong antitumor effect against cancer lesions greater than > 1.0 cm in diameter. **Methods:** Between June 2004 and October 2013, 128 patients (151 lesions) with CLELC underwent NPe6-PDT after the extent of their tumors had been assessed by fluorescence bronchoscopy for photodynamic diagnosis and tumor depth had been assessed by OCT. **Results:** Ninety-four cancer lesions ≦1.0 cm in diameter and 57 lesions >1.0 cm in diameter were identified, and the CR rate was 93.6% (88/94) and 96.5% (55/57), respectively. After the mass of large tumors and deeply invasive tumors, had been reduced by electrocautery, NPe6-PDT was capable of destroying the residual cancer lesions. **Conclusion:** NPe6-PDT has a strong antitumor effect against CLELCs >1.0 cm in diameter, thereby enabling the destruction of residual cancer lesions after mass reduction of large nodular or polypoid type-lung cancers by electrocautery. The PDT guidelines for lung cancers should therefore be revised, because use of NPe6-PDT will enable expansion of the clinical indications for PDT.
Keywords: centrally-located early lung cancers, photodynamic therapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-031 Surgical Management of Bronchial Carcinoid Tumors: A Monocentric Tunisian Experience
Tarek Kilani[1], Adel Marghli[1], Hazem Zribi[1], Sadok Boudaya[1], Sarra Zairi[1], Aida Ayadi[2], Mouna Mlika[2], Tahar Mestiri[1], Faouzi Mezni[2], Hammouda Boussen[3] [1]*Thoracic and Cardiovascular Surgery, Abderrahmane Mami Hospital, Ariana/Tunisia,* [2]*Pathology, Abderrahmane Mami Hospital, Ariana/Tunisia,* [3]*Medical Oncolog, Abderrahmane Mami Hospital, Ariana/Tunisia*

Background: Bronchial carcinoids are rare and account among well differentiated neuroendocrine tumors, with low-grade malignancy. They are divided in two different groups: typical and atypical carcinoids. They have almost a better prognosis than other lung malignancies; however atypical carcinoids are more aggressive. Surgery remains the gold standard with the same requirements as other malignancies, although conservative techniques with broncho-plastic surgery for typical carcinoids are well established. However, their management has to be multidisciplinary, The purpose of this study was to assess the surgical management of primary broncho-pulmonary carcinoid tumors. **Methods:** We reviewed retrospectively 137 cases managed in our thoracic surgery department for bronchial carcinoid tumors during a twenty-three-year period, between 1992 and 2014. **Results:** There were 64 men and 73 women (sex-ratio: 0.87), with a mean age of 44.2 years. One hundred and twenty-one patients had typical carcinoids and 16 patients had atypical carcinoids. Respiratory symptoms were the chief complaint in 98.42%. CT showed a proximal obstructive mass in 52% of the cases, with lung consolidation or atelectasis in 77.2%. Bronchoscopy showed an endo-bronchial tumor in 82.67% of the cases. Anatomical resection had been achieved among 119 patients (86.9%) (Pneumonectomy: 24 cases, bilobectomy: 27 cases, lobectomy: 68), with extended resection to the left atrium in 2 cases and to the adjacent upper lobe in 1 case. Conservative resection was performed in 18 patients (13.1%) with typical carcinoid tumor (bronchotomy and resection of the tumor: 3 cases, anatomical segmentectomy: 3 cases, sleeve lobectomy: 12 cases). Lymph node metastases were present in 12.6% of the cases. The postoperative course was uneventful in 89.05% of the cases and complicated in 10.94%, with atelectasis being the most reported in 5 cases. One patient was readmitted and reoperated two months after surgery for post operative empyema. 2 patients deceased in the post operative course (1.4%). Follow-up revealed recurrence in one patient with a typical carcinoid and distant metastasis in 4 others (2 atypical and 2 typical carcinoids). The 5-year survival rate was 45% for atypical carcinoid vs 95% for typical carcinoid. Reported prognostic factors for typical carcinoids were sex (male), the size of the tumor and lymph nodes involvement. **Conclusion:** Carcinoids are rare malignant tumors, almost with a favorable outcome after surgery, given that their resection is complete, with a thorough lymph node dissection. However, local recurrence and metastases can occur with both typical and atypical carcinoid tumors, justifying the need for early diagnosis and long-term follow-up. Survival rates in our series were largely influenced by the pathological type, distant metastasis and mediastinal lymph node involvement.
Keywords: Surgery, Typical carcinoid tumor, Atypical carcinoids, Prognosis

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-032 Phase II Clinical Trial of Stereotactic Ablative Radiotherapy (SABR) in Surgically Operable Stage I Non-Small Cell Lung Cancer (STARS)
Joe Y. Chang[1], Reza Mehran[2], Peter Balter[1], Stephen Mcrae[3], Lei Feng[4], Donald Berry[4], Ritsuko U. Komaki[1], Jack Roth[2] [1]*Radiation Oncology, MD Anderson Cancer Center, Houston/United States of America,* [2]*Thoracic Surgery, MD Anderson Cancer Center, Houston/AL/United States of America,* [3]*Radiology, MD Anderson Cancer Center, Houston/AL/United States of America,* [4]*Biostatistics, MD Anderson Cancer Center, Houston/AL/United States of America*

Background: Standard therapy for operable clinical stage I non-small cell lung cancer (NSCLC) is lobectomy with sampling or dissection of mediastinal lymph nodes. Stereotactic ablative radiotherapy (SABR) has produced local control rates in excess of 95% and has become standard care for medically inoperable stage I NSCLC. However, the role of SABR in operable stage I NSCLC remains controversial due to concerns about the risk of local or nodal recurrence after SABR, either of which could lead to worse OS than that after standard surgery. We report here the preliminary outcome using SABR in clinically operable stage I NSCLC. **Methods:** Patients with clinical T1A(≤3 cm)N0M0 biopsy proven operable NSCLC who meet criteria for lobectomy are being enrolled. All patients are staged with chest CT, PET/CT imaging, and EBUS. 54 Gy in 3 fractions was used for peripheral lesions and 50 Gy in 4 fractions for central lesions, respecting critical normal tissue dose volume constraints. SABR plans are typically optimized by using 6 to 12 coplanar or non-coplanar 6-MV photon beams (3-D CRT or IMRT) or Cyberknife or one to three arcs (VMAT). Daily CT-on-rail or a cone-beam CT scans or tumor tracking was used during each radiotherapy fraction. **Results:** Enrollment was started in September 2009, temporally closed in 2013 with 20 patients and re-opened in 2014. The study is ongoing and 58 patients have been enrolled up to date. The median follow-up time for the first 20 patients was 40 months; for all patients, median follow up was 7 months (range 0.8-49.6 months, interquartile 4.7, 22.8 months). No deaths have occurred to date. There was one local failure in the treated lobe that was salvaged with lobectomy. There were 5 cases of regional mediastinal lymph node progression treated with concurrent chemo/radiotherapy. Three of these cases had suspicious lymph nodes by CT and PET before SABR but were enrolled because EBUS was negative. One patient developed distant metastasis and was treated with chemotherapy. No one had grade 3-5 toxicity. Six patients had grade 2 chest wall pain (10.3%) and three patients developed grade 2 pulmonary toxicity (5%). **Conclusion:** SABR is well tolerated with minimal toxicity and promising local control and survival. More stringent mediastinal staging is recommended in the future.
Keywords: operable Stage I lung cancer, stereotactic radiotherapy, SBRT, SABR

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-033 Actual Situation of Adjuvant Chemotherapy for NSCLC in Japan
Ryu Nakajima, Hidetoshi Inoue, Michitaka Kimura, Takuma Tsukioka, Makoto Takahama, Ryoji Yamamoto *General Thoracic Surgery, Osaka City General Hospital, -- Miyakojima-Hondori Miyakojimaku Osaka/Japan*

Background: Several Clinical Trials were revealed survival advantage of adjuvant chemotherapy (AC) for completely resected NSCLC (increased 5 year survival rate by 4% to 15%), and AC has been standard of care for completely resected stage II to IIIA NSCLC. Further more, on JLCSG study has been revealed survival advantage of

adjuvant UFT treatment for Japanese stage I (size>2cm) patients. To investigate the practical situation of Adjuvant chemotherapy (AC) for completely resected NSCLC in our institution. **Methods:** We retrospectively reviewed completely resected NSCLC patients who were p-stage IA (Size > 2cm) to IIIA at our institution between 2005 and 2010. Enforcement status of AC, regimen and survival were analyzed. **Results:** Of the 648 had oncological indication of AC, but only 123 patients (19%) were received AC. Poor postoperative physical condition (25%), age (24%) and doctor's decision (Tumor size nearly 2cm, AIS) (22%) were popular reasons for avoid to AC. Ten presents of patients refuse AC by their intention. Forty-nine percent of patients were received AC by platinum doublet regimen and 33% were UFT regimen. Treatment related death and severe adverse event were not observed in all AC treatment. **Conclusion:** AC is standard of care for completely resected stage II to IIIA NSCLC and safety performed in practical situation. But majority of patients could not receive it. **Keywords:** NSCLC, adjuvant chemotherapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-034 Induction Therapy with Intercalated TKI and Chemotherapy in NSCLC with Activating EGFR Mutation in Stages II-IIIB: NeoIntercal

Frank Griesinger[1], Martin Sebastian[2], Monika H. Serke[3], Christian Grohé[4], Lars Hillejan[5], Bernward Passlick[6], Nils Reinmuth[7], Ullrich Graeven[8], Anne C. Lueers[9], Susanne M. Radke[10], Aysun Karatas[11], Markus Tiemann[12], Lukas Heukamp[12], Tobias Overbeck[13]
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Background: EGFR TKI treatment is standard of care in patients with metastasized NSCLC carrying an activating EGFR mutation. 1st and 2nd generation agents lead to response rates of up to 70% in metastatic EGFRM+ NSCLC. Recently, new light has been shed on intercalated regimens of chemotherapy and TKI have shown improved PFS as well as OS in the metastatic setting in an unselected Asian population (Wu *et al.* 2013 *The Lancet Oncology* 14 (8): 777-86). Response is a predictor of PFS and OS in limited and locally advanced NSCLC. Chemotherapy induction alone leads to pCR rates of no more than 15%. No data have been generated for induction therapy including EGFR TKI in EGFRM+ NSCLC. Four cases treated in one center have demonstrated the feasibility and tolerability of an intercalated induction therapy concept (Lüers *et al. 2013* Abstract WCLC). **Methods:** Therefore, NeoIntercal a single arm phase II study has been initiated in 9 centers in Germany. In a first step, patients with stage II to IIIB staged according to local standards will be screened for EGFR mutations by a ring certified pathologist. EGFRM+ patients will receive gefitinib 250 mg / die p.o. on d-12 to -1 (d1 = first day of first cycle of chemotherapy) followed by 3 cycles of taxane and platinum containing chemotherapy with intercalated gefitinib on d4-d20 of each cycle. After 2 cycles, restaging CT is performed and patients are scheduled to undergo surgery during the 4th or 5th week of the last cycle of CTx-gefitinib. Pathologic response rate is the primary endpoint. If more than 30% of patients achieve pCR (regression grades IIB and III according to Junker) in the mediastinal lymph nodes, it is planned to additionally enroll 28 patients in the 2nd part of the study. Secondary endpoints include OS, PFS, relapse rate and pattern, toxicity and feasibility. A liquid biopsy project is included in the study to correlate EGFR mutation status from tumor biopsy results with ctDNA plasma analysis. Furthermore, therapy effects will be monitored by liquid biopsy. **Results:** Study preparation and recruitment of clinical trial centers is nearly completed and the enrollment of the first patient is planned for 3Q2015. An interim analysis will be performed approximately 12 months after enrollment initiation with data from 21 patients. Should the interim analysis be positive and an additional 28 patients are included, the study is scheduled to end in approximately 2019 after a follow up period of 24 months. **Conclusion:** According to our knowledge, NeoIntercal is the first study in the neoadjuvant setting with curative intent applying an intercalating combination of chemotherapy and targeted therapy. The NeoIntercal study group believes that this study will potentially contribute to the improvement of EGFRM+ NSCLC therapy. **Keywords:** EGFR TKI, activating mutation, gefitinib, neoadjuvant therapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-035 Is There an Optimal Time to Initiate Adjuvant Chemotherapy in Order to Predict the Benefit of Survival in Non-Small Cell Lung Cancer?

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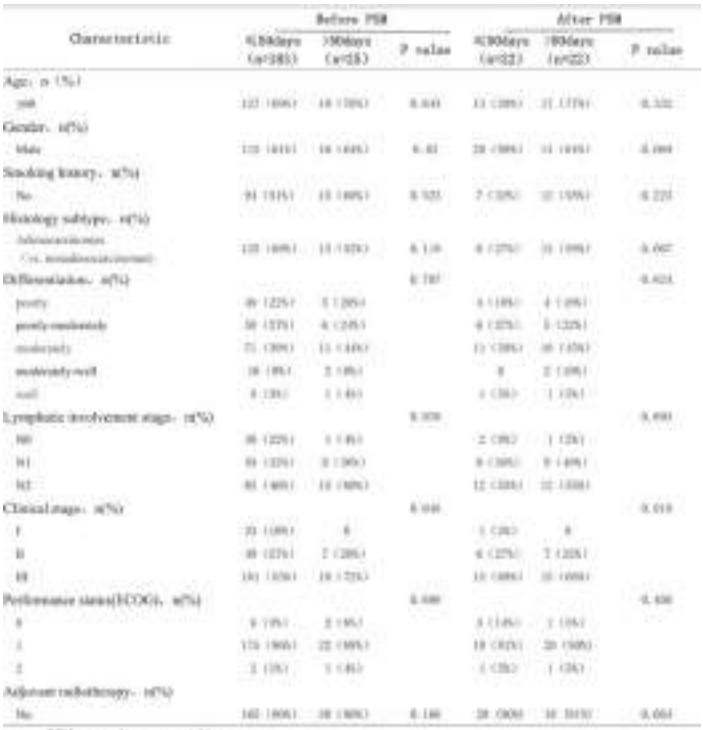
Background: Adjuvant chemotherapy (ACT) improves the survival for completely resected non-small cell lung cancer (NSCLC) patients. However, there are very few reports to explore the correlation between time of initiation of adjuvant chemotherapy (TTAC) and survival. **Methods:** 208 completely resected NSCLC patients received adjuvant chemotherapy in Cancer Hospital, Chinese Academy of Medical Sciences from 2001-2010 were analyzed. TTAC was measured from the date of surgery to initiation of ACT. Disease-free survival (DFS) was defined as the duration from the surgery to the time of relapse or last follow-up. Optimal cutoff value of the TTAC was determined by maximally selected log-rank statistics. Survival analysis was performed using Kaplan–Meier estimates, log-rank tests and Cox's proportional hazards regression analysis. Propensity score matching (PSM) was used, and a survival analysis of the match data was carried out. **Results:** The best discriminating cutoff value of TTAC was the 50th day(Figure 2). According to the cutoff value of 50, patients were divided into 2 groups, group1 (≤50days, n=183) and group2 (>50 days, n=25). Figure 1 shows the baseline characteristics of the two groups of patients before and after PSM .There was significant difference in DFS between the two groups (mDFS: 737days vs. 369days, P=0.005)(Figure 2), and the TTAC was found to be a significant predictive factor for DFS in multivariable analysis (P =0.035).Unfortunately, DFS was not continually significant difference in 22 PSM pairs (mDFS:576days vs. 369days,P=0.122) (Figure 2).



Characteristic	Before PSM			After PSM		
	≤30days (n=183)	>30days (n=25)	P value	≤30days (n=22)	>30days (n=22)	P value
Age, n (%)						
Gender, n(%)						
Smoking history, n(%)						
Histology subtype, n(%)						
Differentiation, n(%)						
Lymphatic involvement stage, n(%)						
Clinical stage, n(%)						
Performance status(ECOG), n(%)						
Adjuvant radiotherapy, n(%)						

PSM propensity score matching

Figure 1. Patients demographic characteristics and propensity score-matched characteristics between two groups.

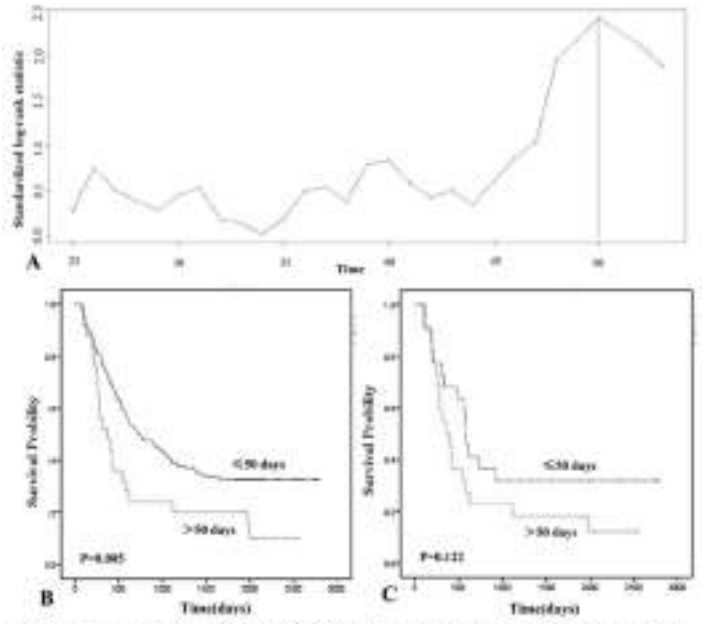


Figure 2. A.Optimal cutoff values of the TTAC by maximally selected log-rank statistics. Kaplan-Meier curve for NSCLC disease-free survival(DFS) according to interval between surgery and chemotherapy initiation.B.In all patients,there was significant difference in the DFS between patients who received adjuvant chemotherapy within 50 days and later than 50 days(P=0.005). C.In propensity score-matched pairs,DFS was not significant difference between the 2 groups(P=0.122).

Conclusion: TTAC does not appear to be associated with DFS in NSCLC. The conclusion was limited by the small sample size; therefore the number of patients between the groups was not close. Larger sample of cases should be warranted in future. **Keywords:** non-small cell lung cancer, adjuvant chemotherapy, time to adjuvant chemotherapy, disease free survival

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-036 Radiation Therapy Alone in cT1-3N0 Lung Cancer Patients Who Are Unfit for Surgery or Stereotactic Ablative Radiation Therapy Yong Chan Ahn, Wonkyung Cho, Jae Myung Noh, Dongryul Oh, Hongryull Pyo *Radiation Oncology, Samsung Medical Center, Seoul/Korea*

Background: High dose radiation therapy (RT) alone is recommended to cT1-3N0 lung cancer patients, who are unfit for surgical resection or stereotactic RT based on medical comorbidity, tumor size and location. This study is to evaluate clinical outcomes and costs following definitive RT alone using 2 modest hypo-fractionated dose schemes. **Methods:** Retrospective review on 116 patients who received high dose RT alone from January 2001 till December 2013 was done. Median age was 74 years and 91 patients (78.4%) were male. All had cT1-3N0 disease and 65 patients (56.0%) had squamous cell carcinoma, followed by adenocarcinoma in 35 (30.2%). Dose-fractionation scheme of 60 Gy in 20 fractions over 4 weeks was applied to 79 patients from 2001 till 2010 (68.1%, Group I). Meanwhile, 2 dose-fractionation schemes were used from 2011 till 2013: 60 Gy in 20 fractions to 17 patients (14.7%, Group II); and more hypo-fractionated scheme of 60 Gy in 15 fractions over 3 weeks to 20 patients (17.2%, Group III). 60 Gy in 15 fractions was chosen on individual basis if RT-related acute side effects (bronchitis, esophagitis) could be avoided based on tumor location and geometry. Group I/II patients had central tumors (defined as within 2 cm from lobar bronchi) more frequently (78.5% vs. 64.7% vs. 35.0%, p<0.0001), and larger mean tumor size (4.2 cm vs. 5.0 cm vs. 3.8 cm, p=0.0725) than Group III. Elective nodal irradiation to regional lymphatics (median 30 Gy/10 fractions) was delivered to 30 patients: 23 in Group I (29.1%); seven in Group II (41.2%); and none in Group III (0%), respectively (p=0.0341). Local control (LC), progression free survival (PFS), overall survival (OS), and RT-related toxicity profile were estimated and compared. **Results:** After median 19.3 (1.2-119.5) months' follow-up, 68 patients (58.6%) experienced disease progression, and 66 (56.9%) died. 2-year LC and PFS rates of all patients were 62.0% and 39.3%, respectively, which were not different between Groups (59.3% and 36.1% vs. 52.1% and 26.9% vs. 78.8% and 61.6%, p=0.3010 and 0.1620, respectively). 2-year OS rate of all patients was 57.5%, and was significantly better in Group III (51.3% vs. 69.1% vs. 83.0%, p=0.0232). Grade ≥2 pneumonitis developed in 27 patients (23.3%), and was not different between Groups (19.0% vs. 35.3% vs. 30.0%, p=0.1908), while Grade ≥2 esophagitis developed in 22 patients (19.0%), however, none in Group III (22.8% vs. 23.5% vs. 0%, p=0.0373). Good performance status (ECOG 0-1 vs. 2-3) and low cT-stage (T1-2 vs. T3) were significantly favorable factors affecting LC, PFS, and OS, however, central location of tumor was not. Costs incurred by RT under Korean Health Insurance Policy were 6,080,000 KW in Groups I and II and 4,707,500 KW in Group III, respectively. **Conclusion:** Hypo-fractionated RT delivering 60 Gy in either 15 or 20 fractions could lead to reasonably favorable and comparable clinical outcomes in cT1-3N0 lung cancer. 60 Gy in 15 fractions in selective cases as in Group III, however, seems more cost-effective and attractive by virtue of shorter RT duration, lower cost, and increased patients' convenience. **Keywords:** non-small cell lung cancer, hypofractionated radiation therapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-037 Evaluation of the Dosimetric Characteristics of Salvage Lung SBRT with Image Deformable Registration Technique Kaile Li[1], Eward Jung[2] [1]*Radiation Oncology, John R Marsh Cancer Center, Hagerstown/United States of America,* [2]*Radiation Oncology, John R Marsh Cancer Center, Hagerstown/AL/United States of America*

Background: Treatment planning for salvage radiation therapy after failing initial treatment is challenging. Many factors can contribute to local failure, including inherent aggressiveness of the tumor, target motion localization accuracy, and dose delivery variation. Especially when a patient is re-treated for local failure with repeat lung SBRT at a different institution, or using a different radiation treatment platform or software, treatment planning becomes very complex. In particular, it is crucial to create a reliable composite plan to determine the dose delivered to critical structures to prevent serious complications with repeat lung SBRT. Another factor which has not been well studied is a method to compare temporal changes in dose delivered to the target volume after initial treatment, which can surely affect local control. We present a method to compare lung SBRT treatments and analyze the dosimetric characteristics of salvage lung SBRT by applying image deformation registration techniques with dose distributions, and incorporating temporal changes in dose over time. **Methods:** A patient treated with repeat lung SBRT to a region of local failure involving the left upper lobe was used for analysis. The target volume was initially treated on a CyberKnife radiosurgery unit, and then re-treated with lung SBRT on a Varian Trilogy machine (LINAC). Dosimetric characteristics were compared for these two platforms. Indexes used for analysis include target volume dose coverage, and dose target dose conformity, which is quantified by conformity index (CI), integrated conformity index (ICI), dose spillage level outside of treatment target, and dose to the critical structure. The spillage is defined to be the ratio of maximum dose ouside of the target to the maximum plan dose.Treatment dose effect was described by Biologically Effective Dose (BED) with dose conversion by considering changes in BED over time. CyberKnife SBRT dose distribution was converted for treatment with salvage SBRT with deformable registration by MIM software. **Results:** Parameters were compared for initial CyberKnife SBRT treatment alone, salvage LINAC SBRT treatment alone, and composite sum SBRT with deformable registration. Assuming α/β =10 for the tumor, the calculated BEDs were 100, 138, and 127, respectively. The corresponding CIs were 1.03, 1.18, and 1.28. The ICIs were 0.894, 0.807, and 0.881. Dose spillages were 0.81, 0 .78, and 0.56. V20 was 4.9%, 7.2%, and 5.4% for each plan. **Conclusion:** This study provides a method to estimate the dosimetric characteristics of lung SBRT from different treatment platforms with incorporation of temporal loss of dose between initial and salvage treatments. Deformable registration accuracy and the appropriate parameters affecting local control of lung tumor need further investigation and validation. **Keywords:** Biologically Effective Dose (BED), Deformable Registration, Stereotactic Body Radiotherapy (SBRT), Salvage Lung SBRT

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-038 Clinical Evaluations of Odd/Even Respiratory Phases Based Approach for Determining Internal Target Volume in NSCLC Treated with 4D SABR Xia D. Li[1], Qing-Hua Deng[1], Li-Dan Zhang[1], Yao Ren[1], Jiale Gu[1], Sheng-Lin Ma[1], Zhi-Bing Wu[1], Jia-Hao Wang[1], Gang Li[2] [1]*Radiotherapy, Hangzhou Cancer Hospital, Hangzhou/China,* [2]*Radiotherapy, Xiaoshan Hospital of Zhejiang, Hangzhou/China*

Background: Appropriate definition of the target volume with an efficient approach remains a major challenge for early stage NSCLS treated with SBRT technique; one of crucial disturbed factors in delineation of target volume is the tumors movement due to irregular respiration patterns(3), to account for tumor motion, the ICRU Report 62 introduced the concept of an internal target volume (ITV), defined as the clinical target volume (CTV), plus an additional margin to account for geometric uncertainties due to variable tumor motion (4), Conventionally, a free-breathing three-dimensional (3D)-CT scan was adopted to acquire the patient's anatomic information which leads to geometric distortions (5). To account for these geometric uncertainties, large target volumes are needed, thereby limiting the effectiveness of the radiotherapy (6). To reduce geometric uncertainties in 3D-CT images, time related four-dimensional CT (4D-CT) scanning techniques have been developed in radiation therapy to obtain information about volumetric organ motion associated with respiration. And various methods for definition of the target volume using 4D-CT scans in treatment planning have been reported recently(7,8,9,10), the most accurate method of determining ITV is combined by contouring in each phase of the 4DCT dataset (typically 10 phases). Although this method is widely accepted as a golden standard for delineation of ITV , it poses more efforts and time consuming due to the increased workload for radiation oncologists. To Improve work efficiency many efforts has been done to reduce the workload meanwhile maintain a reasonable ITV, the maximal intensity projection (MIP) dataset has been widely applied in the clinic to define ITV in the early stage; some other researchers investigated ITV from 4D-CT such as ITV2ep(including two extreme phases) and ITV4phase= ITV2ep+ two phases (20% and 70%) , The matching index (MI) was adopted to evaluate the marching degree between different determining approaches,in this research, we will proposed a new approach to definite an ITV with the best marching index meanwhile with the least time and human resource. **Methods:**December 2013 and March 2014, 46 patients who underwent SABR were included in this retrospective study. All patients underwent imaging with 4DCT scans, The MI and DI index were evaluated $ITV_{10,}$ $ITV_{Yeo,}$ $ITV_{EI+EE,}$ And combining GTV from five odd phasesITVodd, Accordingly the ITV_{EVEN} , and ITV_{AVG} ,ITV_{MIP} were Contoured from two reconstructed 4D-CT Sequences, finally, a method which was not sensitive to the tumor volume and motion Characteristic was selected for clinical use. **Results:** The mean tumor motion (RLR, RAP, RCC, and R3D) were 3.5mm(1.4mm~8.4mm), 4.5mm(1.1mm~8.6mm), 9.5mm(0mm~10mm), 12.3mm (2.5-55.3 mm) respectively. IGTVx volume were Underestimated by25.7%、35.6%、17.9%、12.8%、3.6%、4.8% (P=0.000) respectively. MI index comparisons between six ITV generation methods and ITV_{10} showed statistical significance: 0.69、0.62、0.80、0.86、0.93、0.91 (P=0.006) , DI index showed no statistical significance: 0.98、0.98、0.97、0.97、0.99、0.98 (P=0.13) , the tumor size and motion amplitude were certified not the independent factors for the MI index of ITV_{odd} and ITV_{EVEN} **Conclusion:** $IGTV_{ODD/EVEN}$ based on odd or even 4D-CT phases was not sensitive to tumor size or motion characteristic and was proved to have a good marching with ITV_{10} meanwhile Maintaining a reasonable contouring efficiency, it can be recommend to the institutions which not equipped with the deformable registration systems. **Keywords:** non-small cell lung cancer, Stereotactic ablative radiotherapy, internal target volume, 4DCT

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-039 Patterns-Of-Care Study of Stereotactic Ablative Radiotherapy for Lung Cancer in Korea Sanghyuk Song[1], Hak Jae Kim[2], Jin Hee Kim[3], Jae-Sung Kim[4], Yong Chan Ahn[1], Yeon Sil Kim[5], Si Yeol Song[6], Sung Ho Moon[7], Moon June Cho[8], Seon Min Youn[9], Won Il Jang[10] [1]*Samsung Medical Center, Seoul/Korea,* [2]*Seoul National University Hospital, Seoul/Korea,* [3]*Keimyung University, School of Medicine, Taegu/Korea,* [4]*Seoul National University Bundang Hospital, Seongnam/Korea,* [5]*Seoul St. Mary'S Hospital, Seoul/Korea,* [6]*Asan Medical Center, Seoul/Korea,* [7]*National Cancer Center, Goyang/Korea,* [8]*Chungnam National University Hospital, Daejeon/Korea,* [9]*Eulji University Hospital, Daejeon/Korea,* [10]*Korea Institute of Radiological & Medical Sciences, Seoul/Korea*

Background: Stereotactic ablative radiotherapy (SABR) is an emerging effective technique for early stage lung cancer. We investigated the current practice patterns for stereotactic ablative radiotherapy (SABR) for lung cancer in Korea. **Methods:** A nationwide survey about experience with SABR for lung cancer was sent by e-mail to the radiation oncologists of 85 institutions in May 2014. SABR was defined as hypofractionated radiotherapy (1–8 fractions). The survey contained 23 questions, and those regarding technical details allowed multiple choices. **Results:** Of the 59 institutions that responded to the survey, 33 (56%) had used SABR for lung cancer. Thirty-seven radiation oncologists from these 33 institutions responded to the survey. Seventy-five percent of the oncologists had been treating lung cancer with SABR for less than 5 years, while 89% treat less than 20 cases annually. The most common planning method was rotational intensity-modulated technique (59%), followed by static intensity-modulated technique (49%). A wing board (54%) was most frequently used for immobilization, followed by the vacuum lock system (51%). Respiratory motion was managed by gating (54%) or abdominal compression (51%), and 86% of the planning scans were obtained with 4-dimensional computed tomography. More than half of the respondents (62%) treated daily if a multi-fraction

regimen was used. **Conclusion:** The results of our survey indicated that SABR for lung cancer is being used increasingly in Korea, and that the majority of radiation oncologists using this therapy have limited experience in its use. There was wide variation among institutions with regard to the technical protocols, which indicates that standardization is necessary prior to the initiation of further nationwide multi-center, randomized studies. **Keywords:** lung cancer, Stereotactic ablative radiotherapy, Patterns-of-care, Survey

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-040 Clinical Outcome of Fiducial-Less CyberKnife Stereotactic Ablative Body Radiotherapy for Stage I Non-Small Cell Lung Cancer Inhye Jung, Si Yeol Song, Jinhong Jung, Byungchul Cho, Jungwon Kwak, Hyoung Uk Je, Wonsik Choi, Nuri H. Jung, Eun Kyung Cho *Radiation Oncology, Asan Medical Center, Seoul/Korea*

Background: CyberKnifeTM is a dedicated system for radiosurgery, with a capability of real-time tumor tracking; Synchrony® Respiratory tracking system. Xsight® lung tracking system with Synchrony® Respiratory tracking system make possible direct lung tumor tracking without fiducial markers. However, there was no established indication of fiducial-less Cyberknife Radiosurgery (CKRS). So, to ascertain whether indication of fiducial-less CKRS can be extended or not , we had evaluated treatment outcome of fiducial-less CKRS using Xsight® lung tracking system at AMC and tested accuracy of CyberKnife Xsight® lung tracking system without fiducial marker by phantom experiment. Here are the results of fiducial-less CKRS using Xsight® lung tracking system for stage I NSCLC. **Methods:** From June 2011 to November 2013, 58 patients received Cyberknife Radiosurgery to lung at Asan medical center. We retrospectively reviewed records of 44 patients of stage I lung cancer exclude 14 patients (6 with Advanced NSCLC, 6 with Rec. lung cancer within 5 years, 2 with lung metastasis from other primary cancer). All analyses were performed using SPSS, version 21. **Results:** Median age at diagnosis was 75 years. Man was 37 (84.1%). Most of patients were inoperable primary lung cancer with poor PFT (mean FEV1: 63.0 % (range 24-138%), mean DLCo: 50.8 % (range 43- 96 %)) or comorbidity or old age. Clinical stage was IA in 30 (68.2 %), IB in 14 (31.8 %) patients. Mean tumor size was 2.6 cm. (1.2 cm-4.8cm, smaller than 2 cm was 12 (27.3%)) Radiation dose were 48 – 60 Gy per 3 - 4 fx. With median follow-up of 23.1 months, there were LR in 3 patients (1Y LRFSR: 94.9%, 2Y LRFSR: 90.4%) and DM in 13 patients (DM only, n= 7). All patients tolerated the radiosurgery well, only 2 patients had grade 3 dyspnea (1 of 2 suffered from ILD aggravation). Most common complication was RT-induced fibrosis & pneumonitis. Eight patients have died due to cancer progression.(1Y OSR: 86%, 2Y OSR: 80.3%) **Conclusion:** Fiducial-less cyberknife radiosurgery showed good local tumor control and survival in medically inoperable stage I NSCLC, which was comparable with that of linac-based stereotactic body radiosurgery or CKRS with fiducial marker. Even though there were some limitations to apply Xsight ® lung tracking system without fiducial marker, but it could be used safely in relatively small tumor located in not recommended site. **Keywords:** lung cancer, cyberknife radiosurgery (CKRS), fiducial marker

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.02-041 Stereotactic Body Radiotherapy (SBRT) or Surgery in Early Stage (I & II) Non Small Cell Lung Cancer (NSCLC) Hirsh Koyi[1], Gunnar Hillerdal[2], Signe Friesland[3], Karl Gustav Kölbeck[2], Olov Andersson[2], Per Bergman[4], Lotta Orre[4], Per Liv[5], Eva Brandén[1] [1]*Department of Respiratory Medicine, Gävle Hospital, Gävle/ Sweden,* [2]*Deartment of Respiratory Medicine, Karolinska University Hospital, Stockholm/ Sweden,* [3]*Dept of Oncology, Karolinska University Hospital, Stockholm/Sweden,* [4]*Deprtment of Thoracic Surgery, Karolinska University Hopsital, Stockholm/Sweden,* [5]*Centre for Research and Development, Uppsala University/County Council of Gävleborg, Gävle/Sweden*

Background: For patients with NSCLC clinical stages I and II disease with no medical contraindications, surgery is treatment of choice showing 5-year survival rates of about 60–80% for stage I and 40–50% for stage II, respectively. However, for patients who are medically or technically unfit for surgery and for patients refusing surgery, SBRT) is an alternative with local control rates >90% at 3 years. **Methods:** Medical journals in all patients with stage I or II NSCLC who were underwent surgery and treated with SBRT at the Department of oncology or thoracic surgery, Karolinska University Hospital, Sweden from 2003 to 2009 were retrospectively reviewed. **Results:** In all, 186 (78.2%) underwent surgery and 52 (21.8%) were treated with SBRT. Mean, median and range of age among the surgery group was 69.29, 70.52 and 45-85 years, while in the SBRT group, these figures were 78.04, 80.03 and 61-89 years. The difference in age between the groups was significant (p=0.03).There were significantly more comorbidites in the SBRT group. Among the surgery group, 91.3% were smokers or former smokers. The figures for SBRT group was 94.1%. There was a significant difference in performance status (PS) between the groups (p<0.001) with with PS 0-1 in 98.9% in the surgery group compared with 69.2% in the SBRT group. There was a significant difference in lung function with mean FEV1 2.15 liter in surgery group compared to 1.45 in the SBRT group. The figures for mean FEV1% was 83% respectively 57.5%. The median overall survival was 97 months for the surgery group and 61.8 months for the SBRT group (p<0.001). **Conclusion:** The much worse median overall survival in the SBRT group can be explained by the selection of patients, but still, a survival of more than 5 years in an elderly group with so many comorbidities and a bad PS indicates that SBRT has been of value. **Keywords:** early stage, Surgery, stereotactic body radiotherapy

SESSION: POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC TUESDAY, SEPTEMBER 8, 2015

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-001 Perioperative Cardiac Events in Patients with Coronary Artery Stent Undergoing Lung Resection for Lung Cancer Takayuki Ibi, Taichiro Ishizumi, Tatsuya Inoue, Akira Sato, Kyoshiro Takegahara, Toriyama Sayuko, Jitsuo Usuda *Thoracic Surgery, Nippon Medical School Hospital, Tokyo/Japan*

Background: Many patients with coronary artery disease (CAD) receive coronary artery stents. Some of them require major lung resection for non-small cell lung cancer (NSCLC). Patients with coronary artery stent have problems with antiplatelet therapy. After coronary artery stent, patients need dual antiplatelet therapy for a while to decrease the risk of stent thrombosis. The ACC/AHA Guidelines recommended continuation of dual antiplatelet therapy for 4 to 6 weeks after bare-metal stent (BMS) placement and 12 months for a drug-eluting stent (DES). Lung resection with discontinuation of antiplatelet therapy may increase a risk of perioperative coronary event in patients with CAD. Many patients with coronary artery disease (CAD) receive coronary artery stents. Some of them require major lung resection for non-small cell lung cancer (NSCLC). Patients with coronary artery stent have problems with antiplatelet therapy. After coronary artery stent, patients need dual antiplatelet therapy for a while to decrease the risk of stent thrombosis. The ACC/AHA Guidelines recommended continuation of dual antiplatelet therapy for 4 to 6 weeks after bare-metal stent (BMS) placement and 12 months for a drug-eluting stent (DES). Lung resection with discontinuation of antiplatelet therapy may increase a risk of perioperative coronary event in patients with CAD. **Methods:** This retrospective analysis is based on all patients with coronary artery stent requiring major lung resection for NSCLC between January 2011 and December 2013 at Nippon Medical School Hospital, Tokyo, Japan. We retrospectively examined major adverse cardiac events (MACE) and perioperative management of the patients with coronary artery stent requiring major lung resection for NSCLC. **Results:** There were thirteen patients (5.8%) with coronary artery stent in two hundred twenty six patients who underwent radical lung cancer resection. The stent group had more males (p = 0.020). There were no differences in age, histological type, operative procedure, intraoperative blood loss, pathological stage and perioperative complication. Thirty-day MACE occurred one patient in the no-stent group (0.4%). There was no patient of MACE in the stent group. Overall 3-year survival rates were 93.2% and 92.3% in the no-stent group and the stent group, respectively (p = 0.545). In the stent group, all patients were managed by cardiologists to estimate the coronary risk and preoperatively discontinued aspirin and clopidogrel. Eight patients had taken cilostazol by three days before operation day, instead of aspirin. **Conclusion:** In this retrospective study, patients with coronary stent undergoing surgical therapy for NSCLC were not at risk of for perioperative MACE. Larger prospective studies are required to conclude the risk of in-stent thrombosis in patients with coronary stent required lung resection. **Keywords:** lung cancer, ischemic heart disease, coronary, stent

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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P2.03-002 Surgery for Locally Advanced Lung Cancer after Induction Concurrent Chemo-Radiation Therapy Kazunori Okabe[1], Hiroyuki Tao[2], Toshiki Tanaka[2], Tatsuro Hayashi[2], Kouichi Yoshiyama[2], Masashi Furukawa[2], Kumiko Yoshida[2], Hiroshi Ueoka[2], Tsuneo Matsumoto[2] [1]*Thoracic Surgery, Yamaguchi Ube Medical Center, Ube/Japan,* [2]*Yamaguchi Ube Medical Center, Ube/Japan*

Background: The prognosis of locally advanced non-small-cell lung cancer is very poor. According to the American Cancer Society website, 5-year observed survival rate of Stage IIIA is 14%, and that of IIIB is 5%. A highly effective treatment strategy is needed to improve it. Surgery after induction concurrent chemo-radiation therapy for locally advanced non-small-cell lung cancer in our hospital over the last 8 years was retrospectively reviewed. **Methods:** Our standard induction chemo-radiation therapy consisted of cisplatin 40 mg/m^2 and docetaxel hydrate 40 mg/m^2 given on days 1, 8, 29, and 36 plus concurrent irradiation of 46 Gy (2 Gy/day) to the tumor, hilum, and mediastinum. Surgery was performed between 4 and 6 weeks after completion of the radiotherapy. 37 consecutive patients with 21 cases of lobectomy and 16 cases of pneumonectomy were reviewed. The median age at surgery was 62 (41 – 74) years old. There were 6 females and 31 males. Adenocarcinoma was present in 18, squamous cell carcinoma in 13, large cell neuroendocrine carcinoma in 2, adenosquamous cell carcinoma in 1, giant cell carcinoma in 1, NSCLC in 1, and atypical carcinoid which was preoperatively diagnosed as squamous cell carcinoma in 1. The pretreatment stage was IIIB in 11, IIIA in 20, IIB in 3, IIA in 1, and IB in 2. The pretreatment very high tumor marker levels in blood were as follows: CEA 367, 337, 266, 180, 154, 151, 105 ng/ml, CYFRA 47, 23, 20 ng/ml, and SCC 15, 10 ng/ml. Survival was calculated using the Kaplan-Meier method, and analyzed by the Log-Lank test. **Results:** Toxicity was manageable, and no serious complication was noted. All 37 cases were R0 resection. The median operation time of 21 cases of lobectomy and 16 cases of pneumonectomy were 5 hr 4 min and 4 hr 35 min, respectively. The median bleeding time of 21 cases of lobectomy and 16 cases of pneumonectomy were 200 ml and 175 ml, respectively. A pathologically complete response was obtained in 11 (30%) patients. The pathological stage was complete response in 11, IIIB in 3, IIIA in 6, IIB in 5, IIA in 4, IB in 2, and IA in 6. All abnormal blood tumor marker levels went down to normal. At a median follow-up period of 3 years 4 months (5 months - 8 years 8 month), 5-year survival rate of all 37 patients was 80%, and that of 21 lobectomy patients was 63%. Although 2 patients

had recurrent tumors, 16 pneumonectomy patients were all alive without oxygen therapy. The prognosis of pneumonectomy was significantly better than lobectomy ($p < 0.05$). **Conclusion:** Surgery after induction concurrent chemo-radiation therapy for locally advanced non-small-cell lung cancer is feasible and highly effective. This treatment strategy has greatly improved the prognosis of locally advanced non-small-cell lung cancer. **Keywords:** lung cancer, multimodality treatment, surgery, induction chemo-radiation

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

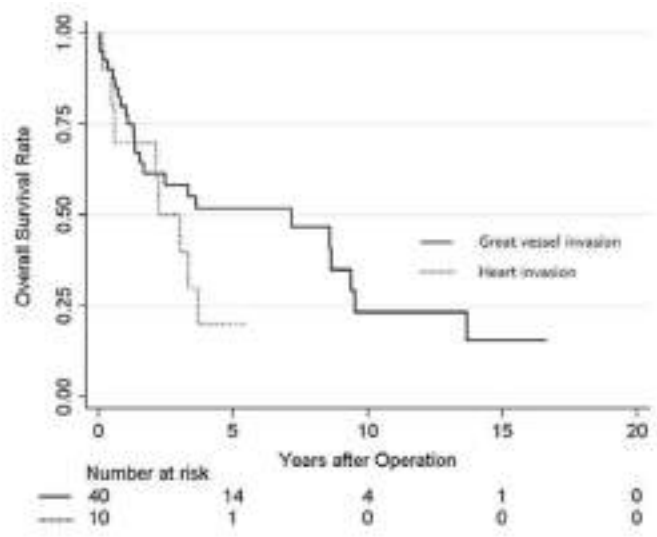
P2.03-003 Video Assisted Thoracoscopic Anatomical Resection for Non Small Cell Lung Cancer (NSCLC) Is Increasingly Safe Diego M. Avella[1], Ujala Bokhary[2], Brittany Lapin[2], Ki W. Kim[2], John Howington[2] [1]*Surgery, University of Chicago, Chicago/IL/ United States of America,* [2]*Thoracic Surgery, Northshore University Healthsystem, Evanston/ IL/United States of America*

Background: We analyze our institutional clinical data of patients that underwent video assisted thoracoscopic (VATS) anatomical lung resection for Non-small cell lung carcinoma (NSCLC). **Methods:** This is a retrospective analysis from January 1st of 2009 to December 31st of 2013. We extracted the data through standard queries and by manual extraction from the Electronic Data Warehouse of the NorthShore University Health System. The patients were selected based on surgical description of anatomical resection defined as lobectomy, bilobectomy or segmentectomy for proven NSCLC. Patients with more than one procedure performed, diagnosis of carcinoid tumor or incomplete data were excluded. The variables evaluated included demographics, preoperative workup and clinical evaluation, pathology reports, intra-operative data and post-operative outcomes. **Results:** A total of 224 patients were included. The mean age at the time of diagnosis was 70.9 years, 63% were females, 81.5% were Caucasian with a 37 pack-year smoking history. The most common comorbidities encountered were hypertension, COPD and coronary artery disease. Sixty four percent of patients were diagnosed with pathologic stage I, 20.5% with stage II and 13.2% with stage III disease. Eighty nine percent of patients had FEV_1 whereas DLCO was available in 83.6% of the patients. VATS lobectomy was performed in 84% of the patients and VATS segmentectomy in 14% of the patients. The mean procedure time was 157 minutes, the median length of chest drainage with tube thoracostomy was 2 days. Twenty three percent of the patients required admission to the Intensive Care Unit (ICU) with a median length of stay in the ICU of 1.1 days. The length of stay in the hospital was 3 days. The overall rate of complications was 30% with atrial fibrillation (17.9%), prolonged air leak (>5 days) (9.8%) and atrial arrhythmia (3.8%) being the most frequent complications. Atrial Fibrillation had a postoperative onset in 50% of the patients whereas 50% of the patients with history of atrial fibrillation did not have atrial fibrillation perioperatively. The median follow-up was 26 months. There were only two in-hospital deaths (0.9%). Recurrences occurred in 18.2% of the patients with a mean time of 1.5(±1.0) years after surgery (local: 62.7%/1.7 years; distant: 37.3% 1.3 years). The overall mortality rate was 12% with 90 day mortality of only 1% (unrelated to the procedure). The 1 and 3-year overall survival was 96.6% and 93.8% for stage I, 93.7% and 73.9% for stage II and 97.1% and 52.2% for stage III. The 1 and 3-year disease-free survival was 96.3% and 89.8% for stage I, 93.4% and 68.8% for stage II and 96.7% and 52.7% for stage III. **Conclusion:** Our data suggests that over the last several years the rate of complications, need for ICU admission, length of hospital stay and overall mortality associated with the VATS anatomical resection for all stages of NSCLC has decreased in comparison with reported analysis from national data. In our series the 1-year and 3-years survival of VATS anatomical resection are similar to the reported data for open thoracotomy. **Keywords:** Long term survival NSCLC

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-004 Surgical Outcomes of Locally Advanced Non-Small Cell Lung Cancer Invading Great Vessels and Heart Byungjoon Park[1], Hong Kwan Kim[2], Yong Soo Choi[3], Jae Ill Zo[3], Young Mog Shim[3], Jhingook Kim[2] [1]*Thoracic and Cardiovascular Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Seoul/Korea,* [2]*Thoracic & Cardiovascular Surgery, Samsung Medical Center, Seoul/ Korea,* [3]*Department Thoracic & Cardiovascular Surgery, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul/Korea*

Background: The role of surgery has been debated in locally advanced lung cancer, especially in cases with great vessel or cardiac invasion. The aim of this study was to evaluate predictive factors and clarify whether surgical resection is beneficial in lung cancer with great vessels and heart involvement. **Methods:** Patients who were surgically treated and pathologically diagnosed as T4N0/1 non-small cell lung cancer (NSCLC) with great vessel or heart invasion were enrolled and evaluated for surgical outcomes. Patients with other structural invasion to trachea, carina, esophagus, and vertebrae were excluded. Patients with previous history of other malignant disease or double primary cancer were also excluded. **Results:**We included 50 patients and mean age was 63 9 years old. The structural involvement included main pulmonary artery (54%), pulmonary vein (38%), aorta (12%), superior vena cava (10%) and heart (10%). Complete resection was achieved in 45 patients (90%) and 5 patients underwent tumor resection under cardio-pulmonary bypass. In-hospital mortality was 12% and 5-year overall and disease-free survival rate was 44% and 40%, respectively. Multivariate analysis demonstrated that right sided cancer ($p = 0.023$), grossly incomplete resection (R2; $p = 0.032$), pneumonectomy ($p = 0.029$), and large cell neuroendocrine cancer ($p < 0.001$) were significant unfavorable prognostic factors for overall survival. NSCLC with heart invasion showed worse 5-year overall survival than NSCLC with great vessel involvement (53% vs. 20%), but did not show statistical significance ($p = 0.143$) due to small number of patients (Figure).

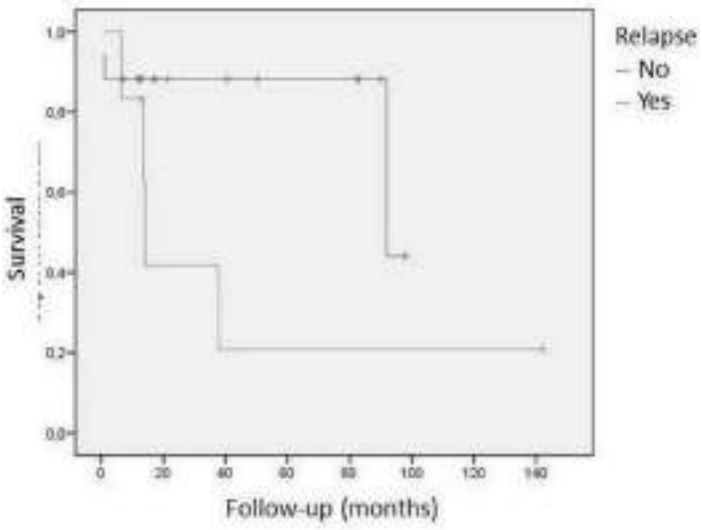


Conclusion: Surgical resection of locally advanced lung cancer involving great vessels or heart showed an important role with affordable outcomes. **Keywords:** non-small cell lung cancer, locally advanced lung cancer, great vessel, Surgery

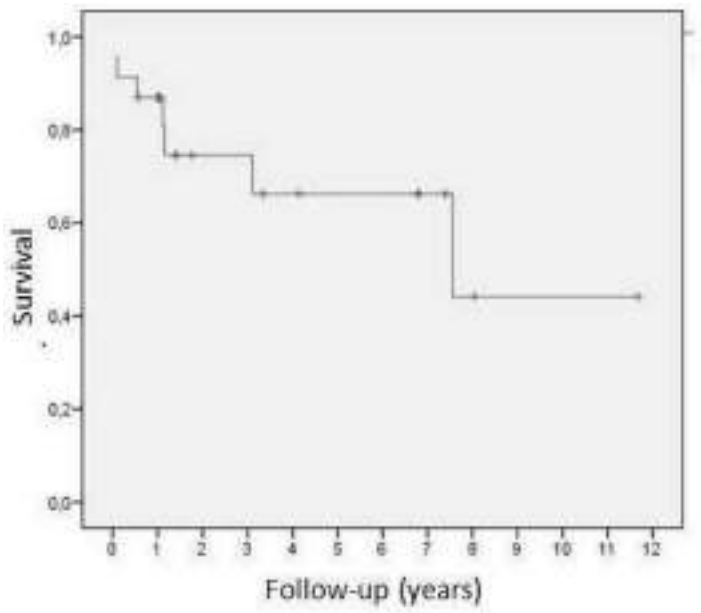
POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-005 Surgical Resection after Definitive Chemoradiotherapy Laura Romero Vielva, José A. Maestre, Santiago Viteri, Maria Gonzalez Cao, Daniela Morales, Rafael Rosell *Thoracic Surgery, Dr. Rosell Oncology Institute, Quiron Dexeus University Hospital, Barcelona/Spain*

Background: Approximately, 30% of non-small-cell lung cancer (NSCLC) patients are diagnosed with locally advanced disease (IIIA-B). Treatment of these patients is controversial, with recommendations including definitive chemoradiotherapy, induction chemotherapy followed by surgery or induction chemoradiotherapy followed by surgical resection. Salvage surgery is defined as resection after high doses of radiation (>50Gy), planned as a primary curative intent, and usually more than 12 weeks after radiotherapy. Lung resection after high-dose radiotherapy has traditionally been avoided due to high rates of morbidity and mortality. **Methods:** The aim of this review is to analyze the outcome of patients referred to our institution for surgical resection after definitive chemoradiation. We reviewed 23 NSCLC patients who underwent surgical treatment after definitive chemoradiation between 2003 and 2014. **Results:** There were 15 men and eight women with a median age of 54.64 years (range 33-69 years). Fifteen patients were diagnosed with adenocarcinoma (65.2%), and the most frequent cTNM stage was T3N2M0 (34.8%) followed by T2N2M0 and T4N2M0. The type of surgical resection included five lobectomies, six bilobectomies and 12 pneumonectomies (seven right and five left pneumonectomies). Four patients showed a complete pathological response after treatment (pT0N0M0 17.4%). There was only one postoperative death due to a bronchopleural fistula. All patients received platinum-based chemotherapy and definitive radiotherapy, with a median dose of 65Gy (range 45-70Gy). Median time from radiotherapy to surgical resection was 8.28 months (0.9-35.47 months). Six patients suffered recurrence after surgery, three to a distant site and three local recurrences. Median disease free survival for the group of patients who relapsed after surgery was 7.7 months (3.9-17.5 months).



Median overall survival was 88.3 months (CI 95% 57.6–118.9), with 1, 3 and 5 year survival rates of 87%, 74.5% and 66.3% respectively.



Conclusion: Salvage surgery after definitive chemoradiotherapy is feasible, with low postoperative complication rates and encouraging survival. **Keywords:** salvage surgery, definitive chemoradiotherapy, outcome

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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P2.03-006 Survival Rates after Surgery for Stage-3A (N2) Non-Small Cell Lung Cancer with Induction versus Adjuvant Chemotherapy+/-Radiation Therapy
Eric M. Toloza[1], Tawee Tanvetyanon[1], Dung-Tsa Chen[2], Alberto Chiappori[1], Benjamin Creelan[1], Thomas Dilling[1], Jacques Fontaine[1], Jhanelle Gray[3], Eric Haura[1], Mary Pinder-Schenck[1], Lary A. Robinson[1], Craig Stevens[1], Charles Williams[1], Scott J. Antonia[1]
[1]*Thoracic Oncology, Moffitt Cancer Center, Tampa/FL/United States of America,* [2]*Immunology, Moffitt Cancer Center, Tampa/FL/United States of America,* [3]*Thoracic Oncology, Moffitt Cancer Center, Tampa/United States of America*

Background: We compared survival of stage-3A non-small cell lung cancer (NSCLC) patients (pts) after surgery without or with induction versus adjuvant chemotherapy ± radiation therapy (chemo±XRT). **Methods:** We retrospectively analyzed pts with clinical stage-3A (cStage3A) NSCLC and who had surgery without or with induction chemo±XRT or who were pathologic stage-3A (pStage3A) and had adjuvant chemo±XRT. Kaplan-Meier survival curves were compared for these 3 groups, with significant differences at $p \leq 0.05$ by Chi Square test, with Log Rank (Mantel-Cox), Breslow (Generalized Wilcoxon), and Tarone-Ware pairwise comparisons. **Results:** From 1/1986 to 12/2010, there were 300 NSCLC pts who were cStage3A at surgery. Another 52 pts were not cStage3A at surgery, but were then pStage3A. Of these 352 pts, 192 had curative resection, with 56 pts having surgery alone (SURG), 43 pts having surgery after induction therapy (NEOADJ), and 93 pts having surgery then adjuvant therapy (ADJ). Kaplan-Meier survival for SURG was worse than that for either NEOADJ (p=0.03) or ADJ (p=0.005), while NEOADJ and ADJ had similar survival (p=0.90). Median survival was 18±3 mon (95%CI: 12-24 mon) for SURG, 37±6 mon (95%CI: 25-50 mon) for NEOADJ, and 41±5 mon (95%CI: 31- 51 mon) for ADJ. Survival for NEOADJ chemo-alone pts was better than for SURG pts (p=0.031), while that of NEOADJ chemo+XRT pts was similar to SURG survival (p=0.488). Survival for ADJ chemo-alone pts was better than for SURG pts (p=0.007), while that of ADJ chemo+XRT pts was similar to SURG survival (p=0.163). **Conclusion:** Stage-3A NSCLC pts have improved survival with either induction or adjuvant therapy compared to surgery alone. Patients with induction or adjuvant chemo alone, but not those with induction or adjuvant chemo+XRT, have improved survival compared to surgery alone. **Keywords:** non-small cell lung cancer, stage-3A, induction therapy, Adjuvant therapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-007 Pneumonectomy for Non Small Cell Lung Carcinoma: Pre-Operative Comorbidities and Post-Operative Morbidity Affect Long Term Survival
Mathew A. Vandeusen[1], Lana Y. Schumacher[2], Ali H. Zaidi[2], Samantha A. Martin[1], Emily J. Lloyd[2], Athanasios Colonias[2], Gene G. Finley[3], Blair A. Jobe[2], Rodney J. Landreneau[2]
[1]*Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh/PA/United States of America,* [2]*Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh/United States of America,* [3]*Medical Oncology and Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh/PA/United States of America*

Background: Pneumonectomy for NSCLC is commonly associated with significant morbidity and mortality. Patients with pre-existing medical comorbidities experience an increased frequency of post-operative complications. This is of increased importance in this patient population, compared to patients undergoing lesser anatomic resections, as it is associated with a decrease in overall survival. **Methods:** A retrospective review of all patients undergoing pneumonectomy for non small cell lung cancer from 2004 to 2014 was undertaken. IRB approval was obtained. Demographics and pre-existing medical comorbidities, including the utilization of neoadjuvant therapy, were evaluated. Major morbidities occurring in the post-operative period were evaluated. Stage specific survival was evaluated and compared to published survival data following anatomic lobectomy. **Results:** From 2004 to 2014, 84 pneumonectomies were performed for resectable non small cell lung carcinoma. Complete STS data and staging information was available for 81 patients. Demographics and pre-existing medical comorbidities are reported in Table 1. Post-operative major morbidities are reported in Table 2. Mean stage specific survival was 32, 28 and 26 months for Stage I, II and III respectively.

Table 1. Pneumonectomy for NSCLC: Patient demographics, pre-existing comorbidities

Demographics		No. of Patients (%)
Patients		81
Mean Age		65 (34-88)
Gender	*Male*	60 (74%)
	Female	21 (26%)
Side	*Left*	39 (48%)
	Right	42 (52%)
Comorbidities		
Diabetes		14 (17%)
COPD		38 (47%)
CAD		21 (26%)
CHF		1 (1%)
Neoadjuvant Therapy		22 (27%)
Non-Standard Pneumonectomy		30 (37%)
	Intrapericardial	20 (25%)
	Completion	6 (7%)
	Unanticipated	3 (4%)
	Carinal	1 (1%)
	Sternotomy	1 (1%)

Table 2. Pneumonectomy for NSCLC: Post-operative morbidities.

Post-operative Morbidities	No. of Patients (%)
Atrial arrhythmia	27 (33%)
ARDS	11 (14%)
Respiratory failure	10 (12%)
Reintubation	10 (12%)
Ventilation over 48 hours	8 (10%)
Tracheostomy	7 (9%)
Bronchopleural fistula	8 (10%)
Sepsis	7 (9%)
Renal failure	6 (7%)
DVT	3 (4%)
Pulmonary embolus	2 (2%)
Myocardial infarction	2 (2%)

Conclusion: Overall survival is decreased in patients undergoing pneumonectomy for NSCLC compared with patients undergoing lesser anatomic resections. Pre-existing medical conditions may contribute to the increased frequency of post-operative morbidity, resulting in decreased overall survival in these patients. Further evaluation of the severity of pre-existent medical comorbidities and the impact on post-operative morbidity on long term survival following pneumonectomy for non small cell lung carcinoma is warranted. **Keywords:** complications, Comorbidities, NSCLC, pneumonectomy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-008 Surgery for Primary Lung Tumors with Histology Other than Non-Small Cell Lung Cancer: A Single Center Experience Durgatosh Pandey[1], Bharat B. Khurse[1], Rambha Pandey[2], Sunil Kumar[1], Karan Madan[3], Randeep Guleria[3] [1]*Surgical Oncology, All India Institute of Medical Sciences, New Delhi/India,* [2]*Radiation Oncology, All India Institute of Medical Sciences, New Delhi/India,* [3]*Pulmonary Medicine, All India Institute of Medical Sciences, New Delhi/India*

Background: Primary lung tumors with histology other than small cell and non-small cell carcinoma are uncommon, and generally have a better prognosis and differing criteria of resectability. We present our experience of surgery in such tumors over the last three years at a tertiary cancer center in north India. **Methods:** This is an analysis of a prospective database of patients with primary lung tumors undergoing surgery in a three-year period between May 2012 and April 2015 at the Department of Surgical Oncology, All India Institute of Medical Sciences, New Delhi. We included the group of patients with histology other than non-small cell lung cancer (NSCLC). Details concerning the clinical presentation, preoperative therapy, operative procedure, postoperative complications and outcome were retrieved from the database. **Results:** Between May 2012 and April 2015, out of the 101 patients who underwent surgery for primary lung neoplasm, twenty eight (28) patients had histology other than NSCLC. There were 19 males and 9 females, with a median age of 36 (range 6 to 64). They included 18 patients with carcinoid tumor, 3 with mucoepidermoid tumor, 4 with adenoid cystic carcinomas, 2 with myofibroblastic tumor, and 1 with clear cell tumor. Four patients had been previously treated presumptively for pulmonary tuberculosis, and two had received chemotherapy elsewhere before presenting to us. Two patients had prior bronchoscopic debulking. The surgical procedures included lobectomy in 8, bilobectomy in 8, pneumonectomy in 10, and pneumonectomy with carinal resection in 2 patients. Bronchoplastic procedures or sleeve resections were performed in 5 patients. All these surgeries were performed using muscle-sparing thoracotomy approach, except in two patients who underwent left pneumonectomy with carinal resection and reconstruction using median sternotomy approach and cardiopulmonary bypass. Postoperative morbidity was observed in 5 patients (prolonged air leak in 2patients, postoperative lung collapse, pneumonia, and empyema in one patient each). There was one postoperative mortality; this patient had mucoepidermoid carcinoma of the left main bronchus for which he underwent left pneumonectomy with carinal resection under cardiopulmonary bypass through median sternotomy approach. He was re-explored for a pericardial bleed on the first postoperative day, subsequently developed postoperative pneumonia of the solitary lung, and succumbed on 9thpostoperative day. Although the follow-up period is short, there has been no recurrence so far; and all patients are surviving without evidence of disease, except the one patient who died due to postoperative complications. **Conclusion:** Patients with carcinoid tumor, minor salivary gland neoplasm, or other unusual histologies of the lung usually have a better prognosis than those with non-small cell carcinoma. Aggressive surgical approaches should be pursued in such tumors, even in face of advanced local disease that would preclude resection in NSCLC. **Keywords:** carcinoid tumor, minor salivary gland tumor, primary lung neoplasm, Surgery

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-009 Single Institutional Experience of the Surgical Treatment of Second Primary Lung Cancer Hisashi Saji, Hideki Marushima, Rie Tagaya, Hiroyuki Kimura, Noriaki Kurimoto, Haruhiko Nakamura *Chest Surgery, St. Marianna University School of Medicine, Kanagawa/Japan*

Background: Surgical strategies for second primary lung cancer is still a controversial issue. We sought to assess postoperative and survival outcome of surgical resection in the treatment of patients with a second primary lung cancer. **Methods:**From January 2010 to August 2014, 439 patients with lung cancer were underwent surgical resection at our institution. Among them, 18 (4.1%) patients with second primary lung cancer, classified by the criteria proposed by Martini and Melamed, were treated. We retrospectively reviewed these cases for assessment of treatment outcome. **Results:** There are 12 males and 6 females with mean (range) age of 72 (58-85). We had 9 (50%) patients with a synchronous tumor and 9 (50%) with metachronous. Median interval time (range) between metachronous tumors was 42 months (1-194). These second primary located with 9 (50%) cases in right and 9 (50%) cases in left side. Mean (range) tumor size was 20 (7-45) mm with ground glass opacity in 9 (50%) cases. Histology was adenocarcinoma in 15 (83%), large cells in 2 (11%), and small cells in 1 (6%). Pathological stage was IA in 11 (61%), IB in 4 (22%), and IIA in 3 (17%). Mean VC and FEV1.0 were 2.48L and 1.8L, respectively. As second treatment, we performed 3 (17%) lobectomies, 4 (22%) segmentectomies and 11 (61%) wedge resections. Mean operation time and blood loss was 133 min and 47 ml, respectively. Major postoperative complications at second treatment were prolonged air leakage in 2 (11%) cases and interstitial pneumonitis in 1 (5%) case. Operative morbidity and mortality were 16% and 5%, respectively. There years overall survival were 94% with 13 months of median follow up time. Loco-regional and distant recurrence were occurred in 2 (12%) and 1 (5%) cases, respectively. **Conclusion:** From our experience, surgical treatment of second primary lung cancer is feasible. Surgical strategies including lobectomy, segmentectomy, and wedge resection should be selected with considering in the balance with oncological and pulmonary functional status. Furthermore cases need to be collected for detail analysis. **Keywords:** Surgery, second primary lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-010 Sleeve, Semsleeve Lobectomy, Segment Pyramidobasalectomy in Patients with Preoperative Contraindication for Pneumonectomy Fadil Gradica[1], Lutfi Lisha[1], Dhimitraq Argjiri[2], Alma Cani[3], Fahri Kokici[3], Ylber Vata[4], Leon Shpataraku[4], Sali Gradica[5], Perlat Kapisyzi[2], Zef Perduka[2] [1]*Thorax Surgery, University Hospital"Shefqet Ndroqi", Al/Albania,* [2]*Pnemology, University Hospital"Shefqet Ndroqi", Al/Albania,* [3]*Anestesiology Reanimacion, University Hospital"Shefqet Ndroqi", Al/Albania,* [4]*Visceral Surgery, University Hospital"Shefqet Ndroqi", Al/Albania,* [5]*Farmacy, Gradica Farmacy, Al/Albania*

Background: Sleeve and semisleeve lobectomy and segment pyramydobasalectomy is a parenchyma-sparing procedure that is particularly valuable in patients with cardiac or pulmonary contraindications to pneumonectomy. The purpose of this study is to report our experience with sleeve lobectomy for bronchogenic cancer and carcinoid , and to investigate factors associated with long-term survival. **Methods:** Between January 2006 and Novembre 2014,19 patients were treated by saving lung parencima. Patients underwent sleeve lobectomy for non-small-cell lung cancer (n = 3) one patient underwent double sleeve lobectomy or carcinoid tumor (n = 15), including 5 patients underwent sleeve lobectomy (atipic carcinoid) and 10 patients underwent semisleeve lobectomy (tipic carcinois) with a preoperative contraindication to pneumonectomy. Mean age was 52 ± 14 years (range, 19 to 79 years). Vascular sleeve resection was performed in 1 patient and segmentbasalectomy on the right lung. **Results:** Major bronchial anastomotic complications occurred in 2 (13%) patient: One was fatal postoperatively(double sleeve bronchial and vasculare) two weeks after intervent ,because was massive hemoptisia , and one after pyramidbazalectomy 6-th day after intervent because nosocomial difusse pneumonia in the rest lung(shock septic). In the non-small-cell lung cancer group, operative mortality was 13% (2 of 15), and overall 5-year and 10-year survival rates were 60% . By multivariate analysis, two factors significantly and independently influenced survival: nodal status (N0 or N1 versus N2; $p = 0.01$) and microscopic invasion of the bronchial stump ($p = 0.02$). In the carcinoid tumor group, there were no operative deaths, and overall 5-year and 10-year survival rates were 100% and 95%, respectively. **Conclusion:** Sleeve lobectomy achieves local tumor control and is associated with low mortality and bronchial anastomotic complication rates. Long-term survival is excellent for carcinoid tumors. For patients with non-small-cell lung cancer, N2 disease or incomplete resection is associated with a worse prognosis; outcome is not affected by presence of a preoperative contraindication to pneumonectomy.Sleeve lobectomy facilitated the maintenance of residual lung function without serious perioperative complications. This finding suggests that patients with direct tumor invasion to the bronchus might be good candidates for a sleeve lobectomy, but not those with extra-nodal invasion. **Keywords:** sleeve lobectomy ,semisleve,carcinoid ,pyramidbasal segmentectomy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-011 A Phase II Trial of Concurrent Chemoradiation with Consolidation Pembrolizumab in Unresectable Stage III Non-Small Cell Lung Cancer Greg Durm, Nasser Hanna *Simon Cancer Center, Indiana University School of Medicine, Indianapolis/IN/United States of America*

Background: Outcomes for patients with locally advanced non-small cell lung cancer (NSCLC) are poor, and the landscape of treatment in this disease has not changed considerably over the last several years. In those patients with unresectable stage IIIA/IIIB tumors, concurrent chemoradiation has become the standard of care in fit patients, and no alternative approach including induction, consolidation, or maintenance chemotherapy, has been shown to improve overall survival (OS). New treatment paradigms are desperately needed in this setting. Pembrolizumab is a humanized monoclonal antibody that binds to the programmed death-1 (PD-1) receptor on regulatory T-cells (T-reg) and inhibits its interaction with its ligands, PD-L1 and PD-L2. PD-1 exerts an inhibitory effect on T-regs, and blocking this pathway allows for enhanced T-reg activity and an improved anti-tumor immune response. In a phase I trial of previously treated NSCLC patients, Pembrolizumab was well tolerated and demonstrated a 21% response rate by RECIST criteria. Furthermore, preclinical data suggests that the combination of radiation therapy and immunotherapy may have additive or even synergistic effects. Based on these findings, we proposed a phase II trial of consolidation Pembrolizumab following concurrent chemoradiation for patients with inoperable or unresectable stage IIIA or IIIB NSCLC. **Methods:** This study is a multi-institutional phase II trial investigating the PD-1 inhibitor Pembrolizumab as consolidation therapy following initial concurrent chemoradiation in patients with unresectable or inoperable stage IIIA/IIIB NSCLC. Concurrent chemoradiation is defined as platinum-based chemotherapy (Cisplatin/Etoposide or Carboplatin/Paclitaxel) that overlaps with radiotherapy (total dose of 59.4-66Gy). Patients must demonstrate stable disease or disease response following chemoradiation and must have no evidence of metastatic disease. Patients who qualify will receive Pembrolizumab at a dose of 200mg IV every 3 weeks starting a minimum of 4 weeks and a maximum of 8 weeks after completion of chemoradiation. The primary endpoint will be time to distant metastatic disease, defined as disease recurrence outside of the radiated field. Secondary endpoints will include progression free survival (PFS), OS, and toxicity. An exploratory objective will involve assessing PD-L1 expression levels in the tumor samples of participating subjects and correlating that with time to metastatic disease, PFS, OS, and treatment toxicity. Approximately 93 patients will be enrolled. The sample size was calculated based on the hypothesis that consolidation Pembrolizumab will improve time to metastatic disease to 18 months from a historical control of approximately 12 months with a power of 0.80 and a type I error of 0.05. **Results:** Accrual for this trial has begun, and the first patient was enrolled in March 2015. **Conclusion:** This study will determine whether immunotherapeutic consolidation

with Pembrolizumab will increase the time to metastatic disease in patients with stage IIIA/IIIB NSCLC following concurrent chemoradiation. It will also answer questions about the safety and tolerability of this combination of therapies in this patient population. **Keywords:** Immunotherapy, PD-1 inhibitor, NSCLC, pembrolizumab

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-012 Neoadjuvant Chemoradiotherapy or Chemotherapy Followed by Surgery Is Superior to That Definitive Chemoradiation in Stage IIIA (N2) NSCLC
Xiao-Ling Xu[1], Wei Chen[2], Ya-Ping Xu[2], Weimin Mao[1] [1]*Zhejiang Cancer Hospital, Hangzhou/China,* [2]*Zhejiang Cancer Research Institute, Hangzhou/China*

Background: Whether neoadjuvant chemoradiotherapy or chemotherapysurgery followed by surgery is superior to that followed by definitive radiotherapy in Stage IIIA (N2) NSCLC remains controversial. **Methods:** A literature search was performed in the Pubmed, Embase, Medline database (last search updated in March 2015) and a systematic review and meta-analysis of available data was conducted. **Results:** A total of nine studies including five randomized controlled trials and four retrospective studies were enrolled in this meta-analysis. A significant homogeneity ($\chi 2$=49.62 ,p=0.000 , I^2=81.9%) between the four studies with a total of 11948 selected cases was detected between the nine studied investigated overall survival (OS), the random effects model was used to conduct meta-analysis. The combined hazard ratio (HR) of for was 0.65 (95% confidence interval [CI]: 0.60-0.71; p=0.000). Subgroup analysis was investigated according to study design and extent of resection. We observed a statistically significantly better outcome after lobectomy (combined HR: 0.52; 95% CI: 0.47-0.58; p =0.000) than after pneumonectomy (combined HR: 0.82; 95% CI: 0.69–0.98; p=0. 028). Unfortunately, there was no significant difference in randomized controlled studies for the combined HR was 0.94 (95% CI: 0.81-1.09; p = 0. 440). **Conclusion:** Neoadjuvant chemoradiotherapy or chemotherapy followed by surgery is superior to that followed by definitive radiotherapy, particularly in patients with lobectomy. Further study to investigate randomized trial be performed comparing chemoradiation followed by lobectomy vs. definitive chemoradiation in patients with stage IIIA disease is urgently needed. **Keywords:** NSCLC, N2-stage, therapy, surgery

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.03-013 A Phase II Study of S-1 and Thoracic Irradiation for Elderly Pts with Locally Advanced Non-Small Cell Lung Cancer: Okayama Lung Cancer Study Group
Hiroshi Ueoka[1], Katsuyuki Hotta[2], Nagio Takigawa[3], Tadashi Maeda[1], Keisuke Aoe[1], Kenichi Chikamori[1], Daizo Kishino[1], Naoyuki Nogami[4], Shingo Harita[5], Shinobu Hosokawa[6], Kenichi Gemba[7], Keiichi Fujiwara[8], Yoshiro Fujiwara[9], Masahiro Tabata[2], Mitsune Tanimoto[2], Katsuyuki Kiura[2] [1]*Medicine, National Hospital Organization, Yamaguchi-Ube Medical Center, Ube, Yamaguchi Prefecture/Japan,* [2]*Okayama University Hospital, Okayama/Japan,* [3]*General Internal Medicine, Kawasaki Medical School, Okayama/Japan,* [4]*Pulmonary Medicine, National Hospital Organaization, Shikoku Cancer Center, Matsuyama/Japan,* [5]*Medicine, Chugoku Central Hospital, Fukuyama/Japan,* [6]*Red Cross Okayama Hospital, Okayama/Japan,* [7]*National Hospital Organaization, Fukuyama Medical Center, Fukuyama/Japan,* [8]*National Hospital Organaization, Okayama Medical Center, Okayama/Japan,* [9]*Tsuyama Central Hospital, Tsuyama/Japan*

Background: Although thoracic irradiation (TRT) is one of the standarad therapies in elderly pts with locally advanced non-small cell lung cancer (LA-NSCLC), its treatment outcome is still poor. We previously reported safety profiles of S-1, an oral fluoropyrimidine possesing a radio-sensitizing effect, and concurrent TRT in such population [Lung Cancer 2011]. Here, we investigated the efficacy and safety of S-1 with concurrent TRT for elderly pts with LA-NSCLC. **Methods:** Pts with stage III, aged >75 years and PS 0-1, and without any prior chemotherapy were eligible for this study. Pts were treated with S-1 (40 mg/m2/dose b.i.d on days 1-14 and 29-42) and TRT (60 Gy/30 fr over 6 weeks starting on day 1). Primary endpoint was response rate (RR), and required sample siza was 30 pts. **Results:** Between 2007 and 2012, 30 pts were enrolled (24 men; median age, 79 years; PS 1, 15; IIIa, 20; Sq, 12). Median Charlson score was 1 (range; 0-3). The proportion of actual dose schedule relative to the planned one of S-1 and TRT was 95 and 98%, respectively. Partial response was observed in 19 pts (63%; 95% confidence interval: 45-82%), which did not meet the endpoint. At the time of the analysis, 24 (80%) of the 30 had experienced recurrences; 13 (43%) were locoregional, 6(20%) distant, and 5 (17%) both locoregional and distant. At a median follow-up of 23.7 months, median progression-free survival and MST were 13.0 months and 27.9 months, respectively. Toxicities were generally mild, including G3/4 neutropenia (17%), G3 febrile neutropenia (7%) and G3 pneumonitis (10%). No toxic deaths occurred. **Conclusion:** This study did not meet the primary endpoint. However, concurrent S-1 and TRT yielded favorable survival data. Also, it was well-tolerated in elderly pts with LA-NSCLC **Keywords:** locally advanced non-small cell lung cancer, Elderly patients, concurrent chemoradiotherapy, S-1

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-014 Correlation of Response and Prognostic Markers with Survival in Locally Advanced NSCLC Patients Who Have Treated with Neoadjuvant Chemotherapy
Ozden Altundag[1], Nadire Kucukoztas[2], Samed Rahatli[1], Gul Sema Yildiran Keskin[1], Arzu Oguz[1] [1]*Medical Oncology, Baskent University, Ankara/Turkey,* [2]*Medical Oncology, Izzet Baysal University, Bolu/Turkey*

Background: Lung cancer is the most common cause of death from cancer.. NSCLC constitutes 80-85% of all lung cancers. One third of NSCLC is diagnosed at locally advanced. Stage III involves heterogeneous group of patients. Therefore, it is the group of patients with most controversial for treatment. Currently there is no standardized approach to definitive treatment. In this study, we aimed to determine the response to neoadjuvant chemotherapy in patients with stage III NSCLC who had received neoadjuvant therapy. We also aimed to determine the relationship with prognosis and treatment response of the expression of ERCC1 and RRM1. **Methods:** 27 pts with stage III NSCLC were included in this study who received neoadjuvant chemotherapy at the Dept of M. Oncology and had been operated by the at Baskent University 2003 and 2013. Lung tissue biopsies were evaluated by IHC methods for ERCC1 protein expression in patients who received neoadjuvant cisplatin and for RRM1 protein expression in patients who received neoadjuvant gemcitabine. OS and DFS durations were calculated for patients who received neoadjuvant chemotherapy. In addition, the relationship between pathological response and survival of the expression of ERCC1 and of RRM1 were evaluated. **Results:** One (3.7%) women and 26 (96.3%) male pts were enrolled in the study. Median age 59. 14 (51.9%) underwent lobectomy and 13 pts (48.1%) were performed pneumonectomy. According to the TNM staging system; 19 pts (70.4%) were at stage 3A and eight pts (29.6 %) were at stage 3B. All of the patients received neoadjuvant cisplatin-based chemotherapy. 15 patients (55.6%) were identified of relapse during follow-up. The median f/u was 36 mos. In follow-up, 14 pts have died. The average DFS was 26.6 months. The average OS was 48 mos. From the perspective of stage 3A and 3B; DFS (p = 0.379) and OS (p = 0.69) did not differ significantly in terms. 16 pts (59.3%) after receiving neoadjuvant chemotherapy was found viable tumor ratio equal and under 10% in the surgical pathology materials. 11 pts (40%) was found viable tumor above the rate of 10% . When considered from this point of view DFS and OS showed no difference. More patients survived in the group with low ERCC1 expression. Between pts with low ERCC1 expression and pts with high ERCC1 expression showed no difference in terms of survival . (both DFS and OS). Pts with high RRM1 expression showing resistance to gemcitabine and with low RRM1 expression had similar survival rates. **Conclusion:** In patients with stage III NSCLC who received neoadjuvant chemotherapy found longer OS and DFS durations than from literature. Published studies and the results of our study albeit small scale, suggests that in the near future especially for patients with stage IIIA and stage IIIB NSCLC will be suitable for neoadjuvant chemotherapy as standard approach applied. ERCC1 and RRM1 expressions that were predictive markers of response of the treatment for cisplatin and gemcitabine was not correlated to therapy and survival . This may be associated with less number of and is a lack of full-refractory patient population. **Keywords:** RRM1, neoadjuvant, locally advanced, ERCC1

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-015 A Phase II Trial of Individual Trimodality Treatment in Patients with Stage IIIA (N2) Non-Small Cell Lung Cancer: The ZTOG 1202 Study
Yaping Xu, Qixun Chen, Xinmin Yu, Jinshi Liu, Qiang Zhao, Youhua Jiang, Xinming Zhou, Weimin Mao *Zhejiang Cancer Hospital, Zhejiang/China*

Background: Currently, optimal management of clinical stage IIIA (N2) non-small cell lung cancer (NSCLC) is still controversial. We investigated the efficacy and toxicity of individual trimodality treatment using concurrent chemoradiotherapy as a neoadjuvant treatment followed by surgery in patients with stage IIIA (N2) NSCLC. This study is registered with ClinicalTrials.gov, number NCT01926483). **Methods:** Patients with potentially resectable locally advanced stage IIIA (N2) NSCLC received surgery and individual concurrent induction chemotherapy Docetaxel/Cisplatin or Pemetrexed/Cisplatin (Patients received individual chemotherapy regimens depending on the different pathological types: squamous cell carcinoma: Docetaxel 60mg/m^2 d1, Cisplatines 75mg/m^2 d1, repeated every 3 weeks for 2 cycles; non-squamous cell carcinoma: Pemetrexed 500mg/m^2 d1, Cisplatin 75mg/m^2 d1, repeated every 3 weeks for 2 cycles.) plus radiotherapy (46 Gy/23 fractions, 5 days per week) (Fig.1). Primary endpoint was pathological complete remission rate in the mediastinal lymph nodes and we aimed at a rate >47%. Secondary endpoint was a near pathologic complete response (pnCR) (Near pCR: near pathological complete response means only original site exist a small amount of cancer cells, without lymph node metastasis) rate and we aimed for >33%.

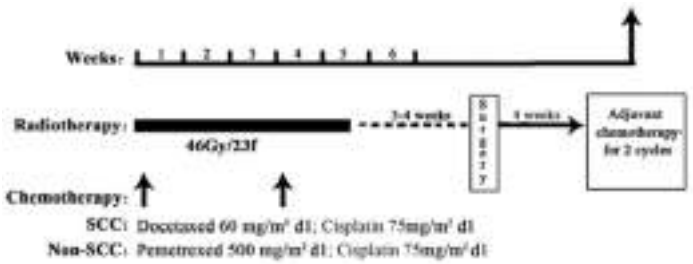

Fig.1 Treatment scheme

Results: Twenty two patients were included in analyses (12 patients with squamous cell carcinoma treated with Docetaxel/Cisplatin, 10 patients with non-squamous cell carcinoma treated with Pemetrexed/Cisplatin). Pathological complete remission rate in the mediastinal lymph nodes was achieved in 11 patients (50%) exceeded the goal per study design. The postinduction pathological findings by T and N category were recorded. The categories were 3 T_0N_0 (13.6% patients) and 6 $T_{near\ 0}N_0$ (27.3% patients). In our study, the prevalence of postoperative complications was low, which was probably

due to the thoracoscopic approach that was employed. No treatment-related deaths were reported. Toxicities associated with induction chemoradiotherapy were similar in both regimens. Neutropenia and esophagitis were the main grade 3 or 4 toxicities (9 [40.9%] and 2 [9.1%], respectively). Other grade 2 or higher toxicities occurring in about 50% of patients included nausea, vomiting, and fatigue. Most side effects were grade 2 and well tolerated by supportive care. **Conclusion:** Individual concurrent chemoradiotherapy based on the pathological type as a neoadjuvant treatment (two cycles of Docetaxel/Cisplatin or Pemetrexed/Cisplatin with 46 Gy/23f of concurrent radiotherapy) followed by resection was safe and well tolerated in patients with stage IIIa (N2) NSCLC. It could improve the pathological complete remission rate in the mediastinal lymph nodes to the preset criterion of 50% and a pnCR rate of 40.9%.
Keywords: N2 non-small-cell lung cancer, Mediastinal nodal involvement, induction chemoradiotherapy, Individual treatment

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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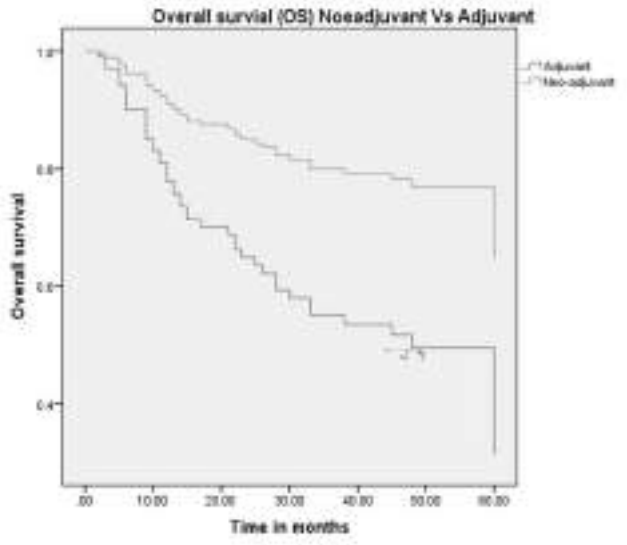
P2.03-016 Comparing Outcomes of Neoadjuvant and Adjuvant Chemotherapy in Non-Small Cell Lung Cancer
Sandhya Sharma[1], Amir Bista[1], Abhash Joshi[2], Kevin Charles[1], Bradley Lash[3] [1]*Internal Medicine, Guthrie-Robert Packer Hospital, Sayre/PA/United States of America,* [2]*Hospitalist, Guthrie-Robert Packer Hospital, Sayre/PA/United States of America,* [3]*Hematology/Oncology, Guthrie-Robert Packer Hospital, Sayre/PA/United States of America*

Background: Lung Cancer is the most common cancer in the US, and the leading cause of cancer deaths. Patient with Non-Small Cell lung cancer (NSCLC) are at substantial risk for recurrence and death even after complete surgical resection, and hence there is rationale for the use of chemotherapy and/or radiation therapy. Cisplatin based regimen is recommended. Adjuvant chemotherapy is most preferred treatment in patients with resectable disease. However, the role of neoadjuvant therapy is unclear. The purpose of this study was to compare the outcome of neoadjuvant and adjuvant chemotherapy in resectable NSCLC. The primary objective was to compare the observed and progression free survival. Secondary objective was to analyze the factors associated with better outcomes in both groups. **Methods:** This is a retrospective study conducted at a community based teaching hospital after IRB approval. A total of 117 patients diagnosed with NSCLC Stage 2 and 3, treated with either adjuvant or neoadjuvant chemotherapy, in addition to surgery, from 2001 to 2013 were included in the study. Chemotherapy consisted of cisplatin based regimen. The patients were followed to a maximum of 5 years. Median follow up period was 31 months. Overall survival and progression free survival was calculated using Kaplan Meyer Curve and compared using Log rank test. **Results:** Median age of diagnosis was 66 years. 26.4% of the patients were in neoadjuvant group. Mean 5 year overall survival was found to be better in neoadjuvant group (80.3%) when compared to adjuvant group (54.7%) with p value of 0.314. Mean 5 year progression free survival was better in neoadjuvant group (63.5%) when compared to adjuvant group (33.6%) with p value of 0.234. As the demographic profile for the patients were not comparable, five year overall survival after adjusting for age, sex and stage at diagnosis was compared using COX proportionate hazard model. This was found to be significantly better for neoadjuvant group compared to adjuvant group with HR of 0.374, 95% CI of 0.152 to 0.919; p value of 0.032.



Conclusion: Overall survival and progression free survival was found to be better in neoadjuvant group, but it was not statistically significant. However, when adjusted for age, sex and stage at diagnosis survival was statistically significant in neoadjuvant group. This study suggests a trend in overall and progression free survival benefit in neoadjuvant group. Further large population randomized trials would be needed to confirm the survival benefit seen in this small retrospective study.
Keywords: NSCLC, Neoadjuvant, Adjuvant, Overall Survival,

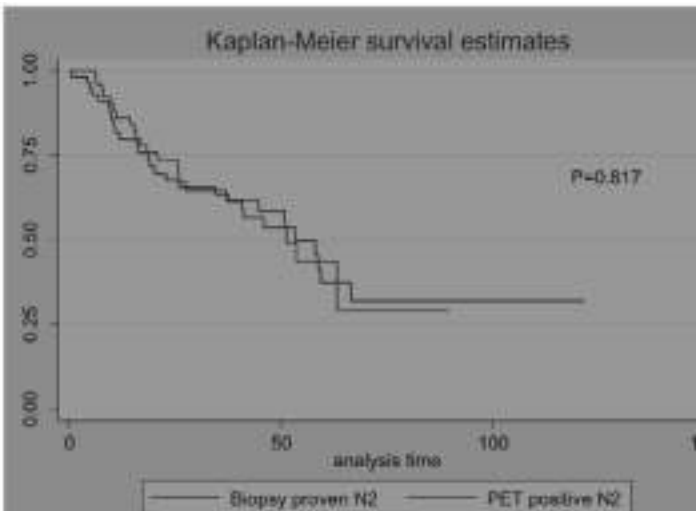
POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-017 Pre-Operative Chemotherapy Followed by Surgery for N2 Non-Small Cell Lung Cancer: A 15-Year Experience
Jonathan D. Spicer[1], Jitesh Shewale[1], Arlene M. Correa[1], John V. Heymach[2], Mara B. Antonoff[1], Wayne Hofstetter[1], Reza Mehran[1], Jack Roth[1], David Rice[1], Boris Sepesi[1], Ara A. Vaporciyan[1], William William[2], Garrett Walsh[1], Stephen Swisher[1] [1]*Thoracic and Cardiovascular Surgery, MD Anderson Cancer Center, Houston/TX/United States of America,* [2]*Medical Oncology, MD Anderson Cancer Center, Houston/United States of America*

Background: The ideal approach to patients with N2 non-small cell lung cancer (NSCLC) remains controversial. While pathological confirmation of nodal status is advocated, in clinical practice patients with suspicious radiographic evidence of N2 disease are frequently assigned to pre-operative therapy without pathological confirmation. Herein, we review our experience with pre-operative chemotherapy followed by surgery in patients with N2 NSCLC and compare outcomes of biopsy proven N2 disease and those patients who were diagnosed based on PET/CT alone. **Methods:** A prospectively entered institutional database was accessed to identify all patients with N2 NSCLC treated by pre-operative chemotherapy followed by surgery from 1999 to 2014. Data were verified by chart review. Patients without biopsy or PET-based evidence of N2 disease were excluded. **Results:** We identified 113 patients of whom 57 had biopsy proof of cN2 and 56 were cN2 based on PET-positivity. See Table 1 for patient demographic and clinico-pathologic variables. Median survival for the cohort was 53.3 months and there was only 1 (0.88%) peri-operative death at 90 days. Three and 5-year survival rates were 63.8% and 39.7%, respectively. Locoregional recurrences occurred in 16.8% of patients. Induction chemotherapy resulted in a significant PET response (SUV reduction > 6) in 38.5% of cases (15/39) where pre- and post-treatment imaging was available. Only 8.77% of patients remained pN2 after pre-operative chemotherapy in those patients who had pre-treatment pathological confirmation. No survival differences were noted between patients with biopsy proven N2 and those with PET-positive N2 nodes (Figure 1).

Demographic and clinico-pathologic variables.

Variables	Biopsy proven N2(N=57)	PET positive N2(N=56)	P value	Totalcohort(N=113)
Median age (range)	64(38-80)	62(43-77)	0.763	63(38-80)
Male gender	25(46.3)	28(54.90)	0.378	53(50.48)
Mean FEV1 (%pred)	85.78	86.54	0.798	86.16
Mean DLCO (%pred)	81.89	82.28	0.916	82.08
Type of surgery			0.743	
Wedge/Segmentectomy	3(5.26)	4(7.14)		7(6.19)
Lobectomy	48(84.21)	44(78.57)		92(81.42)
Pneumonectomy	6(10.53)	8(14.29)		14(12.39)
Post-operative treatment			0.094	
None	24(42.11)	27(48.21)		51(45.13)
Chemo	1(1.75)	15(26.79)		6(5.31)
Radiation	6(5.31)	9(16.07)		41(36.28)
Chemoradiation	6(10.53)	9(16.07)		9(16.07)
Pathological N stage			0.090	
N0	20(35.09)	22(39.29)		42(37.17)
N1	32(56.14)	22(39.29)		54(47.79)
N2	5(8.77)	12(21.43)		17(15.04)



Conclusion: Pre-operative chemotherapy followed by surgery for N2 NSCLC in a well-selected cohort results in good short and long-term outcomes. When pathological confirmation of N2 disease requires invasive staging, it may be acceptable to forgo such tests without compromising patient outcomes. Further prospective studies are needed to determine the ideal treatment regimen for these complex patients. **Keywords:** lung cancer, Surgery, chemotherapy, N2

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-018 Tolerability of Re-Irradiation for Locally Recurrent Lung Cancer
Veronica Finnegan[1], Tyler Underriner[2], Paul Aridgides[3], Seung Hahn[3], Anna Shaprio[1], Mary Kilpatrick[1], Russell Kincaid[1], Weidong Li[1], Jeff A. Bogart[4] [1]*Radiation Oncology, Suny Upstate Medical University, Syracuse/NY/United States of America,* [2]*Suny Upstate Medical University, Syracuse/United States of America,* [3]*Radiation Oncology, Suny Upstate Medical University, Syracuse/United States of America,* [4]*Radiation Oncology, Suny Upstate Medical Center, Syracuse/NY/United States of America*

Background: Treatment of locally recurrent of lung cancer in the setting of prior radiotherapy is a therapeutic challenge, particularly when treating with curative intent. **Methods:** Retrospective review of lung cancer patients treated with 2+ courses of modern radiotherapy, which included image guidance (IGRT). Repeat irradiation was defined as an overlap of the gross tumor volume (GTV) in all treatment courses. **Results:** Thirty-three patients, 25 non-small cell and 8 small cell, received re-irradiation including one patient treated thrice. Thirteen patients initially had early disease (6 stage I, 7 II), and 20 patients had locally advanced or advanced disease. Median interval between treatments was 15 months (range 5 months – 13 years 3 months). 16 patients received concurrent chemotherapy with both courses. 13 additional patients received chemotherapy concurrently during one of the courses of treatment. Seven patients were treated with stereotactic body radiation therapy for one of the courses. 24 patients were treated to the mediastinum twice and 9 additional patients received mediastinal treatment during one of the courses. Cumulative prescribed doses ranged up to 14,000 cGy and 18 patients received > 10,000 cGy. Maximum absolute dose to the lung was 14,000 cGy and to the mediastinum was 14,500 cGy. Ten patients remain alive with a median follow up of 20 months (range 9 months – 36 months). Treatment was generally well tolerated with esophagitis <= grade 3 common during the first or second course of therapy (16% and 24% respectively). Fatigue was noted in 18% of patients following the 2nd course of radiotherapy and only 3% during the initial course but this may be related to concurrent chemotherapy. One patient developed grade 4 dyspnea possibly related to repeat irradiation, though it was the 5th overall course of radiotherapy to the chest. Grade 5 toxicity was not observed and severe late effects were also not reported. **Conclusion:** Re-irradiation, even when concurrent chemotherapy is utilized, appears to be well tolerated with modern treatment planning including the use of IGRT. Further follow-up is necessary to better define local control, overall survival, and potential late toxicity. Additional studies are warranted to further investigate the long-term impact of patients treated more than once to the same region. **Keywords:** Retreatment, recurrent, Re-Irradiation

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-019 A Phase II Multicentre Study of Gefitinib in Combination with Irradiation Followed by Chemotherapy in Patients with Inoperable Stage III NSCLC
Antonin Levy[1], Etienne Bardet[2], Xavier Artignan[3], Pierre Verrelle[4], Cecile Le Pechoux[1] [1]*Radiotherapy, Gustave Roussy, Villejuif/France,* [2]*Centre René Gauducheau, Nantes/France,* [3]*Chp St Gégoire, Saint-Grégoire/France,* [4]*Centre Jean Perrin, Clermont-Ferrand/France*

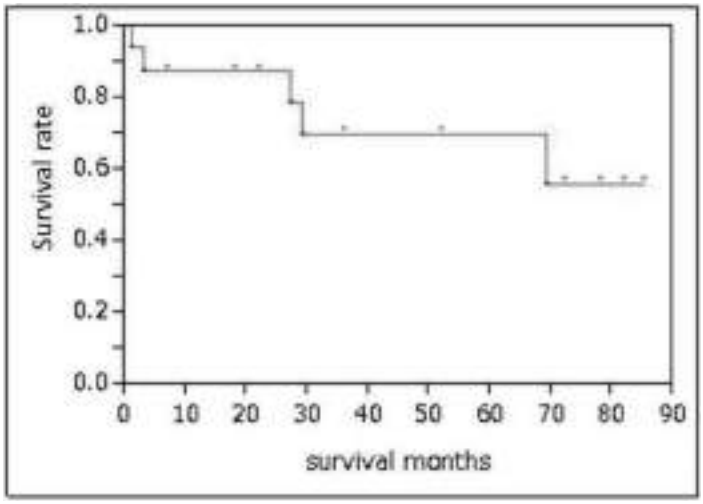
Background: Gefitinib is an oral EGFR TKI approved in first-line treatment for metastatic NSCLC patients with activating mutations of EGFR that may act as a radiosensitizer. **Methods:** This phase II study evaluated the efficacy of gefitinib 250 mg once daily in combination with thoracic radiotherapy (66 Gy in 6.5 weeks, 2 Gy/day, 5 fractions/week) followed by consolidation chemotherapy (IV cisplatin 100 mg/m^2 once every 28 days and vinorelbine 25 mg/m^2 once per week for 3 weeks out of 4) as first line treatment in a population of unselected stage IIIB NSCLC patients according to EGFR status. **Results:** Due to a low recruitment rate in this study, the sample size (n=50) was not reached. Sixteen patients were included in four centers between 2004 and 2006, 50% had adenocarcinoma and 75% were male. Molecular analysis (n=10) revealed that 2, 2, and 4 patients had positive biopsies for pERK, pAKT, and EGFR, respectively. EGFR mutation status was not explored at this time. Four weeks after radiotherapy, 3 patients (19%) had a PR, 6 (38%) had a SD, and 9 had PD (56%).Median OS was 11 months and median TTP was 5 months. At the time of the last contact, 5 patients (31%) were still alive. Compliance was good and all patients completed the combination of gefitinib and radiotherapy. Main toxicities were gastrointestinal (81%), cutaneous (81%), General (56%), and respiratory (50%). Seven (47%) patients had at least one grade 3-4 related adverse event. **Conclusion:** Gefitinib (250 mg daily) in combination with RT is feasible but its impact on outcomes remains to be determined, especially in EGFR mutated patients. **Keywords:** Chemo-radiotherapy, NSCLC, gefitinib, phase II

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-020 Radical Lung Resection after Curative Chemoradiotherapy for Locally Advanced Lung Cancer
Motohiro Yamashita[1], Tsuyashi Ueno[1], Hiroshi Suehisa[1], Sihigeki Sawada[1], Hiromoto Kitajima[2], Daijiro Harada[2], Toshiyuki Kohzuki[2], Naoyuki Nogami[2] [1]*General Thoracic Surgery, Shikoku Cancer Center, Matsuyama/ Japan,* [2]*Thoracic Oncology, Shikoku Cancer Center, Matsuyama/Japan*

Background: The safety and perioperative complications of radical pulmonary resection after concurrent chemoradiotherapy (CRT) for locally advanced lung cancer (LALC) have been problematic. **Methods:** We retrospectively evaluated 16 patients who received CRT and radical surgical resection for locally advanced lung cancer from May 2008 to April 2015. The treatment for LALC consisted of cisplatin and drugs (Docetaxel, Vinorelbine, or TS-1) with curative concurrent thoracic radiotherapy (60Gy.).

Results:



The mean age at the surgery was 61 years (range 46- 71 years), one woman and 15 men. The mean interval from CRT to the surgery was 19 months (range 3-96 months). All patients except one case underwent complete surgical resection with mediastinal nodal dissection including lobectomy in 11 cases, lobectomy with bronchoplasty in 2 cases, pneumonectomy in, 2 cases, and segmentectomy in one case. The bronchial stump was covered with pericardial fat tissue or intercostal muscle. Histological type was adenocarcinoma in 9 cases, squamous carcinoma in 4 cases, large-cell-carcinoma in 2 cases, and combined cell type small-cell carcinoma in one case. The mean operation time was 301 minutes (range 163-649 minutes), and mean blood loss was 842g (range 90-6000g). There was no operative mortality and three cases post-operative morbidity such as arrhythmia in 2 cases, atelectasis in 2 cases, pneumonia and heart failure in each. There was no broncho-pleural fistula or bronchial dehiscence. The 3 and 5 years survival after surgical resection was 70 % and 70 % with 39 months median follow-up period. **Conclusion:** Radical pulmonary resection after curative concurrent chemoradiotherapy for LALC is feasible in careful patient selection, operative procedure and meticulous perioperative care. **Keywords:** Radical pulmonary resection, Salvage resection, Trimodality, Chemoradiotherapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-021 Impact of Radiation on Recurrence Patterns and Survival for Patients Undergoing Lobectomy for Stage IIIA-pN2 Non-Small Cell Lung Cancer
Chi-Fu J. Yang[1], Syed M. Adil[1], Robert R. Meyerhoff[1], Kevin L. Anderson[1], Sameer A. Hirji[1], David Harpole[1], Betty C. Tong[1], Mark W. Onaitis[1], Matthew G. Hartwig[1], Thomas A. D'Amico[1], Mark F. Berry[2] [1]*Surgery, Duke University, Durham/NC/United States of America,* [2]*Surgery, Stanford University, Stanford/CA/United States of America*

Background: There is controversy regarding the optimal multimodality treatment strategy for stage IIIA-pN2 non-small cell lung cancer (NSCLC). This study evaluated the impact of induction and adjuvant radiation on locoregional and distant recurrence and survival when induction chemotherapy and surgery is used. **Methods:** Cancer recurrence and survival of 113 consecutive patients who were treated with lobectomy after induction chemotherapy ± radiation for pathologically staged IIIA-N2 NSCLC between 1995 and 2012 at a single institution were evaluated using Kaplan-Meier, logistic regression, and Cox proportional hazard analysis. **Results:** Induction radiation was used in 58 (51%) patients and adjuvant radiation was used in 29 (26%) patients (Table 1). For the entire cohort (n=113), median survival was 30.1 months (95% CI, 22.0 to 56.4). Five-year overall and recurrence-free survivals were 39.0% (95% CI, 29.1 to 48.7) and 28.2% (95% CI, 18.0 to 39.2), respectively. Recurrent disease occurred in 62 (55%) patients after a median (IQR) time of 11.5 months (4.3, 18.7) after surgery. First recurrence site was locoregional only (n=19), distant only (n=34), and locoregional and distant (n=9) (Table 1). In multivariable analysis, induction radiation was associated with decreased likelihood of developing locoregional recurrence (odds ratio (OR), 0.17; 95% CI: 0.04-0.90; p=0.04) but not improved survival (hazard ratio [HR], 1.47; 95% CI: 0.71-3.03; p=0.04) while adjuvant radiation was not associated with decreased likelihood of developing locoregional recurrence (OR, 0.48; 95% CI: 0.07-3.37; p=0.46) but was associated with improved survival (HR, 0.20; 95% CI: 0.04-0.91; p=0.04) (Table 2).

Table 1. Patterns and Treatments of Recurrence

Characteristics	Locoregional Only (n=19)	Distant (n=43)	*p-value
First site of recurrence (n, %)	0/0		0/0
Brain		18 (28)	
Liver		5 (12)	
Bone		5 (12)	
Adrenal		4 (9)	
Contralateral lung		4 (9)	
Pleural disease		2 (5)	
Chest wall		1 (2)	
Supraclavicular region and GE junction		1 (2)	
Pericardial effusion		1 (2)	
Spine		1 (2)	
Pleural and contralateral pulmonary metastatic disease		1 (2)	
Treatment prior to recurrence			0.49
Adjuvant chemotherapy	7 (37)	11 (26)	
Adjuvant radiation	3 (16)	7 (16)	
Adjuvant chemotherapy and adjuvant radiation	1 (5)	6 (14)	
None	8 (42)	19 (44)	
Detection of recurrence			0.19
Surveillance CT or PET	15 (79)	26 (60)	
Symptoms	4 (21)	16 (37)	
Unavailable data	0 (0)	1 (3)	
Treatment of recurrence			0.02
Surgery	2 (11)	2 (5)	
Radiation	3 (16)	10 (23)	
Chemotherapy	8 (42)	9 (21)	
Surgery and radiation	0 (0)	10 (23)	
Chemoradiation	6 (32)	3 (7)	
Supportive care	0 (0)	5 (12)	
Elected not to have surgery	0 (0)	1 (2)	
Unknown	0 (0)	3 (7)	

*p-values provided are from Chi-square test on categorical variables.

Note: total number of patients with recurrence = 62/113

Table 2. Multivariable Analysis of Recurrence and Survival in Patients with Stage IIIA-N2 NSCLC who have Undergone Induction Therapy Followed by Lobectomy

Cox Proportional-Hazards Analysis of Overall Survival

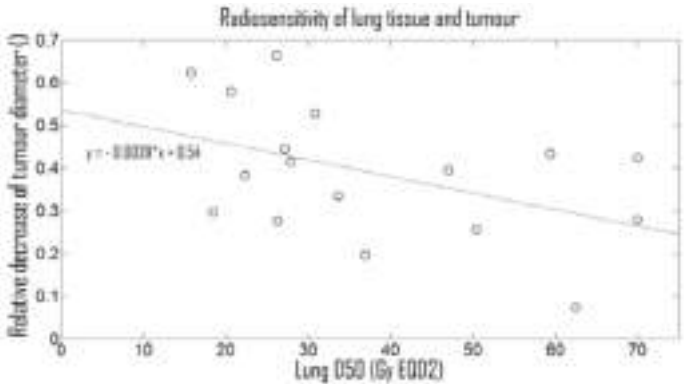
Subgroup	Hazard Ratio	95% CI	p-value
Age/year	1.03	1.00, 1.06	0.07
Sex (ref=female)	1.32	0.75, 2.38	0.33
PRVI	1.00	0.98, 1.01	0.26
Use of Induction Radiation	1.47	0.71, 3.03	0.30
Adjuvant therapy (ref=no treatment)			
Adjuvant chemotherapy	0.69	0.34, 1.29	0.24
Adjuvant radiation	**0.20**	**0.04, 0.91**	**0.04**
Adjuvant chemoradiation	0.58	0.19, 1.33	0.16
Nodal Down-staging (N2 to N1/N0)	**0.46**	**0.23, 0.88**	**0.01**
Operative Year	0.89	0.80, 1.00	0.04

Conclusion: A significant number of recurrences in stage IIIA-pN2 NSCLC patients who undergo induction therapy followed by lobectomy are locoregional recurrences. Use of radiation was associated with improved local control only in the induction setting and may be optimal in terms of survival when given in the adjuvant rather than induction setting.

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-022 Is the Radiosensitivity of the Tumour Related to That of the Lung? A CT-Based Response Analysis of Both Gilles Defraene, Dirk De Ruysscher
Experimental Radiation Oncology, Ku Leuven, Leuven/Belgium

Background: Lung tissue damage after radiotherapy scored as density changes on CT scans proved to be a less multifactorial endpoint compared to dyspnea. Its continuous variation in the patient population is an indication that it could be an expression of patient-specific radiosensitivity variation. This study linked patients' lung damage measures defined on CT with tumour shrinkage. **Methods:** 32 stage I-IV lung cancer patients treated with chemoradiotherapy were studied. Prescribed dose was 66 Gy in fractions of 2 Gy (concurrent) or 2.75 Gy (sequential). Image analysis of the radiation-induced lung damage was performed by comparison of the baseline planning CT_0 and the non-rigidly registered follow-up CT_{fup}. The median Hounsfield Unit increase ($\Delta HU=HU_{fup}-HU_0$) was calculated per dose bin of 5 Gy. The local dose-ΔHU response curve was described using a sigmoidal model. This resulted in a sigmoidal parameter D_{50} (corresponding to 50% of the saturation level of ΔHU) for each patient, as an expression of the patient-specific lung tissue radiosensitivity. On both the CT_0 and CT_{fup} scans, an experienced radiation oncologist delineated the tumour gross target volume (GTV). Volumetric (volume and equivalent diameter) and intensity-based (median, maximal and minimal HU) features were collected for all GTVs. **Results:** The average timepoint of CT_{fup} was 2.3 months after end of radiotherapy. For 25 patients the sigmoidal dose-ΔHU fits were acceptable (sum of squared residuals below 10 HU per datapoint on average). 8 of these patients did not show any dose response in the analysed dose range. The 17 reacting patients showed large variation in D_{50} (median: 30.9 Gy, range: 15,8 Gy-70,0 Gy) and were further analysed. Their median GTV volumes were 25.9cc (range 1.3cc-275.9cc) and 5.2cc (range 0.4cc-42.4cc) on CT_0 and CT_{fup} respectively No correlation of tumour intensity-based features with lung D_{50} was observed. The relative diameter change of tumour however showed moderate correlation (R^2=0.21) with lung radiosensitivity (see Figure). Patients with D_{50} below the population's median showed a mean reduction of tumour diameter of 46.8%, while this was 30.0% in the group with high D_{50} (p=0.03).



Conclusion: The patient-specific D_{50} for lung damage shows correlation with tumour shrinkage. This corroborates the hypothesis that it is a measure of intrinsic radiosensitivity. This study shows that imaging characteristics can provide independent and reproducible measures of radiosensitivity and can play a crucial role in defining patient-specific therapeutic ratio and thus treatment selection. Future radiogenomics studies could also benefit from the input of imaging.
Keywords: radiosensitivity, density change, CT, lung tissue damage

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-023 In-Field Nodal Relapse after Irradiation for Locally Advanced Non-Small-Cell Lung Cancer: Is There a Dose-Effect Relationship? Lisa Van Den Bosch[1], Gilles Defraene[1], Stéphanie Peeters[2], Christophe Dooms[3], Walter De Wever[4], Christophe Deroose[5], Dirk De Ruysscher[1] [1]*Radiation Oncology, University Hospitals Uz Leuven, Leuven/Belgium,* [2]*Department of Radiation Oncology, Ku Leuven - University of Leuven, University Hospitals Leuven, Leuven/Belgium,* [3]*Respiratory Oncology, University Hospital Ku Leuven, Leuven/Belgium,* [4]*Radiology, University Hospitals Uz Leuven, Leuven/Belgium,* [5]*Department Imaging and Pathology, Nuclear Medicine and Molecular Imaging, Ku Leuven - University of Leuven, University Hospitals Leuven, Leuven/Belgium*

Background: We investigated whether prescribed radiation dose is related to in-field nodal relapse. Since in-field nodal relapse is rare according to current literature, the influence of radiation dose on the incidence could be questioned. **Methods:** A retrospective analysis of prospective data was performed. Pathologic lymph nodes were registered based on RECIST 1.1 criteria. An in-field nodal relapse is defined as an increase of at least 20% of the short axis diameter and a minimum absolute increase of 2 mm, taking as reference the short axis diameter measured 3 months (+/-2 months) after radiation therapy. Three subgroups were defined based on EQD2,T (group A: EQD2,T < 50 Gy, group B: EQD2,T 50-55 Gy, group C: EQD2,T > 55 Gy). An actuarial Kaplan-Meier analysis was performed to evaluate the cumulative proportion of in-field nodal relapse per subgroup. A Cox proportional hazards regression analysis was performed to take initial nodal diameter into account. **Results:** A total of 75 patients were reviewed. Sixty-two patients (83%) had stadium IIIA/IIIB disease. Twelve patients (16%) had stadium IV NSCLC who were treated

with a radical oligometastatic approach. One patient (1%) had stadium IIB disease. Sixteen patients (21%) were treated with radiotherapy alone (38% group A, 25% group B, 38% group C). Sequential chemoradiotherapy was given in 47 patients (63%) (32% group A, 45% group B and 23% group C). Twelve patients (16%) received concurrent chemoradiotherapy (33% group A, 66% group B). Group A consisted of 25 patients (median age: 65 years (range 45-88), median follow-up: 6 months (range 1-54)). Thirty-three patients were included in group B (median age: 59 years (range 45-80), median follow-up: 8 months (range 1-86)). Group C consisted of seventeen patients (median age: 67 years (range 54-83), median follow-up: 9 months (range 2-45)). In all three groups median number of follow-up CT scans is 2 (range of 1-11 for group A and C, range of 1-13 for group B). Any relapse occurred in fifty-eight patients (77,3%). Nineteen patients (33%) had a locoregional failure only. Twenty-two patients (38%) had distant failure only, either by progression of a known metastasis or occurrence of a new distant lesion. Seventeen patients (29%) had a locoregional and distant failure at once. A total of 142 lymph nodes were taken into account (55 (39%) in group A, 52 (37%) in group B and 35 (25%) in group C). The average baseline short axis diameter per group was 16,3 mm, 15,8 mm and 14,6 mm for group A, B and C respectively. An actuarial Kaplan-Meier analysis performed on all lymph nodes (n=142) showed no significant difference between subgroups (p=0,24). A Cox proportional hazards regression analysis didn't show a significant effect of baseline nodal diameter on in-field nodal relapse (p=0,82). **Conclusion:** Prescribed radiation dose is not related to the occurrence of in-field nodal relapse. There was no relation between initial lymph node diameter and in-field nodal relapse. **Keywords:** NSCLC, in-field nodal relapse

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-024 PORT-First Strategy After Surgery in Patients with IIIA-N2 Non-Small Cell Lung Cancer Hyun Woo Lee[1], O Kyu Noh[2], Young-Taek Oh[2], Jin-Hyuk Choi[1], Mison Chun[2], Hwanik Kim[2], Jaesung Heo[2], Mi Sun Ahn[1], Oyeon Cho[2] [1]*Department of Hematology-Oncology, Ajou University School of Medicine, Suwon/Korea,* [2]*Department of Radiation Oncology, Ajou University School of Medicine, Suwon/Korea*

Background: Postoperative radiotherapy (PORT) and postoperative chemotherapy (POCT) can be administered as adjuvant therapies in patients with non-small cell lung cancer (NSCLC). The purpose of this study was to investigate the clinical outcomes of the patients treated with PORT-first and following with/without POCT in stage IIIA-N2 NSCLC. **Methods:** From March 1997 to October 2012, 97 patients with stage IIIA-N2 NSCLC who received PORT-first and following with/without POCT were analysed. PORT began within 4-6 weeks after surgical resection, and was delivered using conventional fractionation (1.8 – 2.0 Gy / day) with total dose of 50.4 – 66 Gy. According to the patient's comorbidity, platinum-based POCT was administered 3 – 4 weeks after completion of PORT. We analysed the outcomes and clinical factors affecting survivals. **Results:** Of 97 patients, 32 (33.0%) received POCT with median of 4 cycles (range, 2 – 6). The follow-up time ranged from 3 to 110 months (median, 24) and 5-year locoregional recurrence-free survival (LRRFS), distant metastasis-free survival (DMFS) and overall survival (OS) were 50.6%, 42.2% and 36.6%. Five-year OS of patients treated with PORT and POCT was significantly higher than that of patients with PORT only (62.9% vs. 28.1%, p = 0.005), and no significant differences in LRRFS (58.9% vs. 47.5%, p = 0.935) and DMFS (52.3% vs. 38.8%, p = 0.541). In multivariate analysis, the significant prognostic factors affecting OS were the use of POCT (HR = 0.44, CI, 0.20 – 0.96, p = 0.039), type of surgery (pneumonectomy/lobectomy, HR = 1.83, CI, 1.01 – 3.35, p = 0.047) and the status of resection margin (positive/negative, HR = 3.20, CI, 1.14 – 8.99, p = 0.027). **Conclusion:** PORT-first strategy after surgery appears not to compromise the clinical outcomes in the treatment of stage IIIA-N2 NSCLC. The additional use of POCT showed improving effect on overall survival even in PORT-first setting. **Keywords:** adjuvant chemotherapy, sequence of therapy, non-small cell lung cancer, postoperative radiotherapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-025 Predictors of Relapse and Evaluation of Post-Operative Radiotherapy in Patients with Resected Stage III (N2) Non-Small Cell Lung Cancer William Breen[1], Kenneth Merrell[2], Aaron Mansfield[3], Dennis Wigle[4], Yolanda Garces[2], Kenneth Olivier[5], Christopher Hallemeier[2] [1]*Mayo Medical School, Mayo Clinic, Rochester/MN/United States of America,* [2]*Radiation Oncology, Mayo Clinic, Rochester/ United States of America,* [3]*Medical Oncology, Mayo Clinic, Rochester/United States of America,* [4]*Thoracic Surgery, Mayo Clinic, Rochester/AL/United States of America,* [5]*Radiation Oncology, Mayo Clinic, Rochester/MN/United States of America*

Background: For patients with stage III (N2) NSCLC treated with surgical resection, chemotherapy improves survival, whereas the role of PORT is controversial. The purpose of this study was to evaluate risk factors for recurrence and the role of PORT in a modern series of patients with surgically resected stage III (N2) NSCLC. **Methods:** A retrospective review was performed of patients with Stage III (N2) NSCLC who underwent curative intent surgical resection at our institution between February 1999 and January 2012. Patients who received neoadjuvant RT were excluded. Chi-Square or Fisher's exact tests assessed associations between patient/disease characteristics and receipt of PORT. Local control was defined as lack of disease recurrence within the radiation field for PORT patients, or in the mediastinum or resection area for chemotherapy patients. Overall survival (OS), local control (LC), and metastasis-free survival (MFS) were estimated from the date of surgery using the Kaplan Meier method, with between-group comparisons (PORT vs. no PORT) made with the Log-rank test. Univariate Cox proportional hazards models were used to assess association of patient/disease characteristics and outcomes. **Results:** A total of 76 patients were included. Median age was 62.5 years. Histology was adenocarcinoma in 66%. Clinical N stage was N0 (51%), N1 (4%), or N2 (45%). Baseline positron emission tomography staging was performed in 91%. Pre-operative chemotherapy was administered to 21%. Surgery was pneumonectomy in 16%. Median (range) number of positive pN2 nodes was 1 (0-15). Seven patients with biopsy-proven cN2 had negative pN2 nodes after induction chemotherapy. Extranodal extension occurred in 9%. Surgical margins were positive in 4%. Chemotherapy (preoperative and/or postoperative) was administered to 83%. PORT was administered to 41 patients (54%) with a median (range) dose of 50 (41.4 – 60) Gy. Factors associated with increased likelihood of receiving PORT were increasing age (p=0.006) and no receipt of chemotherapy (p=0.0001). Median follow-up time for living patients was 4.5 (range 0.2 – 15.4) years. For all patients, OS at 5 years was 65%. OS at 5 years for patients receiving PORT vs. no PORT was 71% vs. 58% (p=0.19). For all patients, LC at 5 years was 84%. LC at 5 years for patients receiving PORT vs. no PORT was 89% vs. 77% (p=0.16). Factors associated with decreased LC were male gender (p=0.004), pT3/4 (vs. pT1/2, p=0.008). For all patients, MFS at 5 years was 61%. MFS at 5 years for patients receiving PORT vs. no PORT was 62% vs. 61% (p=0.89). **Conclusion:** In this modern series of patients with surgically resected stage III (N2) NSCLC, patients who received PORT (vs. no PORT) had numerically higher rates of OS and LC, although these differences were not statistically significant, potentially related to limited statistical power. **Keywords:** Post-operative Radiation Therapy, non-small cell lung cancer, Adjuvant therapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-026 Assessing the Risk of Cardiac Toxicity with Esophageal-Sparing Intensity Modulated Radiotherapy for Locally Advanced Lung Cancers Katrina Woodford, Sashendra Senthi, Vanessa Panettieri, Jeremy Ruben *William Buckland Radiotherapy Centre, The Alfred Hospital, Melbourne/VIC/Australia*

Background: Intensity-modulated radiotherapy (IMRT) can be used to reduce high doses to the esophagus for locally advanced non-small cell lung cancer (NSCLC), at the cost of increasing low to intermediate doses to adjacent healthy organs. Care is generally taken to ensure dose to healthy lung is minimized, resulting in IMRT not increasing lung toxicity. Such measures are not normally taken for the heart. Recently, a trial evaluating dose-escalated radiotherapy (RTOG 0617) found that overall survival was impacted by increased low (5Gy) and intermediate (30Gy) cardiac doses. We evaluated the impact of esophageal-sparing IMRT on cardiac doses and predicted toxicity compared to conventional radiotherapy (CRT). **Methods:** Ten consecutive patients with N2 Stage III NSCLC treated to 60Gy in 30 fractions, between February 2012 and September 2014, were evaluated. For each patient, CRT and esophageal-sparing IMRT plans were generated (Eclipse, Anisotropic Analytical Algorithm v11.0.31). For IMRT, treatments were planned such that no radiotherapy beams entered the contralateral lung or heart whenever possible. To compare CRT and IMRT plans, the dose delivered to more than 95% of the target ($D_{95\%}$) was compared. Doses to the esophagus, lung and heart were compared by determining the volume receiving X dose (V_{XGy}) and the normal tissue complication probability (NTCP). **Results:** Seven patients had Stage IIIA disease, while three had Stage IIIB. The median PTV size was 435.5cc (range 175.0-1309.5). CRT treatment plans used 3-4 fields. IMRT plans had the same (30%), one additional (50%) or two additional fields (20%). Dosimetric and NTCP results are summarized in the table below. IMRT resulted in satisfactory target coverage in 90% of patients. In the one patient with unsatisfactory coverage, the target was adjacent to the spinal cord and IMRT improved the $D_{95\%}$ from 42.6Gy to 54.3Gy. Esophageal-sparing was achieved in every patient at all dose levels. There were statistically significant reductions in V_{40Gy} and V_{50Gy} and the NTCP for grade 2 or higher toxicity. IMRT decreased low and intermediate heart doses significantly compared to CRT. This translated into a significantly lower NTCP for cardiac mortality. The cost of this was increased low dose (5Gy) lung exposure, however this did not reach statistical significance, nor did it worsen NTCP for grade 2 pneumonitis.

	CRT	IMRT	p-value
	Mean Dose (Gy)		
Target $D_{95\%}$	55.9	57.5	0.20
Esophagus V_{60Gy}	3.5	0	0.17
Esophagus V_{50Gy}	32	22.9	<0.01
Esophagus V_{40Gy}	36.4	27.4	<0.01
Heart V_{30Gy}	21.2	15.8	0.03
Heart V_{5Gy}	45.7	39.1	0.01
Lung V_{20Gy}	22	21.9	0.95
Lung V_{5Gy}	45.5	48	0.28
	NTCP (%)		
Esophagus	15.4	9.9	<0.01
Heart	5.7	2.8	0.01
Lung	10.0	8.5	0.02

Conclusion: Esophageal-sparing IMRT for locally advanced NSCLC can additionally achieve cardiac-sparing and reduce the theoretical risk of

cardiac death. With careful consideration this can be achieved without compromising target coverage or increasing the risk of radiation pneumonitis. **Keywords:** intensity modulated radiotherapy, Cardiac toxicity, non-small cell lung cancer, esophageal-sparing

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

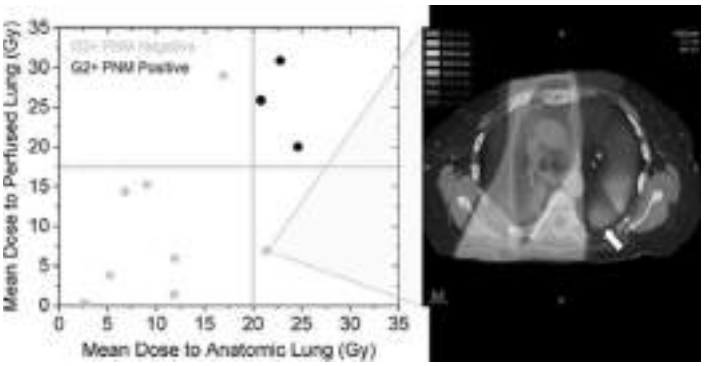
P2.03-027 Predicting the Effect of 7-Days-A-Week Radiotherapy for Locally Advanced Non-Small Cell Lung Cancer Based on Clinicopathological Features
Rafal Suwinski, Katarzyna Galwas, Bogna Klusek, Monika Giglok, Urszula Dworzecka, Bozena Jochymek, Grzegorz Plewicki, Barbara Maslyk *M. Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice/Poland*

Background: Concurrent radiochemotherapy is currently considered as standard treatment for locally advanced non-small cell lung cancer. Some clinical studies suggest, however, that an acceptable treatment outcome can be also obtained with induction chemotherapy followed by accelerated radiotherapy. We explored this direction, considering that not all of the patients are candidates for concurrent treatment. The aim of the present report is to identify clinicopathological features that may help to predict the effect of combined induction chemotherapy and 7-days-a-week radiotherapy. **Methods:** For the purpose of the present report we selected 113 patients from the institutional database that included individuals treated within prospective studies on combined induction chemotherapy and 7-days-a-week radiotherapy . The patients had pathologically confirmed non-small cell lung cancer (74 squamous, 15 adenocarcinoma, 24 NOS), stage IIIA N2 or IIIB. All patients had cisplatin based induction chemotherapy (1-6 courses, median 4) and curative radiotherapy (66-70 Gy, median 69.2 Gy) in 1.8-2.0 Gy per fraction. Fifty seven patients (50.4%) were treated conventionally , 5- days-a- week (CF), while 56 (49.6%) had 7- days-a- week radiotherapy (CAIR). The median dose-intensity of radiotherapy in CF was 9.5 Gy per week compared to 13,4 Gy per week in CAIR. Several clinicopathological features were considered including age, sex, general performance status, gross tumor volume, pathology, Hb concentration, response to chemotherapy and SUV from PET/CT scans. Kaplan-Meier method was used to estimate the overall survival, Cox proportional hazard model was used to assess impact of fractionation in subgroups uniform with respect to the clinicopathological features. **Results:** After median follow-up of 2.8 years the actuarial 3-year survival was 37% in CAIR, compared to 28% in CF, the difference was not statistically significant (HR=0.75, p=0.23). Patients with gross tumor volume smaller than the median of 60 cm^3 tended to benefit from CAIR (3 years survival of 49% vs 21% for CAIR and CF respectively, HR=0.54, p=0.11) unlike the patients with gross tumor volume above the median (3 years survival of 30% vs 28% for CAIR and CF respectively, HR=0.93, p=0.83). Likewise, patients with age of 60 years or less tended to have higher 3 years survival in CAIR vs. CF (42% vs. 8%, HR=0.60, p=0.15) unlike the patients with age over 60 years (3 year survival of 34% in both CAIR and CF, HR=1.01, p=0.97). Some other variables studied (pathology, Hb concentration, SUV) had strong prognostic, but not predictive significance (adenocarcinoma, high Hb concentration and low SUV were prognosticators of favorable overall survival). **Conclusion:** The present data suggest that an improvement in overall survival from 7-days-a-week radiotherapy as compared to conventionally fractionated treatment is relatively small in unselected group of patients with locally advanced non-small cell lung cancer treated in sequential fashion. Patients with small gross tumor volume and those with age of 60 years or less tended, however, to benefit from accelerated radiotherapy, unlike those with large tumor volume or with advanced age. Interestingly, the overall survival was satisfactory both in CAIR and CF, that might be attributed to relatively high total radiation doses given sequentially to chemotherapy. **Keywords:** Accelerated Radiotherapy, predictive factors, overall survival, sequential treatment

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-028 Functional Lung Imaging with Perfusion SPECT/CT Improves Prediction of Radiation Pneumonitis
Jing Zeng[1], Gurleen Dhami[1], Shilpen A. Patel[1], Paul E. Kinahan[2], Robert S. Miyaoka[2], Hubert J. Vesselle[2], Ramesh Rengan[1], Stephen R. Bowen[1] [1]*Radiation Oncology, University of Washington, Seattle/WA/United States of America,* [2]*Radiology, University of Washington, Seattle/United States of America*

Background: Current standard of care relies on CT-based lung dose-volume parameters to predict risk of pulmonary toxicity from radiotherapy. However, this approach remains imperfect as patients treated with radiotherapy for lung cancer still experience up to 20% clinically significant pneumonitis despite efforts to avoid it. We propose to improve prediction accuracy for radiation pneumonitis through incorporation of functional lung radiation dose parameters defined on ventilation/perfusion SPECT/CT. **Methods:** Pre-treatment ^{99}mTc-MAA perfusion and ^{99}mTc-DTPA ventilation SPECT/CT scans were co-registered to planning CT scans in 12 patients who received thoracic radiotherapy: 11 with lung cancer and 1 with lung metastasis. Five patients were treated with IMRT/3DCRT, 3 SBRT, and 4 proton RT. Two patients had clinical grade 2 and one patient had grade 3 pneumonitis (G2+ PNM) defined by CTCAE v4. Total lung minus GTV (TL-GTV) mean dose, V5Gy, V20Gy, and V30Gy were calculated. Threshold percentages of maximum ventilation and perfusion (10-90%) within TL-GTV defined functional dose-volume regions, from which the mean dose ($D_{PERF10\text{-}90\%}$, $D_{VENT10\text{-}90\%}$) and volume fraction of TL-GTV ($V_{PERF10\text{-}90\%}$, $V_{VENT10\text{-}90\%}$) were extracted. Mann-Whitney tests were conducted between patients with and without G2+ PNM. Receiver operating characteristic (ROC) curves identified functional dose-volume thresholds that could predict for G2+ PNM status. Logistic regression of G2+ PNM incidence from anatomic and functional dose-volume parameters was modeled. Spearman rank correlation between predictive anatomic and functional dose-volume parameters was calculated. **Results:** Anatomic TL-GTV parameters were significantly higher in G2+ PNM patients following independent testing, particularly mean lung dose (MLD 23 vs. 9 Gy RBE $EQD2_{\alpha/\beta=3}$, p=0.03) and V20Gy (33% vs. 9%, p=0.03). Perfused lung dose was also higher in patients with G2+ PNM ($D_{PERF70\%}$ 18 vs. 3 Gy, p=0.04). Using a cutoff value of MLD>20 Gy, 3/4 patients had G2+ PNM. The addition of mean perfused lung dose $D_{PERF70\%}$>17.5 Gy to MLD>20Gy improved specificity, with all 3/3 patients who received high MLD and $D_{PERF70\%}$ developing G2+ PNM (See Figure 1). Anatomic and perfused lung metrics were statistically correlated (Spearman R2=0.6, p=0.03). Figure 1. Mean dose to perfused lung vs. anatomic lung for patients with(black circle)/without(gray circle) G2+PNM. Adding perfused lung dose to anatomic lung dose increases specificity for pneumonitis. Radiotherapy plan is highlighted for one false positive case, in which dose to perfused lung is low(white arrow) while dose to anatomic lung is high.



Conclusion: Our data suggests that incorporating perfused lung metrics into radiotherapy planning objectives may improve our ability to predict and mitigate the risk of pneumonitis. Given the limited sample size, further investigation is warranted in a larger population. **Keywords:** Radiation pneumonitis, functional imaging, perfusion SPECT/CT

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-029 SBRT for Localized Central NSCLC Conventional Radiation Failures; Recurrent Laryngeal Nerve Paralysis Is a Novel Toxicity
Ryan Malik[1], Nima Aghdam[1], Richa Bhasin[1], Shaan Kataria[1], Simeng Suy[1], Sean Collins[1], Eric Anderson[2], Brian Collins[1] [1]*Department of Radiation Medicine, Georgetown University Hospital, Washington Dc/United States of America,* [2]*Division of Pulmonary, Critical Care and Sleep Medicine, Georgetown University Hospital, Washington Dc/DC/United States of America*

Background: To report local control, overall survival and toxicity following robotic SBRT for localized central NSCLC conventional radiation failures. **Methods:** Patients presenting with localized central recurrent NSCLC within previously treated radical conventional radiation fields ($\geq$ 60 Gy) salvaged using robotic SBRT in 5 fractions were retrospectively reviewed. Recurrences were considered central if they involved the hilum or mediastinum. **Results:** Twenty patients were treated over a 10-year period and followed for a minimum of 2 years or until death. Eight presented with hilar recurrence and twelve recurrences involved the mediastinum. Seventeen patients had gold fiducials placed for tumor tracking via bronchoscopy; three mediastinal tumors were tracked using the spine as a reference structure. A cumulative dose of 25 to 45 Gy (median, 35 Gy) was delivered to the gross tumor volume (GTV) in 5 fractions. The median GTV was 84 cc (range, 6 to 300). At median potential follow-up of 32 months, the 1-year Kaplan-Meier local control and overall survival estimates were poor at 34% and 40%. However, 1-year Kaplan-Meier local control and overall survival were improved at 67% and 67% when doses greater than 35 Gy were delivered. Two patients with hilar tumors developed acute radiation pneumonitis (Grade III) following 35 Gy and 40 Gy. Two patients with recurrent superior mediastinal tumors unexpectedly developed permanent recurrent laryngeal nerve paralysis (Grade II) 12 months following 40 Gy. One patient with recurrent hilar tumor experienced transient hemoptysis (Grade III) and benign pleural effusion (Grade II) 32 months following 45 Gy. **Conclusion:** Robotic SBRT is a novel salvage treatment option for localized NSCLC central recurrence following radical conventional irradiation. Dose escalation beyond 35 Gy resulted in improved local control and survival. However, doses $\geq$ 35 Gy also resulted in significant toxicity including acute radiation pneumonitis, pleural effusion, hemoptysis and newly described permanent recurrent laryngeal nerve paralysis. **Keywords:** Treatment Toxicity, NSCLC, Stereotactic body radiation therapy, Re-Irradiation

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-030 Adjuvant Radiation Therapy Improves Survival in Pathological Stage IIIA N2 Non-Small Cell Lung Cancer Patients Staged with PET
Mo Mo Tin[1], Catherine Kennedy[2], Daniel Wong[3], Regina Tse[1], Michael Boyer[4], Brian Mccaughan[2] [1]*Radiation Oncology, Royal Prince Alfred Hospital, Camperdown/NSW/Australia,* [2]*University of Sydney, Sydney/NSW/Australia,* [3]*University of Malaya, Kuala Lumpur/Malaysia,* [4]*Medical Oncology, Chris O'Brien Lifehouse, Camperdown/NSW/Australia*

Background: Recent studies suggest a possible survival benefit associated with adjuvant radiation therapy (ART) following curative surgery for patients with pathological stage IIIA N2 (pN2) Non Small-cell Lung cancer (NSCLC) but there is no randomized

data. Lack of survival benefit observed in some of the studies could be due to some of these patients harbouring unexpected distant metastases. 18-FDG Positron Emission Tomography (PET) scanning has been shown to upstage 24% of patients with stage III NSCLC. We hypothesized that survival benefit may become apparent by excluding patients with unexpected distant metastases who would not benefit from ART with the use of PET staging. The objective of this study is to evaluate whether ART improves overall survival in pN2 NSCLC patients staged with PET. **Methods:** Patients with stage IIIA pN2 NSCLC who underwent pre-operative PET staging and curative surgery in a tertiary thoracic oncology facility between January 1995 and June 2014 were identified from a prospectively collected database. 388 patients fit the selection criteria of which 219 patients (57%) received ART (≥ 45Gy). The impact of ART on survival was analysed using the Kaplan-Meier method. **Results:** Median follow up duration was 24 months. 29% of the patients had pneumonectomies. 30 day post-operative mortality was 1.8%. Conformal radiotherapy was used in all patients. 195 patients (51%) received systemic chemotherapy (33% induction, 67% adjuvant). The use of chemotherapy was uncommon in the earlier part of the study. Median age was 65 years (range 29-85 years). The most common histopathology was adenocarcinoma (55%). Patient characteristics, type of resection, complete resection rate, and histopathology subtypes were similar between the group which received ART (219 patients) and the group which did not receive ART (162 patients) but more patients in the ART group received chemotherapy (60% vs.38%). ART group did significantly better in terms of median, 2-year and 5-year Overall Survival (OS) compared to No ART group (median survival 29 months vs. 20 months respectively, 2-year OS 57% vs. 44% respectively, 5-year OS 30% vs.16% respectively, Hazard Ratio 0.62 95% Confidence Interval 0.49 – 0.79; p <0.0001) **Conclusion:** Adjuvant Radiation Therapy improved overall survival in pathological stage IIIA N2 NSCLC patients staged with PET in this series. This is consistent with the growing evidence supporting the use of ART in the modern era. Tri-modality therapy in a large number of patients may have contributed to the superior result in the ART group. **Keywords:** non small cell lung cancer, PET staging, Adjuvant Radiation Therapy,, Pathological Stage IIIA N2

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-031 Subgroup Analysis of East Asian Patients in the Phase III PROCLAIM Trial Luhua (Jingbo) Wang[1], Yi-Long Wu[2], Shun Lu[3], Lei Deng[1], Myung-Ju Ahn[4], Feng-Ming Hsu[5], Neill Iscoe[6], Anwar Hossain[7], Tarun Puri[8], Pinghai Zhang[9], Mauro Orlando[10] [1]*Cancer Hospital, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing/China,* [2]*Guangdong Lung Cancer Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou/China,* [3]*Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China,* [4]*Samsung Medical Center, Gangnam-Gu, Seoul/Korea, Democratic People's Republic of,* [5]*Division of Radiation Oncology, Department of Oncology, National Taiwan University Hospital, Taipei City/ Taiwan,* [6]*Eli Lilly and Company, Toronto/ON/Canada,* [7]*Eli Lilly and Company, Indianapolis/ IN/United States of America,* [8]*Eli Lilly and Company, Gurgaon/India,* [9]*Eli Lilly and Company, Shanghai/China,* [10]*Eli Lilly and Company, Buenos Aires/Argentina*

Background: PROCLAIM is a phase III trial comparing overall survival (OS) in patients with stage III, unresectable, nonsquamous non-small cell lung cancer (NSCLC) receiving pemetrexed (Pem) plus cisplatin (Cis) and concurrent thoracic radiation therapy (TRT) for 3 cycles followed by 4 cycles of Pem consolidation (Pem+Cis arm) versus etoposide (Etop) plus Cis and concurrent TRT for 2 cycles followed by up to 2 cycles of consolidation with a platinum-based doublet of choice (Etop+Cis arm). Overall efficacy and safety results for the intent-to-treat (ITT) population (N=598) will be presented in a separate disclosure. Efficacy and safety results from an East Asia (EA) subgroup analysis are presented here. **Methods:** A subgroup analysis was performed using the EA randomized population (N=97), which consisted of all patients who were randomized to the study from China (n=61), Taiwan (n=25), and The Republic of Korea (n=11). OS and progression-free survival (PFS) were evaluated by the Kaplan-Meier method and hazard ratios (HRs) were calculated using a Cox regression model. The log-rank test was used to compare treatment arms. Objective response rates (ORRs) were compared using an unadjusted, normal distribution approximation for the difference in rates. ClinicalTrials.gov number NCT00686959. **Results:** Baseline characteristics were balanced between treatment arms for EA patients. In the 97 randomized EA patients (n=44 in the Pem+Cis arm; n=53 in the Etop+Cis arm), median PFS was 10.0 months for the Pem+Cis arm and 7.6 months for the Etop+Cis arm (HR: 0.97, 95% confidence interval [CI]: 0.61–1.54, p=0.890). The censoring rate was high for OS (Pem+Cis arm: 43.2%; Etop+Cis arm: 52.8%), and there was no significant difference in OS between the Pem+Cis arm and the Etop+Cis arm (HR: 1.23, 95% CI: 0.70–2.14, p=0.469). The interaction test for region and treatment effect for OS was not significant (p=0.374). The ORRs were 47.7% (95% CI: 32.46–63.31) in the Pem+Cis arm and 34.0% (95% CI: 21.52–48.27) in the Etop+Cis arm. In the 90 treated EA patients (n=44 in the Pem+Cis arm; n=46 in the Etop+Cis arm), the overall incidence of drug-related grade 3/4 treatment-emergent adverse events (TEAEs) was significantly lower in the Pem+Cis arm versus the Etop+Cis arm (61.4% vs. 91.3%; p=0.001). All drug-related grade 3/4 TEAEs occurring in ≥5% of patients had a numerically lower incidence in the Pem+Cis arm than in the Etop+Cis arm except lymphopenia (17 [38.6%] vs. 17 [37.0%]). **Conclusion:** For EA patients with nonsquamous NSCLC, Pem+Cis did not improve OS, but did have a good safety profile and numerically improved PFS and ORR compared to Etop+Cis. **Keywords:** pemetrexed, nonsquamous non-small cell lung cancer, phase III, East Asian patients

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-032 Prognostic Impact of EGFR and KRAS Mutations in Patients with Lung Adenocarcinoma Treated with Definitive Radiation Therapy Federica Oro[1], Mark Sonnick[1], Hongyun Wang[1], Maureen Zakowski[1], Abraham J. Wu[1], Jamie E. Chaft[1], Paul Paik[1], Mazie Tsang[1], Meier Hsu[1], Kenneth Rosenzweig[2], Zhigang Zhang[1], Andreas Rimner[1] [1]*Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York/United States of America,* [2]*Radiation Oncology, Mount Sinai, New York/NY/United States of America*

Background: An association of EGFR and KRAS mutations with radiation sensitivity has been postulated in preclinical studies. Recent clinical studies reported longer local control and survival in patients (pts) harboring EGFR mutations treated with definitive radiotherapy (RT). Here, we sought to evaluate the prognostic impact of EGFR and KRAS mutations in 223 adenocarcinoma pts treated with definitive RT at our institution. **Methods:** Between 2004 and 2013, 466 inoperable pts with non-squamous lung cancer were treated with definitive RT ± chemotherapy. Mutational testing was performed in 223 pts. 44% were male, 56% female. 65% were former, 13% never, and 22% current smokers. Clinical stage was II in 5%, IIIA in 37% and IIIB in 58%. Median size of tumor was 3.8 cm (range 0.5-12.2 cm). 60% received concurrent, 31% sequential chemo-RT and 9% RT alone. The median RT dose was 63Gy (range 50-80Gy). OS was estimated by the Kaplan-Meier method. Cumulative incidence functions were used to estimate local failure (LF) and distal failure (DF), using death without failure as a competing risk. Association of factors with OS was analyzed by Cox regression and association with LF and DF by competing risk regression. **Results:** EGFR status was wild-type in 205 pts (92%) and mutated in 18 (8%). The most common EGFR mutations were exon 19 deletion (8 pts), followed by exon 21 L858R (7 pts), and exon 20 insertion (3 pts). KRAS status was wild- type in 142 pts (64%), mutated in 63 (28%), and not performed in 18 (8%). The most common mutations were G12C (13%), followed by G12V (5%) and G12A and G12D (3% each). With a median follow-up among survivors of 32.7 months (range 0.6-114), the median OS was 38 months for pts with EGFR mutation versus 26 months for pts without (p=0.96); 21 months for patients with KRAS mutation versus 31 months for pts without (p=0.24). 2-year LF was 37% and 46% for pts with and without EGFR mutation, and 48% and 46% for pts with and without KRAS mutation, respectively. 2-year DF was 80% and 64% for pts with and without EGFR mutation, and 62% and 64% for pts with and without KRAS mutation, respectively. On univariate analysis, factors significantly associated with improved OS included KPS ≥ 80 (p=0.01), increasing RT dose (p=0.04) and use of concurrent chemotherapy compared to RT alone (p=0.001). Factors associated with higher risk of LF included stage IIIB (p=0.04) and sequential rather than concurrent chemotherapy (p=0.05). Factors associated with a higher risk of DM included stage IIIB (p=0.03) and lower RT dose (p=0.003). Association of EGFR and KRAS mutations did not reach statistical significance on univariate analysis, thus we did not further investigate their effects by multivariable analysis. **Conclusion:** Despite analyzing the largest patient population to date, we did not identify a significant prognostic impact by EGFR or KRAS mutational status. The lack of an observed association could be related to the low rate of EGFR mutations identified. RT dose and use of concurrent chemotherapy were significantly associated with overall survival. **Keywords:** EGFR mutation, kras mutation, lung adenocarcinoma, radiation therapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-033 ^{18}FDG-PET/CT Improves Lung Cancer Staging and Treatment Selection Accuracy Margarita Majem[1], Nuria Dueñas[2], Nuria Farre[2], Cinta Pallarès[2], Alejandro Fernandez[2], Valle Camacho[2], Alfons Torrego[2], Elisabeth Martinez[2], Anna Virgili[2], Andrea Vethencourt[2], Agustí Barnadas[2] [1]*Hopital de La Santa Creu I Sant Pau, Barcelona/Spain,* [2]*Hospital de La Santa Creu I Sant Pau, Barcelona/Spain*

Background: Integrated [18]F-fluorodeoxyglucose Positron-Emission Tomography - Computed tomography (^{18}FDG-PET/CT) has emerged as the new standard in staging and treatment planning for patients with lung cancer, not only improving the diagnostic accuracy of mediastinal nodal involvement but also the detection of metastases. The aim of this study is to analyse this data in our centre and to evaluate the treatment variations derived from the results of this technique. **Methods:** We included patients with proven or suspected lung cancer diagnosed between September 2010 and February 2014. A computed tomography (CT) and ^{18}FDG-PET/CT were performed in all patients, both explorations were evaluated separately, and a tumour-node-metastasis (TNM) stage and a specific treatment based on its results was established for each technique. We used the 7th TNM edition, and nodal stations were identified according to mapping system of the American Thoracic Society. **Results:** We included 249 patients, the median age was 65 years (23-88), the 78.7% were males and the 21.2% were females. Non-small cell lung cancer (NSCLC) represented an 86.3% and small-cell-lung cancer (SCLC) a 8%. In 14 patients (5.6%) no pathologic diagnosis was established. In 137 of 249 (55%) patients no change in staging between CT and ^{18}FDG-PET/CT was observed: 65 (47.4%) were stage I, 10 (7.2%) stage II, 22 (16%) stage IIIA, 22 (16%) stage IIIB and 18 (7.2%) stage IV. Compared with CT, ^{18}FDG-PET/CT provided additional information in 112 of 249 patients (45 %): 36 patients (14,4%) had downstaging, and a curative treatment was feasible in 13 patients (5.2%) (1 SCLC, 12 NSCLC). Seventy six patients (30.5%) had upstaging, and a palliative treatment was proposed to 49 of them (19.67%) (10 SCLC, 37 NSCLC, 2 without histology). **Of-line: occult metastases were detected in 49 of 249 patients, which represent a 19.67%. **Conclusion:** The study confirms that in our institution, integrated ^{18}FDG-PET/CT improves both lung cancer staging in all histologies and the treatment selection accuracy. **Keywords:** 18FDG-PET/CT, Staging, lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-034 Association of EGFR Mutation Status with Treatment Outcome in Stage III Non-small Cell Lung Cancer Patients Treated with Concurrent Chemoradiotherapy

Shi Feng Nyaw[1], Ka Chai Lee[1], Willian Goggins[2], Sing Hung Lo[1], Wing Yan Tin[1], Yuk Tung[1] [1]*Department of Clinical Oncology, Tuen Mun Hospital, Hong Kong/ Hong Kong,* [2]*Division of Biostatistics, the Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong/Hong Kong*

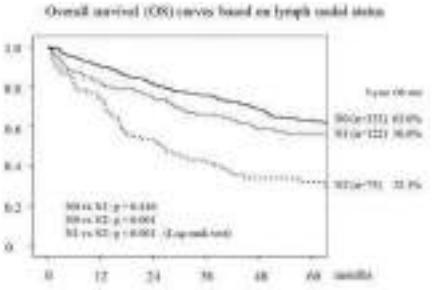
Background: Epidermal growth factor receptor (EGFR) mutation is a biomarker predictive of favorable response to EGFR tyrosine kinase inhibitor in advanced non-small cell lung cancer (NSCLC). Its prognostic value in stage III NSCLC is unclear. The objective of this study is to analyze the association of EGFR mutation with clinical outcome in stage III NSCLC patients treated with concurrent chemoradiotherapy. **Methods:** 91 consecutive patients with stage III non-small cell lung cancer who received concurrent chemoradiotherapy from January 2008 to January 2015 were retrospectively identified. EGFR mutation status was analyzed in 61 patients. Activated EGFR mutations were detected in 17 (28%) patients. Kaplan-Meier method was used to conduct the progression-free survival (PFS) and overall survival (OS) analyses. Univariate and multivariable analyses were performed to investigate the effects of predictor variables including age, disease stage, performance status, histology, EGFR mutation status, radiation dose and surgery after neoadjuvant chemoradiotherapy. **Results:** 51 (56%) patients had stage IIIA and 40 (44%) patients had stage IIIB disease. All patients received at least 2 cycles of platinum-based chemotherapy. Majority (77%) of patients received radiation dose of 60Gy (range 50-66Gy). Among the 17 patients with activated EGFR mutation, 13(76%) of them had disease progression. 12 of them subsequently received EGFR TKI. The median progression-free survival (PFS) was 13.3 months. The median PFS was 12.3 months in patients with mutated EGFR compared with 15 months in patients with wild-type EGFR (log-rank p=0.33). However, in the subgroup analysis of non-squamous histology, there was no significance difference in PFS between patients with or without activated EGFR mutation (Median PFS 12.3 vs. 12.4 months; log-rank p=0.96). In the multivariable analysis with the Cox proportional hazard model, significant predictors of longer PFS include squamous cell histology (HR 0.3; 95% C.I. 0.09, 0.99; p=0.05) and surgery after chemoradiotherapy (HR 0.36; 95% C.I. 0.13, 0.95; p= 0.04). EGFR mutation status was not a significant predictor of PFS (P=0.45) The median overall survival (OS) was 28.6 months. The median OS in patients with mutated EGFR was 33 months while the median OS in patients with wild-type EGFR was 36.7 months (log-rank p=0.24). In the subgroup analysis of non-squamous histology, there was no significance difference in OS between patients with or without activated EGFR mutation (Median OS 33 vs. 31 months; log-rank p=0.65). In the multivariable analysis, significant predictors of longer OS include surgery after chemoradiotherapy (HR 0.16; 95% C.I. 0.04, 0.61; p=0.01), N-stage (p=0.04) and ECOG performance status (p=0.01). A trend of inferior OS was shown in patients with activated EGFR mutation compared with wild-type EGFR (HR 2.6; 95% C.I. 0.9, 7.64; p=0.08). **Conclusion:** In patients with stage III non-small cell lung cancer who received concurrent chemoradiotherapy, EGFR mutation status does not affect the progression-free survival. A trend of shorter overall survival was shown in patients with activated EGFR mutation, which was not statistically significant. This could be due to higher risks of distant metastasis in patients with EGFR mutation. The role of adjuvant EGFR TKI after chemoradiotherapy should be further investigated.
Keywords: Chemoradiotherapy, Prognosis, locally advanced non-small cell lung cancer, Epidermal growth factor receptor

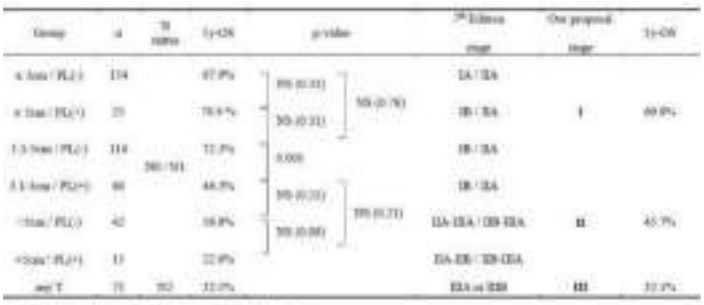
POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-035 Impact of Lymph Node Involvement on Survival in Patients with Completely Resected Pulmonary Squamous Cell Carcinoma

Yujin Kudo[1], Yoshihisa Shimada[1], Ryosuke Amemiya[1], Junichi Maeda[1], Koichi Yoshida[1], Yasufumi Kato[1], Masaru Hagiwara[1], Jun Matsubayashi[2], Masatoshi Kakihana[1], Naohiro Kajiwara[1], Tatsuo Ohira[1], Norihiko Ikeda[1] [1]*Thoracic Surgery, Tokyo Medical University, Tokyo/ Japan,* [2]*Anatomic Pathology, Tokyo Medical University, Tokyo/Japan*

Background: Lymph node involvement is an important prognostic factor in non-small cell lung cancer (NSCLC) patients. However, the prognostic impact varies among the histological types of NSCLC because of the lymph node spread pattern or other factors. We re-evaluated the impact of lymph node involvement and other clinicopathologic factors on survival in patients with pulmonary squamous cell carcinoma (SqCC) and identified high-risk patients who may benefit from additional therapy. **Methods:** Between 1990 and 2010, 530 consecutive T1-4N0-2M0 SqCC patients underwent complete resection with systematic lymph node dissection at our hospital. We statistically analyzed the association between lymph node involvement and clinicopathologic factors, as well as clinical outcomes. **Results:** The 5-year overall survival (5y-OS) rates of the patients with stages I, II, and III were 66.5%, 57.6%, and 30.0%, respectively (stage I vs stage II, NS). Multivariate survival analysis showed that patients with N2 had significant associations with unfavorable prognosis (HR = 2.58, p < 0.0001). The 5y-OS rate for N2 tumors (32.1%) was significantly worse than those for N0 and N1 tumors (63.0% and 56.6%, respectively). In stages I and II, tumor size > 5 cm, pleural invasion (PL), and age over 70 years were found to be significant independent prognostic factors by multivariate survival analysis, but lymph node status (N0 or N1) was not. Thus, tumors ≤ 5 cm without PL and tumors ≤ 3 cm with PL were classified as the new stage I (5y-OS, 69.8%) in the patients with N0 or N1, and tumors > 5 cm without PL and tumors > 3 cm with PL were classified as the new stage II (5y-OS, 45.7%). In contrast, tumors with N2 were classified as the new stage III (5y-OS, 32.1%). There was a statistically significant difference among these groups. **Conclusion:** N2 status was strongly associated with poor outcome in SqCC patients, but not N1 status. Our results indicate that lymph node status should not be incorporated into the staging system for N0-1 SqCC patients This information might prompt the design of clinical trials on additional therapy for these patients.





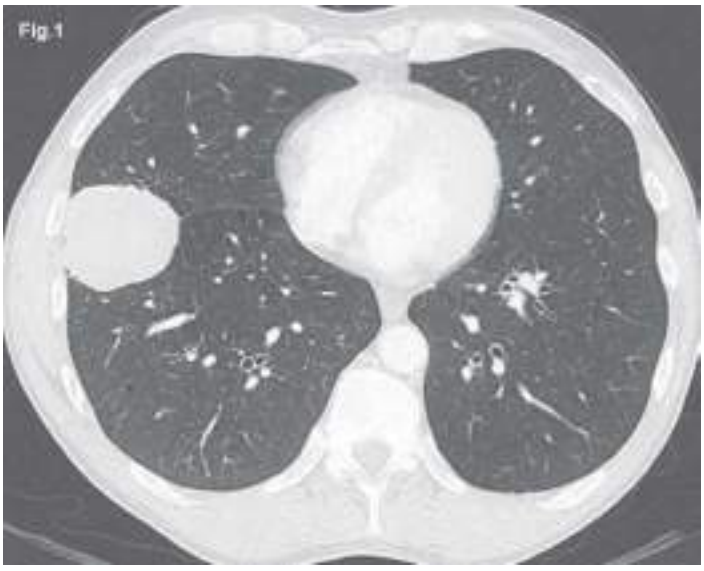
Keywords: Lymph node involvement, N2, N1, Squamous cell carcinoma

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-036 Primary Pulmonary Large Cell Carcinoma with Syncytiotrophoblastic Aspect: Report of a Case

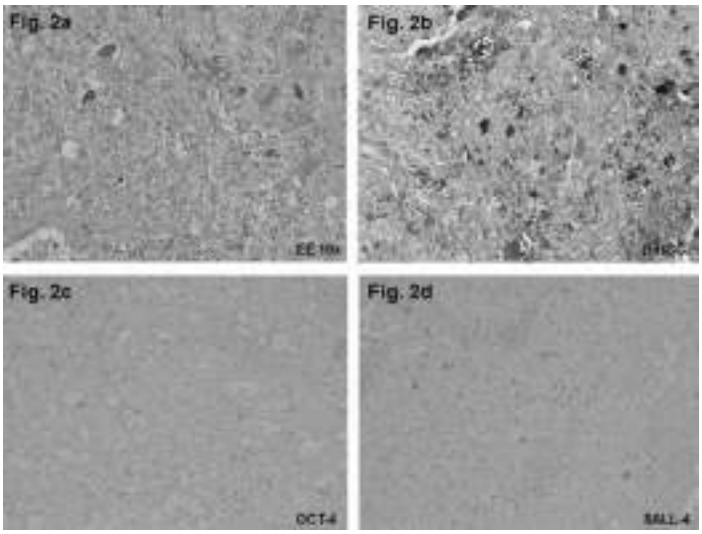
Luigi Ventura[1], Letizia Gnetti[2], Luigi Rolli[1], Michela Solinas[1], Valeria Balestra[1], Livia Ruffini[3], Paolo Carbognani[1], Enrico Maria Silini[2], Michele Rusca[1], Luca Ampollini[1] [1]*Thoracic Surgery, University Hospital of Parma, Parma/Italy,* [2]*Pathology, University of Parma, Parma/Italy,* [3]*Nuclear Medicine, University Hospital of Parma, Parma/Italy*

Background: To present the case of a primary large cell lung carcinoma with syncytiotrophoblastic aspect. **Methods:** A 54-year-old smoking man (60 pack/years), with no significant past medical history, presented for incidental radiological finding of a 5cm mass in the right middle lobe with partial invasion of the lower lobe (Fig.1). A PET/ CT-scan showed a unique intense FDG-uptake of the pulmonary mass. A trans-thoracic fine-needle aspiration led to the diagnosis of non-small-cell lung cancer with sarcomatoid features. Preoperative cardiac and pulmonary function tests were normal.



Results: The patient underwent a right middle lobectomy and wedge resection of the lower lobe and radical lymphadenectomy through a posterolateral thoracotomy. The postoperative course was uneventful; the patient was discharged on the seventh postoperative day. After 52 months the patient is alive and disease-free. Macroscopically, the mass measured 5.5cm, had a greyish colour with lobulated margins. Microscopically, a poor differentiated tumor characterized by giant and medium

pleomorphic cells sometimes with syncytial-trophoblastic features were observed (Fig.2a). Immunohistochemically, tumor cells were positive for beta-human-chorionic-gonadotrophin (Beta-HCG) (Fig.2b), anti-endomisium antibody (EMA), placental alkaline phosphatase (PLAP) e cytokeratin 7 (CK 7); the cells resulted negative for octamer-binding transcription factor-4 (OCT-4) (Fig.2c), spalt like transcription factor 4 (SALL4) (Fig.2d) and glypican-3.A subsequent genital examination and testicular ultrasonography excluded the presence of a primary gonadal choriocarcinoma. Beta-HCG serum levels were undetectable after surgery. Based on the above findings, a diagnosis of primary large cell lung carcinoma with syncytiotrophoblastic aspect was made. Final pathological stage was pT2aN0M0. No adjuvant therapy was proposed.



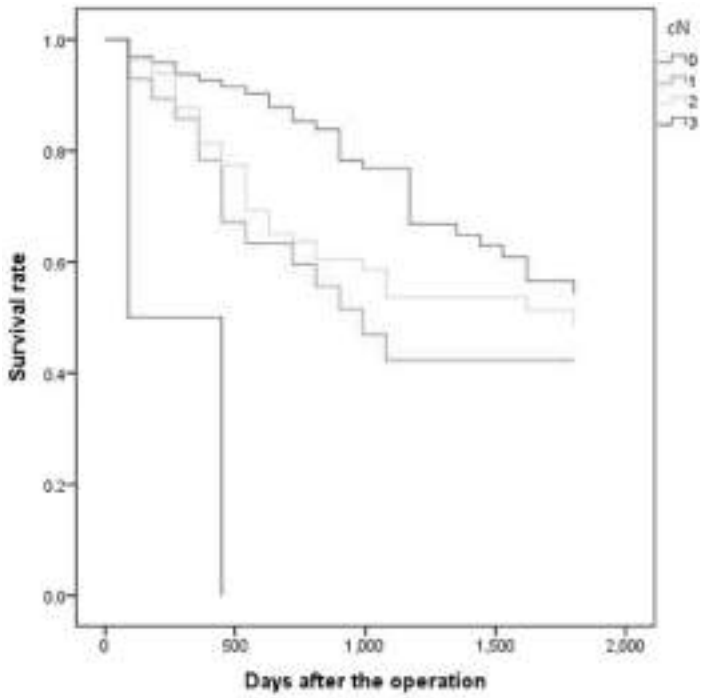
Conclusion: Large cell lung carcinoma with syncytiotrophoblastic aspect is an extremely rare finding. The prognosis is usually poor irrespective of the treatment; a few long-term survivors have been reported. **Keywords:** Surgery, large cell lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-037 Prognostic Factors in Pathologic N2 Non-Small Cell Lung Cancer
Hye-Seon Kim[1], Sukki Cho[2], Kwhanmien Kim[2], Sanghoon Jheon[2] [1]*Department of Thoracic and Cardiovascular Surgery, Hanyang University Seoul Hospital, Seoul/Korea,* [2]*Department of Thoracic and Cardiovascular Surgery, Seoul National University Bundang Hospital,Seoul National University College of Medicine, Seongnam-Si/Korea*

Background: Mediastinal lymph node metastasis is one of the strong prognostic factors in non-small cell lung cancer (NSCLC). Pathologic N2 patients group is heterogenous group consists of stage IIIA to stage IV. Moreover owing to difficulty in preoperative prediction of N2 disease, pathologic N2 patients group shows more variable in clinical stage. We tried to figure out which factors make difference in prognosis of N2 patients. **Methods:** Between May 2003 and December 2013, total 1994 patients underwent pulmonary resection surgery due to lung cancer. Only pathologically proven N2 patients were included in the study. Among them, patients with small cell lung cancer, double primary lung cancer and other malignant disease were excluded. Therefore, 195 N2 patients were analyzed for the study. The patients' clinical information was collected from prospectively recorded database and analyzed retrospectively. Regional N2 disease was defined as upper mediastinal LN involvement for upper lobar disease and lower mediastinal LN involvement for lower lobar disease. Extended N2 disease was defined as involvement of non-regional N2 station.

Results:



Mean follow up duration was 41 months and 5 year survival rate was 50% for the study population. As postoperative stage, majority of the study group was IIIA (84%). Patients' clinical stage and clinical T stage did not make difference in survival and recurrence. However clinical N0 group showed superior result in survival ($p<0.001$) and recurrence ($p=0.46$) even in same stage. In metastatic mediastinal LN extent analysis, extended N2 disease made worse survival than regional N2 disease ($p=0.04$). Total number of metastatic LN did not make any difference in prognosis. **Conclusion:** Owing to heterogeneity, even in same stage group, pathologic N2 patients have showed different prognosis. In this study, we confirmed that clinical N0 was relatively good prognostic factor and extended N2 disease was bad prognostic factor. Deciding postoperative treatment plan, we should take account of these factors. Also, the survival difference between regional and extended N2 disease might be considered in staging revision of NSCLC.
Keywords: lung cancer, mediastinal lymph node

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.03-038 Whole Tumor Perfusion CT in Patients with NSCLC Treated with Endostar Combined with Concurrent Radiotherapy
Lei Shi[1], Ming Chen[2], Guo-Liang Shao[1], Yu-Jin Xu[2], Jing-Jing Sun[1], Xu Wang[1], Jie-Hui Huang[1], Bo Liu[3], Hong-Lian Ma[2], Dan Long[1] [1]*Department of Radiology, Zhejiang Cancer Hospital, Hang Zhou/China,* [2]*Department of Radiation Oncology, Zhejiang Cancer Hospital, Zhejiang Key Laboratory of Radiation Oncology, Hangzhou/China,* [3]*Siemens Ltd.China, Healthcare Sector, Shanghai/China*

Background: Endostar was reported as an anti-angiogenic agent, which could inhibit new vessel formation in tumor. This study is to investigate the NSCLC response to Endostar combined with concurrent radiotherapy using volumetric perfusion CT. **Methods:** This study was performed with the approval of the local Medical Ethics Committee, and all the enrolled patients gave their written informed consent before the inclusion in the study. Six patients with NSCLC were involved in the current study. The histological subtype for each patient was confirmed by biopsy. All patients were treated with Endostar combined with concurrent radiotherapy for 7 weeks. Whole tumor perfusion CT was performed for all patients before treatment (baseline) and 4weeks after combined therapy on a dual-source CT. All images were reviewed in consensus by 2 radiologists. Blood flow (BF), blood volume (BV) and permeability (PMB) values for the whole tumor were calculated by an alternative deconvolution algorithm and then quantitatively assessed. These perfusion parameters before and after therapy were compared to investigate the therapy response of NSCLC. **Results:** Histology revealed adenocarcinoma (AC) in 3 patients and squamous cell carcinoma (SCC) in 3 patients. In SCC group, BF, BV and PMB at baseline were 116.2±34.57, 11.53±3.14 and 21.87±4.86. Four weeks after treatment, those perfusion values were 50.59±16.09, 4.58±1.26 and 10.70±1.05 respectively, which showed obvious decreasing trends compared with baseline data. In AC group, BF, BV and PMB at baseline were 66.58±5.82, 6.66±0.14 and 16.50±1.29, respectively. The parameters were 49.94±5.07, 5.45±1.34 and 13.2±1.67 respectively, which did not show obvious changes compared with baseline data. However, the tendency of perfusion parameters might vary considerably. Of 3 patients with AC, 1 case also showed decreasing trend of BF, BV and PMB after treatment compared with baseline data. On the basis of RECIST criteria, all the four cases (3 cases with SCC and 1 case with AC) that perfusion parameters showed obvious decreasing trend were classified as having a partial response (PR) to therapy, the remaining 2 cases with AC as having stable disease. **Conclusion:** The AC and SCC might respond differently to treatment with endostar combined with concurrent

radiotherapy. The obvious decreasing trend of perfusion parameters after therapy might predict a better response to endostar combined with concurrent radiotherapy. **Keywords:** perfusion CT, Endostar, non-small cell lung cancer

SESSION: POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING TUESDAY, SEPTEMBER 8, 2015

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-001 EGFR Activating and T790M Resistance Mutation in Plasma exoRNA and cfDNA, Detected with Single-Step Isolation Columns and Targeted Resequencing Daniel Enderle[1], Kay Brinkmann[1], Tina Koestler[1], Alexandra Spiel[1], Anne K. Krug[1], Jennifer Emenegger[1], Romy Mueller[1], Stefan Bentink[1], Johan Skog[2], Mikkel Noerholm[1], Vince O'Neill[1] [1]*Exosome Diagnostics Gmbh, Martinsried/Germany,* [2]*Exosome Diagnostics Inc., Ma/MA/United States of America*

Background: After initial responses to tyrosine kinase inhibitors (TKIs), NSCLC patients harboring EGFR activating mutations inevitably show progression, a consequence of acquired resistance (AR). Secondary mutations in the EGFR domains,*e.g.* the gatekeeper mutation T790M, are thought to play a role in clinical resistance of approximately half the patients that experience disease progression during treatment with TKIs, and novel therapeutic agents are in development to circumvent this resistance mechanism. Tissue based assays, requiring repeat biopsy, are fundamentally unattractive, and detection of AR mutations in circulation would be an appealing alternative. Here we present data demonstrating the feasibility of detection of activating and AR EGFR mutations with a targeted resequencing panel, using a combined single-step exosomal RNA (exoRNA) and cell-free DNA (cfDNA) isolation to maximize sensitivity. **Methods:** Plasma from more than 40 lung cancer patients was collected at the time of clinical resistance to EGFR TKI therapy. The plasma samples are complemented by EGFR-genotyping on time-matched tissue from a repeat biopsy. We applied our proprietary column-based method to co-isolate both exoRNA and cfDNA from patient plasma, and analyzed the mutations with a custom procedure for next generation sequencing (NGS). The targeted resequencing panel covers the most important mutation hotspots in NSCLC relevant genes including EGFR mutations on exon 19, 20 and 21. A custom library preparation method and bioinformatics pipeline is used to efficiently call rare mutations in a qualitative and quantitative manner. **Results:** Our data demonstrate the ability to detect low copy numbers of activating and AR mutations in plasma of lung cancer patients by combining the mutation signal from exoRNA and cfDNA and using a focused NGS gene panel. The mutation signal in plasma is highly concordant with data obtained from repeat biopsies, showing the feasibility of the approach. Moreover, EGFR mutations of patients with intrathoracic disease (M0/M1a) are readily detected in the combined exoRNA/cfDNA isolation, in contrast to methods relying only on the isolation of cfDNA. **Conclusion:** Detection of both activating and AR mutations to EGFR therapy in plasma is a feasible alternate to repeat biopsy and the combined isolation of exoRNA and cfDNA offers superior sensitivity. Especially in challenging cases, e.g. with intrathoracic disease, the advantage of combined plasma exoRNA/cfDNA isolation substantially improves the sensitivity over approaches that utilize only cfDNA. **Keywords:** exosomal RNA, cell-free DNA, next generation sequencing, T790M

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-002 Q787Q EGFR Polymorphism as a Prognostic Factor for Lung Squamous Cell Carcinoma Young Wha Koh[1], Jae-Ho Han[2], Changjin Kim[3] [1]*Pathology, Ajou University School of Medicine, Suwon/Korea,* [2]*Ajou University School of Medicine, Suwon/Korea,* [3]*Pathology, College of Medicine, Soonchunhyang University, Chonan/Korea*

Background: EGFR (epidermal growth factor receptor) mutations have been frequently reported in the early stages of non-small cell lung cancer (NSCLC) and have shown survival benefits in advanced lung adenocarcinoma. However, testing for EGFR mutations have rarely been recommended for lung squamous cell carcinoma patients. Previous studies have revealed that the Q787Q polymorphism in exon 20 of the EGFR gene is associated with a poor prognosis in patients treated with gefitinib (an EGFR tyrosine-kinase inhibitor) and is frequently detected in non-adenocarcinoma lung cancer patients. There is no result for an association between Q787Q EGFR polymorphism and EGFR common mutations. The prognostic data of Q787Q EGFR polymorphism was limited to patients treated with gefitinib; therefore, prognostic information for patients without gefitinib treatment is also needed. **Methods:** To determine the presence of Q787Q polymorphism in patients with lung cancer, we performed direct sequencing analyses of four exons for 83 squamous cell carcinomas and 80 adenocarcinomas untreated with EGFR tyrosine-kinase inhibitors. **Results:** When complex mutations were excluded, the Q787Q EGFR polymorphism was more frequently detected in squamous cell carcinoma patients than adenocarcinoma patients (24% and 15.9%, respectively). The group of patients with Q787Q EGFR polymorphism included more males and heavy-smokers compared with other patient groups. The presence of the Q787Q EGFR polymorphism significantly and negatively affected the overall survival (OS) rate in patients with NSCLC (P = 0.024), particularly those with squamous cell carcinoma (P = 0.044). For stage I and II squamous cell carcinoma patients, those with the Q787Q EGFR polymorphism had lower OS rates than those with other mutations or those with a wild type phenotype (P = 0.04).

Table 1. EGFR mutational profile of non-small cell lung carcinoma patients.

Variable	No. of patients (%)
Exon 18	
G719X	2 (1.2%)
T725T polymorphism	6 (3.7%)
Exon 19 (deletion)	15 (9.2%)
Exon 20	
Insertion	2 (1.2%)
Q787Q polymorphism	39 (23.9%)
Exon 21 (L858R)	19 (11.7%)
Complex mutation	
Exon 18(T725T)+ Exon 19 (deletion)	1 (0.6%)
Exon 19 (deletion)+ Exon 20 (Q787Q)	4 (2.4 %)
Exon 21 (L858R)+ Exon 20 (Q787Q)	4 (2.4 %)

Table 2. Multivariate analyses of overall survival according to clinicopathologic variables

Variables		Hazard ratio	*P*value
Age	<60 vs. ≥60	1.836	0.021
Sex	female vs. male	2.071	0.121
Histologic subtype	Adenocarcinoma vs. Squamous cell carcinoma	0.754	0.275
pN stage	0 vs. 1-3	1.552	0.078
Adjuvant radiotherapy	(-) vs. (+)	1.175	0.491
Smoking grade	Non-smoker	reference	
	Ex-smoker	1.907	0.144
	Light-smoker	1.378	0.452
	Heavy-smoker	1.799	0.197
Q787Q EGFR polymorphism	(-) vs. (+)	1.874	0.013

Conclusion: The Q787Q EGFR polymorphism enables the stratification of pulmonary squamous cell carcinoma patients, particularly among those in stage I/II. **Keywords:** Prognosis, Lung Squamous cell carcinoma, EGFR, polymorphism

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-003 Two Methods for Developing in Vitro Erlotinib-Resistant Cell Lines Lead to Distinct RTK Shifts, but Both Result in EMT Kristine R. Jakobsen[1], Anne T. Madsen[1], Christina Demuth[1], Dianna Hussmann[2], Peter Meldgaard[3], Anders L. Nielsen[2], Boe S. Sørensen[1] [1]*Department of Clinical Biochemistry, Aarhus University Hospital, Aarhus C/Denmark,* [2]*Department of Biomedicine, Aarhus University, Aarhus/Denmark,* [3]*Department of Oncology, Aarhus University Hospital, Aarhus/Denmark*

Background: Several studies have investigated resistance mechanisms underlying acquired erlotinib-resistance *in vitro*. To mimic the *in vivo* distribution of the drugs, different approaches such as applying gradually increasing doses of erlotinib to the cells or exposing them to a high fixed concentration of the drug have been used. We demonstrate that two different approaches of developing erlotinib-resistant HCC827 cells results in activation of two distinct RTK bypass-signalling pathways. However, despite these differences both cell lines undergo EMT. Our finding suggests that EMT is a common marker of erlotinib-resistance. **Methods:** Two HCC827 erlotinib-resistant cell lines were established using either gradually increasing doses of erlotinib (0.01 µM – 5 µM) resulting in erlotinib-resistant HCC827ER cells. Alternatively a fixed concentration of 5 µM generated HCC827HD with erlotinib resistance. Growth of the resistant cell lines was investigated using MTS assay in combination with erlotinib, linsitinib and crizotinib. Phospho-RTK arrays (R&D Systems), qPCR and immunofluorescence were used to characterize the cells. **Results:** Phospho-RTK array analysis revealed that the erlotinib-resistant HCC827ER cells had an increased activation of MET, and copy number analysis demonstrated the activation to be caused by a *MET* amplification. Furthermore, HCC827ER showed growth inhibition when treated with the MET-inhibitor crizotinib. The other type of erlotinib-resistant cells, HCC827HD, had increased activation of IGF1R and also responded to the IGF1R-inhibitor linsitinib. However, a common feature is that both HCC827ER and HCC827HD gained EMT features. HCC827ER showed increased expression SLUG, SNAIL and ZEB1, whereas HCC827HD showed increased *SLUG* and *TWIST* expression.

To detect the relevance of MET and IGF1R signalling in accordance to EMT in the two cell lines, we treated the HCC827ER cells with the tyrosine kinase inhibitor crizotinib (MET) and the HCC827HD cells with linsitinib (IGF1R). In both cases, we saw a decrease in EMT-marker transcription after the treatment. **Conclusion:** Our study demonstrates that different approaches to developing erlotinib-resistant cell lines can lead to distinct activation of bypass receptor tyrosine kinase signalling pathways. EMT, however, is induced in both types of erlotinib-resistance. This finding indicates that EMT is a common trait of the phenotype of erlotinib-resistant cells. More research needs to be done to establish the functional role of EMT in erlotinib resistance. **Keywords:** NSCLC, EGFR TKI-resistance, EMT

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-004 The BIM Deletion Polymorphism in Patients with EGFR-Mutant Non-Small Cell Lung Cancer Treated with EGFR Tyrosine Kinase Inhibitors
Ji Yun Lee[1], Bo Mi Ku[2], Sung Hee Lim[1], Haesu Kim[1], Kwai Han Yoo[1], Ki Sun Jung[1], Haa-Na Song[1], Jong-Mu Sun[1], Se-Hoon Lee[1], Jin Seok Ahn[1], Keunchil Park[1], Myung-Ju Ahn[1] [1]*Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/Korea,* [2]*Samsung Biomedical Research Institute, Samsung Cancer Research Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/Korea*

Background: A germline *BIM* deletion polymorphism has been proposed to predict poor treatment response to certain kinase inhibitors. The purpose of this study was to explore whether the *BIM* deletion polymorphism predicts treatment efficacy of epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) in Korean patients with EGFR-mutant NSCLC. **Methods:** Peripheral blood samples from a total of 205 patients with EGFR-mutant NSCLC who were treated with EGFR TKIs between July 2008 and April 2013 were included. The incidence of BIM deletions in these samples was detected by polymerase chain reaction. We compared the clinical outcomes in patients with and without the polymorphism after treatment with EGFR TKIs (gefitinib or erlotinib). **Results:** The *BIM* deletion polymorphism was present in 15.6% (32/205) of patients. One patient was homozygous for the deletion, and the remaining 31 had heterozygous deletions. The majority of patients were < 65 years old (74%), female (68%), never smokers (76%), and had stage IV NSCLC (67%). There were no associations between the BIM deletion polymorphism and clinicopathological features including gender, age, smoking status, histology, stage, and number of metastasis sites. Patients with and without the *BIM* deletion polymorphism had similar ORRs (91% vs. 84%, P = 0.585). Progression-free survival (PFS) and overall survival (OS) did not differ significantly between patients with and without the *BIM* deletion polymorphism (median PFS 12 vs. 11 months, P = 0.160; median OS 31 vs. 30 months, P = 0.452). Multivariate analysis identified significantly predictive markers for clinical outcomes of EGFR TKIs including ECOG PS 0-1, adenocarcinoma histology, recurrent disease, and *EGFR* mutation type. The results were validated in an independent cohort of 69 NSCLC patients. **Conclusion:** It remains to be determined whether the BIM deletion polymorphism provides intrinsic resistance or decreased sensitivity to EGFR TKIs in EGFR-mutant NSCLC patients. **Keywords:** non-small cell lung cancer, Epidermal growth factor receptor, Tyrosine kinase inhibitors, BIM Deletion Polymorphism

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-005 Bevacizumab plus Erlotinib in B901L Xenograft Model of EGFR Mut+ NSCLC
Chinami Masuda, Nobuyuki Ishikura, Toshiki Iwai, Keigo Yorozu, Mtsue Kurasawa, Koh Furugaki, Kaname Yamamoto *Product Research, Chugai Pharmaceutical Co., Ltd., Kanagawa/Japan*

Background: Erlotinib (ERL), an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, has shown clinical efficacy in *EGFR* mutation-positive (*EGFR* Mut+) non-small-cell lung cancer (NSCLC). However, almost all tumors recur and eventually develop resistance to ERL. Bevacizumab (BEV), a humanized anti-vascular endothelial growth factor (anti-VEGF) monoclonal antibody, in combination with standard first-line chemotherapies, has improved clinical outcomes in advanced NSCLC. Recently, the phase II JO25567 study reported that the combination of BEV plus ERL significantly prolonged progression-free survival compared with ERL alone in *EGFR* Mut+ NSCLC (Seto, et al. Lancet Oncol 2014; 15:1236–44). However, the mechanism by which this combination confers efficacy remains unknown. In the present study, we examined the antitumor activity of BEV in combination with ERL and analyzed the mechanism of action in a human *EGFR* Mut+ NSCLC xenograft model. **Methods:** Mice (BALB-nu/nu) were subcutaneously inoculated with the human NSCLC cell line B901L harboring *EGFR* exon 19 deletion. BEV (5 mg/kg) was intraperitoneally administered once a week and oral ERL (60 mg/kg; maximum tolerated dose) was given daily, starting from Day 1. Antitumor activity was evaluated by measuring tumor volume (TV; mm^3) twice a week. Human VEGF protein was quantified by ELISA, and EGFR signaling in tumor tissues was examined by immunoblot analysis. Statistical analysis was performed using the Wilcoxon test. **Results:** In the initial phase, ERL showed remarkable tumor growth inhibition in the B901L xenograft model. However, tumor regrowth was observed in the ERL-treated group during further treatment. In contrast, no significant tumor regrowth was observed in the BEV plus ERL-treated group (WCLC 2013; P2.05-004). In the ERL-treated group, tumor VEGF protein was significantly increased ($p<0.05$) on Day 68 (ERL-refractory phase) compared with Day 4 (ERL-sensitive phase) and the levels of phosphorylation of extracellular signal-regulated kinase (ERK), AKT and signal transducer and activator of transcription 3 were markedly increased on Day 75 compared with Day 5, although phosphorylation of EGFR was still inhibited. In contrast, the combination of BEV plus ERL inhibited phosphorylation of ERK on Day 75, although BEV alone did not. **Conclusion:** The combination of BEV plus ERL demonstrated promising efficacy in the B901L xenograft model of *EGFR* Mut+ NSCLC. The observed continuous inhibition of ERK phosphorylation may contribute to the antitumor activity of BEV plus ERL treatment. Re-induction of VEGF and subsequent VEGF-dependent tumor growth, either directly or indirectly, was suggested as one of the major mechanism of acquired resistance to ERL leading to remarkably prolonged antitumor activity of BEV in combination with ERL in this model. These encouraging preclinical results warrant further investigation in a clinical setting. **Keywords:** NSCLC, bevacizumab, Erlotinib, VEGF

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-006 MiRNA Signature to Assess Sensitivity to FGFR Tyrosine Kinase Inhibitors
Christopher J. Rivard[1], Brad Rikke[2], Murry Wynes[3], Leslie Rozeboom[2], Xian Lu[4], Dexiang Gao[4], Trista Hinz[5], Lynn Heasley[5], Paul A. Bunn, Jr[2], Fred R. Hirsch[2] [1]*Medical Oncology, University of Colorado Denver, Aurora/CO/United States of America,* [2]*Medical Oncology, University of Colorado Denver, Aurora/United States of America,* [3]*Iaslc, Aurora/CO/United States of America,* [4]*Biostatistics and Informatics, University of Colorado School of Public Health, Denver/CO/United States of America,* [5]*Craniofacial Biology, University of Colorado Denver, Aurora/CO/United States of America*

Background: Increased signaling through the FGF/FGFR signaling pathway has been implicated as a driver in a number of different malignancies including lymphomas, prostate cancer, breast cancer, and lung cancer. This pathway also appears to play a role in conferring *de novo* and acquired resistance to cancers driven by EGFR mutations. Consequently, drugs that inhibit FGFRs are being investigated as potential therapeutics for cancer. Here we screened a large panel of miRNAs as potential predictors of sensitivity to FGFR tyrosine kinase inhibitors (TKIs). **Methods:** A panel of 377 miRNAs (Megaplex Card A, Life Technologies) was screened for expression level differences between four lung cancer cell lines that are sensitive (IC_{50} ≤ 50 nM) and four lines that are resistant (IC_{50} > 100 nM) to ponatinib (non-specific FGFR TKI) and AZD4547 (FGFR-specific TKI). Expression levels were assayed by RT-qPCR and analyzed using the Statistical Analysis of Microarrays (SAM) method. Thirty-nine miRNAs having an estimated false discover rate (FDR) of zero and large median fold differences (> 8) between the sensitive and resistant lines were selected for signature development. RT-qPCR assays were incorporated into a custom microfluidics card (Life Technologies), which was used to profile the original 8 cell lines and 10 additional sensitive lines and 16 additional resistant lines (34 lines total). Logistic regression was then used to identify the best signature panel for distinguishing sensitive cell lines from resistant. **Results:** Univariate analysis indicated three miRNAs (let-7c, miR-338, and miR-218) that differed between the sensitive and resistant lines at $p < .05$. The best signature panel consisted of let-7c, miR-200a and miR-200b, which gave an area under the receiver operator characteristic (AUROC) curve of 0.90 (95% CI = 0.8 to 1). This performance was nearly as good as using FGFR1 mRNA alone (AUROC = 0.94). The predominant miRNA in our 3-miRNA signature was let-7c, which also exhibited a suggestive additive effect to using FGFR1 as a biomarker ($p = 0.09$). We also tested whether cell lines with high sensitivity to ponatinib can be made resistant by reducing the high level of let-7c in these lines. We have found that transient transfection of let-7c silencing RNA (Life Technologies) produces a decrease in FGFR1 mRNA levels for some cell lines but not others. **Conclusion:** It appears possible to predict sensitivity to an FGFR1 inhibitor using miRNA expression signatures. More studies, however, are needed to confirm the 3-marker signature developed in this study. Modulating let-7c, the predominant predictor within the signature, appears to modulate FGFR1 levels in a manner consistent with altering ponatinib sensitivity. This effect is most likely indirect as the mRNA of FGFR1 does not contain predicted binding sites for let-7c. **Keywords:** miRNA signature, FGFR, inhibitor, Let-7c

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-007 In Vitro and in Vivo Efficacy of AZD9291 Is Enhanced by Combination with AZD4547 in EGFR Mutant Lung Cancer Cells
Daniel C. Chan[1], Trista K. Hinz[2], Lindsay A. Marek[2], Zhiyong Zhang[1], Teresa T. Nguyen[2], Paul A. Bunn, Jr[1], Lynn Heasley[2] [1]*Medical Oncology, University of Colorado Denver, Aurora/CO/United States of America,* [2]*University of Colorado Anschutz Medical Campus, Aurora/CO/United States of America*

Background: EGFR-specific tyrosine kinase inhibitors (TKIs) provide marked clinical responses in patients bearing EGFR mutated lung tumors, although acquired resistance limits the durability of the response. In light of the frequent emergence of erlotinib and gefitinib-resistant EGFR T790M mutations upon tumor progression, 3rd generation EGFR-specific TKIs have been developed that specifically inhibit gain-of-function EGFR mutants irrespective of T790M status. Recently, we reported a distinct mechanism of acquired resistance whereby specific EGFR mutant lung cancer cell lines including H1650 and HCC4006 cells, but not PC9 cells, undergo an epithelial-mesenchymal transition (EMT) upon chronic *in vitro* treatment with gefitinib. As a result, the adapted cells acquire vulnerability to FGFR inhibitors by virtue of EMT-mediated FGF2 and FGFR1 induction. Herein, we have tested the hypothesis that combination of the FGFR inhibitor, AZD4547, with the 3rd generation EGFR TKI, AZD9291 will yield superior anti-tumor activity relative to AZD9291 alone. **Methods:** Lung cancer cell lines bearing gain-of-function EGFR mutations (HCC4006, H1650 and PC9) were submitted to *in vitro* clonogenic growth assays in the presence of AZD9291 and/or AZD4547 over concentration ranges for 1 to 300 nM for each drug. For *in vivo* measurement of the activity of these drugs, flank xenografts were established in Nu/Nu mice with the 3 lung cancer cell lines and treated by daily oral gavage (5 days on, 2 days off) with diluent, AZD9291 (5 mg/kg), AZD4547 (12.5 mg/kg) and the combination of the two drugs at these doses.

Tumor size was measured with calipers and volume was calculated using the formula, Volume=3.14(short diameter)^2(long diameter)/6. **Results:** HCC4006, H1650 and PC9 cells were highly sensitive to ZD9291 *in vitro* with IC_{50} values of 1.6, 7.4 and 3.3 nM, respectively. In a 2 week clonogenic growth assay, AZD9291 reduced growth of all cell lines by >95%, although viable drug resistant persisters clearly remained. While none of these cell lines exhibited significant growth inhibition in response to AZD4547 alone, combination of AZD9291 and AZD4547 further reduced clonogenic growth of HCC4006 and H1650 cells, but not PC9 cells. In flank xenograft studies, AZD9291 monotherapy induced marked tumor shrinkage (H1650, ~80% at day 10; HCC4006, ~90% at day 30; PC9, 89% at day 25), although regrowth of the tumors occurred with all three xenografts. AZD4547 yielded little or no growth inhibition as a monotherapy, but significantly enhanced the degree of tumor shrinkage and delayed the time to tumor progression in H1650 and HCC4006 tumors, but not PC9 tumors. **Conclusion:** Combination of the FGFR inhibitor AZD4547 with AZD9291 affords greater growth suppression relative to AZD9291 alone in HCC4006 and H1650 cells that undergo EMT and induction of an FGF2-FGFR1 pathway. Predictably, this combination was not more effective compared to AZD9291 alone in PC9 cells that fail to undergo EMT in response to EGFR TKI treatment. The studies support the efficacy of combined AZD9291 and AZD4547 treatment of a subset of lung tumors driven by mutated EGFR, although the features of these particular lung tumors that predict this response is unknown at this time. **Keywords:** AZD9291 and AZD4547, Drug combination, EMT as a resistant mechanism, EGFR mutant lung cancer cells

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-008 IGF1R Expression Is Predictive of Poor Prognosis in EGFR-Mutant Lung Adenocarcinoma Eunhyang Park[1], Hyojin Kim[1], Ping-Li Sun[2], Yan Jin[2], Jin-Haeng Chung[2] [1]*Seoul National University College of Medicine, Seoul/Korea,* [2]*Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seoul/Korea*

Background: Insulin-like growth factor-1 receptor (IGF1R) is a membrane receptor-type tyrosine kinase that has attracted considerable attention as a potential therapeutic target, although its clinical significance in non-small cell lung cancer (NSCLC) is controversial. This study aimed to clarify the clinical significance of IGF1R expression in human NSCLC. **Methods:** IGFIR protein expression was evaluated by immunohistochemistry in 386 patients with NSCLC who underwent surgical resection (150 squamous cell carcinomas [SqCCs] and 236 adenocarcinomas [ADCs]). Correlations of the expression of IGF1R with clinicopathological and molecular features, and prognostic significance were analyzed. **Results:** Membranous and cytoplasmic IGFIR expression was significantly higher in SqCCs than in ADCs. In patients with SqCC, membranous IGFIR expression was associated with lower cancer stage, and better progression-free survival (PFS) (hazard ratio [HR] = 0.60, 95% confidence interval [CI]: 0.36–0.99, p = 0.045). In patients with ADC, IGFIR expression had no significant prognostic value, but in the subgroup of *epidermal growth factor receptor (EGFR)*-mutant ADC, membranous IGF1R expression was associated with vascular, lymphatic and perineural invasion, solid predominant histology, higher cancer stage, and was significantly associated with worse PFS (HR = 2.27, 95% CI: 1.30–5.48, p = 0.008). **Conclusion:** Lung ADC and SqCC showed distinct IGF1R expression profiles that demonstrated prognostic significance. High membranous IGF1R expression was predictive of poor PFS in *EGFR*-mutant lung ADC, while was predictive of better PFS in SqCC. These findings may serve to improve study design for subsequent investigations into IGF1R and NSCLC, and to select patients for future anti-IGF1R therapy. **Keywords:** non-small cell lung cancer, Insulin-like growth factor-1 receptor, Prognosis, Epidermal growth factor receptor

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-009 Potential Predictive Markers with Plasma for Re-Challenge with EGFR-TKIs Tomomi Nakamura[1], Akemi Sato[2], Naomi Kobayashi[2], Hitomi Umeguchi[2], Kazutishi Komiya[2], Shinya Kimura[2], Naoko Sueoka-Aragane[2] [1]*Internal Medicine, Saga University, Saga/Japan,* [2]*Saga University, Saga/Japan*

Background: Epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKI) have produced dramatic anti-cancer effects in non-small cell lung cancer patients carrying *EGFR* activating mutations. However, patients eventually acquire resistance resulting from various mechanisms such as secondary *EGFR* mutation, T790M, *MET* amplification, and hepatocyte growth factor (HGF) overexpression. Recently, the second generation EGFR-TKI, afatinib which was expected for anti-cancer efficacy in T790M positive lung cancer patients has been developed. However, it has not evidenced acceptable anti-cancer efficacy in lung cancer patients who acquired resistance to first generation EGFR-TKI because of difficulty to identify mechanisms of acquired resistance by re-biopsy. The purpose of this study is to investigate whether T790M and HGF in plasma are useful as predictive markers for determination efficacious treatment including re-challenge of the first generation of EGFR-TKI and treatment with the second generation, afatinib after acquired resistance. **Methods:** We analyzed retrospectively 16 re-challenges with first generation EGFR-TKI, and 6 treatments with afatinib after acquired resistance with first generation EGFR-TKI undertaken by investigating T790M and HGF in plasma coupled with clinical characteristics. *EGFR* mutations in plasma DNA were detected using the wild inhibiting PCR and quenched probe (WIP-QP) system for exon 19 deletions, and T790M and L858R were detected using the mutation-biased PCR and quenched probe (MBP-QP) system. HGF level in plasma was measured by enzyme-linked immunosorbent assay; ratio of HGF level before re-challenge or afatinib to that prior to the previous EGFR-TKI treatment was calculated. **Results:** Two re-challenges demonstrated partial response (PR), six remained as stable disease (SD), and eight had progressive disease (PD). Four of five patients with a history of T790M positivity had PD. Seven of eight patients who showed greater than 1.5-fold elevation of HGF before re-challenge with EGFR-TKI suffered PD. Elevation of HGF ratio to above 1.5 was significantly associated with poor response to EGFR-TKI re-challenge (p = 0.005). Having no history of T790M and an HGF ratio less than 1.5 was significantly associated with a good response to EGFR-TKI re-challenge (p<0.001). Afatinib demonstrated one PR and four SD, and one had PD. T790M was detected in four of six patients before afatinib treatment. Three of four patients with a history of T790M positivity had PR or SD. Elevation of HGF ratio to above 1.5 was not detected in six patients who treated with afatinib. **Conclusion:**Combination of T790M detection and HGF quantification using plasma is a potentially useful assay system for predicting the effect of EGFR-TKI re-challenge with not only first generations but also afatinib. Eventually, we strive to develop more effective treatment strategies for NSCLC patients with *EGFR* activating mutations depending on the status of T790M and HGF level in plasma, for example the second or the third generation EGFR-TKI for detection of T790M, MET inhibitor for elevation of HGF level, and EGFR-TKI re-challenge without detection of T790M and elevation of HGF level. **Keywords:** plasma DNA, predictive marker, EGFR-TKI

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P2.04-010 18F-FDG Uptake and CEA between Different EGFR Mutations in Patients with Non-Small Cell Lung Cancer Xiaorong Dong, Xican Gao, Qian Cai, Ruiguang Zhang, Gang Wu *Cancer Center, Union Hospital, Wuhan/China*

Background: Many studies have demonstrated the clinical efficacy of the epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) gefitinib and erlotinib compared with chemotherapy against non–small-cell lung cancer (NSCLC) when used as first-line treatment for patients whose tumors harbor activating *EGFR* mutations. But sometimes the acquisition of adequate tissues for EGFR mutation analysis is not feasible. The aim of this study is to evaluate the relationship between EGFR mutation status, serum carcinoembryonic antigen (CEA) levels, and the SUVmax of [^{18}F]-fluorodeoxyglucose positron emission tomography (FDG-PET) in primary disease and metastatic lymph nodes, and in Chinese non-small cell lung cancer patients. **Methods:** From January 2009 and October 2010, 167 patients with definite pathological diagnosis of NSCLC who underwent [^{18}F]-FDG-PET, EGFR mutation analysis by amplification refractory mutation system (ARMOS) method, and CEA value by Elecsys chemiluminescence immunoassay system were eligible to participate in this study. The associations of EGFR mutation status with patient characteristics, maximal standard uptake value (SUVmax) of primary tumors and metastatic lymph nodes, serum CEA level at diagnosis were analyzed. Receiver-operating characteristic (ROC) curve analysis was performed to quantify the predictive value of these factors. Multivariate logistic regression analysis was used to analyze predictors of EGFR mutations. **Results:** EGFR mutations were identified in 167 patients (73 EGFR-mutant and 94 wild-type). The [^{18}F]-FDG uptake was significantly lower in EGFR-mutant (mean SUVmax=9.3) than wild-type (10.2) NSCLC patients (P=0.045). The CEA value was significantly higher in EGFR-mutant (mean CEA=12.5) than wild-type (5.8) NSCLC patients (P=0.030). The ROC analysis concluded that high FDG uptake (SUV≥9.6) may be predictive of the wild-type *EGFR* genotype, whereas a low normalized SUVmax may predict the presence of *EGFR* mutations less robustly. We also demonstrated that high CEA levels (CEA≥9.25) were positively correlated with histological EGFR gene mutations by ROC analysis. On multivariate analysis, non-smoker, the low SUVmax of the primary tumor and the high CEA value were significantly associated with *EGFR* mutation status. In addition, we also showed that the exon 19 mutation (mean SUVmax=10.6) is strongly correlated with higher SUVmax than exon 21 mutation (mean SUVmax=8.7) (P=0.017). The metastatic lymph nodes in EGFR-mutant patients had lower SUVmax than EGFR wild-type patients (SUVmax 7.3 vs 6.65, P < 0.001). **Conclusion:** The combined evaluation of SUVmax FDG uptake in primary tumor and metastatic lymph nodes, CEA level, and smoking status may be helpful in predicting EGFR mutation status in patients with NSCLC, especially when the tumor sample is inadequate for genetic analysis or genetic testing is not available. **Keywords:** Positron emission tomography, Epidermal growth factor receptor, Carcinoembryonic antigen, NSCLC, ex

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-011 Whole-Genome Copy Number Analyses of NSCLC Tumors Reveal Aberrations Associated With EGFR Mutations and May Have Prognostic Impact Maria M. Bjaanæs[1], Gro Nilsen[2], Steinar Solberg[3], Odd Terje Brustugun[4], Ole C. Lingjærde[2], Åslaug Helland[5] [1]*Department of Genetics, Institute for Cancer Research, Oslo University Hospital-The Norwegian Radium Hospital, Oslo, Norway, Oslo/Norway,* [2]*Department of Computer Science, University of Oslo, Oslo/Norway,* [3]*Department of Cardiothoracic Surgery, Oslo University Hospital-Rikshospitalet, Oslo/Norway,* [4]*Dept of Oncology, Oslo University Hosital,The Norwegian Radium Hospital, Oslo/Norwa, Oslo/Norway,* [5]*Department of Oncology, The Norwegian Radium Hospital, Oslo/Norwa, Oslo/Norway*

Background: Knowledge about genetic alterations in Non-Small Cell Lung Cancer (NSCLC) has given us a significant insight in the biology of these tumors. It is of great clinical importance with consequences for the patients, and DNA mutations and translocations are currently targets for therapy. Aberrations in DNA copy number are frequent events in NSCLC tumors and important in tumorogenesis. In this present study we want to investigate how the copy number changes varies between different subgroups of NSCLC tumors based on the patients' smoking status, histology or *EGFR-*, *KRAS-* and *TP53* mutations. The DNA copy number data will be integrated with global mRNA expression to study the cis-associated mRNA expression changes. Last, we want to investigate whether genomic events, like specific copy number changes or the complex arm-wise aberration index (CAAI), have prognostic impact in patients with

NSCLC. **Methods:** In this study we have included 200 patients with operable NSCLC tumors. Copy number data were obtained by using the Affimetrix Genome-wide human SNP array 6.0. Histopathological information, *EGFR*-, *KRAS*- and *TP53* mutation status were determined and clinical information and follow-up data was obtained for all patients. The mRNA expression was determined by the Agilent 60K mRNA expression array on a subset of 117 patients. The data was analyzed by using bioinformatic tools like ASCAT and integration of the mRNA data and the survival analyses are on-going. **Results:** Preliminary results have shown that copy number aberrations are frequent events in NSCLC tumors, consistent with previous reports. We have identified that the copy number patterns differ between adenocarcinomas and squamous cell carcinomas, and between tumors from patients with different smoking history. However, the largest differences were found between the EGFR-mutated adenocarcinomas compared with *EGFR* wildtype tumors, where we identified a specific pattern of copy number changes in the tumors that harbour *EGFR* mutation. These changes were mainly located at chromosome arm 1p, 2p, 3q, 5q, 7, 12 and 13. Preliminary analyses have also identified specific copy number aberrations with prognostic significance. **Conclusion:** Copy number aberrations are frequent in NSCLC tumors and may have great impact on gene expression and give us valuable prognostic information. EGFR-mutated adenocarcinomas have a specific pattern of copy number changes, which provides new insight of the biology of these tumors. **Keywords:** Copy number aberrations, mRNA expression, Prognosis, EGFR

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P2.04-012 The Development of EGFR Mutation Diagnostic Program for NSCLC Patients in Poland (2011-2014) Joanna Chorostowska-Wynimko[1], Pawel Krawczyk[2], Bartosz Wasag[3], Iwona K. Rzepecka[4], Piotr Wojcik[5], Karolina Tecza[6], Paulina Jagus[1], Tomasz Powrozek[2], Bozena Konopka[4], Agata Gizycka[1], Kamila Wojas-Krawczyk[2], Janusz Limon[3], Barbara Pienkowska-Grela[4], Piotr Pierzchalski[5], Marzena A. Lewandowska[7], Liliana Pieciak[8], Artur Kowalik[8], Piotr Widlak[6] [1]*Department of Genetics and Clinical Immunology, National Institute of Tuberculosis and Lung Diseases, Warsaw/Poland,* [2]*Laboratory of Immunology and Genetics, Department of Pneumonology, Oncology and Allergology, Medical University of Lublin, Lublin/Poland,* [3]*Department of Biology and Genetics, Gdansk Medical University, Gdansk/Poland,* [4]*Department of Pathology and Laboratory Diagnostics, Cancer Center and Institute of Oncology, Warsaw/Poland,* [5]*Oncogene Diagnostics Inc., Cracow/Poland,* [6]*Center for Translational Research and Molecular Biology of Cancer, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice/Poland,* [7]*Molecular Oncology and Genetics Departament, The Inovative Medical Forum, the Franciszek Lukaszczyk Oncology Center, Bydgoszcz/Poland,* [8]*Department of Molecular Diagnostics, Holycross Cancer Center, Kielce/Poland*

Background: Targeted therapy of non-small cell lung cancer necessitates fast and reliable molecular evaluation of tissue/cytologic samples within the routine diagnostic process. Here we present the dynamic development of the *EGFR* mutation screening program for NSCLC patients in Poland within the previous 4 years. **Methods:** In total, 287 samples were analysed for *EGFR* mutations in 2011 (13.3% positive, 3% unsuitable for diagnostics), 1249 (9.2%, 1.5%) in 2012, 2104 (10.1%, 1.9%) in 2013, 4307 (10.2%, 2.7%) in 2014. Adenocarcinomas were 85.9% in 2012, 93.2% in 2014. The percentage of NSCLC NOS materials decreased continuously (10% down to 5.3%). 72% of samples contained >50% of cancer cells, 15% - 20-50%, 5.5% - 10-20%, 7.5% - below 10%. **Results:** Between 2011-2014, 727 activating *EGFR* mutations were identified, including 5.8% in exon 18, 58.5% in exon 19, 35.7% in exon 21, and 83 in exon 20 (10%). Currently, all laboratories employ CE-IVD real-time PCR tests as diagnostic method of choice. Additionally, 3 labs use alternative diagnostic methods as well. Results are available within 48 hrs (1 lab), 3-5 days (3 labs), 6-7 days (2), >8 days (2). All centres participate in the external quality schemes. **Conclusion:** The diagnostic program provides fast and reliable diagnostics of *EGFR* mutation in NSCLC patients in Poland. **Keywords:** non-small cell lung cancer (NSCLC), EGFR Tyrosine-kinase inhibitor (EGFR TKI), EGFR gene mutation detection, molecular diagnostics

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P2.04-013 TraiL Mediates Erlotinib-Induced Apoptosis in EGFR-Mutant Lung Cancer 3D Spheroids Hyun-Kyung Lee[1], Yunock Choi[2], Dario Barbone[3], V. C. Broaddus[3], Dae Young Hur[2] [1]*Division of Pulmonary and Critical Care Medicine, INJE University Busan Paik Hospital, Busan/Korea,* [2]*Department of Anatomy and Tumor Immunology, INJE University, Busan/Korea,* [3]*Lung Biology Center, San Francisco General Hospital, Uc San Francisco, San Francisco/CA/United States of America*

Background: Three-dimentional (3D) spheroid culture model were known to be a good model to study of the multicellular apoptotic resistance in most cancer cell lines. Contrary to the result with other cancer cell lines, we found that 3D spheroids of EGFR-mutant lung cancer cell lines showed more prominent apoptosis to tyrosine-kinase inhibitor (TKI), erlotinib than 2D monolayers in our previous experiments. BIM (the proapoptotic BH3-only BCL-2 family protein) expressions before and/or after treatment of TKI were more prominent in 3D than 2D in several EGFR-mutant lung cancer cell lines. But the other mechanisms of 3D sensitivity to TKI treatment are not studied yet. **Methods:** We used EGFR-mutant cell line, HCC4006 and A549 without EGFR mutation and generated 3D spheroids using poly-HEMA-coated 96-well plates. 2D monolayers and 3D spheroids were treatment with erlotinib. The degree of apoptosis were compared between 2D and 3D. Also the BIM and TNF-related apoptosis-inducing ligand (TraiL) expression were compared. After finding of relatively elevated TraiL expression in 3D, we silenced TraiL by siRNA and compared the degree of apoptosis between 2D and 3D. **Results:** We found that only HCC4006 not A549 showed apoptosis and elevated BIM expression after Erlotinib treatment. In line with our previous results, 3D spheroids showed more apoptosis and elevated BIM expression after Erlotinib treatment compared to 2D. Also we found more elevated TraiL expression in 3D. So we assumed that TraiL is one of the possible mechanisms of more apoptosis to Erlotinib in EGFR-mutant lung cancer 3D spheroids. After silencing the TraiL by siRNA, we found that there was no difference in the degree of apoptosis between 3D spheroids and 2D monolayer. **Conclusion:** Adding to increased BIM, we can suggest that elevated TraiL expression can be one of the possible mechanisms of the more prominent apoptosis in 3D spheroids of EGFR-mutant lung cancer cell lines. So potential therapies that upregulate BIM and/or TraiL expression can improved the efficacy of TKI treatment. **Keywords:** 3D spheroids, BIM, TRAIL, EGFR-mutant lung cancer

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P2.04-014 High Resolution Metabolomics to Discover the Potential Biomarkers in EGFR Mutated Lung Cancer Joon Woo Lee[1], Sung Yong Lee[2], Jeong Eun Lee[3], Youngja Hwang Park[1] [1]*College of Pharmacy, Korea University, Sejong City/Korea,* [2]*Department of Internal Medicine, Korea University Medical Center, Seoul/Korea,* [3]*Chungnam National University, Daejeon/Korea*

Background: Lung cancer is the most common cause of cancer death in the world. The epidermal growth factor receptor (EGFR) is a key target in the treatment of advanced non-small cell lung cancer (NSCLC). EGFR tyrosine kinase inhibitors (EGFR TKIs) have shown good clinical efficacies in EGFR mutation positive patients. For the determination of lung cancer, biopsy has been the method of choice. However, this method is invasive and not safe. Therefore, non-invasive test for the detection of EGFR mutation is required for the safety of the patients. This study aims to discover novel biomarkers which could be utilized in clinical use in the non-invasive diagnosis of EGFR mutation among NSCLC patients. **Methods:** Plasma samples from 15 patients were analyzed to detect biomarkers of EGFR-activating mutations. All patients had histological confirmation of advanced NSCLC. EGFR mutations in tumor tissue were detected using the peptide nucleic acid (PNA)-mediated polymerase chain reaction (PCR) clamping method. Ten (66.7%) of the patients had EGFR mutations in tumor tissue. The mutation groups were divided into exon 21 deletion group (G2) (n=6), and exon 19 deletion group (G3) (n=4). Differences in metabolic profiles of EGFR mutation lung cancer populations and no mutation lung cancer patients (G1) (n=5) were examined through the use of high-throughput mass spectrometry. **Results:** A total of 216 significant metabolites were found to be different between non-mutated and mutated samples. It was found that patients with EGFR mutated NSCLC have a significantly lower levels of leucine. Comparison between G1 and G2 showed that L-proline levels of G2 patients were decreased. Lastly, the comparison between G1 and G3 showed that Butyryl-L-carnitine concentrations of G3 were decreased as compared to G1 patients. **Conclusion:** These findings may not only open a door to a thorough non-invasive diagnosis of an EGFR mutation but also a possibility to classify the type of mutation present. Our results show that changes in metabolite pattern are useful for in diagnosing EGFR mutation. One of the potential biomarkers, leucine discriminates EGFR-mutated lung cancer from that of non-mutated ones. Therefore, high resolution metabolomics can be the potential non-invasive tool to utilize clinically to detect the EGFR mutations in NSCLC patients. **Keywords:** metabolomics, NSCLC, EGFR mutation

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P2.04-015 Screening EGFR Mutations in NSCLC by Immunohistochemistry Rania Gaber[1], Iris Watermann[2], Ekkehard Vollmer[2], Torsten Goldmann[2] [1]*Pathology, Faculty of Medicine, University of Alexandria, Egypt, Alexandria/Egypt,* [2]*Clinical and Experimental Pathology, Research Center Borstel, Borstel/Germany*

Background: EGFR mutations are important targets for therapy in NSCLC. EGFR mutations, receptor overexpression and increase gene copy number are main factors inducing EGFR tumorigenic activity. The aim of the present study was to detect EGFR mutations in NSCLC by immunohistochemistry (IHC) and investigate its relation to mutations detected by DNA sequencing, level of wild type EGFR protein overexpression, gene copy number gain and clinicopathological data. **Methods:** The study was performed in a cohort of 216 tumor tissues of primary chemotherapeutic naïve NSCLC. Expression of EGFR mutations was identified by immunohistochemistry (IHC), using the specific antibodies 6B6 and 43B2 (Cell Signaling Technology) followed by DNA sequencing of positive cases for NSCLC-associated EGFR mutations (Applied Biosystems). IHC was scored by two systems: (a) a modified H-score ranging from 0 to 300 (% cancer cells with membranous/cytoplasmic EGFR protein staining multiplied by the staining intensity rank from 0 to 3+) with score 100 as the positive threshold and (b) a qualitative score with cut off for positivity as ≥10% cells with 1+ to 3+ membranous or cytoplasmic staining for the mutation specific antibodies and 2+ and 3+ membranous staining for the wild form of EGFR. Wild EGFR protein expression determined by the 31G7 antibody (Zymed laboratories, CA). Gene copy number was investigated by Fluorescence In Situ Hybridization (FISH) using the SPEC EGFR/CEN7 dual color probe (ZytoLight) and specimens were scored according to the Colorado scoring system with high copy number defined as high polysomy (HP), low amplification (EGFR/CEN7=2.1-3) or high amplification (EGFR/CEN7=3). **Results:** Forty-one cases (19.9%) were positive to mutated EGFR by IHC, and 8 of them showed EGFR specific mutations on exons 18-21 by DNA sequencing. All the mutation confirmed cases had membranous or cytoplasmic staining intensity 2+ and 3+ with the different positive cut-off points of the two scoring systems. 6/10 (60%) of the genotyped NSCLC- associated mutations cases were positive to 43B2 and 4/10 (40%) were positive to 6B6 antibody. 7/10 (70%) of these cases showed 3+ membranous staining in ≥10% of tumor cells, 3/10(30%) showed 2+ cytoplasmic staining in ≥ 10% of tumor cells. All 8 cases (100%) positive for mutations by sequencing had adenocarcinoma histology. Positive correlations were found between EGFR mutations, by IHC and sequencing, and both overexpression of wild EGFR and increase

gene copy number (p=0.002 and p<0.001, respectively). Also, positive correlation was detected between EGFR mutations and high tumor grade and clinical stage (p<0.001 for both). **Conclusion:** IHC staining using mutation specific antibodies was demonstrated as a useful sensitive screening test before DNA sequencing. EGFR mutations play synergistic role with EGFR overexpression and increased gene copy number in NSCLC poor prognosis. Follow up of the cases with further evaluation of expression of EGFR wild and mutated forms after chemotherapy and targeted therapy will be performed. **Keywords:** EGFR mutations, DNA sequencing, NSCLC, Immunohistochemistry

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-016 Minority Exon 19 Deletions Also Have Major Response of EGFR Tyrosine Kinase Inhibitors in Non-Small Cell Lung Cancer Eiji Nakajima[1], Michio Sugita[2], Kinya Furukawa[3], Hiroyuki Miura[1], Hidenobu Takahashi[1], Norihiko Ikeda[4], Fred R. Hirsch[5], Wilbur A. Franklin[2] [1]*Thoracic Surgery, Tokyo Medical University Hachioji Medical Center, Tokyo/Japan,* [2]*Pathology, University of Colorado Health Sciences Center, Aurora/CO/United States of America,* [3]*Thoracic Surgery, Tokyo Medical University Ibaraki Medical Center, Ibaraki/Japan,* [4]*Thoracic Surgery, Tokyo Medical University Hospital, Tokyo/Japan,* [5]*Medical Oncology, University of Colorado Health Sciences Center, Aurora/CO/United States of America*

Background: This study points out an issue of PCR methods to detect exon 19 deletions. Exon 19 deletions are most important among exon 18 to 21 *EGFR* mutations to dictate *EGFR* tyrosine kinase inhibitors (*EGFR*-TKIs) therapy in non-small cell lung cancer (NSCLC), and exon 19 deletions and insertions have over 170 species by catalog of somatic mutation in cancer (COSMIC). PCR methods are used for clinical examination, because they are useful, rapid and cost-effective to detect*EGFR* mutations. Some PCR methods could detect all of exon 19 deletions and insertions, while others could not. We investigated the clinical significance of minority exon 19 deletions, which could not be detected according to the PCR methods, selected majority deletions. **Methods:** The study included a series of 73 NSCLC patients, which were treated with *EGFR*-TKI for recurrent disease after they had undergone surgery from 1992 to 2004. *EGFR* mutations were detected in 34 (47%) in 73 patients. Sixty patients were evaluable for response, and remaining 13 patients who had taken *EGFR*-TKI for less than one month. In 60 assessable patients, exon 19 deletions and exon 21 point mutation were detected from 19 patients and 10 patients, respectively. Patients with *EGFR* mutations had significantly higher response rates to *EGFR*-TKI than those with wild-type (*p*=.047), and exon 19 deletions had still rates (*p*=.024). In 51 samples, including 17 exon 19 deletions and 6 exon 21 mutations, four PCR methods are commonly used in Japan, were performed and compared. PCR-based methods were (1) PCR-Invader for the selected common mutations of exons 18, 19, 20 and 21, and micro capillary electrophoresis for the exhaustive detection of exon 19 deletions and insertions, (2) Peptide nucleic acid-locked nucleic acid (PNA-LNA) PCR clamp for the selected common mutations of exons 18, 19, 20 and 21, and direct sequence for the other mutations, (3) Cycleave PCR for the selected common mutations of exons 18, 20 and 21, and fragment analysis with micro capillary electrophoresis for the exhaustive detection of exon 19 deletions and insertions, (4) Scorpion Amplification Refractory Mutation System (ARMS) for the selected 29 mutations including 19 species of exons 19 deletions and insertions. **Results:** All four methods detected 6 exon 21 mutations as L858R point mutation. However, in exon 19 deletions and insertions including over 170 species, only micro capillary electrophoresis detected all 17 exon 19 deletions. PNA-LNA PCR clamp and direct sequence missed one 9 bp short deletion "L747-E749 del", which had complete response on *EGFR*-TKI therapy. Scorpion ARMS missed one 24 bp deletion and insertion "T751-I759 del ins S", which had stable disease for over 3 years on *EGFR*-TKI therapy. **Conclusion:** This study suggests micro capillary electrophoresis is necessary for the exhaustive detection of exon 19 deletions and insertions, and may identify tumors responsive to *EGFR*-TKIs therapy, especially those with small or unusual deletions. **Keywords:** Exon 19 deletions, PCR methods, non-small cell lung cancer, EGFR Tyrosine Kinase Inhibitors

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P2.04-017 The Study of a Relationship between Thyroid Transcription Factor-1 Expression and EGFR Mutations in Unselected Thai Patients with NSCLC Chaiyut Charoentum[1], Nirush Lertprasertsuke[2], Chumut Phanthunane[2], Theerakorn Theerakittikul[2], Atikun Limsukon[2], Somcharoen Saeteng[2], Apichart Tantraworasin[2], Juntima Euathrongchit[2], Yutthaphan Wannasopha[2], Thatthan Suksomboon charoen[2], Busyamas Chewaskulyong[2] [1]*Internal Medicine, Chiang Mai University, Chiang Mai/Thailand,* [2]*Chiang Mai University, Chiang Mai/Thailand*

Background: Epidermal growth factor receptor (EGFR) mutation status is a important test to guide treatment with EGFR tyrosine kinase inhibitors (EGFR TKI) effectively. However mutation detection by DNA direct sequencing remains expensive and is not readily available for routine practice in advanced NSCLC in Thailand. Thus a simple alternative method of EGFR mutation detection is required in NSCLC treatment. Recent studies have demonstrated a good association of Thyroid Transcription Factor-1 (TTF-1) with common TKI-sensitive EGFR mutations in NSCLC. We investigated the possibility of the routine test of TTF-1 expression by a simple immunohistochemistry (IHC) method as a potential indicator of common TKI-sensitive EGFR status in unselected Thai patients with non-small cell lung cancer. **Methods:** We collected tissue sample from 91 patients with NSCLC whose EGFR mutation status had previously been detected by DNA direct sequencing from January 2010 to January 2015. TTF-1 was detected by immunohistochemistry method. Results of expression of TTF-1 staining were scored as two categories were negative (no immunostaining or <5% stained cells) and positive (more than 5% positive cells with unequivocal nuclear immunostaining). **Results:** A total of 91 NSCLC samples with available results of molecular-based EGFR mutational status were collected. The common TKI-sensitive EGFR mutation was detected in 38/91 cases (42%) which included Exon19 del in 18/91 cases (20%), Exon 21 (L858R) point mutations in 20/91 cases (22%). The others 4 cases were found with uncommon EGFR mutations included Exon 20 (T790M), Exon18 (G719X), Exon 20 S768I and Exon 20 ins. There was 1 case with EGFR mutations at both Exon18 (G719X) and 20 ins. No mutation detected (wild-type, WT) were found in 48/91 patients. Of all 91 tissue samples were available for TTF-1 IHC testing, 80 of 91 patients were positive for TTF-1 (88%). For 80 patients with adenocarcinoma histology and 10 patients with squamous cell carcinoma history, TTF-1 was positive in 93% and 60 % respectively (P<0.05). The expression of TTF-1 in EGFR 19 del and 21 exon (L858R) mutation groups were significantly higher than the WT group (95% vs 81%, P < 0.05). In only 1 of 38 specimens positive for EGFR mutations was TTF-1 negative. The sensitivity was 97 % and specificity was 17%. Estimated negative predictive values (NPV) of TTF-1 expression for common TKI-sensitive EGFR mutation prevalence rates of 42% was 90%. **Conclusion:** These results indicated that positive TTF-1 expression has a significant positive correlation with common TKI-sensitive EGFR mutation at exon 19 and 21. In high prevalence area of EGFR mutation positive in Thailand, TTF-1 could be a valuable marker of EGFR mutation status. **Keywords:** EGFR Tyrosine Kinase Inhibitors, non-small cell lung cancer, TTF-1, EGFR mutations

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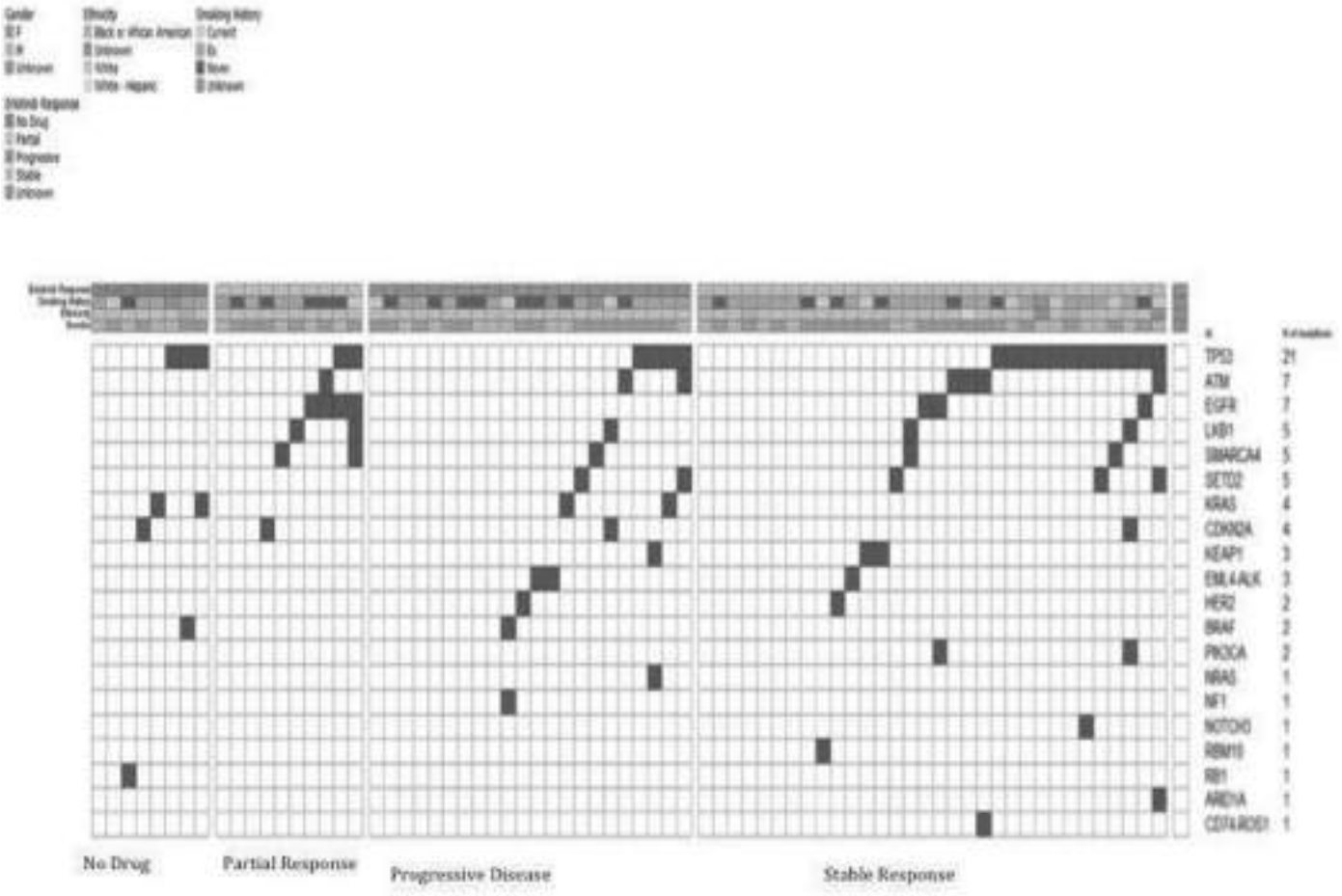
P2.04-018 Whole Transcriptome Analysis of EGFR Wildtype Non-Small Cell Lung Cancer Patients with Clinical Benefit from Erlotinib Michael F. Sharpnack[1], Luiz H. Araujo[1], Tadaaki Yamada[1], Leora Horn[2], Kun Huang[1], David P. Carbone[1] [1]*The Ohio State University Wexner Medical Center, Columbus/OH/United States of America,* [2]*Vanderbilt-Ingram Cancer Center, Nashville/TN/United States of America*

Background: Despite the success of targeted assays of EGFR mutations in defining the non-small cell lung cancer patients who benefit from EGFR-tyrosine kinase inhibition, there still remains a significant portion of patients whose tumors do not harbor EGFR mutations, yet achieve clinical benefit (progression-free survival > 6 months) from erlotinib treatment. We apply whole transcriptome sequencing (RNAseq) to discover expression and mutation changes associated with erlotinib response. **Methods:** We report the results of 108 stage IV non-small cell lung cancer patients treated with first line erlotinib. The primary endpoint assessed was progression-free survival (PFS), to which erlotinib has already shown to be beneficial when compared to placebo. Furthermore, RNAseq was performed on 73 tumors from 29 (40%) males and 44 (60%) females. The RNAseq samples were processed to obtain mutation and expression data. **Results:** 108 patients were followed for PFS, 7 of which declined to be followed, 2 came off erlotinib due to toxicity, 3 died before completion of the first cycle of erlotinib, 5 were ineligible, and 2 have not had tumor recurrence to date. The remaining 92 patients had a mean PFS of 4.71 months (±1.03 months, 95% CI). No patients experienced a complete response, and 14 of 92 (15%) patients had a partial response. Of the tumors analyzed via RNAseq, 7 harbored EGFR mutations, including a complex exon 18 deletion in a patient with a partial response to erlotinib. 14 of 64 (22%) patients without EGFR mutations showed clinical benefit from erlotinib, none of which harbored other known actionable mutations. These EGFR wildtype tumors did not exhibit mutations in other known oncogenes in lung cancer. We hypothesize that they are addicted to EGFR signaling through other means than overactive kinase activity caused by activating mutations.



Conclusion: We present results from a clinical trial of first line erlotinib in stage IV non-small cell lung cancer. We show that there is a significant cohort of EGFR wildtype patients who receive clinical benefit from erlotinib and present preliminary data of their mutation status.
Keywords: Erlotinib, RNAseq, EGFR, targeted treatment

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-019 PD 0332991 Inhibits the Growth of Gefitinib-Resistant Human Lung Cancer Cells in Vitro and in Vivo, When Combined with Gefitinib Hongyu Liu, Ying Li, Minghui Liu, Yongwen Li, Yuli Wang, Jun Chen *Tianjin Medical University General Hospital, Tianjin/China*

Background: Tyrosine kinase inhibitors (TKIs), such as gefitinib and erlotinib, which target the EGFR pathway, have a dramatic effect in the treatment of NSCLC patients, especially for patients with EGFR mutations, which is the leading cause of cancer-related mortality. Unfortunately, despite the success of these drugs, almost all cases progress, and eventually become resistant to such treatment, known as acquired resistance, and current targeted therapeutic strategies for patients with acquired resistance are limited. PD 0332991 is an orally active, highly selective inhibitor of the cyclin D kinases CDK4 and CDK6, with the ability to block retinoblastoma (Rb) phosphorylation. **Methods:** In this study, we evaluated, both *in vitro* and *in vivo*, the therapeutic approach of targeting the CDK4/6 and Rb pathway in PC-9/AB2 cells, which is an EGFR-TKIs acquired resistant lung adenocarcinoma cells. **Results:** PD 0332991 inhibits the growth and proliferation of both gefitinib-sensitive and gefitinib-resistant lung adenocarcinoma cells. In addition, PD 0332991 inhibits Rb phosphorylation in sensitive and resistant cell lines, as well as enhancing apoptosis in lung adenocarcinoma cells, when combined with gefitinib. The combination of PD 0332991 plus gefitinib induced G1 phase arrest for both gefitinib-sensitive and gefitinib-resistant lung cancer cells. This combination treatment also inhibited the growth and relapse of tumors in human PC-9/AB2 tumor xenograft mice, as well as inhibiting proliferation, and induced apoptosis in human PC-9/AB2 tumor xenograft mice. Treatment with PD 0332991 and gefitinib also inhibited angiogenesis in human PC-9/AB2 tumor xenograft mice. **Conclusion:** These findings provide the rationale for evaluating PD 0332991 combined with gefitinib for a novel therapeutic approach for overcoming acquired resistance to gefitinib in lung cancer.

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P2.04-020 Epidermal Growth Factor Receptor (EGFR) Testing among Veterans Diagnosed with Lung Cancer Julie Lynch[1], Brygida Berse[2], Andrew Freedman[3], Kelly Filipski[3], Scott Duvall[4], Scott Kulich[5], Michael Kelley[6] [1]*Veterans Health Administration, Utah/United States of America,* [2]*Boston University Medical School, Ma/United States of America,* [3]*National Cancer Institute, Dc/DC/United States of America,* [4]*Veterans Health Administration, Utah/UT/United States of America,* [5]*Veterans Healthcare Administration, Pa/PA/United States of America,* [6]*Veterans Health Administration, Nc/NC/United States of America*

Background: Molecular profiling has resulted in new, targeted therapies that may improve survival for non-small cell lung cancer patients (NSCLC). Erlotinib is used in stage-IV patients and requires testing patients' tumors for EGFR mutations. In 2010, guidelines recommended screening for EGFR gene mutations in non-squamous, stage IV NSCLC patients. Current guidelines recommend testing for all patients diagnosed with adenocarcinoma. Data on population-level implementation of molecular tests are sparse, yet are crucial to evaluate differences in access and outcomes. **Methods:** Patient-level test orders and results from January 2011 until December 2013 were provided by reference laboratories that conduct molecular testing for VA medical centers (VAMCs). The VA Central Cancer Registry (VACCR) reported clinical characteristics of lung cancer patients diagnosed in 2011 and 2012. We analyzed rate of testing, prevalence of EGFR mutations, clinicians' perspectives regarding testing, and characteristics that predicted likelihood to undergo testing. **Results:** Our previous data showed that in 2010, 15 VAMCs ordered 93 assays. Lab data from 2011 to 2013 identified 986 tests ordered by 70 VAMCs, of which 352 were newly diagnosed patients included in the VACCR for 2011/2012. Patient characteristics of those tested were: 95% male, age (M=67, range 23 to 93). VACCR data (95% male, age (M=68, range 28 to 97) showed that 2,889 (19.64%) of Veterans diagnosed in 2011/2012 were eligible for EGFR testing. Clinicians reported an expected low rate of EGFR mutations among the Veteran clinical phenotype (histology, smoking status, gender). Lab and VACCR data confirmed this. Activating EGFR mutations were detected in 5.6% of cases. The 2361G>A polymorphism, missense mutations expected to be clinically insignificant, and variants of unknown significance were detected in 16.7%,

2.3% and 0.8% of patients, respectively. 70.1% of patients were negative for EGFR mutations. 4.4% of tests were not processed for technical reasons. **Conclusion:** Veterans have a much lower rate clinically actionable EGFR mutations than the reported average of 15%. Among Veterans diagnosed with lung cancer, 52% are current smokers, 40% are former smokers, which may explain the low rate of EGFR mutations. **Keywords:** Cancer Registry, reporting actionable mutations, Veterans prevalence of EGFR mutations

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P2.04-021 Predictive Value of Initial Maximal Standardized Uptake Value of 18F-FDG PET/CT in Patients with Lung Adenocarcinoma Treated with Erlotinib

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Background: Targeted therapies like erlotinib, afatinib, gefitinib, crizotinib and ceritinib were suggested to be used in the first line treatment of non-small cell lung cancer (NSCLC) according to EGFR mutation and EML-4/ALK fusion gene analysis. EGFR mutation rate is about 10% in NSCLC and Exon 9 deletion and Exon 21 L858R are indicators of a longer progression free survival (PFS). According to guidelines thyrosine kinase inhibitors can also be used as switch or maintenance therapy after progression first-line therapy independent of EGFR mutation. This retrospective analysis indicates the predictive value of initial PET-CT SUVmax. in patients treated with erlotinib. **Methods:** This retrospective study about erlotinib was performed on patients with diagnosis of lung adenocarcinoma, treated with erlotinib as first-line, switch or maintenance therapy and after progression of first line chemotherapy in Gaziantep University Hospital Department of Medical Oncology, between 2008 and 2014. Preatreatment PET-CT imagings in last six months were scanned and peak SUVmax values of primary mass or metastasis were noted. Mean SUVmax values was 10,8. Thus, patients stratified as SUVmax above 10,8 and SUV max below 10,8. Also patients were grouped as EGFR muation positive (+), negative(-), and unknown. PET-CT and CT were used for follow-up and 3 months PFS and 6 months PFS ratios were enlisted according to RECIST criteria. **Results:**50 patient enrolled to this study. 27 of patients had SUV max. value below 10.8. Three months PFS rate of these patient was 77.8% *(p:0.020),* while it was 43.5% in patients who have SUV max. above 10.8. Also these rates were 66.7% and 21.7% for 6 months PFS *(p:0.020).* Subgroup analysis according to EGFR mutation status showed that 3 months PFS rates were %75.0, 54.5%, 52.6% in EGFR (+), EGFR (-) and EGFR unknown group respectively *(p:0,301).* These rates were %50, 45.5%, 42.1% for 6 months PFS *(p: 0,884).* In subgroup analysis of EGFR (+) patients, 3 months PFS rate was %100 in patients who have SUVmax below 10,8 and %66,7 in patients who have SUVmax above 10,8. These rates were %100 and %33,3 for 6-months PFS. **Conclusion:** Erlotinib showed better PFS ratios in EGFR positive patients who have low SUVmax values. Also erlotinib is an available drug for EGFR negative and unknown patients in consequent treatment of lung adenocarcinoma. SUVmax could be a predictive value for response. Predictive value of SUVmax could effect treatment decisions with multicenter studies proving this effect. **Keywords:** Erlotinib, PET-CT, Lung cancer,

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P2.04-022 Development of Microfluidic Devices for Rapid, Low-Cost Detection of EGFR Mutations in Cytological Samples from Patients with Lung Cancer

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Background: *Epidermal Growth Factor Receptor (EGFR)* mutation testing plays an important role in selecting patients for targeted therapy with EGFR-tyrosine kinase inhibitors (TKIs). However, a currently available PCR-based sequencing is time-consuming and expensive. In order to overcome these problems, we have developed microfluidic devices which enable rapid and specific detection of mutant EGFR proteins at low-cost in cytological samples from patients with non-small cell lung cancer (NSCLC). **Methods:** The diagnostic device consisted of the capture antibody against EGFR and photo-reactive polymer. The antibody-immobilized photo-reactive polymer wall (40 μm width, 40 μm height and 4 mm length) was constructed at the center of a microchannel (1 mm width, 40 μm height and 8.5 mm length) by ultraviolet light irradiation. The substrate was made of cyclic olefin polymer by using injection molding. The inner wall of the microchannel was blocked with bovine serum albumin. By using the diagnosis devices, the sandwich-type fluorescence immunoassay procedure was conducted. The sample, detection antibody reagent (mutation specific monoclonal antibody against EGFR with the E746_A750 deletion in exon 19 or the L858R point mutation and control EGFR antibody), and fluorescence-labeled anti-IgG antibody reagent were injected in turn. Between each injection, we performed a washing procedure, in which the microchannel was filled with the washing buffer for 1 minute followed by flushing with 5 μL of the same washing buffer. The amount of the sample and reagents to fill the microchannel was 1 μL. Incubation times were 15 minutes, 30 seconds, and 30 seconds for capture antibody-antigen reaction, antigen-detection antibody reaction, and detection antibody-fluorescence-labeled antibody reaction, respectively. After the immunoassay, fluorescence images were captured by using a digital CCD camera. Malignant pleural effusions (MPEs) were obtained from patients with NSCLC with written informed consent. After centrifugation, the cell pellets of MPEs were lysed in 200μl of lysis buffer. **Results:** First, we performed a pilot study by using cell lysates of 3 lung cancer lines expressing wild-type (H358) or E746_A750del mutant (HCC827) or L858R mutant (H3255) EGFR. Using our newly developed diagnostic device, we were able to specifically distinguish EGFR mutant proteins from that of wild-type EGFR in all of these cell lines. Next, we tested the device for detecting *EGFR* mutations in cytological samples of MPEs. Results of the mutation testing of the lysates using this device were consistent with those obtained by commercially available techniques in Japan although the number of samples assessed in this experiment was limited. The cost was less than a few dollars per assay. **Conclusion:** These results suggest that our device may be possible candidates for the next generation companion diagnostics devices for EGFR-TKI. Further investigation will be needed to elucidate the most appropriate detection method of *EGFR* mutation as a companion diagnostics. **Keywords:** EGFR mutation testing

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P2.04-023 Global Epidemiology of EGFR Mutation in Advanced Non-Small Cell Lung Cancer

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Background: Lung cancer is a leading cause of cancer-related mortality worldwide. Subsets of patients with driver oncogenes can be treated with targeted therapies achieving longer survival than the general population of patients with advanced non-small cell lung cancer. Epidermal growth factor receptor (EGFR) mutations represent an important predictive factor for responses to EGFR inhibitors. This study aims to describe the prevalence of EGFR mutations throughout the world. **Methods:** We used MEDLINE to searched for articles describing the prevalence of EGFR mutations in countries around the world. Key search terms included "lung cancer", "NSCLC" and "non-small cell lung cancer" in combination with the following terms: "EGFR", "EGFR mutation" and "epidermal growth factor receptor". The search was limited to human studies published in English, Portuguese or Spanish. No date limits were included. All studies describing the prevalence of EGFR mutations were included, provided they used any of the validated testing methods.We excluded the following types of studies: (i) animal xenograft experiments using human cancer cell lines, and (ii) abstracts, letters and posters for which the full study was not published. **Results:** Our search retrieved 2,369 articles dated from 1989 to 2015, of which 324 were selected based on the criteria described above. 213 of these studies (65.8%) were published between 2011 and 2015; 15 (4.7%) were clinical trials and 306 (98%) were cohort studies, case series or epidemiological series. We found articles from 37 different countries throughout the world, accounting for 121,109 patients. The global prevalence of EGFR mutation was 14.62% (CI 95%; 7.64-21.60%). In an exploratory subgroup analysis by region of the world, gender, smoking status and histology, we found higher prevalence of EGFR mutation in South/East Asia (41.67%; 95%CI: 37.99-45.35%; p<0.001), women (39.68%; 95%CI: 31.49-47-87; p<0.001), non-smokers (54.61%; 95%CI: 45.91-63.31; p<0.001) and adenocarcinoma (35.28%; CI 95%: 28.68-41.90%; p<0.001).

Table 1 summarizes the results.

Table 1 Global prevalence of EGFR mutation in NSCLC

Region	Country	Number of studies	Number of patients	Mean Prevalence of EGFR Mutation (95%CI)
Asia – South/ East	Bangladesh	1	61	22.95%
	China	60	24,638	43.95%
	India	9	5,027	36.94%
	Japan	70	11,938	38.30%
	Malaysia	3	1,180	43.59%
	Singapore	1	30	50.00%
	South Korea	15	5322	45.40%
	Taiwan	5	1373	50.78%
	TOTAL	164	47,553	41.67% (37.99% - 45.35%)
USA/Canada	Canada	3	2,647	19.48%
	USA	44	13,593	25.02%
	TOTAL	47	16,240	24.48% (20.98% - 28.17%)
Latin America	Argentina	1	244	19.26%
	Brazil	2	138	7.78%
	Chile	1	1,164	14.26%
	Colombia	1	322	24.80%
	Mexico	2	444	34.65%
	Peru	1	283	67.00%
	TOTAL	8	2,515	26.25% (9.70% - 42.81%)
Europe	Belgium	2	297	10.77%
	Czech Republic	1	223	7.17%
	Denmark	2	1,623	8.84%
	England	4	715	32.78%
	Finland	1	528	10.98%
	France	9	17,838	18.13%
	Germany	5	2,142	21.59%
	Greece	4	277	18.31%
	Italy	6	1,367	10.45%
	Lithuania	1	103	9.71%
	Netherlands	2	1,178	12.20%
	Poland	2	2464	18.78%
	Portugal	2	812	15.02%
	Slovenia	1	40	45.00%
	Spain	5	583	23.80%
	TOTAL	50	30,549	18.14% (15.55% - 22.74%)
Rest of the world	Australia	3	2,276	19.92%
	Morocco	1	137	20.44%
	Pakistan	1	94	28.72%
	Russia	1	147	19.05%
	Turkey	2	75	40.75%
	TOTAL	6	2,727	26.88% (17.86% - 34.98%)

Conclusion: To our knowledge this is the most comprehensive study of EGFR mutation prevalence in NSCLC worldwide. Our finds corroborate the estimate that EGFR mutations occur in around 20% of patients and the higher incidence among southeastern populations in Asia, females, non-smokers and adenocarcinoma. Policy makers can use this information to supporting testing of all non-smokers and of patients with adenocarcinoma worldwide. **Keywords:** EGFR, non-small cell lung cancer, epidemiology, PREVALENCE

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P2.04-024 NGS reveals potential druggable targets and molecular heterogeneity in EGFR mutant NSCLC with acquired resistance to EGFR TKIs
Choong-Kun Lee[1], Sora Kim[2], Jae Seok Lee[3], Hye Ryun Kim[1], Joo-Hang Kim[1], Sang Woo Kim[2], Byoung Chul Cho[1] *[1]Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul/Korea, [2]Severance Biomedical Science Institute, Yonsei University College of Medicine, Seoul/Korea, [3]Department of Pathology, Yonsei University College of Medicine, Seoul/Korea*

Background: Although patients with non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor (EGFR) mutations respond to EGFR tyrosine kinase inhibitors (EGFR-TKIs), acquired resistance to these agents eventually occurs. To date, there has been no study on the comprehensive genome-wide alterations using next-generation sequencing (NGS). **Methods:** At pre-EGFR-TKI and post-progression, we collected formalin-fixed paraffin-embedded tumor/normal pairs form 19 NSCLC patients. Ion AmpliSeqTM Comprehensive Cancer Panel was used to identify alterations across all exons of 409 target genes. The predicted mutated gene associated with resistance to EGFR-TKIs was subjected to *in vitro*functional assay. **Results:** All patients satisfied the clinical definition of acquired resistance to the EGFR-TKIs. The patients characteristics were as follows; median age of 58 years, male/female (n=7/12), pretreatment with erlotinib/gefitinib (n=2/17), and exon 19 deletion/L858R/others (n=14/3/2). Median progression-free survival (mPFS) of all patients on EGFR-TKIs was 6.7 months (2.4 to 27.8) and best overall response was partial responses in 10 patients and stable diseases in 8 patients. Tumors were sequenced to a median coverage of 607x. Cancer genomes are characterized by 1,398 somatic single-nucleotide variants (788 missense, 74 nonsense, and 20 splice-site) and 1,774 frameshift and in frame insertions/deletions, with a median of 93.42 mutations per Mb (18.03 to 692.03 mutations per Mb). Overall, there was no significant difference in number and type of somatic mutation between pre-EGFR-TKI and post-progression tumors. In post-progression samples, patients with T790M mutation (n=12, 63.2%) had significant better mPFS and median overall survival (mOS) compared to patients who maintained EGFR activating mutation without evidence of acquired T790M (n=5) or without T790M nor EGFR activating mutation (n=2) (12.4 vs. 3.9 months for mPFS, *P*=<0.0001; 28.9 vs. 11.7 months for mOS, *P*=0.0306). No pre-EGFR-TKI tumor had a preexisting T790M mutation, suggesting that tumors acquired T790M mutations during progression or after the acquisition of resistance to EGFR-TKI. Statistical analysis confirmed that T790M (-) patients group had significant enrichment of mutated genes belonging to the angiogenesis (*P*=0.003394) and extracellular matrix (*P*=0.00905) pathways before treatment of EGFR-TKI compared to T790M (+) patients. One patient with poor response (PFS = 3.6 months) lost EGFR activating mutation (allele frequencies from 20.8% to 0%) without detectable T790M mutation after EGFR-TKI treatment. We identified a novel missense mutation (T263P) of the extracellular domain (subdomain II) of EGFR, concurrently with an activating EGFR G719A mutation in pre- and post-EGFR-TKI samples of a lung adenocarcinoma showing poor response to erlotinib. Transfection of T263P vectors conferred resistance to erlotinib in PC-9 cells. **Conclusion:** NGS of pre-EGFR-TKI and post-progression tumor samples provides insight into the complex molecular mechanisms of acquired resistance to EGFR-TKIs in EGFR-mutant NSCLC. **Keywords:** non-small cell lung cancer, Epidermal growth factor receptor, tyrosine kinase inhibitor resistance mechanism, next-generation sequencing

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P2.04-025 Frequency of EGFR Mutation in Nsclc and Its Relationship with Clinicopathological Features: A Multicenter Asmo Trial
Sinemis Yuksel[1], Hilmi Kodaz[2], Ibrahim Yildiz[3], Hatice Odabas[1], Ayse Ocak[4], Ibrahim V. Bayoglu[3], Ilhan Hacibekiroglu[2], Ozlem Ercelep[1], Ahmet S. Ekinci[5], Bulent Erdogan[2], Aslihan G. Mert[1], Halit Karaca[4], Tarik Salman[3], Serkan Menekse[6], Ozge Gumusay[7], Basak O. Ustaalioglu[8], Mehmet N. Aldemir[9], Caglayan Geredeli[10], Meltem Baykara[11], Mukremin Uysal[12], Alper Sevinc[13], Asude Aksoy[14], Arife Ulas[15], Mevlude Inanc[4], Ozgur Tanriverdi[16], Nilufer Avci[17], Nedim Turan[18], Mehmet Aliustaoglu[1], Mahmut Gumus[19] *[1]Medical Oncology, Kartal Dr.Lutfi Kirdar Research and Training Hospital, Istanbul/Turkey, [2]Medical Oncology, Trakya University Medical School, Istanbul/Turkey, [3]Medical Oncology, Katip Celebi University Medical School, Izmir/Turkey, [4]Medical Oncology, Erciyes University Medical School, Kayseri/Turkey, [5]Medical Oncology, Abdurrahman Yurtaslan Oncology Research and Training Hospital, Ankara/ Turkey, [6]Medical Oncology, Celal Bayar University Medical School, Manisa/Turkey,[7]Medical Oncology, Gazi University Medical School, Ankara/Turkey, [8]Medical Oncology, Haydarpasa Numne Research and Training Hospital, Istanbul/Turkey, [9]Medical Oncology, Erzurum Research and Training Hospital, Erzurum/Turkey,[10]Medical Oncology, Necmettin Erbakan University Medical School, Konya/Turkey, [11]Medical Oncology, Sakarya Research and Training Hospital, Sakarya/Turkey, [12]Medical Oncology, Kocatepe University Medical School, Afyon/Turkey,[13]Medical Oncology, Gaziantep University Medical School, Gaziantep/ Turkey, [14]Medical Oncology, Firat University Medical School, Elazıg/Turkey, [15]Medical Oncology, Bursa Oncology Hospital, Bursa/Turkey, [16]Medical Oncology, Mugla University Medical School, Mugla/Turkey, [17]Medical Oncology, Balikesir State Hospital, Balikesir/ Turkey, [18]Medical Oncology, Malatya State Hospital, Malatya/Turkey, [19]Medical Oncology, Bezmialem Vakif University, Istanbul/Turkey*

Background: There has been important developments in NSCLC since the understanding of molecular pathways and the initiation of targeted treatments. The aim of the study is to find the EGFR mutation frequency and its correlation to survival and clinicopathological features. **Methods:** In this multicenter study, 827 NSCLC patients were included retrospectively to find out the EGFR mutation status with age, sex, performance status, histopathological diagnosis, smoking status and stage. Survival correlates were determined. The primary aim was to find out the EGFR mutation status with all of the features in the database. The secondary aim was to find out the effects of EGFR mutation status on survival with multivariate analysis. **Results:** The median age was 59 (24-87) years. Median follow-up period was 14 (2-117) months. 29,7% were female. 85,2% were stage IIIB-IV and 94% was adenocarcinoma. EGFR mutation frequency was 21,6% including exon 19 (62,3%). There was no correlation between mutational status and age, performance status and stage at diagnosis (p>0,05). However, there was a correlation between sex, smoking, and the metastatic area (p= 0.000, 0,000 ve 0.04 relatively). The frequency of mutation in female subjects was more pronounced in non-smokers/ex-smokers and less metastatic sites. Median progression-free survival was 9 months and overall survival was 20 months. The overall survival was 27 (SE:5; 95% CI 17-36) months in EGFR positive cases whereas 19 (SE:1; 95% CI 16-21) months in EGFR negative cases (p=0,008). The multivariate analysis showed good performance status, ealy stage diseaase and presence of EGFR mutation as a prognostic factor (p<0,05). **Conclusion:** Presence of EGFR mutation seems to be correlated with survival. The determination of EGFR mutation will lead the pathway for a better treatment outcome and individualised therapy. **Keywords:** EGFR mutation, non small cell lung cancer, molecular testing, survival

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P2.04-026 Second Generation EGFR TKIs Inhibit Tumor Growth in a Chemo-Resistant Squamous Cell Lung Cancer Patient Derived Xenograft Model
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Background: In clinical trials testing the efficacy of first generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs), occasional responses were observed in patients with lung squamous cell carcinomas (LSCC) (Shepherd FA, et al. New Engl J Med 2005) and survival benefit was confirmed for erlotinib in a subset analysis of male, ever-smokers with LSCC (Clark GM, et al. Clin Lung Cancer 2006). Currently, the LUX-Lung 8 phase III clinical trial is comparing afatinib versus erlotinib in the second-line setting for LSCC after cisplatin-based chemotherapy (Goss GD, et

al. ESMO 2014). Preclinical data indicate that high EGFR protein expression may be predictive of response to erlotinib in *EGFR* wild type LSCC (Cranston et al, AACR 2013). Herein we assessed and compared the anti-tumor efficacy of different EGFR inhibitors in chemo-resistant squamous cell lung cancer patient derived xenograft (PDX) models with high EGFR expression and *EGFR*amplification. **Methods:** The cryopreserved PDX model established from a resected early stage LSCC was revived in non-obese diabetic severe combined immunodeficient mice (NOD SCID), expanded and subsequently treated with chemotherapy (cisplatin 3 mg/kg and vinorelbine 7 mg/kg intraperitoneally [IP]), cetuximab 20 mg/kg IP, and daily oral schedules were followed for erlotinib 50 mg/kg, afatinib 20 mg/kg, dacomitinib 3 mg/kg. For each model, 6 mice were used in each of the different treatment and the control arms. Treatment was initiated in the PDXs at a tumor average volume of 150 mm^3. **Results:** The PDX was derived from a 57 year old male, smoker, following right pneumonectomy for a stage IIIB (T4N1M0) LSCC. This patient received adjuvant cisplatin/vinorelbine, but relapsed three weeks after the end of cycle 4 and died a week later. The tumor had a high EGFR expression by immunohistochemistry (H score = 300) and *EGFR*amplification (clusters) by fluorescent in situ hybridization. The PDX was *EGFR* wild type by Illumina exome sequencing and OncoCartaTM MassArray mutation screen (Sequenom), also was refractory to cisplatin/vinorelbine. Reduced growth rate (stable disease, SD) was obtained with erlotinib and cetuximab. Treatment with afatinib and dacomitinib resulted in tumor growth inhibition (partial response, PR). The PDX developed resistance to dacomitinib after 100 days of treatment, but continued to be inhibited by afatinib after 215 days of treatment. **Conclusion:** This study shows the efficacy of second generation especially afatinib irreversible EGFR TKIs in a chemoresistant LSCC PDX, with high wild type EGFR expression and*EGFR* amplification. Our results lend further support to the LUX-Lung 8 trial, and also the use of PDX to model therapeutic responses in lung cancer. **Keywords:** Patient derived xenograft model, EGFR TKI, Squamous cell lung carcinoma

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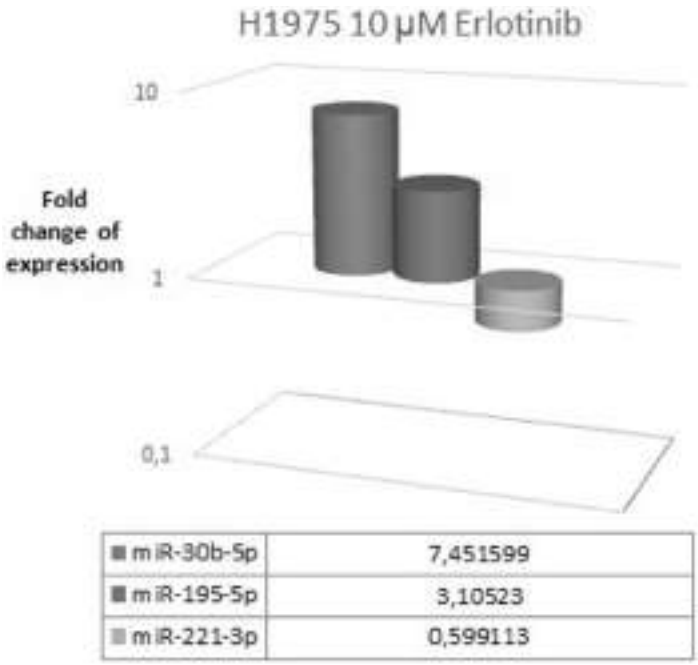
P2.04-027 Erlotinib Induce miRNA Alterations in T790M EGFR Mutated NSCLC: Preclinical Study Jorge Chacartegui[1], Marco Giallombardo[2], Nele Van Der Steen[3], Patrick Pauwels[4], Christian Rolfo[1] [1]*Phase I-Early Clinical Trials Unit&Centre for Oncological Research (Core), Antwerp University Hospital & Antwerp University, Edegem/Belgium,* [2]*Phase I- Early Clinical Trials Unit, Antwerp University Hospital & Palermo University, Edegem/Belgium,* [3]*Center for Oncological Research (Core), Antwerp University, Edegem/Belgium,* [4]*Molecular Pathology Unit & Core, Antwerp University Hospital & Antwerp University, Edegem/Belgium*

Background: Lung cancer is one of the leading causes of cancer-related deaths worldwide. In the most common type, non-small cell lung cancer (NSCLC), an array of oncogenic driver mutations affecting growth factor receptors and signaling pathways, such as EGFR, KRAS, c-Met or ALK translocation has driven the development of directed-drug therapies with tyrosine kinase inhibitors (TKIs) and monoclonal antibodies. Nevertheless, the appearance of resistance mechanisms, such as c-Met amplification or *de novo* mutations in EGFR, decreases the effectiveness of these therapies. Therefore, we analyzed the levels of miRNA which have proved to be involved in disease progression (miR-30b-5p,195-5p,221-3p) in NSCLC cells that are resistant (H1975) or sensitive (HCC827) against first generation TKI (erlotinib) treatment, to assess whether they are markers of response to the treatment. **Methods:** The H1975 cell line (EGFR mutations T790M/L858R) was cultured in RPMI 1640 medium, supplied with 10% FBS, 2 mM L-glutamine and 1% penicillin/streptomycin (Gibco). The sulforhodamine B assay was performed to assess cell proliferation. The cells were treated during 72h with 10μM erlotinib (SelleckChem) or DMSO. After collection, cells were lysed and RNA was extracted through commercial kit (RNA Mini Spin, GE Healthcare). The miRNAs profile analysis was performed through TaqMan Real-Time PCR and miRNA RNU-48 was used as endogenous control. Data was processed according to the formula 2-Δ Δct. Control values (H1975 + vehicle) are used as baseline and results are shown in logarithmic scale (Image). **Results:** Cells treated with 10μM erlotinib show an increased expression of miR-30b-5p, miR-195-5p compared to control values. On the other hand, we detected that the expression of the miR-221-3p was strongly down-regulated in respect the control values. **Conclusion:** H1975 carries the T790M mutation in EGFR, associated in NSCLC with appearance of resistance to TKIs treatment. However, we observed after treatment an increase of onco-suppressor miR-30b-5p and decrease of the oncogenic mir-221-3p, which are reported to correlate with good prognosis (Garofalo 2013, Zhong 2014). Moreover, mir-195-5p, another miRNA related with onco-suppression, is also upregulated, which has been reported to correlate with good response (Liu, 2015). Overall, our data suggests that erlotinib treatment alters miRNA in an EGFR mutated cell line. Further analysis of miRNA in exosomes produced by H1975, and comparison with HCC827 exosomal and cellular miRNA levels is currently undergoing in our group to confirm their value as response to treatment biomarkers.



miR-30b-5p	7,451599
miR-195-5p	3,10523
miR-221-3p	0,599113

Keywords: Erlotinib, T790M mutation, TKI resistance, miRNA profile

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-028 BIM Deletion Polymorphisms in Hispanic Patients with Non-Small Cell Lung Cancer Who Carriers EGFR Mutations (CLICaP) Andrés F. Cardona[1], Oscar Arrieta Rodriguez[2], Claudio Martin[3], Hernan Carranza[1], Carlos A. Vargas[1], Jorge M. Otero[1], Leonardo Rojas[4], Mauricio Cuello[5], Rafael Rosell[6] [1]*Clinical and Translational Oncology Group, Foundation for Clinical and Applied Cancer Research - Ficmac, Bogotá/Colombia,* [2]*Unidad Funcional de Oncología Torácica Y Laboratorio de Medicina Personalizada, National Cancer Institute, Mexico City/Mexico,* [3]*Clinical Oncology, Instituto Fleming, Buenos Aires/Argentina,* [4]*Centro Javeriano de Oncologia, Hospital Universitario San Ignacio, Bogota/Colombia,* [5]*Clinical Oncology, Hospital de Clínicas - Udelar, Montevideo/Uruguay,* [6]*Hospital Germans Trias I Pujol, Catalan Institute of Oncology, Barcelona/Spain*

Background: Germline alterations in the proapoptotic protein Bcl-2-like 11 (BIM) can have a crucial role in diverse tumors. To determine the clinical utility of detecting BIM deletion polymorphisms (par4226 bp/ par363 bp) in EGFR positive non-small-cell lung cancer (NSCLC), we examined outcomes of patients (pts) with and without BIM alterations **Methods:** We studied 89 NSCLC pts with EGFR mutation who were treated with erlotinib between January 2009 and November 2014. BIM deletion was analyzed by PCR in formalin-fixed paraffin-embedded (FFPE) tissues of tumor biopsies. We retrospectively analyzed clinical characteristics, response rate, toxicity, and outcomes among patients with and without BIM deletion (del)**Results:** BIM deletion was present in 14 pts (15.7%). There were no significant differences between pts with and without BIM del in clinical characteristics or type of EGFR mutation; however, pts with BIM del had a worse overall response rate to erlotinib (42.9% vs. 73.3% for pts without BIM del; p=0.024) as well as a significantly shorter progression-free survival (PFS) (10.8 del+ vs. 21.7 months for pts without BIM del; p=0.029) and overall survival (OS) (15.5 del+ vs. 34.0 months for pts without BIM del; p=0.035). Multivariate Cox regression analysis showed that BIM deletion was an independent indicator of shorter PFS (HR 3.0; 95%CI 1.2-7.6; p=0.01) and OS (HR 3.4; 95%CI 1.4-8.3; p=0.006) **Conclusion:** The incidence of BIM del found in pts from Colombia is similar to that previously described in Asia; this alteration is associated with a poor clinical response to erlotinib and represents an independent prognostic factor for pts who had NSCLC with EGFR mutations **Keywords:** EGFR mutations, non-small cell lung cancer, BIM DELETION

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-029 Could EGFR Gene Mutations Provide a Selective Advantage to Malignant Cells in Specific Sites? New Perspectives in Lung Adenocarcinoma Biology Tindara Franchina, Alessandro Russo, Veronica Franchina, Antonio Picone, Giuseppina R.R. Ricciardi, Giuseppa Ferraro, Maria Picciotto, Giuseppe Toscano, Vincenzo Adamo *Department of Human Pathology, University of Messina & Medical Oncology Unit, A.O.O.R. Papardo-Piemonte, Messina/Italy*

Background: There is growing evidence about differences in metastatic spread among distinct subsets of nonsmall cell lung cancer (NSCLC) characterized by activation of different driver oncogenes at the time of diagnosis. It is hypothesized that the dominant oncogenes in NSCLC would be associated with distinct patterns of metastatic spread. Aim of this study was to analyze the pattern of metastasization in lung adenocarcinomas according to EGFR mutational status. **Methods:** A total of 104 consecutive patients (60 M/44 F) with stage

IV adenocarcinoma and an EGFR mutation (25.9%), or wild-type (74.1%) were included. We compared the incidence rates of metastatic spread at a given site between EGFR mutated and wild type. Descriptive analysis was performed on the two molecularly defined groups and associated clinical data. **Results:** 37% of pts with EGFR activating mutations had bone metastases and 44% lung metastases. Moreover, BM were reported in 18%. Lung metastases were more common among pts harboring exon 19 deletions (10/12 pts). In the subgroups of EGFR wild type pts BM were present in 15%, while bone and lung metastases in 17% and 22% of pts, respectively.The difference between the incidence of metastases in the different sites according to EGFR mutational status was not statistically significant. An interesting trend toward significance was observed in the evaluation of the incidence of lung metastases in EGFR mutated pts (p=0.1). **Conclusion:** The biomolecular characteristics and the pathways involved in the different lung cancer subtypes may directly influence the metastases formation and evolution. This report underline the need to better define the clinical and molecular characteristics in adenocarcinoma subtype related to EGFR mutational status, to improve therapeutic choices and obtain relevant clinical results. **Keywords:** Metastatic spread, Adenocarcinoma, EGFR mutational status

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-030 Activating and Resistance Mutations of EGFR in Peruvian Patients with Metastatic NSCLC Juan C. Gomez De La Torre[1], Claudia Barletta[1], Angelo M. Storace[2], Christian Piscocha[1], Jose Landa[1], Carlos Roe[1], Eduardo Roe[1], Manuel Leiva[1], Luis Mas[3], Sandro Casavilca[4], Carlos Barrionuevo[4] [1]*Laboratorio Roe, Lima/Peru,* [2]*Roche Farma Peru, Lima/Peru,* [3]*Oncosalud-Auna, Lima/Peru,* [4]*Instituto Nacional de Enfermedades Neoplásicas (Inen), Lima/Peru*

Background: The evaluation of EGFR mutational status of the EGFR in non-small cell lung cancer (NSCLC) is crucial to select the adequate targeted therapy and to know the prognostic of patients. Our aim was describe to determine the frequency of activating and resistance mutations of EGFR in a large cohort of Peruvian patients. **Methods:** We tested metastatic tumor samples from 436 NSCLC patients for known EGFR mutations involving exon 18 (G719X), exon 19 (deletions), exon 20 (T790M, S768I and insertions) and exon 21 (L858R). Samples were from a mutational testing program sponsored by a pharmaceutical company. All samples were processed at a central reference laboratory (Roe laboratory, Lima-Peru) under protocolized laboratory procedures. **Results:** A total of 398 out of 436 samples were evaluable for determination of EGFR mutational status. Fifty five percent of patients were male. EGFR mutations was present in 36.7% of cases (n = 146). In regard to specific mutations, G719X (in exon 18) was present in 1% (n = 4); deletions in exon 19 had a frequency of 19.6% (n = 78). Mutations in exon 20 were present in 3.5% (n = 14). In patients with exon 20 mutated, 8 cases had insertions, 5 cases had the mutation T790M and 1 case had the mutation S768I. Mutation L858R (exon 21) in 14.1% (n = 56) of cases. Coexistence of two mutations were present in exon 19/exon 20 (n = 3) and exon 20/ exon 21 (n = 3). Female patients were more likely to have any EGFR mutation with a Relative Risk = 1.92 and a P < 0.001, in the Chi-square test. In tumors with EGFR mutated. The sensible profile for EGFR tyrosine kinase inhibitors (TKI´s) was present in 94.5% of cases (n=138) while 8 cases (5.5%) had mutations associated with resistance to TKI´s. **Conclusion:** Most patients with metastatic NSCLC and EGFR mutations will benefit from anti-EGFR targeted therapy. Our frequency of EGFR activating or resistance mutation was similar to other Latin American countries where mutations in exon 19 are the most frequent. **Keywords:** lung cancer, Adenocarcinoma, EGFR, Targeted therapy

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P2.04-031 EGFR Mutation Associated with Histologic Subtype According to the IASLC/ATS/ERS Adenocarcinoma Classification: A Meta-Analysis Chen H. Ma[1], Qian Li[1], Ya F. Liu[2], Yan W. Yao[3], Yong Song[3] [1]*Department of Respiratory Medicine, Nanjing University School of Medicine, Nanjing/China,* [2]*Department of Respiratory Medicine, Nanfang Medical University, Nanjing/China,* [3]*Department of Respiratory Medicine, Jinling Hospital, Nanjing University School of Medicine, Nanjing/China*

Background: In 2011, the International Association for the Study of Lung Cancer, American Thoracic Society and European Respiratory Society (IASLC/ATS/ERS) proposed the new lung adenocarcinoma histologic classification. The purpose of this meta-analysis is to determine the relationship between EGFR mutation states and different predominant histologic subtypes. **Methods:** We carried out a comprehensive search for published articles from 2011 to February, 2015, using the PubMed, EMBASE databases and Cochrane Library. The main key words used for search were: IASLC/ATS/ERS, new lung adenocarcinoma classification, EGFR. By searching the databases and further checking the reference lists of the publications, we obtained the initial articles. Next, we performed the preliminary screening through reading the titles and abstracts and excluded the obviously irrelevant articles. Then, we downloaded the full texts and read these articles intensively, excluding articles not giving the detailed data for meta-analysis. We extracted information from all eligible studies as follows: author, publish year, region, total cases, mean age, number of a certain histologic subtype, number of EGFR mutation in certain histologic subtype, total number of other histologic subtypes, total number of EGFR mutation in other histologic subtypes. This meta-analysis was completed using the Stata software (version 11.0; StataCorp LP, College Station, TX, USA). Detailed numbers in each included study were pooled to evaluate the association between EGFR mutation and histologic subtype. A random-effect model was used to calculate the pooled relative risks (RRs), 95% confidence interval (95%CI), and P values. Two-sided P values less than 0.05(P<0.05) were considered statistically significant. **Results:** The micropapillary predominant subtype was found to be tended with EGFR mutation (RR=1.37, 95%CI=1.08-1.74, p=0.011). On the contrary, the solid predominant subtype has a low EGFR mutation frequency (RR=0.74, 95%CI=0.59-0.93, p=0.009). Obvious correlation with EGFR mutation states is not found among other histologic subtypes. **Conclusion:** Taken together, the new IASLC/ATS/ERS lung adenocarcinoma classification is a very useful predictor of EGFR mutation frequency, the micropapillary predominant subtype has higher EGFR mutation frequency, on the contrary, the solid predominant subtype with lower frequency. **Keywords:** NSCLC, IASLC/ATS/ERS adenocarcinoma classification, EGFR mutation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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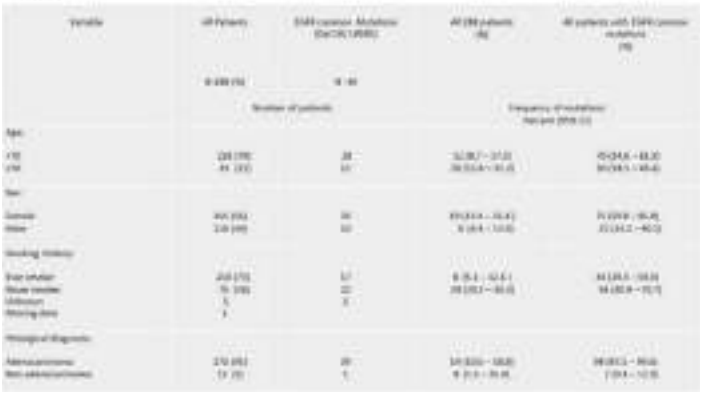
P2.04-032 Epidemiology and Clinical Outcomes of Epidermal Growth Factor Receptor (EGFR) Mutant Patients at the Brazilian National Cancer Institute (INCA) Pedro M. Domingues, Tatiane Montella, Mauro Zukin, Clarissa Baldotto, Carlos Ferreira *Department of Thoracic Oncology, Brazilian National Cancer Institute, Rio de Janeiro/Brazil*

Background: It is largely recognized the relationship between ethnicity and frequency of *EGFR* mutation. In Eastern Asia *EGFR* mutation prevalence in unselected lung adenocarcinoma reaches 52% as reported by large molecular studies. In withe populations, such as in European and North-American data, the *EGFR* mutation frequency decreases to 13-24%. Latin-America is a large and heterogeneous region with an elevated frequency of non-small-cell lung cancer (NSCLC) tumors. However, with the hurdles to access a high quality molecular test and targeted drugs, data regarding *EGFR* epidemiology in this region are lacking. For instance, in Brazil is estimated that less than 15% of advanced non-squamous cell lung cancer are tested. In this study, we describe the epidemiology and clinical outcomes of *EGFR*-mutant patients with advanced NSCLC after the implementation of *EGFR* reflex testing at a Brazilian public hospital. **Methods:** From May-2011 to Dec-2014 we retrospectively collected data from *EGFR* reflex test at INCA. The test was recommended for all advanced non-squamous NSCLC patients treated at the institution. *EGFR* exons 18, 19, 20 and 21 were examined using either Cobas® platform or Sanger sequencing. **Results:** From May 2011 to Dec 2014, 288 samples were screened for *EGFR* mutations and 40 (13.9%) harbored common *EGFR* mutations (del19-L858R). Of all tested patients, 21% had >70 years-old, 56% were women and 26% were never-smokers. Most patients had adenocarcinoma (95%). Results were obtained from cytological specimen in 65 cases (23%). Sanger sequencing was performed in the majority of patients (73%). *EGFR* mutation frequency was significantly higher in females than in males (19%[13.4–25.4] *vs* 8%[4.4–13.9]), and in never-smokers (29%[20.2–40.4] vs 8%[5.1–12.6] in ever-smokers)[Table 1]. The median Overall Survival (OS) of the entire cohort was 15.1 months. *EGFR*mutation was associated with better OS, as compared with *EGFR*-WT (26.4 vs 13.7 months [HR-0.37;*p*<0.001], respectively). Other prognostic factors identified were age>70y (*p*=0.01) and stage IV (*p*=0.008). In the 40 EGFR-mutant patients, 32 received EGFR-TKI. The exposure to EGFR-TKI was associated with better survival as compared with no TKI treatment (62.9 vs 9.8 months [HR-0.25;*p*<0.01], respectively).

Table 1



Conclusion: Our results have demonstrated that the epidemiology and clinical outcomes of EGFR-mutant patients in a Brazilian cohort are in line with previous western studies. Further data with a higher number of patients and a wider extension are needed to confirm this results and point out possible intraregional differences. **Keywords:** epidermal growth factor receptor (EGFR), epidemiology, lung cancer

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P2.04-033 Patterns of *EGFR* Mutations in a Cohort of 395 Patients from a Single Institution in Brazil Augusto O. Saito, Vladmir C.C. Lima, Aldo L.A. Dettino, Mariana P. Macedo, Izabela W. Cunha, Graziela Z. Dal Molin, Helano C. Freitas
Oncologia Clínica, A C Camargo Cancer Center, Sao Paulo/Brazil

Background: Lung cancer is among the most common malignancies in Brazil. Nevertheless, so far, there are no official data on *EGFR* mutation frequency in the country, the test is not routinely offered in the public system and there seems to exist great disparities in patient access to *EGFR* testing across regions. In this study we describe the frequency and patterns of *EGFR* mutations from a single brazilian

institution. **Methods:** DNA samples were obtained either by slide scraping or by laser microdissection of tumoral cells from paraffin embedded tissue blocks. Exons 18, 19, 20 and 21 of *EGFR* gene were tested for mutation by direct sequencing or by pyrosequencing using standard protocols. We used chi-square statistics, or Fisher's exact test when appropriate, to compare proportions among groups. **Results:** From Aug/2010 to Jun/2014, 395 patients were tested for *EGFR* mutation at AC Camargo Cancer Center, Sao Paulo. Among tested patients, median age was 64y, 51% were female, 91% had adenocarcinoma, 27% were smokers/former smokers with median 12 pack year smoking history. The presence of EGFR mutations was associated with non-smoking status (p=0.023). Twenty six percent of patients (105/395) had EGFR mutations, 28.6% (30/105) of them were L858R, 42.9% (45/105) were exon 19 deletions and 28.6% (30/105) were composed of rare or complex mutations. Among patients with rare mutations, 56.6% (17/30) had more than one mutation detected. Rare/complex mutations were more frequently associated with non-adenocarcinoma histology (p=0.014), smoking history (p=0.03) and smoking intensity (p=0.02). **Conclusion:** In this cohort, the mutation frequency was higher than that reported in other western countries series. The high proportion of rare and complex mutations is also worthnoting and was more frequently seen in heavy smokers with non-adenocarcinoma histology. **Keywords:** EGFR testing, NSCLC, Rare EGFR mutations, EGFR mutation frequence

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-034 The Study of EGFR Mutation Specific-Antibody for Detection of EGFR Status in Non-Small Cell Lung Cancer Chaiyut Charoentum, Chumut Phanthunane, Nirush Lertprasertsuke, Theerakorn Theerakittikul, Atikun Limsukon, Somcharoen Saeteng, Apichart Tantraworasin, Juntima Euathrongchit, Yutthaphan Wannasopha, Thatthan Suksomboncharoen, Busyamas Chewaskulyong, Sumitra Thongprasert *Internal Medicine, Faculty of Medicine, Chiangmai University, Chiangmai/ Thailand*

Background: Specific somatic mutations of the epidermal growth factor receptor (EGFR) associate with increasing response to EGFR tyrosine kinase inhibitors (TKIs) treatment in NSCLC. Assessment of EGFR mutation status by gene-based assay remains expensive and is not routinely reimbursed in Thailand. The objective of this study is to test a simple immunohistochemical (IHC) method using EGFR mutation-specific antibodies for detection of EGFR status. **Methods:** Specimen from 76 NSCLC patients whose EGFR mutation status had been detected by DNA direct sequencing were collected from January 2010 to July 2014 as the reference standard. We performed IHC analyses using 2 EGFR mutation-specific antibodies to E746-A750 del in exon 19 and the other to L858R in axon 21 for all samples. IHC staining were score as 0 (no, or faint staining intensity in <10% tumor cells), 1+ (faint, staining >10%), 2+ (moderate) and 3+ (strong). **Results:** The reference DNA sequencing showed exon 21 L858R EGFR mutations in 17 (22.4%) patients, exon 19 deletions in 12 (15.8%) patients, G719X mutation in 1 (1.3%) patients, exon 20 insertion in 1 (1.3%) patients, multiple sites mutation in 1 (1.3%) patients and no mutation detected in 46 (52.9%) patients. With the DNA sequencing results were set as the reference standard, the prevalence of mutation detected by IHC-based analyses was 25.8% (8/31), 44.4% (8/18), 100% (7/7) and 66.7% (8/12) respectively, for samples with scores 0, 1+, 2+ and 3+. At IHC cut point value 2+, sensitivity and specificity for antibodies L858R were 52.9% wand 98.3 respectively. Likewise for antibodies E746-A750, cut point value 2+ showed sensitivity and specificity as 50.0% and 95.3% E746-A750 respectively. Additional, indicate similar cut point as score 2 ,PPV and NPV were 66.7% and 91.0% for antibodies E746-A750 and 90.0% and 88% for L858R antibodies. **Conclusion:** A simple IHC-based analysis using EGFR mutation-specific antibodies in this study have good correlation with gene-based for EGFR mutation analysis. In Thailand, these simple IHC cost less for five times, have shorter turn around time than gene-based for EGFR mutation analysis and could be useful where molecular-based assay is not readily accessible. **Keywords:** lungcancer, EGFR, Immunohistochemistry, thailand

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-035 Methods for Evaluating Early Response to Erlotinib Treatment Using FDG-PET/CT Joan Fledelius[1], Anne W. Larsen[2], Azza Ahmed Khalil[2], Jørgen Frøkiær[3], Peter Meldgaard[4] [1]*Nuclear Medicine, Herning Hospital, Herning/Denmark,* [2]*Department of Oncology, Århus University Hospital, Århus/Denmark,* [3]*Department of Nuclear Medicine and Pet Centre, Århus University Hospital, Århus/Denmark,* [4]*Department of Oncology, Aarhus University Hospital, Aarhus/Denmark*

Background: Early evaluation of response to treatment with Fluoro-deoxy-glucose-Positron-Emission-Tomograpy-CT (FDG-PET/CT) is increasing rapidly, but which method is the ideal to use is not clear. In this study early response (1-2 weeks) evaluation was performed using three different methods and compared to clinical response at three months. **Methods:** Forty-three patients with metastatic pulmonary adenocarcinoma had FDG-PET/CT scans performed prior to erlotinib treatment and after 1-2 weeks of treatment. The scans were evaluated by one experienced nuclear medicine specialist. The scans were evaluated by three different methods using Siemens Syngovia software: Visual evaluation, as according to Hicks et al, % change in SULpeak as according to PERCIST 1.0 , and finally calculating the % change in total tumor glycolysis (TLG) proposed in PERCIST 1.0. The early response was compared to response on CT at 12 weeks and to progression free survival (PFS) **Results:** The results are shown in figure 1. Defining response as "not progression" on CT at 12 weeks (10 in total), visual evaluation identifies 6 correctly, and 5 of 33 non-responders as responders. One patient classified as a responder who had a PFS of 0.9 months, had stopped treatment because of side effects. The SULpeak method identifies the same 6 responders correctly, and 3 of 33 non-responders as responders. TLG change identifies 4 responders correctly and 3 of 33 non-responders as responders. Looking at early progression (16 in total) , visual evaluation identified 6 correctly, The SULpeak method identified 4 correctly, the TLG method identified 2 early progressions correctly

.

Visual	SULpeak	TLG	PFS	CT 12w
1	**1**	**1**	19.0	1
1	**1**		11.0	2
2	2	2	9.1	2
1	**1**	**1**	8.3	1
2	2	2	8.2	1
1	**1**	**1**	7.2	1
2	2	2	5.8	*
2	2	2	5.6	2
1	**1**		5.3	1
1	**1**	**1**	4.8	2
2	2	2	3.4	3
1	2	2	3.2	3
2	2	2	2.9	3
3	3	2	2.9	3
1	1	1	2.9	3
1	1	1	2.8	3
1	2	1	2.8	3
2	2	2	2.8	3
3	3	3	2.7	3
2	2	2	2.7	3
2	2	2	2.7	3
2	2	2	2.7	3
2	2	2	2.6	3
2	2	2	2.6	3
3	3	2	2.5	3
2	2	2	2.5	3
2	2	2	2.4	3
2	2	2	2.3	*
3	2	2	2.1	3
3	**3**	2	2.0	3
2	2	2	1.7	3
2	2	2	1.5	3
2	2	2	1.5	3
2	2	2	1.5	*
3	2	2	1.5	*
3	**3**	**3**	1.3	*
2	2	2	1.2	**
2	2	2	1.2	**
2	1	2	0.9	3
2	2	2	0.9	3
3	**3**		0.9	3
1	2	2	0.9	**
3	**3**	**3**	0.8	3

Table 1: Response groups by patient, ordered by PFS (in months) as found by the three methods. 1 partial response, 2 stable disease and 3 progression. "true" progression and response values are highlighted in **bold.** Division lines in bold separates response and early progression from the middle group as according to PFS and CT. * Not Available, ** treatment stopped early because of side effects . **Conclusion:** Visual evaluation identified more responders and patients with early progression during treatment with erlotinib. The more objective method based on calculation of SUV calculations identified less responders as well as less patients with early progression, suggesting a lower sensibility for this method. This suggests that the 40% cut off in % change used in this study (as suggested by Wahl et al in the PERCIST criteria), and perhaps the 30% cut off used for SULpeak change are too high for very early evaluation. **Keywords:** FDG-PET/CT, Adenocarcinoma, Erlotinib, response evaluation

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P2.04-036 The Association of EGFR Mutations with Stage at Diagnosis in Lung Adenocarcinomas Jaeyoung Cho[1], Sun Mi Choi[1], Jinwoo Lee[1], Chang-Hoon Lee[1], Sang-Min Lee[1], Jae-Joon Yim[1], Chul-Gyu Yoo[1], Young Whan Kim[1], Sung Koo Han[1], Doo Hyun Chung[2], Young Sik Park[1] [1]*Internal Medicine, Seoul National University Hospital, Seoul/ Korea,* [2]*Pathology, Seoul National University Hospital, Seoul/Korea*

Background: The prognostic role of epidermal growth factor receptor (*EGFR*) mutations in patients with lung adenocarcinomas remains controversial and the association between *EGFR* mutations and stage at the time of the initial diagnosis is debatable. Here we evaluated the association of *EGFR* mutations with initial stage in lung adenocarcinomas. **Methods:** From June 2011 to December 2014, 1004

consecutive patients who were diagnosed with lung adenocarcinomas and tested for *EGFR* mutations were retrospectively analyzed. As screening detects lung cancer at early stage, screening was incorporated as a confounder in multivariable analysis. **Results:** Among 1004 patients with lung adenocarcinomas, *EGFR*mutations were detected in 49.2% (494 of 1004). In multivariable analysis, *EGFR* mutations were significantly associated with early stage (stage I to II) at diagnosis (OR, 0.65; 95% CI, 0.49 to 0.87; $P = 0.003$). When adjusted for age, sex, smoking status, and screening, adjusted proportion of *EGFR* mutations significantly decreased according to stage. Adjusted proportion of *EGFR* was 57.6% (95% CI, 51.7% to 63.3%) in stage I, 47.9% (95% CI, 36.9% to 59.0%) in stage II, 47.5% (95% CI, 39.6% to 55.5%) in stage III, and 43.4% (95% CI, 38.3% to 48.6%) in stage IV ($P = 0.0082$). **Conclusion:** The presence of *EGFR* mutations is significantly associated with early stage at initial diagnosis in lung adenocarcinomas after adjusting for age, sex, smoking status, and screening. This finding implies that *EGFR* mutations may play a role as a positive prognostic marker. **Keywords:** lung cancer, Adenocarcinoma, EGFR, stage

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-037 Frequency of EGFR Mutations in NSCLC Patients of the Lung Center of the Philippines Maria Teresa A. Barzaga[1], Francisco Iii M. Heralde[2], Jose Luis J. Danguilan[3], Nelia S. Tan-Liu[1] [1]*Pathology, Lung Center of the Philippines, Quezon/ Philippines,* [2]*Biochemistry and Molecular Biology, University of the Philippines - Manila, Manila/Philippines,* [3]*Thoracic Surgery, Lung Center of the Philippines, Quezon/Philippines*

Background: In 2014, the Lung Center of the Philippines embarked on a program to offer Epidermal Growth Factor Receptor (EGFR) mutation testing to its Non-Small Cell Lung Carcinoma (NSCLC) patients to support the diagnostic and decision-making capability of its allied oncologists towards anti-EGFR targeted therapy. As previous clinical studies indicated significant benefit from Tyrosine Kinase Inhibitor (TKI) therapies among Asian patients, enrolling patients on a TKI program based on anti-EGFR profile would realize the Lung Center of the Philippines' objective of providing better chemotherapy to its patients. Meanwhile, early reports showed variable frequency of EGFR mutations among NSCLC patients from two private Philippine hospitals (i.e. San Juan De Dios, 52.3% EGFR positive in 2012 and Saint Luke's Medical Center, 38.9% EGFR positive in 2015). This study will report the profile of EGFR mutation among NSCLC patients from a government tertiary hospital catering to the general Philippine population. **Methods:** Tissue samples from 80 patients clinically diagnosed with NSCLC at stages II to IV via histopathologic sections of biopsy derived specimens, were subjected to EGFR mutation analysis following the Roche EGFR protocol using the Roche EGFR mutation detection kit and the Cobas Quantitative Real Time PCR. The patients' background data were obtained via a survey questionnaire at the time of sample submission and followed up through telephone interview. The patients were made to execute informed consents following the guidelines of the Institutional Ethics Review Committee of the Hospital. **Results:** Out of the 80 NSCLC samples analyzed, 55% (44/80) were from males and 45% (36/80) were from females with a mean age of 61.3 (SD: 11.5) years old. There were 47.5% (38/80) specimens that were positive for EGFR mutations of which 39.5% (15/38) were from males and 60.5% (23/38) were from females. Majority of the EGFR positive patients were non-smokers with only 13.8% (11/80) confirmed to be smokers and only 18.2% (2/11) of the smokers showing positive EGFR mutation. For patients showing positive EGFR mutations, 73.7% (28/38) were Exon 19 deletions, 23.7% (9/38) were Exon 21 L858R, and 2.6% (1/38) was a double mutation comprising Exon 19 deletion and Exon 20 insertion, and is a non-smoker. **Conclusion:** EGFR mutation frequency in LCP's NSCLC patients were midway between the reported values in two Philippine private hospitals and consistent with the reported preponderance among females. Smoking appears not to be a driver for EGFR mutation. Majority of the EGFR mutations detected were on Exon 19 deletion. How these mutation patterns correlate with the chemotherapeutic response would be an important area for future follow-up. **Keywords:** Non-small-cell lung cancer, EGFR testing, Lung Center of the Philippines, Exon 19 deletion

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P2.04-038 EGFR Mutation Prevalence and Epidemiological Profile of Patients with Metastatic Nonsquamous Non Small Cell Lung Cancer Maria Fernanda E. Simões, Eldsamira Mascarenhas, Tercia V. Reis, Clarissa Mathias *Núcleo de Oncologia Da Bahia, Bahia/Brazil*

Background: Presence of epidermal growth factor receptor (EGFR) mutation in patients with non small cell lung cancer (NSCLC) is very important for therapeutic choice, since these patients benefit from the use of targeted therapies, such as EGFR tyrosine kinase inhibitors (TKIs). There are different types of EGFR mutation causing deletions in exons 18, 19, 20 and 21. Presence of this mutation is commonly found in female, Asian ethnicity, never smokers and adenocarcinoma histology. Patients with EGFR mutations have benefit of use TKIs because these drugs inhibit tyrosine kinase activity, enabling apoptosis of tumor cells. However, there are cases of TKI resistance due to mutations at EGFR second site, resulting in T790 mutation (T790M), which prevents TKI connection to tyrosine kinase. This study aimed to determine the percentage of patients with metastatic nonsquamous NSCLC which realized molecular analysis for EGFR mutation, especially T790M, and to describe epidemiological profile of these patients. **Methods:** Observational, retrospective, single-institutional study in metastatic nonsquamous NSCLC patients, in attendance during January 2012 and December 2014. Variables analyzed: age, sex, race, smoking, number of metastatic sites, first-line therapy, presence of EGFR mutation and T790M. **Results:** There were 93 eligible patients, 79 (84,94%) of them were tested for EGFR and 23 patients (29.11%) of 79 were mutated. From all patients tested, 15 patients (18.98%) were positive for exon 19, three patients for exon 21 (3.79%), two patients (2.53%) for exon 20 (T790M), two patients (2.53%) for exon 20 (T790M) and exon 21 (L858R) and one patient (1.26%) for exons 20 (R776C) and 21 (L858R). No patients were positive for exon 18. Therefore, percentage of patients with T790M was 5.06% of all patients tested for EGFR mutation. Among patients with positive EGFR, 56.21% was female, 95.65% had adenocarcinoma and 4.34% large cell. About 69.56% was brown, 21.73% white and 8.69% black; 73.91% never smoked, 17.39% former smokers, while 8.69% was current smoker. The mean age was 55.95 and median of 57 years. Approximately 47.82% of patients had one metastatic site, 39.13% 2 metastatic sites and 13.04% 3 metastatic sites. As for first-line therapy, 52.17% of patients used TKIs (Afatinib or Gefitinib or Erlotinib), while 43.47% used platinum-based chemotherapy, 4.34% used only Pemetrexed. **Conclusion:** The percentage of patients who tested EGFR mutation was high and presence of T790M was also quite significant. Other study found that 81% of patients with stage IIIb/IV NSCLC were tested for EGFR before first-line therapy administration. In a multicenter study, about 90.7% of newly diagnosed NSCLC patients were tested for EGFR mutation and mutation rate was 11.6% for exons 19 and 21. Some of our patients have not been tested for EGFR mutation because they were supportive patients or because the sample was insufficient/ inadequate. The profile of patients with positive EGFR was similar to that found in literature. Some patients did not use TKI as first-line treatment because the result of mutation delayed to arrive. Molecular study in NSCLC patients is essential for the best treatment choice and TKIs should be started as soon as there is positive result of mutation. **Keywords:** EGFR mutation, T790 EGFR mutation, non small cell lung cancer

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P2.04-039 A World of EGFR Screening Test Mélodie Carbonnaux, Pierre Jean Souquet, Sébastien Couraud *Service de Pneumologie Aiguë Spécialisée & Cancérologie Thoracique, Institut Du Cancer Des Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Pierre Bénite/France*

Background: EGFR mutation status has emerged as a crucial issue in the management of lung cancer. In France, the national cancer institute has launched a network of EGFR screening test facilities for daily practice. There is however very little information about EGFR screening test and TKI drugs availability in routine at a worldwide level. We also hypothesized that inequalities might occur in the EGFR test availability regarding country development. Thus, the aim of this study was to edit a map of routine EGFR test and drugs availability and cost subsequently associated to development indicators. **Methods:** We conducted a prospective expert opinion survey. An electronic questionnaire, edited in French or English, was addressed to experts in thoracic oncology in each country of the world. Experts were selected by three different ways: (i) email lists of partner institutions (the *European Respiratory Society,* the Asian Pacific Society of Respiratory, the A*sociacion Latinoamericana del Torax*, the *Thoracic society of Australia and New Zealand*), (ii) manual research on the internet, and (iii) the IASLC member. Interpretation of multiple answers was performed according to an *a priori* determined algorithm. Questionnaire contained 10 multiple-choice questions on availability, and cost of EGFR screening test and EGFR tyrosine kinases inhibitors (TKI). Country development was estimated by the human development index (HDI) provided by UN development program. **Results:** We obtained answer from 74 countries, covering 78% of world population according to UN data. Experts (n=100) were mainly clinicians and worked in hospitals or cancer centers. Non-responding countries were mainly from Africa and Asia, and had a significantly lower HDI than responding countries. EGFR screening test was routinely available in whole the country or only in some region for 57 countries (70% of the world population; figure 1). The remaining-cost of the test was less than 500 US$ in 49 countries (42.5% of the population). Availability and cost of the test were both significantly linked to HDI. The delay to obtain test result was less than 30 working-days in 71% of the population. Erlotinib, Gefitinib, Afatinib and Icotinib were routinely available in 75%, 66%, 31% and 23% of the world population respectively. Availability and cost of erlotinib, gefitinib and afatinib were also associated to HDI.

Figure 1 – Availability of EGFR test in routine practice

Conclusion: EGFR screening test and EGFR TKI are widely accessible in routine worldwide. However, there are large discrepancies in the access and the cost of this innovative process regarding development index. **Keywords:** EGFR mutation, EGFR Tyrosine Kinase Inhibitors, worldwide mapping

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P2.04-040 Impact of Ethnicity on Incidence of Brain Metastasis in Patients with EGFR-Mutant Lung Cancer Jiexia Zhang[1], Huiyu Wen[2], Di Cai[1], Hahn La[2], David R. Gandara[2], Jianxin He[1], Lihong Qi[3], Tianhong Li[2] [1]*Guangzhou Institute of Respiratory Disease, Guangzhou/China,* [2]*Division of Hematology & Oncology, Uc Davis Comprehensive Cancer Center, Sacramento/CA/United States of America,* [3]*Department of Public Health Sciences, University of California, Davis, Davis/CA/United States of America*

Background: Better systemic control and longer survival have been cited as the reason for the higher incidence of brain metastasis observed in patients with EGFR-mutant lung cancer compared to patients with EGFR wild-type lung cancer. The prevalence of EGFR mutation is particularly dependent on patient's ethnicity: 30-40% and 10-16% in East Asian and Caucasian patients, respectively. However, the incidence of brain metastasis in EGFR mutant lung cancer at initial diagnosis in these ethnic groups is less well defined. The objective of this study was to investigate the incidence of brain metastasis at diagnosis in East Asian and Caucasian patients with EGFR-mutant lung cancer. **Methods:** This retrospective study included 163 consecutive patients with EGFR-mutant metastatic NSCLC from a Chinese (N=72) and a US academic (N=91) institution. The EGFR mutation status was determined by the institutional laboratory in China and CLIA-certified laboratory in the US. East Asians in Northern California and Chinese patients in China had a similar incidence of brain metastasis at diagnosis (10/23=43.5% and 30/72=41.7%, respectively), and were combined as East Asians in the analysis. Descriptive statistics were generated for demographics, smoking habits, histology, and EGFR mutation subtypes, stratified by status of brain metastasis at diagnosis. Chi-squared tests and t-tests were used for testing associations of categorical variables and continuous variables with brain metastasis at diagnosis, respectively. Logistic regression models were used to study the association between race and brain metastasis at diagnosis, with and without adjusting for age at initial diagnosis, gender, EGFR mutation type, smoking status, and histology. Odds ratio (OR) and corresponding 95% confidence intervals (CI) were obtained. All analyses were two sided and a p value <0.05 were considered significant. **Results:** Three patients who were neither East Asian nor Caucasian were ineligible for analysis. Among the remaining 160 patients, 44.2% were Caucasians and 55.8% East Asians. Higher incidence of brain metastasis at diagnosis was detected in East Asian patients than Caucasian patients (42.1% vs 13.8%, p= 0.0001). There is no significant difference in the mean age (62 and 59 years old), smoking history (34.2% vs 26.5%), histology (93.8% adenocarcinoma in both groups), type of EGFR mutation (Exon 19 Deletion: 47.8% vs 48.0%; L858R: 35.4% vs 38.0%) between patients without brain metastasis and with brain metastasis at diagnosis. Comparing to Caucasians, East Asians had significantly higher incidence of brain metastasis at diagnosis (OR = 4.53, 95% CI: 2.01–10.20, p= 0.0003). The result remained significant after adjusting for other factors (aOR = 4.24, 95% CI: 1.76–10.18, p= 0.001). **Conclusion:** Regardless of place of residence (Northern California or China), East Asians were more likely to have brain metastasis at initial diagnosis than Caucasian patients, suggesting ethnicity-related genomic and pharmacogenomic differences and less impact of environmental factors on tumorigenesis and clinical course of EGFR-mutant lung cancer. Further study is indicated to understand the impact of ethnicity and population-related genomics and pharmacogenomics on tumor biology of EGFR-mutant lung cancer. **Keywords:** EGFR-mutant lung cancer, Ethnicity, Brain metastasis

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P2.04-041 Characterization of EGFR Activating Mutations in Brazilian Patients with Pulmonary Adenocarcinoma Cheng T. Yen[1], Rafael C. Bitton[1], Luiz G.C.A. De Lima[1], Alex V. Amadio[2], Tiago K. Takahashi[1], Andrea M. Marini[1], Tereza Y. Takagaki[1], Ricardo M. Terra[1], Evandro S. Mello[1], Gilberto De Castro Jr[1] [1]*Medical Oncology, Instituto Do Cancer Do Estado de Sao Paulo - Icesp, Sao Paulo/Brazil,* [2]*Usp, Sao Paulo/Brazil*

Background: The presence of EGFR activating mutations in pulmonary adenocarcinoma is predictive of exquisite response to EGFR-tyrosine kinase inhibitors. Here we studied the frequency of EGFR activating mutations in pts consecutively treated in our institution. **Methods:** It is a retrospective, uniinstitutional study of all consecutively tested samples from pts diagnosed with pulmonary adenocarcinoma and treated in our Institute. All samples were formalin-fixed and paraffin-embedded. Tumor areas were selected and macrodissected, followed by whole DNA extraction and amplification by PCR. EGFR genotyping was performed through DNA sequencing (exons 18, 19, 20 and 21) by Sanger´s methodology. **Results:**417 pts had tumor samples genotyped between Aug/2011 and Sep/2015. Median age was 62 y (17-91), 237 (57%) female. According to ethnicity, 357 pts were Caucasian (86%), 37 African-American (9%) and 21 Asian (5%); 140 pts were classified as never-smokers (34%), 37 (9%) as light-smokers (≤ 10 p.y.) and 238 (57%) as current smokers/> 10 p.y. EGFR activating mutations could be identified in 103 out of 417 samples (24.7%): 78 were exon 19 deletions (76%), 23 were L858R mutation in exon 21 (22%), and two were rare mutations (G719S in exon 18, and V774M and S768I in exon 20). These mutations were found to be more frequent in females than in males (32% vs. 15%, p=0.0001), and in never-smokers and light-smokers than in current smokers/> 10 p.y. (65% vs. 16%, p<0.0001). It is noteworthy to mention that EGFR mutations were detected in 31 current smokers/> 10 p.y. pts. With the exception of 2 cases, all tumors harboring EGFR activating mutations presented TTF-1 expression by immunohistochemistry, and among those TTF-1-negative adenocarcinomas, no mutation was detected in 36/38 samples (p=0.0011). In a median follow-up of 12 months, the median overall survival was 16.3 months among those pts with stage IV and ECOG-PS 0-1, whose tumors presented EGFR-activating mutations. **Conclusion:** In this Brazilian pts, the frequency of EGFR activating mutations was 28%, being more frequent in females, and never-smokers or light smokers. These results reinforce the importance of diagnosing EGFR activating mutations in all pts with TTF-1-positive, pulmonary adenocarcinoma. **Keywords:** EGFR activating mutations, pulmonary adenocarcinoma

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P2.04-042 Mutation of Epidermal Growth Factor Receptor (EGFR) in Patients with Non-Small Cell Lung Cancer (NSCLC) in a University Hospital in Latin America Luz F. Sua[1], Lisa X. Rodriguez[2], Liliana Fernandez[3], Carlos A. Muñoz[4], Juan G. Restrepo[5] [1]*Department of Pathology and Laboratory Medicine and Phd Biomedical Sciences, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [2]*Department of Pathology and Laboratory Medicine and Phd Human Genetics, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [3]*Interventional Pulmonology, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [4]*Medical Research, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [5]*Hemato-Oncology Clinic, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia*

Background: The presence of activating gene mutations in the epidermal growth factor receptor of non-small cell lung cancer patients is predictive. It improved progression-free survival and improved response rate when treated with small molecule tyrosine kinase inhibitors. Together, exon 19 deletion and exon 21 L858R gene substitution are present in about 10% of Caucasian patients and in 20–40% of Asian patients. Moreover, guidelines now suggest EGFR gene mutation testing should be conducted in all patients with lung adenocarcinoma or mixed lung cancers with an adenocarcinoma component, regardless of characteristics such as smoking status, gender or race. The success of targeted therapies in non-small cell lung cancer patients has changed the treatment paradigm in metastatic non-small cell lung cancer. We describe the frequency of mutations in exons 19 and 21 of the EGFR gene in (NSCLC) in our hospital **Methods:** Between June 2013 and March 2015, 73 samples of lung tissue of patients with NSCLC were obtained in Fundacion Valle del Lili Cali-Colombia. Microdissection cuts on paraffin-embedded lung tissue was performed with the objective of increasing the amount of tumor DNA. DNA was extracted with DNA FFPE Tissue Kit QIAamo Kit (Qiagen), then amplified with PCR and exons 19 and 20 of EGFR mutations studied for amplification. Visualization was performed using microfluidic electrophoresis in the Agilent Bioanalyzer. **Results:** We analyzed tumor samples from 73 patients with NSCLC by PCR and RFLP. Good quantity and quality of DNA in 96% (70) cases was obtained. The average age was 65.6 years ± SD, 69% (48) women and 31% (22) men. EGFR mutations were observed in 21% (15) of the samples with 80% (12) in females. 47% of mutations were in exon 19 and 53% in exon 21. 80% of cases with mutations were adenocarcinomas. 53% of patients with mutations were in stage IV disease and 33% of patients received the tyrosine kinase inhibitor. **Conclusion:** In patients who are properly selected for EGFR-positive gene mutations, EGFR-TKIs have been shown to improve symptom control and quality of life, especially in frail elderly patients who desire to avoid the systemic side effects of cytotoxic chemotherapy while achieving a certain level of clinical efficacy. As more clinical trials for novel third-generation EGFR TKIs and other alternative therapies mature, better understanding may be gained through the use of these agents in improving treatment efficacy in adenocarcinoma or even squamous cell histology of metastatic NSCLC.

Table 1. Variables series study

	Total = 70	With the mutation	Without the mutation
Population Characteristics	**n (%)**	**n (%)**	**n (%)**
Age ǂ, years	65,6	62,1	66,6
Gender			
Female	48 (68,6)	12 (25)	36 (75)
Male	22 (31,4)	3 (13,6)	19 (86,4)
Sample collection technique			
EBUS	2 (2,9)	0 (0)	2 (100)
FBO	26 (37,1)	3 (11,5)	23 (88,5)
CT-guided puncture	6 (8,6)	2 (33,3)	4 (66,7)
Thoracoscopic biopsy	34 (48,6)	9 (26,5)	25 (73,5)
Thoracentesis	2 (2,9)	1 (50)	1 (50)
Diagnosis			
Adenocarcinoma	57 (81,4)	12 (21,1)	45 (78,9)
Squamous cell tumor	4 (5,7)	0 (0)	4 (100)
Large tumor cells	4 (5,7)	0 (0)	4 (100)
Adenosquamous tumor cells	4 (5,7)	2 (50)	2 (50)
Giant Cell Carcinoma	1 (1,4)	1 (100)	0 (0)
Tumor stages			
IA	3 (4,3)	1 (33,3)	2 (66,7)
IB	2 (2,9)	1 (50)	1 (50)
IIA	1 (1,4)	(0)	1 (100)
IIB	5 (7,1)	1 (20)	4 (80)
IIIA	2 (2,9)	1 (50)	1 (50)
IIIB	9 (12,9)	3 (33,3)	6 (66,7)
IV	48 (68,6)	8 (16,7)	40 (83,3)
Exons evaluated			
Exon 19	70 (100)	7 (10)	63 (90)
Exon 21	70 (100)	8 (11,4)	62 (88,6)
Treatments*			
Surgical treatment	11 (15,7)	3 (27,3)	8 (72,7)
Palliative treatment	20 (28,6)	3 (15)	17 (85)
Chemotherapy	44 (62,9)	9 (20,5)	35 (79,5)
Tyrosine kinase inhibitor	9 (12,9)	5 (55,6)	4 (44,4)
Radiotherapy	8 (11,4)	1 (12,5)	7 (87,5)
Observation	3 (4,3)	1 (33,3)	2 (66,7)
Survival			
Mortality	10 (14,3)	3 (30)	7 (70)
Survivors	40 (57,1)	10 (25)	30 (75)
No data	20 (28,6)	2 (10)	18 (90)

* A patient may have had more than one treatment

Keywords: EGFR, PCR, NSCLC, TKIs

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P2.04-043 A Successful Case in Which Electromagnetic Navigation Bronchoscopy Identified an EGFR Mutation in Small Peripheral Lung Lesions

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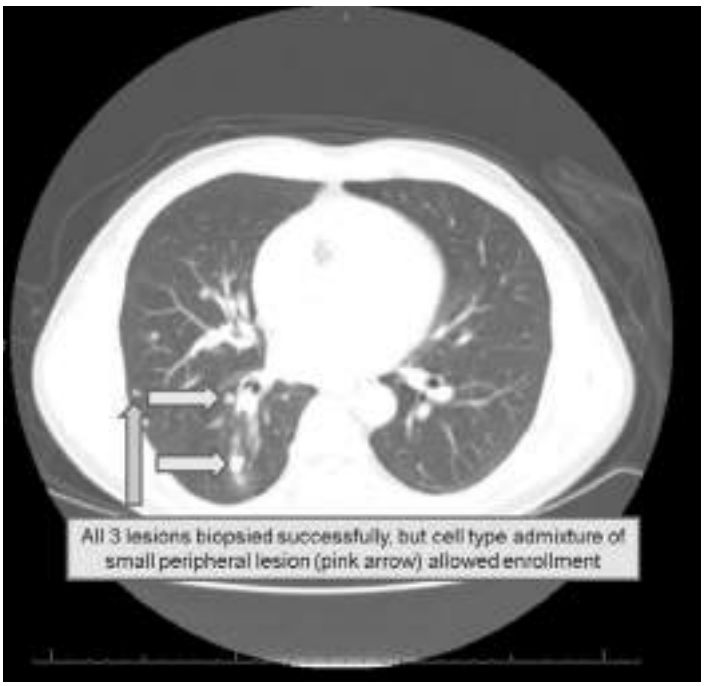
Background: Our institution participated in a Phase I National Trial that treats patients with advanced NSCLC. Clinical enrollment not only required repeat biopsy of tissue for histopathological analysis and molecular testing, but the target lesions were technically challenging due to size, number of lesions, risk, and and time constraints. Utilization of electromagnetic navigation bronchoscopy (ENB) was used to enroll a patient in a clinical trial in which multiple target lesions were identified, but the only viable target lesion was a mere 6mm in diameter in the periphery of the lung. **Methods:** A 54 year old Asian male showed disease progression in a follow-up chest CT after 9 months of treatment with Erlotinib, suggesting that an acquired resistance to Erlotinib had developed after an initial successful response. Additional tissue specimens were needed to determine if the patient was eligible to participate in a Phase I National Clinical Trial that is attempting to prevent EGFR mutations from acquiring resistance mechanisms. An electromagnetic navigational bronchoscopy (ENB™) guided forceps biopsy tool was utilized to obtain tissue samples from 3 separately identified lesions.



Results: All 3 lesions were successfully navigated and tissue samples were all adequate for molecular testing. NSCLC favoring adenocarcinoma was diagnosed for all 3 sites. However, the admixture of cell types (bronchial epithelial, inflammatory cells, etc) meant that only the smallest 6mm peripheral right middle lobe lesion tissue sample biopsy could be used for this specific trial. Based on these pathology results this patient was enrolled. **Conclusion:** Newer minimally invasive biopsy technologies such as ENB™ guidance can facilitate biopsies of multiple pulmonary sites in one procedure; such procedures are safe and feasible in a community based setting. Moreover, these procedures are increasingly important to meet the expanding needs for advanced histological and molecular testing in oncology. This procedure enabled us to enroll this patient in a Phase I National Trial that may potentially address his acquired resistance to Erlotinib treatment.
Keywords: bronchoscopy, EGFR, navigation, molecular testing

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P2.04-044 Analysis of the Intra-Tumor Heterogeneity and Consistency between FGFR1 Gene Amplification and Protein Expression in Squamous Cell Lung Cancer

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Background: Preclinical data have shown that inhibition of fibroblast growth factor receptor 1 (FGFR1) could be a promising therapy for lung tumors with *FGFR1* amplification or expression. The candidate predictive biomarkers *FGFR1* amplification and protein overexpression has been reported respectively in 10-20% or 10-41% patients (pts) with squamous cell lung carcinoma (SqCLC). Therefore, there is an urgent need to assess relationship between both, as well as the heterogeneity of their intratumoral distribution as the potential confounding factors for testing reliability. **Methods:** 3 to 5 FFPE sections from different regions of each of 20 SqCLC tumors were analyzed. *FGFR1* gene copy number was assessed by FISH method using probes specific for the 8p12 locus and the chromosome 8 centromere (CEN8). Criteria of *FGFR1* amplification were as follows: *FGFR1*/CEN8 ≥2.0 or the average number of *FGFR1* signals per cell >6 or >10% of tumor cells containing ≥15*FGFR1* signals. FGFR1 protein expression was determined by immunohistochemistry (IHC). Expression was defined as staining intensity 2+ or 3+ (graded from 0 to 3+) in >1% of the cancer cells. For the heterogeneity analysis only patients with ≥4 slides per tumor were taken into account (15/20 pts). Different definition of heterogeneity was considered. Finally, tumor was classified as heterogeneous, when >25% of slides showed different results of FISH or IHC. Statistical calculation of correlation between FISH and IHC results (19/20 pts) was performed using the GraphPad Prism software using Spearman test. **Results:** *FGFR1* amplification was observed in 6/20 (30%) SqCLC tumors. The average *FGFR1* gene copy number per cell ranged from 1.9 to 10.9 (mean: 4.6) and the mean *FGFR1*/CEN8 ratio was 2.3 (range: 0.7–3.7). The mean content of tumor cells with ≥15 *FGFR1* copies was 2.2%. In IHC(+) tumors (5/20, 25%) the percentage of stained cancer cells with intensity ≥2 was low - only 10/78 samples contained more than 10% of them. In total, 62 FFPE samples from 15 SqCLC patients were analyzed for tumor heterogeneity. *FGFR1* amplification was homogeneous in all pts (15/15), in contrast to expression, as 1/15 tumor was confirmed heterogeneous. The FISH and IHC results were consistent in 52% SqCC patients (n=19), including 1/19 (5.2%) double-positive and 9/19 (47.3%) double-negative

tumors. In 9/19 pts results were discordant: 5/19 (26.3%) IHC(-) FISH(+), while in 4 (21%) pts IHC(+) FISH(-). *FGFR1* amplification did not correlate with protein expression (P=0.543; r=-0.149) for 19 SqCLC tumors . **Conclusion:** Our study demonstrated relative SqCLC tumor homogeneity in terms of *FGFR1* amplification and expression. However, *FGFR1* amplification did not relate to protein expression. Therefore, further more detailed evaluation of both biomarkers *FGFR1* amplification and protein expression regarding their predictive diagnostic value towards anti-FGFR therapy is needed. **Keywords:** Squamous cell lung cancer, biomarker, FGFR1 expression, FGFR1 amplification

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P2.04-045 Targeting eIF4A1 and eIF4A2 mRNA Helicases in Pulmonary Adenocarcinoma Farheen Raza[1], Junichi Tanaka[2], John Le Quesne[1] [1]*Medical Research Council Toxicology Unit, Leicester/United Kingdom,* [2]*University of the Ryukyus, Okinawa/ Japan*

Background: Neoplasia is frequently associated with dysregulated mRNA translation. This dysregulation facilitates tumour growth by promoting proliferation, survival and angiogenesis. Translation is mostly regulated at the initiation stage during which translation initiation factors facilitate positioning of the translation-competent ribosome at the start codon of mRNA. Eukaryotic initiation factors 4A1 and 4A2 are ATP-dependent DEAD-box helicases that unwind 5' UTR as a subunit of the eIF4F complex. eIF4A2 shares 91% amino-acid sequence identity with eIF4A1 and has been implicated in mRNA-mediated silencing. Studies have suggested separate roles for the two eIF4A isoforms. High-level expression of eIF4A1 in early stage non-small cell lung cancer (NSCLC) primary tumours was shown to be associated with poor survival, and, recently, downregulation of eIF4A2 was shown to promote NSCLC progression. Small molecule inhibitors of eIF4A have been shown to have anticancer effects in cell culture and xenograft models. Thus, eIF4A1 and eIf4A2 hold promise as important mediators in lung cancer. This study aims to elucidate the role of eIF4A1 and eIF4A2 in the development of malignant phenotype in pulmonary adenocarcinoma. **Methods:** This study employed two human cancer cell lines as a model for pulmonary adenocarcinoma: HCC364 and H2228. eIF4A activity was modified by using hippuristanol, a non-specific allosteric small molecule inhibitor of both eIF4A isoforms, and siRNA-mediated knockdown of eIFA1 or eIF4A2. Cell cycle analysis was performed using EdU labelling and flow cytometry and cell proliferation was measured by cell counting, xCELLigence and WST metabolic assays. Effects of eIf4A inhibition on protein translation were studied through polysome profiling. **Results:** Both adenocarcinoma cell lines showed significant reduction in S-phase cell population and metabolic activity when treated with hippuristanol. Polysome profiling of HCC364 cells treated with hippuristanol revealed a substantial decrease in polysomal fractions accompanied with the liberation of ribosomal units. Although siRNA-mediated silencing of eIF4A1 markedly suppressed cell proliferation in HCC364 cells, the H2228 cells were unaffected. Interestingly, silencing of eIF4A2 in H2228 cells sometimes results in marked hyperproliferation. **Conclusion:** Our data suggest very different roles of eIF4A isoforms in lung cancer, which have major implications for possible anti-eIF4A therapies. In particular, it suggests that inhibition of eIF4A2 may have a growth-promoting effect in some tumours. As current small molecule inhibitors are non-specific between the two isoforms, this has major implications for the use of similar compounds in a clinical setting. **Keywords:** eif4a, Adenocarcinoma, helicase

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P2.04-046 Kinome RNAi Screens Identify Essential Genes and Therapeutics In 'Driver Negative' Non-Small Cell Lung Cancer Jihye Kim[1], Daniel Foster[2], Rangnath Mishra[2], Jeffrey Kern[2], Aik-Choon Tan[1], James H. Finigan[2] [1]*Division of Medical Oncology, University of Colorado Som, Aurora/CO/United States of America,* [2]*Oncology, National Jewish Health, Denver,Co/CO/United States of America*

Background: Lung adenocarcinoma is a leading cause of cancer-related death worldwide. The discovery of "driver" mutations in genes such as the epidermal growth factor receptor (EGFR) which are required for malignant transformation have revolutionized lung cancer care as chemotherapy directed against these proteins has resulted in dramatic improvements in survival. Approximately 75% of the non-small cell lung cancer (NSCLC) patients harbor a driver gene (KRAS, EGFR, ALK, ROS etc) from the recent molecular characterization of lung adenocarcinomas by The Cancer Genome Atlas. Unfortunately, ~25% of the patients are "driver negative". Therefore, identifying genes essential for malignant pathogenesis in these "driver negative" NSCLC may serve as new therapeutic targets for these patients. **Methods:** Four "driver negative" NSCLC cell lines – H292, H1703, H228, and H322C – were used in the kinome RNAi essential screen. Cells were transduced with a short-hairpin loop lentiviral kinome library (~3700 shRNAs targeting ~600 kinases) developed by The RNAi Consortium (TRC 1.0/1.5). Cells were cultured and harvested after 2, 7, and 14 days of transduction. ShRNAs from surviving cells were extracted, reverse transcribed and barcoded for individual replicates. These samples were sequenced on the Illumina HiSEQ 2000. BiNGS! software was used for analyzing and interpreting the essential screen. Kinases were considered essential if were present at day 2 but they were lost (i.e. knocked out causing cell death) at both day 7 and day 14. We then queried these essential kinases to K-Map, a bioinformatics platform that systematically connects a kinase profile with a reference kinase inhibitor database and predicts the most effective inhibitor for a queried kinase profile. **Results:** All samples from four cell lines had on average 85% of mapping rates (70% - 92%) with 5 to 24 million mapped reads per sample. In total, twenty kinases were identified as essential kinases for these "driver negative" cell lines. For example, MAPK4 for H292; ERBB3 for H322C; ATR for H228; and KDR for H1703. We queried the K-Map using the twenty essential and potentially transformative kinases to connect them to drugs. One of the top kinase inhibitors connected by K-Map was sunitinib. From published papers, we found that H1703 has been validated to be sensitive to sunitinib, supporting the K-Map prediction of inhibitors on the essential kinases. Further validation will be performed and presented in the conference. **Conclusion:** Functional genetic screens have the potential to identify genes essential for cancer cell survival and proliferation, providing a "functional" map in "driver negative" NSCLC. Using a series of novel bioinformatics analyses, specifically connecting the essential kinases with small molecules based on inhibition activities, we have identified that candidate drugs effectively inhibits the essential kinases in "driver negative" NSCLC cell lines resulting in cell death. Further investigation of these candidate drugs and the functional role of these essential kinases could provide personalized treatment for the "driver negative" lung cancer patients. **Keywords:** RNAi screen, kinases, NSCLC, Bioinformatics

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P2.04-047 Mitochondrial Activation- A Potential Therapy in Lung Cancer Ronen Shavit[1], Maya Ilouze[2], Tali Feinberg[3], Yaacov Richard Lawrence[1], Nir Peled[2], Yossi Tzur[1] [1]*Thoracic Cancer Reasearch and Detection Center, Sheba Medical Center Tel Hashomer, Ramat Gan/Israel,* [2]*Thoracic Cancer Unit, Davidoff Cancer Center, Petach Tiqwa/ Israel,* [3]*Physiology and Pharmacology, Tel Aviv University, Tel-Aviv/Israel*

Background: Lung cancer is the leading cause of cancer related deaths in the United States with an overall 5- year survival rate of all stages of~ 17%. Radiation therapy plays a key role in lung cancer treatment. However, many lung cancer patients show resistance to radiation. There is a growing body of evidence indicating that mitochondria may be the primary targets for cancer therapeutics: The unique metabolism of most solid tumors, including lung cancer, stems from remodeling mitochondrial functions to produce a glycolytic phenotype and a strong resistance to apoptosis (Warburg effect). Cancer specific remodeling can be reversed by a small molecule named dichloroacetate (DCA) which promote mitochondrial activation by increasing the influx of pyruvate. Sodium oxamate- another molecule that interferes with cells metabolism, inhibits the formation of the lactate-the end product of glycolysis. Here, we tested whether mitochondrial induction (using DCA and sodium oxamate) may increase the sensitivity of non-small cell lung cancer (NSCLC) cells to radiation through this mechanism. Moreover we tested whether sodium oxamate, increases the effect of DCA on radiation. **Methods:** Two representative NSCLC cell lines (A549 and H1299) were tested for their sensitivity to radiation with and without pre-exposure to DCA and sodium oxamate. The treatment efficacy was evaluated using a clonogenic survival assay. An extracellular flux analyzer was used to assess the effect of DCA on cellular oxygen consumption as a surrogate marker for mitochondrial activity. **Results:** We found that DCA increases the oxygen consumption rate in both A549 and H1299 cells by 60 % ($p=0.0037$) and 20 % ($p=0.0039$), respectively. Pre-exposure to DCA one hour before radiation increased the cytotoxic death rate 4-fold in A549 cells (55 to 13 %, $p=0.004$) and 2-fold in H1299 cells (35 to 17 %, $p=0.28$) respectively, compared to radiation alone. Sodium Oxamate radisosensitized H1299 cells as well. Double treatment with DCA and Sodium Oxamate enhances the radiosensitivity of H1299 cells. **Conclusion:** Mitochondrial activation may serve as a radio-sensitizer in the treatment of non-small cell lung cancer. Inhibition of the end stage of glycolysis increases the effect of mitochondrial activation on radiation. **Keywords:** DCA, Radiation, Warburg effect, Non small cell lung cancer, radiosensitization

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P2.04-048 Analysis of Gene Expression in the Re-Replication Pathway and Selective Blockade with Checkpoint Inhibitors as a Therapeutic Option in NSCLC Daniela Morales-Espinosa[1], Miguel A. Molina-Vila[2], Ana Gimenez-Capitan[2], Silvia García-Román[2], Jordi Bertrán-Alamillo[2], Pedro Méndez-Romero[3], José L. Ramírez-Serrano[4], Santiago Viteri[5], Niki Karachaliou[6], Rafael Rosell[7] [1]*Translational Lung Cancer Research Laboratory, Germans Trias I Pujol Health Sciences Institute and Hospital, Catalan Institute of Oncology, Badalona/Spain,* [2]*Laboratorio de Oncología/Pangaea Biotech. Hospital Universitario Quirón Dexeus. Barcelona, Barcelona/Spain,* [3]*Thoracic Oncology Laboratory, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco/CA/United States of America,* [4]*Hospital Germans Trias I Pujol, Catalan Institute of Oncology, Badalona/Spain,*[5]*Dr Rosell Oncology Institute, Quirón Dexeus University Institute,, Barcelona/Spain,* [6]*Translational Research Unit, Dr Rosell Oncology Institute, Barcelona/Spain,* [7]*Hospital Germans Trias I Pujol, Catalan Institute of Oncology, Barcelona/Spain*

Background: Targeted lung cancer therapy has undoubtedly made a difference to the treatment of *EGFR* mutation and ALK translocation carriers. However, targeted therapies for other subgroups like squamous cell carcinoma are still scarce. Re-replication of the genome could initiate gene amplification and cause chromosomal translocation and loss, contributing to tumor progression. It has been shown that cell cycle checkpoints and DNA damage response are activated when re-replication is induced. Cell cycle checkpoints, mediated by *CHK1* and *2*, are essential to prevent re-replication and maintain genomic integrity. Specific *CHK1* inhibitors such as LY2603618 have been shown to delay tumor growth when given in combination with pemetrexed in NSCLC xenograft models. **Methods:** We selected a panel of NSCLC adenocarcinoma and squamous cell carcinoma cell lines representing different genetic backgrounds with *TP53, KRAS* and *EGFR* mutations. In addition, six PC9-derived, TKI resistant cell lines were included (PC9-ER, PC9-GR1 to GR5). Expression of genes involved in the re-replication pathway (*MDC1, ATR, ATM, CHEK2, Rap80, Cdc1, Cdc6, MYC, SLX4, CHEK1, BRCA1, BRCA2, p53, ORC4, ORC5, ORC6* and *GMNN*) was analyzed by RT-PCR. All cell lines were treated with *CHK1* and a *CHK1/2* inhibitors, and the IC50 was determined by the MTT assay **Results:** We observed different expression levels of key genes involved in

the re-replication pathway. Interestingly, a *p53* mutated **squamous cell line** (SK MES1), which has high expression levels of CHK1 and CHK2 (22.31 and 18.66, respectively), showed the **lowest IC50 in our study (IC50= 0.024 mM)** with a *CHK1*selective inhibitor (LY2603618). Also, two EGFR-resistant cell lines, one harbouring the T790M mutation, were highly sensitive to *CHK1* inhibition (IC50 of 0.19μM for PC-GR5; 0.40 μM for PC9-GR4). Interestingly, when using **a dual CHK1-CHK2, the IC50 is significantly higher in the SK MES1 cell line (84.62 μM vs 0.024 μM) when compared to single CHK1 inhibiton**

Half maximal inhibitory concentrations (IC50s) of CHK1 and CHK1-2 inhibitors		
Cell line	**CHK1 (IC50 μM, mean)**	**CHK1-2 (IC50 μM, mean)**
SK-MES1	0.027	84.62
A549	0.8	15
HCC78	1.2	33.4
H2228	2	0.5
H3255	8.1	12.6
H1975	22.6	9.6

Conclusion: A great advance has been made in targeted therapy for NSCLC during the last 10 years. Nevertheless, few specific therapeutic options exist for squamous cell carcinoma of the lung nowadays. Different expression of genes involved in the re-replication pathway, and the sensitivity of some NSCLC cell lines (such as SK-MES1, a squamous carcinoma cell line) to selective *CHK-1* and dual *CHK1-CHK2* inhibitors identify this pathway as a possible therapeutic target worthy of further investigation. **Keywords:** NSCLC, Targeted therapy, Re-replication pathway, CHK1 inhibition

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P2.04-049 Efficacy of Focal Adhesion Kinase (FAK) Inhibition in RAS Mutant and EGFR Mutant Non-Small Cell Lung Cancer (NSCLC) Hao Zhang[1], Shao Huanjie[1], Hongbin Chen[1], Vita Golubovskaya[2], William Cance[2], Alex Adjei[1], Grace Dy[1]
[1]*Medicine, Roswell Park Cancer Institute, Buffalo/NY/United States of America,* [2]*Surgery, Roswell Park Cancer Institute, Buffalo/NY/United States of America*

Background: Focal Adhesion Kinase (FAK) is overexpressed in many types of tumors, including lung cancer. We sought to determine the antitumor activity of various FAK inhibitors in NSCLC cell lines with RAS mutations as well as in epidermal growth factor receptor (EGFR) mutant cell lines with known resistance to EGFR tyrosine kinase inhibitors (TKIs). **Methods:** The effects of FAK inhibitors (NVP-TAE226, PF-562271, PF-573228, Y15) were tested against a variety of lung cancer cell lines (H157, H358, H460, H727, H1299, A549, H1650, H1975). Cell viability and clonogenic assays were performed to determine the IC50 of each agent. Western blot analysis was performed to determine alterations in relevant signaling proteins. RNA interference studies were done to elucidate mechanisms of action. Xenograft experiments were conducted to evaluate the efficacy of Y15 *in vivo*. **Results:** Y15 is more potent compared to the most selective FAK inhibitor PF-574228, with comparable to slightly more potent activity compared to PF-573228 and TAE-226 (Table 1). Y15 blocked autophosphorylation of FAK in a time- and dose-dependent manner. It caused dose-dependent decrease of lung cancer cell viability and clonogenicity. Apoptosis through Bcl-2 and Bcl-xL downregulation induced by Y15 occurs in an Akt-independent manner via JNK activation. Moreover, knockdown of Bcl-2 or Bcl-xL potentiated the effects of Y15. The combination of various inhibitors of the Bcl-2 family of proteins with FAK inhibitors demonstrated synergy in multiple lung cancer cell lines *in vitro*. Y15 blocked tumor growth of RAS mutant (A549 with KRAS mutation and H1299 with NRAS mutation) as well as EGFR mutant cell lines with known resistance to EGFR TKIs (H1650 and H1975) in xenograft experiments.

Table 1. The IC50 values of FAK inhibitors in lung cancer cell lines as determined by MTS assay.

		H157	**H358**	**H460**	**H727**	**H1299**	**A549**	**H1650**	**H1975**
TAE226	IC50 (uM)	7.46	3.18	4.32	0.30	2.98	2.59	2.30	2.88
PF-562271	IC50 (uM)	5.76	6.38	4,26	2.26	3.94	5.41	5.31	5.47
PF-573228	IC50 (uM)	11.39	27.49	6.17	2.80	9.18	9.08	20.70	13.20
Y15	IC50 (uM)	2.1	2.72	3.16	1.30	3.88	3.49	1.9	1.56

Conclusion: FAK inhibition using Y15 demonstrated efficacy both in vitro and in vivo in lung cancers with either oncogenic RAS or EGFR mutations. The combination of FAK inhibitors with inhibitors of the Bcl-2-family of anti-apoptotic proteins has synergistic activity in these RAS and EGFR mutant NSCLC cell line models. **Keywords:** focal adhesion kinase, RAS mutation, bcl-2, EGFR mutation

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P2.04-050 Basaloid Squamous Cell Cancers Arising from the Lung: Next Generation Sequencing Reveals PTCH1 Mutations in the Hedgehog Pathway Bob T. Li[1], Natasha Rekhtman[2], Helen Won[2], Maria E. Arcila[2], Charles M. Rudin[1], Mark G. Kris[1], Michael Berger[2], Paul Paik[1] [1]*Department of Medicine, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [2]*Department of Pathology, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America*

Background: Basaloid squamous cell lung cancers are a defined variant of non-small cell lung cancers associated with a high mitotic count and rapid clinical progression. Due to its morphologic similarities with basal cell carcinoma of the skin, distinguishing between the two can be difficult. We sought to define the molecular characteristics of basaloid squamous cell cancers that were clinically defined as possible lung primaries in an effort to aid in the diagnosis of this disease. **Methods:**We reviewed a total of 179 patients who were diagnosed with squamous cell lung cancers and had undergone tumor next generation sequencing at Memorial Sloan Kettering. Through the MSK-Integrated Mutation Profiling for Actionable Cancer Targets (MSK-IMPACT), the illumina HiSeq platform was used to detect 341 potentially actionable genetic alterations, including single base substitutions, indels, copy number alterations and selected gene fusions. Data on clinicopathologic characteristics, smoking history were reviewed, and their mutational profile described. **Results:** A total of 6 of 179 (2%) patients with squamous cell lung cancers were found to have basaloid features. Of the 6 patients with basaloid features, 5 (83%) were men, 2 (33%) were never-smokers, 6 (100%) were white Caucasians, 3 (50%) had resected lung specimens, and 2 (33%) presented with stage IV disease. Three cases (50%) had protein patched homolog 1 (PTCH1) mutations in the hedgehog pathway (H652Y, V1057splice, V579fs), identical to those found in basal cell carcinoma of the skin. Two of these patients had a history of basal cell carcinoma of the skin, raising the possibility of metachronous metastatic basal cell carcinoma of the skin. One patient had no such history of basal cell skin cancer. **Conclusion:** Basaloid squamous cell cancers that appear to arise from the lung frequently harbor PTCH1 mutations. Metachronous metastatic basal cell carcinoma of the skin needs to be considered as a possibility in patients with a history of superficial skin lesions. Patients diagnosed with these basaloid cancers that harbor PTCH1 mutations, whether from skin or lung origin, may benefit from hedgehog pathway inhibitors such as vismodegib. **Keywords:** Squamous cell carcinoma, Basaloid features, hedgehog pathway, PTCH1 mutation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-051 The Pluripotency Factor Musashi-2 Is a Potential Target for Lung Cancer Therapy Mary Zhang, Sichuan Xi, Yin Xiong, Shakirat Oyetunji1, Julie A Hong, David Straughan, Saïd Azoury, Emily Reardon, Haobin Chen, David S. Schrump
Tgib, Nci/Ccr/Nih, Bethesda/MD/United States of America

Background: Recent studies have demonstrated that mithramycin represses multiple pathways critical for stem cell signaling and pluripotency in lung cancer cells. This phenomenon coincides with decreased side population (SP) fraction, and dramatic dose-dependent growth arrest of lung cancer cells in-vitro and in-vivo. The present study was performed to further examine the effects of mithramycin on stem cell signaling in an attempt to identify novel targets for lung cancer therapy. **Methods:** Microarray, quantitative RT-PCR (qRT-PCR) and immunoblot techniques were used to examine stem cell gene expression and proliferation of human lung cancer cells and normal/immortalized human respiratory epithelial cells (SAEC/NHBE/HBEC) cultured in the presence or absence of mithramycin, or lung cancer cells following stem cell gene knockdown. Micro-array and qRT-PCR techniques were used to assess effects of systemic mithramycin exposure on stem cell gene expression in subcutaneous lung cancer xenografts in athymic nude mice. qRT-PCR and immunoblot techniques were used to examine endogenous levels of selected stem cell genes in induced pluripotent stem cells (iPSC) derived from SAEC, as well as primary lung cancers and paired normal respiratory tissues. siRNA techniques were used to knockdown Msi-2 to confirm potential mechanisms of action of mithramycin-mediated cytotoxicity in lung cancer cells. **Results:**Preliminary microarray analysis of cultured lung cancer cells and xenografts demonstrated that mithramycin decreased expression of musashi-2 (Msi-2), a RNA binding protein which mediates self-renewal in normal stem cells and aggressive phenotype of several human cancers. Subsequent qRT-PCR and immunoblot experiments confirmed that mithramycin depletes Msi-2 in lung cancer cells in a time and dose-dependent manner. Expression levels of Msi-2 were significantly elevated in non-small cell as well as small-cell lung cancer lines relative to normal/immortalized human respiratory epithelial cells ($p < 0.001$). Consistent with these findings, Msi-2 mRNA levels in primary lung cancers were significantly higher than those detected in adjacent paired normal lung parenchyma ($p< 0.0003$). Msi-2 expression was enriched in SP fractions of cultured lung cancer cells, and was significantly increased in SAEC following reprogramming to pluripotency. si-RNA-mediated knock-down of Msi-2 decreased expression of Oct4, Nanog and Myc, and transiently inhibited proliferation of lung cancer cells. Attempts to permanently knockdown Msi-2 by shRNA techniques thus far have been unsuccessful, suggesting a strong selective pressure to maintain Msi-2 expression in these cells. **Conclusion:** Mithramycin depletes Msi-2 in lung cancer cells. Pharmacologic depletion of this pluripotency factor may be a novel strategy for lung cancer therapy. **Keywords:** NSCLC, SCLC, stem cell signaling, Mithramycin

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P2.04-052 Targeting Oncogenic Eukaryotic Protein Translation in Thoracic Malignancies with Small-Molecule Inhibitors Zeeshan Ahmad[1], Blake Jacobson[1], Aniekan M. Okon[2], Manish Patel[1], Ezzideen B. Al Rawi[1], Gabe Vattendahl Vidal[3], Carston R. Wagner[2], Robert Kratzke[1] [1]*Hematology/Oncology/Transplant, University of Minnesota, Minneapolis/MN/United States of America,* [2]*Dept. Medicinal Chemistry, University of Minnesota, Minneapolis/MN/United States of America,* [3]*Department of Medicine, University of Minnesota, Minneapolis/MN/United States of America*

Background: Hyperactivation of cap-mediated translation can induce oncogenic transformation by enhancing the translation of a subset of mRNAs involved in the genesis, maintenance and progression of cancer.In this investigation, disabling the eIF4F complex by disrupting the eIF4E-mRNA-cap interaction is evaluated as a therapy for mesothelioma and non-small cell lung cancer (NSCLC). **Methods: Cell lines and culture**. H513 and H2373 were from American Type Culture Collection (ATCC) and cultured in either RPMI 1640 containing 10% calf serum supplemented with 10% calf serum and maintained at 37oC. **Cell proliferation assay**. 5000 cells were seeded into wells of 96 well plates. Following overnight incubation cells were treated with varying doses of cpd 267, 272 or pemetrexed for 72 h. Viable cells were counted employing Cell Counting Kit 8 (Dojindo). **Cap-affinity assay**. Cell lysate was mixed with 50 mL of a 50% mixture of m^7GTP-Sepharose resin with and without 400 mM of cpd 267 for 2 h at 4oC to capture eIF4E and eIF4G. The captured bound proteins were eluted and prepared for immunoblot analysis. **Immunoblot analysis**. Protein samples were separated by SDS-PAGE and transferred to Hybond PVDF membrane. Blots were probed for eIF4E and eIF4G (both from Cell Signaling and diluted 1:1000). Detection was carried out using ECL Plus Western Blotting System (Amersham) to visualize the bands of interest. **Results:**Mesothelioma and NSCLC cells were treated with small-molecule inhibitors [compounds 267 and 272] that mimic the cap structure that displace capped mRNAs from the eIF4F complex resulting in suppression of cap-dependent translation of malignancy-related proteins. Treatment with the compounds resulted in a dose dependent decrease in cell viability. Combination therapy of the compounds with cytotoxic agents further decreased cell survival. Binding to a synthetic cap-analogue was employed to assess the strength of eIF4F complex activation in lysates exposed to the compounds. **Conclusion:** These novel compounds reduce cancer cell proliferation,reduce eIF4F complex formation and sensitizes mesothelioma and NSCLC cells to cytotoxic agents. **Keywords:** Small molecule inhibitors, non-small cell lung cancer, Mesothelioma, Cap-dependent translation

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P2.04-053 Patient-Derived Xenograft Studies Suggest FGFR1 Amplification Is Insufficient to Predict Response to FGFR Inhibitors in Lung SqCC Shingo Sakashita[1], Nhu-An Pham[1], Philipp Alberts[2], Olga Ludkovski[1], Ming Li[1], Christine Ng[1], Dennis Wang[1], Ghassan Allo[1], Lucia Kim[1], Naoki Yanagawa[1], Chang-Qi Zhu[1], Ming S. Tsao[1] [1]*Departments of Laboratory Medicine and Pathobiology, University of Toronto, University Health Network, Toronto/ON/Canada,* [2]*University of Toronto, Toronto/Canada*

Background: FGFR1 amplification has been reported in 16%-20% of lung squamous cell carcinoma (SqCC). Early phase clinical trials with anti-FGFR small molecule inhibitors are in progress. It remains unclear whether genomic changes involving FGFR1 is associated with a dependency in FGFR-driven oncogenic activity that could be inhibited with pharmacologic agents. We evaluated a pan-FGFR inhibitor (BGJ398) in four SqCC patient-derived xenograft (PDX) models with amplification of the FGFR1 gene. **Methods:** FGFR1 gene copy changes were assessed by fluorescence in-situ hybridization. PDX models were established by implanting surgical resected tumor fragments into the subcutaneous tissue of non-obese diabetic severe combined immune deficient (NOD-SCID) mice. Protein and mRNA expression levels were assessed by immunohistochemistry/western blot and RT-qPCR, respectively. **Results:** FGFR1 amplification was observed in 13 of 60 (22%) SqCC patient tumors, with all amplified tumors forming PDX. PDX models with FGFR1 gene amplification displayed higher levels of mRNA and protein compared to non-amplified tumor, excluding polysomy cases. One model demonstrated an average of 50% decrease in tumor volume in the BGJ398 treated group compared to control group, 21 days post-treatment. This model also expressed high FGFR1 and high cMYC protein. BGJ398-resistant PDX models included one model with high FGFR1 but low cMYC protein levels, and two models with low FGFR1 and high cMYC protein levels. **Conclusion:** The lack of growth arrest to a pan-FGFR small molecule inhibitor in the 4 PDX models evaluated suggests that FGFR1 amplification alone was not a sufficient predictive marker for pan-FGFR1 inhibitor activity. FGFR1 protein and MYC protein are putative markers. **Keywords:** FGFR1 amplified Squamous cell lung cancer, Patient derived Xenograft, FGFR inhibitor

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P2.04-054 Targeting DNA Methylation in Chromatin Weiguo Han[1], Amos Yan[2], Miao Shi[1], Matthew Levy[2], Simon D. Spivack[1] [1]*Medicine/Pulmonary, Albert Einstein College of Medicine, Bronx/NY/United States of America,* [2]*Bichemistry, Albert Einstein College of Medicine, Bronx/NY/United States of America*

Background: DNA methylation is heritable during mitosis, and has been reported to serve as a strong molecular mark for gene silencing memory. Therefore, to more permanently down-regulate a gene's expression than by siRNA or other means, target-directed DNA methyltransferases are desirable. Recently, the first gene-specific targeted DNA methylation using a zinc finger protein fused to the catalytic domain of DNMT3a (DNMT3a-CD) was reported in a chromatin context for the tumor suppressor gene MASPIN, and the oncogene SOX2, and showed definite but modest activity, but require that a new protein be re-engineered for every new target site. Cas9 directed constructs can potentially be retargeted by simply changing the identity of the guide RNA (gRNA) sequence. **Methods:** We synthesized a Cas9x-DNMT3a-P2A-EGFP fusion in which the catalytic domain of DNMT3a (DNMT3a-CD) is fused to the carboxy terminus of Cas9 D10A-H840A mutant (Cas9x) along with a fluorescent reporter (EGFP) for targeting to the SOX2 promoter. The constructs was transfected into 293T cells and the transfected cells were sorted by flow cytometry. DNA methylation was analyzed by bisulfite sequencing and SOX2 expression was determined by real-time RT-PCR. **Results:** We sorted transfected 293T cells with flow cytometry and found ~50% of the GFP positive cells were methylated with an average methylation level of ~17% (~4 of 21 CpG sites with the target region, but vaired from clone-to-clone); the Cas9x-only expressing vector (as control) showed no methylation. SOX2 mRNA expression was reduced 31% compared to the Cas9x control. Cell adhesion was disrupted, as was growth in culture, compared to empty vector Cas9x controls. Replication studies in A549 lung cancer and other cells are ongoing, as are optimization refinements.

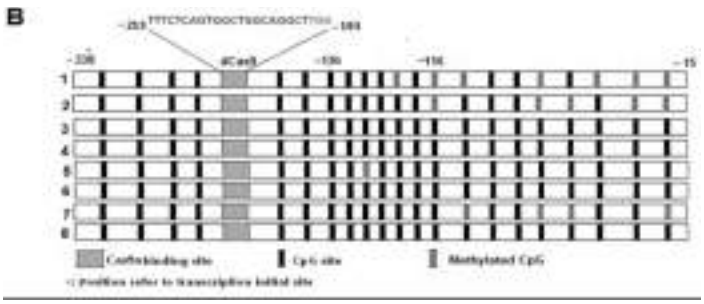

Figure. The methylation state of SOX2 promoter targeted by Cas9x-DNMT3a-CD. The Cas9x-DNMT3a-2A-GFP expression vector was transfected into 293Tcells with LipoFectamin 2000. The sgRNA-targeted site is depicted in yellow. GFP expressing cells were sorted with flow cytometry. Genomic DNA was extracted. After bisulfite treatment, the 400 bp promoter region was amplified and cloned into sequencing vector. Four out of eight colonies (50%) showed some degree of targeted methylation (red marks) adjacent to the Cas9x binding site. **Conclusion:** These results suggest that one can use de-activated Cas9 to direct methyltransferases to specific sites within the genome and regulate gene expression. This has not previously been reported, and may represent a significant advance in the ability to methylate and regulate specific target sites in the cancer genome on a heritable basis.

Keywords: Cas9, DNA methylation, targeting

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-055 Anti-Glut-1 Antibody as a Novel Therapeutic Modality against Breast and Lung Cancers Viral Vaghani[1], Patrick Nassarre[2], Harry A. Drabkin[3], Robert M. Gemmill[4], George R. Simon[5] [1]*University of Texas, Houston/TX/United States of America,* [2]*Hematology/Oncology Division, Medical University of South Carolina, Charleston/SC/United States of America,* [3]*Medicine, Medical Univ. of South Carolina, Charleston/United States of America,* [4]*Medicine, Medical Univ. of South Carolina, Charleston/SC/United States of America,* [5]*Thoracic Medical Oncology, MD Anderson Cancer Center, Houston/TX/United States of America*

Background: The growth and survival of many tumors are dependent upon high glucose uptake to meets it energy needs. A family of glucose transporters proteins (GLUTs) facilitate glucose uptake by cancer cells. There are at least 12 known isoforms of glucose transporter proteins. These transporter proteins differ in their kinetics and its expression is tailored to the requirement of the individual cell type. Although more than one Glut transporter protein may be expressed by a particular tumor cell type, tumors frequently over express Glut-1 which is a high affinity glucose transporter protein allowing the tumor to internalized a relatively large amount of glucose. Indeed tumoral Glut-1 expression correlates with the intensity of glucose uptake seen in a PET scan. We have previously demonstrated that anti-Glut-1 monoclonal antibody inhibited proliferation and induced apoptosis in breast cancer and lung cancer cell lines in vitro. Here we report the results of our in vivo studies where we investigated the ability of anti-Glut-1 monoclonal antibody to retard tumor growth in orthotopically implanted MDAMB-231 cell line in female athymic nude mice. We also examined the ability of the Glut-1 antibody to augment the retardation of tumor growth induced by cisplatin, paclitaxel, tamoxifen, and trastuzumab in the study. **Methods:** MDA-MB-231 breast cancer cells were orthotopically implanted in female thymic nude mice. Cohorts of tumor bearing mice were treated with control solution (PBS) or different dose levels of anti-Glut 1 antibody through tail vein injections. The Glut-1 monoclonal antibody used in the studies detailed here was generated from the clone SPM498. Once an optimal dose of Glu-1 antibody was selected we tested its ability to augment the growth retardation induced by cisplatin, paclitaxel, tamoxifen and trastuzumab. Tumors were measured as treatments continued. At the sign of earliest distress the animals were sacrificed and the organs were harvested and examined for evidence of toxicity and metastases. The harvested tumors were then subjected to Western blot and immunohistochemical analysis to look for markers of apoptosis and proliferation. All the organs and peripheral blood were examined to look for evidence of organ toxicity as a consequence of treatment by the Glut-1 antibody. **Results:** Anti-Glut 1 antibody can be administered safely in high doses to mice. No consistent organ

toxicities associated with Glut-1 treatment were observed. Specifically, there was no central nervous system side effects noted in the mice given that the brain accounts for approximately 30% of the total glucose consumption. Treatment with Anti-Glut-1 antibody did not demonstrate significant single agent activity; however an increase in survival was observed in mice treated with the combination of tamoxifen and the anti-Glut-1 antibody compared with tamoxifen alone. The results of the detailed analyses will be presented at the meeting. **Conclusion:** Our studies demonstrate that anti-Glut1 antibody can be safely administered to mice without major organ toxicity including CNS toxicity. It demonstrated limited anti-tumor efficacy as a single agent, but it shows an increased anti-tumor effect when combined with tamoxifen. Further studies evaluating the combination of anti-Glut-1 antibody with targeted and hormonal agents are warranted. **Keywords:** Breast cancer, Anti-Glut-1 Antibody, Glut-1, lung cancer

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P2.04-056 Analysis of EGFRvIII, PIK3CA, and DDR2 Mutations in Chinese Lung Squamous Cell Carcinoma Patients Min Li, Jian An, Jun Tan, Qi H. Gu, Cheng P. Hu
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Background: As the role of targeted therapy of lung adenocarcinoma affirming, people pay more attention to targeted therapy of squamous cell lung cancer . EGFRvIII , PIK3CA and DDR2 genes become research hotspots as targeted therapy of potential squamous cell lung cancer. However there are few reports on the state of these genes in Chinese patients. Therefore, this study intends to conduct PIK3CA, DDR2 and EGFRvⅢ genetic testing on the surgical specimens from Chinese lung squamous cell carcinoma patients, in order to understand the gene status of Chinese lung squamous cell carcinoma patients and its relationship with clinical factors. **Methods:** This study collected 100 surgical tissue samples of lung squamouscarcinoma patients from Xiangya Hospital of Central South University. All patients had not received preoperative radiotherapy and chemotherapy. EGFRvIII gene was detected by Immunofluorescence, PIK3CA and DDR2 was detected by direct sequencing. X^2 test was applied to analyze the relationship of each gene mutation, expression and clinical characteristics (age, gender, smoking status, tumor stage, tumor differentiation), and two-sided test $P < 0.05$ is considered statistically significant. **Results: Patient Enrollment** A total of 100 cases met eligibility for this study. Clinicopathologic characteristics of 100 patients are shown in Table 1.

Table 1 Detailed Clinicopathologic Characteristics of 100 Lung Squamous Cell Carcinomas

Variable	No. (%)
Total patients	100
Age	
ơ60y	59(59)
≥60y	41(41)
Sex	
Male	92(92)
Female	8(8)
Smoking	
Smoker	82(82)
Never Smoker	18(18)
TNM stage	
Stage I	20(20)
Stage II	23(23)
Stage IIIa	57(57)
Stage IIIb	0(0)
Stage IV	0(0)
Differentiation	
Poor	26(26)
Moderate	65(65)
Well	9(9)

EGFRvIII expression and mutational spectrum of PIK3CA, DDR2 In the 100 cases of lung squamous cell carcinoma specimens, 15 cases were positive of EGFRvIII gene staining (15%); 5 cases of PIK3CA mutation (5%), of which all occurred on 9th exon E545K; among all tested specimens, no DDR2 mutation was found. **Correlation between clinicopathologic characteristics and status of EGFRvIII expression, and PIK3CA mutantion** The EGFRvIII gene expression and PIK3CA gene mutation in the patients' age, gender, smoking, TNM stage and tumor differentiation had no statistically significant difference. **Conclusion:** This study found out that the PIK3CA mutation rate in Chinese lung squamous cell carcinoma patients was higher than in Westerners. **Keywords:** Lung Squamous cell carcinoma, EGFRvIII, PIK3CA, DDR2

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-057 Targeting PIM Kinase in NSCLC Kathy Gately[1], Susan Heavey[1], Stephen P. Finn[1], Sinead Cuffe[1], Niamh Leonard[2], Siobhan Nicholson[2], Ronan Ryan[3], Vincent Young[3], Kenneth J. O'Byrne[4], Martin Page[5], Michael O'Neill[5], Martin P. Barr[6]
[1]*Clinical Medicine, Trinity College Dublin, Dublin/Ireland,* [2]*Department of Histopathology, St. James'S Hospital, Dublin/Ireland,* [3]*Department of Cardiothoracic Surgery, St. James'S Hospital, Dublin/Ireland,* [4]*Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane/Australia,* [5]*Inflection Bioscience Ltd, London/United Kingdom,* [6]*Thoracic Oncology Research Group, Trinity College Dublin/St. James'S Hospital, Dublin/Ireland*

Background: PIM proteins belong to a family of serine/threonine kinases composed of 3 isoforms, PIM1, PIM2 and PIM3, that play a key role in cell cycle regulation, have potent anti-apoptotic activity and play a role in the homing and migration of metastatic cells. Furthermore, PIM kinases have also been shown to be activated in response to Akt pathway inhibition, indicating a role in adaptive responses to inhibition of this pathway potentially leading to treatment resistance. Thus, there is a strong rationale for combining PIM kinase inhibition with inhibition of the Akt pathway (i.e., inhibitors of EGFR, PI3K, Akt and mTOR). PIM kinase has been recognised as a therapeutic target particularly in haematological malignancies however the role of PIM kinases in solid tumours and NSCLC in particular are less well characterised. This study is the first to elucidate the expression of all 3 PIM isoforms in NSCLC cell lines and patient tumours as well as to examine the effect of Inflection Bioscience Ltd novel dual PI3K/PIM kinase (IBL-202) and triple PI3K/mTOR/PIM kinase (IBL-301) targeted therapies *in-vitro* and *in-vivo*. **Methods:** PIM 1/2/3 protein expression was quantified by western blot analysis in a panel of NSCLC cell lines and 40 matched normal/tumour tissues from NSCLC patients (20 adenocarcinoma and 20 squamous cell carcinoma). PIM kinase expression was correlated to patient clinicopathological characteristics and survival data. The effectiveness of IBL-202 and IBL-301 on proliferation and apoptosis in NSCLC cell lines were examined by BrdU and Annexin V/PI FACS analysis, respectively. A head-to-head *in-vivo* study of IBL-202 vs. IBL-301 in xenograft nude mice formed using H1975 cells is ongoing. **Results:** All 3 isoforms of PIM kinase are highly expressed across a panel of NSCLC cell lines. PIM kinase is expressed in ~ 90% of NSCLC tumour tissues across all stages of the disease. IBL-202 and IBL-301 induced apoptosis and decreased cell proliferation in NSCLC cell lines at micromolar concentrations *in-vitro*. The *in-vivo* study is ongoing and results will be presented. **Conclusion:** PIM kinase is a promising new therapeutic target for the treatment of NSCLC patients. Dual PI3K/PIM kinase (IBL-202) and triple PI3K/mTOR/PIM kinase (IBL-301) targeted therapies have demonstrated pro-apoptotic and anti-proliferative activity *in-vitro* and *in-vivo* and should be considered in the treatment of NSCLC patients. **Keywords:** PIM kinase, PI3K, IBL-202, IBL-301

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-058 Neutrophil-Lymphocyte Ratio (NLR) as a Prognostic Marker in Locally Advanced Non-Small Cell Lung Cancer (LANSCLC) Katherine A. Schrenk, Søren M. Bentzen, Vincent K. Lam, Pranshu Mohindra, Elizabeth M. Nichols, Melissa Vyfhuis, Neha Bhooshan, Steven J. Feigenberg, Martin Edelman, Josephine L. Feliciano
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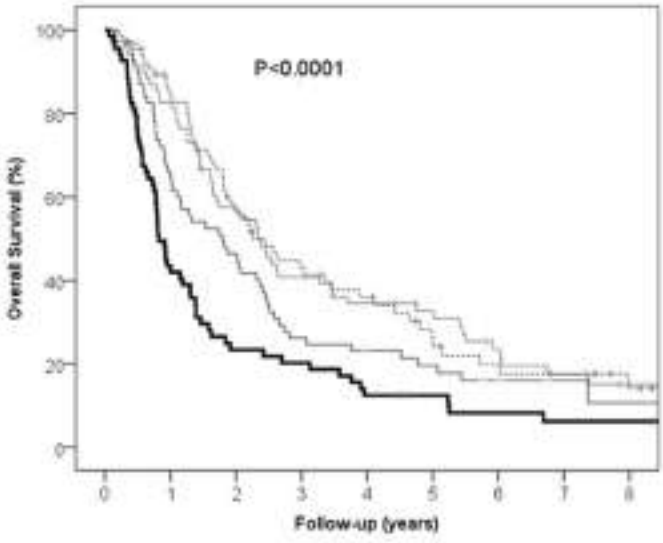
Background: NLR is a measure of systemic inflammation which appears prognostic in localized and advanced NSCLC. Increased systemic inflammation portends a poorer prognosis in cancer patients. We hypothesize that low NLR measured at diagnosis is associated with improved overall survival (OS) in patients with LANSCLC. **Methods:** Records from 276 patients with stage IIIA and IIIB NSCLC treated with definitive chemoradiation with or without surgery at our institution between 2000 and 2010 with adequate data were retrospectively reviewed. Baseline patient demographic data and pre-treatment absolute neutrophil and lymphocyte counts were collected. Patients were grouped into quartiles based on NLR. OS was estimated using the Kaplan-Meier method and the logrank test was used to compare mortality between groups. A linear test-for-trend was used for the NLR quartile groups. The Cox proportional hazards model was used to adjust for other prognostic factors in a multivariable analysis. Distributions of NLR in subgroups were compared using the Mann-Whitney U test. All P-values are 2-tailed. **Results:** NLR was a highly prognostic factor for overall survival ($p<0.0001$). Median survival [95% CI] for the first, second, third and fourth quartile groups of the population distribution of NLR were 27 months [19-36], 28 months [22-34], 22 months [12-31] and 10 months [8-12], respectively. NLR correlated with race, gender, stage and performance status. Even after adjusting for stage (IIIA vs. IIIB), NLR remained predictive of overall survival ($p=0.001$).

Table 1. Baseline patient characteristics and NLR (n=276).

Patient characteristic	Frequency (%)	Median NLR	P-value
Stage			
IIIA	149 (54.0%)	2.86	P=0.001
IIIB	127 (46.0%)	3.90	
Race			
Black	114 (41.3%)	2.66	P=0.021
White	162 (58.7%)	3.37	
Gender			
Female	117 (42.4%)	2.83	P=0.008
Male	159 (57.6%)	3.65	
ECOG Performance Status			
0	134 (48.6%)	2.82	P<0.0001
1	115 (41.7%)	3.40	
2	15 (5.4%)	5.24	
3	9 (3.3%)	6.96	
N/A	3 (1.0%)	–	

Figure 1. Kaplan-Meier Curve.



Legend to figure:

Thin stippled line: First Quartile (NLR≤2.12)

Thin solid line: Second Quartile (2.12<NLR≤3.22)

Medium solid line: Third Quartile (3.22<NLR≤5.18)

Thick solid line: Fourth Quartile (NLR>5.18)

Conclusion: To our knowledge, this is the first large series evaluating NLR as a prognostic indicator in LANSCLC. Pre-treatment NLR is strongly associated with OS in LANSCLC. NLR is an inexpensive biomarker which is significantly prognostic even after adjusting for race, gender and stage. It can be easily utilized at the time of LANSCLC diagnosis to help predict life expectancy. As an indicator of inflammatory response, it should be explored in the context of immunomodulatory therapy. **Keywords:** inflammation, neutrophil-lymphocyte ratio, non-small cell lung cancer, Prognosis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-059 Structural and Functional Characterization of the Hemolymphangiogenic Microenvironment in Lung Cancer Federico Quaini[1], Denise Madeddu[1], Bruno Lorusso[1], Angela Falco[1], Andrea Gervasi[1], Costanzaannamaria Lagrasta[2], Gallia Graiani[1], Paolo Carbognani[3], Luca Ampollini[3], Eugenio Quaini[4], Konrad Urbanek[5] [1]*Clinical and Experimental Medicine, University of Parma, Parma/Italy,* [2]*Pathology, University of Parma, Parma/Italy,* [3]*Thoracic Surgery, University of Parma, Parma/Italy,* [4]*Cardiac Surgery, University of Milan, Milan/Italy,* [5]*Pharmacology, Univesity of Naples, Naples/Italy*

Background: The hypothesis of the existence of a Lung Cancer Initiating Cell (LCIC) offers new pathogenetic and therapeutic options. CICs express vascular-related molecules in order to induce neoangiogenesis and establish an aberrant vascular niche. Conversely, tumor angiogenesis and formation of a cancer vascular niche contribute to the maintenance of CIC. The limited success of anti-angiogenic strategies in lung cancer imposes a better knowledge of the biology and architecture of the tumor vascular microenvironment. The aim of our study was to characterize the structural and functional changes of blood and lymphatic vasculature in human lung cancer. **Methods:** Fresh samples of the neoplastic (T) and spared distal (Dist) lung from 30 patients affected by NSCLC (21 Adeno and 9 Squamous) and 9 Neuroendocrine tumors were processed for immunohistochemical analysis and cell isolation. Control healthy lung (CTRL) was represented by 12 samples collected at autopsy from patients who died in the absence of respiratory diseases and 6 surgical specimens of pneumothorax. Immunofluorescence and confocal microscopy were employed using specific antibodies to detect blood (CD31, vWF, a-SMA) and lymphatic (Podoplanin Pdn, Lyve-1 and Prox-1) vessels. Moreover, the distribution of cells expressing stem/progenitor cell associated antigens (c-kit, CD133, CD34 and PDGFR) was assessed. Phenotypical and functional characterization on immunomagnetically sorted hematic (CD31pos) and lymphatic (CD31pos/Pdnpos) endothelial cells was performed on cells isolated from Dist and T lung samples. **Results:** Results indicated that, compared to CTRL capillary density increased by 77% and 74% in Dist and T portions of the lung, respectively. Conversely, the numerical incidence of venules did not show significant difference. These parameters were similarly represented in the three different tumor histotypes. A significant increase in arteriolar density was observed in all tumor types compared to CTRL. Moreover, the number of arterioles within T was increased by 3-fold compared to Dist portion. The quantitative analysis of lymphatic vessels showed similar values in all types of cancer specimens although rarefaction of these vascular structures was observed compared to CTRL. Moreover, lymphatic vessels density was 10-fold higher in Dist lung than in T. Immunofluorescence confocal analysis documented a positive gradient of c-kitpos, CD34pos and PDGFRpos progenitor cells from Dist towards T in all cancer samples. However, compared to CTRL, cells expressing c-kit and CD34 were more numerous both in the Dist and T portion of the lung, while the increase in PDGFRpos cells was present only in T. Blood (BEC) and lymphatic (LEC) endothelial cells isolated from Dist and T samples of the lung, showed different growth properties and variable expression of Tumor Endothelial Marker (TEM) and receptor tyrosine kinases as VEGFR 2 and 3, PDGFRbeta, EGFR, IGF-1R, and c-met. Functional assays indicated that T derived LEC possess higher tube forming ability on matrigel than Dist LEC while this phenomenon was not observed in BEC. Moreover, wound healing assay showed a VEGF-C independent reduced migratory capacity of LEC isolated from T samples compared to the Dist counterpart. **Conclusion:** Specific changes in the composition and function of the tumor hemolymphangiogenic environment occur in lung cancer providing innovative pathogenetic and therapeutic approaches. **Keywords:** tumor lymphangiogenesis, cancer initiating cells, vascular niche, tumor microenvironment

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P2.04-060 Analysis of Lung Microbiome From Patients Undergoing Bronchoscopy Glen J. Weiss[1], Mark Linhart[2], Daniel A. Nader[3], J. F. Turner[4], J. B. Ross[1], J. G. Caporaso[2], Paul Keim[2], Brandy Harmon[1], Heather Barilla[1], Talima Pearson[2] [1]*Western Regional Medical Center, Cancer Treatment Centers of America, Goodyear/AZ/United States of America,* [2]*Northern Arizona University, Flagstaff/United States of America,* [3]*Southwestern Regional Medical Center, Cancer Treatment Centers of America, Tulsa/AL/United States of America,* [4]*University of Tennessee Graduate School of Medicine, Knoxville/AL/United States of America*

Background: Recent studies have demonstrated diversity in the lung microbiomes of chronic obstructive pulmonary disease and healthy individuals. Lung microbial communities may not just serve as a predictor of cancer development, but also as a target of pharmacological cancer prevention strategies. We sought to characterize the lung microbiome diversity within patients with lung cancer for comparison to those without lung cancer. **Methods:** Signed informed consent was obtained from patients ages 18 years and older that underwent a bronchoscopy during the course of clinical evaluation at one of two cancer centers. A bronchial lavage was collected for research purposes after routine bronchoscopic procedures were completed. The lavage sample was collected in a sterile collection container and immediately placed on dry ice. Subsequently, samples were diluted 1:1, incubated with dithiothreitol to aid in mucus dissolution, and then mechanically homogenized. DNA was extracted and 515F/806R 16S rRNA primers used to amplify Variable Region 4. Amplicons were sequenced using the Illumina MiSeq. Sequences were clustered into operational taxonomic units (OTUs) using QIIME's open reference OTU picking workflow, and taxonomy was assigned to OTUs by classification against the Greengenes database using the RDP Classifier. Microbial communities were compared using phylogenetic beta diversity metrics based on 16S rRNA reads. Statistical significance of diversity between samples was determined by comparing the UniFrac distances between pairs of samples using parametric and non-parametric Monte Carlo-based t-tests. Differences in alpha diversity were tested using a t-test comparing the distributions of diversity values across the sample types. **Results:** None of the patients undergoing a research-related bronchial lavage experienced a significant adverse event from the procedure. There were seven lung cancer patients with a median age of 56.0 years (range 45-75). Of these, six were current/former smokers with an average of 32.5 pack-years. All seven lung cancer patients were Caucasian with five using prescription inhalers and none on recent antibiotics. Five patients had adenocarcinoma and one each of squamous cell carcinoma and small cell lung cancer. There were six non-lung cancer patients with a median age of 57.5 years (range 39-68). Of these, three were current/former smokers with an average of 40 pack-years. All six non-lung cancer patients were Caucasian with three using prescription inhalers and one recently taking antibiotics. Analyses of the microbiota present in lung samples show the presence of multiple bacterial taxonomic groups in each sample, however, the phylogenetic diversity of the bacterial community is low compared to other body sites. Fusobacteria represented a significant portion of the bacterial community of lavage samples. Not surprisingly, the community composition of these samples is most similar to human oral communities, however, a portion of these communities is unlike communities from other characterized human body sites and we are still actively investigating these differences. **Conclusion:** Microbiota associated with lung cancer have not been well-characterized or associated with treatment and outcome. Our analyses suggest that bacterial communities may play an

important role in cancer development and present an opportunity to better characterize these communities and their components. Updated results will be presented at WCLC.
Keywords: microbiota, bronchial lavage, lung cancer, non-lung cancer

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P2.04-061 Tumor-Associated Fibroblasts Increased Density in Non-Small Cell Lung Cancer Is Mediated by Microenvironment Through β1/FAK Signaling
Noemi Reguart[1], Marta Gabasa[2], Marta Puig[2], Jose Ramirez[3], Oscar Busnadiego[4], Fernando Rodríguez-Pascual[4], Aleix Prat[1], Pere Gascon[5], Jordi Alcaraz[2] [1]*Medical Oncology, Hospital Clinic, Translational Genomics and Targeted Therapeutics in Solid Tumors, Institut D'Investigacions Biomèdiques August Pi I Sunyer (Idibaps), Barcelona/Spain,* [2]*Unitat de Biofísica I Bioenginyeria, Facultat de Medicina, Universitat de Barcelona, Barcelona/Spain,* [3]*Pathology, Hospital Clinic, Barcelona/Spain,* [4]*Centro de Biología Molecular Severo Ochoa, Csic, Madrid, Spain., Madrid/Spain,* [5]*Medical Oncology, Hospital Clinic, Centre de Recerca Biomèdica Cellex, Barcelona/Spain*

Background: The current paradigm assumes that the abundance of tumor-associated fibroblasts (TAFs) is largely driven by soluble growth factors as in generic repair responses irrespective of the tumor type or subtype. We recently challenged this assumption by showing that the increased population of lung cancer squamous (SQC)-TAFs in culture was largely driven by matrix stiffening rather than by soluble growth factors (i.e. serum), whereas lung adenocarcinoma (ADC)-TAFs were poorly responsive to exogenous mechanical cues (i.e. matrix rigidity). Moreover, we described that the differential mechano-responses observed in SQC- and ADC-TAFs were associated with increased FAK and a β1 integrin expression. **Methods:** To check whether β1 integrin was necessary for the larger TAF density observed, we treated CCD-19Lu fibroblasts with increasing concentrations of the β1 integrin-inhibitory monoclonal antibody AIIB2 and the monoclonal b1 integrin–activating antibody TS2/16. To further confirm the requirement of β1 integrin through FAK we either depleted or overexpressed FAK in mouse embryonic fibroblasts (MEFs) by transducing with adenoviral infection with FAK (Adv-FAK). **Results:** We observed a dose-dependent decrease in cell density in cells cultured in stiff (30 kPa) gels treated with AIIB2. Moreover, activating β1 integrin with TS2/16 antibody was sufficient to increase both cell density and FAKpY397 expression of CCD-19Lu fibroblasts in soft (1 kPa) gels. As in CCD-19 Lu fibroblasts, matrix stiffening enhanced cell density and FAK expression in wild-type MEFs (FAK+/+), whereas such increases were not observed in FAK null fibroblasts (FAK-/-). Conversely, overexpressing FAK in wild-type MEFs (FAK+/+) was sufficient to markedly increase both cell density and FAK expression in 1 kPa gels compared with control MEFs. **Conclusion:** Abnormally high intrinsic mechano-sensing through β1 integrins and FAK can bypass the inhibitory (protective) role of an extrinsic soft microenvironment. Inhibition of either β1 integrin or FAK signaling may be a suitable approach to target tumor-supporting TAFs in SQC-NSCLC.

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P2.04-062 Temporal Programming of Murine Pulmonary Macrophages in N-Nitroso-Tris-(2-Chloroethyl) Urea (NTCU)-Induced Squamous Dysplasia
Lori D. Dwyer-Nield[1], Meredith Tennis[2], Kevin S. Choo[3], Robert L. Keith[3], Elizabeth F. Redente[4] [1]*Pharmaceutical Sciences, University of Colorado Denver, Aurora/CO/United States of America,* [2]*Pulmonary, University of Colorado Denver Anschutz, Aurora/CO/United States of America,* [3]*Pulmonary Medicine, Denver Veteran Affairs Medical Center, Denver/CO/United States of America,* [4]*National Jewish Health, Denver/CO/United States of America*

Background: Continuous topical application of N-Nitroso-tris-(2-chloroethyl)urea (NTCU) twice per week for 32 weeks causes the development of squamous dysplasia and lung carcinoma (SCC) in certain strains of inbred mice including A/J and FVB mice. In A/J mice, short term/high dose topical application of NTCU induces higher grade squamous lung lesions at earlier times with less toxicity than the 32 week, continuous dosing model. In lung adenocarcinoma, alveolar macrophages become alternatively programmed shortly after carcinogen exposure, before lung lesions are detected indicating that inflammation may be important in lesion development. Herein we examine whether short term/high dose NTCU exposure produces squamous dysplastic lesions in FVB mice. In addition, we characterize macrophage programming as a function of time during lesion development. **Methods:** FVB/N mice were treated with 20mM NTCU twice/week for 2, 4, 8, or 32 weeks and lungs were harvested at 16, 20, 24, 28, and 32 weeks after the initial application. The appearance of squamous lesions was monitored by stereology at the later time point and by the appearance of cytokeratin 5-positive bronchial cells at the earlier time points. Inflammatory cell content was determined by flow cytometry at the 16, 20, 24, and 32 week time in the mice continuously exposed to NTCU and compared to vehicle control. Macrophage programming was assessed by immunofluorescent detection iNOS or arginase I expression . **Results:** Squamous dysplasia appeared in the tracheas of NTCU-treated mice after 16 continual weeks of NTCU exposure, but lung dysplasia was not evident until 8-10 weeks later. The appearance of cytokeratin 5 positive cells in the airways preceded the appearance of these lesions. In mice treated with 8 weeks of NTCU, cytokeratin 5 positive cells in the airways appeared at 24 weeks and dysplastic lesions were also detected. Alveolar macrophage numbers also increased at the 24 week time point in these mice. Data from 28 and 32 week time points is currently being analyzed. Alveolar macrophages displayed little change in iNOS or arginase I staining through 20 weeks, however there were isolated iNOS+ and arginase I+ macrophages at 24 weeks. There were also weakly activated macrophages present in mice treated with NTCU continuously for 32 weeks although alveolar macrophage numbers did not increase significantly. **Conclusion:** The short term/high dose NTCU treatment regimen is less toxic and produces dysplastic lesions at times similar to those in continuous exposure groups. Alveolar macrophage numbers also increase as a function of time in the short term/high dose model whereas there is less reproducibility of this increase in the continuous dosing model. Changes in alveolar macrophage programming occur during dysplastic lesion development, but not to the same extent as that seen in progression of adenomas and adenocarcinomas.
Keywords: squamous dysplasia, mouse models, macrophage programming

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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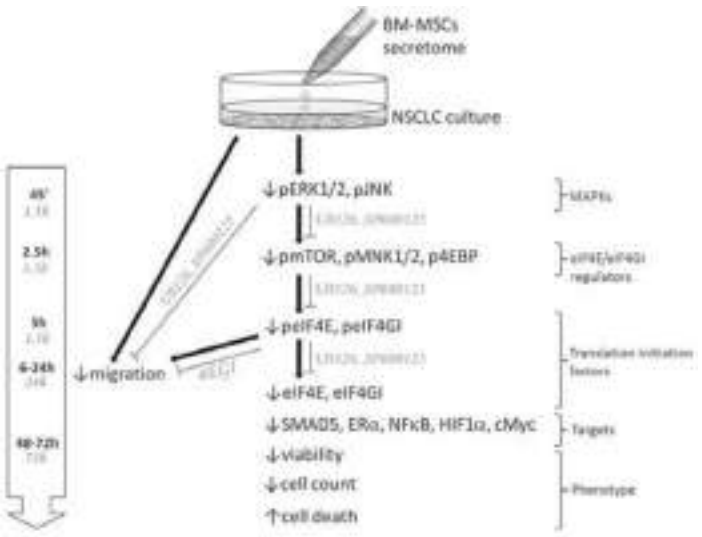
P2.04-063 Secretome of BM Mesenchymal Stem Cells: An Emerging Player in NSCLC Progression
Oshrat Attar-Schneider[1], Victoria Zismanov[1], Liat Drucker[2], Maya Gottfried[3] [1]*Lung Cancer Research Lab, Meir Medical Center, Kfar-Saba/Israel,* [2]*Oncogenetic Lab, Meir Medical Center, Kfar-Saba/Israel,* [3]*Oncology Department, Lung Cancer Unit & Lung Cancer Research Lab, Meir Medical Center, Kfar-Saba/Israel*

Background: Non-small cell lung cancer (NSCLC) remains the most common cause of cancer-related death worldwide. Patients presenting with advanced stage NSCLC have poor prognosis while metastatic spread accounts for >70% of patients deaths. The major advances in treatment of lung cancer have brought only minor improvements in survival; therefore novel strategic treatment approaches are urgently needed. Accumulating data allocate a central role for the cancer microenvironment including mesenchymal stem cells (MSCs) in acquisition of drug resistance and disease relapse. Several studies that investigate MSCs in the lung cancer microenvironment revealed that they exhibit genetic and functional abnormalities compared to their normal counterparts. Furthermore, studies indicate that translation initiation factors are over expressed in NSCLC and negatively impact its prognosis. Importantly, translation initiation is highly modulated by microenvironmental cues. Therefore, we decided to examine the effect of BM-MSCs from normal donors on NSCLC cell lines with special emphasis on the role of translation initiation in the crosstalk. **Methods:** BM samples were obtained from femur head BM samples of normal donors. NSCLC cell lines (H1299, H460) were treated with BM-MSCs' conditioned medium (i.e secretome) for 72 hours after which NSCLC cells were harvested and assesed for changes in the cells' viability, proliferation/ death, and migration. The cells' were immunoblotted for the levels of translation initiation factors (eIF4E, eIF4GI), their targets, and regulators. **Results:** Our results demonstarted deleterious effects on the cells' proliferation, viability, death and migration. We also demonstrated reduced levels of translation initiation factors implicated in cancer progression eIF4E and eIF4GI, their targets, and regulators. Finally, we outlined a mechanism by which BM-MSCs' secretome affected NSCLC's MAPK signaling pathway, downredulated the cells' migration and diminshed translation initiation factors' levles. **Conclusion:** Our study investigates the effects of microenvironmental cues on NSCLC cells' fate and critical translation factors that regulate the cells' tumorigenesis. We showed that there is direct dialogue between the BM-MSCs' secretome and NSCLC cells that manipulates translation initiation and critically affects cell fate. We showed inhibitory effect on the lung cancer cells' migration that is regulated both by MAPK signaling pathways and by translation initiation mechanism. Understanding the molecular events which promote metastasis and improving the means of foretelling their development is a major goal of current clinical research. We suggest that theraputic approach that will sabotage this dialoge, espacially in the BM microenviornment, may diminish lung cancer metastatic spread and morbidity and improve the patients life quality.



Timeline of BM-MSCs' secretome effect on NSCLC cells: The figure presents the signaling activation sequence and phenotype alterations following exposure of NSCLC cells to BM-MSCs' secretome. The schematic presentation describes the timeline of events that emerged from BM-MSCs' secretome, while the thin arrows indicate the trend of change. The gray lines represent the inhibitors effects at the same points. The left arrow depicts the time in which the effects were detected. Here too, the black font represent the time of the effects in the cells that were exposed to the BM-MSCs' secretome, while the gray font is the time for cells treated with the inhibitors. On the right side of the schema specified what was affected in each time point.

Keywords: NSCLC, Translation initiation, Mesenchymal stem cells, Migration

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-064 Microenvironmental Factor of Primary Lung Adenocarcinoma Which Predicts the Effectiveness of Chemotherapy in Patients with Recurrences

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Background: The influence of microenvironmental factors on the effectiveness of chemotherapy is being increasingly recognized. Stromal cells in cancer tissue, such as tumor-associated macrophages (TAMs) and cancer-associated fibroblasts (CAFs), have been shown to influence tumor progression. The associations of CD204-positive cells, which represent an M2 phenotype of TAMs, and podoplanin-positive CAFs, which represent a subpopulation of CAFs with a tumor-promoting phenotype, with a poor prognosis have been identified in patients with lung adenocarcinoma, but whether these associations are involved in the response to chemotherapy remains unknown. The purpose of this study was to investigate the relationships between cancer cell and stromal cell phenotypes in primary tumors and the progression-free survival (PFS) of recurrent lung cancer patients who received platinum-based chemotherapy. **Methods:** We retrospectively analyzed 87 postoperative recurrent lung adenocarcinoma patients treated with platinum-based chemotherapy. The expressions of drug resistance-related proteins including BCRP, Ezrin and ALDH1 in cancer cells, the number of CD204-positive TAMs, and the presence of podoplanin-positive CAFs in the primary tumor were examined. The relationships between the immunohistochemical staining results of primary tumors and the PFS after receiving chemotherapy were also analyzed. **Results:**Among the clinicopathological factors of primary tumors, only an advanced pathological stage was significantly associated with a shorter PFS. As for immunohistochemical staining, no significant relationships were found between the PFS and the expression of BCRP, Ezrin, or ALDH1. The number of CD204-positive TAMs was not associated with the PFS. The presence of podoplanin-positive CAFs, identified in thirty (34%) of 87 samples, was significantly associated with a shorter PFS (median PFS: 5.1 vs. 7.8 months, *P*=0.028), but was not significantly associated with a shorter overall survival (median survival time: 18.1 vs. 23.7 months, *P*=0.156). A multivariate analysis revealed a tendency of podoplanin-positive CAFs to be correlated with a shorter PFS (*P*=0.087). **Conclusion:** The presence of podoplanin-positive CAFs in the primary tumor could be a predictor of a shorter PFS in recurrent lung adenocarcinoma patients who received chemotherapy. These findings suggest that stromal-cell derived factors should be incorporated into predictions of the effectiveness of chemotherapy.
Keywords: Adenocarcinoma, platinum-based chemotherapy, cancer-associated fibroblasts, podoplanin

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P2.04-065 Distant Bystander Effect of REIC/Dkk-3 Gene Therapy through Immune System Stimulation in a Murine Model of Thoracic Malignancies

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Background: We previously identified the tumor suppressor gene *REIC/Dkk-3* whose expression is reduced in many human cancers, and overexpression of REIC/Dkk-3 by an adenovirus (Ad-REIC) exhibited a dramatic therapeutic effect on several human cancers through a mechanism triggered by endoplasmic reticulum (ER) stress. In addition to the direct anti-tumor effect, we also have shown that Ad-REIC has a host-mediated bystander effect on human prostate cancer and scirrhous gastric cancer through REIC-mediated cancer vaccination and production of IL-7. In this study, we examined possible direct and indirect distant bystander effects of Ad-REIC via activation of systemic anti-tumor immunity on thoracic malignancies. **Methods:** We examined anti-tumor effect of Ad-REIC gene therapy on lung cancer and malignant mesothelioma (MM) cell lines *in vitro*. In addition, we examined the direct and distant bystander effect of Ad-REIC in bilateral flank allograft tumor model using immunocompetent BALB/c mice. Mice received intratumoral injection of Ad-REIC into the right-flank tumors, and the effect in bilateral-flank tumors were examined. Dissected bilateral flank tumors after sacrifice were also subjected to immunohistochemical analysis. **Results:** Ad-REIC treatment showed anti-tumor effect in many of lung cancer and MM cell lines *in vitro* due to the activation of c-Jun N-terminal kinase (JNK). REIC/Dkk-3 was highly expressed after Ad-SGE-REIC treatment in Ad-SGE-REIC sensitive cell lines, while it was not or weakly expressed in some cells, which were resist to Ad-SGE-REIC treatment. In an *in vivo* model, Ad-REIC treatment inhibited the tumorigenic growth of not only direct injected tumor but also distant non-injected tumor. In immunohistochemical examination, infiltration of CD49b positive NK cells and expression of MHC Class-I molecules H60 and Rae-1 were revealed in bilateral tumors, suggesting that Ad-REIC treatment showed bystander anti-tumor effect through immune system-mediated apoptosis, and protein expression of MHC class-I molecules induces NK cell infiltration to the tumor. **Conclusion:** We newly revealed that Ad-REIC treatment induced MHC Class-I expression both in primary and distant tumor sites, which lead NK cell infiltration. Ad-REIC treatment showed not only direct anti-tumor effect but also indirect bystander effect through immune system stimulation in immunocompetent mice model. Our findings suggest that Ad-REIC therapy is a promising treatment for MM and lung cancer
Keywords: REIC/Dkk-3, gene therapy, lung cancer, malignant pleural mesothelioma

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-066 Programmed Cell Death Ligand 1 (PD-L1) Overexpression and Low Immune Infiltrate Score Correlate with Poor Outcome in Lung Adenocarcinoma

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Background: PD-L1 is a key immunoregulatory checkpoint which suppresses cytotoxic immune response in a variety of physiologic and pathologic conditions. Thus, inhibition of PD-L1 can lead to reactivating tumor immunity and assist to cancer therapy. PD-L1 overexpression in the tumor cells has been correlated to a lessened immune response and consequent worse prognosis in a variety of cancers. To better understand the immune profiling of PD-L1 expression and its interplay with immune cells, we analyzed the correlation between image analysis-based immunohistochemical (IHC) expression of PD-L1 and tumor infiltrating immune cells density in surgically resected non-small cell lung carcinomas (NSCLC), and the correlation with clinical and pathological features, including patient outcome. **Methods:** IHC for PD-L1, PD-1, CD3, CD4, CD8, CD45RO, CD57, CD68, Granzyme B and FOXP3 were performed in 254 surgical resected stages I-III NSCLC, Adenocarcinoma (ADC=146) and Squamous cell Carcinoma (SqCC=108) from formalin-fixed and paraffin-embedded tissues. PD-L1 membrane expression on tumor cells and density of inflammatory cells were quantified using image analysis in intra-tumoral (IT) and peri-tumoral (PT) compartments. H-score > 5 was used as a cut-off for positive PD-L1 expression and an immune-score (IMS) using CD8/CD4/CD68 was devised. PD-L1 expression and inflammatory cells were correlated with clinico-pathologic features and patient outcomes. **Results:** Positive PD-L1 expression was seen in 26.84% (n=69) of the entire cohort, 23.29% (n=34) of 146 ADC and 23.40% (n=35) of 115 SqCC. In ADC, higher levels of PD-L1 expression were detected in tumors with solid histology pattern compared with other histology patterns (*P*=0.034), and in lifetime smokers compared with non-smokers (*P*<0.0001). In SqCC PD-L1 expression was positive correlation with tumor size (Rho=0.19471,*P*=0.0435). In overall, PD-L1 expression correlated positively with inflammatory cell density in both IT and PT compartments in ADC and SqCC. Patients with *KRAS* mutation (*P*=0.00058), solid tumor (*P*<0.0001) or smoker (P = 0.0446) were more likely to have positive PD-L1 expression tumor cells in ADC. No correlation was detected between *EGFR* mutation and immune markers. Using PD-L1 and CD8/CD4/CD68 IMS expression levels, in ADC and SqCC, we identified 4 groups of tumors (Table 1). Multivariate Cox proportional hazard regression analysis demonstrated that tumors with high PD-L1 expression and low IMS in ADC exhibited significantly poor recurrence-free (HR=4.299; *P*=0.0101) and overall survival (HR=5.632;*P*=0.0010).

Table 1. Summary of the correlation between PD-L1 expression levels and immune-score (IMS=CD8/CD4/CD68) in adenocarcinoma (ADC) and squamous cells carcinoma (SQCC).

PDL-1 H-score (ADC)	IMS (Low)	IMS (High)	Total
<5	61 (41.78%)	51 (34.93%)	112 (76.71%)
≥5	8 (5.48%)	26 (17.81%)	34 (23.29%)
Total	69 (47.26%)	77 (52.74%)	146 (100.0%)
PDL-1 H-score (SqCC)			
<5	37 (34.30%)	36 (33.30%)	73 (67.60%)
≥5	17 (15.70%)	18 (16.70%)	35 (32.40%)
Total	54 (50.00%)	54 (50.00%)	108 (100.0%)

Conclusion: Higher PD-L1 expression is associated with solid pattern in adenocarcinoma and higher level of tumoral immune infiltrate. We developed an immune score which when combined with PD-L1 expression significantly correlates with patient outcome in surgically resected ADCs. (Supported by grants UT-Lung SPORE P50CA70907 and CPRIT RP120713).
Keywords: Non-small cell lung carcinomas, Programmed cell death ligand 1, Immune-score, Survival outcomes

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-067 Clinical Characteristics Associated with PDL1 Positive Status in Resected NSCLC Georgia Geller[1], Brandon S. Sheffield[2], Susanna Zachara-Szczakowski[3], Katy Milne[4], Brad Nelson[4], Diana Ionescu[5], Cheryl Ho[6] [1]*Medical Oncology, BC Cancer Agency, Vancouver/Canada,* [2]*Pathology, BC Cancer Agency, Vancouver/BC/Canada,* [3]*Pathology, Vancouver General Hospital, Vancouver/BC/Canada,* [4]*Biochemistry and Microbiology, BC Cancer Agency, Victoria/BC/Canada,* [5]*Pathology, BC Cancer Agency, Vancouver/Canada,* [6]*Medical Oncology, BC Cancer Agency, Vancouver/BC/Canada*

Background: Multiple different PD1 and PDL1 targeting antibodies have been developed for the treatment of NSCLC. Identifying the population most likely to benefit from PD1/PDL1 direct therapy has focused on PDL1 immunohistochemistry (IHC) of the tumor cells. However, each therapeutic agent has a different companion diagnostic test therefore it is difficult to consistently ascertain the PDL1 status of an individual patient. We proposed to evaluate clinical predictors of PDL1 positive status based on consensus PDL1 immunohistochemistry. **Methods:** Patients with resected Stage II lung adenocarcinoma who underwent adjuvant chemotherapy at the BC Cancer Agency were selected for this study. A tissue microarray (TMA) with matched primary and lymph node was constructed. IHC directed towards PD-L1 was performed with 2 different primary antibody clones: E1L3N (Cell Signaling Technology) and SP142 (Spring Bioscience). PDL1 consensus score was considered positive if there was concordance with both antibodies. Clinical characteristics were abstracted by retrospective chart review. **Results:** Eighty cases of NSCLC were identified and used in TMA construction. 19 primary tumors (24%) were PD-L1 positive by consensus scoring. Lymph node metastases showed a concordant PD-L1 score in 92% cases. Patients were categorized as PDL1 positive based on consensus score of the primary tumor. Baseline characteristics based on PDL1 primary tumor status negative/positive: female 64%/47%, median age 61/65 (NS). Current smoker at the time of diagnosis 34%/58% (p=0.07). The 7 EGFR mutation positive and 2 ALK positive patients were PDL1 negative. PDL1 positivity was examined by pack years of smoking: >10 pk yrs 69%/90% (p=0.13), >20 pk yrs 62%/79% (p=0.26), >30 pk yrs 39/63% (p=0.11) and tumor differentiation: well 13%/5%, moderate 48%/21%, poorly 39%/74% (p=0.03). **Conclusion:** PDL1 positive status is associated with poorly differentiated tumors and demonstrates a trend towards current smokers. This is consistent with the concept that smoking related malignancies and poorly differentiated tumors are more antigenic and therefore require immunosuppression via PDL1 to remain undetected by the immune system. **Keywords:** PDL1, Immunohistochemistry, Adenocarcinoma, clinical characteristics

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-068 PD-L1 Expression in Tumor Infiltrating Immune Cells Determined by Digital Imaging Is Associated with Poor Survival in NSCLC Patients Bernadette G. Reyna Asuncion[1], Zul Fazreen[1], Mohd Feroz Mohd Omar[2], Nur Lina Mohd Salleh[1], Michelle Ann Rozario[3], Min-En Nga[4], Yin Huei Pang[4], Brendan Pang[4], Marie Loh[5], Byoung Chul Cho[6], Barry Iacopetta[7], Richie Soong[1], Ross Soo[3] [1]*Cancer Science Institute, Natl Univ of Singapore, Singapore/Singapore,* [2]*Dept of Pathology, Nus, Singapore/Singapore,* [3]*Dept of Hema-Onco, Nuhs, Singapore/Singapore,* [4]*Dept of Pathology, Nuh-Singapore, Singapore/Singapore,* [5]*Translational Laboratory in Genetic Medicine, Agency for Science Tech and Research, Singapore/Singapore,* [6]*Medical Oncology, Yonsei Cancer Center, Seoul/Korea,* [7]*School of Surgery, University of Western Australia, Perth/ACT/Australia*

Background: Programmed Death-Ligand 1 (PD-L1) has emerged as a potential prognostic marker and as an effective target for therapeutic inhibition in cancer. Using digital slide imaging, we evaluated the clinical, molecular and survival associations of PD-L1 expression in non-small cell lung cancer (NSCLC) according to cell type (tumor and immune cell) and tissue localization (tumor and stroma). **Methods:** Tumor samples from 199 NSCLC patients were stained for PD-L1 by immunohistochemistry (IHC) and quantitatively assessed using the Vectra slide imaging system for PD-L1 tumor membrane expression (TME), PD-L1 positive (+) tumor immune cell density (TICD) and PD-L1+ stroma immune cell density (SICD). Assessment of gene mutation and anaplastic lymphoma kinase rearrangement were performed using the AmpliSeq Cancer Hotspot V2 assay and IHC, respectively. **Results:** High PD-L1 TME correlated with larger tumor size, squamous cell histology and poor differentiation. PD-L1+ TICD was associated with male gender and wild-type EGFR. Univariate analysis revealed that stage (p=0.001), PD-L1 TME (p=0.007) and PD-L1+ TICD (p=0.006) were associated with worse survival. Iterative p-value analysis indicated the optimal thresholds for PD-L1 TME were 30 (p=0.003, 73% of cases) or 160 (p<0.001, 7%), while for PD-L1+ TICD they were 6.9% (p=0.022, 33%) or 20% (p=0.001, 5%). In multivariate analysis, stage (p=0.018), PD-L1 TME≥160 (p=0.040) and PD-L1+ TICD≥6.9% (p=0.015) were independently associated with survival. **Conclusion:** PD-L1 Tumor Membrane Expression (TME) and PD-L1+ Tumor Immune Cell Density (TICD) expression determined by digital analysis have prognostic value in NSCLC. **Keywords:** NSCLC, PD-L1, immune cells, digital slide imaging

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-069 Characteristics and PD-1/PD-L1 Expression of Periphera CD4+CD25+CD127low Treg Cells in Lung Cancer Xue Pan, Yuan An, Hua Shi
Department of Respiration, The Second Affiliated Hospital of Soochow University, Suzhou, China, Suzhou/China

Background: Both regulatory T cells (Tregs) and PD-1/PD-L1 pathway were critically involved in lung cancer. However, the association between them was not well investigated. Herein, we aimed to investigate the characteristics of PD-1 and PD-L1 expression on Tregs and association between them. Also, we analyzed the correlation between Tregs and clinical indicators of lung cancer and between PD-1,PD-L1 expressed by Treg and clinical indicators, thereby preliminary revealed the expression characteristics of PD-1,PD-L1 on Treg and its significant, and providing valuable indicators to clinical diagnosis. **Methods:** The phenotypic characteristics and PD-1 expression of CD4+CD25+CD127lowTreg were studied by flow cytometry. Twenty- two primarily lung cancer patients,ten patients with benign lung disease,twenty-five healthy volunteers were included.The datas were analyzed by SPSS 14.0 software. **Results:** 1.The levels of CD4+CD25+CD127lowTreg in the peripheral blood of patients with lung cancer,with benign lung disease and healthy volunteers were (7.66±2.25%)、(5.73±1.43%)、(3.76±1.06%)respectively.The level of patients with lung cancer was significant higher than those of patients with benign lung disease and healthy volunteers.In the present study, PD-1 and PD-L1 expressions were detected in CD4+CD25+CD127lowTreg in both patients and health controls.The levels of PD-1 expression of CD4+CD25+CD127lowTreg were (46.01±11.33%)、(33.34±13.54%)respectively and the levels of PD-L1 expression of CD4+CD25+CD127low Treg were （73.39±11.64%）、(72.16±12.95%) respectively. Of note, higher level of PD-1 expression was found on tregs in patients with lung cancer. 2.The level of CD4+CD25+CD127lowTreg was not related to pathologic subtype and lymphatic metastasis, but clinical stage(stage Ⅲ6.29±1.18%, stage Ⅳ10.06±1.58%, P<0.01). 3.The level of PD-1 expression of CD4+CD25+CD127lowTreg was not related to pathologic subtype,lymphatic metastasis ,but clinical stage(stage Ⅲ41.85±6.1%, stage Ⅳ56.57±12.52%, P<0.05) .Moreover,the level of PD-L1 expression of CD4+CD25+CD127lowTreg was not associated with pathologic subtype and lymphatic metastasis, but clinical stage(stage Ⅲ48.51±18.17%, stage Ⅳ77.48±8.33%, P<0.05). **Conclusion:** Costimulatory molecule receptor interacting with corresponding ligand mediate positive or negative costimulatory signal and regulate the proliferation of T cells, the production of cytokine, cell toxicity as well as cell apoptosis and existence, which control T cell activation. PD-1 (programmed cell death-1) belongs to the CD28 family and is expressed on activated T, B, and myeloid cells. PD-1 and its ligand PD-L1 deliver inhibitory signals that regulate the balance between effector T cell activation and immune-mediated tissue damage.The proliferation and immune inhibitory function of Treg is related to the costimulatory molecules expressed on its own surface.Our study showed that:1.The level of CD4+CD25+CD127lowTreg cells in the patients with lung cancer increased.The abnormal level of this negative immue cell may play an important role in the development,progression of lung cancer.2.Our study indicated that distinctive characteristics of PD-1 and PD-L1 expression on Tregs in lung cancer suggests associated with impaired adaptive immunity. The cross talk between Treg cells and PD-1/PD-L1 induced inhibition in lung cancer deserved further exploration for lung cancer associated immune pathogenesis. **Keywords:** PD-1/PD-L1 Treg

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-070 Immunological Characterization of PD-L1-Positive Non-Small Cell Lung Cancer Cells Tomoyuki Igarashi[1], Jun Hanaoka[2], Koji Teramoto[1], Yataro Daigo[1] [1]*Department of Medical Oncology, Shiga University of Medical Science, Otsu/Japan,* [2]*Department of Surgery, Shiga University of Medical Science, Otsu/Japan*

Background: The expression of programmed cell death-ligand 1 (PD-L1) on tumor cells plays an essential role in the suppression of anti-tumor immune responses, thus resulting in tumor progression. However, pathological features of PD-L1-positive cancer cells in non-small cell lung cancer (NSCLC) remain unclear.To clarify the characteristics of NSCLCs that are eligible for the-PD-L1-targeted immunotherapy, we examined the immunological feature of PD-L1-positive tumor cells by immunohistochemical analysis. **Methods:** We stained serial sections of formalin-fixed paraffin-embedded NSCLC tissues from 34 patients who had undergone surgery using antibodies to PD-L1 or major histocompatibility complex (MHC) class I. We also identified tumor infiltrated lymphocytes (TIL) in the section, and analyzed the association between PD-L1 expression and MHC class I expression on tumor cells or TIL around tumor cells. **Results:** The patients with median age of 68 years (range, 49-79 years) consisted of 25 males and 9 females. Histological types included 23 adenocarcinomas, 8 squamous cell carcinomas, 2 adeno-squamous cell carcinomas and 1 pleomorphic carcinoma. PD-L1 and MHC class I were expressed on tumor cells in 28 (82.3%) and 29 (85.3%) of 34 cases, respectively. In 18 of 34 cases (52.9%), MHC class I-positive tumor cells were dominant in the tumor; whereas MHC class I-negative tumor cells were dominant in 16 of 34 cases (47.1%). PD-L1 expression was observed in 14 of 18 (77.7%) NSCLCs that are dominant with MHC class I-positive tumor cells, whereas it was detected in 4 of 16 (25.0%) those mainly containing MHC class I-negative tumor cells. There was a significant association between PD-L1 and MHC class I expressions on NSCLC cells ($p=0.0045$). We next examined the association between the co-expression of PD-L1 and MHC class I on tumor cells and the number of TIL, and found that the incidence of PD-L1+ MHC class I+ tumor cells was likely to associate with the large number of TIL (r=0.42). The frequency of PD-L1-positive cells in MHC class I-positive tumor cells was also associated with the large number of TIL (r=0.33). **Conclusion:** MHC class I expression on tumor cells may be required for their expression of PD-L1, probably through the cell-to-cell interaction with TIL. Further study is warranted, however, the patient with the co-expression of PD-L1 and MHC class I on larger number of tumor cells is likely to be a suitable candidate for PD-L1-targeted immunotherapy. **Keywords:** Immunohistochemistry, PD-L1, MHC class I, non-small cell lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-071 PD-L1 Expression Is Not Associated with Disease-Free Survival in NSCLC Patients Who Underwent Radical Resection Wenhua Liang, Qihua He, Jianrong Zhang, Jianxing He *The First Affiliated Hospital of Guangzhou Medical University, Guangzhou/China*

Background: The expression of Programmed Cell Death Ligand 1 (PD-L1), as a major mechanism of immune escape, has been observed in various malignancies. However, its prognostic impact on non-small cell lung cancer (NSCLC) patients remains controversial, especially those in early stage when theoretically all tumors have been removed. We sought to examine the correlation between PD-L1 expression and prognosis of NSCLC patients after radical resection. **Methods:** A consecutive cohort of 681 patients who underwent radical resection for stage I to III NSCLC in our center between Sep 2009 and Dec 2011 was collected. All available cancerous tissues were collected and were made into tissue arrays. Immunohistochemistry staining using PD-L1 (E1L3N ®) XP ® Rabbit mAb was performed to detect the PD-L1 expression. PD-L1 positive expression was denoted as more than 10% tumor cells with PD-L1 staining, while PD-L1 high expression was denoted as H score≥100. The primary endpoint was disease-free survival (DFS). **Results:** Tissues of 670 patients were available and all of them were eligible for PD-L1 staining. There were 222 events (recurrence/death) and the median follow-up was 3.1 year (range, 0.1 to 5.6). Neither positive expression (HR 0.93, 95%CI 0.69 to 1.25; P=0.61) nor high expression of PD-L1 (HR 0.88, 95% CI 0.59 to 1.31; P=0.54) was associated with DFS (Figure 1). The absence of discrepancies in prognosis did not differ in each stage and histology (Table 1)

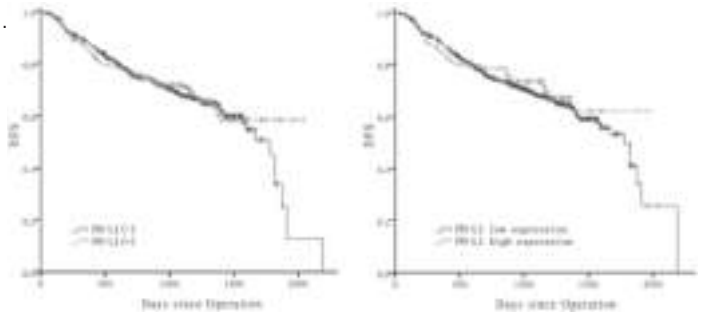

Figure 1. Kaplan-Meier curve. Table 1. Subgroup analyses

Subgroup	No.	HR	95%	CI	Sig.
Stage					
I	340	0.754	0.299	1.897	0.548
II	139	0.827	0.406	1.683	0.600
III	162	0.669	0.355	1.259	0.213
Histology					
Non-squamous without neuro-endocrine differentiation	473	0.840	0.483	1.461	0.537
Squamous	146	0.867	0.445	1.690	0.675
Other or mix	49	0.763	0.225	2.585	0.664

Conclusion: This large scale study showed that PD-L1 is not a prognostic factor in early stage NSCLC after radical resection. These results encourage us to investigate whether the nature of the disease especially regarding immune escape will change after radical resection.
Keywords: NSCLC, PD-L1, survival, Surgery

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-072 Immunohistochemical PDL1 Expression and Clinicopathological Characteristics in 541 Surgically Resected Non-Small Cell Lung Cancers Shohei Mori[1], Noriko Motoi[1], Yosuke Matsuura[2], Hironori Ninomiya[1], Sakae Okumura[2], Makoto Nishio[3], Yuichi Ishikawa[1] [1]*Division of Pathology, The Cancer Institute, Japanese Foundation for Cancer Research, Tokyo/Japan,* [2]*Thoracic Surgery, The Cancer Institute Hospital of Jfcr, Tokyo/Japan,* [3]*Thoracic Medical Oncology, The Cancer Institute Hospital of Jfcr, Tokyo/Japan*

Background: Immune-checkpoint therapy targeting programmed cell death protein 1 (PD1) and programmed cell death protein ligand1 (PD-L1, PDL1, CD274) has been emerging as a new therapeutic strategy for patients with cancer. PDL1 binding to PD1 expressing on the surface of T-cell suppresses activation and proliferation of T-cell. Many types of cancer frequently overexpress PDL1 and escape the immune system. PDL1 expression of tumors may be a useful marker of responsibility for the immune-checkpoint therapy targeting for PDL1. However, the incidence of PDL1 positive cases and related patients' characteristics among NSCLC is still unclear. The aim of this study is to clarify these unsolved questions. **Methods:** The 541 surgically resected non-small cell lung cancers (NSCLC) between 1994 and 2014 were recruited as following criteria; including primary lung cancer, excluding pathological incomplete resection, limited resection, in-situ carcinoma, small-sized carcinoma, large cell neuroendocrine carcinoma, pleomorphic carcinoma, synchronous or metachronous multiple cancer and metastatic cancer. Tissue microarrays (TMA) were constructed using formalin-fixed paraffin embedded (FFPE) tumor specimen of each representative histologic area. Patients' characteristics and outcomes were collected from medical chart. The PDL1 expression was evaluated by immunohistochemistry (IHC) using anti-CD274 (PDL1) antibody (Clone ERP1161 (2), Abcam) as primary antibody on 4-micrometer-thick TMA specimen by an auto-staining machine. The results of IHC were evaluated by microscopy and scored with a combination of intensity and proportion. The intensity was defined as negative: 0, weakly positive: 1+, strongly positive: 2+), the proportion was defined positive cell percentage with 10% increments. Based on PDL1 score defined as Σ [intensity (0, 1, 2) x proportion of each intensity], the tumors were divided as PDL1 positive group (score >50) and PDL1 negative group (score ≤50). We compared between two groups in clinicopathological characteristics and prognosis. **Results:** 541 NSCLCs were classified into PDL1 positive (n = 171, 32%) and negative group (n = 370, 68%). The PDL1 positive group was significantly less differentiated ($p < 0.001$), higher rate of lymphatic ($p = 0.010$), vascular invasion ($p = 0.036$), lymph node metastasis (pN1-3) ($p = 0.012$), and advanced pStage ($p = 0.002$) compared to negative group. There were no significant differences in sex, age, smoking habit, tumor size, pT factor, and distribution of histological types between two groups. Although the prognostic analysis showed no difference between PDL1 positive vs negative groups ($p = 0.861$), the histology-based stratification analysis revealed that PDL1 positive squamous cell carcinoma (SqCC, n=28) showed better overall survival rate compared to PDL1-negative SqCC (n=53) ($p = 0.018$). **Conclusion:** Our data indicated that the PDL1 positive NSCLCs had worse pathological factors, including tumor differentiation, lymphovascular invasion, pN, and pStage, but did not show a statistically significant difference in terms of overall survival rate compared to PDL1-negative group. It is of interest that PDL1 positive SqCC showed a better prognosis than PDL1 negative SqCC.
Keywords: NSCLC, PDL1, Immune-checkpoint, Immunohistochemistry

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-073 PD-L1 Expression Is Induced by MET in an Erlotinib-Resistant Cell Line with MET Amplification Christina Demuth, Morten Nørgaard Andersen, Anne Tranberg Madsen, Kristine R. Jakobsen, Peter Meldgaard, Boe S. Sorensen *Department of Clinical Biochemistry, Aarhus University Hospital, Aarhus C/Denmark*

Background: The programmed cell death receptor 1 (PD-1) and its ligand PD-L1 have proved to be of significant importance in lung cancer. Production of PD-L1 helps the cancer cells evade the immune system by inactivating T-cells. Clinical trials investigating the effect of treating lung cancer patients with monoclonal antibodies targeting the PD-L1 and PD-1 shows promising results. Expression of PD-L1 is associated with epidermal growth factor receptor (EGFR) mutational status. Further, expression can be significantly decreased by targeting EGFR with tyrosine kinase inhibitors (TKIs). *In vitro* studies suggest that this initial regulation of PD-L1 expression by EGFR occurs through the Erk pathway. Though, currently not much is known about expression of PD-L1 when TKI-resistance develops. We have developed erlotinib-resistant cell lines. The resistant cell line gained a MET amplification. We demonstrate that PD-L1 is increases in the resistant cells and that this increment is induced by MET signalling. **Methods:** The lung cancer cell line HCC827 with a deletion in exon 19 in the EGFR gene, was treated with increasing concentrations of erlotinib over 5 months until resistance developed. MET gene amplification in the resistant cells was confirmed by PCR. The resistant cell line was used for studying the effect of EGFR and MET inhibitors on PD-L1 expression. **Results:** The HCC827 erlotinib-resistant (ER) cell line gained a MET gene amplification, as seen in previous studies. In the initial phase of erlotinib treatment the expression of PD-L1 decreases. As the dose increases and resistance starts to develop the expression of PD-L1 increases. Activation of Erk is intact in HCC827ER as compared to the parental HCC827 cell line; most likely due to the activation of MET. When HCC827ER cells are treated with the MET inhibitor crizotinib, expression of PD-L1 decreases. When erlotinib is combined with crizotinib an additional effect on PD-L1 expression is observed. These results indicate that increased PD-L1 expression in erlotinib-resistant cell lines may be caused by activation of Erk through MET signalling. **Conclusion:** Our data demonstrates that Erk-dependent PD-L1 expression is increased in cells with erlotinib resistance caused by MET gene amplification. This mechanism might even be general and include several by-pass resistance mechanisms. Our findings suggest that the role of the PD-L1/PD-1 system should also be studied in erlotinib resistant tumors.
Keywords: Resistance, EGFR TKI, PD-L1, MET

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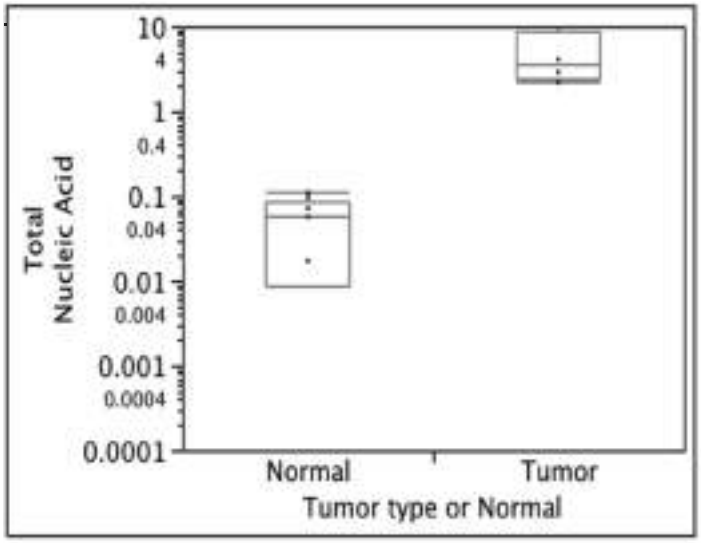
P2.04-074 PD-L1 Gene Expression and Total Cell-Free RNA Measured in Blood Positively Differentiate Healthy Individuals from Metastatic NSCLC Patients Kathleen Danenberg[1], Andreas-Claudius Hoffmann[2], Peter V. Danenberg[3], Joshua Usher[4], Jin Li[1], Yahya Elshimali[1], Xu Huang[1], Mai Dang[1], Todd Sturdevant[5], Yolanda Jaimes[1], Robert Findlater[1], Mary Grino[1] [1]*Liquid Genomics, Inc., Torrance/CA/United States of America,* [2]*Medical Oncology, West German Cancer Center, Essen/Germany,* [3]*Biochemisty & Molecular Biology, University of Southern California, Los Angeles/CA/United States of America,*[4]*Applied Biostatistics, University of Southern California, Los Angeles/CA/United States of America,* [5]*Research & Development, Liquid Genomics, Inc., Torrance/CA/United States of America*

Background: Cell-free DNA (cfDNA) released into the bloodstream by tumors allows non-invasive identification of tumor-specific mutations. However, not all molecular changes in

tumors involve DNA mutations; in many cases it is also the quantity of a particular gene (i.e., gene expression) that is important. In this study, we investigated the use of cell-free RNA (cfRNA) released into the blood in order to monitor PD-L1 gene expression in NSCLC patients. The PD-1/PD-L1 pathway is a promising therapeutic target and anti-PD-L1 agents have shown encouraging activity in a variety of tumor types. **Methods:** Blood samples were collected from NSCLC patients at various times during therapy. Additionally, non-cancer bearing blood samples were obtained from healthy volunteers ("control group"). Plasma was fractionated from blood samples and nucleic acids were extracted. RNA was reverse-transcribed into cDNA using random primers, and then analyzed by quantitative RT-PCR using appropriate gene-specific primers. The cDNA of PD-L1 was quantitated in both cancer patients and the control group. ERCC1 expression was also quantitated as an example of a non-tumor-specific gene. β-actin expression was used as the denominator gene representing total RNA. **Results:** PD-L1 expression was detected in the cfRNA of 60% (3/5 plasma samples) from the NSCLC patients, but was not detected in any samples from the control group (0/9), (p = 0.0005, Fisher's Exact Test). ERCC1 expression was detected in 100% (5/5) of NSCLC patients and 67% (6/9) of the control group but its median expression value was about 8-fold higher in the plasma of cancer patients (p = 0.0045, Pearson's chi-square). Median relative β-actin expressions in cancer patients and the control group were 19.3 (7.9-68.9) and 0.41 (0-0.75), respectively (p < 0.0062, Pearson chi-square) (Fig. 1)



Conclusion: These data demonstrate the potential value of using cfRNA from blood to measure gene expressions for detection of cancer and its recurrence, and in selecting and monitoring therapies. The presence of PD-L1 cfRNA in blood may be a specific indicator of cancer, although its sensitivity of tumor detection is less than 100% because it is not expressed in all cancer patients. ERCC1 expression, while not specific for tumors, nevertheless shows considerably higher overall levels in cancer patients. The surprisingly large (about 50-fold) difference in median total cfRNA between cancer patients and healthy individuals without any overlap in the ranges of expression suggests that total cfRNA may be useful as a sensitive preliminary indicator of the presence of cancer and for recurrence monitoring. **Keywords:** Cell-free RNA, NSCLC, Gene Expression, PD-L1

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-075 Network Analysis of Anti-CTLA4-Induced Regressing Tumours Identifies Novel Synergistic Drug Combinations Willem Joost Lesterhuis[1], Anna K. Nowak[1], Catherine Rinaldi[1], Anya Jones[2], Ian Dick[1], Bruce W.S. Robinson[1], Anthony Bosco[2], Richard A. Lake[1] [1]*School of Medicine and Pharmacology, University of Western Australia, Perth/WA/Australia,* [2]*Telethon Kids Institute, University of Western Australia, Perth/Australia*

Background: Antibodies blocking immune checkpoint molecules such as CTLA-4 have been shown to be effective in several cancer types, with some patients displaying durable complete regression. However, many patients do not respond to treatment. It is not known what molecular events control the response nor which co-treatments are likely to combine effectively with checkpoint blockade. Current strategies involve empirically testing different combinations of checkpoint blocking antibodies with other immunotherapeutic strategies or conventional anti-cancer drugs. We provide an alternative approach. **Methods:** Through performing network analysis of gene expression data from responding versus non-responding AB1-HA mesothelioma tumours from mice treated with anti-CTLA-4, we identified genetic modules and hub genes within these modules that were associated with responsiveness. We subsequently identified synergistic anti-CTLA-4/drug combinations using two different approaches: first, by pinpointing drugs that modulated hub genes within these response-associated modules, and second, by interrogating overlaps in the modular response patterns and drug-perturbation signatures in drug repurposing databases. The approaches were validated by testing the identified drugs *in vivo*, in combination with anti-CTLA-4 in murine cancer models. **Results:** We identified and validated several drugs that increased the response rate to anti-CTLA-4 in a highly synergistic manner. We identified four drug classes with the capacity to increase the cure rate from 10% for anti-CTLA-4 alone to 60-80% as combination therapy. These repurposed drugs are normally used in completely unrelated conditions such as cardiovascular or skin diseases. **Conclusion:** Together, our results show that using network analysis of gene expression data from immunotherapy-responsive tumours generates testable hypotheses for the identification of novel synergistic drug combinations. **Keywords:** immune checkpoint, systems biology, combination therapy, drug discovery

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-076 Dynamics of Soluble PD-1 during Treatment with EGFR-TKI in Advanced NSCLC Patients Steffen F. Sorensen[1], Christina Demuth[2], Boe S. Sorensen[2], Peter Meldgaard[1] [1]*Department of Oncology, Aarhus University Hospital, Aarhus C/Denmark,* [2]*Department of Clinical Biochemistry, Aarhus University Hospital, Aarhus C/Denmark*

Background: The programmed cell death receptor-ligand pathway (PD-1/PD-L1) is hijacked by tumors in order to evade immune response. Therapy with monoclonal antibodies against PD-1 or PD-L1 in patients with advanced NSCLC has shown promising results in recent clinical trials. Preclinical studies indicate that the PD-L1 expression on tumor cells, and subsequently the PD-L1/PD-1 interaction, is increased when resistance to EGFR-TKI treatment in EGFR mutated NSCLC tumors occur. A soluble form of PD-1 receptor is present in the blood plasma, and can be detected in healthy individuals and in increased amounts in patients with autoimmune diseases and cancer. The dynamics of soluble PD-1 (sPD-1) during treatment and at the point of resistance to EGFR-TKI treatment is unknown. The aim of the present study is to assess the dynamics in plasma of EGFR mutated circulating tumor DNA and sPD-1 longitudinally during treatment with EGFR-TKI, and to study if the level of sPD-1 will increase at the time of resistance to EGFR-TKI treatment. **Methods:** Consecutive blood samples taken before initiation of treatment with erlotinib, during treatment, and at disease progression while on erlotinib from 20 patients with EGFR wildtype and 20 patients with EGFR mutated advanced NSCLC, has been collected, and will be analyzed. The amount of EGFR mutated circulating tumor DNA (in the EGFR mutated patients) and sPD-1 (all patients) will be detected by use of the Cobas® instrument (RMD) and ELISA (R&D systems), respectively. These results will be described and correlated to the clinico-pathological characteristics of the patients. **Results:** Preliminary results show that sPD-1 can be detected in plasma from lung cancer patients. The final results of the analysis will be presented at the conference. **Conclusion:** The present study is to our knowledge the first to describe the dynamics of soluble PD-1 during EGFR-TKI therapy in both EGFR mutated and EGFR wildtype patients treated with erlotinib. The results will elucidate on the role of sPD-1 as a potential biomarker of resistance to EGFR-TKI therapy. The clinical time point of increased sPD-1 in plasma could indicate a "window of opportunity", in which these patients could be highly responsive to anti-PD-1 or anti-PD-L1 immunotherapy. Such findings have to be further investigated in prospective clinical trials. **Keywords:** PD-1, Circulating Tumor DNA, Erlotinib, EGFR mutation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-077 PDL1 Expression in Metastatic Non-Small Cell Lung Cancer Patients from Colombia (CLICaP) Andrés F. Cardona[1], Leonardo Rojas[2], Carlos A. Vargas[1], Hernan Carranza[1], Jorge M. Otero[1], Oscar Arrieta Rodriguez[3], Claudio Martin[4], Luis Corrales[5], Mauricio Cuello[6], Rafael Rosell[7] [1]*Clinical and Translational Oncology Group, Foundation for Clinical and Applied Cancer Research - Ficmac, Bogotá/Colombia,* [2]*Centro Javeriano de Oncología, Hospital Universitario San Ignacio, Bogotá/Colombia,* [3]*Unidad Funcional de Oncología Torácica Y Laboratorio de Medicina Personalizada, National Cancer Institute, Mexico City/Mexico,* [4]*Clinical Oncology, Instituto Fleming, Buenos Aires/Argentina,* [5]*Clinical Oncology, Hospital San Juan de Dios, San José/Costa Rica,* [6]*Clinical Oncology, Hospital de Clínicas - Udelar, Montevideo/Uruguay,* [7]*Hospital Germans Trias I Pujol, Catalan Institute of Oncology, Barcelona/Spain*

Background: Programmed cell death-1-ligand 1 (PD-L1) is involved in the ability of tumor cells to escape the host's immune system. PD-L1 is selectively expressed in a number of tumors. The blockade of interactions between PD-1 and PD-L1 enhances the immune function in vitro and mediates antitumor activity in preclinical models. Recent studies have suggested that antibody-mediated blockade of PD-L1 induced durable tumor regression and prolonged stabilization of the disease in certain cancers including NSCLC. A recent study demonstrated that immunohistochemical (IHC) analysis detected no objective response in PD-L1-negative patients. However, 36% of the patients with PD-L1-positive tumors had a positive response. **Methods:** PD-L1 was assessed by IHC (Dako MAb) in 115 NSCLC patients, considering as positive a staining intensity ≥ 2 in more than 5% of cells. The driver mutation epidermal growth factor receptor (EGFR) was examined by direct sequencing and allele specific PCR. ALK FISH was performed using the Vysis ALK Break-Apart Probe. The correlations of PD-L1 expression with major clinicopathologic parameters and outcomes were analyzed. **Results:** Mean age was 64.3 years (SD+/-10.7), 66% were females, 83% had adenocarcinoma and 58% were former/current smokers. Fourteen patients (18%) had mutations in the EGFR and 19 (25%) were PD-L1+. PD-L1 was positive in fifty-nine patients (51%) and this condition was more frequent in the light or never smokers (p=0.05). In the same way PD-L1 positivity was significantly associated with presence of EGFR mutations (p=0.03), in tumors with a higher grade of differentiation (p=0.023) and in presence of vascular invasion (p=0.038). Patients with positive PD-L1 expresion had a longer progression free survival (PFS) (6.4 months vs. 3.0 months, p=0.001) and overall survival (OS) (28.2 vs. 12.4 months; p=0.001). **Conclusion:** Although the study sample is small, PD-L1 positivity correlates with PFS and OS. This results supports that PD-L1 might be a critical factor in the use of NSCLC immunotherapy. **Keywords:** Immunotherapy, PD-L1, NSCLC, survival

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-078 Functional Characterization of NK Cells in Non-Small Cell Lung Cancer Oscar Arrieta Rodriguez[1], Ángel Gómez-Gallegos[2], Renato Morales-Flores[3], Angeles Garcia-Vicente[2], Edgar Montes-Servín[3], Fernanda Salinas-Parra[3], Lourdes Barrera[4] [1]*Laboratory of Experimental Oncology and Thoracic Oncology Unit, National Institute of Cancer, Mexico City/Mexico,* [2]*Laboratory of Integrative Immunology, National Institute of Respiratory Diseases Ismael Cosío Villegas, Mexico City/Mexico,*[3]*Laboratory of Experimental Oncology, National Institute of Cancer, Mexico City/Mexico,* [4]*Business Oncology Unit, Astrazeneca, Mexico City/Mexico*

Background: Lung cancer is the leading cause of cancer death worldwide and most of the patients are diagnosed with advanced disease. Lung cancer is the leading cause of cancer death worldwide. Natural killer (NK) cells are important effector cells in control of infected, malignant, and tumor cells. The aim of this study was to investigate the activation state and cytotoxic potential of NK peripheral cells in patients with Non-Small Cell Lung Cancer (NSCLC). **Methods:** We investigated the relationship between NK cells apoptosis and Fas expression. NK cell apoptosis, Fas and Fas-L, NKG2D, CD69, KIR, CD244, CD122 and CD161 receptors were evaluated with multiparametric flow cytometry. We further evaluated the cytotoxic activity of NK cells and IFN-gamma expression. For this purpose, we simultaneously analyzed the loss of intracellular perforin and the surface expression of CD107a/b as well as the intracellular IFN-gamma expression with multiparametric flow cytometry. **Results:** Our results showed that Fas-positive NK cells in lung cancer patients were higher than healthy controls ($P<0.001$). These results also showed that up-regulation of Fas expression is related to increased apoptosis of circulating NK cells. Regarding the cytotoxic capacity, our results showed that upon PMA stimulation, the expression of surface CD107a/b and loss of intracellular perforin of NK cells from patients with NSCLC were not correlated indicating an impaired functional cytotoxic activity. Interestingly, we also found that, IFN-gamma ($P<0.005$) and NKG2D expression were also impaired significantly ($P<0.001$). **Conclusion:** The results from this study suggest a possible NK cells anergy state. Our description will help to provide a mechanistic insight into tumor immune escape via negative regulation of NK cell innate function; however, the underlying mechanisms remained to be addressed. **Keywords:** NK cells, NSCLC, Tumor escape, biomarker

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P2.04-079 Targeting Antigen Presentation by Tumor Infiltrating B Cells to CD4 T Cells in Non-Small Cell Lung Cancer Patient Tumors Tullia C. Bruno[1], Brandon Moore[1], Peggy Ebner[1], Daniel Munson[1], Jeffrey Kern[2], Jill E. Slansky[1] [1]*Immunology and Microbiology, University of Colorado School of Medicine, Aurora/CO/United States of America,* [2]*Oncology, National Jewish Health, Denver,Co/CO/United States of America*

Background: B cells in tumors (TIL-Bs) are detected in non-small cell lung cancer (NSCLC) and their frequency correlates with improved survival, however, the functional mechanism of TIL-Bs in solid tumors is not well understood. We hypothesize that TIL-Bs help generate potent, long-term immune responses against cancer by presenting tumor antigens to CD4 tumor infiltrating lymphocytes (TILs) in primary human lung tumors. **Methods:** not applicable **Results:** Using un-manipulated, primary human B cells from fresh tumor, tumor-adjacent, and normal (cancer-free) lung tissue we observed that the total number of B cells at the site of the tumor versus the tumor-adjacent tissue was increased compared to other immune subsets. Further, in analyzing B cell markers of activation and exhaustion, we observed a spectrum of activation of TIL-Bs. Finally, we showed that TIL-Bs present autologous tumor antigens to CD4 TILs in a subset of NSCLC patients, and that depending on the activation or exhaustion profile of the TIL-Bs, differentiate CD4 TILs to T regulatory cells (Treg). These data suggest that some patients with TIL-Bs have differential function that is influenced by their activation or exhaustion phenotype. **Conclusion:** In conclusion, the anti-tumor functon of TIL-Bs can be stimulated in some NSCLC patients, and TIL-Bs that cannot be stimulated have increased immune exhaustion and promote Treg differentiation. Ultimately, results from this study will help predict which TIL-B functions to target in future TIL-B-specific immunotherapies or in combination with current immunotherapies for NSCLC patients like blockade of the inhibitory receptor, PD-1. **Keywords:** non-small cell lung cancer, Immunology, B cell, T cell

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-080 Novel Biomarkers for Non Small Cell Lung Cancer (NSCLC) Lukman Tijani, Cynthia Jumper, Leonardo Mirandola, Hassan Kaleem, Mohamed Shanshal, Maurizio Chiriva-Internati *Internal Medicine, Texas Tech Health Sciences Center, Lubbock/TX/United States of America*

Background: Abstract Cancer testis antigens (CTA) are a class of tumor associated antigens, showing a restricted expression in cancer, strong immunogenicity, and weak expression in normal tissues. Sp17/AKAP4/PTTG1 have been previously investigated, showing promising results as a target. Our aim was to investigate the expression of Sp17/AKAP4/PTTG1 in lung cancer patients. **Methods:** We analyzed 2 lung cancer cell lines, one normal bronchus cell line, a panel of normal tissues and patients cells by RT-PCR, flow-cytometry, immunocytochemistry (ICC), and immunofluorescence (IF). CTA immunogenicity was investigated by measuring circulating specific antibodies in the sera of lung cancer patients. **Results:** ELISA analyses show the presence of circulating CTA-specific antibodies in the sera of lung cancer patients, indicating the immunogenicity of Sp17, AKAP-4 and PTTG-1. Sp17/AKAP4/PTTG1 were detected only in the cells of lung cancer patients. **Conclusion:** We showed that CTA, Sp17, AKAP-4 and PTTG-1 can be detected in both sera and tissue of patients with NSCLC.

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P2.04-081 The Role of B7-H4–Expressing Macrophage in Malignant Pleural Effusion Jian An Huang[1], Chen Cheng[1], Xiao Hui Zhang[2] [1]*Respiratory Medicine, The First Affiliated Hospital of Soochow University, Suzhou/China,* [2]*The First Affiliated Hospital of Soochow University, Suzhou/China*

Background: B7-H4 is a novel protein of the B7 family which regulated tumor immune escape through inhibition of T-cell activation and cytokine secretion. Tumor-associated macrophages (TAM) are a major component of cancer-related inflammation and play a central role in tumor promotion. Previously, some study have shown that B7-H4–expressing macrophage in peripheral blood from lung cancer patients was significantly higher than that from healthy donors and tuberculosis patients. However, the role of B7-H4–expressing macrophage in malignant pleural effusion is unknown. **Methods:** Pleural effusion mononuclear cells (PEMC) were isolated using Histopaque gradient centrifugation. The percentages of B7-H4–expressing CD68+cells were estimated by comparing the proportions of labeled cells with respect to total number of CD68+cells from the subjects studied. Intracellular staining was performed with FITC-TGF-beta1 mAb through the Cytofix/Cytoperm™ Fixation/Permeabilization Solution Kit. The detection of EMT related proteins by Western blotting and Flow cytometry. Using ROC curve to evaluate the diagnostic values of B7-H4+cell percentage in total macrophages in malignant pleural effusion caused by lung cancer. **Results:** In this study, we found that malignant pleural effusion caused by lung cancer have higher level of B7-H4–expressing macrophage than tuberculous pleural effusion, which have diagnostic value for malignant pleural effusion （CD68+B7-H4+ 16.97±10.32%vs 7.17±5.52%, $P<0.01$) Further studies indicated that B7-H4–expressing macrophage is a source of TGF-β1, which is the most important factors of epithelial-mesenchymal transition (EMT). As supported, we proved malignant pleural effusion of lung cancer and TGF-β1 can both induce the EMT of A549 cells, accompanying with enhancement of A549 cell migration and invasion ability. **Conclusion:** Taken together, it is suggested that B7-H4–expressing macrophage may promote pleural metastasis of lung cancer though regulate the process of EMT by secreting TGF-β1. **Keywords:** B7-H4, macrophage, malignant pleural effusion

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P2.04-082 Diagnostic Value of Survivin-Expressing Circulating Tumor Cells in Patients with Non-Small Cell Lung Cancer Mi-Hyun Kim[1], Jung Seop Eom[2], Min Ke Lee[1] [1]*School of Medicine, Pusan National University, Busan/Korea,* [2]*Pusan National University Hospital, Busan/Korea*

Background: The most widely used circulating tumor cell (CTC) isolation techniques rely on antibody-based capture of CTCs, which express epithelial cell surface markers that are absent from normal leucocytes. Among these, epithelial cell adhesion molecule (EpCAM) is most commonly used. Although this platform is the most standardized of any current technology, it suffers from relatively low sensitivity. Survivin is a member of the inhibitor of apoptosis protein gene family that is highly expressed in most cancers. Several studies have shown the prognostic value of survivin in various malignancies, including lung cancer. But the diagnostic significance of survivin for non-small cell lung cancer (NSCLC) remains controversial. The purpose of this prospective study was to evaluate the diagnostic value of survivin-expressing CTCs in peripheral blood of patients with NSCLC. **Methods:** Blood samples were collected from patients with NSCLC before treatment and healthy volunteers. The EpCAM- and survivin- expressing CTCs were detected by real-time quantitative PCR. **Results:** To date, 43 patients with NSCLC stages I-IV and 15 healthy controls, all aged 52-79 years were enrolled in the study. Survivin mRNA was detected in the CTCs. Survivin- expressing CTCs were upregulated with more than 2-fold difference as compared with controls (p=0.004). EpCAM was not significantly different between NSCLC patients and controls (p=0.409). No correlation between the survivin-expressing CTCs levels and the stage of disease and histology can be made at this point. **Conclusion:** We demonstrated the significant difference in the levels of survivin-expressing CTCs between NSCLC patients and controls. These results suggest that survivin might be useful molecular marker for CTCs. **Keywords:** survivin, non-small cell lung cancer, Circulating tumor cell

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P2.04-083 Influence of Surgery on EGFR Mutation Abundance among Patients with Early-Stage Non–Small-Cell Lung Cancer Chengliang Yang[1], Yi Ren[1], Ye Gang Ma[1], Dan Yang[2], Bo Dong[2], Wen Yuan Shang[2], Xue Qiao[2], Yang Zhou[2], Yongyu Liu[1] [1]*Department of Thoracic Surgery, Liaoning Cancer Hospital & Institute, Shenyang/China,* [2]*Lab of Lung Cancer, Liaoning Cancer Hospital & Institute, Shenyang/China*

Background: Detecting circulating plasma cell-free DNA (cfDNA) in patients with early-stage cancer has the potential to change how oncologists recommend systemic therapies for solid tumors after surgery. However, it remains unclear whether surgery affects epidermal growth factor receptor (EGFR) mutation abundance in early-stage non–small-cell lung cancer (NSCLC). We investigated the influence of surgery on *EGFR* mutations in plasma and tumor tissues from patients with early-stage NSCLC. **Methods:** In this prospective study, primary lung tumors and matched pre- and postsurgery blood samples were collected from patients with early-stage NSCLC (n=96). We detected *EGFR* mutations (exon19 deletions, T790M and L858R) in 96 early-stage lung cancer samples using droplet digital PCR (ddPCR) and amplification refractory

mutation system (ARMS). *EGFR* mutation abundance was determined and analyzed to reveal potential impact of surgery. **Results:**Presurgery plasma samples (n=96) matched tumor tissue samples (n=96) were analyzed for *EGFR* mutations using ddPCR and ARMS respectively. Of the 56 *EGFR* mutations detected in tumor tissues by ARMS, 48 of the corresponding mutations were detected in presurgical cfDNA, whereas no mutations were found in plasma from patients with *EGFR* wild-type tumors (sensitivity 85.71%, specificity 100%). Forty patients with mutation-positive cfDNA presurgery had ddPCR analysis of postsurgery plasma, with twenty-four patients having detectable cfDNA postsurgery. The decrease in *EGFR* mutation abundance was statistically significant (0.22 vs 0.04, P <0.05). **Conclusion:** This study demonstrates accurate mutation detection in plasma using ddPCR, and that cfDNA can be detected in blood before and after surgery in patients with early-stage lung cancer. Our results suggest that surgery may reduce EGFR mutation abundance in early-stage NSCLC patients with mutation-positive cfDNA presurgery. Future studies can now address whether monitoring the change of EGFR mutation abundance after surgery identifies patients at risk forrecurrence, which could guide therapy decisions for individual NSCLC patients.
Keywords: EGFR Mutation Abundance, Early-stage NSCLC, droplet digital PCR, Surgery

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-084 Next-Generation Sequencing with Digital Droplet PCR for Circulating Tumor DNA Quantification in Non-Small-Cell Lung Cancer Patients
Nicolas P. Pécuchet[1], Eleonora Zonta[2], Audrey Didelot[2], Pierre Combe[3], Laure Gibault[4], Nadege Rice[5], Pierre Laurent-Puig[6], Valerie Taly[2], Helene Blons[6], Elizabeth Fabre[1]
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Background: We aimed to compare different methods to assess the dynamics of circulating tumor DNA (ctDNA) in metastatic NSCLC pts. **Methods:** A cohort of advanced NSCLC pts was followed by serial plasma blood samples and RECIST assessments every 2 months. Plasmatic cell-free DNA was extracted with the QIAsymphony DSP Virus/Pathogen kit (Qiagen). EGFR and KRAS mutations were assessed in plasmatic DNA using Q-PCR and picoliter droplet based digital PCR (ddPCR, Raindance) with CAST probes. Nexte-Generation Sequencing (NGS) was performed using the Lung and Colon Cancer Panel v2 (Iontorrent, AmpliSeq, Lifetechnologies) with a target of 10,000X (Proton). For NGS and dPCR, the limit of blank was determined for each mutation. **Results:** We included 37 pts treated by TKI (n=21) or chemotherapy (n=16), in 1rst (n=31) or 2nd line (n=6). Median follow-up, progression-free survival (PFS) and overall survival were 12, 6 and 31 months, respectively. Tumor mutations were: EGFR [L858R (n=9), Del19 (n=9), L861Q (n=1), Ins20 (n=2)], KRAS (n=2), TP53 (n=4). No mutation was found in 8 pts. At baseline, ctDNA was positive by one of the 3 technics in 22/29 (76%) pts, with 2 pts being positive by dPCR only. ctDNA quantification was highly correlated between NGS and ddPCR r^2=0.74), but not with Q-PCR. The fraction of ctDNA (‰) was associated with radiological outcome (ROC AUC 0.87 and 0.81 for NGS and dPCR). The relative change of ctDNA between 2 consecutive samples did not improve the prediction of tumor evolution (AUC 0.74 and 0.76). RECIST tumor progression was best predicted by pDNA >1.1‰ in NGS (sensitivity 0.85, specificity 0.80), and >1.4‰ in dPCR (sensitivity 0.82, specificity 0.74). Persistence of >1‰ ctDNA under treatment was associated with a short PFS (2.2 months vs. 8 months, log-rank P = .0002). **Conclusion:** In this cohort, the persistence of plasmatic tumor DNA using NGS (10,000 X) or dPCR was associated with treatment failure in NSCLC patients. A threshold of 1/1000 mutation ratio was clinically meaningful using both technics. Plasmatic tumor DNA normalization could be evaluated in addition to standard RECIST criteria as clinical endpoints for clinical trials.
Keywords: digital droplet PCR, circulating DNA, next generation sequencing

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-085 A Comparative Analysis of Cancer Hotspot Mutation Profiles in Circulating Tumour Cells, Circulating Tumour DNA and Matched Primary Lung Tumour
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Background: Blood based mutation profile analyses are becoming an increasingly important non-invasive form of mutation screening in cancer. Many have reported on single mutation comparisons between blood based and primary tumour tissue, but limited information is available on multiplex comparisons between the DNA extracted from circulating tumour cells (CTC), circulating free tumour DNA in the plasma (ctDNA) against the current standard of FFPE analysis of primary tumour. **Methods:** Pre-operative whole blood samples were collected from 30 patients who underwent thoracic surgery. CTCs were isolated using ScreenCell MB devices from 6ml of whole blood, and 1ml aliquots of plasma were removed from 9ml of EDTA samples. Matching FFPE samples were retrieved from post-resection primary tumour tissue in three 10µm PCR rolls. DNA was extracted from the CTCs, ctDNA and matched FFPE tissues using Qiagen kits (QIAamp DNA Micro kit, QIAamp DNA blood mini kit and QIAamp FFPE tissue kit, respectively). The 90 (30 matched triplicates) DNA samples were sequenced by Illumina HiSeq using Z3 cancer panel (Illumina, San Diego). Agreements of variant calls were compared between the three DNA substrates and a kappa statistic was reported using Stata 13. **Results:** Between 2011 and 2013, samples from 30 consenting patients were obtained. In total, 10 had primary lung cancer, 19 had secondary lung cancer, and 1 (intentionally included) had no evidence of cancer. From the 90 samples, a total of 18,821 variant calls were identified after the removal of known 1,048 germline variants. Within the hotspot panel alone, the mean (SD) number of variant calls per patient was 151 (44) on FFPE samples, 136 (49) on CTC samples and 463(108) on ctDNA samples. There was good agreement between CTCs and FFPE of 79.8% with a Kappa statistic of 0.42 (P<0.001). Agreement between ctDNA and FFPE was much poorer at 12.7% with a Kappa statistic of -0.40 (P=1.000). The results also suggested poor agreement between CTC and ctDNA of 16.1% with a Kappa statistic of -0.32 (P=1.000). Focusing on single gene comparisons on the multiplex platform, agreement was considerably better for *KRAS* and *EGFR* for CTCs compared to ctDNA at 44% versus 11% for *KRAS* and 92% versus 9% for *EGFR* respectively. Discordances were largely due to an increased number of variants that were identified in ctDNA and not in CTC or FFPE tissue. **Conclusion:** Our results suggest on a next generation sequencing platform that the global genetic variant profile between DNA extracted from CTC had good agreement with FFPE primary tumour tissue, and the agreement for ctDNA and FFPE was much poorer. This was observed to be an increase in the number of variants detected on single gene analysis and may be due to processing, sample or analytic difficulties with ctDNA.
Keywords: next generation sequencing, ctDNA, Circulating Tumour Cells, Mutation profile

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-086 An Effective In Vivo Liquid Biopsy Tool for High-Yield Isolation of Circulating Tumor Cells
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Background: Analysis of tumor biopsy material represents only assessable tumor and represents the state at the time of diagnosis. This approach neglects tumoral heterogeneity changes occurring during disease progression. However, during systemic therapies tumors undergo molecular changes and usually develop resistance mechanisms. Reevaluation of tumors after therapy, at disease progression and before new treatment initiation would be informative for the selection of appropriate next steps. However, re-biopsies are not often feasible and can cause morbidity. . Liquid biopsy, i.e. isolating and analyzing circulating tumor cells (CTCs), can be an additional source of diagnosis, prognosis, evaluation of treatment efficacy, and molecular tumor evolution and metastatic sites. Commonly, CTCs are isolated from small blood volumes (5-10 ml) in in vitro approaches. This approach has limited sampling volume particularly in detecting low frequency CTC. To overcome this limitation, the GILUPI CellCollectorâ, an intravascularly in-dwelling device, screens a large volume (>1 liter) of blood for CTCs directly in the vein of the cancer patient. The device has specific monoclonal antibodies attached to pull down epithelial derived CTCs. We demonstrate the application of the CellCollector in the assessment of CTC in non-small cell lung cancer (NSCLC) patients. The novel study demonstrates a novel in vivo approach of assessing CTC in different stages of NSCLC. **Methods: :** In this study a total of 25 non-small cell lung cancer (NSCLC) patients stage IA to IIIB, were applied for CTC isolation before (n=50) time and after surgery how long after (n=25). CTC validation and enumeration was conducted by immunofluorescence (IF) microscopy. Following this, isolated CTCs were analysed for mutations in KRAS and EGFR genes commonly found in NSCLC using the PointMan DNA mutation enrichment assay. Primary tumor tissue was analysed for the same mutations to investigate concordance. **Results:** In a previous studies have shown a significantly higher isolation efficacy compared to the FDA-cleared CellSearchâ System. In the current study we focused on the comparison of the status of driver mutations in KRAS and EGFR in CTCs compared to the primary tumor tissue. Overall, successful isolation of CTCs with the CellCollectorâ was detectable in 77% of the samples. The pre-surgical isolation rate was 79%, slightly higher than the post-operative rate of 72%. In this cohort of patients, EGFR and KRAS mutations could be detected in all patients? Frequency level need to given and were compared by analysis of the respective primary tumor sgive concordance. **Conclusion:** The GILUPI CellCollectorâ overcomes blood volume limitations of other CTC extraction approaches and thereby increases the diagnostic sensitivity of CTC isolation. It allows CTC enumeration, molecular characterization, and biomarker expression analysis, which could help guide treatment strategies and monitoring therapy efficacy.
Keywords: molecular diagnostic, NSCLC, Oncology, CTC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-087 Detection of Mutations from Peripheral Blood in Patients with Non-Small Cell Lung Cancer with Fast Turn-Around
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Background: In non-small cell lung cancer (NSCLC) several genetic changes that have clinical consequences for targeted treatment approaches have been identified. As for EGFR Mutations there are already options for more than one line of treatment. For those patients with secondary changes like the T790M-mediated resistance to EGFR inhibitors irreversible tyrosine kinase inhibitors (TKI) seem to be a promising alternative. These options may however be limited to missing proof of such changes as with progressing tumor burden patients may be susceptible to higher mortality with necessary invasive procedures. The so called "Liquid Biopsy" – using peripheral blood to obtain timely information on genetic information in solid malignancies – seems to be the urgently needed solution to this problem. Methods are needed that hold the promise of fast-turn around and broad availability. **Methods:** Serum was tested from 130 patients with adenocarcinoma or squamous cell cancer of the lung. All patients received at least one line of systemic therapy. Frequencies of EGFR ex19dels, EGFR L848R and EGFR T790M were tested as well as KRAS G12C, D and V. The detected frequencies were correlated with expected frequencies obtained from published data (mycancergenome.com). Furthermore the results from serum were correlated to results obtained from the available tumor tissue. Additional samples of fresh blood were tested. **Results:** Correlation of mutation detection results from serum correlated significantly with measurement of the available tumor specimen. Furthermore expected frequencies were in line with published occurrence of genetic changes. There was however a potential bias as T790M mutations were higher than expected which may be due to cancer center specific patient selection. These results were in line with the fresh blood samples tested. Turn-Around of fresh samples was three (3) days. **Conclusion:** Mutation detection is feasible from peripheral blood with fast turn-around and high sensitivity and specificity. In addition samples can be used either fresh or as stored serum probes. This will allow faster treatment decisions and higher patient satisfaction due to shorter intervals until start of therapy. The Liquid Biopsy is a clear and medically needed alternative to analyzing tissue samples. Especially in cases of secondary changes to tumors during systemic therapy this method will be crucial. **Keywords:** liquid biopsy, cell-free DNA, EGFR, KRAS

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-088 Surrogate or Not: The Role for Cell Free Circulating DNA in Detecting EGFR Mutations Present in Tumor Tissue Satya Das[1], Lyudmila Bazhenova[2], Veena Singh[3], Lyle Arnold[3], Vassilios Alexiadis[3], Tim Watanaskul[3]
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Background: Identification of molecular drivers such as EGFR in non-small cell lung cancer (NSCLC) has increased our capability to deliver personalized cancer therapy. EGFR tyrosine kinase inhibitors (TKI) are very effective in patients with EGFR sensitive mutations, but resistance ultimately develops. Determining mechanisms of secondary resistance requires post progression biopsies which carry non-trivial complication risks for patients and thus are not suitable means for serial monitoring. Cell free circulating DNA (cfcDNA) could represent an alternative method to detect molecular mechanisms of secondary resistance. **Methods:** Single institution observational study of 13 patients with EGFR mutant Stage IV lung adenocarcinoma. Two 8-10 ml tubes of blood were collected from patients who progressed on erlotinib. Patient samples were tested for T790M mutations using the Biocept Selector assay as well as MET using FISH amplification. Results from these "liquid-biopsies" were then compared to results obtained on standard tissue biopsy. **Results:** 13 patients with secondary resistance were enrolled, all 13 had adenocarcinoma. Median age was 61 with an age range 52-76, male to female ratio 7:6, 8/13 (62%) had deletion 19, 5/13 (38%) had an L858R mutation. Median duration of EGFR TKI therapy prior to cfcDNA sample collection was 16 months, range 5.2-64.4 months. 9/13 patients underwent a post-progression tissue biopsy with 8/13 found to have the T790M mutation, 1/13 with c-MET amplification, and 1/13 with both. 11/13 patients were found to have T790M in cfcDNA. Average concentration of T790M clone in cfcDNA was 4% with a range from .004-27.6% (from 3mL of blood). Average copy number of T790M in cfcDNA was 2310 with a range from 7-20507 (from 3mL of blood). Average copy number of the EGFR gene in cfcDNA was 39404 with a range from 4308-169628 (from 3mL of blood). Among the 10 patient thus far whose post-progression biopsies and cfcDNA sampling was completed, the sensitivity and positive predictive value (PPV) of Selector was 88% and 88% respectively. Concordance was 80% between cfcDNA and tissue. 7/9 patients with tissue confirmed T790M were switched to third generation TKI with 6/7 currently with stable disease after an average of 7 months (5-9). 1/7 passed away after one month on the next generation TKI due to disease progression. **Conclusion:** Biocept's blood based assay detecting T790M and MET amplifications from cfcDNA is highly concordant with mutations present in tumor tissue and therefore a non-invasive surrogate for determining mutational status of patients' who progress on TKI therapy. **Keywords:** Advanced Stage NSCLC, EGFR sensitizing mutation, T790M, Cell Free Circulating DNA

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-089 Detection of Epidermal Growth Factor Receptor (EGFR) Mutations in Circulating Tumor DNA During EGFR-Tyrosine Kinase Inhibitor Treatment In-Jae Oh, Hyun-Ju Cho, Chul-Kyu Park, Young-Chul Kim, Ju-Sik Yun, Sang-Yun Song, Kook-Joo Na, Mee-Sun Yun, Sung-Ja Ahn, Hyun-Ju Seon, Yoo-Duk Choi *Lung and Esophageal Cancer Clinic, Chonnam National University Hwasun Hospital, Jeonnam/Korea*

Background: Epidermal growth factor receptor (EGFR) mutations are predictive marker of EGFR-tyrosine kinase inhibitor (TKI) therapy. We compared the sensitivity of EGFR mutation detection techniques between tumor tissue and peripheral blood sample in patients with EGFR-TKI treatment. **Methods:** We collected plasma and serum sample before EGFR-TKI and after acquired resistance in 11 patients with EGFR mutations (5 cases of 19 deletion and 5 cases of L858R) from paraffin-embedded tissues using PNAClampTMEGFR Mutation Detection kit. DNA extraction from plasma and serum was performed using the QIAamp MinElute virus spin kit. EGFR mutation analysis for blood was done by pyrosequencing and PANAMutyperTMR EGFR kit. The degree of agreement was evaluated by Cohen's kappa value. **Results:** The median EGFR-TKI duration of total 11 (7 male, 4 female) cases was 6 months (range 4-24). The sensitivity of plasma EGFR mutations were 33.3% in pyrosequencing. The sensitivities of PANAMutyperTMR were 72.7% in plasma and 45.5% in serum sample. The degree of agreements between tissue and blood sample were better in plasma PANAMutyperTMR (k=0.429, p=0.033) and serum PANAMutyperTMR (k=0.290, p=0.026) than plasma pyrosequencing (k=0.194, p=0.087). After the development of acquired resistance, plasma EGFR mutations were still detected in 4 cases by PANAMutyperTMR. One of them showed 19 deletion and T790M mutation at the same time. **Conclusion:** The sensitivity and the strength of agreement of PANAMutyperTMR test were better than pyrosequencing. So this technique can be useful to detect EGFR mutation in peripheral blood. **Keywords:** Circulating tumor cell, Epidermal growth factor receptor mutations, Sensitivity

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-090 Changes in Circulating Epidermal Growth Factor Receptor (EGFR) during Radiotherapy in Non-Small Cell Lung Cancer (NSCLC) Patients Ping Ye[1], Jing Zhao[2], Nita Maihle[2], Shulian Wang[2], Jianyue Jin[2], Feng-Ming (Spring) Kong[1]
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Background: Epidermal growth factor receptor (EGFR) is overexpressed in a variety of malignant tumors including lung cancer. A circulating isoform of EGFR has been detected in the blood of lung cancer patients. Previous reports suggest that low baseline plasma EGFR concentrations are associated with reduced survival in patients with stage IV non-small cell lung cancer (NSCLC) post-chemotherapy. The goal of the present study was to determine whether: 1) plasma EGFR concentrations change during- and/or after radiotherapy, 2) the changes are associated with overall survival (OS) in stage I-III NSCLC following radiation treatment. **Methods:** Patients enrolled in prospective studies in which platelet poor plasma samples had been collected were eligible. All patients received radiation-based treatment. Patient age, gender, ECOG score, clinical stage, pathology, smoking history, chemotherapy and radiotherapy were all included in this analysis. Blood samples were collected pre-radiotherapy (pre-), during radiotherapy (2 weeks) (2w), during radiotherapy (4 weeks) (4w) and post-radiotherapy (more than 4 weeks post-radiotherapy). Plasma EGFR concentrations were measured using a commercial enzyme-linked immunoassay kit (BosterBio Inc., Pleasanton, CA) that detects the extracellular domain of EGFR. The primary endpoint was OS. **Results:** 183 patients with median age of 66, 143 male and 40 female, were included in this study. The median OS was 15.5 months (95% confidence interval [CI]: 20.8-27.3). The mean plasma concentration of EGFR was 35.6 ng/ml for pre- (n=116, 95% CI: 33.9-37.4); 22.4 ng/ml for 2w (n=114, 95% CI: 20.8-24.0); 34.5 ng/ml for 4w (n=114, 95% CI: 31.4-37.7); and 45.0 ng/ml for post (n=114, 95% CI: 40.1-49.9). The plasma level at 2w was significantly lower than pre-levels ($p < 0.01$). The plasma EGFR level at 4w was significantly higher than at 2w ($p < 0.01$), though it was not significantly different from that of pre-RT levels. There is a significant increase in EGFR levels in post-RT treated patients ($p < 0.01$). Post-treatment levels are above all other points observed in cancer patients, including at baseline and during-RT. However, no significant correlation between the levels of EGFR and OS, or between the ratio 2w/pre or post/pre and OS were observed. Kaplan-Meier survival analysis showed pre- EGFR concentrations [22.2 months (95% CI: 6.8-37.7) versus 23.5 months (95% CI: 14.1-32.9) ($p = 0.527$)] and fold changes of 2w/pre- [24.5 months (95% CI: 11.2-35.9) versus 23.7 months (95% CI: 12.2-42.3) ($p=0.928$)] respectively. **Conclusion:** In parallel with previous reports for the treatment of NSCLC patients with gefitinib, RT results in a decrease in EGFR plasma concentrations shortly after therapy (2 weeks), but an increase relative to baseline levels by 4 weeks, followed by a further increase (to above baseline levels) by 3 months post-treatment. In patients treated with gefitinib, this increase correlated with worse response to therapy. Here there does not appear to be a correlation between increased plasma EGFR levels and OS following RT. The biologic mechanism(s) underlying these observations, and their clinical implications warrant further study. **Keywords:** NSCLC, Radiotherapy, EGFR

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-091 Digital PCR Analysis of Plasma Cell-Free DNA as a Noninvasive Detection of the Drug Resistance Mechanisms in EGFR Mutant NSCLC Hidenobu Ishii[1], Koichi Azuma[1], Kazuko Sakai[2], Takaaki Tokito[1], Kazuhiko Yamada[1], Kazuto Nishio[2], Tomoaki Hoshino[1] [1]*Division of Respirology, Neurology, and Rheumatology, Department of Internal Medicine, Kurume University School of Medicine, Kurume/Japan,* [2]*Department of Genome Biology, Kinki University Faculty of Medicine, Osaka-Sayama/Japan*

Background: Although the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKI) have shown dramatic effects against EGFR mutant non-small-cell lung cancer (NSCLC), patients demonstrate resistant by various mechanisms, such as second-site point mutation that substitutes methionine for threonine at position 790 (T790M) in EGFR, and amplification of mesenchymal-epithelial transition (*MET*) proto-oncogene and human epidermal growth factor receptor 2 (*HER2*). With the development of overcoming resistance to EGFR-TKIs, identification of the mechanisms of drug resistance

is urgently needed. However, tumor samples for detecting the resistant mechanisms were not easily available in patients with *EGFR*mutation-positive NSCLC relapsed after EGFR-TKIs treatment. Here, we examined the correlation of *T790M* mutation, activating *EGFR* mutations, *HER2* amplification, and *MET* amplification in relapsed NSCLC patients between plasma and tumor samples using digital PCR assay as an alternative and noninvasive method. **Methods:** A total of 18 patients obtained pairs of tumor and blood samples after resistance to EGFR-TKI treatment were enrolled in this study. T790M mutation, activating*EGFR* mutations, *MET* amplification, and *HER2* amplification in relapsed NSCLC patients after EGFR-TKIs treatment were analyzed by digital PCR. **Results:** Digital PCR analysis of T790M mutation in plasma had a sensitivity of 81.8% and specificity of 85.7%, with the overall concordance between plasma and tissue samples 83.3%. Analysis of primary active mutation in plasma showed inconsistent results with lower sensitivity of 66.7% and concordance of 70.6% compared to those of T790M mutation. *MET* gene copy number gain of tumor DNA by digital PCR was observed in three patients. Of these patients, one patient exhibited positive for *MET* amplification by FISH, whereas no patient demonstrated *MET* and *HER2* copy number gain in plasma DNA. **Conclusion:** Digital PCR analysis in plasma is feasible and accurate method for detecting the T790M mutation in NSCLC resistance to EGFR-TKIs treatment. **Keywords:** digital PCR, EGFR, T790M, plasma

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P2.04-092 Sequencing of Actionable EGFR Mutations from PtDNA in NSCLC: A Feasibility Study of Non-Invasive Analysis of Sensitivity to TKI Svitlana Tarasevych[1], Marta Castiglia[1], Birgitta I. Hiddinga[1], Patrick Pauwels[1], Christian Rolfo[2], Jan P. Van Meerbeeck[1] [1]*Thoracic Oncology, Multidisciplinary Oncology Centre Antwerp, Antwerp University Hospital, Edegem/Belgium,* [2]*Phase I-Early Clinical Trials Unit&Centre for Oncological Research (Core), Antwerp University Hospital, Edegem/Belgium*

Background: In ~10 % of Caucasian patients with non-small cell lung cancer (NSCLC), the presence of an activating epidermal growth factor receptor (EGFR)-mutation has resulted in a more favourable prognosis by its exquisite sensitivity to a targeted treatment with tyrosine kinase inhibitors (TKI's). However, in up to 20% of those patients, the presence of "driver" alterations cannot reliably be established due to an inadequate diagnostic sample and/or impossibility to re-biopsy a patient. Activating EGFR-mutations can be accurately detected in plasma with a high concordance to matched tumour tissue with allele-specific PCR assays of plasma tumor DNA (ptDNA). This 'liquid biopsy' can replace response to treatment, allow detection of early relapse in the follow-up and estimate prognosis. The aim of this study is to assess the feasibility of detecting ptDNA in patients with EGFR mutations, to assess the concordance of ptDNA levels to mutations in matched tissue samples and to correlate ptDNA levels with clinical response or relapse after start of TKI-treatment. **Methods:** Tumour tissue samples of 20 patients (10 with/10 without activating EGFR-mutations), was assessed for the presence of the respective mutation in matched ptDNA, obtained either at presentation or during follow up. DNA was extracted from aliquots (1ml) of plasma with the use of Qlamp circulating nucleic acid kit (Qiagen). The target DNA is amplified and detected on the cobas z 480 analyzer using the amplification and detection reagents provided in the cobas EGFR Mutation Test kit. The concordance was estimated with Bayesian variables. **Results:** 26 tissue and 34 plasma samples were collected from 20 Caucasian patients with median age of 67 years (54 to 84), 60% female, 30% non-smokers, 100% adenocarcinomas and 95% histologically or cytologically confirmed stage IV NSCLC. The median number of samples per patient was 3 (2 - 5). In the tissue samples 6 patients had an exon 19 deletion, 1 had exon 18 mutation, 2 had exon 20 mutation and in 1 patient a simultaneous exon 19 deletion and T790M mutation. The Bayesian characteristics of ptDNA determination are as follows:

		A: at sample level (n = 34)	B: at study population level (n = 20)
1.	Prevalence of mutation	8.8%	10%
2.	Sensitivity	12.5%	20%
3.	Specificity	100%	100%
4.	PPV	100%	100%
5.	NPV	32.2%	55%
6.	Accuracy	38%	60%
7.	Concordance	11.5%	7.7%

Conclusion: Detection of ptDNA in EGFR-positive patients is feasible. However, ptDNA mutation testing by cobasR 4800_Blood Test was not reliable due to the low analytical sensitivity and the heterogeneity of the patient population. Further studies with other methods as next-generation sequencing or digital droplet PCR are warranted. **Keywords:** plasma tumor DNA, tyrosine kinase inhibitor, non-small cell lung cancer, Epidermal growth factor receptor

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-093 Assessment of Clinical Applications of Circulating Tumor DNA in Lung Cancer Using an Enhanced TAm-Seq Platform Davina Gale[1], Andrew Lawson[1], Jordi Remon[2], Vincent Plagnol[1], Sarah Smalley[1], Espereanza Perez[2], Karen Howarth[1], Michelle Pugh[1], Tim Forshew[1], Abdelaziz Fahem[1], Amanda Bettison[1], John Beeler[1], Ludovic Lacroix[2], Emma Green[1], Michael Stocum[1], Benjamin Besse[2], Nitzan Rosenfeld[1] [1]*Inivata Ltd, Cambridge/United Kingdom,* [2]*Institut Gustave-Roussy, Villejuif/ France*

Background: Novel biomarkers are required to assess tumor burden and response in lung cancer as conventional biopsies are invasive, costly and only provide a snapshot of the mutational profile at a given time and location. A promising biomarker is the detection of genomic material released from tumors into the blood plasma of patients, known as circulating tumor DNA (ctDNA). ctDNA has been detected in plasma for a wide range of solid tumors and can be distinguished from other (germline) cell-free DNA by the presence of tumor-specific DNA alterations or known hotspot mutations. However, the potential of ctDNA as a biomarker in lung cancer has not yet been fully realized due to technical challenges associated with its detection and analysis, including the short fragment sizes (140-170 bp), small number of amplifiable copies and low/ variable allele fractions of ctDNA. To further develop applications of ctDNA in lung cancer, we have developed a process to analyse ctDNA and utilise it in a range of clinical studies. **Methods:** We have developed an enhanced platform for tagged-amplicon deep sequencing (TAm-Seq). Using a combination of improved library preparation and bespoke data analysis methods, this platform can be used to sequence established cancer hotspots and the entire coding regions of selected genes, while preserving high levels of specificity and sensitivity. **Results:** Using this approach, we have developed an assay that analyzes ~20 kb of the genome (including regions of interest in more than 30 genes) with sensitivity down to a few mutant copies. Performance of this assay has been demonstrated using spike-in experiments, dilution series and clinical sample cohorts from lung cancer patients. **Conclusion:** Our proof of concept studies show the potential of ctDNA to be used to assess tumor mutation status, monitor tumor dynamics, assess response to treatment and identify mutations associated with acquired drug resistance and disease progression. This non-invasive approach - a "liquid biopsy" - offers a revolution in how cancer can be detected, monitored and treated. Further studies in lung cancer are being developed and will be presented. **Keywords:** Circulating tumour DNA, personalised medicine, liquid biopsy

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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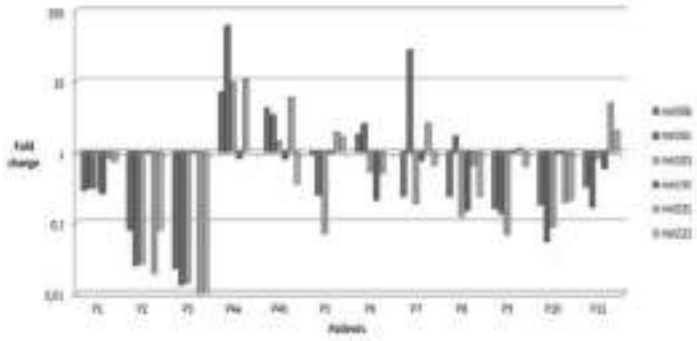
P2.04-094 Exosomal MiRNA Analysis of Non-Small Cell Lung Cancer (NSCLC) Liquid Biopsies. Mirror of the Disease Status?: Proof of Concept Study Marco Giallombardo[1], Jorge Chacartegui[2], Laure Sober[3], Jan P. Van Meerbeeck[4], Sofie Goethals[5], Riccardo Alessandro[6], Patrick Pauwels[3], Christian Rolfo[7] [1]*Phase I- Early Clinical Trials Unit, Antwerp University Hospital & Palermo University, Edegem/ Belgium,* [2]*Phase I- Early Clinical Trials Unit, Antwerp University Hospital, Edegem/ Belgium,* [3]*Molecular Pathology Unit & Core, Antwerp University Hospital & Antwerp University, Edegem/Belgium,* [4]*Thoracic Oncology, Antwerp University Hospital, Edegem/Belgium,* [5]*Molecular Pathology Unit, Antwerp University Hospital, Edegem/ Belgium,* [6]*Department of Medical Biotechnology - Dibimed, University of Palermo, Palermo/ Italy,* [7]*Phase I-Early Clinical Trials Unit, Department of Medical Oncology & Core, Antwerp University Hospital & Antwerp University, Edegem/Belgium*

Background: The discovery of the alterations in EGFR, c-Met or ALK in NSCLC has driven the development of targeted-drug therapy using tyrosine kinase inhibitors (TKIs). To optimize the use of these TKIs, the discovery of new biomarkers for early detection and disease progression is needed. The exosomes extracted from blood samples could be non-invasive and regularly updated biomarkers. Here we analyze selected exosomal miRNAs to evaluate its biomarker potential in NSCLC. **Methods:** 1 ml of serum/plasma sample from 11 NSCLC patients, with different mutations and treatments (and 6 healthy donors as controls), were used as exosome sources. Exosome were isolated through commercial-kit or D_2O/sucrose density-gradient ultracentrifugation. After exosome characterization (Western-Blot, Transmission Electron Microscopy) a panel of miRNAs (30b-5p, 30c-5p, 103,195,221-3p,222-3p), correlated with NSCLC disease (Garofalo et al, 2013), was analyzed. The miRNAs profile analysis was performed through TaqMan Real-Time PCR and mir-1228-3p was used as endogenous control. The data was processed according to the formula $2\text{-}\Delta\Delta ct$. Control values are used as baseline and results are shown in logarithmic scale (figure). **Results:** Patients without molecular alterations (WMA): The levels of miR-30b-5p/30c-5p/103/221-3p/222-3p were down-regulated relative to the healthy controls. The patient with docetaxel treatment (P2) has an increased down-regulation of these miRNAs compared to the non-treated patient (P1). Patient with BRAF G464V: We observed an increased up-regulation of miR-30b-5p/30c-5p/103/221-3p/222-3p just after stopping Erlotinib treatment (P4a) compared with one month after the treatment (P4b). Patients with C-Met 3+ over-expression: We detected an increase of expression of miR-30b-5p/30c-5p and a decrease of expression of mir221-3p/222-3p in a patient treated with Crizotinib (P6) compared to a non-treated patient (P5). Patients with EGFR (exon 19 del): We observed a decrease of expression of mir221-3p/222-3p in a patient treated with Afatinib beyond progression (P8) compared to a non-treated patient (P7). Patients with ALK t(2p23): We detected a decrease of expression of miR-30b-5p/30c-5p/103 compared to healthy controls. No differences between treated (P9-P11) and non-treated (P3) patients were observed. Nevertheless, mir221-3p/222-3p differs significantly between patients treated with Ceritinib one week (P10) and one month (P11) after the treatment was started. **Conclusion:** This panel of exosomal miRNAs derived from patients with varying mutations is responsive to different treatments. The down-regulation of miR-30b-5p/30c-5p in exosomes of patients with

WMA and ALK t(2p23) mutations, mirrored the reported low levels of these miRNAs in NSCLC tissue (Zhong et al.,2014). Follow-up analysis to correlate clinical progression and exosome miRNAs profile is currently ongoing.



Keywords: liquid biopsies, exosomes, miRNA analysis, molecular profile

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P2.04-095 Detection of Mutations in Tumor and Blood Samples from Lung Adenocarcinoma Patients Using Two Different Techniques Jose M. Clavero[1], Claudia Hurtado[2], Mauricio Moreno[2], Tania Quiroz[2], Marcela Figueroa[2], David Lazo[1], Patricio Rodriguez[1], Alvaro Ibarra[3], Manuel Alvarez[4] [1]*Thoracic Surgery, Clínica Las Condes, Santiago/Chile,* [2]*Laboratorio de Oncología Y Biología Molecular, Clínica Las Condes, Santiago/Chile,* [3]*Department of Pathology, Clínica Las Condes, Santiago/Chile,* [4]*Clinic Cancer Center, Clínica Las Condes, Santiago/Chile*

Background: Adenocarcinoma is currently the most common type of lung cancer in which genetic alterations with prognostic and predictive value have been identified. EGFR mutations are predictive of response to TKI and mutually exclusive with KRAS mutation. Molecular analyses from tissue biopsies are nowadays mandatory in initial pathology studies and recommended if TKI resistance develop. Molecular analysis in circulating cell-free DNA (cfDNA) appeared as an easier method to perform these studies. cfDNA analysis from plasma or serum in lung cancer have identified mutations in EGFR, KRAS, ALK and HER-2, that correlated with those observed in the primary tumor. This study compared two different techniques to determine KRAS and EGFR mutations in tissue and blood samples from patients with lung adenocarcinoma. **Methods:** Patients with suspected lung cancer admitted to Clinica Las Condes between October 2012 and March 2014, were offered to enter the Study. Previous to biopsy, 20ml of blood was drawn and samples of plasma and serum stored. When an adenocarcinoma was diagnosed EGFR and KRAS mutations of the biopsy were analyzed by COBAS® KRAS/ EGFR Mutation Tests and by SSCP (Single Stranded Conformational Polymorphism) and confirmed by Sanger sequencing. Blind analysis of stored plasma and serum was performed, isolating cfDNA using QIAamp® Circulating Nucleic Acid kit, and tumor DNA by QIAamp® DNA FFPE Tissue kit. Clínica Las Condes Ethics Board approved the study, and informed consent obtained in all patients. **Results:** Twenty-one patients entered the study; two were excluded because final pathology showed Atypic Hyperplasia. Of the reminding 19 patients: 14 had invasive Adenocarcinoma, 3 in situ Adenocarcinoma and 2 Adenosquamous carcinoma. Tissue biopsies were obtained from the primary tumor in 14 cases, pleural metastases in 2, lymphnode metastases in 2 and brain metastases in one. Two patients had Adenocarcinoma in situ, 10 stage I, 1 stage II, 2 stage III and 4 stage IV. Seven patients have mutations detected by COBAS® and SSCP in tissue biopsies: 3 EGFR and 4 KRAS mutations. EGFR mutations were detected in 2 stage I, and one stage IV patients. KRAS in 1 ACAis, 2 stage I and one stage IV. In these patient´s plasma only 1 mutation was detected in cfDNA (KRAS mutation in one stage IV patient), correlation between tissue biopsy and cfDNA 1 out of 7 (14%). No mutations were detected in cfDNA from serum samples. **Conclusion:** In our study EGFR and KRAS mutations rates were lower than expected for Chilean population, but it could be due to the small sample size. We had poor general correlation between mutations in tissue biopsies compared with those detected in cfDNA (14%). In stage IV correlation was better (50%). No EGFR mutations were detected in cfDNA, but again could be due to the sample size. COBAS® technique was useful to determine KRAS mutations in plasma cfDNA. Both SSCP and COBAS techniques allow determining mutations in tumor samples. cfDNA analysis could be used to determine KRAS mutations in patients with advanced disease. Its use to determine EGFR mutations need to be investigated in larger studies.
Keywords: KRAS, EGFR, lung cancer, cell free DNA

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P2.04-096 Liquid Biopsies in Patients with EGFR Mutated Non-Small Cell Lung Cancer Undergoing Curative Treatment Eva B. Hansen[1], Boe S. Sorensen[2], Peter Meldgaard[3] [1]*Oncology, Aarhus University Hospital, Aarhus/Denmark,* [2]*Dept. of Clinical Biochemistry, Aarhus University Hospital, Aarhus C/Denmark,* [3]*Dept. of Oncology, Aarhus University Hospital, Aarhus C/Denmark*

Background: A blood based test for detection of EGFR mutations has been developed. Studies have shown a correlation between level of mutations in the blood and course of the disease in stage IV patients, suggesting that the test could be used as a monitoring device. No studies have been conducted examining whether the blood test can be used to monitor patients who undergo curative treatment. **Methods:** Six patients with EGFR mutated tumors were monitored with continuous blood samples from the time of diagnosis until relapse, death or present date. The blood samples were tested for the level of EGFR mutations using the Cobas® EGFR Mutation Test developed for plasma DNA (Roche Molecular Systems, Inc.). Results were compared to the clinical course of the disease. **Results: Operated without adjuvant chemotherapy** (n=3, all patients with T1N0M0 disease). In two patients there were no measurable mutations in the blood samples at any point. One patient is at present date without sign of relapse after 3 years and attends follow up. The other patient died of non-cancer related causes. The third patient had declining level of mutations the first two years after the operation but the mutated DNA has never reached zero. **Operated with adjuvant chemotherapy** (n=1, T2N2M0). Mutations were measurable before operation and declined to zero after. One year after the operation, metastatic disease (CNS) was discovered along with a rise in mutation level, which again declined after local irradiation and initiation of erlotinib treatment. **Chemoradiotherapy** (n=2, T2N2-3M0). One of these patients had measurable levels of mutations initially, which declined to zero during the course of treatment with chemoradiotherapy and a supplement of erlotinib. Metastatic disease (CNS) was found during the treatment, and the patient proceeded with erlotinib treatment and cerebral irradiation. The patient died due to disease progression 9 months later, no measurable mutated DNA was identified. In contrast, another patient had no measurable mutations until after relapse was detected. **Conclusion:** Our results suggest that in some cases monitoring the level of EGFR mutations in the blood might be a valuable tool in the detection of relapse in patients who have undergone curative treatment for their lung cancer. Further investigations are warranted to elucidate the subject. We have initiated a project, where we prospectively follow all patients with EGFR mutated NSCLC regardless of stage and treatment modality and we examine their blood for EGFR mutations every time a blood sample is drawn.
Keywords: liquid biopsies, Curative treatment, NSCLC, EGFR mutations

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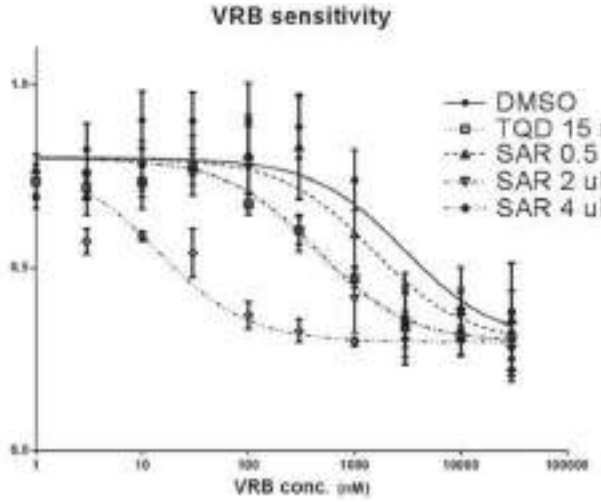
P2.04-097 Vinorelbine Resistance in Lung Cancer; Role of Focal Adhesion Signaling Pathways Takao Nakanishi, Toshi Menju, Kei Shikuma, Terumasa Sowa, Hiroyuki Cho, Shinya Neri, Makoto Sonobe, Hideki Motoyama, Kyoko Hijiya, Toshihiko Sato, Akihiro Aoyama, Fengshi Chen, Hiroshi Date *Thoracic Surgery, Kyoto University, Graduate School of Medicine, Kyoto/Japan*

Background: Vinorelbine (VRB) combined with cisplatin is a widely used regimen for the treatment of non-small cell lung cancer, but their curative effect is unsatisfactory. The resistance to these drugs is the main cause of chemotherapeutic failure. Several factors are reported to be related with VRB resistance, however their validity remains controversial. In the present study, we compared the gene expression and protein phosphorylation between parental (P) and induced VRB resistant (VR) cell lines to elucidate candidate mechanisms for VRB resistance. **Methods:** First we established VR lung cancer cells (H1299) with the exposure to the graded increase in VRB concentration. Then, transcriptional changes were measured with DNA microarray and pathway analysis by comparing VR line to the parental. Protein expression and its activation in the candidate pathway were examined by western blot analysis. Cell viability about VRB and Src / ABCB1 inhibitors was assessed by 'WST-8 assays'. **Results:** Half-maximum inhibitory concentration (IC50) of VR cells to VRB were 190 times higher than that of parental cells. VR cells had cross resistance to docetaxel and etoposide, but they did not have cross resistance to cisplatin. VR cells highly expressed ABC transporter (ABCB1: fold change = 13.4) and focal adhesion (FA) related genes, such as integrins and underlining molecules (ITGB3: fold change = 3.7, Src: fold change = 1.1). Western blot analysis confirmed the high expression of intergrin $\beta 1$, $\beta 3$ and the activation of the FA pathways including Src, and Akt in VR cells. VRB sensitivity in VR cells was recovered with ABCB1 inhibitor (tariquidar: TQD). Although single usage of Src inhibitor (dasatinib: DAS) did not show any effectiveness, TQD and DAS had synergistic effect on VRB sensitivity. VRB IC50 concomitant use with DMSO, DAS 50 nM, TQD 15 nM, and DAS 50 nM + TQD 15 nM were 1261 nM, 1125 nM, 466.5 nM, and 75.58 nM, respectively. Saracatinib (SAR), a dual inhibitor of Src and ABCB1, recovered VRB sensitivity (Fig.).



Conclusion: Indeed, ABCB1 is the main cause of VRB resistance and multi-drug resistance in lung cancer. Genome-wide gene expression analyses revealed another candidate, focal adhesion pathways, except for drug efflux in VRB resistance. Our results show the potential of Src inhibitor to overcome these drug resistance. **Keywords:** Chemotherapeutic resistance, vinorelbine, Focal Adhesion Signaling Pathways, Src

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P2.04-098 Acquired Resistance to Anti-VEGF Therapy in Non-Small Cell Lung Cancer Is Not Associated with Angiogenic Compensation Robin E. Frink, Laura A. Sullivan, Wenting Du, Ashley Barraza, Rolf A. Brekken *Hamon Center for Therapeutic Oncology Res, UT Southwestern, Dallas/TX/United States of America*

Background: The vascular system provides nutrients and oxygen to cells and tissues via the circulation of blood. Tissues require an efficient vascular network to maintain homeostasis. Angiogenesis, the process of expansion and remodeling of the vascular network, is driven by the expression and secretion of angiogenic growth factors that stimulate endothelial cell migration, proliferation and survival. Induction of angiogenesis is an early event in the progression of tumors, including non-small cell lung cancer (NSCLC). Vascular endothelial growth factor-A (VEGF) is a principal angiogenic growth factor in NSCLC and as a result is an attractive therapeutic target. Despite promising preclinical results, therapies targeting VEGF have shown only modest improvements in progression free survival and overall survival in NSCLC patients. Many NSCLC patients that initially respond to anti-VEGF therapy develop resistance with continued use. We sought to determine factors associated with acquired resistance to anti-VEGF monoclonal antibodies (mAbs). r84 is a fully human anti-VEGF mAb that inhibits human and mouse VEGF binding to VEGF receptor 2 (VEGFR2) but not VEGFR1 and is currently in Phase I clinical trials. Bevacizumab is a humanized mAb specific for human VEGF that blocks VEGF from binding VEGFR1 and VEGFR2 and is currently approved for treatment of NSCLC. **Methods:** Acquired resistance to anti-VEGF therapy was driven in NSCLC cell lines (H1975, H1993, and H2073) by prolonged in vivo therapy with r84 or bevacizumab. Over 20 cell lines (e.g., H1975-81) were generated by ex vivo culture from tumors that displayed acquired resistance to therapy. In addition, tumor cell lines were generated from tumor-bearing mice treated with saline (e.g. H1975-713). A subset of control and resistant cell lines were implanted in vivo and evaluated for response to anti-VEGF therapy. Tumor microvessel density was determined by immunohistochemistry. **Results:** Two of five acquired resistance cell lines were verified as resistant upon reimplantation and treatment with r84 and bevacizumab demonstrating that the changes induced by prolonged anti-VEGF therapy in these cell lines are heritable. Conversely, tumor xenografts from saline control tumors remained sensitive to anti-VEGF therapy. Anti-VEGF therapy with r84 or bevacizumab reduced microvessel density in each tumor regardless of whether therapy reduced tumor growth or not. **Conclusion:** Anti-VEGF therapy significantly reduces angiogenesis even in tumors that show resistance to therapy, suggesting that compensation by other angiogenic growth factors is not a significant contributor to tumor response to anti-VEGF therapy. Further, prolonged treatment with anti-VEGF can induce heritable changes in NSCLC cells that confer resistance to anti-VEGF therapy. **Keywords:** angiogenesis, NSCLC, bevacizumab

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P2.04-099 Differential Regulation of DNA Repair Genes in Cisplatin Resistant Non-Small Cell Lung Cancer Cells Yuexi He[1], Sinead Cuffe[1], Stephen Finn[2], Kenneth J. O'Byrne[3], Martin P. Barr[1] [1]*Thoracic Oncology, St James'S Hospital & Trinity College Dublin, Dublin/Ireland,* [2]*Histopathology, St James'S Hospital & Trinity College Dublin, Dublin/Ireland,* [3]*Cancer and Ageing Research Program, Princess Alexandra Hospital and Queensland University of Technology, Brisbane/Australia*

Background: In the absence of specific treatable mutations, cisplatin-based doublet chemotherapy remains the gold standard treatment for NSCLC patients. However, its clinical efficacy is hindered in many patients due to both intrinsic and acquired resistance to this drug. Alterations in the DNA repair capacity of damaged cells is now recognised as an important factor in mediating this phenomenon. DNA repair is therefore a vital target to improving cancer therapy and overcoming resistance of tumour cells to DNA damaging agents currently used in the treatment of NSCLC patients. **Methods:** DNA Repair Pathway RT^2 Profiler Arrays were used to elucidate the key DNA repair genes implicated in cisplatin resistant NSCLC cells using cisplatin resistant (CisR) and corresponding parental (PT) H460 NSCLC cells previously established in our laboratory. The regulation of the trans-activation of p53 in response to DNA damage was studied by examining protein accumulation, post-translational modifications (p53Ser^{15}) and whether depletion of the novel DNA repair protein, hSSB1, affects the regulation of p53 in response to cisplatin. The repair of cisplatin-induced double strand breaks (DSBs) was examined by immunofluorescence imaging of γH2AX foci. Expression of p53Ser^{15} (phosphorylated & total) in addition to hSSB1 was also assessed by HCA and Western blot analysis. **Results:** We identified a number of critical DNA repair genes that were differentially regulated between parental and cisplatin resistant NSCLC cells, some of which are known to be implicated in the nucleotide and mismatch repair pathways. H2AX was shown to be a reliable and specific marker of DNA double strand DNA breaks induced by platinum agents such as cisplatin. Cisplatin induced the translocation of p53 from the cytoplasmic compartment of H460 PT cells to the nuclear compartment, while significant levels of p53 were retained within the cytoplasmic compartment of CisR cells. Using both HCS and Western blot analysis, hSSB1 protein was undetectable. **Conclusion:** To date, despite reports that differential expression of components of the various DNA repair pathways correlate with response to cisplatin, translation of such findings in the clinical setting are warranted. The identification of alterations in specific proteins and pathways that contribute to these unique DNA repair pathways in cisplatin resistant cancer cells may potentially lead to a renewed interest in the development of rational novel therapies for cisplatin resistant cancers, in particular, lung cancer. **Keywords:** DNA repair, cisplatin, resistance, p53, NSCLC

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P2.04-100 Platin-Induced ATM Activation in Non-Small Cell Lung Cancer Jarrett Moore[1], Lars F. Petersen[1], Anifat A. Elegbede[2], Gwyn Bebb[3] [1]*Oncology, Tbcc Translational Labs, University of Calgary, Calgary/AB/Canada,* [2]*Oncology, Tbcc Translational Labs, University of Calgary, Calgary/Canada,* [3]*Alberta Health Services, Calgary/AB/Canada*

Background: Platinum based antineoplastic therapies (platins) are a first line treatment prescribed for non-small cell lung cancer (NSCLC), but unfortunately have many adverse side effects. Cytotoxicity is caused by the generation of DNA adducts, which create single and double stranded DNA breaks and stimulate DNA damage response pathways. A key mediator of this response is ataxia telangiectasia mutated (ATM), which is responsible for the activation of several downstream targets involved in DNA repair, cell cycle arrest, and apoptosis. Of great interest are platin sensitivity markers that help identify patients more susceptible to these treatments. Previous research on predictive markers of platin sensitivity has focused on ERCC1 and RRM1 with varying levels of success. Our lab has shown that cells lacking ATM have increased sensitivity to some platin therapies. We hypothesize that ATM signaling may be invoked by platin exposure and that tumours deficient in ATM may have innate sensitivity to platin therapies. Here we assess the molecular action of ATM in response to different platin therapies to determine whether low activity in ATM-deficient cells is predictive of platin sensitivity. **Methods:** Six NSCLC cell lines were assessed for the presence of ATM by western blot. Those cell lines for which ATM was not found were deemed ATM-deficient. Cell lines were treated with varying concentrations of platinum based therapies (cisplatin, carboplatin and oxaloplatin) for two hours or overnight. ATM activation was determined by assessment of phosphorylated-ATM protein levels using western blots. Additionally, downstream targets of ATM were probed to determine ATM pathway activation. **Results:**NSCLC cell lines H226, H460 and H522 were found to be ATM-proficient whereas cell lines H23, H1373 and H1395 were found to be ATM-deficient. ATM-proficient cell lines demonstrated an increased level of phosphorylated-ATM in response to treatments with cisplatin, carboplatin, and oxaliplatin. In addition, downstream targets of ATM also showed increased levels of activation when compared to non-treated controls. ATM-deficient cell lines showed no increased levels of phosphorylated-ATM however, downstream targets of ATM showed some activation in ATM-deficient cell lines. **Conclusion:** We have shown that cisplatin, carboplatin and oxaliplatin treatments induce the phosphorylation of ATM, a prominent regulator of the DNA damage response. In addition, the ATM-deficient cell lines showed reduced activation of ATM to platin treatments. It is clear that platin exposure induced an ATM mediated signalling response, however its predictive capabilities of platin sensitivity is still unclear. Activation of DNA repair by platins may leave ATM-deficient tumours at a disadvantage when mounting repair responses to these treatments. This data suggests that individuals with low or non-functioning ATM may be candidates for precision low-dose therapies that exploit this deficiency. **Keywords:** ATM, NSCLC, DNA damage, Cisplatin

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P2.04-101 Ganetespib Resistance in KRAS Mutant NSCLC Is Mediated through Reactivation of the RAF/MEK/ERK and PI3K/MTOR Pathways Suman Chatterjee, Timothy F. Burns *Department of Medicine/ Division of Hematology Oncology, University of Pittsburgh Cancer Institute, Pittsburgh/PA/United States of America*

Background: One third of all malignancies and approximately 25% of non-small cell lung cancer (NSCLC) patients have *KRAS* mutations which leads to the activation of several growth regulatory signaling pathways including RAF/MEK/ERK and PI3K/AKT/MTOR. Unfortunately, there are no current therapies targeting this critical oncogene. Heat shock protein 90 (HSP90) is a molecular chaperone required for the stability of 'client' oncoproteins, many of which are effectors of KRAS. Unfortunately, limited efficacy was observed in early clinical studies of single agent HSP90 inhibitors (HSP90i) in *KRAS* mutant NSCLC. Here, we examined the mechanism(s) of acquired resistance to ganetespib, a Phase 3 HSP90i, in *KRAS*mutant NSCLC to develop rationale combinations with ganetespib. **Methods:** Growth inhibition was determined through the colony formation and MTS assays. Ganetespib resistant (GR)-*KRAS* mutant NSCLC cell lines were derived to identify resistance mechanism(s). Flow-cytometry was performed to generate cell-cycle profiles. Genetic (shRNA) and pharmacologic inhibition of candidate mediators of resistance was performed. **Results:** Ganetespib was cytotoxic in a panel of *KRAS*mutant NSCLC cell lines and decreased expression and activity of both RAF/MEK/ERK and PI3K/AKT/MTOR pathways. In order to identify the mechanisms of ganetespib resistance in *KRAS* mutant NSCLC, we derived three *KRAS* mutant NSCLC ganetespib resistant (GR) cell lines. GR cells were cross-resistant to a first generation HSP90i, 17-AAG, suggesting that altered metabolism of ganetespib is unlikely to explain this resistance. Moreover, the ganetespib-induced G_2/M checkpoint arrest observed in A549 parental cells was significantly diminished in A549-GR cells. These results suggest that bypass of this checkpoint may contribute to the observed ganetespib resistance. Furthermore, we demonstrated that GR cells were cross-resistant to docetaxel, an anti-microtubule agent. In addition, expression and activity of the PI3K/AKT/MTOR pathway members as well as the RAF/MEK/ERK pathway members were significantly increased suggesting that reactivation of these pathways may be responsible for the observed resistance. To test this hypothesis, we treated parental and GR cells with inhibitors of

the PI3K/AKT/MTOR pathway (dual PI3K/mTOR inhibitor, BEZ235 and PI3K inhibitor PX866) or the RAF/MEK/ERF pathway (ERK inhibitor, SCH772984). Remarkably, GR cells were more sensitive to these inhibitors compared to the parental ones suggesting that the acquired ganetespib resistance lead to increased dependence on the both RAF/MEK/ERK and PI3K/MTOR pathways. Interestingly, the expression/activity of the key ERK and PDK1 substrate and activator of the PI3K/MTOR pathway, p90 ribosomal S6 kinase (RSK) was strikingly increased in the GR cells. Since RSK has been implicated as a key mediator of crosstalk between these two pathways, as well as in promoting G2/M progression, we examine the effect of genetic (shRNA) or pharmacologic (BI-D1870 and SL0101) inhibition of RSK in two GR cell lines. Remarkably, the GR cells showed increased dependency on RSK activity compared to the parental cell lines. **Conclusion:** These data suggests that the combination of inhibitors for HSP90 and PI3K/mTOR or a RSK inhibitor may prevent ganetespib resistance and/or help overcome the resistance after single agent treatment, providing the preclinical rationale for our planned Phase I/II trial of the combination of ganetespib and a dual PI3K/MTOR inhibitor in *KRAS* mutant NSCLC.
Keywords: KRAS, HSP90 inhibitor, p90RSK, Acquired resistance

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P2.04-102 Targeting Inflammatory Mediators to Overcome Intrinsic and Acquired Cisplatin Resistance in Non-Small Cell Lung Cancer
Anne-Marie Baird[1], Peter Godwin[2], Susan Heavey[2], Kazuo Umezawa[3], Martin P. Barr[2], Anthony Davies[4], Derek Richard[1], Kathy Gately[2], Kenneth J. O'Byrne[5] [1]*Cancer and Ageing Research Program, Queensland University of Technology, Brisbane/QLD/Australia,* [2]*Thoracic Oncology Research Group, Trinity College Dublin/St. James'S Hospital, Dublin/Ireland,* [3]*Dept. of Molecular Target Medicine Screening, Aichi Medical University, Aichi/Japan,* [4]*Translational Cell Imaging Queensland, Queensland University of Technology, Brisbane/QLD/Australia,* [5]*Cancer and Ageing Research Program, Princess Alexandra Hospital and Queensland University of Technology, Brisbane/Australia*

Background: Cisplatin based doublet-chemotherapy is commonly used in non-small cell lung cancer (NSCLC) treatment with an initial objective response rate of 40-50%. However, intrinsic and acquired chemo-resistance constitutes a major clinical obstacle. The mechanisms of resistance have yet to be fully understood. We have previously demonstrated that NF-κB levels are elevated in cisplatin resistant cells (CisR) and that the use of an NF-κB inhibitor, DHMEQ, resulted in greater CisR cell death. The goal of this project is to elucidate the mechanistic links between NF-κB regulated pathways and the development of cisplatin resistant NSCLC. **Methods:** The expression of NF-κB mediators and immune regulators were assessed in an isogenic NSCLC cell line model of cisplatin resistance using qPCR arrays (252 genes). A number of targets were identified and validated using PCR. The effect of drug combinations (Cisplatin and DHMEQ) was also determined. Comet assays (DNA damage) were also performed to determine the effect of DHMEQ alone or in combination with irradiation (6 Gy). **Results:** Various chemokines and their receptors were elevated in cisplatin resistant (CisR) cells compared with cisplatin sensitive (PT). In addition, a number of key TLRs and regulators of the innate immune pathway were altered. DHMEQ enhanced cellular sensitivity to cisplatin in both PT and CisR cell lines ($p<0.05$). This drug also overcame the chemo-protective effect of a number of chemokines and enhanced irradiation induced DNA damage. An animal study will commence shortly using DHMEQ alone and in combination with cisplatin. **Conclusion:** Immune-modulators such as DHMEQ may be a novel viable option in addressing inflammatory mediated acquired and intrinsic NSCLC chemo-resistance. In addition, immune regulators identified in this project may provide innovative targets for immuno-oncology therapy.
Keywords: inflammation, Cisplatin resistance, Chemokines, NSCLC

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P2.04-103 A Goodpasture Antigen-Binding Protein Kinase Inhibitor to Treat Drug-Resistant Metastatic Lung Cancer
Juan Saus[1], Fernando Revert[2], Aida Artigot[2], Raül Blasco[2], Juan F. Sanz-Cervera[3], Enrique Pérez-Paya[4], Ernesto López-Pascual[2], Alejandra Pérez-Sastre[2], Roberto Gozalbo-Rovira[2], Francisco Revert-Ros[2] [1]*Biochemistry and Molecular Biology, University of Valencia Medical School, Valencia/Spain,* [2]*Research & Development, Fibrostatin Sl, Paterna - Valencia/Spain,* [3]*Organic Chemistry, University of Valencia, Burjassot-Valencia/Spain,*[4]*Biochemistry and Molecular Biology, University of Valencia, Burjassot-Valencia/Spain*

Background: Goodpasture antigen-binding protein (GPBP) is a secretable Ser/Thr kinase which regulates the organization of the type IV collagen network in the extracellular matrix. Current evidence suggests that this network interacts directly with Cancer Stem Cells (CSC) and forms a protective shield against anti-tumor therapies. CSC are recognized as responsible for tumor's drug resistance and invasiveness. Remarkably, expression of *COL4A3BP*, the gene coding for both GPBP kinase and cytosolic ceramide transporter CERT, has been associated with multidrug resistance and poor prognosis in breast and lung cancer patients. Here, we have developed T12, a highly specific small molecule inhibitor of GPBP kinase and demonstrated its potential to treat drug-resistant and metastatic non-small cell lung cancer. **Methods:** The yeast two-hybrid system was used to identify a five-residue motif responsible for GPBP multimerization and enhanced kinase activity. We then generated a series of peptidomimetic compounds featuring a terphenyl structure. The compound 3-[4''-methoxy-3,2'-dimethyl-(1,1';4',1'')terphenyl-2''-yl] propionic acid, referred to as T12, exhibited a suitable kinase inhibitory activity and toxicokinetics, and as a result was selected for additional testing using relevant *ex vivo* and *in vivo* models of human non-small cell lung cancer (A549 and patient-derived primary cultures). **Results:** T12 treatment reduced the viability of human lung cancer cells exhibiting a prevalent mesenchymal-invasive phenotype, but had no effect on human lung cancer cells with a predominant epithelial phenotype. Conversely, the latter responded to T12 when combined with doxorubicin, an inducer of the epithelial-to-mesenchymal transition (EMT). Consequently, we suggest that the GPBP kinase activity and concomitant type IV collagen expression stabilize the privileged niche of the mesenchymal drug-resistant CSC in human lung cancer. Accordingly, down-regulation of either GPBP kinase activity or type IV collagen expression using siRNA or T12 treatment, compromised human lung cancer cell viability only after EMT induction. Moreover, the pivotal role of GPBP in stabilizing the tumor invasive phenotype was further demonstrated by exhibiting reduced tumor implantation and metastasis formation in GPBP -/- mice. Finally, confirmation that T12 inhibition of GPBP kinase was responsible for anti-tumor activity in mice was accomplished by showing analogous therapeutic effects following administering of N26, a GPBP-specific monoclonal antibody that inhibits GPBP binding to type IV collagen. **Conclusion:** The general mechanism for multidrug-resistance and poor prognosis associated with *COL4A3BP* expression depends by and large on its affiliated kinase activity. Thus, T12 emerges as a First-in-Class drug candidate to specifically treat drug-resistant and metastatic non-small cell lung cancer.
Keywords: GPBP, CERT, collagen IV, COL4A3BP

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P2.04-104 Regulating the Response to Cisplatin in Lung Cancer Cells through the Transcription Factor TCF4: A New Potential Role for Wnt Signaling
Javier De Castro[1], Olga Vera[2], Olga Pernia[2], Ana Sastre Perona[3], Rocío Rosas[2], Pilar Santisteban[3], María Palomares-Bralo[4], Inmaculada Ibáñez De Cáceres[2] [1]*Medical Oncology. Laboratorio de Epigenética, Ingemm. Terapias Experimentales Y Biomarcadores En Cáncer N33 Idipaz., Hospital Universitario La Paz, Idipaz, Madrid/Spain,* [2]*Laboratorio de Epigenética, Ingemm. Terapias Experimentales Y Biomarcadores En Cáncer N33 Idipaz., Hospital Universitario La Paz, Idipaz, Madrid/Spain,* [3]*Instituto de Investigaciones Biomedicas Csic/Uam, Madrid/Spain,* [4]*Laboratorio de Genómica Estructural Y Funcional, Ingemm. N29. Idipaz. Ciber de Enfermedades Raras (Ciberer), Hospital Universitario La Paz, Idipaz, Madrid/Spain*

Background: The standard treatment for non-small cell lung cancer (NSCLC) is Platinum-based chemotherapy, although the main clinical problem associated is the progression of the disease to a platinum-resistant state. This fact has limited its efficacy in these tumor types, which is one of the first causes of cancer deaths in developed countries. Thus, it is of great interest to identify predictive molecular biomarkers that could help in the patient treatment selection. **Methods:** In this study we used array-CGH to analyze the cytogenetic alterations that arise in NSCLC and ovarian cancer cells after cisplatin treatment, by using four paired sensitive(S) and resistant(R) cell lines: H23S/R, H460S/R, A2780S/R and OVCAR3S/R. **Results:** Our experimental approach revealed the presence of a common deletion of the gene TCF4 in a mosaic manner in at least 50% of the resistant cells in both tumor types, while a decrease in TCF4 expression was confirmed through qRT-PCR in the same cells. As TCF4 is a downstream transcription factor of Wnt signaling, we analyzed its potential role regulating the CDDP response in resistant cells through its action in the Wnt pathway. Combination of Top-Fop vectors and TCF4-cDNA overexpression plasmids showed firstly, that resistant cells responded easily to the activation of Wnt pathway, an effect in part mediated by the decrease in TCF4 expression; secondly the overexpression of TCF4 induced an increase in the Cisplatin sensitivity. These results indicate that TCF4 could be acting as a Wnt transcriptional repressor, maintaining the sensitivity to Cisplatin in A2780-S cells. **Conclusion:** Our translational approach in a total of 40 ovarian and lung primary tumors and in 14 normal tissues confirmed that TCF4 expression is frequently downregulated in these tumor types. Altogether we present a novel role for Wnt signaling pathway, regulating the response to CDDP, which could be a potential target for cancer treatment.
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Keywords: Biomarkers, Wnt signalling, non-small cell lung cancer, Cisplatin resistance

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P2.04-105 PARP Inhibition Sensitises ATM Deficient NSCLC Cells to Cisplatin Treatment
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Background: We have previously demonstrated that non-small cell lung cancer (NSCLC) cells with low or undetectable ATM are sensitive to synthetic lethality with PARP inhibitor as a single agent. In contrast, lack of ATM alone does not seem to predict sensitivity of these cells to other agents such as cisplatin, a part of standard chemotherapy often used in NSCLC with limited efficacy. Because Cisplatin can induce some DNA damage that can activate ATM, we sought to determine whether PARP inhibition will improve cisplatin efficacy in NSCLC cells that are ATM deficient. **Methods:** A panel of NSCLC cell lines (NCI-H23, NCI-H460, NC1-H522, NCI-H1373) were assessed for ATM status by western blot in terms of a) ATM protein levels and b) ATM functionality by examining active phosphorylated ATM and downstream targets of ATM e.g. p53 and KRAB-associated protein 1 (KAP1) in irradiated cells. The biological effects of PARP-1 inhibition and cisplatin on viability of these cells were examined using the clonogenic survival assay. **Results:** Two NSCLC cell lines H23 and H1373 were found to be ATM deficient and they show increased sensitivity to the combination of cisplatin with PARP inhibition using olaparib, (Table 1).

	Percentage cell survival (%)					% decrease in cell survival with Cisplatin/ PARPi relative to Cisplatin alone
NSCLC	ATM status	PARPi @ 0.5μM	PARPi @ 1μM	Cisplatin @ 1μM	PARPi @ 0.5μM + Cisplatin @ 1μM	
H23	-	41	8	19	10	47
H460	-	90	38	33	31	4
H522	-	71	33	7	6	14
H1373	-	68	26	23	15	29

Table 1: Percentage cell survival following treatment of NSCLC cells with PARP inhibitor and Cisplatin in clonogenic survival assays (PARPi – PARP inhibitor)

Conclusion: Here, we show that PARP inhibitor sensitized ATM deficient NSCLC cells to cisplatin. These results suggest that a significant treatment response could be achieved in ATM deficient NSCLC cells with low dose cisplatin and PARP inhibition. We have evidence to suggest that ATM deficiency may be present in as much as 20 - 25% of NSCLC patients. This cohort may be able to benefit from modified therapy using lower dose chemotherapy, producing milder side effects and better quality of life. **Keywords:** Cisplatin, PARP inhibitor, ATM, Lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

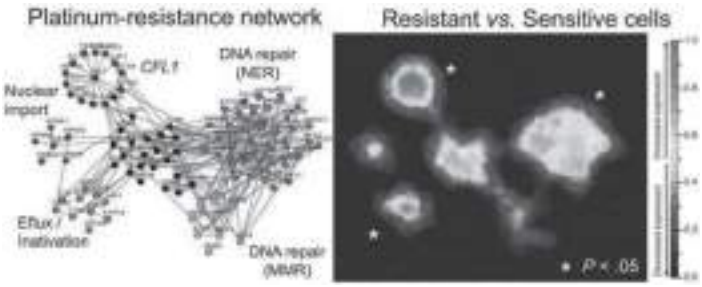
P2.04-106 Expression of AEG-1 Associated with Increase of TS Contributes to Chemoresistance of Pemetrexed in Lung Adenocarcinoma Chung-Yu Chen[1], Ying-Yin Chen[1], Kuan-Yu Chen[2], Jin-Yuan Shih[2], Yih-Leong Chang[2], Chong-Jen Yu[2] [1]*National Taiwan University Hospital Yunlin Branch, Douliou/Taiwan,* [2]*National Taiwan University Hospital, Taipei/Taiwan*

Background: Previous studies have suggested that astrocyte-elevated gene-1 (AEG1) contributes to a broad spectrum of resistance to various chemotherapeutics. Expression of thymidylate synthase (TS) has implication for effectiveness of pemetrexed in treatment of lung cancer. In this study, we investigated the AEG-1 activity to determine whether its expression is correlated with TS increasing resulted in chemoresistance of pemetrexed in patients with advanced lung adenocarcinoma. **Methods:** Patients with advanced lung adenocarcinoma treated with pemetrexed plus cisplatin as first-line chemotherapy were enrolled. Re-biopsy was performed until disease progression. Immunohistochemical stain of AEG-1 and TS were studied in all patients' tissue before chemotherapy and after disease progression. The primary antibodies used were anti-AEG-1 (1:1,000; chicken polyclonal), anti-actin (1:1,000; rabbit polyclonal; Santa Cruz), and anti-TS (1:1,000; mouse monoclonal; Abcam). The expression of TS and AEG-1 were calculated by H-score. The medical records were reviewed and analyzed, including data on age, gender, smoking status, epidermal growth factor receptor (EGFR) mutation status, treatment responses, and survival. **Results:** A total of six patients (3 male and 3 female) received first-line chemotherapy as pemetrexed/cisplatin for 6 cycles and continuation maintenance therapy with pemetrexed. The mean age was 57.2 years old. Overall best treatment response were partial response. The median of progression-free survival was 5.8 months. Re-biopsy was performed in all of them after disease progression. The expression of AEG-1 level increased from baseline to disease progression (mean, AEG-1, 133.3 to 175.0, $p = 0.001$), associated with elevation of TS level (mean, TS, 57.9 to 116,1, $p = 0.01$). **Conclusion:** Expression of AEG-1 associated with increase of TS contributes to chemoresistance of pemetrexed in lung adenocarcinoma. TS expression might be regulated by AEG-1 associated with development of chemoresistance to pemetrexed. **Keywords:** astrocyte-elevated gene-1, Thymidylate Synthase, pemetrexed, chemoresistance

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-107 Cofilin-1 as a Biomarker for Non-Small Cell Lung Cancer and a Potential Predictor to Platinum-Based Chemotherapy Resistance Juliano Cé Coelho[1], Carolina Beatriz Muller[2], Marco Antônio De Bastiani[2], Matheus Becker[2], Mariane Araújo Branco[3], Cristiano Feijó Andrades[4], Mauro Antônio Alves Castro[5], Fábio Klamt[2] [1]*Medical Oncology, Hospital de Clínicas de Porto Alegre, Porto Alegre/Brazil,* [2]*Department of Biochemistry, Universidade Federal Do Rio Grande Do Sul, Porto Alegre/Brazil,* [3]*Universidade Federal Do Rio Grande Do Sul, Porto Alegre/Brazil,*[4]*Hospital de Clínicas de Porto Alegre, Porto Alegre/Brazil,* [5]*Universidade Federal Do Paraná, Curitiba/Brazil*

Background: Non-small cell Lung cancer (NSCLC) is a highly lethal disease, whose symptoms are not common in the early stages, making detection difficult in this scenario. Biomarkers may be important for prognosis and prediction of therapy, resulting in more effective treatments and lower mortality rates. The expression of several genes have been tested for its potential as a biomarker for lung cancer, but none was positive as a prognostic factor. Cofilin-1 (*CFL1*) was first described in breast and ovarian cancer and emerges as a potencial biomarker for NSCLC. **Methods:** To identify and validate *CFL1* as a prognostic biomarker for NSCLC, independets cohorts obtained from published NSCLC microarray data (GSE3141/GSE42127/GSE13213) were used and the results were validated in a retrospective cohort. A semi-quantitative immunohistochemistry method was established measuring the intensity of IHC reaction using images software. The *CFL1*potential in predicting drug resistance was also explored. A panel of 120 anticancer compound and the *CFL1* levels in human NSCLC cell lines were analysed and an *in vitro* model for intrinsic and acquired cisplatin resistance protocols was established. A network graphic determining the association of *CFL1* expression and cisplatin drug resistance was drawn applying a spring model algorithm. Using the STRING database all proteins directly interacting with *CFL1* were retrieved and crossed with gene expression data of cisplatin-resistant cells. **Results:** *CFL1* levels in biopsies are able to discriminate between good and bad prognosis at early tumor stages, where high *CFL1* levels are correlated with lower overall survival rate ($P < 0.0001$). *In vitro* evidences suggest that *CFL1* is a biological predictor of cisplatin resistance. Cell lines with high *CFL1* expression are resistant to 21 of 30 alkylating drugs (including cisplatin and carboplatin). Intrinsically cisplatin resistant (ICR)-A549 cells presented a six-fold increase in cisplatin GI_{50} value and an increased in *CFL1* protein levels ($P < 0.01$). Also, a high activity of the *CFL1* gene network was found in cisplatin-resistant cells ($P < 0.01$) and in response to acute cisplatin treatment.



Conclusion: *CFL1* emerges as a biomarker of a more aggressive cancer phenotype. The potential of *CFL1* in screening patients less sensitive to alkylating agents represents a major impact with regard to the therapeutic strategy and should be explored further. Using a retrospective clinical cohort of NSCLC we intend to confirm the laboratory results in clinical patients. Also, we aim to establish a cutoff value of *CFL1*, and test it for predicting treatment response and patient survival. **Keywords:** Non-small cell long cancer, Chemotherapy resistance, biomarker, Cofilin-1

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-108 The Role of miR-30c-2* in Clinical Outcome and Drug Resistance in HPV-Infected Non-Small Cell Lung Cancer Ya-Wen Cheng *Graduate Institute of Cancer Biology and Drug Discovery, Taipei Medical University, Taipei/Taiwan*

Background: Lung cancer is leading cause of cancer death in Taiwanese women who are mostly to be life-time never smokers. Majority of drugs and combinations are used to treat with smoking lung cancer patients, not for nonsmokers. However, the 5-year survival rate in lung cancer patients remains ~15% during the past three decades. Therefore, dissolving tumor recurrence and drug resistance is urgent needed for improving outcome in lung cancer, especially in nonsmokers. Mir-30c-2* has been considered to be tumor suppressor gene in various cancers. MiR-30c-2* levels were associated with in gemcitabine sensitivity of lung cancer cells. Down-regulation of miR-30c promotes tumor invasion via an increased in MTA1 expression. **Methods:** We examined whether miR-30c and HPV oncoprotein expression could be associated with patients' outcome by collecting 150 lung tumors from patients with NSCLC to determine miR-30c, MTA gene expression,HPV 16/18 infection, and HPV 16/18 E6 and p53 protein expression by PCR-RFLP, nested-PCR, and immunohistochemical analysis. **Results:** Our previous reports have indicated that HPV16/18 infection may be involved in Taiwanese lung tumorigenesis. Preliminary data showed that miR-30C-2* levels were elevated 45-fold in E6-knockdown TL-1 cells as compared with parental cells with non-specific RNAi tranfection. More interestingly, MTA-1 expression was negatively correlated with miR-30C-2* in lung tumors from lung cancer patients. Expression levels of MTA-1 were positive correlated with tumor stage and nodal metastasis in tumor tissues of lung cancer patients. Our cell model studies also found that miR-30C-2* suppressed by E6 could contribute to tumor metastasis and drug resistance via an increased in MTA-1 expression. **Conclusion:** These results were showed that miR-30C-2* levels in patients' tumor tissues could be useful to predict outcome and therapeutic response and to select useful therapy drugs for lung cancer patients, especially in patients with HPV-infection. **Keywords:** HPV, tumor metastasis, poor prognosis, miR-30c

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.04-109 Epithelial-To-Mesenchymal Transition (EMT) and Acquired Resistance to PI3K-mTOR Inhibition in NSCLC Kathy Gately[1], Paul Dowling[2], Martin P. Barr[1], Niamh Kelly[1], Sinead Cuffe[1], Stephen P. Finn[1], Bryan Hennessy[3], Sinead Toomey[4], Kenneth J. O'Byrne[5], Susan Heavey[1] [1]*Thoracic Oncology Research Group, Trinity College Dublin/St. James'S Hospital, Dublin/Ireland,* [2]*Biology, Nui Maynooth, Kildare/Ireland,* [3]*Beaumont Hospital, Dublin/Ireland,* [4]*Royal College of Surgoens, Dublin/ Ireland,* [5]*Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane/Australia*

Background: The PI3K-Akt-mTOR pathway regulates cell growth and proliferation and is often dysregulated in NSCLC, making it an attractive therapeutic target in this setting. GDC-0980 is a selective dual inhibitor of PI3K and mTOR, which is currently in Phase II clinical trials for solid tumours. As with all targeted therapies, acquired resistance to GDC-0980 is anticipated to be a major hurdle in the success of this drug. The aims of this project are to (i) elucidate the frequency of PIK3CA mutations in an Irish cohort of

NSCLC patients and (ii) develop and characterise three cell line models of resistance to GDC-0980, each representing a different molecular subtype of NSCLC, in order to identify biomarkers of response/resistance to the drug that may dictate beneficial treatment strategies. **Methods:** DNA was extracted from 250 NSCLC patient tissue samples, and screened for 547 clinically relevant mutations in 46 genes using the Sequenom platform. H460, A549, and H1975 cells were cultured in GDC-0980 at IC50 concentrations over a period of several months, along with matched 'parent' cell lines. Development of resistance was assessed by monthly BrdU proliferation assays. Cell growth patterns were compared across the sensitive and resistant cell lines in real time using the xCELLigence platform. Cell lines were then interrogated for alterations in DNA (Sequenom), mRNA (SABiosciences arrays profiling expression of >150 genes), miRNA (Exiqon expression profiling of 2100 miRNAs) and protein (R&D Phospho Kinase array expression profiling of 43 kinases and 2 associated total proteins, PTMScan® Ubiquitin Remnant Motif (K-ε-GG) Kit from CST and Western blot analysis). **Results:** PIK3CA mutations occur in ~5% adenocarcinomas & 12% squamous cell carcinomas. H1975 cells (PIK3CA mutant and activated pAkt (Ser473/Thr308), pmTOR, pS6R) were most sensitive to GDC-0980, however they were the first to develop resistance to the drug. Results obtained from xCELLigence studies identified H1975 resistant (H1975R) cells as having the highest cell index out of all parent and resistant cell lines after 100 hours of cell growth, suggesting that these are the most aggressive cells. Initially a 33 miRNA signature was identified contrasting H1975P and H1975R. qPCR validation of miR-205 (a regulator of EMT) identified expression in H1975P cells but miR-205 was undetectable in H1975R cells. mRNA expression of Zeb1 & Zeb2 (direct targets of miR-205) were increased in H1975R cells compared to H1975P cells. 1,200 proteins were found to be differentially expressed between H1975P and H1975R cells. Increased expression of EMT proteins vimentin, desmin and filamin was detected in H1975R cells ($p < 0.05$, fold change >2). Vimentin overexpression in H1975R cells was confirmed by western blot analyis. Activation of EMT was identified as one potential mechanism of resistance to GDC-0980 in H1975R cells. **Conclusion:** The PI3K-mTOR pathway is frequently mutated in NSCLC, in particular squamous cell carcinoma, making it an ideal therapeutic target. Acquired resistance to GDC-0980 developed rapidly in NSCLC cell lines, (4-6 months) and correlates to the induction of EMT. Further elucidation of EMT regulation is under investigation and is crucial to the design of improved treatment protocols. **Keywords:** EMT, PIK3CA, PI3K-mTOR, Resistance

SESSION: POSTER SESSION/ PREVENTION AND TOBACCO CONTROL TUESDAY, SEPTEMBER 8, 2015

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-001 Assessment of Faculty and Staff Smoking Behavior at Total Ban on Smoking in Campus

Tomoyasu Uno *Health Care Center, Fukushima University, Fukushima-City/Japan*

Background: Recently, tobacco was positioned "the essence of smoking is nicotine addiction" and conjunction with advanced of scientific research. However, not only the social situation and also tobacco-free (TF) campus has not been fulfilled in Japan. Therefore, we investigated the current state about smoking and analyzed for improvement the recognition and for change behavior in non-medical TF campus since 2010. **Methods:** The questionnaire for all faculty members(employees) in our campus was performed. Subjects in this survey conducted in 2012-13 who enrolled over 20 years of age was examined in 132 cases that consent were obtained. **Results:** Base of analyzed subjects' characteristics were male/female(%)=60.6/39.4, 44.6±11.6 yrs (mean±SD), respectively. Current smoking prevalence was 8.3% and Ex was 25.0%. The starting smoking age was 17.9±3.2 (Mean±SD, [Range 6;32]),opportunity(%) was "Out of interest/Incidentally/Because neighboring smoke":11.7/10.2/8.6 were accounted for a large number (*multiple answers act). Tobacco products(connect with the Japanese government) sold in domestic market are required to have health warnings in Japanese, however, low level of recognition. This may be due to text size of tobacco package warning documents (Risk of Lung cancer, Secondhand smoke, etc.) are small, mild message and include educational problems. Currently, the people of quit smoking several decades has led to resmoking has been occasionally observed. After the Great East Japan Earthquake, resmoking rate was turned out to be themselves/ blood relationship persons 1.9%/3.3%. Surprisingly found that awareness of TF within the campus, 10.8% was unknown and continuing smoke. **Conclusion:** The results revealed that stood out that lack of information on the status of tobacco and TF campus, and be considered sharing the critical issue. Road to TF campuses is difficult now in Japan, however, we should be make as the realization. Awareness of TF was poor, therefor the necessity of further education about stop smoking was indicated. Alongside we need a certain degree of understanding about resmoking status according to psychological damage factors of post-disaster, however, faculty members should be effort to critical that leads to a complete TF campus for youth-adult student in low-dose radiation exposure risk area. We would like to further advance a this research. For this purpose, the achieving completely TF campus, not only our university, we think need initiatives of the entire university in Japan. In addition, by resolving the current college students and faculty/staff problems, the younger generation, it aims to contribute to that improvement will be prevention and cessation education to (e.g. elementary and junior high schools), smoking current situation that is later than other countries. **Keywords:** Smoke-Free Campus, Health Care Education

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-002 The Risk of Lung Cancer among Women Who Start Smoking as Teenagers

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Background: To examine the effect of smoking on lung cancer risk in a large population-based cohort of women, many of whom started smoking as teenagers **Methods:** We followed 102,098 women, ages 30 to 50 years, completing a mailed questionnaire at recruitment to the Nigerian-Ethiopian Cohort Study in 2011/2012, through December 2013. We used Cox proportional hazard regression models to estimate relative risk (RR) of lung cancer associated with different measures of smoking initiation, duration, and intensity adjusting for confounding variables. We conducted analyses on the entire study population, among women who had smoked for at least 20 years, among non drinkers, and separately for each country**Results:** Altogether, 1,240 women were diagnosed with incident, invasive lung cancer. Compared with never smokers, women who smoked for at least 20 years and who smoked 10 cigarettes or more daily had a RR of 1.34 (95% CI, 1.06-1.70). Likewise, those who initiated smoking prior to their first birth (1.27, 1.00-1.62), before menarche (1.39, 1.03-1.87), or before age 15 (1.48, 1.03-2.13) had an increased risk. The increased RR associated with smoking was observed among nondrinkers of alcohol, women with and without a family history of lung cancer, pre-menopausal and post-menopausal women, and in both countries **Conclusion:** Our results support the notion that women who start smoking as teenagers and continue to smoke for at least 20 years have increased lung cancer risk **Keywords:** lung cancer, smoking, teenagers, cancer risk

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-003 Poor & Heavy Smokers in Nigeria Face Higher Risk of Lung Cancer DNA Damage

Emmanuel Odiase *Epidemiology, University of Ibadan, Abuja/Nigeria*

Background: Many poor smokers in Northen Nigeria who started smoking at teenage, smoked for at least 15 years, have the least access to medical attention and who probably smoke more sticks and/or packets because of the cheap price of cigarettes may face a higher risk of entire DNA damage from lung cancer **Methods:** There were 98,500 men, ages 30 to 55 years involved in a community-based tobacco control/smoking cessation study through questionnaires in English and the local languages for two Nigerian geo-political zones which are the North western and North eastern with the most smoking prevalence in the country. The Nigerian Cohort Study was from 2007 through December 2013. Relative Risk (RR) of tobacco-related lung cancer associated with different measures of smoking initiation, duration, and intensity adjusting for confounding variables were estimated. There were also analyses conducted on the entire study population, among men who had smoked for at least 15 years, most of whom started smoking at youth. Study was separately for each geo-political zone. **Results:** From the entire number participating in the study, 19,200 men or about 20% were diagnosed with tobacco-specific lung cancer. Compared with never smokers, men who smoked for at least 15 years and who smoked 10 cigarettes or more daily had a higher Relative Risk (RR). On the other side, men who had smoked for at least 15 years, but were priviledged to periodic hospital visits or started smoking after teenage, had their lung cancer risk reduced and/or averted. The increased RR of DNA damage from lung cancer associated with smoking was higher amongst "I dont care" smokers in both geo-political zones in Northern Nigeria. **Conclusion:** Results here show that young initiation, poverty, high tobacco consumption, duration of smoking and inacesability to regular medical check up very well increases the risk of lung cancer leading to entire DNA damage. **Keywords:** lung cancer, DNA damage, tobacco, nigerian

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-004 ETS Exposure Presents a High Risk of Lung Cancer to Restuarant/ Bar Workers in Nigeria

Emmanuel Odiase *Epidemiology, University of Ibadan, Abuja/ Nigeria*

Background: Several studies have proved that over ninety percent of lung cancer cases are caused by tobacco. Smoking causes numerous cancers but surely has lung cancer on the highest. The alarming issue at the hand is that exposure to Environmental Tobacco Smoke-ETS may result to lung cancer among innocent non smoking employees in work places or elsewhere. **Methods:** Further from an earlier study where about 200 restuarant and bar non-smoking staff in four states in Nigeria-Lagos, Kano, Port-Harcourt and Abuja from were examined, we scaled up to conduct a similar expanded study among 450 non-smoking bar employees and regular non smoking bar users to reteirate our claims in 4 additional states. Level of ETS exposure was compared with survey results from participants. Duration of employment and level of exposure(number of hours daily) to Environmental Tobacco Smoke (ETS) for each person was also taken into account. **Results:** We discovered that participants exposed to workplace second-hand smoke were more likely to have any detectable level of NNAL (P=.005) and higher mean levels of NNAL ($P < .001$) compared with non-exposed participants. Increased levels of NNAL were also associated with hours of a single workplace exposure. Furthermore, some risks were noticed from non smoking daily bar users. **Conclusion:** Non-smoking employees left unprotected from workplace secondhand smoke exposure had elevated levels of a tobacco-specific carcinogen in their bodies. All workers—including bar and restaurant workers—should be protected from indoor workplace exposure to cancer-causing secondhand smoke. This calls for countries without a comprehensive National Tobacco Control Law to pass one as soon as possible in line with the WHO Framework Convention on Tobacco Control- FCTC. **Keywords:** tobacco, lung cancer, non smokers, ETS

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-005 Radon Exposure Prevention of Lung Cancer Policies in Brazil
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Background: Lung cancer is the leading cause of cancer death in the United States and other industrialized countries. The most important risk factor is still smoking. However, given the increased incidence of lung cancer in non-smokers, it is necessary to increase knowledge of the other risk factors. The Radon (Rn) is a noble gas and is the most important natural source of human exposure to ionizing radiation. Exposure to high levels of this radioactive gas are related to increased risk of developing lung cancer. **Methods:** We have conducted a survey on the website of the Brazilian National Health Surveillance Agency (ANVISA), LAMIN (Mineral Analysis Laboratory), CPRM (Geological Survey of Brazil), Ministry of Health and Pubmed The objective was to highlight the importance of measuring the concentration of this gas indoors and identify which steps should be taken for radiological protection. **Results:** We emphasize that lung cancer is a major public health problem and the exposure to Rn indoors should be considered as a risk factor in patients with non-smokers lung cancer. Buildings or houses with high concentrations of radon should be identified. However, currently, there is not in Brazil, a country with great potential of mineral extraction, any regulated recommendation for control of exposure to Rn. **Conclusion:** Exposure to indoor Rn should be considered as the main risk factor in patients with non-smokers lung cancer and second risk factor in smokers. Buildings or houses with high concentrations of radon should be identified. It is essential that regular reviews of radon levels are carried out at these sites **Keywords:** lung, Cancer, Radon

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-006 Meta-Analysis of Radon Indoor Concentrations and Risk of Lung Cancer
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Background: Our ongoing research is assessing stem cells alterations in cancer due to indoor radon exposure. Therefore, we performed a meta-analysis of previous studies on radon exposure and lung cancer to evaluate the strength of the statistical and radon-detection methods for determining exposure-response risk levels. **Methods:** Literature search used PubMed. **Inclusion criteria:** a), original case-control studies; b), use of alpha track detectors; c), report weighted average values of radon concentrations over time and/or cumulative exposure rates; d), include only lung cancer diagnosis by pathology and/or imaging; e), frequency-matched controls by age, gender and smoking status; f), enough samples and data for odds ratio estimation and variations; g), published in English. **Data Extraction:** Statistical data extracted from the selected studies. Studies selected were stratified by level of exposure to evaluate the dose-response relationships. Adjusted odds ratios (CI 95%) extracted for radon concentrations expressed in Bq/m-3). All data was later adjusted to WHO's categories 0-99, 100-199, 200-299 and >300 Bq/m-3. **Meta-analysis:** For each study, analysis of the weighted linear regression of log-adjusted odds ratio was performed according to the average radon concentrations. Coefficients and 95% confidence intervals were calculated according to the various levels of radon concentration. **Sensitivity analyzes:** Separate meta-analysis was performed by grouping studies with similar characteristics **Results:** The log-OR for lung cancer risk was 1.22 higher at radon indoor levels >Bq/100-3, being such levels more frequent in the homes of lung cancer cases. As for smokers, the 1.14 metanalytical measure indicates a log-OR of 3.19 (CI: 95%). **Conclusion:** This meta-analysis suggests a statistical significant higher risk of lung cancer in individuals exposed to indoor radon levels >Bq/100-3. **Keywords:** lung cancer risk, environmental factors, indoor radon gas, alpha particles detectors

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-007 Role of Carbon Monoxide Analyser and NRT in Smoking Cessation
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Background: Tobacco consumption is increasing day by day world wide. In developed countries, the pattern of using tobacco is in the form of smoke where as in developing or underdeveloped countries both form (smoke & smokeless) of tobacco is in use. In developing countries like India, more than 2200 people are dying daily because of consuming tobacco in various forms, data issued by WHO & GATS. Dentist can play an important role in tobacco cessation , as they closely deal the patient of any gender and of any age groups. Smoking is very common among age of 20-45 years. Most of the dental problems arises during this age group and may be because of smoking. Dentist can counsel and motivate the patient by taking case history of the patient on Dental chair to quit this habit. He can use Carbon Monoxide analyser as a helping tool to tell the amount of carbon monoxide in patients lungs. CO analyser can be used as threating tool for smokers and later we can advice Nicotine replacement therapy according to the dependency on nicotine. **Methods:** Carbon monoxide analyser is a device which is used to measure the amount of carbon monoxide in smokers lung. It is of various types:- a) CO analyser with USB port which can be attached to Computer and printer ,b) Baby Carbon monoxide analyser. Benefit of CO analyser with USB port- it can be used in clinic and we can save data as clinic record and can give print out to the patient as their motivational agent. where as Baby CO analyser can be used for masses in camps. It immediately show the level of CO through their indicator lights. CO Analyser parts , it consists of D piece and instrument body. 1st step- ask the patient to take deep breath and hold it for 15 seconds then patient will blow the air slowly in D piece which is attached to anlyser , aiming to empty the lungs completely. The instrument will then display the level of Carbon monoxide by the relevant indicatror lights. CO is calculated in PPM. Normal Range - a) 0-6ppm- Normal (green light - less then 1 cigarette): b) 7-10ppm- Orange light (light smoker- 2-5 cigarette) ; c) 11-15ppm- regular smoker (red light) ; d) 16-25ppm- red light with beep sound(chronic smoker). After this, we can do nicotine urine test by centrifugal method and prescibing the NRT products depending upon the investigation result. NRT is of differnt types- Gums, Patch, Nicotine nasal spray, Lozenges,Inhaler, etc. **Results:** CO anlyser can be helpful in knowing "SWOT" analysis of the patient. It will be a beneficial tool in counselling and helping the smokers to quit the habit. "SWOT - Strength, Weakness,Opportunity, Threatning analysis. **Conclusion:** By using CO analyser & NRT, we can help tobacco user to quit the habit by eliminating the exposure to 2nd hand smoke, prevent quiting among young and adults. Prevent initiation among youths at Dental clinics. **Keywords:** CO analyser, NRT products, Dentist as Tobacco therapist

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-008 The Role of Haplotype in 15q25.1 Locus in Lung Cancer Risk: Results of Scanning Chromosome 15
Xuemei Ji[1], Jiang Gui[1], Younghun Han[1], Paul Brennan[2], Yafang Li[1], James Mckay[2], Neil Caporaso[3], Pier A. Bertazzi[4], Maria T. Landi[5], Christopher I. Amos[1] [1]*Biomedical Data Science, Dartmouth College, Hanover/NH/United States of America,* [2]*International Agency for Research on Cancer, Lyon/France,* [3]*National Institutes of Health, Bethesda/MD/United States of America,* [4]*University of Milan, Milan/Italy,* [5]*National Cancer Institute, Bethesda/NH/United States of America*

Background: The role of haplotypes and the interaction of haplotypes and smoking exposure in the etiology of lung cancer have not been well characterized. **Methods:** We analyzed data from an Italian population-based case-control study among 1815 lung cancer cases and 1959 healthy controls in discovery phase and performed a validation using a case-control study comprising 2983 lung cancer cases and 3553 healthy controls of European ancestry for replication. Haplotype analyses and logistic regression were used to explore the casual haplotype and its association with lung cancer risk. **Results:** Sliding window haplotype analysis within chromosome 15, evaluating 4,722,250 haplotypes, and pair-wise haplotype analysis identified that rs16969968-rs588765 was the most significant haplotype associated with lung cancer risk (omnibus $p = 8.35 \times 10^{-15}$ in discovery and 7.26×10^{-14} in replication), and improved the prediction of case status over that provided by the individual SNPs rs16969968 or rs588765 (likelihood ratio test $p = 0.006$ for rs16969968 and 3.83×10^{-14} for rs588765 in discovery, 0.009 for rs16969968 and 4.62×10^{-13} for rs588765 in replication, compared with rs16969968-rs588765). Compared to the wild type homozygous diplotype, the CA/CA homozygote exhibited an approximately 2-fold increase risk for lung cancer (OR = 2.12; 95% CI, 1.46 - 3.07 in discovery, and OR = 2.01; 95% CI, 1.51 - 2.67 in replication). Even among never-smokers, individuals with CA/CA homozygous diplotype had an increased risk of lung cancer with borderline significance in the discovery (adjusted OR = 1.75, 95% CI, 0.96 – 3.19) and statistical significance in the replication (adjusted OR = 2.10, 95% CI, 1.12 – 3.96), compared to those with combined genotypes (CG/CG + CG/TG). We also found that smokers with the CA/CA homozygous diplotype had a more than 13-fold increased risk for lung cancer in the discovery (adjusted OR = 13.42, 95% CI, 8.21 – 21.95) and 15-fold increased risk in the replication (adjusted OR = 15.52, 95% CI, 9.85 – 24.45), compared to nonsmokers with the combined genotypes (CG/CG + CG/TG). **Conclusion:** The rs16969968-rs588765 haplotype modifies lung cancer risk more than effects from individual variations at rs16969968 or rs588765, may be a marker of genetic susceptibility to lung cancer even among never-smokers, and has a joint effect with smoking exposure on lung risk.This knowledge may facilitate our understanding of lung cancer etiology and identifies a particularly high risk. **Keywords:** genetic factor, lung cancer, haplotype, smoking

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-009 Tobacco Addiction and Perception of Risk of Lung Cancer in Vulnerable Populations
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Background: Social indicators of vulnerable populations are associated with increased rates of comorbidities and risk factors for cancer but not with screening attendance, as previously shown by the French EDIFICE surveys. The present work sought to determine whether living in poor economic social conditions is associated with specific behavior or beliefs that increase exposure to the risk factors for lung cancer. **Methods:** The 4th French nationwide observational survey, EDIFICE 4, was conducted by phone from June 12 to July 10, 2014 among a representative sample of 1602 individuals aged between 40 and 75 years, using the quota method. Individuals were questioned about their smoking habits. Tobacco addiction was evaluated in current smokers using the Fagerström Test for Cigarette Dependence (FTCD) score, which ranks participants into one of four groups: no dependence, low, moderate, and high dependence. Risk perception compared to the average-risk population was self-assessed. Data were analyzed according to the validated EPICES vulnerability score. **Results:** Vulnerable individuals (N=455) were more frequently current smokers than non-vulnerable individuals (N=941) (34.1% vs 19.9%;

P≤0.01) and less frequently former smokers (25.9% vs. 35.8%; P≤0.01). Compared to the non-vulnerable population, current and former cigarette smokers in the vulnerable population were more likely to have started smoking before the age of 15 (33.8% vs. 25.5%, P≤0.05), and had a higher average consumption (16.6 pack-years [SD 16.25] vs. 13.59 pack-years [SD 16.44]; P≤0.01). Vulnerable individuals were also more likely to stop smoking for periods of less than 1 year or for 1-9 years (18.6% vs. 10.4% and 29.2% vs. 19.4%, respectively; P≤0.05) but were less likely to quit for longer periods (10-19 years, 17.6% vs. 27.1%, P≤0.05; 20-29 years, 17.2% vs. 22.5% and ≥30 years, 17.5% vs. 20.3%, not statistically different). Likewise, vulnerable individuals had higher average FTCD scores (3.24 [SD 2.38] vs. 2.55 [SD 2.16], P≤0.01) and were more frequently ranked as moderately or highly dependent on cigarettes (32.0% vs. 21.5%, P≤0.05). Respondents were asked about the number of cigarettes per day they considered to be associated with no risk of lung cancer; average replies were 3.01 (SD 5.40) in the vulnerable population vs. 1.93 (SD 3.90, P≤0.01) in the non-vulnerable population. The former were also less likely to spontaneously cite a number of lung cancer risk factors (unhealthy life-style 93.8% vs. 97.5%, active smoking 91.3% vs. 95.5%; passive smoking 60.4% vs. 72.0%; P≤0.01). But they were more likely to rank their own risk of lung cancer as higher than that of the average population (22.6% vs. 16.6%, P≤0.01) and to consider screening as more distressing than reassuring (25.9% vs 18.3%, P≤0.01). **Conclusion:** Because they develop a heavy, long-lasting consumption of tobacco and are less likely to quit smoking permanently, vulnerable individuals are more exposed to the tobacco-consumption-related risks of lung cancer. Paradoxically, they also appeared both less concerned and more anxious about the risks of lung cancer than non-vulnerable populations. These results highlight the urgency of implementing information campaigns, prevention messages, and smoking cessation support specifically targeting this vulnerable population. **Keywords:** tobacco addiction, lung cancer risk, vulnerable population

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-010 The Chronic Respiratory Infection as a Background of the Lung Cancers Tsutomu Yoshida, Takayuki Nakagawa, Kiyomi Shimoda, Miyako Hiramatsu, Yuji Shiraishi *Chest Surgery Division, Respiratory Disease Center, Fukujuji Hospital, Japan Anti-Tuberculosis Association, Tokyo/Japan*

Background: It had been pointed out about the respiratory infectious disease that the tuberculosis patients had increased risk of lung cancers, and the lung cancer patients had increased risk of tuberculous infection. In recent years, primary lung cancer cases are increased, despite of decreasing of tuberculosis infection and, on the other hand, of increasing of chronic respiratory infectious diseases such as the pulmonary non-tuberculous mycobacteriosis or mycosis. A purpose of this study is to research the chronic respiratory infectious diseases as a background of the lung cancer treatment. **Methods:** From January, 2010 to December, 2014, 431 cases of radical operations for primary lung cancers were performed in our institute. A bacteriological search by the expectoration and bronchus absorption sputum was examined in 389 cases preoperatively. Among these cases, we retrospectively researched about the fungal infections and mycobacterial infections. **Results:** Among the 431 primary lung cancer cases, 19 cases of fungal infections were detected, 12 cases of non-tuberculous mycobacterium infections were detected, four were co-existing and none was tuberculosis. In the patient background of mycosis, gender was 15 cases of male and four of female, the mean age was 69.7±8.1 years old (53-88 years old), and mean smoking index was 1073 (0-2640). The histological types of the lung cancers were eight cases of squamous cell carcinoma, seven of adenocarcinoma, each one of small cell lung cancer, pleomorphic carcinoma and LCNEC. The pathological stages of the lung cancers were nine cases of stage I, five of stage II, four of stage III and two of stage IV. The detected species of bacteria were nine cases of *Candida spp.*, eight of *Candida albicans*, two of *Aspergillus fumigatus* and one of *Aspergillus niger*. The patients had past history of tuberculosis in three cases, cancer in four, diabetes in 6 and continuous treatment by steroid in two. In the patient background of non-tuberculous mycobacteriosis, gender was 7 cases of male and 5 of female, the mean age was 71.7±10.2 years old (50-88 years old), and mean smoking index was 556 (0-1800). The histological types of the lung cancers were six cases of adenocarcinoma, three of LCNEC, two of squamous cell carcinoma, one of small cell lung cancer. The pathological stages of the lung cancers were eight cases of stage I, one of stage II, two of stage III and one of stage IV. The detected species of bacteria were 11 cases of *Mycobacterium avium* complex and one of *Mycobacterium mucogenicum*. The patients had past history of cancer in two cases and continuous treatment by steroid in two, but none of tuberculosis and diabetes. The five year survival rate of the lung cancer cases with the chronic respiratory infections was 63.0% and that without the chronic respiratory infections was 76.6%. The lung cancer cases with chronic respiratory infections showed tendency of poor prognosis, although there was no significant difference between two groups (p=0.087). **Conclusion:** The lung cancer cases with chronic respiratory infections had past history of coexisting disease, and showed tendency of poor prognosis. **Keywords:** mycosis, mycobacteriosis, lung cancer

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.05-011 Presence of Pleural Plaques and/or Asbestosis and the Risk of Lung Cancer in a Crocidolite Asbestos Exposed Population from Western Australia Fraser Brims[1], Bill Musk[1], Alison Reid[2], S C Pang[1], Peter Franklin[3], Susan Peters[3], Nick De Klerk[3] [1]*Respiratory Department, Sir Charles Gairdner Hospital, Perth/Australia,* [2]*Curtin University, Perth/WA/Australia,* [3]*University of Western Australia, Perth/WA/Australia*

Background: Asbestos exposure is associated with dose-dependent risk of benign pleural disease, lung cancer and mesothelioma. While an association between asbestosis and lung cancer (even after adjustment for asbestos exposure) is well established [Reid et al, OEM 2005], the link between lung cancer and the presence of pleural plaque remains controversial. **Methods:** We followed 2,218 subjects exposed to crocidolite asbestos as miners (n=1286) or mine township residents, monitored with annual review, chest radiography (CXR) and outcome linkage to national cancer and mortality registry data over a 25-year period. Subjects were followed up from the date of their latest x-ray taken a year or more before the date of death, cancer incidence, or end of follow-up. Hazard ratios for lung cancer were estimated by Cox regression, with age as the underlying matching time variable, for sex, tobacco smoking, asbestos exposure estimates (time since first exposure and fibre/ml years), International Labour Organisation CXR readings for asbestosis (defined as profusion score ≥ 1/0) and presence (and extent) of pleural plaques. **Results:** Mean age at follow up was 60.6 years, 1,575 (71%) were male, 328 (14.8%) had any pleural plaque and 359 (16.2%) had asbestosis. 103 (4.64%) lung cancers were recorded. 1568 (70.7%) were ever-smokers with a mean tobacco exposure of 39.3 pack years.

	HR	Lower 95% CI	Upper 95% CI	p-value
Log (yrs) SFE	1.77	.60	5.22	0.298
Ever smoker	18.1	2.5	132	0.004
Pack years	1.009	1.005	1.01	<0.0005
Female	0.75	.38	1.48	0.408
Profusion: 0/1	1.88	1.14	3.10	0.013
1/0	1.64	0.87	3.07	0.124
1/1	3.64	1.83	7.24	<0.0005
1/2	6.10	2.03	18.3	0.001
≥ 2/1	2.18	0.64	7.49	0.215
Log f/ml yrs	1.223	1.076	1.390	0.002
Any PP	1.048	0.601	1.826	0.869
SFE = since first exposure; f/ml = fibres / ml; PP = pleural plaque; HR = hazard ratio; CI = confidence interval				

Table 1. Hazard ratios for diagnosis of lung cancer **Conclusion:** In our population, the presence of pleural plaque is not associated with an increased risk of subsequent lung cancer. This is contrary to a recent report that had smaller numbers of lung cancer and used death certificates [Pairon, AJRCCM, 2014]. As we have demonstrated previously, the presence of asbestosis and cumulative asbestos exposure both contribute to increased subsequent lung cancer risk, although previous tobacco smoke exposure remains the strongest risk factor. **Keywords:** lung cancer, asbestos, pleural plaque, epidemiology

SESSION: POSTER SESSION/ SCREENING AND EARLY DETECTION TUESDAY, SEPTEMBER 8, 2015

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-001 Community-Based Low-Dose Computed Tomography (LDCT) Lung Cancer Screening in the Histoplasmosis Belt of the United States Emilia A. Porubcin, Judith A. Howell, Steven A. Cremer *Unity Point Medical Center, Moline/IL/United States of America*

Background: LDCT lung cancer screening has been incorporated into most major American medical societies' screening guidelines and has recently been approved for reimbursement by the Centers for Medicare and Medicaid Services. However, its performance in a non-tertiary care community setting with a high prevalence of fungal infections has not been sufficiently studied. **Methods:** Beginning in April 2013, high-risk adults ages 55-80 with at least a 30 pack-year smoking history, including former smokers who had quit within the previous 15 years, were prospectively evaluated with an LDCT scan performed at our community hospital (Unity Point Health Medical Center in Quad Cities, Illinois). Standard National Lung Screening Trial exclusion criteria were followed with the exception of previous chest CTs being allowed up to 12 months rather than 18 months prior to study entry and extension of age of the studied population to 80 years. An oncology nurse navigator contacted and monitored all participants. The CTs were interpreted by a local radiology group with two radiologists spearheading the program and ensuring consistent interpretations. **Results:** As of April 2015, we have evaluated 176 participants, 86 of whom were men (49%). Median age of the studied population was 64 years (range 55 - 80). Screening adherence was 97% with a total of 36 participants (20%) having at least one follow-up LDCT. 40 participants (23%) had a positive baseline screening test. 1 patient had a baseline screening test positive for pneumonia and was subsequently diagnosed with stage IV non-small cell lung cancer (NSCLC). 135 patients

(77%) had a negative baseline screening test. Benign appearing calcified granulomas were detected in 60 participants (34%) with a nearly identical relative distribution between those with negative and positive screening tests. Only seven follow-up PET-CT scans were necessary. One was performed for staging purposes after a histologically proven cancer diagnosis. Six were performed for evaluation of lesions felt to be highly suspicious on LDCT. Four of the six PET-CTs were positive and led to a diagnosis of malignancy. A total of five malignancies (2.8%) were detected as a direct result of the screening. Four were NSCLC, of which three were stage I and one was stage IV. One participant was diagnosed with Marginal Zone Non-Hodgkin Lymphoma of the lung. All biopsies that were performed were positive for malignancy. No unnecessary biopsies were performed. No biopsy-related complications occurred. Four out of five patients with detected malignancies are still alive and doing well. Two patients (1%) died during the follow-up. One patient died secondary to an advanced NSCLC detected by the screening program; the other death was due to an unrelated cause, pneumonia. **Conclusion:** To our knowledge, this is the first community hospital-based study evaluating the results of LDCT lung cancer screening in an area of the United States endemic for both Histoplasmosis and Blastomycosis. LDCT cancer screening in such a setting can be done effectively without significant false positive results due to fungal infections. A significant number of early stage lung cancers were detected without excessive testing or complications. **Keywords:** community-setting, Screening, lung cancer, histoplasmosis

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-002 Preliminary Results of Early Stage Lung Cancer Detection Using Low-Dose Computed Tomographic Screening Huimin Wang[1], Jiajun Teng[1], Yanwei Zhang[1], Qunhui Chen[2], Jianding Ye[2], Jiatao Lou[3], Rong Shi[4], Bo Jin[1], Xueyan Zhang[1], Jianlin Xu[1], Xue Dong[1], Yuqing Lou[1], Baohui Han[1] *[1]Department of Pulmonary, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai/China, [2]Department of Radiology, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai/China, [3]Department of Clinical Laboratory, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai/China, [4]Department of Public Health, Shanghai Jiaotong University, Shanghai/China*

Background: The overall 5 years survival for lung cancer patients is approximately 16%, a survival advantage is noted for early stage lung cancer, with 5-year survivals up to 65%. However, only 10% patients are diagnosed when the primary tumor is resectable. Our trial was conducted to improving the early stage lung cancer detection rate using low-dose CT. **Methods:** Eligible participants enrolled in our trial were local residents in 6 communities located in Xuhui District, Shanghai, China, aged from 45 to 70 years and with either of the following risk factors: 1) history of cigarette smoking ≥ 20 pack-years, and, if former smokers, had quit within the previous 15 years; 2) malignant tumors history in immediate family members; 3) personal cancer history; 4) professional exposure to carcinogens; 5) long term exposure to second-hand smoke; 6) long term exposure to cooking oil fumes. From November 2013 to November 2014, the high risk residents received free chest low-dose CT (LDCT) scans at Shanghai Jiao Tong University Affiliated Shanghai Chest Hospital. The findings of CT scan were identified by three experts. The shadows on the lungs were grouped accordingly. If imaging was highly suggestive of malignancy, the expert group would have further discussion. The residents would be assigned to undergo biopsy or surgical resection directly. **Results:** Up to January 2015, 2933 participants were received LDCT screening. According to the inclusion criteria, 2892 persons at high risk for lung cancer were included in our trail, and 41cases were finally excluded. Of the 2892 aged 45 -70 years old cases, the median age was 61years old. Of the included participants, 1151 cases were male, and 1741 cases were female. Pulmonary small nodules were found in 742 cases; small nodules detection rate was 25.66% (742/2892). 69 cases were suspected of lung cancer. Accounting for pulmonary small nodules was 9.30% (69/742), and was 2.39% (69/2892) of the total number of screening high risk population. 23 cases underwent surgery, with 22 lung cancer (10 males and 12 females) and 1 hamartoma, representing a positive lung cancer detection rate with low-dose CT screening of 0.76% (22/2892). 21 of the 22 cases resected lung cancers were stage I (95.45%) and 1 was stage II (4.55%), with 21 adenocarcinomas (95.45%) and 1 squamous lung cancer (4.55%). **Conclusion:** The application of low-dose CT screening prompted an increase detection rate of early stage lung cancers (stage I and II) in the high risk population. **Keywords:** high risk population, lung cancer, Screening, low-dose CT

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-003 A System-Wide Lung Cancer Screening Program: First Year Experiences John C. Ruckdeschel[1], Andrew T. Miller[2], Patricia Kruger[3], Braden Row;Ey[3], Teresa J. Robertson[4], William T. Sause[5], Karen Connor[6], Denitza P. Blagev[7] *[1]Thoracic Oncology, Synergy Cancer Center, Las Vegas/NV/United States of America, [2]Internal Medicine, Intermountain Healthcare, Murray/UT/United States of America, [3]Oncology, Intermountain Healthcare, Murray/UT/United States of America,[4]Clinical Information Systems, Intermountain Healthcare, Murray/UT/United States of America, [5]Radiation Oncology, Intermountain Healthcare, Murray/UT/United States of America, [6]Diagnostic Radiology, Intermountain Healthcare, Murray/UT/United States of America, [7]Division Ofpulmonary Medicine, University of Utah, Salt Lake City/UT/United States of America*

Background: The United States Preventive Services Task Force (USPSTF) and National Comprehensive Cancer Network (NCCN) recommend screening with Low-Dose Computed Tomography (LDCT) for asymptomatic patients at high risk of lung cancer. It remains unknown, however, how well these recommendations will translate to the medical community at large. Here, we report on the initial year of a statewide lung cancer-screening program implemented at Intermountain Healthcare. **Methods:** We developed a comprehensive lung cancer screening program open to patients aged 55-80 with either a 30 pack-year smoking history (USPSTF criteria) or a 20 pack-year smoking history plus a risk factor (NCCN criteria) who continue to smoke or have quit within the past 15 years. At the time of patient enrollment, a nurse coordinator was supposed to complete an electronic intake form that assessed patient screening eligibility, smoking history, symptoms, and environmental carcinogen exposure. Radiographic reporting and nodule evaluation were standardized. **Results:** From September 4, 2013 to October 1, 2014, 258 patients were referred to the lung cancer-screening program. Thirty-four patients were ineligible for screening based on the aforementioned guidelines while 17 patients declined screening. Of the 207 patients who met USPSTF or NCCN criteria, forty-five were not processed by the coordinator primarily due to physician office staff calling radiology directly. Of the 162 properly processed patients the mean age was 65.7 +/- 5.5 years, 50.6% (82) were active smokers, 45.7 %(74) had additional environmental exposures and 61.1% (74) reported symptoms at the time of intake. Of the 74 patients with symptoms 66 (89%) reported cough. Of the total of 207 who were screened 48.3%(100) had no nodules, 30.4% (63) had a nodule >6mm requiring follow up studies, 6.8% (14) had a nodule suspected of being cancer and 14.5% (30) had significant incidental findings. Eight of the 14 patients with suspicious lesions had been evaluated at the time of review. Three were found to have lung cancer (stages 1A, 2A and 4) and 2 others had a non-lung malignancy (renal, lymphoma). Three patients had benign lesions (2 hamartomas and 1 fibrosis). **Conclusion:** Despite vigorous attempts to standardize the process and broad discussion of the indications with physician groups, numerous patients who were ineligible were referred and several underwent screening when physician's office staffs were able to bypass the coordinator step. Cough as a symptom needs further clarification as a significant majority of patients present with cough. The CMS recommendation for physician counseling is likely to have little impact as most physicians are not knowledgeable about the nuances of screening for lung cancer. For lung screening to realize its true potential these technical issues must be resolved. **Keywords:** lung cancer screening, lung nodule

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-004 Lung Cancer Screening Perceptions in Vermont Edmund Folefac *Medicine, Unversity of Vermont, Burlington/VT/United States of America*

Background: In 2014 the University of Vermont Cancer Center obtained accreditation for the new Lung Cancer Screening Program from the American College of Radiology. During the first 6 months of the LDCT screening program, there were 100 participants in the program. Patient understanding of lung cancer screening did not seem to be clear. **Methods:** We conducted a preliminary survey to define the perceptions of the first 76 participants enrolled in the program. A 30 question questionnaire was done by telephone survey. Descriptive statistics were used. **Results:** Thirty-six participants (47%) responded to the survey. Referral of the majority of participants was done by less than primary care providers. 32Participants did not know about the program before they were told by their doctor. Although 92% of respondents knew they had a "lung X-Ray" done, 14% did not know why the test was done and only 28% knew they had undergone a LDCT of the lungs. All 36 patients knew they had received the results of the test and 26 (72%) had a follow-up appointment with their provider. Fourteen percent had further testing and 3 were diagnosed with early stage lung cancer. Only 25% received education material on lung cancer screening program. Eleven participants (30%) would have liked more information. Interestingly, 45% were not interested. Twenty-two percent incurred additional expenditure from $10 to $1200. Over 90% of the participants would agree to refer a family member to the program if this was an option. Most patients (75%) reported that the test did not affect their mood. The highest level of anxiety was in those who were diagnosed with cancer. Of the current smokers (N=20), only 17 (85%) were counseled to quit smoking. Of the 17 participants who received counseling, 9 followed the advice and sought help to quit, 2 did decrease smoking, and 7 did not follow the advice. Over 97% of patients (35/36) wanted to know what other anomalies were diagnosed on the LDCT. Interestingly, these 35 patients thought they would be more likely to quit if they had a better understanding of the damage done by tobacco. **Conclusion:** LDCT scan is an effective tool to diagnose early stage lung cancer and does not affect the mood of the majority of the participant, but it is still much underutilized mainly because of the knowledge gap among providers responsible for educating and referring at-risk patients. Most of the participants were satisfied with the program but there is a need to better educate the public and primary providers about the purpose of the study and the importance of smoking cessation. Finally showing participants the LDCT images of their lungs and counseling them about tobacco related changes in their lungs found during screening can be a power tool to help them quit smoking. **Keywords:** lung cancer screening

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-005 Lung Cancer Risk Perception: Findings from the PAIRS-COPD Study Stephen P. Brummell[1], Angela M. Tod[2], Trevor Rogers[3], Dawn Bowen[4], Mark Boon[4] *[1]Health and Wellbeing, Sheffield Hallam University, Sheffield/United Kingdom, [2]University of Manchester, Manchester/United Kingdom, [3]Doncaster Royal Infirmary and Hon. Senior Lecturer, University of Sheffield, Doncaster/United Kingdom,[4]Conisbrough Group Practice,, Doncaster/United Kingdom*

Background: Detecting new or early lung cancer symptoms in people who have COPD is especially difficult as early signs of disease may be masked by existing chronic respiratory symptoms. Public awareness of lung cancer symptoms remains low despite recent media campaigns. A lack of knowledge and understanding of their condition and associated risks may account for patient symptom reporting delay. Over 60% of UK

lung cancer patients are diagnosed at a stage where curative treatment is no longer an option. Early reporting and diagnosis can provide curative treatment options and improved outcomes. New, cost effective interventions that promote timely detection and diagnosis and that are acceptable to patients are required. Prospective Assessment of Incident Respiratory Symptoms (PAIRS-COPD) is a feasibility study that evaluated four-monthly telephone reviews of COPD patient's respiratory symptoms, by a primary care nurse. This abstract presents findings that identify the intervention's effectiveness in prompting symptom reporting and referral and explores participant's perceptions of their chest condition and lung cancer risk. **Methods:** Mixed methods were used. Quantitative analysis of frequency of identification of indications for a chest X-ray was undertaken with COPD patients on a primary care register (n=77). A purposive sample (n=12) were selected for semi-structured telephone interviews (7 women and 5 men) to evaluate patient perceptions and experiences and acceptability of the intervention. Interviews were audio taped and transcribed. Thematic analysis was used. **Results:** Interviewees revealed that living with respiratory symptoms for protracted periods resulted in a high level of symptom tolerance. New symptoms were assumed to be an inevitable and expected part of their normal illness trajectory or of aging more generally. Awareness of prognostic implications and lung cancer risk was low. The interviewees reported the belief that decline was inevitable. This, combined with their worsening respiratory condition and high symptom tolerance, had made delay in reporting new or deteriorating symptoms inevitable. However, as a consequence of the intervention, symptoms recommended to prompt a chest X-ray by the National Institute of Clinical Excellence (NICE) were identified in 27% of the 77 volunteers over the 12-month study period. In 5%, criteria for an urgent lung cancer referral were met. Importantly, the interviewees described how the intervention was acceptable and accessible as it did not require additional travel and visits to the doctor. It successfully provided them with a more nuanced understanding of their chest condition, increased knowledge of early indicators of acute exacerbation and enhanced their self-management skills. The calls also heightened interviewees' appreciation of their increased risk of lung cancer and awareness of the associated symptoms. They reported adopting more proactive help seeking behaviours. **Conclusion:** This study reveals how the PAIRS-COPD intervention can help COPD patients identify and report new symptoms that may otherwise be accepted or missed. In the study symptoms requiring further investigation and referral were uncovered surprisingly frequently. For a client group with a significant symptom burden, the lack of disruption was a primary reason for the acceptability of the intervention. **Keywords:** lung cancer detection, COPD patients, Telephone based intervention, Primary care nurse

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-006 Diagnostic Accuracy of CT-Guided Transthoracic Needle Biopsy for Solitary Pulmonary Nodules Yong Song, Wen Yang, Wenkui Sun *Jinling Hospital, Nanjing/China*

Background: To evaluate the diagnostic accuracy of computed tomography (CT)-guided percutaneous lung biopsy for solitary pulmonary nodules. **Methods:** Three hundred and eleven patients (211 males and 100 females), with a mean age of 59.6 years (range, 19–87 years), who were diagnosed with solitary pulmonary nodules and underwent CT-guided percutaneous transthoracic needle biopsy between January 2008 and January 2014 were reviewed. **Results:** All patients were confirmed by surgery or the clinical course. The overall diagnostic accuracy and incidence of complications were calculated, and the factors influencing these were statistically evaluated and compared. Specimens were successfully obtained from all 311 patients. A total of 217 and 94 cases were found to be malignant and benign lesions, respectively, by biopsy. Two hundred and twenty-five (72.3%) carcinomas, 78 (25.1%) benign lesions, and 8 (2.6%) inconclusive lesions were confirmed by surgery and the clinical course. The diagnostic accuracy, sensitivity, and specificity of CT-guided percutaneous transthoracic needle biopsy were 92.9%, 95.3%, and 95.7%, respectively. The incidences of pneumothorax and self-limiting bleeding were 17.7% and 11.6%, respectively. **Conclusion:** Taking account of all evidence, CT-guided percutaneous lung biopsy for solitary pulmonary nodules is an irreplaceable, efficient, and safe diagnostic method associated with few complications. **Keywords:** specificity, Percutaneous lung biopsy, solitary pulmonary nodules, Sensitivity

POSTER SESSION/ SCREENING AND EARLY DETECTION
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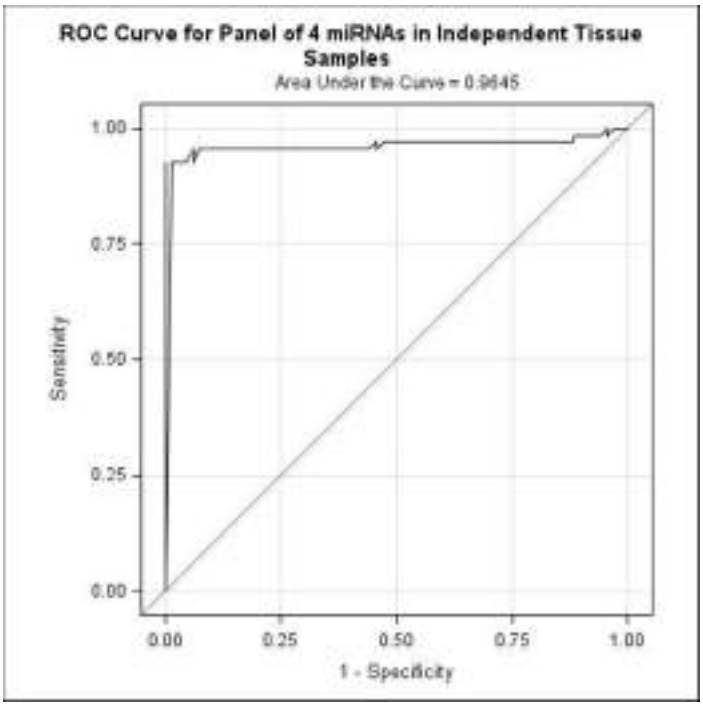
P2.06-007 A miRNA Signature Derived From Independently Replicated Biomarkers of Non-Small Cell Lung Cancer Christopher J. Rivard[1], Brad Rikke[1], Leslie Rozeboom[1], Ashley A. Kowalewski[1], William J. Feser[2], Anna E. Barón[2], York E. Miller[3], Paul A. Bunn, Jr[1], Fred R. Hirsch[1] [1]*Medical Oncology, University of Colorado Denver, Aurora/CO/United States of America,* [2]*Biostatistics and Informatics, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora/CO/United States of America,*[3]*Pulmonary and Critical Care Medicine, University of Colorado Anschutz Medical Campus, Aurora/United States of America*

Background: miRNAs have shown exceptional promise as biomarkers of lung cancer; however, no miRNA signatures have yet reached the clinic. Towards developing a signature with a high likelihood of being validated externally for clinical use, we screened a panel of 50 miRNAs shown to be effective biomarkers in at least two previous studies for distinguishing human lung cancer samples from non-cancer samples. **Methods:** Sixty tumor-normal pairs (33 adenocarcinoma, 27 squamous cell carcinoma) were used to identify the best-performing combination of 4 miRNAs for distinguishing tumor samples from normal. The miRNA levels were measured by RT-qPCR using Taqman custom-made microfluidics cards and primer pools purchased from Life Technologies. All possible combinations of 4 miRNAs were tested, and best performance was defined as the highest median area-under the receiver operating curve (AUC) obtained from 1000 bootstrap replicates. A second, independent set of 68 tumor-normal samples (half adenocarcinoma, half squamous) was used as a test set, and bootstrapping was used to determine the 95% confidence interval for the AUC. **Results:** The median AUC for the top-performing panel of 4 miRNAs in our training set was 0.96. Several other miRNA combinations exhibited AUCs > 0.95 as well. In our test set, the top-performing panel (and only panel tested) exhibited an AUC of 0.97 (0.93, 0.99). This panel consisted of miRs 26a, 145, 183 and 486. miRs 145 and183 have previously been shown, when used individually, to be significant lung tumor biomarkers in at least 4 previous studies; miR-486 has been replicated 8 times.



Conclusion: Consistent with previous studies, we've identified a panel of 4 miRNAs that shows excellent potential for diagnosing lung tumors. Each of these miRNAs has been replicated as a biomarker of lung cancer in at least two previous studies, suggesting a high likelihood of achieving clinical validation. Several previous studies have also shown that these four miRNAs are potentially useful as biomarkers for diagnosing lung cancer using blood samples, and we are currently pursuing such validation studies. **Keywords:** Biomarkers, miRNA signature, NSCLC

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P2.06-008 Diagnostic Yield of Autoantibody Panel for Patients with Ground-Glass Nodules (GGNs) or Solid Nodules in Chinese Population Caicun Zhou, Shengxiang Ren, Yayi He *Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

Background: Autoantibodies is an attractive diagnostic approach for early detection of malignant tumors. Our previous studies found a panel of 7 TAAs(p53 , PGP9.5, SOX2, GAGE7, GBU4-5, MAGE A1, CAGE) was associated with lung cancer. We performed this large-scale clinical trial to validate their ability to aid early diagnosis of lung adenocarcinoma presenting with GGNs or solid nodules in Chinese population. **Methods:** The 7 TAAs were selected from 43 candidate TAAs from our previous studies. These samples including lung adenocarcinoma presenting with GGNs (n = 170) or solid nodules (n = 100) and healthy volunteers (n = 200). The sensitivity and specificity from 7 TAAs and the traditional cancer biomarkers CEA, NSE, and CYFRA21-1 were compared. **Results:** The sensitivity and specificity of autoantibody assay were 53% and 91% respectively, which were similar in different subgroups such as age, gender, smoker status and histological type. The sensitivity of autoantibody assay was 50% in lung adenocarcinoma presenting with GGNs. The sensitivity of autoantibody assay was 58% in lung adenocarcinoma presenting with nodules. The results were significantly higher than 27% when using the combination of CEA, NSE, and CYFRA21-1 to detect patients with lung cancer. **Conclusion:** Our study suggested that the 7 TAAs autoantibody panel might be helpful to aid diagnosis of lung cancer with GGNs or solid nodule. Large scale trial to validate our finding of patients with GGNs is ongoing in our institute. **Keywords:** ground-glass nodules (GGNs), solid nodules, autoantibody panel, lung adenocarcinoma

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P2.06-009 Oral Glucose Tolerance Test as a Diagnostic Tool in Lung Cancer
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Background: Previous studies have demonstrated that volatile organic compounds (VOCs) in exhaled breath can distinguish between healthy and affected individuals, and can even discern between SCLC and NSCLC and within the subtypes of lung cancer (LC) and its mutations status. The current study assessed the differences in glucose metabolism on the volatile signature in LC through an oral glucose tolerance test (OGTT). **Methods:** This cohort included forty participants (22 control participants whom are at high risk for LC, 18 study participants whom have active, naïve lung cancer). Pre-OGTT and Post-OGTT blood glucose levels and exhaled breath samples were measured with a lay period of 90 minutes. A proton transfer reaction mass spectrometer (PTR MS) detected and measured the VOCs. The data was then analyzed using a series of feature selection methods to identify relevant inputs for multilayer perceptron (MLP) models to distinguish LC patients from controls, with and without the consideration of the glucose effect. **Results:** The feature selection method "infogain" revealed a combination of 14 masses (m/e) that were different between the two groups without considering the glucose effect. All the average values of these masses were higher in the LC group except for m/e 52, which was higher in the high-risk group. These 14 masses enable us to distinguish between the two groups with an average accuracy of 91.67% for three internal validation tests of a MLP (threshold set at 0.45). The analysis of the effect of glucose revealed that several m/e increased more for the control group whereas others increased more for the LC group. Moreover, three feature selections, each with a different combination of 4 masses, allowed the design of three MLPs that yielded 90% for K-fold cross-validation accuracy. **Conclusion:** This study showed that breath analysis could discriminate between the high-risk and LC group. Furthermore, it demonstrated that glucose metabolism leaves a unique VOC pattern in the LC group. These findings may assist in the development of a non-invasive screening method for lung cancer.
Keywords: warburg effect, volatile organic compounds, oral glucose tolerance test, lung cancer screening

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P2.06-010 Exhaled Biomarkers for Lung Cancer Screening
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Background: Lung cancer is the leading cause of global cancer death in both males and females. Figures on disease outcome are disappointing despite advances in treatment since 86% lung cancer patients die within 5 yrs of diagnosis. However with early detection and treatment, 5-year survival improves from 20% stage III to 70% stage I disease. Breath chemical tests have been applied in respiratory disorders and we sought to determine if exhaled breath volatile compounds (VOC) could discriminate patients with lung cancer from pulmonary tuberculosis (TB) by comparing them against age matched controls. **Methods:** Subjects seen at outpatient respiratory clinics with CXR suspicious of lung cancer were recruited. Diagnosis of lung cancer or TB was established via bronchoscopic, CT lung biopsy or sputum cultures and exhaled breath was collected. Patients with other lung diseases but gender and age matched were recruited as controls. Analysis of VOC was performed by Thermal Desorption-Gas Chromatography mass spectrometry (TD-GC/MS) using Unity Series 2 Thermal Desorber (Markes International Limited) and 6890 GC system (Agilent Technologies), interfaced with 5973 MSD (Agilent Technologies). Data were analyzed by MZmine 2.11 for peak alignment and normalization, and OPLS for statistical clustering analysis. Additional univariate and receiver operating characteristic analysis were performed with SPSS. **Results:** Statistical clustering analysis OPLS Fig1 showed breath profile differences between lung cancer (n=17) and those with other lung diseases (CON, n=19). Fig2 indicated that breath profile of lung cancer patients was also different from those with Tuberculosis (TB). Specific VOC that contribute to these breath differences will be identified by TD-GC/MS. Individual breath VOC was reproducible in triplicates.

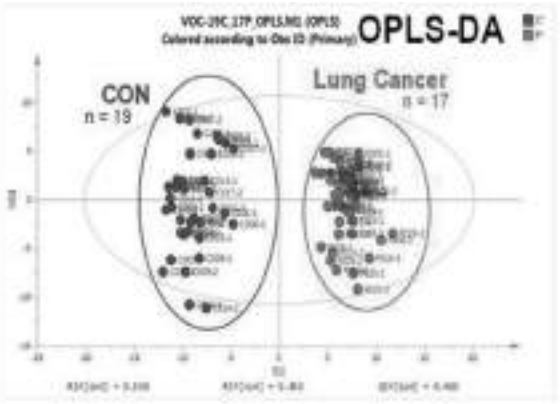

Fig. 1. Two Group OPLS Clustering Analysis. VOC profile differences between CON (Other lung diseases) and Lung cancer

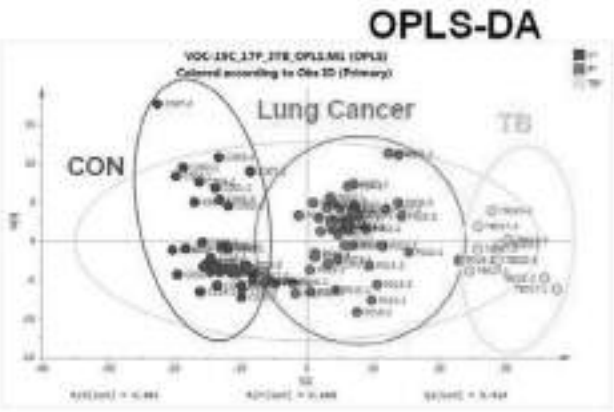

Fig. 2. Three Group OPLS Clustering Analysis. VOC profile differences among CON (Other lung diseases), Lung cancer and TB (Tuberculosis).

Conclusion: These exciting preliminary results suggest that exhaled breath collected from subjects attending respiratory clinic may serve as screening test to aid the physician in the identification of patients with lung cancer and pulmonary tuberculosis from other respiratory diseases.
Keywords: lung cancer tuberculosis exhaled breath

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P2.06-011 Periostin Investigational Use Only Automated Immunoassay for Abbott ARCHITECT®
Philip M. Hemken[1], Nicolette Jeanblanc[1], Maria Datwyler[1], Susan Brophy[1], Scott Manetz[2], Roxanne Lee[2], Meina Liang[2], Partha Choudhury[2], Reena Varkey[2], Ethan Grant[2], Katie Streicher[2], Lydia Greenlees[2], Koustubh Ranade[2], Gerard Davis[1] [1]*Research and Development, Abbott, Abbott Park/IL/United States of America,* [2]*Medimmune, Gaithersburg/MD/United States of America*

Background: Periostin is an 836 amino acid, 93314 Da, protein secreted by airway epithelial cells that induces cell attachment and spreading and plays a role in cell adhesion. Specifically, it functions to enhance incorporation of BMP1 in the fibronectin matrix of connective tissues, and subsequent proteolytic activation of lysyl oxidase. Its expression is induced by the Th2 cytokine IL-13. Periostin serum levels have shown to be elevated in some asthmatic patients. Therefore, it is hypothesized that periostin may be useful as a surrogate marker for IL-13 up-regulation and to identify asthmatics more likely to benefit from IL-13 targeted therapy. The clinical utility of the assay is being explored in patients with uncontrolled severe asthma in Phase III trials of tralokinumab, an investigational anti-IL13 monoclonal antibody. An analytically robust investigational use only (IUO) immunoassay was developed to quantitate serum periostin on the ARCHITECT® immunoassay*i*System. **Methods:** The ARCHITECT® Periostin assay is a monoclonal antibody (mAb) sandwich twostep immunoassay for the quantitative determination of periostin in human serum using Chemiluminescent Magnetic Immunoassay (CMIA) technology. Periostin is captured by microparticles coated with an anti-periostin mAb and detected with a mAb conjugated with acridinium. Chemiluminesence is triggered, and signal is measured as relative light units (RLUs), which directly reflect to the quantitative amount of periostin. ARCHITECT® *i*System has throughput of 200 tests per hour. The analytical performance of the assay was assessed for sensitivity, linearity, precision, endogenous and drug interfering substances, specimen handling/ preanalytics, and periostin isoform reactivity. The assay was standardized using gravimetrically prepared periostin isoform 1 with protein concentration determined

using an extinction coefficient established by amino acid analysis. **Results:** Prototyping was performed on ARCHITECT® iSR2000. Numerous antibody formats were evaluated for key analytical performance prior to final pair selection and completion of extensive analytical performance testing. Limit of quantitation is </= 4 ng/mL. Specimen dilution analysis yielded linear results across the dynamic range of the assay (4-100 ng/mL). Five-day total precision results ranged from 3.4 to 6.4 %CV across 3 controls and 3 serum based panels. No endogenous sample and drug interferences were observed. Drugs assessed for interference were selected as representatives from drug classes that are commonly used to treat asthma. Periostin in serum separator tubes (SST) was stable at room temperature or refrigerated for up to 24 hours. Serum samples are stable for up to 2 freeze/thaw cycles. Beyond 24 hours of collection, freezing (-10oC or colder) for long term storage is recommended. All known periostin isoforms expressed in the lung (2-4, 7, 8) are detected with the ARCHITECT® Periostin assay. Using this newly developed IUO assay, periostin levels were measured in over 1000 serum samples from patients with severe asthma. The periostin levels ranged from 5.2-73.3 ng/mL with a median level of 16.4 ng/mL. **Conclusion:** The IUO ARCHITECT® Periostin immunoassay is a robust and reliable test for the measurement of serum periostin. Periostin testing is in progress in Phase III trials for tralokinumab, an anti-IL-13 human IgG4 mAb. **Keywords:** periostin, Abbott ARCHITECT®, tralokinumab, companion diagnostic

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P2.06-012 A Model Incorporating Clinical, Radiographic, and Biomarker Characteristics Predicts Malignancy in Indeterminate Pulmonary Nodules
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Background: The high false-positive rate associated with low-dose computed tomography (CT) lung cancer screening results in unnecessary testing, cost, and patient anxiety. We hypothesized that an algorithm incorporating clinical, radiographic, and serum biomarker data would be capable of differentiating benign from malignant pulmonary nodules. **Methods:** An institutional biorepository was used to identify 84 patients with ≤ 2 cm indeterminate pulmonary nodules identified on CT scan, including 50 patients with biopsy-proven, node-negative, non-small cell lung cancer (NSCLC) and 34 patients with benign, non-calcified, solitary pulmonary nodules. Clinical and radiographic data were collected from patient charts and imaging studies. Serum specimens were evaluated in a blinded manner for 55 biomarkers using multiplex immunoassays. Random forest analyses were used to generate a multivariate cross-validation prediction model incorporating clinical, radiographic, and serum biomarker data. **Results:** A total of 84 patients were identified with a median nodule size of 5 mm for benign nodules and 15 mm for NSCLC. Median smoking histories were 21 and 28 pack-years and patient age was 62 and 70 years, respectively. An algorithm incorporating serum biomarker profile (IGFBP-4, IGFBP-5, IL-10, IL-1ra, IL-6, SDF-1alpha, IGF-2), age, sex, BMI, COPD, smoking history, hemoptysis, previous cancer, nodule size, nodule location, spiculation, nodule type, and nodule count provided the optimal performance with a sensitivity 92%, specificity 65%, NPV 85%, and PPV 79%. This model performed with an overall accuracy of 81% with a cross-validated AUC=0.904. **Conclusion:** An algorithm incorporating clinical, radiographic, and serum biomarker characteristics may help differentiate benign from malignant pulmonary nodules. This model is currently being externally validated in a second-site patient cohort.

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P2.06-013 Verification of the Biomarker Candidates for Non-Small-Cell Lung Cancer Using a Targeted Proteomics Approach
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Background: Lung cancer, with its high metastatic potential and high mortality rate, is the worldwide leading cause of cancer-related deaths. High-throughput "omics"-based platforms have accelerated the discovery of biomarkers for lung cancer, and the resulting candidates are to be evaluated for their diagnostic potential as non-invasive biomarkers. The evaluation of the biomarker candidates involves the quantitative measurement of large numbers of proteins in bodily fluids using advanced mass spectrometric techniques. In this study, a robust method based on targeted proteomics was developed for biomarker verification in plasma samples and applied to verifying lung cancer biomarker candidates. **Methods:** Sample acquisition: Blood samples were obtained from 72 patients diagnosed with non-small-cell lung cancer (NSCLC) (stages I-IV), and 30 healthy volunteers with the approval of the National Research Ethics Committee. Sample processing and Liquid Chromatography-Selected Reaction Monitoring (LC-SRM): Two most-abundant plasma proteins were depleted from each sample. Proteins were digested by trypsin to generate peptide mixtures. Peptides representing the potential biomarker proteins were selected. Stable isotope-labeled (SIL) peptides of the selected target peptides were synthesized to be used as internal standards, and spiked-in the processed plasma samples. A peptide banking system equipped with a local spectral library of synthetic peptides was used to facilitate automatic generation of LC-SRM methods. Multiplexed LC-SRM assays for >100 potential markers for NSCLC were generated to screen the plasma samples. **Results:** In the first set of screening for 190 peptides, a total of 60 peptides corresponding to 44 proteins were detectable by LC-SRM in the plasma. Among them, 17 proteins exhibited higher expression levels in the NSCLC patients compared to the control. For those proteins, additional peptides were prepared in order to increase the coverage of the protein sequence, and the number of samples were expanded (72 NSCLC and 30 controls). After differential analysis of the SRM results, 17 proteins were finally verified as potential diagnostic markers. The verified targets include ACTN1, ALDOA, ENO1, FLNA, G6PD, GPI, HSP90B1, ICAM1, ILK, LDHB, MSN, PGK1, PKM2, SPP1, TALDO1, THBS1, and ZYX. The expression levels were cross-validated by ELISAs if available. A novel plasma-based biomarker, ZYX, showed a potential of early diagnostics as its plasma level increases from the early stages (stages I and II). The overall pattern of the plasma levels of four ZYX peptides and the ELISA results were correlated. The role of ZYX in cancer has been recently discussed as a key player in epithelial-mesenchymal transition mechanism, and the association to lung cancer was reported in several studies. To the best of our knowledge, the potential use of ZYX protein as a tumor biomarker in plasma for lung cancer has been verified for the first time in this study. **Conclusion:** A targeted proteomics-based, analytical pipeline was designed for a large-scale biomarker verification and successfully applied to verifying a set of potential biomarkers for NSCLC. The robust workflow is critical to the early-stage screening where the attrition rate tends to be high (68% in this study). Several novel targets were verified as plasma-based NSCLC biomarkers, and ZYX showed a potential of early diagnostics. **Keywords:** biomarker, NSCLC, targeted proteomics, plasma

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P2.06-014 A Czech Page in the Lung Cancer Multiplicity
Teodor Horvath[1], Radek Vesely[2], Jan Savolt[2], Martin Sobotka[2], Ilona Kocakova[3], Ivo Kocak[3], Stanislav Spelda[3], Edvard Geryk[4], Radim Stampach[5], Petr Kubicek[5], Helena Bartonkova[3], Milan Prasek[3], Drahomira Chasakova[2], Sylva Rybnickova[3], Ivo Capak[3], Jan Dolezel[3], Daniel Macik[3], Richard Feranec[3], Renata Kalabova[3], Ilona Kantorova[2], Barbora Garajova[1], Tomas Racek[2], Marie Horvathova[6] [1]*Faculty Hospital, Dept. of Surgery, Faculty of Medicine, Masaryk University, Brno/Czech Republic,* [2]*Department of Traumatology at the Medical Faculty, Masaryk University, Trauma Hospital Brno, Brno/Czech Republic,* [3]*Masaryk Memorial Cancer Institute, Brno/Czech Republic,* [4]*Department of Preventive Medicine, Masaryk University, Brno/Czech Republic,* [5]*Department of Geography, Masaryk University, Faculty of Science, Brno/Czech Republic,* [6]*Early Diagnosis, Cbc Vznik S.R.O., Brno/Czech Republic*

Background: There are estimated in the National Czech Cancer Registry since 1976 to 2010 among 203, 858 cancers a total of 16 622 lung cancers (LCs) in males associated with other neoplasms, presented 10 % of 166 239 (81,5%) newly registered LCs in males. They were 4,395 (2.6 %) primary and 12,227 (7.4 %) subsequent LCs; A total of 5,322 LCs in females, presented 14.1 % of 37,619 (18,5%) newly registered LCs in females, of which were 1,022 (2.7 %) primary and 4,300 (11.4 %) subsequent LCs. Their representation at the early clinical stages decreased gradually from 53% to 22 %, at the advanced stages increased from 20 % to 64 %; One third of subsequent neoplasms in early stage and one fifth in advanced stage evaluated replenish 51,2% of unknown stage in men and 47,4% in women. High proportion of LCs at unknown stages limited detailed analysis. Dichotomous question of early diagnosis is inquired. **Methods:** Miscellaneous group of 548 individuals (260 females and 288 males) with high risk of lung cancer was formed predominantly from South Moravia region of the Czech Republic, EU. They were enrolled since 2001 to 2010. Approximately one third (n=185) from the group had undergone surgery due to cancer of head and neck, gastrointestinal, gynecological including breast, urological and skin location (n=86) and due to pulmonary malignancy (n=99) . The follow up scheme for this subgroup represents four time yearly careful clinical investigation with monitoring of appropriate TM levels during first three years, then three time in the year during fourth and fifth years, and two time yearly follow up investigation during sixth to tenth year in connection with yearly paraclinical set of CT of thorax and USG of abdominal spaces on even-numbered, and X-rays of thorax and CT of abdomen on odd-numbered years, two-year period bone scan, endoscopy, and yearly laboratory screening tests – serology, hematology, and basic urine investigation. Another parts of the risk group are represented by persons (n=203) with high risk of lung cancer (uranium miners with long term professional exposure to Rn222, heavy smokers minimally 20 yrs with 1 to 2 packs cigarettes per day (n=60), pts with hemoptysis (n=15) and persons with other kind of risk (n=85). These were screened one time yearly by clinical, laboratory, and bronchoscopy examination and imaging alternately yearly X rays / thoracic CT scan and abdominal USG. Classification of malignant tumours TNM-7 and Program Microsoft Excel® were used to data analysis. **Results:** Among 548 persons from the risk group followed during ten years period they were found in 29 individuals (5,3%) counting 11 females and 18 males a total of 40 lung cancers. They were 14 primaries and 26 subsequent LC with two cases of triplicity. The early diagnosis in the stage (I, II) was established 32-times (i.e. 4/5) versus 8-times diagnosed advanced stage (III, IV) of disease (i.e. 1/5). Appropriate treatment was organized and follow up continues to evaluate survival. **Conclusion:** Early diagnosis in patients with lung cancer multiplicity seems attainable despite of certain limitation. **Keywords:** early diagnosis, lung cancer, Primary and Subsequent Neoplasms

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P2.06-015 Detecting Obstructive Lung Diseases with Aerosol Breath Test: A Non-Invasive Diagnostic Method Using Fractal Analysis and SVM Classification
Jinxiang Xi[1], Jiayao E. Yuan[2], Xiuhua A. Si[3] [1]*School of Engineering and Technology, Central Michigan University, Mt Pleasant/MI/United States of America,* [2]*School of Engineering and Technology, Central Michigan Univresity, Mt Pleasant/MI/United States of America,* [3]*Mechanical Engineering, California Baptist University, Riverside/CA/United States of America*

Background: Each lung structure has a unique pattern of exhaled aerosols (*aerosol fingerprint*), whose deviation from the normal pattern may indicate an anomaly inside the airway. Therefore, an exhaled aerosol test can be used to detect and monitor lung diseases non-invasively. The key challenge is accurately interpreting the exhaled aerosol fingerprints and quantitatively correlating them to lung diseases. **Methods:** In this study, a novel integrated algorithm was developed to evaluate the feasibility of the exhaled aerosol tests. This algorithm has four steps: data generation via physiology-based modeling, image feature extraction using sub-regional fractal analysis, data classification using a support vector machine (SVM), and data quality assessment using principle component analysis. **Results:** By employing the 10-fold cross-validation method, we achieved 100% classification accuracy among four asthmatic models using an ideal 108-sample dataset and 99.1% accuracy using a more realistic 324-sample dataset. The fractal-SVM classifier has been shown to be robust, highly sensitive to structural variations, and inherently suitable for investigating aerosol-disease correlations. **Conclusion:** For the first time, this study quantitatively links the exhaled aerosol patterns with their underlying diseases and sets the stage for the development of a computer-aided diagnostic system for non-invasive detection of obstructive respiratory diseases. The proposed aerosol breath test is especially suitable for the use of screening to detect lung tumors at early stages, and to monitor tumor growth or therapeutic outcome of medical interventions. **Keywords:** Obstructive respiratory diseases, aerosol breath test, computer-aided diagnostic system, lung tumor early detection

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P2.06-016 An Epidemiological Study on Detection of Chronic Obstructive Pulmonary Diseases and Lung Cancer by Regional Lung Cancer Mass Screening
Takehiko Fujisawa[1], Yasuo Sekine[1], Ryoko Yanagibori[1], Kiminori Suzuki[1], Haruko Yamaji[1], Atsuko Tokuda[1], Sonomi Sugiyama[2] [1]*Respiratory Medicine, Chiba Foundation for Health Promotion and Disease Prevention, Chiba/Japan,* [2]*Diagnostic Radiology, Chiba Foundation for Health Promotion and Disease Prevention, Chiba/Japan*

Background: Lung cancer is a major cause of death in the world and chronic obstructive pulmonary disease(COPD) are at risk for lung cancer. Both the diseases have common etiologies, including cigarette smoking. We aimed to clarify the effectiveness of lung cancer screening by chest X-ray and by low-dose computed tomography (LDCT) among patients with COPD tested by pulmonary function test(PFT) by using regional lung cancer mass screening. **Methods:** A total of 7,067 residents including 2,720 males and 4,347 females of Togane City, Chiba, Japan received lung cancer screening between May and July, 2011. All residents underwent chest X-ray and answered questionnaire, including smoking history , chronic respiratory symptoms and lifestyle-related disease for selecting COPD. We hypothesized that individuals with a positive smoking history with chronic respiratory symptoms or lifestyle-related disease considered COPD candidates and advised to undergo PFT. COPD candidates whose forced-expiratory volume in 1 second/ forced vital capacity less than 70 % were considered COPD who underwent LDCT. They were followed additional two years by high resolution CT for detecting lung cancer. **Results:** Chest X-ray showed normal in 6,749 and abnormal in 318(4.5%). Among participants with normal chest x-ray, positive COPD candidates were 1,686(23.9%) and negative COPD candidates were 5,381(76.1%), according to the questionnaire. 1,500 of 1,686 underwent PFT and diagnosed COPD in 171(2.4%). 151(2.1%) of them received LDCT. Six of 318(1.9%) cases with abnormal chest X-ray were finally diagnosed lung cancer (86/100,000). One case at initial time and three cases during follow-up periods were diagnosed lung cancer by LDCT in COPD patients (0.88 % per year). **Conclusion:** Chest X-ray and LDCT for COPD patients may be effective for lung cancer surveillance in community-based lung cancer screening. **Keywords:** lung cancer,COPD, screening, LDCT

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P2.06-017 Incidental Detection of Lung Cancer by Pre-Operative Evaluation, a Series of 6 Cases
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Background: American Society of Anesthesiologists (ASA) classification is an useful pre-operative evaluation system which helps clinicians in prediction of possible complications and risks due to surgery. In ASA classification, surgical candidates are divided into six groups according to their risk status. Following ASA classification, grading is done according to the severity of the operation. Grades are determined due to the severity and the duration of the operation. After determining ASA classes and grades, necessary tests are performed according to age groups to complete the pre-operative assessment. However, in this evaluation, randomly determined pathologies can dramatically change the assessment results in those cases without any symptoms. For this purpose, we retrospectively analyzed the results of the patients received pre-operative pulmonary evaluation during the last one year. **Methods:** Pre-operative pulmonary evaluation results of 520 cases were analyzed retrospectively who were referred to our clinic between January 2014-January 2015. **Results:** Through them, 6 (1.2%) patients (4 men, 2 women) with mass and/or nodule images in their chest radiographs, were histopathologicaly diagnosed with lung cancer. 3 of these cases were planned for inguinal herniorrhaphy, and other 3 cases for knee replacement surgery. The common points of these cases were being asymptomatic and included into ASA 1 - grade II group. The mean age of the patients was 71.1 (65- 87). Lung cancer diagnosis was proven by transthoracic needle biopsy in 3 cases, bronchoscopy in 1 case and thoracentesis + pleural biopsy in 1 case with pleural effusion. All of the cases are non-small cell lung cancer; 3 adenocarcinoma and 3 squamous cell lung carcinoma. 4 cases were found to be in stage IIIB and over, while the other 2 patients who were underwent lobectomy were in stage IB. Chemoradiotherapy was performed to the inoperable cases. **Conclusion:** Pre-operative tests conducted according to current ASA classification are still useful in terms of determining the possible complications and risks. However, in some cases, as in ours, examinations broader than recommended may be necessary. According to ASA classification; ASA group 1describes healthy person with no systemic problem accept for current surgical pathology, and grade 2 describes short timed operations (30 minutes - 1 hour) in which vital organs are affected minimum (inguinal herniorrhaphy, tonsillectomy, arthroscopy, cystoscopy, etc.). ASA recommends preoperatively complete blood count, serum electrolytes, blood glucose, blood urea nitrogen, creatinine tests for ASA group 1- grade II patients aged 61 years and older. Chest radiography is not routinely recommended in these patients with no obvious symptoms or signs. However, in our own clinical approach for pre-operative evaluation of patients aged over 65 years, chest radiograph is a preferred test. Considering that 6 asymptomatic lung cancer patients were determined by this approach, the benefits of pre-operative chest radiograph which is a cheap, fast and easy examination are remarkable in pre-operative pulmonary evaluation. We presented this case series in order to emphasize this subject. **Keywords:** ASA, lung cancer, pre-operative, chest radiograph

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-018 Health Disparities Assessment in a Newly Established Lung Cancer Screening Program
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Background: Lung cancer incidence and mortality rates differ depending on race, ethnicity, and gender. African American (AA) men have significant higher incidence and mortality from lung cancer compared to white men (incidence 87.3 vs. 72.5; mortality 70.1 vs. 57.8 per 100,000). Lung cancer screening is an effective lifesaving tool. The National Lung Screening Trial (NLST) showed a 20 percent reduction in lung cancer mortality with low-dose computerized tomography (LDCT) versus chest X-ray screening, but the study population was 91% white and only 4.5% AA. Could the reduction in lung cancer mortality be even greater if the NLST population included a larger minority population? UI Health has a large community outreach that serves minority populations in Chicago (48% AA, 24% classified as "other", 16% White, 7% Hispanic). In March 2015, UI Health began a comprehensive lung cancer-screening program. **Methods:** The program coverage and eligibility is broadly advertised to patients and primary practitioners in our community. Previously, low cost lung cancer screening was available but coverage was a concern for patients and practitioners. Lung cancer screening eligibility criteria used is set by the CMS (age 55-77, current smoker or one that have quit within the past 15 years, smoking history of > 30 pack-years) and the U.S. Preventive Services Task Force (including ages up to 80 for non-Medicare patient). American College of Radiology LungRADS system is used for standardized image reporting, and recommended management for positive screens. Data elements include age, gender, race/ethnicity, insurance type, LDCT findings, and treatment modalities for diagnosed lung cancer is collected in a secure registry. **Results:** In our first month, 13 patients have been screened between the ages of 56-76, 7 females/6 males. Race/ethnicity make-up: 54% AA, 31% White, 15% Hispanic. Estimated volume of LDCT screens is 200 per year. As yet, there are no significant findings requiring intervention. Of note, in the greater than 2 years that screening was an option but coverage was not clarified by CMS, fewer than 10 patients participated, suggesting that lack of coverage by CMS or commercial carriers was a barrier for our patients. **Conclusion:** Coverage by CMS and commercial carriers for LDCT screening has a significant impact on our patient population. Analysis from this study will assess if we can reach a large underserved group with a screening program and whether it will result in decrease of lung cancer mortality in this population. **Keywords:** Screening Program, low-dose computerized tomography (LDCT), high-risk population, health disparities

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-019 Prognosis of Lung Cancer Patients Diagnosed with National Health Surveillance
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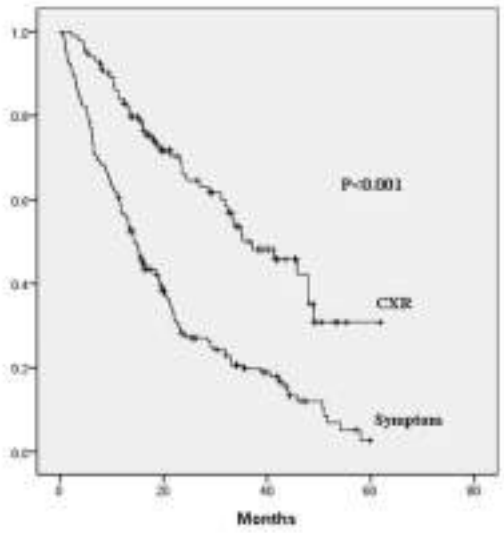
Background: National health surveillance with chest X-ray is performing in our country every two years. The present study was performed to evaluate the differences in clinical characteristics and survival outcomes of patients with non-small cell lung cancer (NSCLC) according to detecting the disease by health surveillance with chest X-ray (CXR) or presenting symptoms (SX). **Methods:** We identified 294 patients (male/female ratio: 226/68; mean age: 68.7 years old) in tertiary university hospital between Jan 2010

and Dec 2012. The patients were divided into two categories according to method of detection. The clinical characteristics and treatment outcomes were estimated according to CXR group and SX group. **Results:** CXR group was 102 patients and SX group was 192 patients. There were significant shift to early TNM stage distribution, cancer cell type, initial treatment modality and type of surgery in the CXR group compared with SX group (table 1). Median survival times were 35.2 months (95% confidence interval (CI): 24.1–46.3) in CXR group, and 14.2 months (95% CI: 12.1–16.3) in SX group. There were statistically significant differences in overall survival between CXR and SX groups (P=0.001) (figure1).

Table 1. Clinical characteristics of patients with non-small cell lung cancer according to the modes of detection.

	CXR (n=102)	Symptom (n=192)	P value
Mean age	69.8	68.1	0.144
Sex (Male) (%)	76 (74.5%)	150 (78.1%)	0.561
Smoking (%)	62 (64.6%)	142 (74.0%)	0.102
PYRS	26.7	34.7	0.013
Cell type (%)			0.025
Squamous cell	24 (23.5%)	89 (46.4%)	
Adenocarcinoma	60 (58.8%)	66 (34.4%)	
Adenosquamous cell	6 (5.9%)	24 (12.5%)	
Large cell	12 (11.8%)	13 (6.8%)	
Clinical stage (sum %)			<0.001
IA/IB	21/9 (29.4%)	6/9 (7.8%)	
IIA/IIB	11/5 (17.6%)	15/15 (15.6%)	
IIIA/IIIB	15/9 (23.5%)	19/20 (20.3%)	
IV	30 (29.4%)	108 (56.3%)	
Initial Treatment modality (%)			<0.001
Thoracic surgery	54 (52.9%)	24 (12.5%)	
Chemotherapy	12 (11.8%)	102 (53.1%)	
Chemoradiation Tx	36 (35.3%)	66 (34.4%)	
Type of surgery			<0.001
Lobectomy	40 (37.3%)	15 (7.8%)	
Bi-lobectomy	2 (20.%)	0	
Pneumonectomy	0	1 (0.5%)	
Wedge resection	5 (4.9%)	2 (1.0%)	
Segmentectomy	9 (8.8%)	6 (3.1%)	

Fig. 1. Comparative analysis of overall survival curves between radiographically detected [chest radiography (CXR)] non-small cell lung cancer patients and symptom-prompted patients.



Conclusion: Lung cancer screening by national health surveillance with chest X-ray contributed to better clinical outcome in patients with NSCLC. **Keywords:** lung cancer, Screening, symptom, survival

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-020 Comparison of Cytological Diagnosis Between Solitary and Semi-Solitary Lung Nodules in Biopsy Samples: Experience from a Single Academic Center Gary Gong[1], Haiyan Wang[1], Russell Hales[1], Derek B. Allison[2], Susan Geddes[2], Edward Gabrielson[3], Frederic Askin[2], Qing Kay K. Li[2] [1]*Radiology, Johns Hopkins Medical Institutions, Baltimore/United States of America,* [2]*Pathology, Johns Hopkins Medical Institutions, Baltimore/MD/United States of America,* [3]*Pathology, Johns Hopkins Medical Institutions, Baltimore/United States of America*

Background: The recent large scale National Lung Cancer Screening Trial in the United States (NLST) demonstrated an increased detection of stage I lung cancers. This approach was associated with a 20% reduction of lung cancer-related deaths in the screening population. However, the current clinical guideline for the management of lung nodule is primarily based on studies of non-calcified solitary pulmonary nodules (SPN). Although several recent studies have addressed the issue of the management of semi-solitary and/or partially calcified lung nodules, the evidence-based study is still necessary. Clinically, the diagnosis of small pulmonary nodules involves the combination of radiological surveillance and the morphological examination of pulmonary cells, such as bronchoscopic sampling of the lesion, including bronchial brushing and/or transbronchial fine needle aspiration biopsy (TBNA) with or without ultrasound guidance. In this study, we correlated cytomorphological diagnoses of lung nodules with radiological characteristics, and compared them with findings of mediastinal lymph nodes (LN) fine needle aspiration (FNA) biopsy. **Methods:** A total of 300 lung and mediastinal LN cases over a one-year period were identified by a computer search, including 117 lung and 183 lymph nodes biopsies. All cases were divided into three categories: solitary, semi-solitary and partially calcified nodules/lesions according to radiographic image. The cytological diagnoses of all cases were correlated with radiographic findings. **Results:** In lung biopsies, the average sizes of the solitary, semi-solitary and calcified lesions were 1.952+/-2.225, 1.333+/-1.827, and 1.152+/-1.984 cm, whereas, in lymph nodes the average sizes of the solitary, semi-solitary and calcified lesions were 1.696+/-2.225, 0.909+/-1.041, and 2.788+/-3.371 cm. The cytological diagnosis was summarized in the table.

Lesions	Lung (n=117)			Lymph node (n=183)		
	Malig-nant	Benign	Suspi-cious	Malig-nant	Benign	Suspi-cious
Solitary (lung n=88) (LN n=156)	58 (65.9%)	23 (26.1%)	7 8.0%)	136 (87.2%)	20 (12.8%)	0
Semi-solitary (Lung n=23) (LN n=23)	8 (34.8%)	12 (52.2%)	3 (13.4%)	21 (91.3%)	2 (8.7%)	0
Calcified (Lung n=6) (LN n=4)	2 (33.3%)	3 (50%)	1 (16.7%)	4 (100%)	0	0
Total	68 (58.1%)	38 (32.5%)	11 (9.4%)	161 (88%)	22 (12%)	0

Conclusion: In suspicious solitary and semi-solitary lung nodules, the malignancy was diagnosed as 65.9% and 34.8%, respectively. In suspicious solitary and semi-solitary lymph nodes, the malignancy was diagnosed as 87.2% and 91.3%, respectively. In lung lesions with partial calcifications (we only had very limited number of cases), approximately 50% were malignant lesions. In addition to radiological evaluation, the cytomorphological evaluation of semi-solitary and partially calcified nodules is still crucial for the accurate diagnosis and the appropriate clinical management of lung nodules patients. **Keywords:** cytological diagnosis, Lung nodule FNA, semi-solid lung nodule, partial calcified lung nodule

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-021 Analysis of Autofluorescence Bronchoscopy Used for Characterisation and Identification of Bronchopulmonary Cancer Xiaoxuan Zheng[1], Baohui Han[2], Hongkai Xiong[3], Yong Li[3], Jiayuan Sun[1] [1]*Department of Endoscopy, Shanghai Jiaotong Univ. Affiliated Shanghai Chest Hospital, Shanghai/China,* [2]*Department of Pulmonary Medicine, Shanghai Jiaotong Univ. Affiliated Shanghai Chest Hospital, Shanghai/China,* [3]*Department of Electronic Engineering, Shanghaijiaotong University, Shanghai/China*

Background: The aim of the study is to introduce a more effective quantitative method(optimal identification index and reference value) for characterizing the AFB images within the region of interest and to explore the value of AFB in diagnosis of different types of lung cancer. **Methods:** Patients with one or more preinvasive bronchial lesions were entolled, followed-up by white light bronchoscope(WLB) and AFB. A quantitative analysis based on color space(red-to-green value, R/G value) was conducted and the result was compared with the final diagnosis obtained by the pathology of biopsy and/or by surgical pathology. **Results:** A retrospective analysis was conducted on 218 cases with 1,208 biopsies. 173 cases were diagnosed as positive by WLB associated with AFB, which included 151 true positive cases and 22

false positive cases. There were 45 cases in 151 true postive cases which included 13 false negative cases and 32 true negative cases. WLB associated with AFB was able to differentiate between benign and malignant lesion lymph nodes with a high sensitivity, specificity, positive predictive value and negative predictive value(92.1%, 59.3%, 87.3% and 71.1%, respectively). The quantitative method of R/G value allowed an more excellent discrimination and yielded a high sensitivity and specificity(82.3% and 80.5%), based on a cut-off level of 1.485. **Conclusion:** AFB associated with WLB is a promising method which allows characterisation and differentiation of benign and malignant lesions with a high sensitivity, specificity based on R/G value. **Keywords:** medical image processing, autofluorescence bronchoscopy, white light bronchoscopy, lung cancer

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-022 Multiple Primary Malignancies - A Retrospective Analysis
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Background: With the increase in survival of cancer patients over the past three decades, both as a result of improved treatments and earlier diagnosis, the likelihood of developing a second cancer has increased. The aim of our study was to assess the frequency of multiple malignancies in patients hospitalised at the Centre for Pulmonary Diseases in Olsztyn, Poland. **Methods:** We performed a retrospective review of medical records of 1112 patients hospitalised at our Centre between January 2013 and September 2014. We selected cases with at least two malignancies. We recorded the number and locations of the tumours in the patients and their relatives, risk factors and co-morbidities. The inclusion criteria were met by 56 patients (18 women and 38 men). **Results:** Among the patients with multiple primary neoplasms we identified 52 cases where at least one of the primary cancers was lung cancer and 4 cases where none of the primary cancers was lung cancer. The mean age at diagnosis of the first and the second cancer was 62,16 (SD 12,04) years an 67,20 (SD 9,68) years, respectively. The mean interval between the diagnosis of the first and the second cancer was 3,84 (SD 13,03) years. We identified 4 cases of triple primaries and 1 case of quadruple primaries. Regarding the sequence of diagnosis, lung cancer was the first malignancy in 11 cases (1 - non-small-cell carcinoma, 4 - adenocarcinoma and 5 - squamous cell carcinoma, 1 - undiagnosed), the second malignancy in 39 cases (4 - non-small-cell carcinoma, 12 - adenocarcinoma, 10 - squamous cell carcinoma, 7 - small-cell carcinoma and 6 - undiagnosed) and the third malignancy in 2 cases (1 - squamous cell carcinoma, 1- undiagnosed). The other malignancies diagnosed as the first ones and the second ones were:

	First	Second
Prostate cancer	6	4
Breast cancer	5	2
Vocal cord cancer	1	1
Renal cel carcinoma	4	1
Uterine cancer	4	0
Colorectal cancer	8	0
Skin cancer	3	0
Bladder cancer	2	3
Adrenal cancer	2	1
Lymphoma	1	3
Laryngeal cancer	3	0
Gastric cancer	1	1
Brain cancer	2	0
Tongue cancer	1	0
Salivary gland cancer	1	0
Ovarian cancer	1	0
Thyroid cancer	0	1

We identified the following co-morbidities: hypertension (28), COPD (17), coronary artery disease (8), atrial fibrillation (6), myocardial infarction (3) type 2 diabetes mellitus (4), thyroid diseases (4), chronic renal failure (2), peripheral artery disease (1), stroke (1) and connective tissue disease (1). **Conclusion:** · Lung cancer occur more frequently as the second malignancy. · Patients with multiple neoplasms make up 5,04% of all patients with lung cancer and the number seems to increase. · Generally synchronous neoplasms occur later (medium age; 67,31; SD 11,64), while metachronous neoplasms occur earlier (medium age of the first cancer: 60,12; SD 11,55 and the second one 67,17; SD 9,15), p=0,0014. **Keywords:** frequency, multiple neoplasms, retrospective analysis

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-023 A Complete Thoracic Navigation System to Allow for Nodal and Parenchymal Molecular Assessment in NSCLC: A Prospective Human Study
Lonny Yarmus[1], David Feller-Kopman[1], Jason Akulian[2], Hans Lee[3] [1]*Johns Hopkins University, Baltimore/United States of America,* [2]*University of North Carolina, Chapel Hill/ NC/United States of America,* [3]*Johns Hopkins University, Baltimore/MD/United States of America*

Background: Peripheral pulmonary nodules (PPN) remain a diagnostic challenge for physicians. Minimally invasive biopsy methods for molecular analysis include endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA), navigational bronchoscopy (NB) and transthoracic needle aspiration under computer tomography (CT) guidance. Recently, a combined thoracic navigation system (TNS) allowing for NB and electromagnetic navigational trans-thoracic needle aspiration (N-TTNA) has become available allowing for all necessary procedures to obtain diagnostic and molecular analysis for NSCLC to be performed during a single procedural session. **Methods:** This study was a prospective single arm study examining the success in obtaining molecular tissue in NSCLC cases from the lymph nodes and/or PPN using a novel combined diagnostic approach with TNS (EBUS, NB and N-TTNA) in a single procedural setting. Consecutive patients who consented with a PPN undergoing bronchoscopy were enrolled. All patients underwent convex EBUS for full lymph node staging followed by NB and N-TTNA. All non-diagnostic biopsies were followed with radiographic interval imaging revealing a decrease in size or resolution or a surgical biopsy was performed. The primary outcome was successful acquisition and testing of tissue for molecular analysis. **Results:** Twenty-four subjects with PPN were enrolled in this study (9 male and 15 female) with a median age of 70 years (range 52-85). An EBUS with NB and/or N-TTNA was completed in 24/24 (100%) of the patients. In this cohort, there were seven cases of Adenocarcinoma in which adequate tissue for molecular analysis was obtained in all (100%) of the cases. PPN diagnostic tissue that was adequate for molecular testing was achieved in six out of seven patients (85%). Four patients had evidence of nodal disease on EBUS and all four (100%) nodal samples were adequate for molecular analysis. When a complete TNS is performed combining convex EBUS with the combined TNS procedure for complete staging, the overall diagnostic yield was 92%. No bleeding or hemoptysis events were encountered during the study. There were two (8%) subjects required small bore pigtail catheter placement secondary to pneumothorax. **Conclusion:** This is the first human study demonstrating the sampling adequacy for both nodal and parenchymal tissue sampling for NSCLC molecular analysis in a single procedural setting. Multicentered prospective studies are needed to confirm the utility of these findings in an era of expanding need for tissue acquisition in a minimally invasive setting. **Keywords:** molecular testing, bronchoscopy, TTNA

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-024 Study on the Clinical Application of CT-Guided Percutaneous Lung Biopsy
Peng Zhang, Feng Long, Youzhi Zhang, Haihua Yang *Department of Respiratory Medicine, Huashan Hospital North, Fudan University, Shanghai/China*

Background: To research the clinical value and complications of CT-guided percutaneous lung biopsy **Methods:** 116 patients with pulmonary lesion were applied percutaneous lung biopsy, using the BRAND 18 G automatic puncturing pistol, under 64-slice spiral CT guiding. **Results:** 114 patients succeed to get the biopsy of lung,2 cases failed due to sever pneumothorax,the achievement rate was 98.3%. Among them, 95 were diagnosed as malignant,91 cases being lung cancer (including 18 squamous cell carcinoma, 54 adenocarcinoma,2 small cell lung carcinoma,3 large cell lung carcinoma, and 4 are unclassified).The others contained 2 pleural mesothelioma,2 non-Hodgkin lymphoma,19 non-cancerous lesions (all of these cases,9 with tuberculosis,5 with organized pneumonia,2 with sarcoidosis, 2 with Vasculitis, 2 with inflammatory pseudo tumor).There were 26 patients presenting side effects or complications, the total incidence was 22.4%. Among these, 18 patients had pneumothorax (2 serious, ending puncture), 11 patients had lung bleeding, 2 patients with both pneumothorax and lung bleeding, 8 patients also had chest pain, nausea or other discomfort reactions. **Conclusion:** CTguided percutaneous lung biopsy has the advantages of security and accuracy ,was important method to identify pulmonary lesion. **Keywords:** Lung biopsy, CT-guided

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-025 New PET/CT Criterion for Nodal Staging in Lung Cancer: Area of SUV ≥ 2.5 / Lymph Node Area
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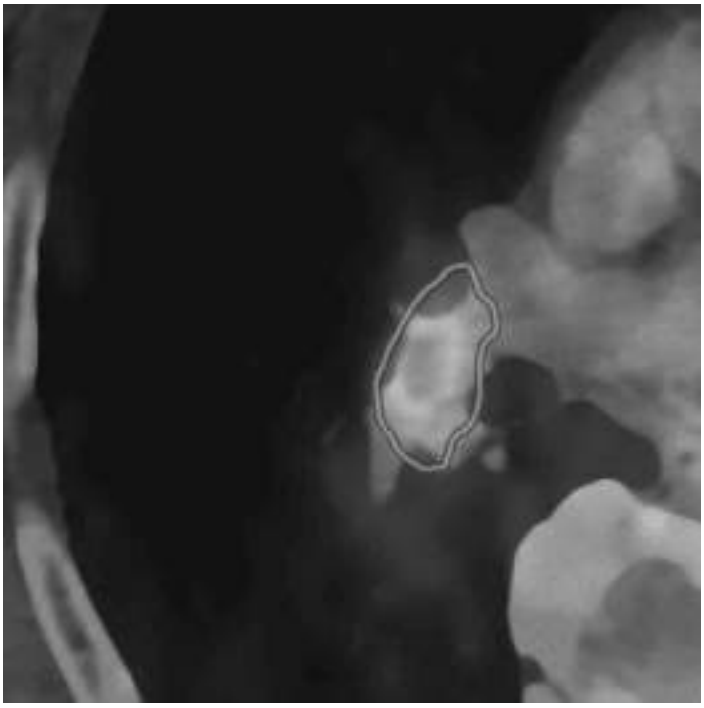
Background: Surgical resection is the accepted standard of care for patients with non-small cell lung cancer (NSCLC) at an early stage, patients have a favorable prognosis. Unfortunately, however, only about 25% of NSCLC patients are eligible for surgery, and once the surgical candidates are selected, mediastinal staging is mandatory because up to 50% of these patients have regional metastasis. Accurate nodal staging is crucial for determining optimal treatment strategies and optimizing prognoses. The aim of the present study was to use surgical and histological results to develop a simple noninvasive technique for improving nodal staging using routine preoperative PET/CT in patients presenting with localized and clinically resectable NSCLC. **Methods:** The institutional review board approved this retrospective study, and written informed consent to perform

the initial and follow-up CT studies was obtained from all patients. Preoperative PET/CT findings (n=163 patients with resectable NSCLC) and pathological diagnoses after surgical resection were evaluated. Using PET/CT images, lymph node surface area (SA), the maximum standardized uptake value (SUV_{max}), SA of SUV ≥2.5 (Figure) and ≥3.0 were drawn freehand and measured using caliper software. Receiver operating characteristic (ROC) curves were then used to analyze those data.



Results: Based on ROC analyses, the cut-off values for SA of SUV ≥2.5, SA of SUV ≥3.0, SUV ≥2.5 SA / node SA ratio and SUV ≥3.0 SA / node SA ratio for diagnosis of lymph node metastasis were 200 mm^2, 30 mm^2, 1.0 and 0.4. When the conventional SUV_{max} ≥2.5 was used for diagnosis, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy of nodal staging were 61.1%, 62.2%, 28.9%, 86.4%, 62.0% , respectively. SUV ≥2.5 SA / node SA ≥1.0 had the highest negative predictive value, and when a cut-off value of SUV ≥2.5 SA / node SA ≥1.0 was used for diagnosis, the sensitivity, specificity, PPV, NPV and accuracy were 61.1%, 73.4%, 36.7%, 88.2% and 70.9%, respectively. **Conclusion:** When diagnosing nodal staging based a lymph node SUV ≥2.5 SA / node SA ratio of ≥1.0, we achieved a higher performance level than was achieved using the conventional of SUV_{max} criterion. Furthermore, determination of this ratio from PET/CT images is a simple noninvasive procedure. **Keywords:** lymph node, metastasis, PET CT, lung cancer

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-026 Advanced Bronchoscopies for Diagnosing Precancerous or Cancerous Lesions: A Meta-Analysis Jianrong Zhang[1], Jieyu Wu[2], Yujing Yang[3], Hua Liao[4], Long Jiang[1], Zhiheng Xu[5], Ziyan Liang[6], Jun Huang[7], Huishan Wei[8], Xiaoru Deng[9], Gongle Zhong[10], Minzhang Guo[1], Xuewei Chen[1], Yi Zhang[11], Qihua He[1], Shengyi Zhong[1], Liqi Yang[12], Miao Chen[12], Minyi Yang[13], Yonghong Chen[11], Jingyi Chen[1], Xusen Zou[1], Ying Chen[1], Wenhua Liang[1], Jianxing He[1] [1]*Department of Thoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou/China,* [2]*Department of Pathology, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou/China,* [3]*Department of Clinical Laboratory, Guangdong General Hospital, Guangzhou/China,* [4]*Department of Cadre Health Care, The First Affiliated Hospital of Guangdong Pharmaceutical University, Guangzhou/China,* [5]*Department of Cadre Health Care, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou/China,* [6]*Department of Neonatology, The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou/China,* [7]*Medical Equipment Section, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou/China,* [8]*The Jockey Club School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong/China,* [9]*Library, Guangzhou Medical University, Guangzhou/China,*[10]*Department of Gynaecology, Dongguan Kanghua Hospital, Dongguan/China,* [11]*Guangzhou Medical University, Guangzhou/China,* [12]*Department of Pulmonary Medicine, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou/China,* [13]*Department of Radiotherapy, Sun Yat-Sen University Cancer Center, Guangzhou/China*

Background: Conventional white light bronchoscopy (WLB) has been used for decades. Some technical advances in bronchoscopies are available for detecting lung precancerous and cancerous lesions currently. Our aim was to investigate the performance of autofluorescence bronchoscopy (AFB), AFB combined with white light bronchoscopy (AFB+WLB), narrow-band imaging bronchoscopy (NBI) and, additionally, to directly compare these new techniques with WLB alone. **Methods:**Pubmed, Embase, Web of Science, Ovid, ProQuest, Scopus and the Cochrane Library were searched for relevant articles. Eligible studies should study any of the new techniques with histopathology as a golden standard, and should have sufficient data to construct 2×2 contingency tables. We used random-effects bivariate models to pool sensitivity, specificity, diagnostic odds ratio (DOR) and the area under the receiver operating curve (AUC) with 95% confidence interval. **Results:**Fifty-three studies involving a total of 6543 patients and 18458 biopsy specimens were included. Single arm synthesis of the new techniques showed that the overall sensitivity of AFB, AFB+WLB, NBI and WLB was 87% (82%-90%), 88% (82%-93%), 96% (78%-99%) and 54% (46%-61%); overall specificity was 65% (58%-72%), 59% (48%-68%), 84% (70%-92%) and 79% (73%-84%); and AUC was 85% (81%-87%), 82% (78%-85%), 94% (91%-96%) and 72% (68%-76%) respectively. In direct comparison, AFB, AFB+WLB and NBI had higher overall sensitivity, DOR and AUC, but lower specificity than WLB alone, regardless of precancerous or cancerous lesions (see in Table 1). In exploratory subgroup analysis, the sensitivities of all techniques were relatively higher in studies with higher proportion of elder patients, or in those with higher proportion of 'high risk' patients who had prior/suspected lung cancer or head & neck cancer.

Table 1. Direct comparison

Techniques	Overall Performance						Cancerous Lesions				Precancerous Lesions			
	Sen	P	Spe	P	AUC	P	Sen	P	Spe	P	Sen	P	Spe	P
AFB	86%	<0.001	62%	0.002	84%	<0.001	97%	0.013	47%	<0.001	83%	<0.001	72%	0.168
WLB	51%		79%		72%		89%		69%		24%		83%	
AFB+WLB	88%	<0.001	57%	<0.001	82%	0.083	95%	0.102	61%	0.025	91%	<0.001	23%	0.022
WLB	51%		83%		77%		81%		86%		15%		77%	
NBI	79%	<0.001	71%	0.043	89%	0.030	100%	0.050	40%	0.313	90%	0.002	85%	0.211
WLB	29%		82%		66%		89%		68%		17%		88%	

Sen: Sensitivity; Spe: Specificity

Conclusion: Based on this pooled analysis, the performance of AFB, AFB+WLB or NBI is superior to WLB alone for diagnosing both lung precancerous and cancerous lesions. Its application might be preferably encouraged in populations with higher risk for non-benign lesions. **Keywords:** autofluorescence bronchoscopy combine with white light bronchoscopy, autofluorescence bronchoscopy, Lung cancerous and precancerous lesions, narrow-band imaging bronchoscopy

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-027 Pleural Fluid Reactive Oxygen Species Modulator 1 (Romo1) as a Diagnostic and Prognostic Marker in Lung Cancer Patients with Malignant Effusion Seung Hyeun Lee[1], Eun Joo Lee[2], Kyung Hoon Min[2], Gyu Young Hur[2], Seung Heon Lee[2], Sung Yong Lee[2], Je Hyeong Kim[2], Sang Yeub Lee[2], Chol Shin[2], Jae Jeong Shim[2], Kyung Ho Kang[2], Kwang Ho In[2] [1]*Department of Internal Medicine, Kepco Medical Center, Seoul/Korea,* [2]*Division of Respiratory and Critical Care Medicine, Department of Internal Medicine, College of Medicine, Korea University, Seoul/Korea*

Background: Reactive oxygen species modulator 1 (Romo1) is a novel protein that is critical in mitochondrial reactive oxygen species (ROS) generation. It is increased in most cancer cell lines and is associated with resistance to chemotherapy *in vitro*. Recently, serum Romo1 has been suggested as a potential diagnostic marker for non-small cell lung cancer (NSCLC), and increased tissue Romo1 protein expression has been related with poor prognosis in patients following surgical resection for NSCLC. The clinical significance of pleural fluid Romo1 is unknown. We evaluated the clinical usefulness of pleural fluid Romo1 as a potential diagnostic and prognostic marker in patients with lung cancer-associated malignant effusion. **Methods:** Romo1 level was measured in pleural fluid using enzyme-linked immunosorbent assay in four groups: lung cancer-associated malignant effusion (n =24; 15 adenocarcinomas, 7 squamous cell carcinomas and 2 small cell lung cancers), tuberculous pleurisy (n = 14), parapneumonic effusion (n =15) and transudative effusion (n = 16). The discriminative power in lung cancer-associated malignant effusion and the association with survival of Romo1 was determined using receiver operating characteristic (ROC) curve and Kaplan-Meier survival analysis, respectively. **Results:** Pleural fluid Romo1 level was significantly higher in lung cancer-associated malignant effusion compared with other groups (all $p < 0.001$). In the ROC curve analysis, the optimal cutoff value for lung cancer-associated malignant effusion was 451.5 pg/mL with a sensitivity of 81.9% and specificity of 84.8%, with an area under the curve of 0.838 (95% confidence interval: 0.789 - 0892, $p < 0.01$). In addition, at the cutoff determined by median Romo1 level, high Romo1 expression was related with reduced overall survival in patients with NSCLC ($p = 0.03$). For all patients, pleural fluid Romo1 level was not related with age, gender, smoking status, tumor differentiation, histological type, glucose, protein, albumin and lactate dehydrogenase level. **Conclusion:** Romo1 discriminated lung cancer-associated malignant effusion from non-malignant effusions with considerable sensitivity and specificity. Also, high Romo1 level was associated with poor prognosis in lung cancer patients. Pleural fluid Romo1 could be a potential diagnostic and prognostic marker in patients with lung cancer-associated malignant effusion. **Keywords:** pleural effusion, biomarker, reactive oxygen species, non-small cell lung cancer

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

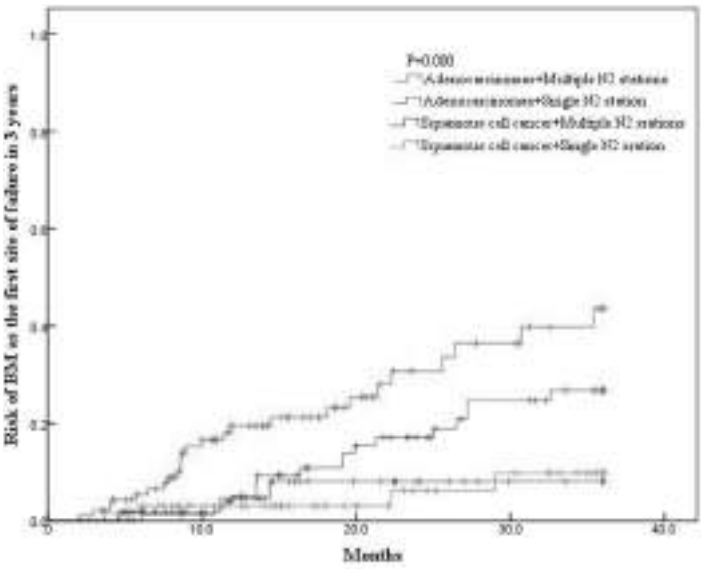
P2.06-028 Accumulation of 18F-FDG Might Predict the Survival of Early-Stage Lung Cancer Patients Masashi Yanada, Katsuhiko Nishiyama, Hiroshi Okazaki *General Thoracic Surgery, Japanese Red Cross Kyoto Daini Hospital, Kyoto/Japan*

Background: In recent years, the outcome of surgically treated early lung cancer patients have improved steadily. However postoperative recurrence following early stage lung cancer surgery can occur: 10-20% possibility of recurrence presents within 5 years after the initial operation. Numerous reports of various malignancies have revealed that 18-Fluoro-2-deoxy-D-glucose (18F-FDG) accumulation, evaluated by positron emission tomography, can be used to predict the prognosis of patients. Our purpose in this retrospective study was to determine if the maximum standardized uptake value (SUVmax) of a primary tumor predicts survival for patients of surgically treated early lung cancer. **Methods:** A total of 170 patients (99 males and 71 females) with curatively operated early lung cancer (p-stage I/II) were enrolled in this study between April 2010 and February 2015 at Japanese Red Cross Kyoto Daini Hospital. Lobectomy 160 cases, segmentectomy 20 cases, and wedge resection 4 cases. The FDG uptake of all primary lung tumor lesions diagnosed by conventional CT was evaluated by 18F-FDG PET/CT. The relation between SUVmax and patient survival was analyzed retrospectively. The postoperative survival rate was analyzed by Kaplan-Meier method, and the differences in survival rates were assessed by log-rank test. A probability value of <0.05 was considered significant. The optimal cut-off value of SUVmax for postoperative recurrences was determined using a receiver operating characteristic (ROC) curve. **Results:** The SUVmax of 170 patients ranged between 0 and 23.7. The median SUVmax was 3.5 for all cases, 3.5 for stage IA, 7.2 for stage IB, 8.2 for stage IIA, and 12.8 for stage IIB (P<0.01). Tumor recurrence occurred in 26 cases (15.3%). According to a survey by the ROC curve, the optimal cut-off value of SUVmax for postoperative recurrences was set at 3.75 with 81% sensitivity, 63% specificity. The survival between patients with SUVmax cut-off value 3.75 or more and patients with SUVmax less than 3.75 were statistically different. The 5-year survival for patients with SUVmax more than 3.75 was 76.6% and the 5-year survival for patients with SUVmax less than 3.75 was 90.6% (P=0.0196). However, the number of patients and the follow-up period were still not extensive enough to settle this important problem conclusively. **Conclusion:** The survival of patients with surgically treated early lung cancer might be predicted by evaluating their SUVmax using 18F-FDG -PET/CT. Among early lung cancer patients, there are potentially advanced lung cancer. The present findings suggested that SUVmax of more than 3.75 in lung cancer patients is predictive of a higher likelihood of recurrence. We recommended close clinical follow-up of the early lung cancer patients with SUVmax more than 3.75 for early diagnosis of recurrence. **Keywords:** early lung cancer, 18F-FDG -PET/CT, maximum standardized uptake value

POSTER SESSION/ SCREENING AND EARLY DETECTION
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.06-029 Risk Factors of Brain Metastases in Completely Resected Stage IIIA(N2) Non-Small Cell Lung Cancer Qin Zhang *Radiation Oncology, Hanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China*

Background: As the first failure, the rate of distant failure was much higher than local failure in patients with completely resected stage IIIA(N2) NSCLC . Brain was the most common site of distant failure as the first failure, and more than 90% Brain metastases (BM) developed in 3 years.We aimed to identify the risk factors of BM as the initial site of failure in 3 years and to define the highest-risk patients who are most likely to benefit from prophylactic cranial irradiation (PCI). **Methods:** The medical records of 301 consecutive patients with pathological stage IIIA (N2) NSCLC who underwent complete surgery were reviewed between January 2005 and July 2012. We observed the correlation between clinical, pathological, microenvironmental factors and BM to find out the risk factors of BM. Main outcome measure was BM as the first site of failure in 3 years. The cumulative incidence of BM as the first site of failure were determined using the Kaplan–Meier analyiss. To assess the risk factors of BM as the first site of failure in 3 years, the log-rank test was used for univariate analysis, and Cox regression was used for multivariate analysis. **Results:** The 1-, 2-, and 3-year risks for patients developing BM as the initial site of failure were 9.3%, 17.7% and 25.8%, respectively. Univariate analysis showed that adenocarcinomas (P = 0.000), multiple N2 stations (P = 0.025), multiple regions of mediastinal lymph node (MLN) involvement (P = 0.023), and highest MLN metastasis (P=0.023) were significantly associated with an increased risk of developing BM as the first site of failure in 3 years. Patients with the tumor budding >5 experienced increased BM in 3 years versus patients with the tumor budding ≤5 (P=0.068) Multivariate analysis showed that adenocarcinomas and multiple N2 stations were significantly associated with the high risk of BM as the initial site of failure in 3 years. In patients with adenocarcinomas and multiple N2 stations, the 3-year actuarial risk of BM as the initial failure was 43.5%.



Conclusion: In patients with completely resected stage IIIA (N2) NSCLC, adenocarcinomas and multiple N2 stations were independent risk factors of BM as the initial failure in 3 years. Patients with the tumor budding >5 had a tendency to experience more BM. Patients with adenocarcinomas and multiple N2 stations are at the highest risk of BM, and are most likely to benefit from PCI. **Keywords:** stage IIIA(N2), NSCLC, risk factor, brain metastases

SESSION: POSTER SESSION/ SMALL CELL LUNG CANCER TUESDAY, SEPTEMBER 8, 2015

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-001 CK2α Is Highly Expressed and Could Represent a Suitable Therapeutic Target in Small Cell Lung Cancer Zhilong Zhao[1], Hongsheng Xue[1], Haili Qian[2] [1]*Thoracic Department, Zhongshan Hospital, Dalian University, Dalian/China,* [2]*State Key Laboratory of Molecular Oncology, Cancer Institute and Hospital, Chinese Academy of Medical Sciences, Beijing/China*

Background: Protein kinase CK2 has long been associated with increased cell growth and proliferation in both normal and malignant cells. CK2α (a catalytic subunit) is highly expressed and pivotal for survival and proliferation in multiple malignancies; however, whether CK2α functions in small cell lung cancer (SCLC) malignant behavior and whether it is feasible to be used as a therapeutic target have not been evaluated. **Methods:** The expression levels of CK2α were analyzed in SCLC tissue microarray and cell line (NCI-H446) by immunohistochemistry and immunofluorescence. After knocking down the CK 2α level by specific siRNA sequence, biological consequences on proliferation, migration, invasion and apoptosis were evaluated. **Results:** CK2α was detected in 66.7% of cases with a trend towards a stronger CK2α immunostain in SCLC tissues compared to normal lung tissues. CK2α silencing had potent suppressive effects on SCLC proliferation, migration and invasion, resulted in abrogation of tumor-cell pseudopod formation, however, did not lead to cell arrest and apoptosis. Western-blot analysis confirmed elevated PML/Bcl-2 protein levels as well as reduced E-Cadherin protein level in the CK2α-silenced SCLC cells.

Patient Characteristics	No. of Cases	%
Gender (F/M)	9/31	22.5/77.5
Stage		
Ⅰ	10	25
Ⅱ	21	52.5
Ⅲ	9	22.5
Tumor		
T1/T2	36	90
T3/T4	4	10
N0	12	30
N1/N2	28	70
Normal Lung Tissue	10	

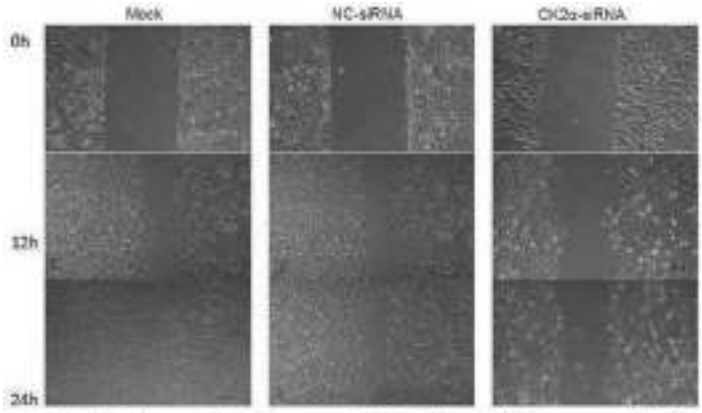


Figure4. CK2α downregulation suppresses SCLC cell motility in the wound healing assay (magnification, ×200).

Conclusion: The results suggest that CK2α negative regulation of the protein levels of tumor suppressor PML/Bcl-2 and activation of the E-Cadherin pathway could be involved in SCLC malignant behavior. Depleting CK2α level may serve as a promising therapeutic strategy for human SCLC. **Keywords:** Protein Kinase, CK2α, Small cell, Lung cancer

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-002 Effects of Eribulin and Radiation on a Panel of Small Cell Lung Cancer (SCLC) Cell Lines Barbara Helfrich[1], David Raben[2], Dexiang Gao[3], Paul A. Bunn, Jr[4] [1]*Medicine, University of Colorado Denver-Amc, Aurora/United States of America,* [2]*Radiation Oncology, University of Colorado Denver-Amc, Aurora/United States of America,* [3]*Biostatistics & Informatics, University of Colorado, Aurora/CO/United States of America,* [4]*Medicine, University of Colorado, Aurora/United States of America*

Background: Background: Chemotherapy produces high response rates in extensive stage SCLC and a modest improvement in 5-year survival rates when combined with chest radiation in limited stage SCLC. Chemotherapeutic agents for SCLC have not changed in 20 years. Eribulin is a microtubule inhibitor that arrests cells in the G2/M fraction of the cell cycle with established activity in breast cancer. Radiobiological studies demonstrated that cells in the G2/M phase of the cell cycle are less efficient at repairing radiation induced DNA damage. Thus, we investigated the effects of eribulin, radiation and the combination on growth and cell cycle distribution in a panel of SCLC cell lines. **Methods:** Methods: Growth inhibition (GI) by varying concentrations of eribulin alone, radiation alone and the combination was assessed by MTS assay at 5 days post-treatment. Growth inhibition or fraction affected (FA) was determined by 1-(x/y) where x is the MTS signal for the experimental condition and y is the MTS signal for the untreated control cells. Our goal was to use a dose of radiation that alone induced a FA of about 0.5 allowing determination of the combination effects with eribulin. Changes in the G2/M distribution of cells treated with eribulin alone, radiation alone and the combination were evaluated at 24 and 48 hours post treatment by propidium iodine staining and analysis by FACS. **Results:** Results: Four of the eight SCLC cell lines were very sensitive to eribulin with half maximal growth inhibitory concentration (FA<0.5) of < 2nM. Four lines had 0.5 FA values > 2nM. 2 Gy radiation produced 32% to 58% growth inhibition in all 8 lines irrespective of their eribulin sensitivity. Low eribulin concentrations (≤ 1.25nM) and 2Gy radiation produced >70% growth inhibition in the 4 sensitive lines, which was significantly more growth inhibition than either alone. Eribulin concentrations of >2.5nM were required to increase growth inhibition over either alone in the 4 more resistant lines and the maximal GI was less in these lines (48%-70%) even at higher concentrations. With respect to G2/M, in the 4 most sensitive eribulin lines, there was a significant increase in the G2/M fraction following eribulin alone (0.625-1.25nM), radiation alone (2 or 3Gy) and a further increase occurred with the combination treatment. In these eribulin sensitive lines, 59% to 93% of the cells were in the G2/M phase by 48 hours. In 3 of the 4 less sensitive eribulin lines, higher concentrations of eribulin (>2.5nM) were required to increase the G2/M fraction to >50% and 2 or 3 Gy irradiation increased the G2/M fraction to 59% to 64%. The combination produced maximal G2/M fractions of 64%-79%. The one most eribulin resistance line never had more than 50% GI or > 40% of cells in G2/M at any concentration or radiation dose up to 4 Gy. **Conclusion:** Conclusions: SCLC cell lines are sensitive to eribulin and radiation and the combination produced significantly more growth inhibition and cell cycle arrest then either alone. The combination warrants further evaluation in in vivo models and potentially clinical trial study in patients with SCLC. **Keywords:** SCLC eribulin radiation

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-003 Attempt to Validate Drug Repositioning for Metastatic Small Cell Lung Cancer (SCLC) Therapy Identifies Statins Associated with Survival Benefit Zoltan Lohinai[1], Peter Dome[2], Zsuzsa Szilagyi[1], Gyula Ostoros[3], Judit Moldvay[1], Balazs Hegedus[4], Balazs Dome[1], Glen J. Weiss[5] [1]*Department of Tumor Biology, National Koranyi Institute of Pulmonology, Budapest/Hungary,* [2]*Department of Clinical and Theoretical Mental Health, Kútvölgyi Clinical Center,, Semelweis University, Budapest/Hungary,* [3]*8Th Dept. of Pulmonology, National Koranyi Institute of Pulmonology, Budapest/Hungary,* [4]*Translational Thoracic Oncology Laboratory, Department of Thoracic Surgery, Comprehensive Cancer Center, Medical University Vienna, Vienna/Austria,* [5]*Medical Oncology, Cancer Treatment Centers of America, Goodyear/AZ/United States of America*

Background: SCLC is an aggressive malignancy with limited treatment options. Based on in vitro data and results of a recent drug repositioning study, some medications approved by the FDA for the treatment of various non-malignant disorders were demonstrated to have anti-SCLC activity in preclinical models. Drug dose levels that demonstrated anti-cancer activity were similar to those used in the clinics. The aim of our study is to confirm whether use of these medications is associated with survival benefit in a large cohort of SCLC patients from a single institution. **Methods:** Consecutive patients with cytologically or histologically confirmed, metastatic SCLC evaluated between 2000-2013 at the National Koranyi Institute of Pulmonology were analyzed in this retrospective analysis. Patients that were prescribed statins, aspirin, clomipramine (a tricyclic antidepressant [TCA]), selective serotonin re-uptake inhibitors (SSRIs), doxazosin, and prazosin were identified. Next, we evaluated the associations amongst these various medications, clinicopathological characteristics (including gender, age, and Eastern Cooperative Oncology Group performance status [ECOG PS]), and overall survival (OS) in univariate and multivariate analyses with Bonferroni correction applied. **Results:** There were a total of 876 patients (508 men and 368 women) with a median age of 61 years (range, 33-86). 75% of the chemotherapy administered in the first line setting was platinum-based. Aspirin, statin, SSRIs, doxazosin, prazosin, and TCA were administered in 138, 72, 20, 14, 14, and 5 cases; respectively. Univariate analysis identified age, ECOG PS, and statin treatment as significant prognostic factors ($p<0.001$; $p<0.001$; and $p=0.002$; respectively). A statistically significant increase in OS was observed only in statin-treated patients when compared to those not receiving any of the aforementioned medications (median OS, 8.4 vs. 6.1 months; respectively). The administration of SSRIs, TCA, aspirin, prazosin, or doxazosin did not result in a statistically significant OS benefit (median OS, 8.5, 7.2, 6.8, 6.8, and 4.6 months; respectively). The multivariate Cox model showed that besides age and ECOG PS, statin treatment was an independent survival predictor (Hazard Ratio, 1.41; 95% confidence interval, 1.1–1.8; $p=0.007$). **Conclusion:** Statins appear to provide a statistically significant survival benefit in metastatic SCLC. Other classes of medications analyzed in this study did not validate the preclinical drug repositioning studies previously reported. Drug repositioning studies using only preclinical data or small numbers of patients should be treated with caution before application in the clinic. **Keywords:** small cell lung cancer, Drug repositioning, statins

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-004 The Relationship between UGT1A1 Gene Polymorphism and Irinotecan Effect on ED-SCLC Xiao Xiaoguang, Xia Shu, Mei Qi, Yuan Chen
Department of Oncology, Tongji Hospital, Tongji Medical College of Huazhong University of Science and Technology, Wuhan/China

Background: NCCN recommends IP program as a first-line chemotherapy of ED-SCLC. Several clinical study conducted in colorectal cancer showed that the polymorphism of UGT1A1*28 gene can evaluate the risk of severe neutropenia and diarrhea occurred in patients receiving irinotecan chemotherapy. The purpose of this research is to analyze the distribution of UGT1A1 gene polymorphisms in Chinese Han patients with ED-SCLC, and to evaluate correlations between UGT1A1 gene polymorphisms and toxicity and efficacy of irinotecan in patients with ED-SCLC. **Methods:** Analysis of UGT1A1*28 and UGT1A1*6 gene polymorphisms were performed by peripheral blood gene sequencing. From June 2011 to Nov 2013, 67 cases admitted to hospital with ED-SCLC treated by irinotecan(CPT-11) based regimen were enrolled in this study. We observe the relationship of PFS , OS and AEs between different genotypes.

Results:

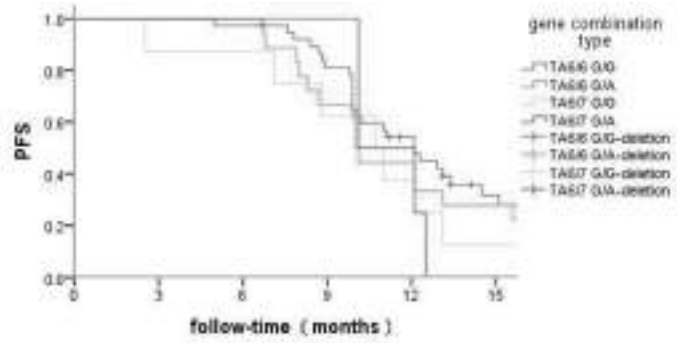


figure 1 the PFS and different gene type

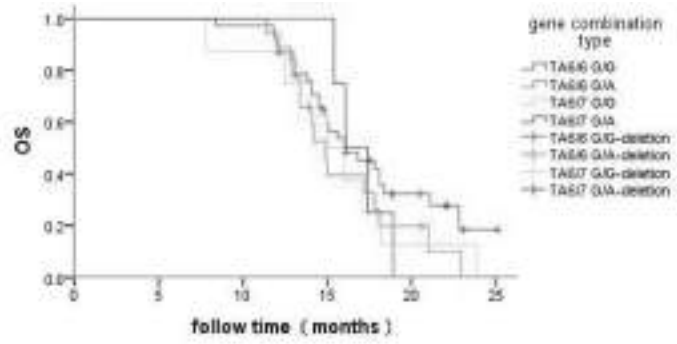


figure 2 the OS and different gene type

The median PFS of wild type UGT1A1*28 (TA6/6) and mutant (TA6/7) was 9.9 months and 10 months respectively; the median PFS of wild type UGT1A1*6 (G/G) and UGT1A1*6 mutant (G/A) was 9.7 months and 9.9 months respectively. The median OS of wild type UGT1A1*28 (TA6/6) and mutant (TA6/7) was 13.9 months and 14.5 months respectively; the median OS of wild type UGT1A1*6 (G/G) and UGT1A1*6 mutant (G/A) was 13.8 months and 14.1 months respectively. No significant difference of PFS and OS was observed between different genotypes($p>0.05$). The incidence of grade 3 and 4 delayed diarrhea and neutropenia in patients carrying UGT1A1*6 G/A was higher than that in the WT genotype(36.4% vs. 6.6% $p<0.05$; 27.2% vs. 4.4% $p<0.05$ respectively); The patients simultaneously carrying UGT1A1*28 TA6/7 and UGT1A1*6 G/A were prone to suffering 3 and 4 delayed diarrhea and neutropenia. **Conclusion:** Although UGT1A1 polymorphisms failed to predict the efficacy of CPT-11 in ED-SCLC, the prediction of adverse effect may worth attention. **Keywords:** gene polymorphism, irinotecan, adverse effect, small cell lung cancer

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-005 AVE plus Valproate for Refractory/Relapsing SCLC: A Phase II Study by the ELCWP Thierry Berghmans[1], Jean-Jacques Lafitte[2], Arnaud Scherpereel[2], Marianne Paesmans[3], Lieveke Ameye[3], Anne-Pascale Meert[1], Luc Willems[4], Nathalie Leclercq[1], Jean-Paul Sculier[1] *[1]Intensive Care and Thoracic Oncology, Institut Jules Bordet, Brussels/Belgium, [2]Pneumology, CHU Lille, Lille/France, [3]Data Centre, Institut Jules Bordet, Brussels/Belgium, [4]Gembloux Agro-Bio Tech and Interdisciplinary Cluster for Applied Genoproteomics, University of Liège, Liège/Belgium*

Background: Salvage chemotherapy (CT) for relapsing or refractory small cell lung cancer (SCLC) to platinum-etoposide remains disappointing. *In vitro* experiments are suggesting that valproic acid, by inhibiting histone deacetylases (HDAC), could increase apoptosis of SCLC cell lines exposed to doxorubicin, vindesine and bis(2-chloroethyl) amine. The primary objective of this phase II study is to determine if epigenetic modulation with valproic acid in addition to a doxorubicin, vindesine, cyclophosphamide (AVE) regimen may allow adequate improved 6-months progression-free survival (PFS) in refractory/relapsing SCLC. **Methods:** Patients (pts) with previously pathologically proven SCLC, either primary or secondary refractory to prior chemotherapy regimen including platinum derivatives and etoposide, Karnofsky performance status ≥ 60, adequate haematological, hepatic, renal, lung and cardiac functions were eligible. After central registration, pts received AVE (doxorubicin 45 mg/m^2, vindesine 3 mg/m^2, cyclophosphamide 1 g/m^2 every 3 weeks) plus daily oral valproic acid to obtain serum concentration in the range of the recommended values for the treatment of epilepsy (50-100 µg/ml). Response was assessed after 3 courses and responders continued treatment until best response, unacceptable toxicity or cumulative dose of doxorubicin > 500 mg/m^2. The trial was designed to show that 6-months PFS was > 18%, powering the trial to detect an increase to at least 39%. With this assumption, at least 43 pts assessable for PFS had to be registered (a 10%, b 10%). **Results:** From 11/2008 to 12/2013, 64 pts were registered of whom 6 were ineligible. The main characteristics of the 58 eligible pts were: male/female 38/20 pts, PS 60-70/80-100 17/41 pts, median age 60 years, 19 pts received two or more previous lines of CT. Seven pts did not receive any CT leaving 51 pts assessable for the primary endpoint. Objective response rate was 19.6% (95% CI 8.7%-30.5%). Median PFS was 2.75 months (95% CI, 2.46 to 3.61) and 6-months PFS was 6%. Median survival time was 5.9 months (95% CI, 4.7 to 7.5) with 6 and 12-months survival rates of 50% and 6%. As expected, toxicity was mainly haematological with 88% and 26% grade 3-4 neutropenia and thrombopenia, respectively. **Conclusion:** Despite an interesting response rate, the addition of valproic acid to AVE did not translate into adequate PFS in relapsing/refractory SCLC to platinum/etoposide. This regimen cannot be recommended for further investigation. **Keywords:** small cell lung cancer, epigenetics, valproic acid

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-006 Study on Feasibility of Hippocampal Avoidance Prophylactic Cranial Irradiation Mao Zhang, Tao Sun, Mingwei Bu, Xiao Guo, Jin Zhang *Departement of Radiation Oncology, Jilin Province Cancer Hospital, Changchun, Jilin/China*

Background: To investigate the dosimetric characteristics, feasibility and risk of Hippocampal avoidance prophylactic cranial irradiation (HA-PCI), in intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT). **Methods:**Sixteen patients with limited-stage small-cell lung cancer (LS-SCLC) achieved complete remission after chemoradiotherapy accepted HA-PCI. After image evaluation by fusing CT and MRI, hippocampal avoidance regions were created in the hippocampus. A 5 mm area around the hippocampus was plotted as radiation dose deduction area. Patients were randomly assigned to accept intensity-modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT). The prescription dose was DT25Gy per 10 fractions.The dose distribution of whole brain, hippocampus and hippocampal plus 5mm were calculated. **Results:** The mean value of Hippocampal volume in the sixteen patients was 2.76 cm^3(range 2.56cm^3-3.01cm^3). Using IMRT and VMAT, the mean value of radiation dosein hippocampus was 9.04Gy (range 8.92Gy-9.39Gy)and 10.32Gy (range 10.13Gy-10.82Gy), respectively, reduced by 66.03% and 61.17% compared with whole-brainirradiation.The mean dose in the avoidance regions for IMRT and VMAT was 13.57Gy (range 13.47Gy-13.67Gy),and 14.86Gy (range 14.33Gy-15.89Gy), respectively, reduced by 49.00% and 44.29% compare with whole-brain radiation. **Conclusion:** HA-PCI in IMRT and VMAT is feasible in clinical practice and can achieve adequate whole brain coverage, as well as reduce exposure dose in hippocampus. HS-PCI can protect patient's neurocognitive function. **Keywords:** Lung neoplasms, prophylactic cranial irradiation, hippocampal avoidance, radiotherapy technique

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-007 Prophylactic Cranial Irradiation for Extensive Stage Small Cell Lung Cancer Yu Yang Soon[1], Huili Zheng[2], Shaun Z. Ho[3], Wee Yao Koh[1], Su Woon Kim[3], Cheng Nang Leong[1], En Yun Loy[2], Jeremy Tey[1], Balamurugan Vellayappan[1], Swee Peng Yap[3], Kam Weng Fong[3], Ivan Tham[1] *[1]National University Cancer Institute Singapore, Singapore/Singapore, [2]Health Promotion Board, Singapore/Singapore, [3]National Cancer Centre Singapore, Singapore/Singapore*

Background: The survival benefit of prophylactic cranial irradiation (PCI) in extensive stage small-cell lung cancer (ES-SCLC) reported by an EORTC randomized trial in 2007 has been questioned recently, as a Japanese study with similar trial design failed to show similar results. This retrospective cohort study aims to evaluate the uptake of PCI and its impact on the survival of ES-SCLC before and after publication of the EORTC randomized trial. **Methods:** All patients diagnosed with ES-SCLC without brain metastases and had stable disease or better after first line chemotherapy in the only two Singapore national cancer centers from 2003 to 2010 were identified using the institutions' pathology registries. We linked the treatment records to the national death registry. We described the utilization of PCI and compared survival of patients diagnosed from 2003 to 2006 (pre-adoption cohort) with patients diagnosed from 2007 to 2010 (post-adoption cohort). Characteristics between pre and post-adoption cohorts were analyzed using chi-square test. Survival was determined from date of diagnosis to death using Kaplan-Meier method. Predictors for improved survival were determined using multivariate analysis. **Results:** 71 patients were identified. The demographic and clinical characteristics were similar between the two cohorts save for more patients in the post-adoption cohort having second line therapy (49% versus (vs) 16%, P = 0.01) and receiving PCI (32% vs 10%, P = 0.04). There was no difference in overall survival between the two cohorts (Hazard ratio [HR] 0.70; 95% Confidence Interval [CI] 0.43 to 1.13, P = 0.148). Multivariate analysis showed that PCI (HR 0.47; 95% CI 0.24 to 0.91, P = 0.024) and thoracic radiotherapy (HR 0.49; 95% CI 0.28 to 0.86, P = 0.013) was associated with lower risk of death. **Conclusion:** There was an increase in the uptake of PCI for ES-SCLC since 2007. The use of PCI and thoracic radiotherapy has been shown to be predictors for improved survival in ES-SCLC who had stable disease or better after first line chemotherapy. A larger population based outcome study is warranted to confirm these observations. **Keywords:** prophylactic cranial irradiation, small cell lung cancer

POSTER SESSION/ SMALL CELL LUNG CANCER
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P2.07-008 CTC 11-001: Phl Study of Carfilzomib (C) + Irinotecan (I) in Relapsed, Irinotecan Sensitive Solid Tumors Susanne M. Arnold[1], Kari Chansky[2], Markos Leggas[3], Michael Thompson[4], John Hamm[5], Rachel E. Sanborn[6], Glen J. Weiss[7], Kamal Chatta[8], Maria Q. Baggstrom[9] [1]*Medical Oncology, University of Kentucky, Lexington/KY/United States of America,* [2]*Biostatistics, Cancer Research and Biostatistics, Seattle/United States of America,* [3]*College of Pharmacy, University of Kentucky, Lexington/KY/United States of America,* [4]*Cancer Center, Aurora Research Institute, Wauwatosa/WI/United States of America,* [5]*Medical Oncology, Norton Cancer Institute, Louisville/KY/United States of America,* [6]*Medical Oncology, Providence Portland Medical Center, Portland/OR/United States of America,* [7]*Medical Oncology, Cancer Treatment Centers of America, Goodyear/AZ/United States of America,* [8]*Medical Oncology, Virginia Mason Cancer Institute, Seattle/WA/United States of America,* [9]*Division of Oncology, Washington University School of Medicine, St. Louis/MO/United States of America*

Background: Inactivation of proteasome function allows for increased apoptosis and the potential for enhanced antitumor effect by chemotherapy. Carfilzomib (C) and Irinotecan (I) potentially synergize by increasing camptothecin-induced apoptosis and interfering with topoisomerase-I degradation, preventing DNA damage repair. This report describes the initial phase I study of C + I in adults with relapsed, irinotecan-sensitive cancers including small cell lung cancer (SCLC). **Methods:** The primary endpoint was determination of the MTD of 28-day cycle 1 of I (D1,8,15) and C (D1,2,8,9,15,16) using a standard 3+3 Ph1 design. Toxicity and response were evaluated using NCI CTCAE (v4) and RECIST (v1.1). Pharmacodynamics endpoints (proteasome activity, topo-1 expression, and gamma-H2AX protein expression in PBMC) were assessed on C1D1 and C1D2. **Results:** 16 patients were enrolled at 3 dose levels of C (mg/m2/d) using stepped-up dosing: 20 mg given C1D1 & C1D2 then increased to the dose indicated: 20/27 (N=4), 20/36 (N=9), 20/45 (N=3) and I dosed at 125 mg/m2d. Median age: 64 (range 56-78), 8 M/8F. Tumor types included: SCLC (N=13), non-small cell lung cancer (NSCLC) (N=2) and ovarian (N=1). 6 subjects completed 2 or more cycles of therapy, 4 subjects were not evaluable for dose-limiting toxicity (DLT) secondary to rapid progressive disease (PD) or withdrawal and were replaced. 2 DLTs were observed in cohort 3, Grade (Gr)4 thrombocytopenia lasting ≥ 7 days and Gr3 diarrhea lasting ≥ 7 days) and 1 DLT in cohort 2 (Gr3 diarrhea lasting ≥ 7 days). Serious adverse events (SAEs) by dose level: 20/27: Gr3 Dysphagia and recurrent laryngeal nerve palsy, (unrelated); Gr3 peripheral motor neuropathy and Gr3 urinary incontinence, (unrelated); 20/36: Gr3 fatigue, multiple occurrences; Gr3 diarrhea with dehydration; Gr3 cholelithiasis with dehydration (unrelated); 20/45: Gr3 dehydration, Gr3 anemia, Gr2 anemia and Gr3 acute on chronic kidney disease. Common Gr3/4 AEs were: fatigue (19%), thrombocytopenia (19%), diarrhea (13%), anemia (6%), neutropenia (6%), and leukopenia (6%). One patient (25%), five patients (55%), and two patients (67%) experienced Gr3/4 AEs in cohorts 1, 2, and 3, respectively. The maximum tolerated dose was exceeded at 20/45. Antitumor activity (stable disease or better) was observed in 3 SCLC subjects to date, with updated follow-up to be reported. **Conclusion:** C and I is a well-tolerated combination with anti-tumor activity in heavily pretreated patients. The recommended phase 2 dose of Carfilzomib is 20/36 mg/m2/d in combination with Irinotecan 125 mg/m2/d. A phase 2 study in SCLC is ongoing through the Lung Cancer Research Team (LCRT). This study was supported by Onyx Pharmaceuticals, a subsidiary of Amgen Corporation. Clinical trial information: NCT01941316. **Keywords:** camptothecins, phase I clinical trial, pharmacokinetics

POSTER SESSION/ SMALL CELL LUNG CANCER
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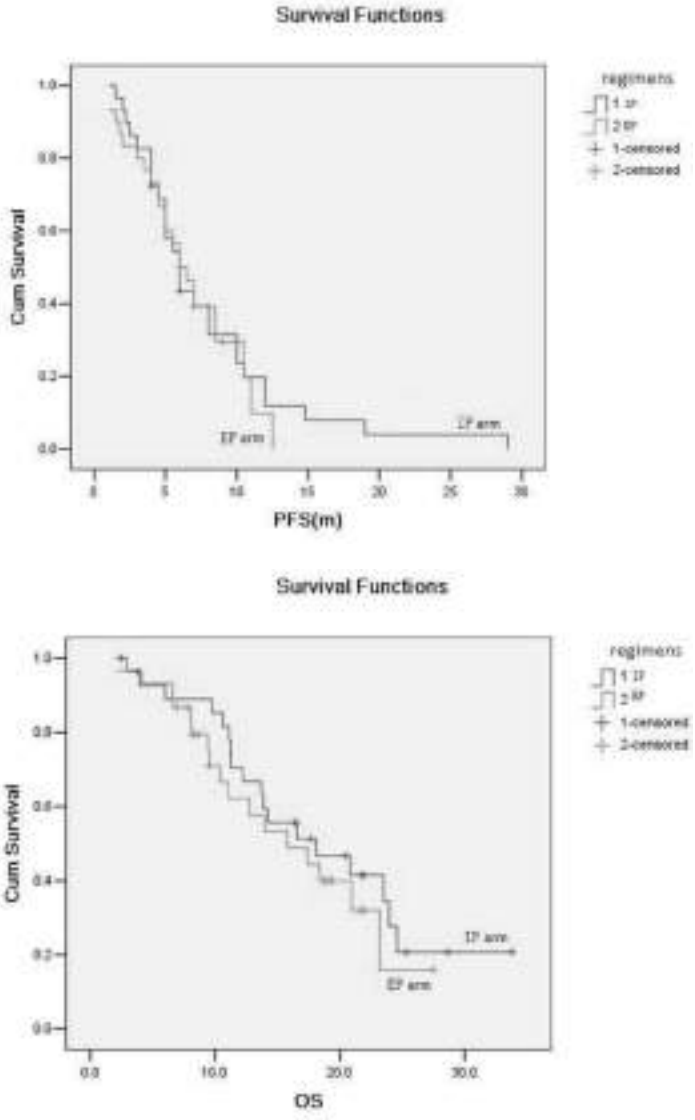
P2.07-009 Cisplatin Combined with Irinotecan or Etoposide for Untreated Extensive-Stage Small Cell Lung Cancer Yuankai Shi[1], Xingsheng Hu[1], Yi Hu[2], Xiaohong Han[1], Xue Li[3], Lin Lin[1] [1]*Department of Medical Oncology, Cancer Institute and Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing Key Laboratory of Clinical Study on Anticancer Molecular Targeted Drugs, Beijing/China,* [2]*Chinese PLA General Hospital, Medical School of Chinese PLA, Beijing/China,* [3]*China-Japan Friendship Hospital, China-Japan Friendship Hospital, Beijing/China*

Background: This study aims to evaluate the efficacy and safety of irinotecan/cisplatin (IP) and etoposide/cisplatin (EP) in extensive-stage small cell lung cancer (ES-SCLC) and the distribution of UGT1A1. Simultaneously, the relationship between UGT1A1 genotypes and patient outcomes were assessed. **Methods:** Patients with untreated ES-SCLC were randomly assigned to receive either IP or EP, and blood specimens were collected to test the genotypes of UGT1A1*28 and UGT1A1*6. The association of efficacy and toxicity of IP regimen with UGT1A1 genotype was analyzed. **Results:** Of the 62 patients enrolled from three institutions, 30 patients were in the IP and 32 patients were in the EP arms, respectively. Disease control rates (DCR) with IP and EP were 83.3% and 71.9%, respectively (P=0.043). Median progression-free survival (PFS) for IP and EP were both 6 months. Median overall survival (OS) for IP and EP was 18.1 and 15.8 months respectively, without significant difference. Grade 3-4 thrombocytopenia was more common with EP (18.8% versus 6.7%, P=0.035), while the incidence of diarrhea was higher with IP (70% versus 15.6%, P=0.008). The incidence of grade1-4 late-onset diarrhea of wild-type, heterozygous and homozygous UGT1A1*28 were 65.0%, 85.7% and 66.7% respectively (P=0.037). UGT1A1*28 polymorphisms, Eastern Cooperative Oncology Group (ECOG) performance status, chemotherapy cycles were the essential factors affecting grade1-4 late-onset diarrhea in a logistic regression analysis.



Conclusion: The efficacy of IP regimen was similar to EP regimen for untreated ES-SCLC. UGT1A1 polymorphisms was associated with late-onset diarrhea, however it has no influence on efficacy. **Keywords:** irinotecan, extensive-stage small cell lung cancer, etoposide, UGT1A1

POSTER SESSION/ SMALL CELL LUNG CANCER
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P2.07-010 Alisertib (MLN8237)+Paclitaxel versus Placebo+Paclitaxel for Relapsed SCLC Taofeek K. Owonikoko[1], Tibor Csoszi[2], Kristiaan Nackaerts[3], Edgardo Santos[4], Christina S. Baik[5], Erzesbet Juhasz[6], Vitezslav Kolek[7], Gyula Ostoros[8], Jaromir Roubec[9], Hossein Borghaei[10], Alberto Chiappori[11], Christos Chouaid[12], Margarita Majem[13], E Jane Leonard[14], Jungah Jung[15], Claudio Dansky Ullmann[14], David Spigel[16] [1]*Hematology & Medical Oncology, Emory University School of Medicine, Atlanta/GA/United States of America,* [2]*Department of Oncology, Hetenyi G Korhaz, Onkologiai Kozpont, Szolnok/Hungary,* [3]*Department of Respiratory Diseases, Respiratory Oncology Unit, Ku Leuven-University of Leuven, University Hospitals Leuven, Leuven/Belgium,* [4]*Department of Oncology, Lynn Cancer Institute/Florida Atlantic University, Boca Raton/FL/United States of America,* [5]*Division of Medical Oncology, Thoracic, Head, and Neck Program, University of Washington, Seattle Cancer Care Alliance, Seattle/WA/United States of America,* [6]*Orszagos Koranyi Tbc Es Pulmonologiai Intezet, Budapest/Hungary,* [7]*Department of Klinika Plicnich Nemoci A Tuberkulozy, Fakultni Nemocnice Olomouc, Olomouc/Czech Republic,* [8]*Viii. Tudobelosztaly, Orszagos Koranyi Tbc Es Pulmonologiai Intezet, Budapest/Hungary,* [9]*Klinika Plicních Nemocí A Tbc, Fakultní Nemocnice Ostrava-Poruba, Ostrava/Czech Republic,* [10]*Department of Medical Oncology, Fox Chase Cancer Center, Philadelphia/PA/United States of America,* [11]*Department of Thoracic Oncology, H. Lee Moffitt Cancer Center and Research Institute, Inc, Tampa/FL/United States of America,* [12]*Service de Pneumologie, Centre Hospitalier Intercommunal de Créteil, Créteil/France,* [13]*Department of Oncology, Hospital de La Santa Creu I Sant Pau, Barcelona/Spain,* [14]*Oncology Clinical Research, Millennium Pharmaceuticals, Inc., A Wholly Owned Subsidiary of Takeda Pharmaceutical Company Limited, Cambridge/MA/United States of America,* [15]*Statistics, Millennium Pharmaceuticals, Inc., A Wholly Owned Subsidiary of Takeda Pharmaceutical Company Limited, Cambridge/MA/United States of America,* [16]*Sarah Cannon Research Institute/*

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Background: Small cell lung cancer (SCLC) is an aggressive malignant disease comprising approximately 14% of all lung cancers, with approximately 31,000 new diagnoses each year in the USA. SCLC has a very poor prognosis, particularly in patients presenting with extensive stage disease. Platinum-based combinations are standard first-line therapy for SCLC; however, relapse is almost universal (≥85%) and patients require further treatment in subsequent lines. Effective new targeted therapies are needed to improve the poor outcomes observed in SCLC. Alisertib is an investigational, orally available, selective inhibitor of Aurora A kinase. Alisertib has shown single-agent antitumor activity in preclinical *in vivo* models of SCLC and has demonstrated synergism with paclitaxel in this setting. Single-agent alisertib has demonstrated promising efficacy in patients with relapsed/refractory SCLC (Melichar B, et al. Lancet Oncol 2015;16[4]:395–405). Further, phase 1 and 2 evaluation of alisertib+paclitaxel in patients with relapsed ovarian cancer and breast cancer has suggested the antitumor activity of this combination (Falchook G, et al. Int J Gynecol Cancer 2013;23[8] Suppl_1:abstract; Coleman R, et al. Ann Oncol 2014;25[Suppl_4]:abstract 8760). Here we describe the design and objectives of an ongoing phase 2, randomized, double-blind, placebo-controlled study of alisertib+paclitaxel versus placebo+paclitaxel in patients with relapsed SCLC and previously treated with only one line of platinum-based therapy (NCT02038647). **Methods:** Approximately 166 adult patients with relapsed SCLC after standard first-line platinum-based therapy, measurable disease by RECIST v1.1, and Eastern Cooperative Oncology Group performance status 0 or 1 will be enrolled at approximately 80 sites in the USA and Europe. Patients will be randomized 1:1 (stratified by type of relapse [sensitive vs resistant/refractory] and presence of brain metastases) to receive 28-day cycles of either alisertib 40 mg or matched placebo PO twice daily on days 1–3, 8–10, and 15–17, plus paclitaxel 60 or 80 mg/m^2 IV, respectively, on days 1, 8, and 15, until disease progression or unacceptable toxicity. The primary endpoint of the trial is progression-free survival (PFS). Assuming a hazard ratio of 0.6 for PFS, a total of 138 progression/death events will be required to provide 85% power (two-sided alpha=0.05). Secondary endpoints include: overall and complete response rates; disease control rate; duration of response; overall survival; safety (NCI-CTCAE v4.03); alisertib pharmacokinetics; and symptom-related endpoints (symptom score, time to symptom relief, time to symptom progression). Evaluation of candidate biomarkers in tumor tissue specimens and in circulating tumor cells (CTC)/circulating tumor DNA, change from baseline in CTC numbers, and health-related quality of life (EORTC QLQ-C30/QLQ-LC13 instruments) are exploratory endpoints. As of 10 April 2015, there are 60 sites open in 6 countries with 90 patients randomized. The study continues to enroll patients. **Results:** not applicable **Conclusion:** not applicable
Keywords: small cell lung cancer, alisertib, paclitaxel, relapsed

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P2.07-011 Maintenance with Lanreotide in SCLC Patients, Expressing Somatostatine Receptors, after Response to First Line Therapy Antonio Santo[1], Elisa Roca[2], Francesca La Russa[3], Francesco Grossi[4], Carlo Genova[5], Adolfo G. Favaretto[6], Angela Sibau[7], Alessandro Follador[7], Alessandra Bearz[8], Giampiero Romano[9], Maximilian Papi[10], Alberto Caprioli[2], Annamaria Catino[11], Domenico Galetta[12]
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Background: Small cell lung cancer (SCLC) is a rapidly progressive disease, characterized by rapid progression in spite of initial responsiveness to first-line chemotherapy. In this setting, an effective and safe maintenance therapy might result in improved disease control; to date, no maintenance strategy has been registered for SCLC yet. Since SCLC cells express a neuroendocrine phenotype, some tumors may express significant levels of somatostatin (SST) receptors; this feature might be exploited for new therapeutic approaches. The aim of our study is to investigate the activity of lanreotide, a SST analogue, as maintenance for patients with SCLC who have achieved a complete response (CR) or partial response (PR) to standard platinum-based chemotherapy (CHT) alone or combined with radiation therapy (RT) , in order to improve progression-free survival (PFS). **Methods:** In this prospective, open-label, multicenter, randomized phase III trial, patients with confirmed diagnosis of SCLC (limited or extended disease) expressing SST receptors (assessed by SST receptor scintigraphy) and with objective response (CR or PR) after CHT or CHT/RT are randomized (1:1) to one of the following arms: maintenance therapy/consolidation with 120 mg lanreotide, by deep subcutaneous injection, every 28 days up to progressive disease (PD) or one year (Arm A); or observation (Arm B). The patients were re-assessed every two months until documented PD during the first year after randomization, and then every three months. The planned enrollment period is 24 months, followed by a period of maintenance of 12 months and further 6 months for the completion of follow-up; the planned global period of the study is 3 years and a half. **Results:** This study is still ongoing; therefore, it is not possible to show its final results yet. However, relevant preliminary data can be described. Currently, out of 76 expected patients, 53 were enrolled; of these, 11 patients (37.96%) in Arm A had limited disease and 18 (62.06%) extended disease. In Arm B, 11 patients had limited disease (45.83%) and 13 (54.17%) had extended disease. After one year of follow-up, among 29 patients randomized to Arm A, 1 patient died (3.45%), while 12 patients experienced PD (41.38%), and 16 are still on study (55.17%); among 24 patients randomized to Arm B, 2 deaths occurred (8.33%), while 11 patients experienced PD (45.83%) and 11 are still on study (45.83%). In Arm A, no significant adverse events were reported. **Conclusion:** This study will determine whether maintenance with lanreotide could prolong PFS of patients with SCLC expressing SST receptors and responsive to upfront CHT or CHT/RT. Moreover, the final results of this study might establish if this treatment could result in an improved overall survival rate after two years. To date, lanreotide has demonstrated an excellent safety profile in all the treated patients. On behalf of FONICAP (Forza Operativa Nazionale Interdisciplinare contro il Cancro del Polmone)
Keywords: SCLC, maintenance, SST analogue

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P2.07-012 Accelerated Hypofractionated Radiotherapy and Concurrent Etoposide / Cisplatin in Patients with Limited-Disease SCLC (LD-SCLC) Sherif Abdelwahab, Wesam Elghamry, Ali Azmy, Iman Fouad, Zeinab Elsayed *Clinical Oncology, Ain Shams University, Cairo/Egypt*

Background: The optimal TRT dose/fraction for LS-SCLC remains debatable, and due to increasing number of population in Egypt and number of patients as well, so reducing the duration of radiation therapy is favored. This study was conducted using etoposide and cisplatin (EP) concurrently with accelerated hypofractionated thoracic radiation therapy to evaluate the response and toxicity of this protocol in the treatment of patients with limited-disease small cell lung cancer (LD-SCLC). **Methods:** Thirty patients with previously untreated LD-SCLC were enrolled into this study between June 2012 and February 2015. All patients received etoposide 100 mg/m^2 days 1 to 3 and cisplatin 25 mg/m^2 days 1 to 3 with start of accelerated hypofractionated thoracic radiation therapy on first day of the second cycle of chemotherapy of 55 Gy,2.5 Gy/ fraction over 30 days. Chemotherapy was given 4-6 cycles. Prophylactic cranial irradiation 25 Gy in 10 daily fractions was given for patient who achieved complete remission. **Results:** The median age was 61 years; 28 patients (93%) were men. ECOG PS was 0 in 6 (20%) patients , 1 in 20 (67%) patients and 2 in 4(13%) patients. Five (17%) patients achieved a complete response (CR), 22 (73%) patients achieved a partial response (PR), while 2 patients (7%) had progressive disease (PD) and 1(3 %) patients achieved stable disease; therefore, the overall response rate was 90%. The median survival time was 26.4 months and 1- and 2-year survival rates were 78% and 58.3%, respectively. The median progression-free survival (PFS) was 16.7 months, and 1- and 2-year PFS times were 60% and 41.4%, respectively. Among the hematologic toxicities neutropenia was the most prevalent toxicity and it was evident as grade 3-4 in 12 patients (40%). Grade 3-4 Asthenia was the most prevalent nonhematological toxicity, in 12 patients (40%); esophagitis occurred in 7 patients (23%). No treatment-related deaths (due to sepsis or bleeding) were reported in the study. **Conclusion:** Using etoposide and cisplatin concurrently with accelerated hypofractionated thoracic radiation therapy for the treatment of patients with LD-SCLC showed an encouraging outcomes and acceptable toxicity and warrants further research.
Keywords: LD-SCLC, Elderly, Accelerated Hypofractionated Radiotherapy

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P2.07-013 Medically Inoperable Early Stage Small Cell Lung Cancer: Patterns of Failure after SBRT Gregory M.M. Videtic[1], Chandana Reddy[2], Neil Woody[2], Kevin Stephans[2] [1]*Radiation Oncology, Cleveland Clinic, Cleveland/OH/United States of America,* [2]*Cleveland Clinic, Cleveland/United States of America*

Background: To report on the patterns of failure for medically inoperable early stage small cell lung cancer (SCLC) when stereotactic body radiotherapy (SBRT) manages the primary lung tumor. **Methods:** We queried our institutional IRB-approved SBRT registry for the period 2004-2014 for any early stage SCLC patients with a minimum of 6 months follow up. All patients had biopsy proven disease and were deemed medically inoperable after multi-disciplinary review. Routine staging consisted of PET/CT and MRI brain scans only. The treatment model consisted of SBRT to the primary followed by adjuvant platinum-based chemotherapy (CHT) and then prophylactic cranial irradiation (PCI). SBRT was delivered employing a stereotactic-specific LINAC with vacuum-bag based immobilization, and infrared-based X-ray positioning system+/- CBCT for image-guidance. **Results:** Of 747 definitively treated cancers over 10 years , 16 (2%) were SCLCs meeting study criteria. Patient characteristics revealed: median KPS was 80 (range 50-90), median age was 69 years (range 45-87), 50% of patients were female, median BMI was 28.2 (range 17.4-41.2). Tumor characteristics revealed: median tumor size was 3.25cm (range1.4-7.2), 4 (25%) tumors were "central" (per RTOG 0813 criteria), median PET-SUVmax was 10.3 (range 2.8-21.1). Median time to SBRT from diagnosis was 2.1 months (range 0.6-6.7). SBRT schedules were: 60 Gy/3 fractions in 25%, 50 Gy/5 fractions in 68.75%, 30 Gy/1 fraction in 6.25% of cases. Mean follow up was 15 months. Fifteen (94%) received at least 2 cycles CHT, of which 2 (12.5%) received CHT before SBRT. Nine patients (56%) received PCI and of the 7 (44%) that did not, 1 developed brain metastases prior, 1 refused, and 5 died of non-cancer issues before PCI . There was no grade 3 or higher toxicity; rate of grade 2 or less toxicity was 12.5%. Seven patients (43.75%) were alive at analysis and of the 9 deaths, 2 (22%)were cancer, 5 were non-cancer (56%), 2 unknown cause(22%). Local control was 100% with 13 patients (81.25%) without any failure. Crude rates of failure were one (6.3%) distant and regional nodal and two (12.5%) distant. Median survival was 39 months. Three-year actuarial overall and progression-free survivals were 50.5% and 76%, respectively. **Conclusion:** SBRT for stage I medically inoperable SCLC yields excellent local control. The absence of regional nodal failure lends support to PET for mediastinal staging. The primary pattern of failure is distant.
Keywords: small cell lung cancer, early stage, SBRT, patterns of failure

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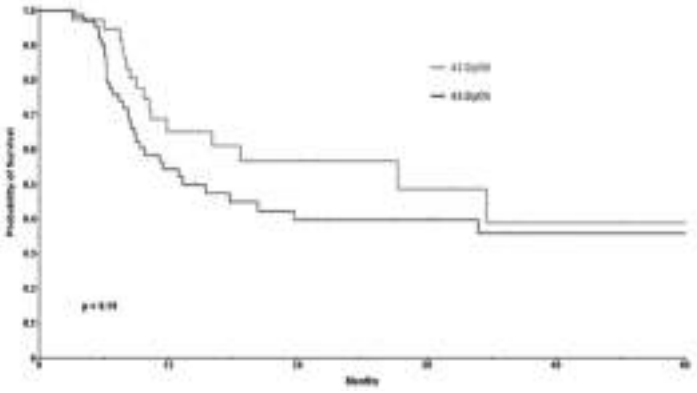
P2.07-014 Does Prophylactic Cranial Irradiation Improve Overall Survival of Elderly Patients with Limited-Stage Small Cell Lung Cancer? Ritsuko U. Komaki, Xiong Wei, Pamela K. Allen, Emma B. Holliday, Ahsan Farooqi, Steven H. Lin, James W. Welsh, James D. Cox *Radiation Oncology, MD Anderson Cancer Center, Houston/TX/United States of America*

Background: Prophylactic cranial irradiation (PCI) has led to improved overall survival (OS) for patients with small cell lung cancer (SCLC) that has responded completely to chemotherapy and thoracic radiotherapy. However, whether PCI is indicated for elderly patients remains unclear. **Methods:** We reviewed 658 patients with limited-stage SCLC treated in 1986-2009 at a single institution with definitive concurrent chemoradiation to a total radiation dose of 45-70 Gy. Variables investigated for possible association with OS included patient sex, age, ethnicity, Karnofsky performance status (KPS) score, year of diagnosis and treatment period (1986-1999 vs. 2000-2009), tumor size, radiation dose, cycles of induction chemotherapy, use of intensity-modulated-radiation-therapy (IMRT), and fractionation. Groups were compared with chi-square tests for categorical variables or medians tests for continuous variables. Kaplan-Meier estimates were constructed for overall survival (OS), disease-free survival (DFS), local-recurrence-free survival (LRFS), distant metastasis-free survival (DMFS). **Results:** Among 658 patients, 507 patients were <70 years old (Group A) and 151 patients were ≥70 years old (Group B). Median survival time was significantly longer in the younger group (25.6 months vs. 20.3 months, *P*=0.007), but no differences were found in DFS, LRFS, or DMFS time by age. Of the 151 patients aged ≥70 years (54 of whom received PCI and 89 did not), those treated in 2000-2009 (vs. 1986-1999) had better brain MFS than those treated in 1986-1999 (*P*=0.048); those who received PCI had better brain MFS than those who did not (*P*=0.033). Multivariate analysis showed that among patients aged ≥70, receiving PCI, not receiving induction chemotherapy, and local-regional control were associated with fewer brain metastases (for PCI, subdistribution hazard ratio [SHR]=0.40, 95% confidence interval [CI] 0.17-0.95, *P*=0.037; for induction chemotherapy, SHR=0.43, 95% CI=0.19-0.96, *P*=0.039; and for local-regional failure, SHR=0.996, 95% CI=0.993-0.998, *P*=0.001). Among patients ≥70, receipt of PCI seemed to have been associated with better OS for those with small-volume disease (primary+nodal disease <5 cm, *P*=0.0545) but not for those with larger-volume disease (*P*=0.7387). **Conclusion:** Patients aged ≥70 years with small-volume limited-stage SCLC seemed to show a benefit in OS from the use of PCI, but those with larger-volume disease did not. Improved brain MFS was associated with use of PCI, no induction chemotherapy, and locoregional control. **Keywords:** prophylactic cranial irradiation, Elderly patients, Limited-stage small cell lung cancer

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-015 Pattern of Failure after Definitive Radiotherapy for Small Cell Lung Cancer Siri S. Rasmussen[1], Olfred Hansen[2], Karin H. Hansen[2], Tine Schytte[3] [1]*Department of Oncology, Odense University Hospital, Odense/Denmark,* [2]*Department of Clinical Oncology, Odense University Hospital, Odense C/Denmark,* [3]*Department of Oncology, Odense University Hospital, Odense C/Denmark*

Background: The standard of care for limited disease SCLC is chemo-radiotherapy. The recommended radiotherapy schedule is 45 Gy/30 F bi-daily (BD-RT) for patients in good performance status according to various guidelines. However, a large proportion of these patients are not able to fulfill the bi-daily schedule due to frailty. For these patients 45 Gy/25 F, once-daily (OD-RT) has been the standard of care at our institution. The aim of this study was to investigate the pattern of failure and survival after chemo-radiotherapy with the 2 different radiotherapy schedules. **Methods:** Records of 106 patients with limited disease SCLC treated from 2007 to 2013 with definitive chemo-radiotherapy in our institution were reviewed. The chemotherapy regimen was a platinum doublet with etoposide. The radiotherapy schedule for 69 patients was treatment OD-RT (45 Gy/25 F), whereas 37 patients were treated BD-RT (45 Gy/30 F). Log rank tests were used to compare overall survival (OS) and local failure free survival (LFS) between the groups. **Results:** In the OD-RT 23 patients (33%) were either alive or dead without evidence of recurrence, and 15 patients (41%) in the BD-RT. In the OD-RT 21 patients (30%) had locoregional recurrence only, 12 patients (17%) had locoregional and distant relapse, and 13 patients (19%) had distant metastasis only. In the BD-RT 8 patients (22%) had locoregional recurrence only, 8 patients (22%) had locoregional and distant failure, and 6 patients (16%) had distant relapse only. Statistically significant (p<0,05) differences in patient characteristics between the two groups were observed: fraction of Performance Status 0-1 93% vs 67%, fraction treated with PCI 78% vs 54% and mean age of 62 vs 67 years for the groups BD-RT and OD-RT respectively. No differences were observed in S-sodium, LDH or gender. The mean follow-up was 24 months. Median overall survival was 18 months in OD-RT and 24 months in BD-RT, and 2 year OS was 45% vs 43% respectively (p=0.23). Median local-failure free survival was 13 months in OD-RT vs 33 months in BD-RT, and 2 year LFS was 57% vs 40% respectively (p=0.19) Local failure free survival:



Conclusion: In this study the locoregional control and overall survival was not significantly better in the bi-daily regimen with 45 Gy/30 F compared to once-daily treatment with 45 Gy/25 F. This was unexpected, because the two groups differed significantly in PS, PCI and age in favour of the bi-daily regimen. But the size sample was small and follow-up time short. **Keywords:** SCLC, definitive radiotherapy, pattern of failure

POSTER SESSION/ SMALL CELL LUNG CANCER
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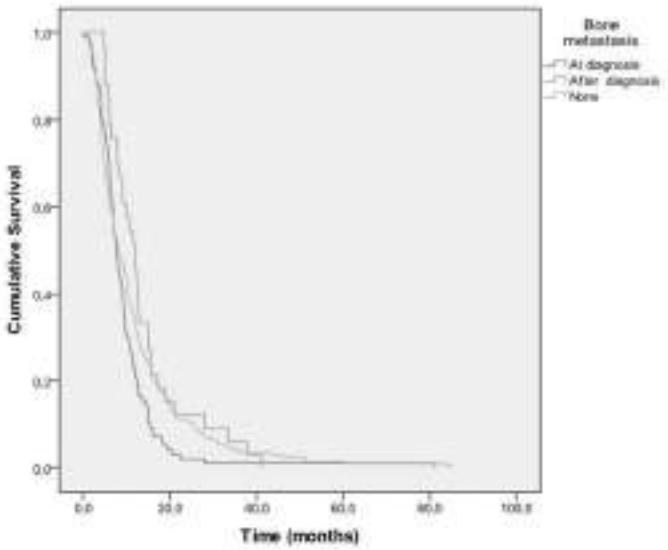
P2.07-016 Prognostic Impact of Bone Metastases in Small Cell Lung Carcinoma Konstantinos Syrigos, Dimitris Vassos, Paraskevi Boura, Sotirios Tsimpoukis, Alexandra Kopitopoulou, Andriani Charpidou, Ioannis Gkiozos *University of Athens, Athens/Greece* **Background:** Metastatic bone disease is associated with increased morbidity as it may cause disabling pain and lead to other skeletal-related events (SREs), such as pathologic fractures, spinal cord compression or hypercalcemia of malignancy, with significant consequences on quality of life and overall functioning of patients, potentially affecting survival as well. The aim of the present study was to further explore the potential impact of bone metastases (BMs) and their therapeutic management on the overall prognosis of patients with small cell lung carcinoma (SCLC). **Methods:** A retrospective analysis of medical records of 363 patients with SCLC was performed. Clinicopathological features and survival data were correlated with the presence of BMs, their time point of development (early versus late onset) and their treatment modality (radiotherapy, bisphosphonates or both), in the entire study population and in the subgroups of patients with limited or extensive-stage disease (LD or ED-SCLC, respectively) at diagnosis. **Results:** Overall, 35.8% of our patients were diagnosed with BMs, either at diagnosis (early onset BMs, 26.7%) or at a subsequent time point (late onset BMs, 9.1%). Patients with early onset BMs had a worse survival time compared to those with late-onset BMs or those without BMs (log rank test, p=0.020; figure 1). No statistically significant associations were observed between OS and the presence of BMs in the ED and LD subgroups of patients (p=0.926 and p=0.144, respectively). Treatment modality of BMs had no impact on OS either (p>0.05). Multiple Cox regression analysis showed that increased age, poor performance status, presence of BMs and early onset BMs were independently associated with reduced OS.



Conclusion: The presence of early-onset BMs may represent an independent prognostic factor in patients with SCLC. In contrast, the type of modality employed for treatment of BMs had no statistically significant impact on survival in our study population. **Keywords:** bone metastases, overall survival, Prognosis, small cell lung carcinoma

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-017 Body Composition Analysis Using Computed Tomography in Patients with Small Cell Lung Cancer Eun Young Kim[1], Young Saing Kim[2], Inkeun Park[2], Hee Kyung Ahn[2], Eun Kyung Cho[2] [1]*Department of Radiology, Gachon University Gil Medical Center, Incheon/Korea,* [2]*Division of Hematology and Oncology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon/Korea*

Background: Although the clinical significance of body composition has been recognized as associated with performance status and prognoses for solid tumors, no study has specifically evaluated baseline body composition in detail using computed tomography (CT) images for patients with small cell lung cancer (SCLC). **Methods:** We analyzed skeletal muscle mass and fat mass in 150 patients with pathologically proven SCLC between January 2010 and November 2014 in our institution. Cross-sectional areas of skeletal muscle (Hounsfield unit, HU ranges -29 to 150) and fat tissue (HU, -190 to -30) were measured on the level of 3rd lumbar vertebra using the baseline CT images. Data on clinical characteristics were retrospectively collected. **Results:** Mean age was 69 ± 9 years (85.3% were male). At the time of diagnosis, mean body mass index (BMI) was 22.1, with 40.7% of patients being overweight or obese (BMI ≥ 23). Only 16.7% overall were underweight as conventionally understood (BMI < 18.5). The overall prevalence of severe muscle depletion (sarcopenia) was 53.3% and was present in patients in all BMI categories (84.0% in underweight patients, 45.2% in overweight and obese patients). A much higher proportion of men (60.2%) than women (13.6%) met the criteria of sarcopenia. **Conclusion:** Wasting of skeletal muscle is a prominent feature of patients with small cell lung cancer, despite normal or heavy body weights. **Keywords:** body composition, sarcopenia, tomography, X-ray computed, small cell lung cancer

POSTER SESSION/ SMALL CELL LUNG CANCER
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.07-018 The Association of Hyponatremia with the Prognosis of Patients with SCLC Kong Yue *Department of Radiation Oncology, Zhejiang Cancer Hospital, Zhejiang Province/China*

Background: Lung cancer is still one of the leading causes of cancer patients,which has a high incidence and poor prognosis. Hyponatremia is found in about 15% patients with small cell lung cancer(SCLC) at different disease stages. This study aims to analyze the association of hyponatremia with the prognosis of patients with SCLC. **Methods:** The clinical materials of 489 patients with SCLC treated in ZheJiang cancer hospital between January 2010 and December 2012 were retrospectively analyzed. Kaplan- Meier and Log-Rank test were used to analyze the data. Prognostic factors were analyzed by multivariate Cox proportional hazards model. **Results:** Hyponatremia occurred in 17.9%、13.3%、12.5% and 18.9% patients at 4 different clinical stages(before treatment, after 2 cycles of chemotheropy, after radiotheropy and after all the treatments). The serum sodium level was not significantly different among patients of different gender, age, BMI, KPS, hypertension and diabetes mellitus history, tumor stage, smoking history and tumor metastasis (P>0.05). Univariate analysis showed that hyponatremia significantly affected the survival of patients. Multivariate analysis showed that hyponatremia was the independent prognostic factor for SCLC. The relative risk of death of patients with hyponatremia was elevated by 1.297 times (95%CI:1.160~1.449, P<0.001), 1.366 times (95%CI:1.023~1.825,P=0.035), 1.77 times (95%CI:1.168~2.682,P=0.007) and 1.507 times (95%CI:1.167~1.944,P=0.002). **Conclusion:** Hyponatremia is an independent prognostic indicator for the survival of initially treated patients with small cell lung cancer(SCLC). **Keywords:** Prognosis, small cell lung cancer, Hyponatremia

SESSION: POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

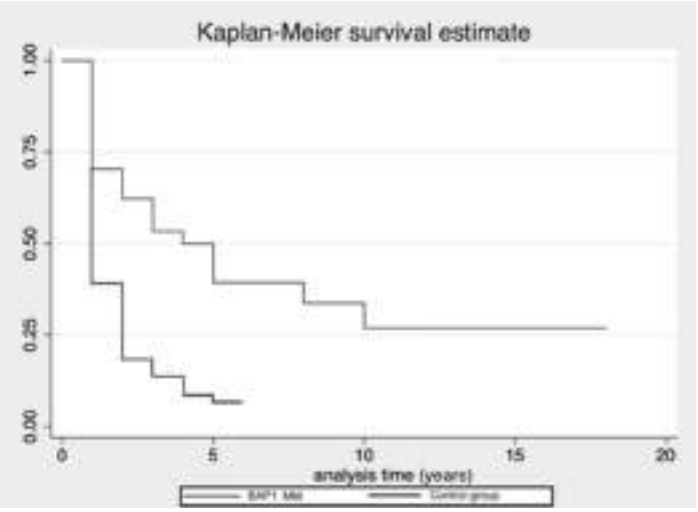
P2.08-001 A Randomized, Placebo-Controlled Study of Amatuximab in Combination with Pemetrexed and Cisplatin (P/C) in Subjects with Pleural Mesothelioma Bruce A. Wallin[1], Julis D. Maltzman[1], Alex Dmietrienko[2], Kimberly Hoffman[1], Megan Mclaughlin[1], Raffit Hassan[3] [1]*Clinical Development, Morphotek, Exton/PA/United States of America,* [2]*Quintiles, Overland Park/KS/United States of America,* [3]*Thoracic and Gastrointestinal Oncology Branch, National Cancer Institute, Bethesda/MD/United States of America*

Background: Amatuximab is a chimeric monoclonal antibody that binds to mesothelin, which is highly expressed in malignant mesothelioma and largely absent from normal tissue. In vitro studies indicate that amatuximab potentially has anti-tumor activity via antibody-dependent cellular cytotoxicity. Amatuximab was studied in a Phase 2 malignant pleural mesothelioma (MPM) trial which demonstrated that the safety profile of amatuximab in combination with P/C was consistent with that seen previously for the P/C regimen. Although PFS was not significantly different from historical results of P/C alone, the median OS was 14.8 months (as compared to 13.3 months for P/C). The post-hoc PK/PD analysis demonstrated that amatuximab trough concentrations were a significant predictor of both OS and PFS where higher concentrations were associated with longer OS (583 days; p=0.0202) and PFS (238 days; p<0.001). **Methods:** 560 subjects with previously untreated, unresectable malignant pleural mesothelioma (MPM) will receive P/C and are randomized 1:1 to receive weekly amatuximab, 5 mg/kg or saline placebo IV in this global study. The primary endpoint of the study is to demonstrate whether amatuximab in combination with P/C has superior OS compared with P/C in subjects with MPM. The secondary endpoints are to compare amatuximab versus placebo with regard to PFS, ORR, duration of response, health-related QOL (LCSS-Meso), and the safety of amatuximab when administered with P/C. Clinical trial information: NCT02357147. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** Maligant Pleural Mesothelioma

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-002 Germline BAP1 Mutation Is Associated with a Significant Increased Survival and Multiple Cancer in Mesothelioma Patients Francine Baumann[1], Erin Flores[1], Andrea Napolitano[1], Emanuela Taioli[2], Harvey I. Pass[3], Haining Yang[1], Michele Carbone[4] [1]*Cancer Center, University of Hawaii, Honolulu/HI/United States of America,* [2]*Department of Population Health, Hofstra-North Shore LIJ School of Medicine, Great Neck/NY/United States of America,* [3]*Department of Cardiothoracic Surgery, New York University Langone Medical Center, New York/NY/United States of America,* [4]*Cancer Center, University of Hawaii, Honolulu/United States of America*

Background: Because the diagnosis is often made at a late stage, malignant mesothelioma (MM) prognosis is very poor, with a median survival of 6-12 months and a five-year survival of less than 5%. We found that germline *BAP1* mutation is associated with a new cancer syndrome, including rare malignancies such as MM and uveal carcinoma (UV), and other cancers. We noted that some MM cases that we followed from *BAP1* mutated families had prolonged survival. We carried out a pooled analysis of *BAP1* mutated MM patients to test the hypothesis that they had a better survival compared to sporadic MM. **Methods:** : We included all published *BAP1* germline mutated MMs with available data on *BAP1* status, site of MM, age at diagnosis, gender, and age at death or status at end of follow-up, in addition to the *BAP1* mutated MM cases from families that we are following. Twenty-three *BAP1* MM patients were included. Using the Kaplan-Meier method and Wilcoxon test, we compared survival among *BAP1* mutated MM patients with that of all MMs (N = 10 556) recorded in the US SEER data from 1973 to 2010. **Results:** In our *BAP1* cohort, ten patients had peritoneal MM, ten pleural MM, and three MM in both locations. Thirteen patients had one or more malignancies in addition to MM. Actuarial median survival for the MM patients with germline *BAP1* mutations was five years, as compared with less than one year in the SEER MM control group. Five-year survival was 47%, 95%CI [24-67%], as compared with 6.7% [6.2-7.3%] in the SEER MM control group. The small size of our *BAP1* cohort did not allow for significant statistical comparisons. However, patients with peritoneal MM (median survival of 10 years, P=0.0571), or with a second malignancy in addition to MM (median survival of 10 years, P=0.0716), survived for a longer time compared to patients who only had pleural MM, or MM patients without a second malignancy, respectively.



Conclusion: MM patients with germline *BAP1* mutations have an overall seven-fold increased survival, independently of sex and age. This better prognosis was associated with multiple cancer and/or peritoneal MM. Appropriate genetic counseling and clinical management should be considered for MM patients who are also *BAP1* mutation carriers. **Keywords:** Mesothelioma, survival, BAP1 germline mutation, Multiple cancer

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-003 MDM2 Inhibitor plus rhAPO2L/TRAIL: A Promising Strategy for Malignant Pleural Mesothelioma Treatment Loredana Urso[1], Micol Silic-Benussi[1], Vincenzo Ciminale[1], Federico Rea[2], Pierfranco Conte[1], Adolfo Favaretto[3], Giulia Pasello[3] [1]*Surgical Oncologic and Gastroenterological Sciences Department, University of Padova, Padova/Italy,* [2]*Thoracic Surgery Unit, University of Padua, Padua/Italy,* [3]*Second Medical Oncology Unit, Istituto Oncologico Veneto, Padua/Italy*

Background: Malignant Pleural Mesothelioma (MPM) is an aggressive tumor characterized by chemoresistance. Most MPM tumor specimens have wild type p53 but show a deletion of INK4A/ARF locus (70-80%) which contains p14/ARF gene. The p14 lack increases MDM2 activity and subsequently down-regulates p53. The role of MDM2 is not only related to p53 control but it is also involved in regulation of cell proliferation, apoptosis and angiogenesis in p53 independent manner. Tumor necrosis factor (TNF)-Related Apoptosis-Inducing Ligand (Apo2L/TRAIL) is a promising agent for antitumor treatment because its ability to selectively kill cancer cells through the extrinsic apoptotic pathway. The aim of our study is to investigate, the anticancer effect of the MDM2 inhibitor, Nutlin 3a, in association with rhAPO2L/TRAIL in MPM *in vitro* and *in vivo*. **Methods:** In vitro apoptosis assay was performed using PI staining, positive cells were detected by flow cytometry. Cycle analysis was performed by PI staining and flow cytometry detection, DNA content was analyzed by MODFIT software. p53, p21 and survivin protein expression levels were detected by western blot analysis. TRAIL receptors levels were assessed by flow cytometry analysis. mRNA expression levels were evaluated by real-time PCR. *In vivo* experiments were performed in 32 SCID male mice, intraperitoneally injected with sarcomatoid MPM cells trasduced with lentiviral Luciferase vector and treated with Nutlin and/or rhAPO2L/TRAIL. **Results:** Nutlin 3a treatment provoked p21 induction and cell cycle arrest in p53 wild type cells (M14K epithelioid, MSTO-211H biphasic and ZL34 sarcomatoid) but had no effect in p53 mutated cells (ZL55 epithelioid). Interesting, apoptosis assay showed a synergistic cell death induction of Nutlin3a *plus* rhAPO2L/TRAIL in both p53 wild type and p53 mutated MPM cells with a greater effect in ZL34 cell lines that expressed higher mRNA and protein levels of MDM2. Nutlin 3a increased the expression of DR4/DR5 TRAIL death receptors and inhibition of survivin only in p53 wild type cells. As a consequence, western blot analysis of Caspase 8 activation showed that the MDM2 inhibitor induced an increase of extrinsic apoptosis signal only when p53 was functional. Finally, antitumor activity tested in ZL34 *in vivo* mouse model showed a strong inhibition of tumor growth in mice treated with Nutlin 3a plus Apo2L/TRAIL compared to Nutlin 3a or Apo2L/TRAIL used as single agents. **Conclusion:** The results demonstrate that the combination of Nutlin 3a plus Apo2L/TRAIL may be a promising strategy for MPM treatment independently to p53 status. Further esperiments are needed in order to clarify the role of p53 status as selection criterium for treatment and to explore p53-independent MDM2 functions.

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-004 Healthcare Professional Perceptions of Chemotherapy in Treatment of Malignant Pleural Mesothelioma (MPM) Steven Kao[1], Haryana Dhillon[2], Anne Warby[3], Janette Vardy[4] [1]*Medical Oncology, Chris O'Brien Lifehouse, Sydney/Australia,* [2]*University of Sydney, Sydney/Australia,* [3]*Asbestos Diseases Research Institute, University of Sydney, Sydney/ACT/Australia,* [4]*Concord Cancer Centre, University of Sydney, Sydney/ACT/Australia*

Background: Background: An evidence-based chemotherapy utilisation model for MPM suggests rates of use should be around 65%. Actual Australian rates are about 54%. Aim: To examine healthcare professional perceptions of chemotherapy use and barriers to it in MPM patients. **Methods:** Methods: Healthcare professionals caring for people with MPM were invited via email from professional groups, to complete a purpose designed online survey. Data were collected from January-July 2014. Descriptive data are presented. **Results:** Results: Surveys were completed by 102 doctors (Respiratory Physicians=53, Medical Oncologists (MO)=35, Other=15) and 19 nurses. Doctors mean age 47 (31-75) years, 74% male, 49% worked only in public system, 57% did not have lung cancer nurse specialist, and saw mean of 7 new patients with MPM annually. Nurses mean age 45 (29-68) years, all female, 53% worked only in public system, and saw mean of 12 (1-40) new patients with MPM annually. 74% of doctors and 53% of nurses believed >11% of MPM patients potentially eligible for chemotherapy do not receive it. Clinician barriers most commonly endorsed include: clinician nihilism 70%, 37%; non-referral to MO 47%, 63%; lack of cancer services 43%, 53%; no MDT review 40%, 32% for doctor, nurse respectively. 74% of nurses also indicated delayed diagnosis and 58% lack of clinician knowledge about treatment. **Conclusion:** Conclusions: Healthcare professionals' estimates of potentially eligible patients with MPM who do not receive chemotherapy are consistent with or higher than evidence-based estimates. Barriers to chemotherapy access endorsed suggest strategies to increase knowledge of evidence-based treatment and address clinical nihilism are required. **Keywords:** Mesothelioma, chemotherapy treatment, decision-making, healthcare professionals

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-005 Vinorelbine as Second or Third-Line Therapy in Pemetrexed-Pretreated Malignant Pleural Mesothelioma (MPM) Patients Giovanni L. Ceresoli[1], Paolo A. Zucali[2], Federica Grosso[3], Manlio Mencoboni[4], Philip Bonomi[1], Hector J.M. Soto Parra[5], Giulia Pasello[6], Diego Cortinovis[7], Matteo Perrino[2], Alberto Muzio[8], Andrea Bruzzone[4], Fabio De Vincenzo[2], Daniela Degiovanni[9], Matteo Simonelli[2], Giordano D. Beretta[1], Laura Giordano[10], Armando Santoro[2] [1]*Oncology, Cliniche Humanitas Gavazzeni, Bergamo/Italy,* [2]*Oncology, Humanitas Cancer Center, Rozzano, Milan/Italy,* [3]*Oncology, Ospedale Ss Antonio E Biagio, Alessandria/Italy,* [4]*Oncology Unit, Villa Scassi Hospital, Asl 3 Genovese, Genova/Italy,* [5]*Oncology, Policlinico Universitario Vittorio Emanuele, Catania/Italy,* [6]*Medical Oncology 2, Istituto Oncologico Veneto, Padova/Italy,* [7]*Medical Oncology Unit, San Gerardo Hospital, Monza/Italy,* [8]*Oncology, Ospedale Santo Spirito, Casale Monferrato (Al)/Italy,* [9]*Palliative Care Unit, Ospedale Santo Spirito, Casale Monferrato (Al)/Italy,* [10]*Biostatistic Unit, Humanitas Cancer Center, Rozzano, Milan/Italy*

Background: There is no standard treatment for patients (pts) with MPM progressing during or after pemetrexed/platinum-based chemotherapy (PBC). Single agent chemotherapy is often administered in everyday practice, although its use is poorly supported by clinical trials. The aim of this retrospective study (NCI01865045) was to analyze the efficacy and toxicity of second (2nd) and third (3rd) line vinorelbine (VNR) in a large cohort of PBC-pretreated MPM patients. **Methods:** The clinical records of MPM pts consecutively treated in 8 Italian Centers with intravenous (iv) or oral (po) VNR as 2nd or 3rd line treatment following PBC were reviewed. Radiological response was assessed by modified RECIST criteria. Toxicity was reported according to CTCAEv4 criteria. Relative dose-intensity (DI) of VNR was calculated. Progression-free survival (PFS) and overall survival (OS) were estimated and correlated to clinical variables: age, gender, histological subtype, ECOG performance status (PS), line of VNR therapy (2nd vs 3rd) and outcome of first-line treatment. **Results:** From August 2001 to September 2014, 161 pts (M/F 120/41) were treated, 128 with iv and 33 with po VNR. Most of the cases included (92%) were treated after 2007. Histological subtype was epithelioid in 134, biphasic in 15, sarcomatoid in 8 and unspecified in 4 pts. Median age was 67 years (range 41-82). VNR was administered as 2nd or 3rd line treatment in 94 and 67 pts, respectively. Median number of VNR cycles was 3 (range 1-26), median relative DI was 88%. Main grade 3-4 toxicities were neutropenia in 9%, fatigue in 4% and constipation in 5% of pts. No toxic death occurred. A partial response was observed in 10 pts (6%), stable disease in 57 (35%), for an overall disease control rate of 41%. Median PFS and OS were 2.5 and 6.7 months, respectively. In multivariate analysis, only ECOG PS (0 vs 1-2) was significantly associated with improved PFS and OS. An analysis of molecular predictors of VNR response is ongoing. **Conclusion:** In this large retrospective patient cohort, 2nd and 3rd line VNR had modest but definite activity in PBC-pretreated MPM patients, with an excellent toxicity profile. Although inclusion in prospective clinical trials of new agents should be always considered in this setting, single agent VNR remains a reasonable option for palliation. **Keywords:** Mesothelioma, chemotherapy, Second-line, vinorelbine

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-006 The JmjC Family of Lysine Demethylases Are Overexpressed and Potential Therapeutic Targets in Malignant Pleural Mesothelioma Maeve Breslin[1], Sian Cregan[1], Leah Quinn[1], Sigrid Wennstedt[1], Gerard Roche[1], Yun Gao[2], Kim Griggs[3], Michaela B. Kirschner[4], Kenneth J. O'Byrne[5], Stephen P. Finn[6], Sinead Cuffe[7], Sonja Klebe[3], Glen Reid[4], Steven G. Gray[1] [1]*Thoracic Oncology Research Group, Trinity College Dublin/St. James'S Hospital, Dublin/Ireland,* [2]*Department of Oncology, Aerospace Central Clinical Medical College of Peking University, Beijing/China,* [3]*Anatomical Pathology, Flinders University, Adelaide/SA/Australia,* [4]*Asbestos Diseases Research Institute, Sydney/NSW/Australia,* [5]*Cancer and Ageing Research Program, Princess Alexandra Hospital and Queensland University of Technology, Brisbane/QLD/Australia,*[6]*Department of Pathology, University of Dublin, Trinity College and St. James'S Hospital, Dublin/Ireland,* [7]*Hope Department, St.James'S Hospital, Dublin/Ireland*

Background: Malignant pleural mesothelioma (MPM) is an aggressive rare cancer affecting the pleura and is predominatly associated with prior exposure to asbestos. Treatment options are limited, and most patients die within 24 months of diagnosis. The current standard of care for MPM patients is a combination of cisplatin and pemetrexed (or alternatively cisplatin and raltitrexed), yet most patients die within 24 months of diagnosis. There is therefore an urgent unmet need to identify new therapeutic options for the treatment of MPM. Asbestos fibres contain of transition metals and their ability to both adsorb and accumulate these metals was one of the first mechanisms suggested for explaining the toxic and particularly carcinogenic effects of asbestos. One of the transition metals in asbestos fibres is iron, and therefore asbestos fibres may cause an alteration of iron homeostasis in the tissue. In addition, asbestos fibres have also been shown to have high affinity for histones, and therefore may result in high accumulation of iron around chromatin. Lysine Demethylases (KDMs) containing a JmjC domain require both Fe2+ and 2-oxoglutarate as co-factors to regulate gene expression by "erasing or removing" methylation on histones in chromatin. Members of this family are frequently found to have aberrant expression in cancer and currently are actively pursued as candidate pharmaceutical therapeutic targets. Given that asbestos increases iron levels, this may result in aberrant KDM activity, and these KDMs could therefore be novel candidate targets in mesothelioma. We therefore examined the expression of several JmjC containing KDMs in MPM and assessed their potential for therapeutic intervention in mesothelioma using existing small molecule inhibitors. **Methods:** A panel of MPM cell lines were screened for expression of KDM4A-D, KDM5A/B and KDM6A/B by RT-PCR. mRNA levels were subsequently examined by RT-PCR in a cohort of snap-frozen patient samples isolated at surgery comprising benign, epithelial, biphasic, and sarcomatoid histologies. IHC was performed for KDM4A on a cohort of FFPE specimens. The effects of treatments with small molecule inhibitors targeting these proteins on both cellular health and gene expression were assessed. **Results:** The expression of the various KDMs was detectable across our panel of cell lines. In primary tumours the expression of these KDMs were significantly elevated in malignant MPM compared to benign pleura ($p<0.05$), and significant differences were also observed when samples were analysed across different histological subtypes. Treatment of mesothelioma cell lines with various small molecule inhibitors caused significant effects on cellular health and on the expression of a panel of genes. **Conclusion:** The expression of KDMs are significantly altered in MPM. Small molecule inhibitors directed against these KDMs show potential therapeutic efficacy with significant anti-proliferative effects. We continue to assess the effects of these compounds on gene expression and cellular health to confirm their potential utility as novel therapies for the treatment of MPM. **Keywords:** JumonjiC, Mesothelioma, epigenetics, therapeutic target

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P2.08-007 The Efficacy and Safety of Re-Challenge Platinum plus Pemetrexed Combination Therapy for Recurrent Malignant Pleural Mesothelioma Mariko Morishita, Masahiro Morise, Tetsunari Hase, Mitsuo Sato, Masashi Kondoh, Yoshinori Hasegawa *Department of Intgrated Medicine, Nagoya University Graduate School of Medicine, Nagoya/Japan*

Background: Malignant pleural mesothelioma (MPM) is associated with poor prognosis and 5-year survival rate was only 23.1%.Tri-modality therapy (induction chemotherapy followed by pleural pneumonectomy and adjuvant radiation), bimodality therapy (induction chemotherapy followed by pleural decortication) and chemotherapy alone viable treatment option for MPM. These initial therapies are selected according to IMIG staging, performance status, and the severity of comorbidity. These treatment options all include platinum plus pemetrexed combination therapy, which is regarded as the standard regimen for advanced MPM. However, the majority of patients showed disease relapse even when treated with multimodality strategy and the treatment options for recurrent MPM are limited. Under these findings, the current study investigated the efficacy and safety of re-challenge platinum plus pemetrexed combination therapy for recurrent MPM. **Methods:**We retrospectively reviewed 36 patients pathologically diagnosed as MPM between April 2007 and April 2015. The patients who received re-challenge platinum plus pemetrexed combination therapy as second line therapy for recurrent MPM were eligible for this study. **Results:** Of these 36 patients, 15 showed disease relapse after receiving the first treatment. 7 patients received monotherapy or best supportive care after the relapse. After all, 8 patients received re-challenge platinum plus pemetrexed combination therapy. The characteristics of the 8 patients were as follows, male/female:6/2, median age:58 years (range 49-69), performance status 0/1:2/6, epithelioid/sarcomatoid/biphasic/unknown: 6/0/1/1. Prior therapy tri-modality/bimodality/chemotherapy alone:5/0/3, treatment free interval from the completion of initial therapy <90days/≧90days; 0:8. 1 partial response and 6 stable disease were observed in 8 patients, respectively. Median progression free survival and median overall survival was 8.3 and 17.3 months, respectively. In terms of toxicity, grade 3 leukopenia was observed in one patient. No grade 3-4 thrombocytopenia was observed. In addition, grade 2 erythema was observed in one patient. Over all, the combination therapy was well tolerated. **Conclusion:** The re-challenge platinum plus pemetrexed combination was active and well tolerable for recurrent MPM. **Keywords:** malignant pleural mesothelioma, recurrent, Platinum, pemetrexed

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P2.08-008 A Phase 1 Dose Escalation Study of VS-5584, a PI3K/MTOR Inhibitor, Administered with VS-6063, a Focal Adhesion Kinase Inhibitor, in Mesothelioma Udai Banerji[1], Dean A. Fennell[2], Hedy Lee Kindler[3], Marjorie G. Zauderer[4], Mitchell Keegan[5], Joanna Horobin[6] [1]*Royal Marsden NHS Foundation Trust, London/United Kingdom,* [2]*University of Leicester & Leicester University Hospitals, Leicester/ United Kingdom,* [3]*Section of Hematology/Oncology, University of Chicago, Chicago/IL/ United States of America,*[4]*Medicine/Thoracic Oncology, Mskcc, New York/NY/United States of America,* [5]*Verastem, Boston/AL/United States of America,* [6]*Verastem, Boston/United States of America*

Background: Malignant mesothelioma is a rare, but aggressive pleural or peritoneal tumor which is highly invasive and progresses rapidly. The median survival of patients with mesothelioma is between 9 and 13 months, and survival has not been significantly affected by most currently available therapeutic interventions. There are no approved therapies following first line treatment. VS-6063 is an oral inhibitor of focal adhesion kinase (FAK) currently being evaluated in a randomized phase 2 study in patients with malignant pleural mesothelioma who have stable disease or better after front line chemotherapy. VS-5584 is an oral dual inhibitor of PI3K/mTOR currently undergoing phase I testing in solid tumors. Previously reported literature has shown that dual PI3K/ mTOR inhibitors have activity in patients with relapsed mesothelioma. In preclinical models, the combination of VS-6063 and VS-5584 have demonstrated synergy in tumor models of malignant mesothelioma supporting the potential exploration of this combination clinically. **Methods:** This is a multi-center, open-label, phase 1 trial in subjects with relapsed malignant mesothelioma. The study is comprised of two sequential parts: Part 1 (Dose Escalation of VS-5584 with a fixed dose of VS-6063) and Part 2 (Expansion). Patients receive VS-5584 orally on an intermittent dosing schedule and VS-6063 400 mg orally BID. Primary endpoints are to determine the maximum tolerated dose, recommended Phase 2 dose/schedule and to assess safety and tolerability of the combination in this patient population. Secondary endpoints include assessing the pharmacokinetics of VS-5584 and VS-6063 when co-administered. Exploratory endpoints include response rate and biomarker correlation with response and PD. The study is currently enrolling across 4 sites in the United States and United Kingdom. Clinical trial: NCT02372227. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** Mesothelioma, PI3K, mTOR

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P2.08-009 Malignant Pleural Mesothelioma: A Retrospective Analysis of Clinicopathological and Survival Data in Egyptian Patients Mona K. Jomaa, Ahmed Nagy, Nesreen Mosalam, Mostafa Mohamed, Marwa Ezzat *Clinical Oncology and Nuclear Medicine, Ain Shams University, Cairo/Egypt*

Background: The incidence of Malignant pleural mesothelioma (MPM) in Egypt showing a steady increase which mandate more intension. This study was conducted to study the clinico-epidemiological data and different treatment modalities offered for (MPM) patients and to evaluate their impact on survival **Methods:** Data was retrospectively collected from the medical files of 103 cases presented as MPM to Department of Clinical Oncology and Nuclear Medicine, Ain Shams University Hospitals from January 2011 to December 2013. Demographics, risk factors, morphological status and treatment received were described using frequencies. Survival outcome was described using Kaplan Meier curves stratified according to morphology and treatment received. **Results:** A steady increase in the number of cases was detected, from 30 in 2011 and 40 cases in 2013. Male/female ratio was 0.98 ($p = 0.989$). The median age was 58 years (range 28-85). About 60 patients (58.3 %) came from endemic areas. Only one patient underwent decortication surgery. About 70.9 %, 21.4 % and 5.8% of the patients received chemotherapy (CT) in 1st line, 2nd line and 3rd line respectively and median OS was 5 months (Range 1-48). Only 5.5%, 21.7% and 33.3% of the patients received Pemetrexed in 1st line, 2nd line and 3rd line CT respectively.Kaplan-Meier survival for sex, age, residence and the pathological types was insignificant. The median survival for epithelial versus non-epithelial pathological types was 6 and 5 months respectively (P= 0.165).The median survival for the patients who received 1st line, 2nd line and 3rd line CT versus best supportive care (BSC) was 3 and 8 months ($P = 0.001$), 12 and 5 months ($P < 0.001$) and 12 and 5 months ($P = 0.417$) respectively.There was a significant difference ($P = 0.001$) between the median survival for patients who received CT (8 months, 95% CI 5.422-10.578) and those who were offered BSC (3 months, 95% CI 1.715-4.285). Another factor that affected the survival negatively was non-platinum based CT in the 1st line (2 months versus 9 months $P = 0.001$). Cox regression analysis revealed that the factors that predicted better OS were patients being offered CT rather than BSC especially patients who received 1st and 2nd line of CT ($P = 0.004$). **Conclusion:** MPM is a growing health burden in Egypt which is underestimated and need more support to offer new treatment modalities. The CT prolongs survival compared to BSC in patients with MPM. Moreover, using platinum based CT provides survival advantages. **Keywords:** Chemotherapy; epidemiology; malignant pleural mesothelioma.

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P2.08-010 Phase II Study of the Anti-PD-1 Antibody Pembrolizumab in Patients with Malignant Mesothelioma Hedy Lee Kindler[1], Theodore Karrison[2], Arun Khattri[1], Zhixiang Zuo[1], Nanna Sulai[1], Buerkley Rose[1], Mehwish I. Ahmad[1], Samuel Armato[3], Ravi Salgia[1], Tanguy Seiwert[1] [1]*Section of Hematology/Oncology, University of Chicago, Chicago/IL/United States of America,* [2]*Department of Public Health Sciences, University of Chicago, Chicago/IL/United States of America,* [3]*Department of Radiology, University of Chicago, Chicago/IL/United States of America*

Background: Mesothelioma is a frequently "inflamed" tumor. We previously identified PD-L1 expression, a CD8 infiltrative pattern, and the presence of PD-1/PD-L1 immune checkpoints in about 1/3 of mesothelioma tumors, similar to the phenotype found in malignancies such as melanoma that benefit from immune checkpoint blockade (Kindler and Seiwert, *ASCO* 2014). Based on these data, we have initiated a single-center phase II trial (NCT02399371) of the anti-PD-1 antibody pembrolizumab in previously-treated mesothelioma patients. The rationale for this study is further supported by recent data from a phase IB multi-cohort study of pembrolizumab in PD-L1 positive solid tumors, in which an objective response rate of 28% and a disease control rate of 76% was observed in 25 pleural mesothelioma patients, who received 10 mg/kg pembrolizumab every 2 weeks (Alley, *AACR* 2015). **Methods:** Eligible patients have histologically-confirmed pleural or peritoneal mesothelioma, measurable disease, PS 0-1, disease progression on or after treatment with pemetrexed plus cis- or carboplatin, no more than 2 prior lines of cytotoxic therapy, normal organ function, and tissue available for correlative studies. Patients receive a flat dose of 200 mg pembrolizumab intravenously every 3 weeks. CT scans are obtained every 9 weeks. The primary objectives are: 1) to determine the objective response rate in A] an unselected population and in B] a PD-L1 positive population, and 2) to determine the optimal threshold for PD-L1 expression using the 22C3 antibody-based IHC assay. Secondary objectives include progression-free and overall survival, disease control rate, and toxicity. Correlative studies are intended to characterize the T-cell inflamed phenotype in mesothelioma via CD8, CD4, and PD-L1 staining, immune related gene expression signatures (Nanostring), and determination of other immune escape mechanisms including T-regulatory cells (FOXP3 expression), IDO expression, MDSCs, and other checkpoints/co-stimulatory signals by immunohistochemistry and/or flow cytometry. A single-stage binomial design will be used. Part A requires ≥ 3 responses in 35 patients. Part B, which uses PD-L1 pre-selection (optimal expression pattern and threshold determined in cohort A), requires ≥ 6 responses in 30 patients. Funded in part by a grant from the Mesothelioma Applied Research Foundation. **Results:**Not applicable. **Conclusion:** Not applicable. **Keywords:** phase II trial, Mesothelioma, PD-1, pembrolizumab

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P2.08-011 Surgical Cytoreduction and HITHOC for Malignant Pleural Tumors Michael Ried[1], Reiner Neu[1], Berthold Schalke[2], Hans-Stefan Hofmann[1] [1]*Department of Thoracic Surgery, University Medical Center Regensburg, Regensburg/ Germany,* [2]*Department of Neurology, University of Regensburg at the District Medical Center, Regensburg/Germany*

Background: Combination of surgical cytoreduction and hyperthermic intrathoracic chemotherapy (HITHOC) is performed for therapy of pleural malignancies within a multimodality treatment concept. We describe the perioperative management and our clinical experience. **Methods:** Between September 2008 and January 2015 a total of 23 patients with malignant pleural mesothelioma (MPM) and 27 patients with thymoma/

thymic carcinoma with pleural involvement (Masaoka-stage IVa) were prospectively enrolled. Perioperative management, postoperative morbidity and mortality were analyzed. **Results:** Included were 17 female and 33 male patients with a mean age of 54.6 years (25 to 72 years). All patients received multimodality therapy depending on tumor stage, histology and their overall condition. Histologic subtype of patients with MPM was epitheloid (n= 19; 83%) or biphasic (n= 4; 17%). WHO-classification of thymoma patients was: B1 n= 2, B2 n= 10, B2/B3 n= 6, B3 n= 4 and C n= 5. All patients underwent radical surgical cytoreduction with pleurectomy/decortication (P/D; n= 25), extended P/D (P/D + resection of pericardium and/or diaphragm; n= 19) or extrapleural pleuropneumonectomy (EPP; n= 6) followed by HITHOC perfusion at 42°C for one hour. HITHOC was performed with an increasing concentration of cisplatin (100 mg/m^2 n= 14; 150 mg/m^2 n= 18; 175 mg/m^2 n= 2) or combination of cisplatin/doxorubicin (175 mg/m^2 / 65 mg n= 16). Macroscopic complete resection (R0/R1) was achieved in 46 patients (92%). Severe chemotherapy-related complications were not observed. Operative revision was necessary in seven patients (14%). Postoperative renal insufficiency was observed in six patients (12%) with two patients requiring temporary postoperative dialysis (4%). Prolonged bronchopleural fistula was documented in five patients (11%) after lungsparing P/D or extended P/D. 30-day mortality was 4%, both after EPP. **Conclusion:** Surgical cytoreduction in combination with HITHOC can be performed with acceptable morbidity and mortality rates in selected patients. Patients should be evaluated interdisciplinary to determine their eligibility for this multimodality approach. Early clinical results may encourage the use of additional HITHOC to provide better local tumor control. **Keywords:** Pleural mesothelioma, thymoma, surgical cytoreduction, hyperthermic intrathoracic chemotherapy

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P2.08-012 Differentiation of Mesothelioma from Lung Cancer and Healthy Individuals Using Human Serum by ATR-FTIR Spectroscopy Coupled with Chemometrics Salih A. Emri[1], Dilek Yonar[2], Abdulsamet Sandal[3], Ulku Yılmaz[4], Feride Severcan[2] [1]*Hacettepe University, Mesothelioma and Medical Geology Research and Application Center, Ankara/Turkey,* [2]*Biological Sciences, Middle East Technical University, Ankara/Turkey,* [3]*Chest Disases, Hacettepe University, School of Medicine, Ankara/Turkey,* [4]*Chest Diseases, Atatürk Chest Diseases and Chest Surgery Training Hospital, Ankara/Turkey*

Background: Malignant pleural mesothelioma (MPM) is a rare, aggressive cancer that progresses in the thin layer of pleura. The inhalation of microscopic asbestos fibers primarily the main reason of the disease. Early symptoms of pleural mesothelioma often are confused with other respiratory ailments. Therefore, MPM can only be diagnosed in the advanced stage. Consequently, it is important to develop a new approach with high specificity and sensitivity for the differential diagnosis of MPM. Fourier Transform Infrared (FTIR) spectroscopy is a novel and non-invasive method that has potential to diagnose cancer with high specificity and sensitivity. Hence, we used ATR-FTIR spectroscopy coupled with chemometric methods to differentiate MPM from healthy individuals and lung cancer patients. **Methods:** FTIR spectra of the samples collected from patients diagnosed with malignant pleural mesothelioma (MPM), lung cancer (LC), and healthy control (C) were recorded in the 4000-650 cm-[1]spectral region. Recording the spectra and analysis of the spectral data were obtained with Perkin Elmer Spectrum One Program. Both unsupervised Principal Component Analysis (PCA) (The Unscrambler X 10.3, CAMO Software) and Hierarchical Cluster Analysis (HCA) (OPUS 5.5, BRUKER) were applied for differentiation MPM from other groups. **Results:** Cluster analysis of the samples demonstrated that MPM and lung cancer successfully differentiated from healthy controls at whole spectral region (4000-650 cm-[1]). Moreover, successful clusters of these three groups were obtained in the fingerprint (1800-650 cm-[1]) and 1500-800 cm-[1] regions. In addition, some special bands such as DNA band at 832 cm-[1] gave very successful differentiation by PCA from serum samples. **Conclusion:** These findings indicate that FTIR spectroscopic analysis of serum coupled with chemometric analyses enabled differential diagnosis of mesothelioma from lung cancer patients and healthy individuals. *This work was supported by the Scientific and Technical Research Council of Turkey (TUBITAK), SBAG-113S294 Research Fund. **Keywords:** ATR-FTIR Spectroscopy, Mesothelioma, Diagnosis, Chemometric Analysis

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P2.08-013 A Phase II Trial of TTFields with Chemotherapy for First Line Treatment of Malignant Mesothelioma Uri Weinberg[1], Ori Farber[2] [1]*Novocure Gmbh, Lucerne/Switzerland,* [2]*Novocure Ltd., Haifa/Israel*

Background: Tumor Treating Fields (TTFields) are an anti-mitotic, regional treatment modality, which is based on low intensity alternating electric fields delivered non-invasively using a portable, home use, medical device (NovoTTF-100L, Novocure Ltd.). In-vitro, human mesothelioma cells were found to be highly susceptible to TTFields. When applied to the thorax, TTFields were found to be safe and efficacious in a clinical trial of 42 patients with advanced non-small cell lung cancer, where the only common device-related adverse event was mild to moderate skin reaction. Malignant pleural mesothelioma (MPM) is always fatal when unresectable, and existing therapies provide very limited clinical benefit. Since MPM normally progresses regionally within the thorax, the addition of a regional therapy to systemic chemotherapy is an appealing treatment approach. However, the use of radiation therapy as a loco-regional treatment is limited, due to significant pulmonary toxicity. TTFields may therefore serve as a potential non-toxic regional therapy in MPM. **Methods: The STELLAR Clinical Trial** Eighty (80) patients with unresectable and previously untreated MPM will be treated with pemetrexed and cisplatin or carboplatin in combination with TTFields. The patients will be followed up every 3 weeks (CT scan every 6 weeks) until disease progression. **Objectives** To test the efficacy and safety of TTFields combined with standard chemotherapy in this patient population. **Endpoints** The primary endpoint is overall survival (OS) and secondary endpoints are response rate, progression free survival and treatment-emergent toxicity. **Statistical Considerations** This is a prospective phase II, single arm, multicenter study for 80 patients. The sample size (71 + 12% loss to follow up) is based upon the asymptotic distribution provided by Lachin (2000) using the log of the hazard rate. The historical control is assumed to have an exponential distribution with a constant hazard rate of 0.03938 calculated from the median survival of 12.1 Months reported by Vogelzang et al. The sample size provides 80% power with a two sided alpha of 0.05 to detect an increase of 5.5 months in OS which is equivalent to a Hazard Ratio of 0.67 compared to the historical control data for OS. **Major Eligibility Criteria** Patients are 18 years of age or older with good performance status (ECOG 0-1). The patients must have pathological or histological evidence of MPM with at least one measurable or evaluable lesion according to modified RECIST criteria. The disease should be previously untreated and not amendable for curative treatment (surgery or radiotherapy). Untreated brain metastases and contraindications to any of the study treatments are exclusionary. **Treatment** Continuous TTFields at 150 kHz is applied to the thorax using the NovoTTF-100L System. The System is a portable medical device allowing normal daily life activities. The device delivers alternating electric fields to the thorax using 4 Transducer Arrays. The experimental treatment is administered on top of the standard of care chemotherapy – pemetrexed/platinum doublet. **Results:** not applicable **Conclusion:** not applicable **Keywords:** Tumor Treating Fields, TTFields, malignant pleural mesothelioma, Unresectable

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P2.08-014 Therapeutic Effectiveness of MET/RON Small Molecule Inhibitor BMS-777607 on Cell Viability of Human Malignant Pleural Mesothelioma Cell Lines Bashir M. Mohamed[1], Melad A. Aswisi[1], Steven G. Gray[2] [1]*Clinical Medicine Department, Trinity College Dublin and St James`S Hospital, Dublin/Ireland,* [2]*Thoracic Oncology, St James'S Hospital & Trinity College Dublin, Dublin/Ireland*

Background: Overexpression of c-Met receptor tyrosine kinase has been highly associated with oncogenic progression of non-neoplastic mesothelial progenitor cells to malignant pleural mesothelioma (MPM). Moreover, activated c-Met receptor tyrosine kinase transduces signals that regulate tumorigenic activities including cell growth, migration, survival, and invasion of extracellular matrixes. A small molecule MET kinase inhibitor (BMS-777607) is an inhibitor of tyrosine receptor currently under clinical trials. Previous studies reported the effect of this inhibitor on cancer cells such as breast, hepatic and prostate cancer. However, its inhibitory effect on malignant pleural mesothelioma (MPM) cells has not yet been evaluated. In our study, we aimed to investigate the therapeutic usefulness of this small molecule on MPM. **Methods:** Human MPM cell lines such as REN and NCI-H2373 and a human lung carcinoma cell line (NCI-H226) were used. LP-9 cell line, which resembles normal human mesothelial cells, was used as control. These cells were cultured and exposed to BMS-777607 at concentrations 1uM, 5uM and 10uM. Cell cycle, cell viability, lysosomal mass/pH changes and mitochondrial membrane potential were examined using immunofluorescent staining methods and data were collected and analysed with high content screening systems such as Cytell and IN Cell Investigator software. **Results:** Both MPM cell lines and the lung cell line showed cell cycle arrest as examined by Cytell in significant dose-dependent manner with maximum effects seen at the highest dose (10 µM) of BMS-777607. Cell viability and other biological cellular markers were also altered upon exposure to this small molecule. Our results showed that BMS-777607 induces negligible changes of these markers examined in the normal mesothelial cells line (LP-9). **Conclusion:** Taken together, these findings indicate that inhibition of MET/RON signalling using a small molecule inhibitor such as BMS-777607 could significantly interrupt the cell cycle stages and alter other cellular compartments (i.e; lysosomal mass/pH, mitochondrial membrane potential) which lead to suppression of MPM cell viability, suggesting that such a targeting strategy may hold promise for the treatment of MPM. **Keywords:** MET/RON kinase inhibitor, BMS-777607, malignant pleural mesothelioma, lysosomal mass/pH

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P2.08-015 The Relationship between the Cost of Treatment and Prognosis in Malignant Mesothelioma in Turkey Guntulu Ak[1], Selma Metintas[2], Tunc Kose[3], Filiz Bogar[4], Nuray Girginer[3], Hasan F. Batirel[5], Nurullah Uckun[3], Muzaffer Metintas[1] [1]*Lung and Pleural Cancers Research and Clinical Center; Medical Faculty Department of Chest Diseases, Esogu, Eskisehir/Turkey,* [2]*Lung and Pleural Cancers Research and Clinical Center; Medical Faculty Department of Public Health, Esogu, Eskisehir/Turkey,* [3]*Faculty of Economics and Administrative Sciences, Esogu, Eskisehir/Turkey,* [4]*Lung and Pleural Cancers Research and Clinical Center, Esogu, Eskisehir/Turkey,* [5]*Medical Faculty General Thoracic Surgery, Marmara University, Istanbul/Turkey*

Background: Malignant mesothelioma (MM) is endemic in the population exposed to asbestos and has high healthcare cost with a limited life expectancy. The aim of this study is to evaluate the relationship between cost according to treatment type and prognosis in MM patients followed up from diagnosis to death. **Methods:** The demographics and healthcare costs of 239 patients with MM were obtained from hospital records in the tertiary university hospital between 2005 and 2014. Variance analysis and t-test were performed to compare the groups. The survival rates were estimated using the Kaplan-Meier method. To clarify health care cost in Turkey, the following information was given according to the national reimbursement price in April 2015. This study was supported by General Directorate of Health Researches, Republic

of Turkey, Ministry of Health. **Results:** The mean age of the patients were 62.9±11.3 years and 125 (52.3%) of them were male. The median survival time was 9.0±0.8 months (95% CI: 7.3–10.7). Patients' numbers according to treatment schema: 52 (21.8%) best supportive care (BSC); 3 (1.3%) BSC+palliative radiotherapy (pRT); 117 (49.0%) chemotherapy; 39 (16.3%) chemotherapy+pRT, 16 (6.7%) pleurectomy/decortication (P/D)+chemotherapy+RT; 4 (1.7%) P/D+chemotherapy; 8 (3.3%) extrapleural pneumonectomy (EPP)+chemotherapy+RT. BSC group had the lowest average cost with $1,355 (r:258-4,909) per patient. The average cost was $6,595 (r:1,621-21,371) for patients received only chemotherapy. When pRT added to chemotherapy, cost was increasing to $8,962 per patient. The average cost was $11,691 (r:6,567-19,064) per patient for P/D+chemotherapy+RT group. It decreased to $10,676 without RT. The highest average cost was seen in the group of EPP+chemotherapy+RT with $13,788 (r:6,168-19,577) per patient. The median survival times were 6 months (95%CI:5.3-6.7), 12 months (95%CI:9.8-14.2), 18 months (95%CI:11.5-24.5), 27 months (95%CI:7.6-46.4) for BSC, chemotherapy, P/D+chemotherapy+RT and EPP+chemotherapy+RT group, respectively. The median survival time was significantly different between BSC and chemotherapy groups (Log-Rank:10.607; p=0.001). The average cost of 6 months prolongation of lifetime was $5,239 in chemotherapy group and incremental cost was $873 per month gained. The median survival time was not different between chemotherapy and P/D+chemotherapy+RT groups (Log-Rank: 1.263; p=0.261). However, there was 6 months survival difference between the two groups. The average cost of 6 months prolongation of lifetime was $5,097 and incremental cost was $850 per month gained in EPP+chemotherapy+RT. The median survival time was significantly different between chemotherapy and EPP+chemotherapy+RT groups (Log-Rank: 8.082; p=0.004). The average cost of 15 months prolongation of lifetime was $7,194 and incremental cost was $480 per month gained in EPP+chemotherapy+RT group. There was a difference between surgical groups in terms of median survival (Log-Rank:4.421; p=0.036). The average cost for prolongation of lifetime was $2,097 and incremental cost was $233 per month gained. **Conclusion:** MM has a limited survival time despite antitumor treatment and treatment cost is relatively high by prolongation of lifetime. Treatment should be given to selected patients and EPP should be preferred to P/D as much as possible. It is clear that there is need well designed prospective studies for cost analysis of MM.
Keywords: mesothelioma, cost analysis

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P2.08-016 Pleural Mesothelioma Incidence in Sweden: No Cecrease in Sight
Gunnar N. Hillerdal *Pulmonary Diseases, Karolinska Hospital, Stockholm/Sweden*

Background: Sweden was one of the first countries in the world to ban asbestos, which happened in the early mid-seventies. The use of asbestos in Sweden was thus mainly in the 1960ies. The incidence of mesothelioma started rising from around 1975 and reached a little more tha 100 cases a year in 1985, in parallell to asbestos use 30 years earlier. It has been postulated that it should start sinking in the first decade of the 2000s. **Methods:** The incidence of pleural mesothelioma for both sexes have been taken from the ofiicial Swedish pulblication "Cancer Incidence in Sweden", the latest avialable figures of which is 2012. **Results:** Since 1984, a plateau has been reached, with around 100 cases of new pleural mesotheliomas occurring in Sweden every year, sometimes a little less, more often a little more. No tendency to declining figures can be seen so far. The median age st diagnosis has remained the same since the 1960ies, 54-70 years. Furthermore, the percentage of women is the same, 15-20 % of the total. **Conclusion:** The heaviest exposure took place in Sweden around 1965; after this date, in most working places people became more aware and the exposure was diminished, but continued until early 1970ies. It has been postulated that 40 years after exposure, the risk should decline, and if so those who were 20 years old in 1970 should by now have a decreasing risk, but there are no signs of this. Since the relative risk for men and women is about the same, it is unlikely that general environmental exposure to asbestos explains the lack of decline of the curve. Interestingly, the median age at diagnosis has remained the same though most of those exposed should by now have a fairly advanced age.
Keywords: Mesothelioma, Incidence, Sweden

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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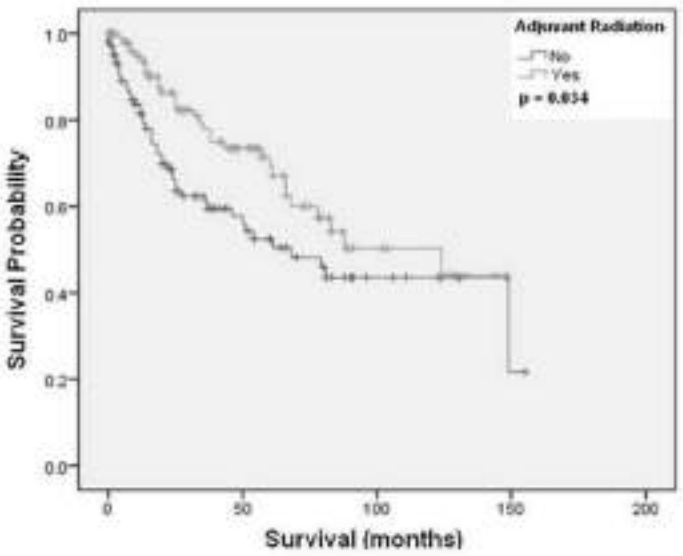
P2.08-017 Chest Wall Soft Tissue Sarcomas: Impact of Adjuvant Radiation Therapy Following Surgical Resection
Adnan M. Al-Ayoubi, Sadiq S. Rehmani, Andrea Wolf, Andrew Kaumfan, Raja Flores, Faiz Y. Bhora *Thoracic Surgery, Icahn School of Medicine at Mount Sinai, New York/NY/United States of America*

Background: Primary chest wall soft tissue sarcomas are rare tumors of the thoracic wall. The objective of this study is to evaluate the impact of adjuvant radiation therapy on survival following surgical resection using the Surveillance, Epidemiology, and End Results (SEER) database. **Methods:** We queried the SEER database for all surgically resected histologically proven primary chest wall soft tissue sarcomas between 1998 and 2010. Exclusion criteria included pediatric sarcomas, multiple malignancies and unknown grade, stage or radiation therapy status. Chi-square tests were performed to identify covariates associated with receiving adjuvant radiation therapy. Coarsened-exact matching was used to generate a matched cohort of patients who received adjuvant radiation following surgery and patients who underwent surgery alone. Cox regression and Kaplan-Meier analyses were performed to determine covariates associated with overall survival. **Results:** A total of 570 patients were included in the cohort prior to matching based on the selection criteria. Histological type (p = 0.003) and tumor grade (p < 0.001) were independently associated with receiving radiation therapy. Cox-regression did not demonstrate reduced hazards of death for adjuvant RT. After coarsened-exact matching, Kaplan-Meier survival analysis of matched groups (105 surgery alone and 104 surgery + RT) showed significant 1-, 3- and 5-year overall survival difference (p = 0.034) in surgery + RT compared to surgery alone. **Conclusion:** In a matched large population cohort, adjuvant radiation therapy appears to improve overall survival following surgical resection of chest wall soft tissue sarcomas. Further trials are required to determine the efficacy of adjuvant radiation therapy in this population.



Keywords: Thoracic Surgery, Chest wall soft tissue sarcoma, radiation therapy

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P2.08-018 The Impact of the Resection Margin on Recurrence and Survival in Bronchopulmonary Carcinoids
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Background: Complete surgical resection is the treatment of choice in bronchopulmonary carcinoids. Previously published data showed no inferiority of sublobar versus lobar resection. Data on the extent of resection margins are lacking, thus we aimed to analyze resection margins in pulmonary carcinoids and correlated them with survival and recurrence. **Methods:** We retrospectively analyzed 85 patients that underwent surgery for atypical (AC) or typical (TC) pulmonary carcinoids. Patient charts were reviewed and clinicopathologic and survival data was collected. Pathology reports were reviewed for length of resection margins. **Results:** The median follow-up period was 42.3 months (range 0.3 - 172.2). There was no statistically significant difference in disease-free survival (DS) when comparing resection margins ≤2 mm to >2 mm (p=0.93, Hazard Ratio (HR)=1.7). When looking at AC alone, a worse DS can be seen if the resection margin was smaller than 2 mm (p=0.06, HR=15.8). In AC likelihood of recurrence was higher when the resection margin was ≤1 cm (Odds ratio=5.1, p=0.28). In TC this tendency was not present (Odds ratio=1.2, p=1). **Conclusion:** There is a trend towards a worse prognosis and higher likelihood of recurrence in smaller resection margins in AC in contrast to TC. Due to low sample size no definitive statements can be made based on this study, however respective data on these rare tumors cannot be drawn from tumor databases. The resection margin is the most critical issue for the treating surgeon and any information on this topic is of highest importance to the field.
Keywords: Resection margin, Surgical treatment, recurrence, bronchopulmonary carcinoids

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P2.08-019 Accuracy of Percutaneous Closed Pleural Biopsy in Thoracic Malignancies
Renata Báez-Saldaña, Uriel Rumbo-Nava, Patricia Castillo-González, Teresa Aguirre-Pérez, María Eugenia Vázquez-Manríquez *Respiratory Oncology, Instituto Nacional de Enfermedades Respiratorias, Distrito Federal/Mexico*

Background: Recently there has been some controversy about the value of percutaneous closed pleural biopsy (PCPB) as a diagnostic procedure for establishing the etiology of pleural effusion. Our objective was to assess the accuracy of percutaneous closed pleural biopsy as a diagnostic procedure for lung cancer and mesothelioma in patients with pleural effusion. **Methods:** We performed a prospective study of all individuals who underwent percutaneous closed pleural biopsy, using Cope needle or Abram's needle in order to establish the etiology of pleural effusion, during a 8/year period in a refering hospital of respiratory diseases in Mexico City. The identification of patients who underwent closed pleural biopsy was obtained from the anatomopathological registries. The information of each patient was obtained by medical record review. In this study, when the pleural biopsy did not establish the definite diagnostic, we used as a gold standard other procedures such as thoracoscopy, open lung/pleural biopsy, fiberoptic bronchoscopy, adenosine deaminase and/or microbiological tests. All cases

were followed up at least three months through medical record review and direct contact with the patient. With 2x2 table we determined the accuracy of PCPB. **Results:** A total of 1034 pleural biopsies were performed. Malignancy was identified in 466 (45.07%) of whom 252 (24.37%) had adenocarcinoma,105 (10.16%) mesothelioma, cancer not differentiated 28 (2.71%), epidermoid 5 (0.48%) small cells cancer 19 (1.84%), giant cells cancer 6 (0.58%), limphomas 11 (1.06%) and others malignancies 40 (3.87%). 116 (%) cases of pleural tuberculosis and 2 (0.19%) parapneumonicos. 378 (36.56%) biopsies were non/specific inflammatory. 171 (19.81%) were excluded to the analysis due to 72 (6.96%) obtaining no pleural tissue and in 99 (9.57%) we can not obtain case information. A total of 863 biopsies were analysed to asses the accuracy.

Indicator	Lung cancer and other malignancies	Mesothelioma
Sensitivity % (CI 95%)	77 (74-79)	81 (78-83)
Specificity % (CI 95%)	98 (97-99)	100
Positive predictive value % (CI 95%)	99 (98-100)	100
Negative predictive value % (CI 95%)	66 (63-70)	97 (96-98)
Likelihood ratio positive	38.5	81
Likelihood ratio negative	0.23	0.19
Prevalence % (CI 95%)	68 (65-71.3)	15 (13-17)

Conclusion: This is a valid, available, accurate and precise diagnostic test which can be applied in patients with pleural effusion to establish cancer or tuberculosis diagnostic. The percutaneous closed pleural biopsy in this setting is useful in our practice due to produces big change from pre-test to post-test probability. **Keywords:** percutaneous closed pleural biopsy, lung cancer, diagnostic test

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P2.08-020 Percutaneous Cryoablation for Pulmonary Metastasis of Soft Tissue and Bone Sarcomas Keisuke Asakura[1], Yoshikane Yamauchi[1], Masafumi Kawamura[2], Seishi Nakatsuka[3], Hideaki Yashiro[3], Masanori Inoue[3], Ikuo Kamiyama[1], Takashi Ohtsuka[1], Mitsutomo Kohno[1], Hisao Asamura[1] [1]*Department of Thoracic Surgery, Keio University, School of Medicine, Tokyo/Japan,* [2]*Department of Surgery, Teikyo University School of Medicine, Tokyo/Japan,* [3]*Department of Diagnostic Radiology, Keio University, School of Medicine, Tokyo/Japan*

Background: The treatment of pulmonary metastases of soft-tissue and bone sarcomas is challenging, as they are highly resistant to both chemotherapy and radiotherapy. Hence, while surgery is the treatment of choice, the treatment options are currently very limited for non-surgical patients. Therefore, the purpose of this study was to evaluate the safety and efficacy of percutaneous computed tomography (CT)-guided cryoablation for pulmonary metastases of soft tissue and bone sarcomas. **Methods:** Hospital records of patients who underwent cryoablation for metastatic lung tumors of soft-tissue and bone sarcomas were reviewed. Percutaneous cryoablation was performed using the Cryocare system (Endocare, Irvine, CA) and multi-slice CT fluoroscopy. CT scans were obtained immediately after the procedure; follow-up CT was performed on days 1, 7, 30, and 90, and subsequently at 6-month intervals. The procedural safety, local progression-free survival, and overall survival were assessed retrospectively. **Results:** Between 2002 and 2011, percutaneous cryoablation was performed on 20 patients (12 men and 8 women; median age, 46 years; age range, 17-83 years) for 56 metastatic lung tumors of soft tissue and bone sarcomas, during a total of 36 sessions. Of the 20 patients, 2 (10%) refused surgery and 18 (90%) were considered inoperable due to multiple tumors or insufficient pulmonary function. Of the 36 sessions, pneumothorax occurred in 12 (33%), transient hemoptysis in 11 (31%), and hemothorax in 1 session (3%). Of the 12 sessions with pneumothorax, 1 (8%) required chest tube insertion. No surgical intervention was required for any of these complications. With a median follow-up of 27 months, 2 tumors (4%) showed disease progression at the original cryoablation site. The local progression-free survival rates at 1 and 3 years after cryoablation were 95% each, and the 1- and 3-year overall survival rates were 77% and 49%, respectively. Four patients were alive over 5 years after cryoablation. **Conclusion:** Percutaneous cryoablation is a feasible and efficient treatment option for inoperable metastatic lung tumors of soft tissue and bone sarcomas. **Keywords:** cryoablation, soft tissue and bone sarcomas, metastatic lung tumor

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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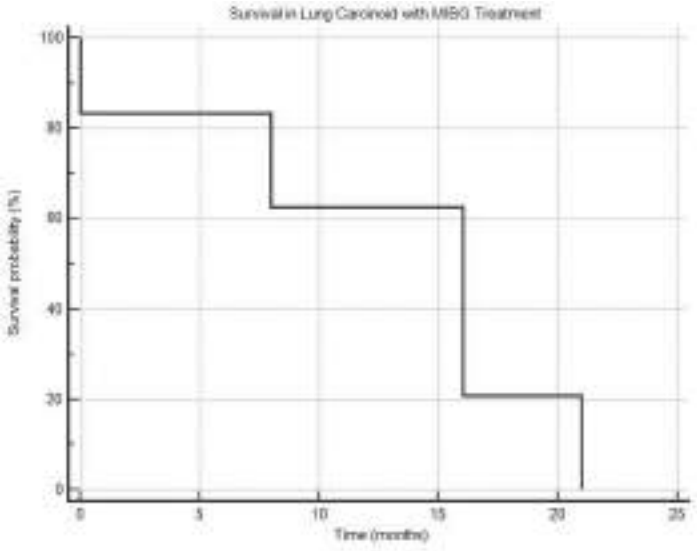
P2.08-021 Radionuclide Therapy with Meta-Iodo-Benzyl-Guanidine (MIBG) for Patients with MIBG Avid Pulmonary Carcinoid Tumors Robert A. Ramirez, David T. Beyer, Richard J. Campeau *Neuroendocrine Tumor Program, Ochsner Medical Center - Kenner, Kenner/United States of America*

Background: Pulmonary carcinoid tumors represent only 2% of all lung tumors. Treatment generally involves surgery which many times is curative, however, once metastasis develops there are no standard treatment options. Radionuclide therapy with MIBG has been shown to be beneficial for gastroenteropancreatic neuroendocrine tumors. We sought to determine the efficacy of MIBG treatment for metastatic pulmonary carcinoid tumors at the Ochsner/Louisiana State University Neuroendocrine Program. **Methods:** All patients who had a diagnosis of a metastatic typical or atypical pulmonary carcinoid tumor and who underwent MIBG treatment at our institution were included. Tumor characteristics, demographic information, response rate and survival was captured. Patients without adequate records were excluded. All patients required MIBG avid disease on MIBG scintigraphy. MIBG treatment consisted on 200 mCi of ^{131}I MIBG delivered over one hour at 30 cc/hour. Follow up CT scans were used to determine response by RECIST 1.1. **Results:** Six pulmonary carcinoid patients were identified who had undergone MIBG treatment. The mean age at initial MIBG treatment was 66 (range 44-89) Females represented 83% of patients. There were five typical and one atypical carcinoid patient included. Two patients achieved a partial response, one patient had stable disease and three patients had progression following MIBG treatment. Overall survival for the entire cohort from the date of MIBG therapy is shown.



Conclusion: In our small cohort, MIBG treatment seemed to be beneficial in 50% of patients with MIBG avid disease with a partial response observed in 33% of patients. This treatment was well tolerated and offered an increased survival in an already heavily pretreated cohort. MIBG may offer some pulmonary carcinoid patients an additional treatment option. Further research should be directed at examining radionuclide therapy in pulmonary carcinoid patients. **Keywords:** carcinoid, radionuclide, neuroendocrine, MIBG

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P2.08-022 Pulmonary Resection of Metastatic Renal Cell Carcinoma Olga Lebedieva, Yurii Kondratsky, Andrii Ganul, Leonid Bororov *Tumors of Thoracic Cavity, National Cancer Institute, Ukraine, Kyiv, Kyiv/Ukraine*

Background: Pulmonary resection for metastases from renal cell carcinoma (mRCC) is a treatment option that can provide long-term disease-free survival. Larger number and size of metastatic nodules, increasing number of lymph node metastases, shorter disease-free interval, and decreased preoperative forced vital capacity are negative prognostic factors in this setting. The potential role of surgery is illustrated by the results from a series of 278 patients with mRCC in which 51 percent underwent removal of all of their metastatic disease with curative intent, 25 percent underwent partial resection of their metastatic disease, and 24 percent were treated without surgery. Metastases were most frequently resected from the lung, brain, bone and soft tissue. **Methods:** Between 1989 and 2014, 73 patients (44 men, 29 women) underwent pulmonary resection of mRCC. Only patients who met the criteria for potentially curative operation, that means, control of primary tumor, ability to resect metastatic diseas were included. All patients received immunotherapy after surgical treatment. **Results:** Pulmonary metastases were bilateral in 15 patients and unilateral in 58 patients. 15 bilateral (9 staged) and 58 unilateral thoracotomies were performed. Wedge resection was performed in 68 and lobectomy in 5 patients. The overall 5-year survival was 72.8 % 10-year survival was 43,9% and 15-year survival was 20,9% among the patients, who had no other extrapulmonary metastases. The 5-year survival of curative resected patients with metachronous metastases was better then patiens with synchronous metastases. The overall 5-year survival was 31,3 % among the patients, who had extrapulmonary metastases. **Conclusion:** Surgical resection of isolated lung metastases in carefully selected patients is safe and effective. Metastasectomy nowadays is the best treatment option in cases with technical resectable metastases with as much as possible good prognostic factors. **Keywords:** pulmonary resection, renal cell carcinoma, metastasis

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P2.08-023 Aberrant Neuroendocrine Lung Tumor Nomenclature in Daily Practice, How Common Is It? Jules L. Derks[1], Ernst-Jan M. Speel[2], Robert Jan Van Suylen[3], Erik Thunnissen[4], Michael Den Bakker[5], Anne-Marie Dingemans[1] [1]*Department of Respiratory Diseases, Grow School for Oncology & Developmental Biology, Maastricht University Medical Center, Maastricht/Netherlands,* [2]*Department of Pathology, Grow School for Oncology & Developmental Biology, Maastricht University Medical Center, Maastricht/ Netherlands,* [3]*Department of Pathology, Jeroen Bosch Hospital, 'S Hertogenbosch/ Netherlands,* [4]*Department of Pathology, VU University Medical Center,, Amsterdam/ Netherlands,* [5]*Department of Pathology, Maasstad Hospital, Rotterdam/Netherlands*

Background: The WHO 2015 classification for pulmonary carcinoids (PC) and high-grade neuroendocrine carcinomas (NEC) has in essence, not been changed compared to the previous one, despite known limitations in the diagnostic process such as 1) the need for resection material or large biopsies 2) reported inter-observer variability and 3) sporadic exposure in daily practice. Furthermore, nomenclature used in previous or different classification systems for neuroendocrine tumors may result in an aberrantly applied description of the WHO 2004 diagnoses. Here we evaluate if nomenclature established in daily pathology practice in the Netherlands is according to that advised by the WHO 2004 for PC, NEC and non-small cell lung cancer (NSCLC) with neuroendocrine differentiation established by immunohistochemistry (IHC). **Methods:** Written conclusions (diagnoses) of pathology reports (2003-2012) were retrieved from the Dutch Pathology Registry. Conclusions describing PC, NEC and carcinomas with neuroendocrine features/ differentiation were selected by multiple queries on anatomic location, diagnosis and keywords (e.g. carcinoma + endocrine). All conclusions were screened in concordance with an experienced pathologist (JLD & RJS) and data on sampling method, diagnoses and origin of primary tumor were collected. Conclusions were excluded if established on autopsy cases or if it reported differential diagnoses, diagnoses of non-pulmonary/ unknown primary, non-neuroendocrine or small cell lung cancer. We compared the retrieved diagnoses with the advised WHO 2004 nomenclature after which all diagnoses were clustered (e.g. typical/well differentiated/grade I carcinoid into "PC"). For statistical analysis the X^2 test was used. **Results:** 4612 conclusions were eligible for analysis of which *N*=698 (15%) described a diagnoses that did not match the WHO nomenclature. Foremost non-WHO diagnoses were: (poorly differentiated) neuroendocrine carcinoma; high-grade neuroendocrine carcinoma/tumor; NSCLC neuroendocrine carcinoma; neuroendocrine tumor and low grade (well differentiated) neuroendocrine carcinoma/ tumor (carcinoids). After discussion, we clustered N=2005 (43%) diagnoses into PC, *N*=1788 (39%) in high-grade NEC, *N*=763 (17%) in carcinoma with neuroendocrine features/differentiation and *N*=56 (1%) in neuroendocrine tumor n.o.s., respectively. Deviations from the WHO nomenclature occurred in 8% (*N*=157) of PC and 21% (*N*=377) of high-grade NEC and this occurred mainly on biopsy/cytology specimens (75% (*N=399)*). In (NSCLC) carcinomas with neuroendocrine features/differentiation diagnoses deviated from the WHO in 14% (*N*=108). Additionally, both the terms neuroendocrine "features" and "differentiation" were used to address positive neuroendocrine IHC staining (16% vs 25%) though differentiation was used slightly more often*(p*=0.001*)*. Finally, 52% (*N*=1045) of PC diagnoses were established on biopsy/cytology specimens and a strong increase in diagnoses of large cell neuroendocrine carcinoma (LCNEC) on biopsy/cytology specimens was observed (<2008 *N*=174 vs. ≥2008 *N*=464, *p*<0.001). **Conclusion:** In daily practice 8% of PC, 21% of high-grade NEC and 14% of (NSCLC) carcinomas with neuroendocrine features/differentiation diagnoses deviated from the WHO 2004 nomenclature. This occurred mainly on biopsy/cytology specimens. Also, the diagnosis (NSCLC) carcinoma with neuroendocrine 'differentiation/features' was unclear and should be specified (i.e. IHC or morphologically based (or both)). Finally, often the diagnosis LCNEC was established on biopsy/cytology specimens whereas this is not advised by the WHO. Whether these findings are due to personal preferences or difficulties applying current classification to limited samples, require further investigation.
Keywords: neuroendocrine, Nomenclature, carcinoid, diagnosis

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P2.08-024 CT Findings of Early Pleural Mesothelioma and Benign Asbestos Pleural Effusion Katsuya Kato[1], Takumi Kishimoto[2], Nobukazu Fujimoto[2], Kenichi Gemba[3], Keisuke Aoe[4], Yukio Takeshima[5], Kouki Inai[6] [1]*Diganostic Radiolgy 2, Kawasaki Medical School, Okayama/Japan,* [2]*Asbestos Study Center, Okayama Rosai Hospital, Okayama/Japan,* [3]*National Hospital Organization Fukuyama Medical Center, Fukuyama/Japan,* [4]*National Hospital Organization Yamaguchi-Ube Medical Center, Ube/Japan,* [5]*Hiroshima University, Hiroshima/Japan,* [6]*Pathological Diagnostic Center, Hiroshima/Japan*

Background: • Malignant pleural mesothelioma is known as disease of the poor prognoses. • Our purpose is to find useful CT findings for correct differentiation between Malignant Pleural Mesothelioma in the early stage (e-MPM) and Benign Asbestos Pleural Effusion (BAPE) to improve prognosis of MPM. **Methods:** • The BAPE group consisted of 36 patients diagnosed at Okayama Rosai Hospital since Jan 2000. In all BAPE patients thoracoscopic biopsies were conducted to exclude malignant diseases including MPM. • In e-MPM group, 66 patients who were diagnosed mesotheliomas with T1 or T2 (IMIG system) by the CT evaluation were studied. The e-MPM patients were selected from 2,742 mesothelioma death cases of Japanese vital statistics of 2003-05. • We evaluated CT scans taken at the time of diagnosis for each group. The evaluating items were presence of asbestosis, pleural plaque (PQ), rounded atelectasis (RA) and diffuse pleural thickening (DPT), as well as the grade and localization of pleural irregularities. **Results:** • In BAPE group (36 cases), the occurrence rate of asbestos-related lesions was significantly higher than in e-MPM group (66 cases) as follows; prevalence of asbestosis 17%/2% (*), PQ 92%/35% (**), RA 44%/0% (**) and DPT 25%/2% (**). (*P=0.0038 **P<0.001) • As for grade of pleural irregularity, no irregularity was found in 22%/9%, low-level irregularity in 72%/54%, high-level irregularity in 5%/23% and mass formation in 0%/14% of BAPE and e-MPM group patients, respectively. • As for localization (including overlap) of pleural irregularity, irregularity in mediastinal pleura was observed in 30%/74%, basal pleura in 91%/77% and interlobar pleura in 0%/55% of BAPE and e-MPM group patients, respectively. The mediastinal pleural thickening was minimal in BAPE group and found regressed in the follow-up CT scans. **Conclusion:** • In BAPE group the occurrence rate of asbestos-related lesions was higher than in e-MPM group. • Because the 5% of BAPE cases presented irregular pleural thickening, the differentiation with MPM was difficult in such case. • The mediastinal pleural thickening, which is considered to be a characteristic of MPM, was also observed in 30% of BAPE cases. However, the finding disappeared during observation. And no BAPE case with interlobar pleural irregularity was found. These findings can be useful for differentiation BAPE and e-MPM cases.
Keywords: Mesothelioma, benign asbestos-related pleural effusion, CT, asbestos

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P2.08-025 Contributing Factors to the Outcome of Primary Malignant Chest Wall Tumors Abdelrahman M. Abdelrahman[1], Rabab Gaafar[2], Mohamed Rahoma[2], Hoda Baki[2] [1]*Suregry, National Cancer Institute, Cairo/Egypt,* [2]*National Cancer Institute, Cairo/Egypt*

Background: Primary malignant chest wall tumors are a heterogeneous group of tumors. They require special experience in designing resection and reconstruction. They account for less than 1% of all primary malignant tumors. This study is designed to clarify different factors contributing to the outcome of patients with primary malignant chest wall tumors in our institution. **Methods:** A retrospective study included 97 patients with pathology proven primary malignant chest wall tumors, treated at the national cancer institute, Cairo University, Egypt, during the period from 2002 to 2012. Computed tomography scan of the chest and upper abdomen was considered the primary staging tool for all patients. Magnetic resonance imaging was requested whenever indicated. Surgical resection and reconstruction was designed according to the site and extent of the lesion. resected. Adjuvant and neo-adjuvant therapy was given according to thoracic oncology committee decision. This study was approved by the ethical committee of our institution and informed patient consent was taken. **Results:** Primary malignant chest wall tumors represented 10.5% of all thoracic malignanciesin our institution. There were 46 males and 51 females, the median age was 41 years. Chondrosarcoma was the commonest tumor histology (20.6%). The mean tumor size was 9.3x6.2cm. Tumor multiplicity was found in 15.4% of patients. Bone resection was performed in 76 patients (78.3%), ribs resection was performed in 62 patients and the average number of resected ribs per patient was 2.57 ribs. Sternal resection was done in 9 patients. R0 resection was achieved in 73% of patients. There was one operative related mortality and 23% of patients suffered procedure related complications. Local recurrence developed in 45.3% of patients. The overall survival for the whole group at 1, 3 and 5 years was 67.1%, 37.2% and 26.1 % respectively and the median survival time was 26 months. Different prognostic variables were used to assess better survival including: age , sex, site , size pathologic subtype , tumor grade,, safety margin Good prognostic factors include female sex, age ≤ 40years, no rib resection, safety margin ≥ 1cm, when the least safety margin involve the soft tissue and not the bone, tumor size ≤ 6cm in diameter. **Conclusion:** rimary malignant chest wall tumors should be treated with highly qualified thoracic surgeon and achieving wide resection margins is of great importance to minimize local tumor recurrence that will have an impact on long-term survival.

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P2.08-026 Molecular Markers of Resected Esophageal Squamous Cell Cancer and Its Correlation with Clinical Outcome Gang Lin, Shuiyun Han, Maohui Yan, Xiaojiang Sun, Yaping Xu, Weimin Mao *Zhejiang Cancer Hospital, Hangzhou/China*

Background: The tumor related molecular markers in esophageal squamous cell cancer(ESCC) remains unknown and requires further investigation in order to promote efficient and rapid development of therapeutic methods. The aim of our study was to evaluate if molecular markers of ESCC correlates with patients' prognosis and the outcome. **Methods:** Protein expressions of EGFR, C-MET, HER2 were detected by immunohistochemistry (IHC) in 180 paraffin-embedded tissue samples from stage IIB-IIIC ESCC patients with esophagectomy at the Zhejiang Cancer Hospital between January 2007 and December 2012. Log-rank test was used for univariate analysis, and Cox's proportional hazards model was used for multivariate analysis. Assessed factors were age, gender, somking, alcohol use , tumor location, stage, differentiation, venous or nerve invasion, radiation, chemotherapy and expressions of EGFR, C-MET, HER2. **Results:** The median survival of all patients was 46 months. Of the all 180 patients, the positive rates of EGFR, C-MET, HER2 were 94.4%, 87.2% and 11.1%, respectively. The high expression rates of EGFR and MET were 47.8% and 46.7%, respectively. On univariate analysis (Tabel 1), stage and high expression MET were the statistically significant unfavorable factors for overall survival, meanwhile, a nonsignificant trend toward dcreased overall survival was found with non chemotherapy patients. The multivariate analysis indicated that independent prognostic risk factors included MET (P=0.029) , chemotherapy (P=0.046) and late stage (p=0.000) with very high statistical significance. In subgroub of the patients with MET high expression, tumor location (p=0.029), non chemotherapy (p=0.043) and late stage (p=0.014) had been the statistically significant unfavorable factors, analyzed by Cox proportional hazards model. In subgroub of the patients with C-MET low or negative expression, non chemotherapy (p=0.043) and late stage (p=0.014) had been the statistically significant unfavorable factors.

Table.1 Prognostic factors for overall survival in univariate analyses

Factors	Category	P-value
Age	≤65 (vs.>65)	0.130
Gender	Male (vs. Female)	0.486
Smoking	Nonsmokers (vs. Smokers)	0.148
Alcohol use	Non use (vs. Use)	0.977
Tumor location	Upper and middle (vs. Lower)	0.193
Stage	IIA-IIIA (vs. IIIB-IIIC)	0.000
Differentiation	Well (vs. moderate and poor)	0.265
Venous or nerve in invasion	Non invasion (vs. Invasion)	0.613
Radiation	Non radiation (vs. Radiation)	0.957
Chemotherapy	Non chemotherapy (vs. Chemotherapy)	0.090
EGFR	>median (vs. ≦median)	0.347
C-MET	>median (vs. ≦median)	0.018
HER2	Positive (vs. Negative)	0.142

Conclusion: In the Chinese population, HER2 expression rate was very low. The high expressions of HER2 and EGFR was not correlated with prognosis. High expression of C-MET may be prognostic factors for IIB-IIIC ESCC patients who underwent esophagectomy. ESCC with high expression of C-MET might be a poorer prognosis than those with C-MET low expression. In conclusion, C-MET is a important molecular marker in esophageal squamous cell cancer(ESCC) and further studies are necessary to explore the role of C-MET.
Keywords: Esophageal squamous cell carcinoma, c-Met, EGFR, HER2

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P2.08-027 Investigation for the Optimum Resectable Pathological Size of Small Solitary Metastasis from Colorectal Cancers
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Background: Surgery is still standard modality for the patients with pulmonary metastases from colorectal cancer in spite of recent remarkable development of chemotherapy. The aim of this multi-institutional retrospective study was to determine which pathological size is the best suited to pulmonary resection, and to evaluate the prognostic factors in the patients with small colorectal solitary metastasis. **Methods:** Patients and Methods Patients with pathologically solitary metastasis were recruited. The retrospective examined sample size was finally 561 who underwent complete resection at 46 facilities in Japan from 2004 to 2009. **Results:** No statistically significant difference was detected between with adjuvant chemotherapy and without in disease free survival (DFS) and overall survival (OS) ($p=0.09$ and $p=0.79$). Disease free survival (DFS) and overall survival (OS) calculated after initial pulmonary resection at 5 years were 71.0% and 41.7%, respectively. Tumors from 8-15mm in diameter showed the lowest incidence of recurrence in this series. Especially, relapse was occurred in all patients with pathological size 5mm (7/7, 100%) among the smallest group in the course of a median 279 days. Although significant difference was not found, a tendency was recognized with 15mm as the border by the recurrence proportion and the receiver operating characteristic curves for DFS. CEA abnormality, pathological size (more than 20 mm), and Disease free interval (more than 2 years) were the prognostic factors for DFS, whereas age (more than 70 years old), CEA abnormality, DFI (more than 2 years), and previous extrapulmonary treatment were the prognostic factors for OS in both univariate and multivariate analyses. **Conclusion:** Our multi-institutional retrospective study proposed that the optimum pathological size up to 15 mm was suitable to pulmonary resection in the patients with solitary metastasis from colorectal cancers, but the smallest nodules (less than 7 mm) had a possibility of re-recurrence within a median one year.
Keywords: pulmonary metastasis , colorectal cancer, solitary metastasis

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-028 Mediastinal Primary Malignant Germ Cell Tumor - Analysis of Prognostic Factors for Patients' Survival. Single Institution Experience
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Background: Primary mediastinal malignant germ cell tumours (MGCT) are a rare entity as typical localization of MGCT are gonads. As there is no concept of how to encode diagnosis of primary mediastinal MGCT (PMMGCT), they are usually reported as mediastinal tumor. The primary aim of the study was to evaluate the prognostic factors for survival of patients with PMMGCT. **Methods:** We analyzed data from patients' medical records who had been diagnosed with a mediastinal tumor and encoded as C38 according to ICD-10. All of them had been diagnosed, treated and followed up in Cancer Center and Institute of Oncology in Gliwice Poland (COI). Patients' medical records were analysed according to the national low regulation. We found 509 patients (pts) with mediastinal tumor diagnosis and reported as C38 according to ICD-10. The most frequently diagnosed tumors were mesothelioma - 32% of pts, and thymoma - 11% of pts. PMMGCT accounted for approximately 4% (19pts). 47% of them had seminoma and 53% non-seminoma diagnosed (the most frequent was tumor mixed). Median age was 28 years (range 19-41). Only 2 pts did not have any disease symptoms and the mediastinal mass has been discovered accidentally during periodic testing. The most frequent symptoms of disease were mediastinal pain and cough, in 79 and 74% of pts, respectively. The impact of the clinicopathological features was analyzed using the chi-squared test with Yates' correction. Survival evaluation was performed using the Kaplan Meier estimate with log rank test. **Results:** Median tumor size was 15cm (range 6,5-20cm). All of pts received cisplatin based chemotherapy. In 53% of pts surgery was the primary treatment and the remaining pts started therapy with chemotherapy. 53% of pts experienced mediastinal radiotherapy. Total median dose was 40Gy (range 12-59,5Gy). All pts with seminoma achieved partial or complete response, disease progression was observed only in pts with non-seminoma tumors. 47% of pts had disease recurrence, including only one pts with seminoma. One pts had two high-dose chemotherapies followed by bone marrow transplant. 53% of the pts died due to disease progression or treatment complication, including one pts with seminoma. Median overall survival was 27,5 months with 5-OS of 53%. Pts with seminoma had smaller tumor size than pts with non-seminoma tumors, $p=0.03$. Pts with a smallers tumor lived longer, $p=0.09$, however, neither surgery nor radiotherapy had an impact on survival, $p=0.5$ and 0.2, respectively. Pts with no general disease symptoms lived significantly longer than those who had any disease symptoms, $p=0.03$. Pts with mediastinal pain at the time at diagnosis lived significantly shorter, $p=0.02$. Pts with seminoma lived significantly longer than pts with non-seminoma tumors, $p<0.001$. **Conclusion:** Primary mediastinal germ cell tumours

occur mostly in males. Pts with mediastinal MGCT had poor prognosis, nonetheless. Pts with seminoma lived significantly longer than pts with non-seminoma tumors, p<0.001. Tumor size and general disease symptoms were the most important prognostic factors. The results of this study have many limitations, mostly due to the group of pts being small. That is why the results should be taken into consideration with caution.
Keywords: primary mediastinal gern cell tumor, chemotherapy, Prognostic factors

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-17:00

P2.08-029 Stereotactic Ablative Radiotherapy (SABR) for Pulmonary Oligometastases and Oligoprogression
Joelle Helou[1], Isabelle Thibault[1], Latifa Yeung L[2], Ian Poon[1], Michael Tjong[2], Andrew Chiang[1], Suneil Jain[1], Hany Soliman[1], Patrick Cheung[1] [1]*Radiation Oncology, Sunnybrook Odette Cancer Centre, Toronto/Canada,* [2]*University of Toronto, Toronto/ON/Canada*

Background: Use of SABR to treat pulmonary oligometastases, and more recently, oligoprogression to delay the need to change systemic therapy, is increasing despite no randomized evidence. This project reviews the outcomes of treating pulmonary metastases from a large single institution. **Methods:** From a prospective SABR database, 180 pulmonary metastases in 120 patients were treated between 11/2008 and 12/2013. Indications for SABR were: 1) oligometastases, where the goal was to irradiate all sites of disease, 2) oligoprogression, where the goal was to irradiate only those tumours which were progressing while a systemic therapy strategy was controlling all other tumours, and 3) dominant areas of progression, where the goal was to irradiate dominant tumours, even if other tumours were progressing, usually in patients with indolent disease not on systemic therapy. Doses of 48-52 Gy in 4-5 fractions were delivered as per institutional policy depending on tumour location and histology. Since 2010 the dose for peripheral colorectal cancer (CRC) metastases was increased to 60 Gy in 4 fractions after a preliminary analysis revealed a higher local failure rate in those tumours. **Results:** Median age of patients was 66.5 years. Median duration of follow-up was 21.1 months. Median biological effective dose (BED) was 120 Gy_{10}. We observed 1 (<1%) grade 5, 1 (<1%) grade 3 and 8 (7%) grade 2 radiation pneumonitis. 2 year local control (LC) of irradiated tumours was 81%. Non-CRC metastases had higher 2 year LC compared to CRC tumours (94% vs 70%, p=0.002). In 18 patients with non small cell lung cancer (NSCLC) pulmonary metastases, 2 year LC was 95%. In the subgroup of 59 patients with CRC metastases, delivering 60 Gy was associated with significantly higher 2 year LC compared to lower doses (88% vs 61%, p=0.011). In 79 patients with oligometastases treated with SABR, the 2 year progression free probability (PFP), progression free survival (PFS) and overall survival (OS) were 63%, 42%, and 73%, respectively. In 27 patients with oligoprogression treated with SABR, the 2 year PFP, PFS, and OS were 42%, 24%, and 70%, respectively. At 2 years, no change in systemic therapy was seen in 56% of the patients irradiated for oligoprogression, with a median time to changing systemic therapy of 30.8 months. In the 12 oligoprogression patients where a change of systemic therapy strategy occurred after SABR, the median time to systemic therapy change was 8.3 months. **Conclusion:** CRC metastases require higher SABR doses to optimize their LC. Outcomes for patients with oligometastases and oligoprogression treated with SABR seem favourable, but prospective clinical trials are needed to confirm these benefits.
Keywords: lung metastases, SABR, Oligometastases, oligoprogression

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-030 Sunitinib in Patients with Advanced Thymoma and Thymic Carcinoma. Retrospective Analysis from RYTHMIC Database
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Background: Sunitinib is a potent oral tyrosine kinase inhibitor of VEGFR, KIT and PDGFR. In a single arm phase 2 study of sunitinib after at least one previous line of chemotherapy, a 26% of partial response rate (PR) was reported in thymic carcinoma (TC) and 6% in thymoma (T), with a median progression free survival (mPFS) of 7.2 months and 8.5 months, respectively. We investigated if off-labelled prescription of sunitinib in this population induced the same efficacy signal. **Methods:** We investigated the database of the French thymic malignancies network. We reviewed advanced T and TC patients (p) who were treated with sunitinib in order to evaluate patient's outcome. **Results:** From October 2011 to January 2015, 28 patients of 7 institutions were identified (20 TC and 8 T). 32% of patients were females and median age was 49.7 y. Fifteen patients (54%) received sunitinib in ≥ 4th line of treatment. Two patients received sunitinib in 1st line treatment (1 T and 1 TC). The 37.5 mg was the initial dose of sunitinib in 16p. In the whole population, the PR rate was 21% (of 20p with TC, 4 (20%) had a PR; and of 8p with T, 2 (25%) had partial responses). Of note, PR to sunitinib was independent of treatment line (1p at 1st lines, 1p at 3rd line, 2 p at 4th line and 2p at ≥ 5th line). 3 TC p were *c-KIT* positive, without a clear relationship with response rate (1 PR, 2 PD). The mPFS in whole population was 103 days. For TC the mPFS was 87 days and 139 days for T. Sunitinib adverse events were manageable and tolerable. 8p stopped sunitinib due to toxicity. The median overall survival (OS) in the whole population was 175 days, with prolonged OS in T *vs*. TC (403 days *vs*. 166 days)**Conclusion:** Sunitinib is an active treatment in thymic epithelial malignancies irrespective of histological subtype, even in a heavy pre-treated population, and treatment line, supporting antiangiogenic therapies as an alternative treatment option for these patients.
Keywords: Sunitinib, efficacy, Thymic, neoplasms

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-031 Usefullness of Positron Emission Tomography in Thymic Lesions' Surgery
Sotirios D. Moraitis[1], Ioannis Gkiozos[2], Konstantinos Kanakakis[1], Dimitros S. Moraitis[1], Dimitrios Angouras[3], Konstantinos Syrigos[2], Theodore Liakakos[4] [1]*Cardiothoracic Surgery, Naval and Veterans Hospital of Athens, Athens/Greece,* [2]*Oncology Unit, 3Rd Internal Medicine Dpt, University of Athens, Medical School, Athens/ Greece,* [3]*Cardiothoracic Surgery Dpt., University of Athens, Medical School, Athens/ Greece,* [4]*1St General Surgery Dpt., University of Athens, Medical School, Athens/Greece*

Background: To evaluate the utilization of positron emission tomography (PET) scan with fluorine-18 fluorodeoxyglucose (FDG) in the selection of the surgical approach for thymic lesions. **Methods:** Twenty-two consecutive patients with thymic pathology, underwent PET-FDG after being evaluated by computed tomography (CT), since 2011. The Standard Uptake Value (SUV) max of the lesion, as well as the SUV of the mediastinum, were estimated. The ratio SUVmax Lesion/Mediastinum was the caliber for selecting thoracoscopic thymectomy (TT) or thymectomy via median sternotomy (TMS), as the therapeutic procedure. If the ratio SUVmax L/M < 1, thoracocscopic thymectomy was preferable. If the ratio was, 1 < SUVmax L/M < 2, the selection was depended on the lesion's dimensions (TT was preferred for lesions < 4 cm). If the ratio was SUVmax L/M > 2, a median sternotomy was the approach of choice. **Results:** There were 14 male and 8 female patients, with a mean age of 41.1 y.o. In 13 patients the ratio SUVmax L/M showed up > 1, while in 4 patients was higher than 2. The histopathology revealed 7 thymomas, 2 thymolipomas, 8 true thymic hyperplasias, 1 non seminomatous tumour, 1 silicone indused lemphadenopathy while 1 patient is waiting for TT and another one (type C thymoma by fine needle biopsy), for TMS. The mean SUVmax for thymomas was 3.02+-1.67, for thymolipomas was 1.48+-0.26, for true thymic hyperplasias was 1.82+-0.42, while the non seminomatous' tumour SUVmax was 12.4. There have been performed 7 TTs, 1 Transcervical approach and 13 TMSs. R0 resection was achieved in all 21 patients, have undergone operation, so far. All patients had an uneventful postoperative course and the mean duration of hospital stay was 4 days for TTs and 7 days for TMSs. **Conclusion:** There is no imaging modality sufficient by itself to identify the nature of thymic lesions. The intensity of FDG uptake is useful for predicting the grade of malignancy, and high FDG uptake may reflect the invasiveness of the malignant nature in thymic epithelial tumors. The creation of a scale of "metabolic biopsy" with the use of the ratio SUVmax L/M, will allow the use of TT to a larger patient population, following of course, the surgical oncology guidelines for the removal of thymic lesions.

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-032 Multimodality Treatment for Advanced Thymoma
Ikuo Kamiyama**, Takashi Ohtsuka, Takao Shigenobu, Yasoo Sugiura, Hisao Asamura** *Department of Surgery, Division of Thoracic Surgery, Keio University, School of Medicine, Tokyo/Japan*

Background: Surgery remains the center of treatment of resectable thymoma. Radiation and chemotherapy have been applied widely as adjuvant treatment. However, the optimal treatment strategy for advanced thymoma remains controversial. This study aimed to evaluate the efficacy of multimodal treatment for patients with advanced stage III, IV thymoma. **Methods:** A total 250 consecutive patients with thymoma were treated in our hospital from January 1985 to December 2013. Among these, 70 patients were staged as Ⅲ and Ⅳ. The overall survival (OS) was analyzed according to clinicopathological factors and types of treatment. **Results:** There were 32 patients with stage III (46%), 35 patients with IVa (50%), and 3 patients with IVb (4%). The 10-year OS rates of patients with III+IV, III, IVa were 76%, 89%, and 64%, respectively. Types of treatment were as follows: surgery alone in 23 patients (33%), surgery followed by radiation in 31 (44%), surgery followed by chemotherapy in 2 (3%), surgery followed by chemo-radio therapy in 8 (11%), chemo-radio therapy alone in 6 (9%). There was no significant difference in OS among the treatment groups. Twenty-eight (40%) patients coexisted with myasthenia gravis (MG). There were no differences in OS between those with and without MG. Significant difference in OS was observed between 49 patients who underwent R0/ R1 resection and 21 patients who underwent R2 resection (P = 0.004). The disease-free survival was worse in patients with combined full-dose mediastinal and low-dose, entire thoracic radiation than in those with full-dose mediastinal radiation alone (P = 0.04). **Conclusion:** In this retrospective study, it was shown that the surgical resection should always try to leave no gross tumor behind to ensure better prognosis. Although the future comparative, prospective study seems difficult because of the limited number of new cases, the multimodal approach with maximal treatment intensity looks promising.
Keywords: radiation, advanced thymoma, Multimodality treatment, sugery

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-033 DNA Methylation on Promotor Region of RASSF1 Gene in Thymic Neuroendocrine Tumor Is Higher than B3 Thymoma and Thymic Squamous Cell Carcinoma
Koichiro Kajiura[1], Kazuya Kondo[2], Seiji Masuda[3], Issei Imoto[3], Yuki Morimoto[4], Daisuke Matsumoto[1], Naoya Kawakita[1], Mitsuhiro Tsuboi[1], Hiroaki Toba[1], Yukikiyo Kawakami[1], Hiromitsu Takizawa[1], Shoji Sakiyama[1], Akira Tangoku[1] [1]*Department of Thoraci,Endocrine Surgery and Oncology, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima City/Japan,* [2]*Department of Oncological Medical Services, Tokushima University, Tokushima/Japan,*[3]*Department of Human Genetics, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima*

City/Japan, [4]Department of Pathology and Laboratory Medicine, Tokushima University, Tokushima/Japan

Background: RASSF1 gene, located in 3p21.3, has eight exons and two promotor regions. RASSF1 is very famous tumor suppressor gene in various cancers. It was reported that DNA methylation on promotor region of RASSF1 in lung cancer, bladder cancer, and breast cancer and so on was higher, additionally low expression of RASSF1 was possible to cause to be poor prognosis. It is few reports about epigenome status in thymic epitherial tumors. We planned to explore DNA methylation in thymic epitherial tumors cyclopedically. **Methods:** ①DNA and RNA were extracted from frozen specimen of B3 thymomas (8cases), thymic cancers (8cases), and thymic neuroendocrine tumors(NET)(3cases). ②DNA was treated by bisulfite conversion. ③DNA methylation level in 470000 CpG sites were measured by infinium methylation assay (Human methylation 450K; ILLMINA) exhaustively. ④DNA methylation on promotor regions of RASSF1 was measured by pyrosequencing (PyroMARKTMsystem;QIAGEN) . ⑤Expression level of mRNA was measured by Real time RT-PCR(Thermal Cycler Dice® Real Time System Single; Takara), using TaqMan Gene Expression Assays (Hs00200394_m1 ; Applied Biosystems). Internal reference gene is GAPDH (Hs02758991_g1 ; Applied Biosystems). ⑥Expression level of protein was analysed by immunostaining. Anti-RASSF1a antibody (Anti-RASSF1a antibody [3F3] ab23950, Mouse monoclonal, abcam) was used by CSAⅡmethod (DAKO CSA II, Biotin-Free Catalyzed Amplification System) . **Results:** Significant difference of DNA methylation was recognized by analysis of infinium methylation assay. All 11 CpG sites were configured on 1α promotor region of RASSF1 in this assay. This assay showed DNA methylation level was highest in NET group. DNA methylation level were 70.9±4.9% in NET, 22.2±20.0% in thymic cancer, 14.3±12.3% in B3 thymoma. (NET vs Cancer/B3 *t-test : P<0.00001*). Pyrosequencing showed DNA methylation level were 24.0±13.1% in NET, 3.0±0.5% in thymic cancer, 3.0±0.9% in B3 thymoma. Real time RT-PCR showed that relative expression level (/ normal thymus) were 0.48±0.31 in NET, 1.02±0.82 in carcinoma, 2.13±2.93 in B3 thymoma (NET vs Carcinoma/B3 *t-test : P=0.16*). Immunostaining of RASSF1 was scored by stain intensity and stain extend. Immunostaining scoring of RASSF1 showed expression inhibition rate were 66% in NET, 50% in thymic cancer, 14% in B3 thymoma. **Conclusion:** The infinium methylation assay showed that DNA methylation on promotor region of RASSF1 in NET is higher than B3 thymoma and thymic cancer. The pyrosequencing validated this result. It was tendency to suppress the mRNA or protein expression of RASSF1 in NET, compared to other tumors. It is possible that aberrant DNA methylation on promotor region of RASSF1 may be specific change in NET among thymic epitherial tumors. Now we collected 8 formalin-fixed paraffin-embedded samples of thymic NETs to perform pyrosequencing and immunostaining of RASSF1 gene. **Keywords:** thymic epitherial tumor, RASSF1, DNA methylation

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-034 'Nerve Sparing' Surgery for Invasive Thymomas Stylianos Korasidis[1], Pietro Bertoglio[1], Marco Lucchi[1], Gabriella Fontanini[2], Alfredo Mussi[1]
[1]*Department of Surgical Medical Molecular Pathology and Critical Care, Divison of Thoracic Surgery, University Hospital of Pisa, Pisa/Italy,* [2]*Department of Surgical Medical Molecular Pathology and Critical Care, Divison of Pathological Anatomy, University Hospital of Pisa, Pisa/Italy*

Background: Masaoka-Koga stage and the radicality of the surgical resection are the most important prognostic factors for thymomas. Infiltration of the phrenic nerve interests 10-40 % of invasive thymomas (stage III and IVA). We report the clinical and oncological outcome of patients operated on for invasive thymoma by a intention-to-treat "nerve sparing" technique. **Methods:** In the period 1992-2012 we have applied the "nerve sparing" surgery in all patients with invasive thymoma, and without pre-operative evidence of phrenic nerve paralysis. In that period we have operated on 72 stage III e 33 stage IVA thymomas. Thirteen out of them had a preoperative radiological evidence of phrenic paralysis (5 stage III and 8 IVA) and they were preliminary excluded. In 30 patients phrenic nerve was partially or completely surrounded by the thymoma and they underwent an attempt of "nerve sparing" surgery. In twenty six cases the resection of the thymoma with a phrenic sparing procedure was possible. All patients underwent subsequent adjuvant radiation (45-60 Gy). **Results:** Twelve male and 14 female have been treated, with a mean age of 56 years (range 26-83). At the hystological analysis there were: 1 Type A, 5 Type AB, 10 Type B1, 5 Type B2, 5 Type B3. Myasthenia gravis and red cell aplasia were associated in fifteen and one case, respectively. Despite the attempt of preserving the phrenic nerve, in five patients phrenic palsy was observed in the immediate postoperative period. Three of them showed a complete phrenic nerve recovery, while in the other 2 cases nerve paralysis was irreversible. Mean follow up was 96 months (DS ±73) with an mean overall survival of 89 months (DS ±68). The mean disease free interval was 81 months (DS ±71). Three patients (11,5%) had a pleural recurrence (2 stage IVA, 1 stage III) requiring further surgical resection. Two patients (7,7 %) died (1 of systemic metastases and 1 for other cause). **Conclusion:** Preserving the phrenic nerve in case of invasive thymomas is feasible and if associated to adjuvant radiotherapy may also allow to achieve good long term disease-free results. In reason of the excellent local control of disease it should be proposed mainly to patients with invasive thymoma and myasthenia gravis or with a poor pulmonary function. **Keywords:** Thymoma, phrenic nerve, Pulmonary Function, disease free survival

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.08-035 Thymoma in Persahabatan Hospital Jakarta, Indonesia 2007 - 2012: An Observational Study Elisna Syahruddin *Faculty of Medicine, Universitas Indonesia, Persahabatan Hospital, Department of Pulmonology and Respiratory Medicine, Dki Jakarta/Indonesia*

Background: In general Indonesian population, mediastinal tumors are rare. However In Persahabatan Hospital Jakarta as National Refferal Hospital in Respiratory Diseases, mediastinal tumors are ranked second in thoracic malignancy after lung cancer, and thymomas are common type. **Methods:** An observational study was done in patients diagnosed as thymoma in Persahabatan Hospital between 2007-2012. Clinical stages, histological types, treatment modalities and survival were analyzed. Histological classification were done based on World Health Organization criteria, and stage of the diseases was determined by Mosaoka Staging System. **Results:** We found that the trend of thymoma cases was increased annually since 2007 to 2012 in Persahabatan hospital Jakarta Indonesia. Among 67 cases diagnosed with thymoma, 43 cases has a complete data and follow up, of which 30 cases were male (69.8%) and 13 female (30.2%) with median age 50 years old (range 16 years old to 79 years old). Myastenia gravis were found in 23 of 43 cases (53.5%). During follow up, 1-year survival rate was 72.1% and 3-year survival rate was 58,1 % respectively. There was no significant difference in survival rate of thymoma based on age, gender and the presence of myasthenia gravis, but Masaoka Staging and histological type were corellated with the survival. Using the Log-Rank test comparisons, We found statistically significant differences between type A-B2 (p 0.009), type A-C (p 0.001), type AB-C (p 0.032) and type B1-C (p 0.018). Masaoka staging has significant differences between stage I - IV A (p 0.012), the I - IV B (p 0.007), II-IV A (p 0.002) and II-IV B (p 0.002). Multivariate analysis showed that the most influential factor on the survival rate in these series was staging,-based on Masaoka Staging system. **Conclusion:** The Masaoka staging system is the most important determinant of survival in surgically cases of thymoma. **Keywords:** survival, Thymoma, Persahabatan Hospital, Indonesia

SESSION: POSTER SESSION/ NURSING AND ALLIED PROFESSIONALS TUESDAY, SEPTEMBER 8, 2015

POSTER SESSION/ NURSING AND ALLIED PROFESSIONALS
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.09-001 Triage Nurse Navigator Implementation: Improvements in NSCLC Resource Utilization Kelly Zibrik, Janessa Laskin, Cheryl Ho *Medical Oncology, BC Cancer Agency, Vancouver/BC/Canada*

Background: Involvement of nurse navigators (NN) in oncology care is becoming increasingly common to facilitate more timely access to diagnostic services and treatment for patients. A lung cancer NN was implemented at the British Columbia Cancer Agency (BCCA) and this role involved developing pathways for triage and staging investigations, initiating molecular tests and coordinating new patient referrals. In the BC publicly funded health care model, reflex molecular testing is not available. The purpose was to evaluate referral practice, timelines and molecular testing for advanced NSCLC patients in cohorts with and without a triage nurse navigator. **Methods:** The study included all advanced NSCLC patients referred to the BCCA – Vancouver Centre in two separate 1 year cohorts for comparison; 2011 and 2014. Timelines between referral and systemic therapy/radiotherapy (XRT) treatments, availability of molecular testing and data on referral patterns were collected. **Results:** A total of 408 patients were included: 212 in 2011, 196 in 2014. Endpoints for medical oncology (MO) comparing 2011 to 2014: overall referral rates remained the same and the proportion of patients receiving systemic treatment increased, 57% vs 69% (p=0.05). Referral to MO consult 18 d vs 15.5 d (p=0.11), referral to systemic therapy initiation was reduced 48 d vs 38 d (p=0.016). Molecular testing: time from referral to EGFR result was reduced 34 d vs 20 d (p<0.001), EGFR results available at MO consult increased 6% vs 37% (p<0.001), rate of molecular testing increased 62% vs 91% (p<0.001), EGFR mutation positive (19% vs 26% p=0.26). For radiation oncology (RO) endpoints: RO consults 87% vs 80% (p=0.05), the same proportion of patients received XRT (91% vs 87%). Time from referral to RO consult 10 d vs 8 d (p=0.005), referral to XRT 18 d vs 11.5 d (p<0.001). **Conclusion:** Implementation of a NN at triage reduced the time period between referral and treatment for MO and RO. The proportion of patients provided with molecular testing increased and the rate of EGFR positive results remained the same, an indication that more patients received appropriate first line targeted therapy. Nurse navigator participation during triage activities suggests that physician, diagnostic and clinical resources are more appropriately allocated. **Keywords:** nurse navigator, NSCLC, triage, wait times

POSTER SESSION/ NURSING AND ALLIED PROFESSIONALS
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P2.09-002 Development of 'Living Well' - A Health and Wellbeing Programme for Thoracic Cancer Patients Paula Tindale-Paul, Tom Fynmore, Pippa Labuc, Olivera Kegey, Emma North *Oncology, Guy'S & St Thomas' NHS Foundation Trust, London/United Kingdom*

Background: In 2013 the Holistic needs assessment (HNA) for newly diagnosed cancer patient, which highlights patient concerns and symptoms, was introduced in the UK. The use of the tool, in a leading cancer centre, identified a need for a multi-disciplinary education and support group to better address the management of patient

symptoms and supportive care needs. The most common physical symptoms reported were; Fatigue/tiredness (74%), sleep (64%), walking/stairs (58%), breathing (56%), appetite/weight changes (46%), and pain (40%). The most common psychosocial concerns were; Fear/anxieties (48%), and sadness (48%). With increasing national focus on cancer survivorship and rehabilitation initiatives for cancer patients there is growing evidence that support programmes can increase quality of life and psychological functioning. A multi-disciplinary team (MDT) was established to develop a health and wellbeing programme for thoracic cancer patients treated at Guy's and St Thomas' NHS Foundation Trust (GSTT). **Methods:** Working as a MDT, consisting of Cancer Nurse Specialists, Physiotherapists, Occupational Therapists and Dietetics, a programme of physical, psychosocial and educational components was devised to address the key symptoms, including the following; 1. Managing your energy 2. Keeping active 3. Eating Well 4. Managing breathlessness 5. Keeping on top of things 6. Time to relax - Qigong Inclusion criteria; Medically stable thoracic cancer patients under GSTT, at any point along their pathway plus carer/family member Exclusion criteria; Anaemia, Hb <80g/L, untreated brain mets/cognitive issues restricting ability to participate in group sessions. Each session was paced to optimise patient care allowing interventions to be tailored to individual's situations, stage of disease, and their wishes. Patient experience questionnaires, which were standardised across all sessions, are handed out and following the end of the programme the CSQ-8 is completed by the patients, allowing for continuous quality control of our service from the patient's perspective. **Results:** Data to February 2015 showed the following; -94% of patients reported an improvement in their ability to self-manage their symptoms -100% of patients reported increased confidence in managing their symptoms -100% of patients reported that anxiety was reduced -Mean CSQ-8 evaluation score = 9.6/10 Patient attendance; -6 week programme format: 9 patients started the programme, 3 completed. -3 week programme format: 21 patients started the programme, 12 completed. -1 week programme format (only 1 programme completed at time of abstract submission): 9 attended and completed entire day **Conclusion:** A programme of this nature represents a valuable intervention output following HNA across the cancer pathway. It supports local and national cancer strategies around survivourship and rehabilitation. With progression free survival in thoracic cancer improving the self-management of physical and psychosocial symptoms, longer term, becomes increasingly relevant. The numbers have been limited, indicative of the symptom and treatment burden for this patient group, however overall results are impressive. This indicates the requirement of a flexible approach. In adapting the format over time patient reported experience remained very positive, moreover attendance improved. Thus making it more accessible for our patient group, as well as enabling, equiping and empowering them to self-manage symptoms and live well with cancer. This model can be adapted and translated into other health care settings and tumor types, both nationally and internationally.
Keywords: multidisciplinary, survivorship, Wellbeing, Self-management

POSTER SESSION/ NURSING AND ALLIED PROFESSIONALS
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P2.09-003 Identifying Research Questions in Disclosure of Risk of Recurrence following Lung Cancer Surgery Using a Critical Synthesis of the Literature
Matthew Johnson[1], Karen Collins[2], Stephen Brummell[2], Angela M. Tod[3] [1]*Cancer Nursing, Royal Brompton and Harefield NHS Foundation Trust, London/United Kingdom,* [2]*Centre for Health and Social Care Research, Sheffield Hallam University, Sheffield/United Kingdom,* [3]*University of Manchester, Manchester/United Kingdom*

Background: Although surgery for lung cancer is often a successful treatment, very little is known about how patients cope and live with the possibility of recurrence of cancer in the future. Two published literature reviews on prognosis disclosure in cancer care have identified no papers focused specifically on risk of recurrence in post-surgical lung cancer patients. Aims were to develop a synthesis of the current literature around prognostic disclosure in cancer care in order to: · Identify a thematic framework that can be used to provide a model for the factors present in prognostic disclosure in cancer care. · Identify research questions that will inform future study into disclosure of recurrence risk in lung cancer patients following potentially curative surgery. **Methods:** A review of published studies on prognostic disclosure in cancer care up until the end of 2003 was used as a starting point. An updated review was undertaken and a systematic approach was taken to searching the literature from 2004 – June 2014. Data were extracted from the identified papers using a comprehensive data extraction form. Codes were assigned to key elements of data within the results and conclusion sections of the papers. Critical interpretive synthesis was used to explore themes by constructing an integrative grid to examine findings between studies and to identify similarities and contradictions. Themes from the original review were identified and compared to the updated findings. A further framework grid was constructed to investigate between-theme relationships and to help identify "synthetic constructs" and a thematic framework. **Results:** Twenty papers were identified in the updated review and were diverse in their objectives and patient groups. Themes were identified in these studies and in the original review covering the nature of prognostic information, patient need for prognostic information, patient need to maintain hope, balancing hope and realism, patient factors, disease factors and clinician factors. A thematic framework was developed. Future research questions were framed around disclosure of risk of recurrence following lung cancer surgery. **Conclusion:** There are no studies looking at prognostic information-giving in post-surgical lung cancer patients. Patients generally want prognostic information, but also want information that supports hope. Patients appear to struggle to fully understand complex prognostic information and value help making sense of information. Working with patients to understand and manage the uncertainty of their situation may be particularly valuable. Future research questions include: · How do patients and their clinical teams manage information disclosure about possible cancer recurrence following lung cancer surgery? · What is the emotional impact on patients of the uncertainty of potential recurrence following lung cancer surgery? · What information do patients want regarding recurrence risk? · What strategies do patients and professionals currently use to help manage the uncertainty of potential recurrence after lung cancer surgery? · Are there strategies or interventions aimed at managing uncertainty in this group that could have wider application for patients?
Keywords: Recurrence-risk, Communication, Information

POSTER SESSION/ NURSING AND ALLIED PROFESSIONALS
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P2.09-004 Prospective Audit of Lung Cancer Nurse Specialists Telephone Link Line Call to Surgical Patients 30 Days Post Hospital Discharge
Maureen King, Lavinia Magee *Thoracic Oncology, Papworth Hospital, Cambridge/United Kingdom*

Background: The Lung Cancer Nurse Specialists (LCNS) at Papworth Hospital provide support and information throughout the surgical patient's pathway. The Thoracic Enhanced Recovery Program has shortened post-operative length-of-stay from 9 days (2010) to 5 days (2013). The aim of this audit was to evaluate the role of a follow up telephone link line call 30 days post-surgery. There is evidence in the literature that telephone contact is beneficial for patients. Patients receive a telephone call from a LCNS within the first week of their discharge and this is considered to be a good means of providing health education and advice, managing symptoms, recognizing complications early and giving reassurance to patients after discharge. However, in order to gain a more detailed account of a patient's recovery / rehabilitation (particularly visits to A&E, readmissions and complications) it was proposed that a second phone call be made by the LCNS at 30 days post discharge. **Methods:** A data collection spreadsheet was designed. From 01/01/2013 to 31/08/2013 patients following a lung cancer resection received a telephone call from a LCNS, 30 days post-surgical discharge. A holistic assessment of the patient's needs, and their progress was explored and actioned. Information regarding advice sought, recovery perception and readmission rates were gained. **Results:** 101 patients underwent surgery, 93 received a 30 day call (61M/32F). 91 (98%) were aware of whom to contact following discharge and were able to name their LCNS. 73 felt ready for discharge, 11 unsure, 9 not ready (8 unanswered). 37 recovered better than expected, 35 as expected, 15 slower and 6 worse than expected. Post-operative pain was more persistent / severe in thoracotomy patients 48/57 (84%) compared to a video assisted thoracoscopy approach 24/36 (66%). 26 patients required advice for constipation, 7 diarrhoea. 60 breathlessness on exertion, 1 discharged home on oxygen. 10 felt low in mood since discharge. 7 were readmitted within 30days. **Conclusion:** The 30 day post discharge link line call has revealed some areas of self-care needs which appear not to have been fully understood or addressed. Patients were perhaps not able to retain the information. The introduction of a structured pre-operative education program may assist with addressing these issues. Also, active telephone follow ups, initiated by the LCNS, appeared relevant to the problems patients face after discharge. With telephone follow-up information can be reinforced, thereby increasing compliance, and ensuring the physical and emotional comfort of the patient. Limitations to this audit include the use of no nationally recognised quality of life tools / scales. A review of the timing and number of calls to a patient with focus given to pain, constipation and psychological support will help deliver a more comprehensive service.
Keywords: post operative, surgical, Lung cancer nurse specialists, telephone

POSTER SESSION/ NURSING AND ALLIED PROFESSIONALS
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P2.09-005 Living With Lung Cancer - Preferred Sources of Patient Support and Information: The Papworth Experience
Georgina Howell, Lavinia Magee *Thoracic Oncology, Papworth Hospital, Cambridge/United Kingdom*

Background: Support groups can help to improve patients' coping and mental adjustment to a cancer diagnosis and treatment. They have also been shown to have a positive impact on psychological wellbeing and reduce anxiety and depression. However, at Papworth Hospital (a regional cardio-thoracic centre), it became increasingly difficult to recruit patients to the lung cancer support group. Consequently, before starting any new initiative, the decision was made to disband the group in December 2013 and to identify alternative and beneficial ways of supporting patients. **Methods:** With patient user involvement, a questionnaire was designed *Living with lung cancer - how can we help you?* From 12/05/2014 to 30/05/2014, 100 questionnaires were distributed to all patients with a confirmed diagnosis of lung cancer who attended a thoracic oncology outpatient clinic. Responses were anonymous and returned to a secure box for review in the audit department. **Results:**81% of the questionnaires were returned. Patients were referred to Papworth from 8 different hospitals in the region. 79% were over 60 years old at diagnosis. 84% recorded a diagnosis within the last 4 years, the remaining recording diagnosis back to 2001. Since diagnosis, the most useful sources of information are listed below as recorded by the patients (please note more than one answer could be selected):

Family/ friends	38
Hospital doctor	62
LCNS / key worker	60
GP	32
District nurses	9
Macmillan nurses	9
Hospice	3
Cancer Centre	3

Of those diagnosed within the last 12 months the Lung Cancer Nurse Specialist (LCNS) was the most useful source of information. The questionnaire proposed a number of topics that might be included in some form of additional support of which 34% were interested. The most common request was for information on symptom control (breathlessness and fatigue), relaxation techniques and treatment options. The questionnaire suggested a number of different formats for providing additional support. Of the 27 respondents, 15 (55%) preferred telephone support from a LCNS. **Conclusion:** The LCNS plays a pivotal role in providing relevant information and support. The challenge is to find new and innovative ways that will help to optimize patients' psychosocial as well as physical wellbeing. Consideration will be given to increasing telephone support to signpost patients to appropriate information on treatment options and symptom control. We plan to audit the effectiveness of LCNS telephone consultations to ascertain the impact on patient wellbeing. Different types of relaxaion techniques such as yoga classes will be explored. Co-ordination of information management within a large geographical area, incorporating many hospitals and local community facilities, is essential. **Keywords:** Patient information, support, wellbeing, telephone

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P2.09-006 A Breathlessness Booklet Carol A. Davies[1], Nuala Galligan[2], Larissa Cowpe[3] [1]*Macmillan Lung Cancer Clinical Nurse Specialist, Aneurin Bevan Univesity Health Board, Monmouthshire/United Kingdom,* [2]*Palliative Care, Aneurin Bevan University Health Board, Newport/United Kingdom,* [3]*Palliative Care Team, Aneurin Bevan University Health Board, Monmouthshire/United Kingdom*

Background: Breathlessness is common amongst lung cancer patients. It leads to inactivity, helplessness and loss of self esteem. As the experience of breathlessness has physical and non-physical aspects, management of the symptom of breathlessness is challenging. It is recognised that non pharmacological intervention for breathlessness is beneficial. In 2012 lung cancer patients expressed the need for an easy to use breathlessness aid. A breathlessness booklet was subsequently developed. Patients were asked to assess the usefulness, understanding and easiness of each entry. The booklet evaluated well with patients and users. The appointment of a Macmillan specialist occupational therapist to the palliative care team was an ideal opportunity to re-examine the breathlessness aid and introduce a multi disciplinary approach. **Methods:** The booklet was reviewed with the layout redesigned and an additional section added on activities of daily living. Information includes anatomy and physiology, breathing control, anxiety management including relaxation techniques, activity pacing and positional aids. **Results:** The revised A5 booklet has since been used by patients and a number of the multi-disciplinary team have had sight of it. Information remains, as intended simplistic but is comprehensive. The booklet is being distributed by the Macmillan lung cancer CNS and palliative care team which includes consultant, CNS's Macmillan OT and healthcare support workers. Patient feedback remains very positive. It suggests patients feel more equipped to cope with their breathlessness. They report it has helped them cope with pacing themselves and controlling breathing when using the stairs. Others enjoy the choice of breathing techniques and tips for managing activities of daily living in and out of the home. **Conclusion:** Interest in this breathlessness aid has been expressed from a variety of specialities and hospitals within Aneurin Bevan Health Board. Requests have been made for the breathlessness leaflet to be available on intranet so that all personnel within ABHB can access information. An additional booklet has been produced on Fatigue. Both booklets have subsequently been presented at The All Wales Lung Cancer Forum 2014 Annual Conference. Delegate feedback was very positive. **Keywords:** breathlessness, Coping techniques, Multi-disciplinary working

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POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-001 The Relationship between Carnitine Pharmacokinetics and Fatigue in Thoracic Cancer Patients Treated with Cisplatin-Containing Chemotherapy Tatsuhiko Kashii[1], Toshiro Miwa[1], Kensuke Suzuki[1], Seisuke Okazawa[1], Kenta Kambara[1], Minehiko Inomata[1], Tomoaki Ikezaki[1], Kouichi Tanabe[2], Hatsuna Yasuda[1], Shinya Kajiura[1] [1]*Toyama University Hospital, Toyama/Japan,* [2]*Meijo University, Nagoya/Japan*

Background: A large majority of patients who receive chemotherapy suffer from fatigue, which lowers their QOL and activities and also has a negative influence on therapeutic efficacy. Although supportive care for those undergoing chemotherapy has steadily progressed, the pathogenesis and treatment of fatigue during chemotherapy is still unknown. Carnitine is an amino acid with a molecular weight of 161, and it plays a critical role in energy production. A decreased level of plasma carnitine has been reported in the case of cancer patients who developed cachexia. It has been reported that carnitine is excreted in the urine after the administration of platinum-type anticancer drugs. We examined the relationship between carnitine pharmacokinetics in patients who received chemotherapy including cisplatin (CDDP) and fatigue. **Methods:** Ten patients (7 male/3 female, median age 66.5 yrs (46-73), 3 SCLC/4 NSCLC/3 malignant mesothelioma, 6 PS0/4 PS1) who received standard chemotherapy including CDDP were examined. We performed 24-hour urine collection and took blood samples on day 1 (before the administration of chemotherapy), day 2, 3, 4, and 8 to measure free carnitine concentration, total carnitine concentration, and acylcarnitine concentration in the plasma and urine. We simultaneously evaluated fatigue levels using the CTCAE, STAT Japanese version, and "Functional Assessment of Chronic Illness Therapy-Fatigue" (FACIT-F). **Results:** The total carnitine concentration in the plasma samples was the highest after 48 hours (day3) of administration and showed significant increase compared to before the administration of CDDP (day1)(65.3±17.6 μmol/L vs. 95.2±28.9 μmol/L, p=0.001). Total urine carnitine concentration was the highest after 24 hours (day2) of administration and showed significant increase compared to day1 (122.3±108.7 μmol/L vs. 632.9±376.6 μmol/L, p=0.003). Fatigue levels were the most severe on day 4 and did not improve thereafter. **Conclusion:** The study suggests an increase of the amount of carnitine excretion within urine is a possible predictive factor for the appearance of fatigue related to chemotherapy. Future studies will be planned to investigate the protective effects of carnitine administration for fatigue in patients treated with CDDP-containing chemotherapy. **Keywords:** Cisplatin, chemotherapy, fatigue, Carnitine

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
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P2.11-002 Identifying Relationship between Symptom Burden and Overall Survival in Patients with Advanced Nonsmall Cell Lung Cancer: A Prospective Study Fatma Ozbaki, Ülkü Yılmaz, Yurdanur Erdoğan, Derya Özaydın Kızılgöz *Atatürk Chest Diseases and Chest Surgery Education and Training Hospital, Ankara/Turkey*

Background: Prognostic factors in nonsmall cell lung carsinoma (NSCLC) has been described in many studies in medical literature. It is unclear the relationship between overall survival and symptom burden. The aim of our study is defining the prognostic factors in advanced NSCLC and to describe relationship between symptoms and overall survival. **Methods:** In this study, the patients newly diagnosed stage 3b and 4 with NSCLC and Eastern Cooperative Oncology Group Performans Status (ECOG PS) of 0 to 2, from August 2011 to May 2013 in Ataturk Chest Diseases and Chest Surgery Education and Training Hospital were included. We obtained the demographic, diseases related and laboratory data for all patients. Symptoms were analyzed with The Edmonton Symptom Assessment Scale (ESAS) before and after chemotherapy. The study was designed prospectively and the patients were followed up to 826 days. Cox model proportional risk analysis was performed at the end of the the followed-up period to assess the beginning symptoms, symptoms differences after chemotheraphy and the relationship between the general characteristics and the survival. **Results:** We conducted a multivariate analysis and it is found that as one of the general characteristics; the stage of the diseases (p= 0,004 HR: 2,373 95% CI: 1,317-4,274) and the histopathologic subtypes (p=0,006 HR: 2,311 95% CI:1,271-4,202) were prognostically significant. The patients with fatigue as the beginning symptoms (p=0,001 HR:2,389 %95 % CI: 1,460-3,908) and the sadness score 4 and over (p= 0,032 HR:2,311 95% CI: 1,271-4,202) had lower survival, it is also found that patients with cough intensity increasing after chemotheraphy (p=0,006 HR: 1,933 95% CI: 1,128-3,314) had lower survival and high mortality risk as well in multivariate analysis. **Conclusion:** During the treatment process, together with performance scores of patients with symptom score monitoring will be meaningful. Further prospective studies including a larger group of patients are required in order to describe better the relationship between the symptoms and the prognosis. **Keywords:** advanced NSCLC, ESAS, Prognostic factors, survival

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P2.11-003 Changes in Quality of Life Through the Early Intervention by a Palliative Care Team for Patients with Advanced Lung Cancer Taro Yokoyama[1], Hiroshi Kunikane[1], Hiroaki Okamoto[2], Tsuneo Shimokawa[2], Yukiko Nakamura[2], Youko Agemi[2], Akira Sato[2], Yuki Misumi[2], Kazuhito Miyazaki[2], Naoto Aiko[2], Mari Ishii[3], Rie Oishi[4] [1]*Department of Palliative Medicine, Yokohama Municipal Citizen'S Hospital, Yokohama-Shi/Japan,* [2]*Department of Respiratory Medicine, Yokohama Municipal Citizen'S Hospital, Yokohama/Japan,* [3]*Department of Medical Oncology, Yokohama Municipal Citizen'S Hospital, Yokohama/Japan,* [4]*Research Support Center, Yokohama Municipal Citizen'S Hospital, Yokohama/Japan*

Background: The change in quality of life (QOL) through the early intervention by a palliative care team was analyzed in patients with advanced lung cancer. The contrast between patients' own evaluation on their QOL and their QOL estimated by their attending physicians was examined as well. **Methods:** The eligibility criteria were newly-diagnosed Japanese patients with stage IV lung cancer, whose ages were over 20- years old, whose Eastern Cooperative Oncology Group Performance Status were from 0 to 3, and those who had written informed consent. For the patients and attending physicians, QOL questionnaires, which were in line European Organization for Research and treatment of Cancer Quality of Life Questionnaire-Core15 （EORTC QLQ c-15）, were conducted at the time of the enrollment and twelve weeks later. The primary endpoint was a change in global QOL score, which ranged from 0 (worst) to 100 (best), after the twelve-week intervention. **Results:** 58 patients out of 96 who were newly diagnosed as stage IV lung cancer were enrolled in this study. 43 patients had the QOL evaluation after twelve weeks. One patient withdrew consent, one patient moved to another hospital and other thirteen patients died during the intervention period. The primary endpoint improved by more than 25% that was originally anticipated (50 points at the enrollment, 64.7 points after the intervention.). All of the following factors including emotional state, nausea, vomiting, pain, constipation improved by more than 25% similarly to the primary endpoints, although other QOL factors showed a slight improvement or no change. While the difference between the QOL score by the patients and the physicians was apparent at the beginning the intervention, it became smaller by every measurement after twelve weeks. In Japan, Palliative care units (PCUs) have a role of hospices as well, and there are not enough number of them, to meet the entire needs for the end-of-life care. Some patients end up dying while on the waiting lists of PCU. Less percentage of patients who had early palliative care (EPC) died while waiting PCU admission, as

compared with other cancer patients who applied for PCU during the same period as the present study. (12.5 % vs 30.4 %) In addition, duration of best supportive care in patients were extended approximately one month, as compared with past patients with stage IV lung cancer in undergoing EPC.(108.7day vs 78day) **Conclusion:** QOL improved in studied Japanese patients after the early interventions by the palliative care team. This result may indicate that discrepancy of QOL evaluation between the patients and physicians was lessened due to the early intervention by the palliative care team, which is considered to have fostered the improvement of the overall QOL. It was suggested that such intervention might support the patients in decision making for end-of-life-care. **Keywords:** palliative care team, early palliative care, advance care planning, lung cancer

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
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P2.11-004 Assessment of Pain Management in Cancer Outpatients Who Receive Chemotherapy Akiko Fujii[1], Yu Yamada[2], Koichi Takayama[1], Takako Nakano[1], Tatsuya Morita[3], Junji Kishimoto[4], Yoichi Nakanishi[1] [1]*Research Institute for Diseases of the Chest, Graduate School of Medical Sciences, Kyushu University, Fukuoka/Japan,* [2]*Saitama Cancer Center, Saitama/Japan,* [3]*Seirei Mikatahara Hospital, Hamamatsu/Japan,* [4]*Research and Development of Next Generation Medicine Faculty of Medical Sciences, Kyushu University, Fukuoka/Japan*

Background: Pain is one of the most frequent and burdensome symptoms in cancer patients. In addition, inadequate pain management may limit anti-cancer active treatment in these patients and impair their quality of life. Chemotherapy in the outpatient settings has become common in Japan in the last decade. However, the adequacy of pain management in patients who receive outpatient chemotherapy is not yet well-known. The primary objective of this study was to assess pain prevalence and intensity in these patients. The secondary objective was to assess the pain management status using the pain management index (PMI). **Methods:** Cancer patients with solid tumors or hematologic malignancies who received chemotherapy in the outpatient setting were enrolled. The PMI scores were calculated using the patient-rated pain score and the analgesic score. The PMI was evaluated twice in each patient on the first day and 3 to 5 weeks later when patients received chemotherapy at Outpatient Chemotherapy Administration Unit, Kyushu University Hospital, Japan. Patients were required to complete questionnaires including Japanese Brief Pain Inventory and the Distress Thermometer and Impact Thermometer. **Results:** Of 740 patients enrolled, 524 patients (71%) who completed the questionnaires at both baseline and follow-up were applied to the statistical analysis. 54% patients experienced any pain and 14% patients had moderate or severe pain. 286 patients (55%) received adequate pain management at both baseline and follow-up, while 238 patients (45%) received inadequate pain management at baseline and/or follow-up. Multivariable analysis revealed that major depression had the most impact on adequacy of pain management. **Conclusion:** Patients who receive outpatient chemotherapy have a high prevalence of pain. The PMI is available to evaluate the pain management status of cancer patients in outpatient setting. Pain management for cancer patients needs to be assessed regularly even though their initial pain management is adequate. **Keywords:** pain management index, Cancer, Pain, outpatient chemotherapy

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-005 The Use of Duloxetine in Chemotherapy-Induced Peripheral Neuropathy Martin E. Richardet, Aldo A. Riso, Matias Molina, Matias Cortes, Patricia A. Hernandez, Luciana P. Acosta, Maria E. Pacher, Eduardo A. Richardet, Pablo Companys *Capital, Ionc (Instituto Oncologico de Cordoba), Cordoba/Argentina*

Background: Approximately 50% to 70% of patients with cancer who receive neurotoxic chemotherapy with taxanes and platinums will develop painful chemotherapy-induced peripheral neuropathy. Duloxetine is a balanced serotonin and noradrenaline reuptake inhibitor licensed for the treatment of major depressive disorders and the management of neuropathic pain associated with peripheral neuropathy. Our objective is to assess the efficacy, compliance and toxicity of duloxetine for treating painful neuropathy. **Methods:** We analyzed data from 79 patients of the Instituto Oncológico de Córdoba (IONC) with breast, lung, colorectal, cervix and endometrium cancer. Eligibility required that patients have grade 2 (G2) or higher sensory neuropathy according to the NCI Common Terminology Criteria for Adverse Events, after paclitaxel, other taxane, or platinum treatment. The initial treatment consisted of taking 1 capsule daily of 30 mg of duloxetine for the first week and 2 capsules of 30 mg of duloxetine daily for 4 additional weeks. **Results:** We enrolled 79 patients with a median age of 63.25 years. Of these, 67% were female and 33% male; 40.5% received adjuvant treatment, 55.6% advanced treatment and 3.7% neoadjuvant treatment. Chemotherapies used were Oxaliplatin (35.4%), paclitaxel (36.5%) carboplatin + paclitaxel (25.3%), and cisplatin (2.5%). At the time of starting treatment with duloxetine, 78.5% of patients had neuropathy G3 and 21.5% G4. 91.5% of them have at least one decrease of neuropathy grade after 30 days of treatment (p = 0.001). 12.6% of patients discontinued treatment due to somnolence (10.8%), vomiting or abdominal pain. 6.3% refused to receive treatment for being a psychotropic drug. **Conclusion:** In our study, treatment with duloxetine showed a response rate, statistically significant, of 91.5% (p: 0,001). Adherence to treatment was 81.1%, with somnolence and vomiting as the primary adverse events. **Keywords:** PERIPHERAL NEUROPATHY LUNG DULOXETINE

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P2.11-006 Impact of Different Comorbidities in Clinical and Molecular Characteristics in a Cohort of Non-Small Cell Lung Cancer (NSCLC) Patients (P) Enric Carcereny, Teresa Morán, Laia Vila, Ana Estival, Maria De Los Llanos Gil, Iris Teruel, Max Hardy-Weber *Medical Oncology, Catalan Institute of Oncology-Hospital Germans Trias I Pujol, Badalona/Spain*

Background: The most common comorbid conditions related to Lung Cancer are age- and tobacco-related illnesses, such us cardiovascular disease, chronic obstructive pulmonary disease(COPD) and other malignancies. Different studies have demonstrated and impact in clinical outcome. We retrospectively review the clinical and molecular characteristics, and the outcome related to comorbidities of an homogeneus cohort of advanced NSCLC. **Methods:** The study included data from all consecutive p who were diagnosed as having advanced NSCLC at our hospital between January 2008 and December 2013. Overall survival (OS) and progression free survival (PFS) were evaluated with Kaplan-Meier curves and groups are compared using the Log-rank test. Variables analyzed included patient characteristics (age, gender, smoking history, Performance Status by ECOG), tumor characteristics (histology, stage, molecular profile, site of metastasis), treatment characteristics (chemotherapy regimen, total cicles per line, total chemotherapy lines, objective response(ORR) according to the RECIST criteria). Comorbidities analyzed were: COPD, Cardiovascular diseases, Other Cancers and Others. **Results:**A total of 580 p were included, 163 p no had comorbidities and 417(71.8%) had at least one. *Table 1* summarized patient's characteristics. Any comorbidity were more frequent in female sex (79.6% vs 64.4%; p0.0002), older patients(mean age 64.3 vs 56.7 yo; p<0.0001), less never-smokers(16.1% vs 25.2; p0.033), less molecular alterations (14.2% vs 22.1%; p0.025) and more squamous histology (25.7% vs 12.9; p0.0043). No differences is ORR, PFS and OS were seen globally. For each comorbidity, COPD was associated to worse ORR (65.9% vs 75.6%; p0.023) and OS (8.1 months vs 14 months; p0.018), and cardiovascular diseases were associated to worse OS (9.1 monthsvs 15.5 months; p<0.0015). In univariate and multivariate analysis COPD, Cardiovascular comorbidity, male sex, age more than 65 yo, and non molecular alteration were related to worse OS. **Table 1. Baseline characteristics (N of patients treated with at least one line: 486).**

	No comorbidities (N=163)	Any comorbididy (N=417)	p-value
Median age Gender (Female) Smoking history (%) -never -former -current -not reported EGFR mut/ ALK translocation Histology -NOS -Adenocarcinoma -Squamous -Adenosquamous -LCC -LCC-NE Site of metastasis -Lung -Brain -Bone -Liver -Adrenal gland	56.7(11.0) 105(64.4) 41(25.2) 63(38.7) 58(35.6) 1(0.6) 36(22.1) 22(13.5) 109(66.9) 21(12.9) 1(0.6) 9(5.5) 1(0.6) 59(36.2) 35 (21.5) 59(36.2) 23(14.1) 25(15.3)	64.3(9.8) 332(79.6) 67(16.1) 209(50.1) 138(33.1) 3(0.7) 59(14.2) 60(14.4) 228(54.7) 107 (25.7) 7(1.7) 8(1.9) 6(1.4) 159(38.1) 96(23.0) 131(31.4) 50(12.0) 53(12.7)	<0.0001 <0.0001 0.033 0.025 0.0043 0.70 0.74 0.28 0.49 0.99

Conclusion: Comorbidities are frequent in patients with advanced NSCLC p, and are age and tobacco related. Patients with COPD have a worse ORR and OS, and patients with Cardiovascular comorbidities have worse OS. In our knowledge, is the first study that relates comorbidities in NSCLC to molecular alterations. **Keywords:** NSCLC, comorbidities

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-007 Geriatric Oncology and Lung Cancer: Comprehensive Geriatric Assessment (CGA) Aspects Related to Outcomes and Important End-Points Aldo L.A. Dettino[1], Marcello F. Fanelli[1], Ludmilla T.D. Chinen[2], Graziela Z. Dal Molin[3], Geraldine E.D. Lima[3], Solange M. Sanches[1], Barbara Figueroa[1], Ana M.M. Leite[4], Marcilei E.C. Buim[2], Helano C. Freitas[1] [1]*Oncologia Clínica, A C Camargo Cancer Center, Sao Paulo/Brazil,* [2]*Oncologia Clínica & Centro Internacional de Ensino E Pesquisa, A C Camargo Cancer Center, Sao Paulo/Brazil,* [3]*Oncologia Clínica - Residency To 2014, A C Camargo Cancer Center, Sao Paulo/Brazil,* [4]*Oncologia Clínica - Geriatric Oncology Unit, A C Camargo Cancer Center, Sao Paulo/Brazil*

Background: Interdisciplinary oncology approach for **geriatric patients** (pts) is essential to improve health care, in the global era of populational aging. A possible way to implement that is to use CGA and interventions directed by its findings. **Lung cancer** (**LC)** treatment is a good scenario to present the importance of CGA, since its pts are usually old and with multiple comorbidities. **Methods:** LC pts with 70+ years

old were found in our cohort of more than 600 pts, evaluated from Jan/12-Dez/12, the period of implementation of CGA in the Geriatric Oncology Unit of A. C. Camargo Cancer Center, a tertiary cancer care institution in Sao Paulo-SP, Brazil. Important geriatric data were extracted to evaluate those pts, to exemplify the importance of a coordinated interdisciplinary treatment plan with better chances of improving favorable clinical endpoints. CGA assessments included scales of: activities of daily living/ADL (basic: Katz; instrumental: Lawton), mini-nutritional assessment, depression (geriatric depression scale/GDS), comorbidities and polypharmacy. Fit pts received mainly full treatment; frail/borderline pts, mainly modified tx and/or specific supportive care. **Results:** Eighty pts with LC were part of a subgroup of the major cohort. Most relevant data at first visit are show in the table below. All pts were assessed with CGA by at least one nurse, before medical oncology evaluation - sometimes, by a psychologist as well. Table 1. Relevant CGA data and elderly with lung cancer (n=80).

Variable	Categories or values		
Age	Median (range)	75 (70-88)	
		n (%)*	
Sex	Male/Female	44/36	**55**/45
ECOG/PS	0-1/2-3	53/23	**63**/29
Histology	Adeno/SCC/Small cel	42/17/8	**53**/21/10
BADL	KATZ = A	60	**75**
	Altered KATZ	20	25
IADL	Lawton = 27	27	34
	Altered Lawton	53	**60**
GDS	Normal (0-4)	43	**54**
	Altered (≥4)	17	21
	Not available (na)	20	25
Nutrition	Undernourished (< 8)	15	19
	Under risk (8-11)	24	**30**
	Normal (12-14)	24	**30**
	na	17	21

* Some subjects may have variable not available. In addition, selected comorbidity count ranged 0-5 (median 2); polipharmacy 0-6 (median 5). Seventeen pts were in follow-up only (21%); 48 (60%) pts were under chemotherapy (isolated or combined with other therapies). Even though CGA domains were altered in around 60% of them, the planned treatment could be offered to 57 (71%) pts. Longer survival probability, in the series, was predicted by performance status (ECOG), BADL (Katz) and mini-nutritional assessment. **Conclusion:** CGA is gaining increasing importance in geriatric oncology. In the present LC subgroup cohort, even though in a small case series, it shows that many pts are vulnerable or even frail; however, interdisciplinary evaluation and multimodal treatment could be offered, without major complications. Limitations include missing data in any domain of CGA, for example. All efforts to better study and define CGA and help to implement interdisciplinary interventions may be utile to improve elderly quality of life and survival in LC care. **Keywords:** Geriatric Oncology, lung cancer, Geriatric assessment

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-008 Association between Heart/Lung Dosimetric Parameters and Subsequent Changes in Quality of Life in Patients Receiving Thoracic Radiotherapy Jing Chen[1], Shiva K. Das[2], Becky Green[2], Stravers Lori[2], Timothy Zagar[2], Toni M. Roth[2], Patricia Rivera[3], Arif Sheikh[4], William Mccartney[4], Lawrence B. Marks[2]
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Background: Thoracic radiotherapy can negatively affect cardiopulmonary function. We herein report on a prospective assessment of the association between heart/lung dosimetric parameters and subsequent changes in the quality of life (QOL) in patients receiving thoracic radiotherapy. **Methods:** Patients about to initiate a course of 3D-planned external beam RT for tumors in/around the thorax were prospectively studied as part of an IRB-approved clinical study. Written informed consent was obtained. Patients had assessments of cardiopulmonary QOL pre-RT and serially post-RT (e.g. 1.5, 3, 6, 12.. months post-RT) using the Functional Assessment of cancer Therapy-Lung (FACT-L) questionnaire. An association between a variety of dosimetric parameters for the heart and lungs (e.g. mean dose, Vx) and changes in pulmonary QOL (e.g. declines in QOL; pre-RT minus post-RT values) were assessed using univariate and multivariate techniques. **Results:** The data from 24 patients treated between 2009-2013 and with evaluable QOL were studied. Their demographics are as follows: median age 68 (range 48-87), 46% male, 92% white, 98% primary tumor from lung, 70% stage III or IV, 50% current or former smokers, 67% having no coexisting lung or heart disease before, 42% also receiving chemotherapy. For the overall group, there were no statistically significant differences between the pre-RT value (QOL score 80.6) and any of the post-RT time points (QOL scores 79.9, 79.9 and 76.3 at 1.5, 3 and 6 months post-RT, respectively). On a per-patient basis, there were no significant associations between any of the lung or heart dosimetric parameters and subsequent declines in QOL, though there was a non-significant trend towards greater declines in QOL with larger lung doses (e.g. mean, V20 and 30). There were no similar trends seen with the heart-based dosimetric parameters. When limiting the analysis to patients whose QOL score declined post-RT, there was a positive correlation between the degree of decline and the V30 and V40 of heart ($p<0.05$). Among patients with lung cancer, the degree of decline in QOL was associated with the heart V20, V30, V40 ($p<0.05$). **Conclusion:** There are no significant associations seen between lung and heart dosimetric parameters and subsequent declines in QOL. Additional analyses involving a larger number of patients are needed to better define predictors of RT-associated declines in QOL. (Supported in part by National Institutes of Health Grant CA69579 , a grant from the Lance Armstrong Foundation) **Keywords:** Cardiopulmonary function, quality of life, thoracic radiotherapy, 3D-planned RT

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-009 Depression and Disability in Lung Cancer Patients in a Nigerian Teaching Hospital Victor Lasebikan[1], Ousoji M. Ige[2], Babalola Faseru[3] [1]*Psychiatry, College of Medicine, University of Ibadan, Ibadan/Nigeria,* [2]*Department of Medicine, Chest Unit, Ibadan/Nigeria,* [3]*Department of Preventive Medicine and Public Health | Department of Family Medicine (Secondary), University of Kansas Medical Center, Kansas/United States of America*

Background: Introduction: Research evidences show that depression and disability are important comorbid conditions in patients with Malignancies. However, little is known regarding the relationship between depression, disability and lung cancer in Nigeria. **Objectives:** The objectives of this study were to determine the prevalence of depression and disability in patients with lung cancer in a teaching hospital. **Methods:** Eighty patients diagnosed with lung cancer aged 35 to 80 years, were matched by age and gender with 80 patients without lung cancer from the Out-Patient Department of the study centre. Depression was assessed using the Mini International Neuropsychiatry Interview (MINI) while the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0), was used to assess disability. All analyses were carried out using SPSS version 16.0. **Results:** Fifty one percent of patients with lung cancer had depression compared to 6.4% in the matched control. Among patients with lung cancer, disability was significantly associated with depression after controlling for smoking OR = 9.1, 95% CI (2.5-28.5), and stage of lung cancer OR = 2.1, 95% CI (1-13-9.42). **Conclusion:** There is a critical need to screen and manage depression in lung cancer patients in other to reduce disability and improve quality of life. **Keywords:** Depression, Disability, Lung Cancer, Early Detection

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-010 Predictors of Thromboembolic Events in Patients with Lung Cancer Bohdan Kadlec, Jana Skrickova *Department of Respiratory Diseases and TB, University Hospital and Masaryk University Brno, Brno/Czech Republic*

Background: Patients with lung cancer experience elevated risk of venous thromboembolism Prothrombotic factors in lung cancer include the ability of tumour cells to produce and secrete procoagulant substances and inflammatory cytokines, and the physical interaction between tumour cell and blood. Other mechanisms of thrombus promotion in malignancy include surgery, metastatic disease and use of chemotherapeutic drugs in combination with novel targeted drugs, such as antiangiogenic agents. Cancer patients with thrombosis have a shorter life expectancy than cancer patients without this complication. The occurrence of VTE worsens the quality of life and may delay, interrupt, or completely halt the cancer therapy. **Methods:** Patients diagnosed with primary lung cancer were followed up between 2006-2010. We recorded demographic data, histology and clinical stage, basic laboratory values of blood and coagulation, frequent and significant comorbidities, and details of initial cancer treatment. In patients with advanced, unresectable or metastatic lung cancer, these parameters were evaluated before the first cycle of chemotherapy or targeted therapy. Thromboembolic events were being detected by standard diagnostic procedure; if detected, the risk of VTE was automatically considered to be high. Statistical analysis included standard descriptive statistics; absolute and relative frequency of each category for categorical variables, median and 5% -95% percentile in the case of continuous variables. Analysis of categorical variables was supplemented with an analysis of frequency tables. **Results:** A total of 950 patients were enrolled, of whom 600 were men and 350 women. The median age of all patients was 64 years. Squamous cell carcinoma was the most frequent histological subtype (27.3%), followed by adenocarcinoma (23.8%), small cell carcinoma (18.4%) and non-small cell NOS. Hypertension was the most frequent comorbidity (39.6%),followed by COPD (38.2%), diabetes mellitus (19.4%), cerebrovascular disease 9.6%, and heart failure (7.7%). Ninety-one thromboembolic events were registered in the entire group (9.6%), of which 80 (87.9%) were severe and 11(12.1%) less severe. In the group of patients with thromboembolic disease, platelet counts were significantly increased at the time of diagnosis of lung cancer – 368 $x10^9$ (191.0 to 540.0). Among comorbidites, heart failure was associated with an increased risk of VTE – OR 13.48 (7.80 to 23.28), followed by cerebrovascular disease – OR 3.17 (1.78 to 5.64), atrial fibrillation – OR 2.96 (1.50 to 5.83), and obesity – OR 2.40 (1.26 to 4.58). Among laboratory parameters, platelet counts above 330,5x109 were associated with the occurrence of severe VTE – OR 3.66 (2.25 to 5.96). **Conclusion:** The incidence of

serious thromboembolic events (8.4%) in our group of lung cancer patients was high, especially in patients with adenocarcinoma, advanced-stage disease, and in patiens on cancer treatment. In patients with thromboembolic disease, significantly higher median platelet counts were observed at the time of cancer diagnosis. In patients treated with chemotherapy, most thromboembolic events were observed shortly after the treatment starts and the majority of thromboembolic events occurred within 6 months after the initiation of chemotherapy. These results justify prophylactic treatment in most patients with advanced or metastatic disease, adenocarcinoma, patients receiving radiotherapy or chemotherapy, and in presence of some associated disorders. **Keywords:** VTE, lung cancer, thrombosis, incidence, predictors

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-011 Utility of Tolvaptan and Demeclocycline in Addition to Systemic Chemotherapy for the Management of Hyponatraemia in Small Cell Lung Cancer Robert L. Metcalf[1], Rachael Mccarthy[2], Claire Higham[3], Raffeale Califano[1], Yvonne Summers[1] [1]*Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester/United Kingdom,* [2]*The University of Manchester Medical School, Manchester/ United Kingdom,* [3]*Department of Endocrinology, The Christie NHS Foundation Trust, Manchester/United Kingdom*

Background: Hyponatraemia due to the syndrome of inappropriate anti-diuretic hormone (SIADH) occurs in 10-25% of small cell lung cancer (SCLC) patients. Management of SIADH includes review of medications, fluid restriction and increased solute intake in addition to commencing chemotherapy. The risk/benefit of the tetracycline derivative demeclocycline and the vasopressin receptor antagonist tolvaptan were recently questioned in a clinical practice guideline for hyponatraemia management (Spasovski, 2014). We sought to evaluate how demeclocycline and tolvaptan were used in addition to chemotherapy in the management of hyponatraemia in patients with SCLC and their effect on serum sodium prior to the publication of this guideline. **Methods:** A retrospective case-note review of 132 patients with SCLC treated at The Christie NHS Foundation Trust between 2009 and 2013 was undertaken to identify patients with serum sodium ≤132 mmol/L at diagnosis. Clinical and laboratory data were collected and change in sodium from nadir to peak values at day 7-14 and day 20-40 was calculated. Patients were divided in three groups: treated with chemotherapy alone, and chemotherapy plus demeclocycline or tolvaptan. Patients with complete data were included in the statistical analysis. Mean values were compared using an unpaired Students t-test. **Results:** Twenty seven patients (20%) had sodium ≤132mmol/L at diagnosis (mean 128 mmol/L, SD 3.9). Measurement of urine and plasma osmolality and urine sodium were performed in 6/27 (22%); thyroid function was measured in 6/27 patients and adrenal function in 4/27. Remaining patients were treated empirically. Patients receiving platinum based chemotherapy alone (12/27 patients receiving 1 to 6 cycles) had the highest mean sodium nadir of 128 mmol/L. Those receiving demeclocycline (13/27 patients) had a mean sodium nadir of 126 mmol/L. Patients receiving tolvaptan (6/27, 4 after prior demeclocycline) had the lowest mean sodium nadir of 121 mmol/L (p=0.0132 comparing with chemotherapy only group). Chemotherapy alone increased mean sodium from 128 mmol/L to 134 mmol/L by day 7-14 (p=0.0062) and 135 mmol/L by day 20-40 (p=0.0007). The addition of demeclocycline increased mean sodium from 126 mmol/L to 130 mmol/L (p=0.0527) and 132 mmol/L (p=0.0102) at the same time-points. The addition of tolvaptan increased mean sodium from a nadir of 121 mmol/L to 135 mmol/L at 7-14 days (p=0.0126) and 133 mmol/L at 20-40 days (p=0.0080). No significant toxicity of demeclocycline or tolvaptan were reported. **Conclusion:** Most cases of hyponatraemia were treated empirically as SIADH using demeclocycline and/or tolvaptan in over half of patients in addition to chemotherapy. Tolvaptan was used to treat patients with the lowest mean sodium most often following failure of demeclocycline. Despite this, these patients had peak sodium levels post treatment equivalent to those in other patients in this study. Clinician choice to treat patients with tolvaptan and/or demeclocycline in adition to chemotherapy was associated with a statistically and clinically meaningful improvement in serum sodium levels in all groups studied. Although this study is limited by the retrospective nature of the analysis, our group is using these data to produce guidelines on the management of hyponatraemia in SCLC to standardise patient management which will be prospectively evaluated. **Keywords:** small cell lung cancer, SIADH, Hyponatraemia, Tolvaptan

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-012 A Retrospective Assessment of Mortality of Patients Who Died in the Respiratory Intensive Care Unit with a Diagnosis of Lung Cancer Nesrin Ocal[1], Deniz Dogan[1], Gurhan Taskin[2] [1]*Chest Diseases, Gulhane Military Medical Faculty, Ankara/ Turkey,* [2]*Intensive Care Medicine, Gulhane Military Medical Faculty, Ankara/Turkey*

Background: According to 2015 data of WHO, lung cancer is still the most common causes of cancer death (1.59 million deaths in 2012) which is more than the combination of next three most common cancers (colon, breast and pancreatic). The number of deaths due to lung cancer has increased approximately 3.5 percent between 1999 and 2012. The number of deaths among men has reached a plateau but the number is still rising among women perhaps related with changesinsmoking habits. The age-adjusted death rate for lung cancer is higher for men than for women. **Methods:** In this study, firstly we retrospectively reviewed the data of 123 patients who died in respiratory intensive care unit of our hospital within last two years. We determined that 63 of them died because of lung malignancies and associated pathologies. Ages, genders, smoking habits, survival times, diagnosis methods, histopathological types of lung cancer, stages, metastatic states of the patients were compiled. In addition; clinical findings just before the death, indications of intensive care unit intake, underlying and immediate death causes were detected. The underlying death cause defines the disorder which initiated the events leading to death.The immediate death cause defines the final disorder or condition resulting in death.Some definitions were used in classifying the cause of death. When the amount of tumor in the lungs was the most important factor in fatal respiratory failure, this death cause was defined as tumor burden. Malfunction of the organs due to widespread metastases was defined as metastatic organ failure. **Results:** 56 cases were primary lung cancer patients. 11 cases were female and 45 cases were male. Mean age of the cases was 71.81 (46-88) in females and 68.91(50-84) in males. 5 of female cases were adenocancer, 4 were squamous cell lung cancer and 2 were small cell lung cancer. 20 of male cases were squamous cell lung cancer, 14 were adenocancer, 11 were small cell lung cancer. Diagnostic methods were bronchoscopy in 33 patients, transthoracic lung biopsy in 12 patients, thoracentesis in 7 patients, metastatic organ biopsy in 4 patients. Mean survival periods were 3.1 months for small cell lung cancer, 6.7 months for squamous cell lung cancer and 8.2 months for adenocancer. All of the small cell lung cancer cases had metastasis at diagnosis time. Pneumonia and MODS-sepsis were the most common death causes in all cases. **Conclusion:** We think that our results would be helpful clinicians about lung cancer and follow up these patients. **Keywords:** lung cancer, mortality, survival, intensive care

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-013 Prognostic Factors Associated with Overall Survival in Croatian Patients with Advanced Lung Cancer Dragan Trivanovic, Lidija Kocic, Marina Dembic, Nika Spasic, Anuska Budisavljevic *Oncology, General Hospital Pula, Pula/Croatia*

Background: In Croatian population Lung cancer (LC) is the most common cancer in male and third most common in women. The age-adjusted incidence rates are 63.5 per 100,000 populations per year. The aim of this study was to investigate the prognostic factors associated with overall survival in patients with cytological and/or histological confirmed advanced (IIIA-IV stage) LC. **Methods:** In this single institution prospective study, 164 consecutive patients were included between September 2008 and January 2013 from Istrian County, Croatia.The prognostic factors evaluated for 2-year overall survival including gender, age, performance status, histology, blood group type, location od tumor, metastatic sites, anemia, elevated WBC, platelets, and diabetes mellitus. All factors with a P value < 0.05 at univariate analysis were entered into a multivariate analysis using Cox proportional-hazards models. **Results:** The median age of patients was 64.0 years (range 36 – 85 years) with males predominance (115 males vs. 49 females). The histological types included: adenocarcinoma 56 (34%), squamous cell carcinoma 50 (30%), small cell carcinoma 33 (20%) other or not-otherwise specified 25 (16%). The median follow-up time was 14.1 months. The 2-year overall survival rate of 164 patients was 27.0%. Female gender and non liver metastatic disease are significantly associated with better overall survival. Data were shown in Table 1. Cox Regression analysis adjusted to tumor stage and age demonstrated that patients with 0 type blood group in adenocarcinoma subpopulation present a worst overall survival when compared to other blood type groups. Not elevated serum platelets in squamous NSCLC and elevated WBC, and female gender are independent prognostic factors in SCLC. Table 1 Significant prognostic factors for overall survival in NSCLC

Baseline prognostic factor	**Univariate analysis**	**Multivariate analysis**		**2-year survival rate %**
	P-value	HR (95% CI)	P-value	
Female* vs Male	0.020	0.62 (0,41-0.93)	0.022	38.0
Non-liver metastasis	0.024	0.60 (0.39-0.95)	0.028	28.8
0 blood group in adenocarcinoma NSCLC	0.008	6.64 (1.38-32.14)	0.019	18.7
Normal serum platelets level	0.013	1.27 (0,45-3.59)	0.654	23
Female* vs Male gender in SCLC	0.01	0.30 (0.11-0.82)	0.019	44
Non-liver metastasis in SCLC	0.027	0.43 (0.18-1.01)	0.055	20
Elevated serum WBC	0.015	0.39 (0.17-0.90)	0.026	19

Abbrevations: *referent, NSCL=Non Small Cell Lung Cancer, SCLC= Small Cell Lung Cancer, WBC= White Blood Cells **Conclusion:** Our results indicated that female gender is powerfull favorable prognostic factor in NSCLC and SCLC. 0-type blood group is significant prognostic factor for short term survival following diagnosis of advanced lung adenocarcinoma and elevated WBC is associated with longer survival in SCLC subpopulation of advanced disease. **Keywords:** Lung Cancer, 0-type blood group, Survival

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-014 Tunneled Pleural Catheters Are Safe in the Setting of Chemotherapy and Immune Suppression Candice L. Wilshire[1], Brian E. Louie[2], Ralph W. Aye[2], Alexander S. Farivar[2], Eric Vallieres[2], Jed A. Gorden[3] *[1]Interventional Pulmonolgy and Thoracic Surgery, Swedish Medical Center and Cancer Institute, Seattle/WA/United States of America, [2]Thoracic Surgery, Swedish Medical Center and Cancer Institute, Seattle/WA/United States of America,[3]Interventional Pulmonolgy, Swedish Medical Center and Cancer Institute, Seattle/WA/United States of America*

Background: The reported rate of tunneled pleural catheter (TPC)-related infections in patients on chemotherapy ranges from 4-20%. Thus, infection is often cited as a contraindication to placement of a TPC in patients with recurrent symptomatic malignant/para-malignant pleural effusions (MPE/PMPE) receiving chemotherapy. Delay in the definitive management of such pleural effusions can result in an increased number of procedures, progressive symptoms and decreased independence in patients with advanced disease. Current data does not directly associate TPC-related infections to a patient's immune status on chemotherapy. We aim to correlate catheter-related infections to immune system competency around the time of chemotherapy. **Methods:** A review of patients with MPE/PMPEs managed with a TPC from 2009-2014 was conducted. We identified 182 patients, of which 109 had chemotherapy within 1 month of TPC insertion or at any time during TPC drainage. An immunocompromised state was defined as the presence of leukopenia [white blood cells (WBC) <4 th/mm^3] when a differential count was unavailable; or lymphopenia [lymphocytes <1 th/mm^3], and/or neutropenia [absolute neutrophil count (ANC) <1.5 th/mm^3]. A pleural infection was defined as the presence of a positive gram stain/culture of pleural fluid. **Results:** Seventy-three (67%) of the 109 patients were identified to be immunocompromised. Only 5 (7%) of the 73 developed a pleural infection. All 5 (100%) received antibiotic treatment. Two of the 5 (40%) pleurodesed and underwent catheter removal, 2 (40%) maintained effective catheter drainage, while 1 (20%) underwent TPC removal and replacement with a pigtail catheter. Of the 5 patients, 4 (80%) demised at a median of 5 months (IQR, 3-8) following the pleural infection. All deaths were considered related to progression of malignant disease and not a consequence of infection. One patient is alive and still undergoing drainage. **Conclusion:** These preliminary results suggest that chemotherapy and immune suppression do not significantly increase the risk of TPC-related infections as the rate is low and comparable to immunocompetent patients. Chemotherapy should not delay the decision to definitely palliate patients with TPCs in the setting MPE/PMPEs. **Keywords:** Infection, immunosuppression, Tunneled pleural catheter, chemotherapy

POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 09:30-16:30

P2.11-015 Factors Related with Reluctance to Treatment in Lung Cancer Jung Hyun Chang *Respiratory and Critical Care Medicine, Ewha Womans University, Seoul/Korea*

Background: Lung cancer is one of increasing cancer in incidence with longer survival of life in Korea. Some patients do not have a condition to receive cancer therapy by the decision of patients themselves and/or family as well as doctors. Refusal or avoidance of active treatment is prone to suffer from cancer symptoms and causes to shorten life survival. The purpose of this study is to define factors related to avoid or refuse active therapy in lung cancer. **Methods:** The population was retrospectively collected from patients' record in one tertiary university hospital from 2010 to 2012. Total 306 subjects were enrolled as lung cancer and 18 subjects were excluded due to incomplete data or follow-up loss. Among 288 subjects, 66 subjects, avoiding cancer treatment were allocated to nontreatment group (NTG), whereas remaining 222 subjects to treatment group (TG). **Results:** Mean age of NTG was older than TG. Previous operation history, low BMI, high ECOG score and Charlson comorbidity index (CCI) score were significant in NTG. Factors of sex, smoking behavior, drinking, offspring number, degree of scholarship, familial history of cancer, pathologic type, TNM stage, presence of chest symptoms or systemic symptoms, and absence of occupation, religion and partner were insignificant. In univariate and multivariate analysis, high ECOG (2-3 vs 0-1; odds ratio [OR]: 6.0; 95% confidence interval [CI]:1.5-23.4) and high CCI score (OR: 1.3; 95% CI; 1.02-1.7) were the significant determinants to the avoidance of treatment. **Conclusion:** Nontreatment decision in lung cancer was associated with performance status and comorbidities, which are considered prior to the guidance of cancer treatment. Patient's personal factors give little influence to the decision of cancer treatment. **Keywords:** lung cancer, avoidance of treatment

SESSION: POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC WEDNESDAY, SEPTEMBER 9, 2015

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-001 Imprime PGG, a Novel Innate Immune Modulator, Combined with Carboplatin, Paclitaxel and Bevacizumab for 1st Line Advanced Nonsquamous NSCLC Walburga Engel-Reidel[1], Folker Schneller[2], Martin Wolf[3], Wolfgang Schuette[4], Jamie Lowe[5], Paulette Mattson[5], Michele A. Gargano[5], Myra Patchen[5], Richard D. Huhn[5], B. Ma[5], A Braun[5] *[1]Kliniken Der Stadt Köln Ggmbh, Koln/Germany, [2]Klinikum Rechts Der Isar, Technical University, Munich/Germany, [3]Klinikum Kassel Gmbh, Kassel/ Germany, [4]Krankenhaus Martha-Maria Halle Dölau, Halle (Saale)/Germany, [5]Biothera, Eagan/ MN/United States of America*

Background: Imprime PGG (PGG) in combination with carboplatin/paclitaxel chemotherapy (C/P) and bevacizumab (Bev) increased objective response rates (ORR) and overall survival (OS) of patients (pts) with previously untreated stage IV non-squamous NSCLC in comparison to C/P + Bev alone in a randomized, controlled, multicenter phase 2 trial (Engel-Riedel W et al, Ann Oncol 25 [Suppl 5], 2014, LBA32). Herein, we report landmark survival analyses at the 1- and 2-year time points. The trial was sponsored by Biothera, ClinicalTrials.gov NCT 00874107, EudraCT 2008-006780-37. **Methods:** 92 pts with stage IV nonsquamous NSCLC were randomized 2:1 to receive PGG (4 mg/kg IV days 1, 8, 15 of each 3-week cycle) + C/P + Bev (PGG group) vs C/P + Bev alone (Ctrl group). C/P was administered for 4 to 6 cycles; Bev +/- PGG were administered until disease progression or intolerable toxicity. The primary endpoint was ORR based on modified RECIST v1.0 and was assessed centrally. Secondary endpoints included overall survival (OS), progression-free survival (PFS), duration of response (DoR) and safety. Imaging assessments (CT of chest and abdomen) were reviewed every 6 weeks. The primary analysis occurred after all pts had either progressed or had the opportunity to complete at least 18 treatment cycles (54 weeks). **Results:** An objective response was achieved by 29 out of 48 evaluable pts (60.4%; 1 CR, 28 PR) in the PGG group and 10 out of 23 (43.5%; 0 CR, 10 PR) in the Ctrl group (p=0.21). Median (m) OS was 16.1 mos with PGG compared to 11.6 mos (HR=0.66; p=0.13) with Ctrl. The mPFS was 11.9 mos vs 10.2 mos (HR=0.86; p=0.59), and mDoR was 10.3 mos vs 5.6 mos (HR=0.92; p=0.90) among subjects receiving PGG vs Ctrl, respectively. Survival rates of pts (95% CI) in the PGG vs Ctrl groups were 62.8% (48.8, 74.0) vs 42.7% (22.7, 61.4) at 12 mos, and 37.0% (22.5, 51.5) vs 24.4% (7.9, 45.7) at 24 mos. Overall, the incidence of adverse events (AEs) was similar across treatment groups. The most common AEs (occurring in ≥ 5 pts) deemed possibly or probably related to PGG by the investigator were chills (13.6%); dyspnea, fatigue (10.2% each); nausea, pyrexia, and infusion-related reactions (8.5% each). Overall, 37.3% of pts receiving PGG and 43.3% receiving Ctrl discontinued the study due to AEs. **Conclusion:** The addition of PGG to C/P + Bev therapy was well tolerated and resulted in clinically meaningful increases in ORR, DoR, and OS. Results did not reach statistical significance in this phase 2 study. Further investigation is warranted to confirm the efficacy and safety of this combination. **Keywords:** Nonsquamous, Immunotherapy, non-small cell lung cancer, Imprime PGG

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-002 PD-L1 Expression and FGFR1 Amplification in Chinese Stage III/IV Lung Squamous Carcinoma Jie Wang, Hua Bai, Sifan Yu, Qinxiang Guo, Minglei Zhuo *Peking University Cancer Hospital and Institute, Beijing/China*

Background: This study aims to explore status of PD-L1 expression and FGFR1 amplification in stage IIIB/IV SQC, further to analyze their correlation with clinicpothological characteristics, efficacy of gemcitabine based chemotherapy and prognosis of SQC patients. **Methods:** 128 stage III/IV SQC patients were enrolled into this study from May 1st 2009 to May 31st 2014, all of which had complete clinical profile. 78 patients received gemcitabine-based chemotherapy. Immunohistochemistry (IHC) was used to detect PD-L1 expression, fluorescence in situ hybridization was applied to detect FGFR1 amplification. SPSS17.0 was used for statistical analysis. **Results:** 80 (62.5%) SQC had IHC positive PD-L1 expression. PD-L1expression was significantly higher in male and smoker population than female and non-smoker, respectively. (gender: 65.5% VS. 22.2%, P=0.011; smoke histology 67.0% VS. 44.0%, P=0.039). PD-L1 expression had no significant relationship with objective response rate (ORR) and disease control rate(DCR) for gemcitabine-based chemotherapy(54.8% VS.59.7%, P =0.434 and P=0.840). However, the overall survival (OS) of PD-L1 negative SQC was significantly longer than PD-L1 positive group (29.8 vs. 20.1 months, P=0.001). 32 cases showed FGFR1 FISH positive (32/128, 25.0%), and stage III patients presented lower rate compared with stage IV SQC (17.1% vs. 36.5%, P=0.013). FGFR1 amplification had no relationship with ORR and DCR in patients treated with gemcitabine-base chemotherapy(32.3% VS.30.6%. P=0.663 and P=0.659). No correlation between PD-L1 expression and FGFR1 amplification was found (P=0.916). **Conclusion:** PD-L1 expression could act as a prognosis factor in Chinese stage III/IV SQC patients. PD-L1 expression and FGFR1 amplification might be irrelevant. **Keywords:** PD-L1 expression, FGFR1 amplification, squamous lung carcinoma

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-003 Patterns of Disease Progression for Stage IV NSCLC While on PD-1 Directed Therapy as Compared to Standard Chemotherapy Monica S. Chatwal[1], Vinicius Ernani[2], Taofeek K. Owonikoko[3], Suresh S. Ramalingam[4], Rathi N. Pillai[5] [1]*Emory University, Atlanta/GA/United States of America,* [2]*Hematology and Medical Oncology, Emory University, Atlanta/GA/United States of America,* [3]*Hematology & Medical Oncology, Emory University School of Medicine, Atlanta/GA/United States of America,* [4]*Medical Oncology, Emory University Winship Cancer Institute, Atlanta/United States of America,* [5]*Winship Cancer Institute, Emory University, Atlanta/GA/United States of America* **Background:** Programmed Cell Death 1 (PD-1) inhibitor therapy is now an established therapeutic modality in certain solid malignancies, including non-small cell lung cancer (NSCLC). The purpose of this study is to determine whether disease progression patterns are different between PD-1 inhibitor therapy or chemotherapy in patients with advanced NSCLC. **Methods:** We performed a retrospective analysis of patients who received PD-1 targeted therapies and systemic chemotherapy for advanced NSCLC treated at the Winship Cancer Institute at Emory University. We reviewed demographic data and treatment history of these patients. RECIST criteria were used to evaluate the patients' baseline tumor burden and their subsequent disease progression from imaging studies (CT, PET/CT, MRI). **Results:** The total cohort included 37 patients with a mean age of 67 years. The PD-1 therapy group included 19 patients (14 males, 5 females), with 9 on MK-3475, 3 on MDPL3280A, and 7 on nivolumab. This group included 3 African Americans and 16 Caucasians. The median number of lines of prior chemotherapy was 3. A comparator group of 18 patients on standard chemotherapy was identified (14 males, 4 females). This group included 8 African Americans and 10 Caucasians. In the PD-1 therapy group, 5 patients had no progression and 14 had disease progression. Of these, 5 progressed at their sites of known cancer (36%), 4 progressed at new sites (28.5%), and 5 progressed at both old and new sites (36%). In the chemotherapy group, 4 patients had no disease progression and 14 had progression. Of those 14, 2 were at old sites only (14%), 4 were at new sites only (29%), and 8 were at both old and new sites (57%). The median time to progression was 3.5 months with PD-1 targeted therapy (range 2-13 months) and 6 months with chemotherapy (range 2-21 months). **Conclusion:** Our data suggests no difference between the progression patterns between PD-1 inhibitor therapy and standard chemotherapy patients. Patients on PD-1 therapy appear to have a shorter time to progression than those on traditional chemotherapy.
Keywords: NSCLC, PD-1 Therapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-004 Paxillin Confers Resistance to TKI via Modulating BIM and Mcl-1 Protein Stability Huei Lee[1], De-Wei Wu[1], Chih-Yi Chen[2] [1]*Graduate Institute of Cancer Biology and Drug Discovery, Taipei Medical University, Taipei/Taiwan,* [2]*Chung Shan Medical University Hospital, Taichung/Taiwan*

Background: Tyrosine kinase inhibitors (TKIs) have been documented to have substantial clinical benefits to non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) mutation. TKI resistance occurs in nearly all patients who receive TKI targeting therapy, resulting in a modest overall survival benefit. Therefore, establishing a biomarker for early prediction and exploring the mechanism of primary TKI resistance is essential for improving the therapeutic efficacy in NSCLC patients. **Methods:** In this study, we provide evidence indicating that paxillin (PXN) overexpression may confer gefitinib resistance in EGFR-mutant lung cancer cells. **Results:** Mechanistically, PXN-mediated ERK activation is responsible for gefitinib resistance via decreased BIM and increased Mcl-1 expression due to modulating their protein stabilities by phosphorylation of BIM at Serine 69 and Mcl-1 at Threonine 163. The mechanistic action in the cell model was further confirmed by the observation of xenograft tumors in nude mice, revealing that the PXN-mediated gefitinib resistance was conquered by ERK inhibitor (AZD6244) and Bcl-2 family inhibitor (obatoclax), but the gefitinib resistance overcome by AZD6244 is more effective than that of obatoclax. **Conclusion:** Therefore, we suggest that PXN expression may be useful in predicting primary TKI resistance, and combining TKI with ERK inhibitors may clinically benefit EGFR-mutant NSCLC patients whose tumors exhibit high PXN expression.
Keywords: Tyrosine kinase inhibitors, Paxillin, EGFR-Mutant

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-005 Clinical Effects of Icotinib for Brain Metastasis in Chinese Non-Small Cell Lung Cancer Patients Harboring an EGFR Mutation Helei Hou, Xiaomei Xu, Xiaofei Wang, Lihua Deng, Airong Tan, Congmin Liu, Wenjun Yu, Chuantao Zhang, Chun Yan, Xiaofeng Cheng, Xiaochun Zhang *Medical Oncology, Qingdao Municipal Hospital, Qingdao University, Qingdao/China*

Background: Icotinib hydrochloride, an oral EGFR tyrosine kinase inhibitor, was proved to be non-inferior to gefitinib in patients with non-small-cell lung cancer (NSCLC). Brain metastasis is a serious factor associated with poor outcomes of NSCLC because systemic chemotherapy usually showed little effects due to the blood-brain barrier. Besides, other treatments such as whole brain or stereotatic radiotherapy may cause neurological complications. There have been some studies showing that gefitinib or erlotinib plus concurrent brain radiotherapy or not was effective in controlling brain metastasis in NSCLC. Herein, we observed the function of Icotinib on brain metastasis in Chinese NSCLC patients harboring an EGFR mutation. **Methods:** The clinical data of 28 NSCLC patients with brain metastasis referred to Qingdao Municipal Hospital from May 2012 to December 2014 were retrospectively analyzed. All the patients had pathological diagnosis of adenocarcinoma. EGFR mutation state was confirmed by ARMS PCR or Sanger sequencing. The patients received first line Icotinib of 125mg three times a day after giving informed consent and they would continue to take Icotinib unless disease progressed or other reasons. No concurrent brain radiotherapy was given during this process. **Results:** Out of the 28 patients treated, 12 achieve partial response, 11 experienced stable disease and 5 experienced progressive disease. The response rate and disease control rate of Icotinib for brain metastasis was 42.8% and 82.1% respectively. After a median follow-up of 15.1 months (range 5-27 months), the median progression-free time was 7.5 months. Rash and diarrhea were the most common adverse events. **Conclusion:** Icotinib might be an alterative treatment for brain metastasis in Chinese NSCLC patients harboring an activating EGFR mutation.
Keywords: non-small cell lung cancer, Brain metastasis, EGFR, icotinib

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-006 Propensity Score Matched Comparison of EGFR TKI for EGFR Mutation 19del vs 21L858R Zhen Zhou, Shun Lu, Xiaoming Niu, Mailing Liao, Chuanjia Li *Lung Cancer Center, Shanghai Chest Hospital, Shanghai/China*

Background: Previously, data of Lux-lung 3 and Lux-lung 6 showed overall survival was improved with the afatinib for patients with 19del EGFR mutations and the absence of an effect in patients with L858R EGFR mutations suggests that EGFR 19del-positive disease might be distinct from L858R-positive disease. We aimed to assess the effect of first-generation reverse EGFR TKI (Gefitinib and Elotinib) on overall survival of patients with EGFR mutation-positive lung adenocarcinoma through an analysis of data from real world practice. **Methods:** This is a retrospective study, 134 patients with EGFRm 19del or 21L858R with reverse EGFR TKI gefitinib or elotinib in clinical practice from Jun.2012 to April.2014 in Shanghai Chest Hospital , follow-up to April.1,2015. To control for selection bias, matched groups of patients were selected using a propensity score matching method. Overall survival and PFS were estimated using the Kaplan-Meier method with log-rank test. The Wilcoxon rank sum test was used for variables not normally distributed. Categorical data are displayed as frequencies and comparisons were made with Chi-square tests (Fisher exact tests if appropriate). **Results:** After1:1 the propensity score matching, matching was based on a one-to-two nearest neighbor matching method with a tolerance level on the maximum propensity score distance (calipers of width 0.2 standard deviation of the logit of the PS). 70 patients were enrolled, the baseline variables (eg, age, sex, smoking , PS, line of EGFR TKI treatment) were comparable between the matched cohorts ($P > 0.05$ for all). Follow-up time: 19del (median 16.2 months, range 1.0-49.2) , 21L858R (median 16.4 months, range 0.4-41.1). m PFS in 19 del and 21L858R was 16.3months, 16.8months, respectively, m OS in 19 del and 21L858R was28.4 months, 32.2 months, respectively, There are no significant difference between EGFR mutation 19del and 21L858R patients with the reversible first-generation inhibitors. **Conclusion:** CONCLUSION: There are no significant difference between EGFR mutation 19del and 21L858R patients with the reversible first-generation inhibitors either PFS or OS. The results maybe related to the sample size, waiting for the results of meta-analysis.
Keywords: Propensity score match, EGFR mutation, First-generation inhibitor, overall survival

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-007 Evaluation of Gefitinib Efficacy According to Body Surface Area, Body Weight, and Body Mass Index in Patients with NSCLC Harboring EGFR Mutations Reiko Sakurai[1], Hisao Imai[2], Tomohito Kuwako[3], Mai Tomizawa[1], Tomomi Masuda[3], Yosuke Miura[3], Kyoichi Kaira[4], Mitsuyoshi Utsugi[5], Akihiro Yoshii[1], Kimihiro Shimizu[6], Noriaki Sunaga[3], Yoshio Tomizawa[1], Shinichi Ishihara[7], Takao Ishizuka[8], Akira Mogi[9], Satoru Watanabe[1], Takeshi Hisada[3], Koichi Minato[2], Atsushi Takise[10], Ryusei Saito[1], Masanobu Yamada[3] [1]*Department of Respiratory Medicine, National Hospital Organization Nishigunma Hospital, Shibukawa/Japan,* [2]*Department of Respiratory Medicine, Gunma Prefectural Cancer Center, Ota/Japan,* [3]*Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Maebashi/Japan,* [4]*Oncology Clinical Development, Gunma University Graduate School of Medicine, Maebashi/Japan,* [5]*Division of Internal Medicine, Kiryu Kosei General Hospital, Kiryu/Japan,*[6]*Department of Thoracic Visceral Organ Surgery, Gunma University Graduate School of Medicine, Maebashi/Japan,* [7]*Division of Internal Medicine, Isesaki Municipal Hospital, Isesaki/Japan,* [8]*Division of Internal Medicine, Public Tomioka General Hospital, Tomioka/Japan,* [9]*Department of General Surgical Science, Gunma University Graduate School of Medicine, Maebashi/Japan,* [10]*Division of Respiratory Medicine, Maebashi Red Cross Hospital, Maebashi/Japan*

Background: Gefitinib is effective as first-line chemotherapy for advanced non-small cell lung cancer (NSCLC) patients harboring sensitive epidermal growth factor receptor (*EGFR*) mutations. Exon 19 deletions and the L858R point mutation are the most commonly encountered sensitive *EGFR* mutations in NSCLC, and have been shown to predict greater efficacy of gefitinib therapy. The objective of this study was to evaluate whether body surface area (BSA), body weight (BW), and body mass index (BMI) affect the efficacy of gefitinib in patients with NSCLC harboring sensitive *EGFR* mutations. **Methods:** We reviewed the medical charts of consecutive patients with advanced NSCLC harboring sensitive *EGFR* mutations who received gefitinib. The median values were used as the cutoffs to evaluate the impact of BSA and BW on the efficacy of gefitinib. BMI was categorized as underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5 to < 25 kg/m^2), and overweight (BMI ≥ 25 kg/m^2). **Results:** The median BSA and BW of the 138 NSCLC patients harboring sensitive *EGFR* mutations were 1.48 m^2 and 53 kg, respectively. The overall response rate, progression-free survival (PFS), and overall survival (OS) were 65.2%, 12.2 months, and 24.2 months, respectively. There were no significant differences

in clinical outcomes between the high-BSA (BSA ≥ 1.43 m^2) and low-BSA groups (BSA < 1.43 m^2), with response rates of 68.5% and 72.0% ($p = 0.92$), median PFS of 12.2 and 11.5 months ($p = 0.73$), and median OS of 25.0 and 21.9 months, respectively ($p = 0.28$). Moreover, there were no significant differences in clinical outcomes between the high-BW (BW ≥ 53 kg) and low-BW groups (BW < 53 kg), with response rates of 63.3% and 67.1% ($p = 0.72$), median PFS of 12.2 and 10.8 months ($p = 0.46$), and median OS of 28.9 and 21.9 months, respectively ($p = 0.22$). For BMI, the median PFS and OS estimated among underweight, normal weight, and overweight patients were 10.6 and 19.2 months, 12.0 and 23.3 months, and 13.1 and 33.1 months, respectively. There were no statistically significant differences in PFS and OS among underweight, normal weight, and overweight patients ($p = 0.52$ and $p = 0.30$, respectively). Finally, to substantiate possible differences in the efficacy in patients who are young (<75 years) vs. elderly (≥ 75 years) and who have exon 19 deletions vs. L858R, we also evaluated these subgroups separately regarding BSA, BW, and BMI. However, there were no significant differences in the PFS and OS between these groups. **Conclusion:** The efficacy of gefitinib in patients with NSCLC harboring sensitive *EGFR* mutations does not differ according to their BSA, BW, and BMI. **Keywords:** non-small cell lung cancer, gefitinib, EGFR mutations, body surface area, body weight, and body mass index

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-008 Gefitinib in Front-Line Treatment of 161 Caucasian Patients with NSCLC of the Czech Republic Jana Skrickova[1], Zbynek Bortlicek[2], Karel Hejduk[2], Milos Pesek[3], Vitezslav Kolek[4], Leona Koubkova[5], Marketa Cernovska[6], Marcela Tomiskova[1], Jaromir Roubec[7], Libor Havel[8], Frantisek Salajka[9], Helena Coupkova[10], Michal Hrnciarik[9], Milada Zemanova[11], Dimka Sixtova[12], Minika Satankova[1], Bohdan Kadlec[1], Miloslav Marel[5] [1]*Department of Respiratory Diseases and TB, University Hospital and Medical Faculty Brno, Brno/Czech Republic,* [2]*Biostatistics, Iba Institute, Brno/Czech Republic,* [3]*Pulmonary Medicine, University Hospital, Plzen/Czech Republic,* [4]*Respiratory Medicine, University Hospital, Olomouc/Czech Republic,* [5]*Pulmonary Medicine, University Hospital,, Praha/Czech Republic,* [6]*Pulmonary Medicine, Thomayer Memorial Hospital, Prague/Czech Republic,* [7]*Pulmonary Medicine, University Hospital, Ostrava/Czech Republic,* [8]*P Neumology and Thoracic Oncology, Municipal Hospital, Prague/Czech Republic,* [9]*University Hospital, Hradev Kralove/Czech Republic,* [10]*Departmen of Oncology, Masaryk Memorila Institute, Brno/Czech Republic,*[11]*Clinical Oncology, General University Hospital Prague, Prague/Czech Republic,* [12]*Respiratory Medicine, General University Hospital Prague, Prague/Czech Republic*

Background: Gefitinib is a potent oral non-cytotoxic, active and selective epidermal growth factor receptor tyrosine kinase inhibitor. This study evaluates treatment outcomes in 161 NSCLC patients from Czech Republic according to activated mutations located in exons 19 and 21. **Methods:** Data treated patients with gefitinib are collected in the TULUNG registry, which is a common project of the Czech Pneumological Society, Czech Oncological Society, and Institute Biostatistics and Analyses Masaryk University Brno. NSCLC patients with EGFR activated mutations were treated in first line between 02/2010 and 12/2014 in 10 institutions. Retrospective analyses were carried out to assess the effectiveness and safety of gefitinib treatment according to activated mutations located in exons 19 and 21. The analysed outcomes include following: treatment response rate, median Overall Survival (mOS), median Progression Free Survival (mPFS) and occurrence of types adverse events. **Results:** Out of 161 treated patients, 105 (70 female, 35 male) had EGFR mutations in exon 19, and 56 (39 female, 17 male) had EGFR mutations in exon 21. Median age was 66 years in the group with mutations in exon 19 and 69 years in the group with mutations in exon 21. There was no statistically significant difference in sex (p=0.727) and in age (p=0.204). No statistically significant difference was observed in the representation in smoking (p=0.354). There was statistically borderline significant difference in adenocarcinoma proportion (p=0.045). In the group with mutations in exon 19 were 96% patients with adenocarcinoma and in the group with mutations in exon 21 were 85% patients with adenocarcinoma. Between these two groups, there was no statistically significant difference according to performance status (p=0.547); no statistically significant difference according to disease control (CR+PR+SD) (p=0.479); no statistically significant difference according the response to the treatment (CR + PR) (p=0.052). There was no statistically significant difference in mOS (p=0.390). In the group of patients with mutations located in exon 19, the overall survival was 22.7 months (CI 95%: 17.7; 27.8), in the group with mutations in exon 21, overall survival was 16.3 months (CI 95%: 10.8; 21.8). There was no statistically significant difference (p=0.202) in mPFS; in the group of patients with mutations in exon 19 it was 11,0 months (CI 95%:9.1; 12.8) and in the group with mutations in exon 21 it was 9.4 months (CI 95% 6.6; 12.2). Similar numbers of adverse effects were observed in either group (35.2% and 35.7%). Almost 70% of patients with mutations in exon 19 and almost 60% of patients with mutations in exon 21 are still alive or were lost to follow up. These patients are censored to the date of last update. **Conclusion:** In both groups of patients, the treatment was very safe. Median PFS and median OS were satisfactory without statistically significant differences between the two groups; however, a better trend was observed in the group of patients with mutations in exon 19. Consequently survival estimates shows great variability and longer potential follow up is needed to confirm these results. **Keywords:** advanced NSCLC, Targeted therapy, EGFR activated mutations, gefitinib

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-009 Impact of EGRR Mutation on Brain Metastasis and Disease-Free Survival in Patients with Surgically Resected Lung Adenocarcinoma Takefumi Akita, Taisuke Akamatsu, Yuichiro Shishido, Satoru Morita, Kazuhiro Asada, Toshihiro Shirai, Takashi Etou, Syunnsuke Eba, Masahide Hirose, Shinichiro Otha *Shizuoka General Hospital, Shizuoka-City/Japan*

Background: Central nervous system (CNS) invasion is a common occurrence in patients with non-small-cell lung cancer (NSCLC) and is associated with poor outcome. For patients who develop CNS invasion, epidermal growth factor receptor (EGFR) mutation derives clinical benefits from EGFR tyrosine kinase inhibitors (TKIs). The clinical manifestation of CNS invasion, EGFR mutation, and prognosis are unclear in patients with resected stage I to III lung adenocarcinoma. **Methods:** The records of 261 patients with completely resected stage I to III lung adenocarcinoma who were hospitalized between March 2002 and January 2013 were reviewed retrospectively. Their pathological records indicated that EGFR mutation testing had been performed. Data on basic patient demographics, EGFR mutation, disease-free survival (DFS), and postoperative recurrence were collected. Kaplan Meier curves were used for survival analysis. **Results:** Of the 261 patients (median age: 68, range: 31-90) identified, 49% were male and 53% were EGFR mutant. Tumor stages were I, II, and III in 153, 47, and 61 patients, respectively.DFS after surgery for stage I, II, and III EGFR-mutant patients were 62 mo, 40 mo, and 29 mo, respectively, and 71 mo, 30 mo, and 74 mo, respectively, for patients with wild-type EGFR, showing no significant difference (p=0.19). Recurrence after surgery occurred in 124 patients (36 with CNS, 23 with bone metastasis, and 87 with other organ metastasis).In patients with CNS relapse, the incidence of CNS relapse as first metastasis was significantly high at 13.3% for EGFR-mutant patients, compared with 4.3% for wild-type EGFR patients (HR 2.5, p=0.046). As for second CNS metastasis, there was no significant difference between EGFR-mutant patients (8.1%) and wild-type EGFR patients (4.2%) (p=0.44).In patients whose first relapse was CNS metastasis, DFS after surgery was significantly longer at 22 months for EGFR-mutant patients, compared with 8 months for wild-type EGFR patients (p=0.012). Patients with recurrence in other organs showed no significant differences in terms of DFS regardless of being EGFR mutant or not. **Conclusion:** The EGFR-mutant patients showed a higher incidence of brain metastasis as the first relapse, and significantly longer DFS than the wild-type EGFR patients. In the present study, the brain metastasis of postoperative lung adenocarcinoma as the first relapse was limited to early in the wild-type EGFR patients, but occurred in later in the EGFR-mutant patients. **Keywords:** EGFR, CNS Metastasis, resected, DFS

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-010 Multivariate Survival Analysis of China IRESSA Charitable Aid Project in Shanghai Hong Jian[1], Baohui Han[2], Qiang Li[3], Shun Lu[1], Xiaolong Fu[4], Chunxue Bai[5], Liang Xue[6], Beili Gao[7], Meilin Liao[1] [1]*Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China,* [2]*Department of Respiratory Medicine, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China,* [3]*Department of Respiratory Medicine, Changhai Hospital Affiliated To Shanghai Second Military Medical University, Shanghai/China,* [4]*Department of Radiotherapy, Shanghai Cancer Hospital, Fudan University, Shanghai/China,* [5]*Department of Respiratory Medicine, Zhongshan Hospital, Fudan University, Shanghai/China,* [6]*Department of Thoracic Surgery, Zhongshan Hospital, Fudan University, Shanghai/China,* [7]*Department of Respiratory Medicine, Ruijin Hospital Affiliated To Shanghai Jiao Tong University, Shanghai/China*

Background: Since Jan 2007, China Charity Federation launched IRESSA Charitable Aid Project for advanced non small cell lung cancer which oral IRESSA was effective for 6 months and have failed previous chemotherapy or received first line IRESSA for EGFR mutation positive. This study investigated the survival and correlation influencing factor of China Charitable Aid Project in shanghai by COX multivariate analysis . **Methods:** A retrospective investigation enrolled advanced non small cell lung cancer patient of IRESSA Charitable Aid Project from Jan 2007 to 30 Jun 2013 at 7 centre in Shanghai . The patients oral IRESSA was effective for 6 months who have failed previous chemotherapy or received first line IRESSA for EGFR mutation positive. IRESSA 250mg QD was taken and prescribed monthly. Tumor assessment was performed every 8 weeks, patients continued to receive IRESSA until disease progression (timely withdraw) or unacceptable toxicity or no benefit from this project which was considered as slower progression(late withdraw). The patient were Followed up until 30 Aug 2014. The primary end point was OS and correlation influencing factor. Using the Kaplan-Meier and COX proportional hazards model analyze the correlation between survival and age, gender, smoking status, pathology, indications and timely withdraw of IRESSA. **Results:** A total of 1066 patients were enrolled, the median age was 64, including 339 cases of greater than or equal to 70. Most patients were female (845,79.3%) and no-smokers (992,93.1%), and 94.1% was adenocarcinoma. Indication for second and multiple line patients were 96.1%(1024). The midian PFS was 33 months (95%CI:29.8-36.2) , and the MST was 37 months (95%CI:32.5-41.5). COX multivariate analysis revealed timely withdraw group was significantly longer OS (hazard ration 1.627; 95%CI:1.378-1.922, p=0.000) , more than 70 years old, smoking and indication for second line patient was significantly worse OS (hazard ration 0.692; 95%CI:0.587-0.816, p=0.000; 0.714; 95%CI: 0.531-0.960, p=0.026; 0.498 ;95%CI: 0.265-0.935,p=0.03 respectively. **Conclusion:** 96.1% of the patient in Iressa charitable aid projects were second or multiple line treatment due to chemotherapy failure, PFS and OS still reached 33 and 37 months, significantly better than the historical reports. The possible reason was enrolled patients with IRESSA effective for 6 months , It could be EGFR mutation positive, of which no-smoking patients ratio were as high as 93.1%, they maybe have a better prognosis. Multivariate analysis showed OS was significantly prolonged in timely withdraw group after disease deteriorate. **Keywords:** non small cell lung cancer, IRESSA, Prognosis

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-011 Antitumor Activity of Tepotinib plus Gefitinib in Asian Patients with Met+ EGFRm+ NSCLC Dong-Wan Kim[1], Ross Soo[2], James Chih-Hsin Yang[3], Keunchil Park[4], Uz Stammberger[5], Huiiling Xiong[6], Christian Ihling[5], Yi-Long Wu[7] [1]*Department of Internal Medicine, Seoul National University Hospital, Seoul/Korea,* [2]*Medical Oncology, National University Cancer Institute Singapore, Singapore/Singapore,* [3]*Department of Oncology, National Taiwan University Hospital, Graduate Institute of Oncology & Cancer Research Center, National Taiwan University, Taipei/Taiwan,* [4]*Innovative Cancer Medicine Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/Korea,* [5]*Merck Kgaa, Darmstadt/Germany,* [6]*Merck Serono Pharmaceutical R&D Co., Ltd, Beijing/China,* [7]*Guangdong Lung Cancer Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou/China*

Background: c-Met abnormalities are key in resistance to EGFR TKIs in EGFRm+ NSCLC patients (pts). The highly selective c-Met inhibitor tepotinib (MSC2156119J) had promising activity in a phase I trial in pts with advanced solid tumors. We report phase Ib data from a trial evaluating tepotinib + gefitinib in pts with Met+ NSCLC (NCT01982955). **Methods:** Asian adults with locally advanced/metastatic NSCLC, Met+ status (2+/3+ c-Met protein overexpression by immunohistochemistry using CONFIRM anti-total c-MET [SP44] rabbit MAb [Ventana] or c-Met gene amplification on IQ FISH [Dako] [c-Met:CEP7 ratio ≥2 or <2.0 with >15 c-Met signals/cell in >10% of cells or clusters in >10% of tumor cell nuclei]) and ECOG PS 0/1 were eligible. EGFR mutation status was assessed using the therascreen® EGFR RGQ PCR Kit (QIAGEN). A 3+3 design was used for the phase Ib part; planned recruitment was 15-18 pts, who received tepotinib 300 or 500 mg p.o. + gefitinib 250 mg/d q3w. Primary objective: determine the RP2D of tepotinib for use in combination; secondary objectives: pharmacokinetics, safety, antitumor activity. **Results:** 14 pts have been enrolled (median age 65 years; male 43%; ECOG PS 0/1 2/12; median prior therapy regimens including an EGFR TKI 3.5). 3 pts received tepotinib 300 mg + gefitinib and 11 tepotinib 500 mg + gefitinib. No DLTs were observed; 4 pts had grade 3/4 treatment-related adverse events (amylase increase [n=3], lipase increase [2], decreased neutrophil count [1]). Best overall response by c-Met status (cut-off Jan 20, 2015) for the 12 evaluable pts is shown in the table. EGFR mutation status for these 12 pts was T790M and L858R mutation (n=2), L858R mutation alone (4), exon 19 deletion (4), no mutation detected using the therascreen® kit (2).

	Best overall response (n)		
n=12	**Partial response**	**Stable disease**	**Progression**
IHC			
2+	0	5	2
3+	4	0	1
FISH			
c-Met:CEP7 ratio >2	1	0	0
≥5 copies in >50% of cells	3	1	1
Negative	0	3	2
Not valid	0	1	0

Conclusion: The RP2D of tepotinib in combination with gefitinib has been confirmed as 500 mg/d in pts with advanced NSCLC. The data show evidence of antitumor activity and that response may be associated with c-Met status. The phase II trial will randomize ≈136 pts with T790M-/c-Met+ tumors who have failed first-line gefitinib to tepotinib 500 mg/d + gefitinib or cisplatin/pemetrexed. **Keywords:** MSC2156119J, EGFR mutation, c-Met, tepotinib

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-012 Efficacy of Chemotherapy after First-Line Gefitinib for EGFR-Mutant NSCLC Patients Tomohito Kuwako[1], Hisao Imai[1], Tomomi Masuda[1], Yosuke Miura[2], Reiko Yoshino[3], Kyoichi Kaira[4], Kimihiro Shimizu[5], Noriaki Sunaga[1], Yoshio Tomizawa[3], Shinichi Ishihara[6], Akira Mogi[7], Takeshi Hisada[1], Koichi Minato[2], Atsushi Takise[8], Ryusei Saito[3], Masanobu Yamada[1] [1]*Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Maebashi/Japan,* [2]*Division of Respiratory Medicine, Gunma Prefectural Cancer Center, Ohta/Japan,* [3]*Division of Respiratory Medicine, National Hospital Organization Nishigunma Hospital, Shibukawa/Japan,* [4]*Department of Oncology Clinical Development, Gunma University Graduate School of Medicine, Maebashi/Japan,* [5]*Department of Thoracic Visceral Organ Surgery, Gunma University Graduate School of Medicine, Maebashi/Japan,* [6]*Division of Internal Medicine, Isesaki Municipal Hospital, Isesaki/Japan,* [7]*Department of Surgical Science, Gunma University Graduate School of Medicine, Maebashi/Japan,* [8]*Division of Respiratory Medicine, Maebashi Red Cross Hospital, Maebashi/Japan*

Background: Gefitinib is an effective first-line chemotherapy for advanced non-small cell lung cancer (NSCLC) patients harboring sensitive *EGFR* mutations. However, whether second-line platinum combination chemotherapy after first-line gefitinib treatment shows similar effects to first-line platinum combination chemotherapy in these patients remains unclear. Therefore, we here aimed to investigate the efficacy of platinum combination chemotherapy after first-line gefitinib treatment in NSCLC patients harboring sensitive *EGFR* mutations. **Methods:** We retrospectively evaluated the clinical effects of second-line platinum combination chemotherapy after first-line gefitinib treatment in NSCLC patients harboring sensitive *EGFR*mutations (exon 19 deletion or exon 21 L858R mutation) at 5 institutions. All patients were initially treated with gefitinib (250 mg/day) followed by platinum combination chemotherapy as second-line chemotherapy. **Results:** Between January 2006 and December 2012, 42 patients (8 men, 34 women; median age, 63 years [range, 39–75 years]) were enrolled. The overall response rate, disease control rate, and median progression-free survival (PFS) were 26.2%, 61.9%, and 5.1 months, respectively, after the second-line treatment. The corresponding values for first-line gefitinib treatment were 69.0%, 95.2%, and 11.1 months, respectively. Moreover, second-line platinum combination chemotherapy with pemetrexed or bevacizumab-containing regimens was indpendently associated with improved PFS. **Conclusion:** Second-line platinum combination chemotherapy after first-line gefitinib treatment in NSCLC patients harboring sensitive *EGFR* mutations was effective and showed equivalent outcomes to first-line platinum combination chemotherapy. After failure of first-line gefitinib therapy, second-line platinum combination chemotherapy with pemetrexed or bevacizumab might result in improved PFS. **Keywords:** Advanced Non-Small Cell Lung Cancer, EGFR mutations, gefitinib, second-line platinum-based chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-013 Combination of Chemotherapy and Gefitinib as First-Line Treatment of Patients with Advanced Lung Adenocarcinoma and Sensitive EGFR Mutations Bo Jin, Yanjie Niu, Yanwei Zhang, Tianqing Chu, Aiqin Gu, Jun Pei, Baohui Han *Shanghai Jiaotong Univ. Affiliated Shanghai Chest Hospital, Shanghai/China*

Background: The results of fastact2 show that chemotherapy plus erlotinib significantly prolonged PFS and OS of patients with NSCLC. However, outcome of the combination therapy are similar to those reported in several trials of single-agent EGFR TKIs. So which is the optimal first-line treatment for patients who harbored a sensitive EGFR mutation? We need a head-to-head study to reply. **Methods:** 77 untreated patients with advanced lung adenocarcinoma who harbored sensitive EGFR mutations, and with ECOG PS 0-1, were randomly assigned to 3 groups. 25 patients were allocated to the combination therapy group (group A), received pemetrexed (500 mg/m(2) on day 1) plus carboplatin (AUC 5 on day 1) combined with gefitinib (250 mg/day on days 5-21) and repeated every 4 weeks for up to six cycles, then continued to receive pemetrexed combined with gefitinib every 4 weeks. 26 patients allocated to the chemotherapy group (group B), received the same chemotherapy regimen alone every 4 weeks for up to six cycles, then continued to receive pemetrexed alone every 4 weeks. 26 patients allocated to the gefitinib group (group C), and received gefitinib alone. All therapies of 3 groups were continued until progression or unacceptable toxicity or death. The primary endpoint was Median PFS. Analyses were done on an ITT basis. **Results:** Median PFS for patients in group A was 19.1months, 95% CI (17.1, 21.1), Median PFS for patients in group B was 5.5months, 95% CI (4.4, 6.8), Median PFS for patients in group C was 9.9months, 95% CI (7.0, 12.7). 6-month PFS was96.0% (24 of 25) in the group A, 38.5% (10 of 26) in the group B, and 73.1% (19 of 26) in the group C. ORR was 80.0% in the group A, 34.6% in the group B, and 61.5% in the group C. The most common grade 3-4 adverse events were neutropenia (3 [12.0%] of patients in the group A vs 4 [15.4%] in the group B vs 0 [0.0%] in the group C), fatigue (2 [8.0%] of patients in the group A vs 2 [7.7%] in the group B vs 0 [0.0%] in the group C), and liver dysfunction (3 [12.0%] of patients in the group A vs 0 [0.0%] in the group B vs 1 [3.8%] in the group C), skin allergy (0 [0.0%] of patients in the group A vs 1 [3.8%] in the group B vs 0 [0.0%] in the group C) **Conclusion:** Patients with lung adenocarcinoma who harbored a sensitive EGFR mutation have longer PFS if they are treated with pemetrexed plus carboplatin combined with gefitinib. **Keywords:** gefitinib, lung adenocarcinoma, EGFR mutation, chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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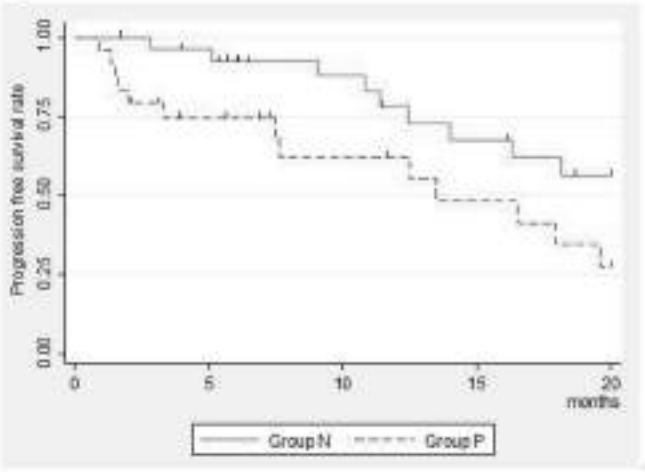
P3.01-014 Interleukin-6 Is a Valuable Predictive Marker for Therapeutic Effect of Gefitinib in Patients with Advanced NSCLC Harboring EGFR Mutations Yuka Kato[1], Katsuyuki Hotta[2], Tomoki Tamura[2], Takehiro Tanaka[3], Koichi Ichimura[3], Kadoaki Ohashi[2], Toshio Kubo[2], Eiki Ichihara[2], Mitsune Tanimoto[4], Katsuyuki Kiura[2] [1]*Center for Innovative Clinical Medicine, Okayama University Hospital, Okayama/Japan,* [2]*Respiratory Medicine, Okayama University Hospital, Okayama/Japan,* [3]*Department of Pathology, Okayama University Hospital, Okayama/Japan,* [4]*Okayama University Hospital, Okayama/Japan*

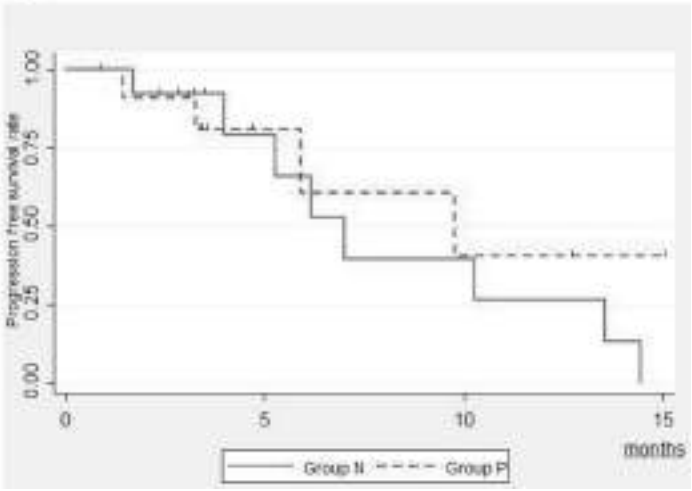
Background: Although epidermal growth factor receptor (EGFR) -tyrosine kinase inhibitors (TKIs) are the key drug in patients with EGFR-mutant Non-small-cell Lung Cancer (NSCLC), some of them can not respond well to its therapy. An overexpression of Interleukin (IL)-6 in tumor cells is postulated as a potential mechanism for such resistance or low sensitivity to EGFR-TKI in the preclinical models (PNAS 2010). Here, we evaluated clinically if tumor IL-6 level can be predictive for the effect of EGFR-TKI therapy. **Methods:** A total of 52 patients with advanced EGFR-mutation NSCLC who had received gefitinib were retrospectively assessed. The protein expression of IL-6 in the tumor cells was immunostained. Each specimen was assessed independently by 2 physicians (YK and TT) and 2 pathologists (KI and TT), and judged as positive if ≥ 50% of 100 tumor cells were stained positively (BJC 1999). Serum IL-6 level was measured by CLEIA in 11 (21%) of 52 patients. **Results:** Patients demographics were as follows: 24 men; median age, 66 yrs; PS 0-1, 48; stage IV, 22; Ad, 49; exon19, 29). Of these, 24 (46%) and 28 (54%) were defined as IL-6-postitive (group P) and IL-6-negative (group N), respectively. Group P had worse PFS (75% v 92% at 6m; p < 0.05), which was retained in the multivariate analysis (HR: 2.38; 95%CI: 1.00-5.68; p=0.05) (Fig1). In contrast, PFS in the platinum-based chemotherapy did not differ in groups P and N (p=0.47). The serum IL-6 level ranged from

0.75 to 23.80 pg/ml (median: 2.90 pg/ml), which correlated neither to that in the tumor cells (regression coefficient: 1.69, p = 0.29) nor PFS in gefitinib therapy (p = 0.44).

<Fig1>



<Fig2>

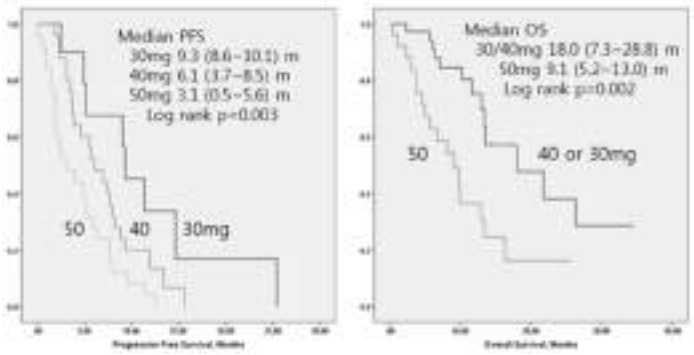


Conclusion: Patients in group P benefited less from gefitinib therapy. This might suggest the inhibition of IL-6 expression can improve the low sensitivity to EGFR-TKI especially in EGFR-mutation tumors with high IL-6 expression. **Keywords:** EGFR-TKI, NSCLC, IL-6, EGFR mutation

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-015 Efficacy, Safety and Dosage of Afatinib in Patients with NSCLC after Failure of Prior EGFR-TKI Young-Chul Kim, Hayoung Choi, Cheol-Kyu Park, In-Jae Oh, Ju-Sik Yun, Sang-Yun Song, Kook-Joo Na, Sung-Ja Ahn, Mee Sun Yoon, Yoo-Duk Choi, Hyun-Ju Seon *Lung and Esophageal Cancer Clinic, Chonnam National University Hwasun Hospital, Jeonnam/Korea*

Background: Afatinib is an irreversible ErbB family blocker that inhibits EGFR with activating mutations as well as the T790M resistance mutations. In Non-Small Cell lung cancer (NSCLC), afatinib has been evaluated in the LUX-Lung trials, with improvement in progression-free survival (PFS) in patients with acquired resistance to prior EGFR tyrosine kinase inhibitor (EGFR-TKI) treatment. This study investigated efficacy, safety and dosage of afatinib under a Named Patient Use (NPU) program in a single institution. **Methods:** We analyzed 60 patients with stage IV NSCLC that had been treated with ≥ 1 platinum based chemotherapy, and with activating EGFR mutation or disease control for ≥ 6 months with prior EGFR-TKIs (gefitinib or erlotinib). The daily dose of afatinib was started with 50mg, which was decreased to 40mg and 30mg according to adverse events and tolerability of patients. Of 60 analyzed patients, 2 received afatinib as 3rd line treatment, 27 as 4th line, 19 as 5th line and 12 as ≥ 6th line. Activating EGFR mutations were detected in 11 (exon 19 deletion) and 7 (L858R) cases. No activating mutation was found in 19 cases, and EGFR status was not studied in 23 cases. **Results:** Thirteen patients achieved partial remission, 33 stable disease, and 12 progression, and 2 not-evaluable resulting in a response rate of 21.7% and a disease control rate of 76.7%. Median PFS was 5.2 months (95% CI, 4.1 to 6.4 months) and median OS was 13.4m (95% CI, 12.6 to 14.2) since the commencement of afatinib. Toxicities leading to drug discontinuation were experienced by 4 patients (6.7%). Grade 3 diarrhea occurred in 10 patients (16.7%), and dosage reductions of afatinib were required in 35 patients, to 40mg in 25 and to 30mg in 10 cases. Patients were grouped by final dosage of afatinib (50mg in 25 cases, 40/30mg in 35 cases). The PFS and OS were significantly longer for patients whose dosage of afatinib were reduced to 40 or 30 mg, compared to patients without dosage reduction (7.5 vs 3.1m and 18.0 vs 9.1m, respectively, p<0.05).



Conclusion: Afatinib showed PFS of 5.2 months and OS of 13.4 months in selected patients after failure of prior EGFR-TKIs. Aggressive dosage reduction should be considered in the course of treatment with afatinib. **Keywords:** Dose, afatinib, EGFR-TKI, EGFR

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-016 Does Sequence of Cranial Radiotherapy Matter in EGFR Mutant Non-Small Cell Lung Cancer Patients with Brain Metastasis? Seonggyu Byeon, Jun Soo Ham, Se-Hoon Lee, Jong-Mu Sun, Jin Seok Ahn, Keunchil Park, Myung-Ju Ahn *Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Seoul/Korea*

Background: The incidence of brain metastasis in EGFR mutant advanced non-small cell lung cancer (NSCLC) is higher than EGFR wild type at the time of diagnosis. Although cranial radiotherapy is considered standard treatment for brain metastasis, EGFR tyrosine kinase inhibitors (TKIs) alone have shown promising activity with up to 80% of response in EGFR mutant NSCLC patients with brain metastasis. However, the role of sequential cranial radiotherapy in EGFR mutant NSCLC treated with EGFR TKIs remains to be determined. **Methods:** Advanced NSCLC patients harboring EGFR mutation (exon 19 deletion or L858R) with brain metastasis who were treated with EGFR TKIs were retrospectively reviewed. To investigate the role of cranial radiotherapy, we analyzed the clinical outcomes between patients treated with EGFR TKIs alone and those treated with cranial radiotherapy (WBRT or SRS) followed by EGFR TKIs (combination therapy). The primary end point was overall survival (OS) and secondary end points included intracranial and extracranial progression free survival (PFS). **Results:** A total of 573 patients who identified EGFR mutation and received EGFR TKIs treatment for NSCLC with brain metastasis from Jan 2007 to Dec 2013 at Samsung Medical Center were enrolled for analysis. Of all 573 patients, 121 patients had brain metastasis in initial work up. There were 38 males and 83 female, a median age was 59.5 years (range 30 – 80). All 121 patients were received gefitinib (n=103) or erlotinib (n=18) as EGFR TKI treatment for 1st line chemotherapy. 74 patients were treated with combination therapy (34 patients were taken SRS, 28 patients WBRT, 12 patients both), and 47 patients were treated with EGFR TKI alone. In combination therapy group, 32 patients had brain metastasis related symptoms.The median OS was 38.7 months [95% Confidence Interval 35.0 to 42.5] in combination therapy group and 28.6 months [95% CI 24.3 to 32.8] in EGFR TKI alone group (p=0.295). There were no significant differences in intracranial PFS (18.6 vs 19.7 months, p=0.343) and extracranial PFS (15.7 vs 15.3 months, p=0.574) between two groups. **Conclusion:** In this retrospective analysis, the combination therapy with cranial radiotherapy followed EGFR TKI did not improve OS and intracranial PFS compared with EGFR TKI alone therapy in EGFR mutant NSCLC patients with brain metastases. Further prospective studies are needed to refine the role of sequential cranial radiotherapy in EGFR mutant NSCLC treated with EGFR TKIs. **Keywords:** EGFT TKI, intracranial radiotherapy, NSCLC, Brain metastasis

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-017 P53 Disruptive Mutation Is a Negative Predictive Factor in EGFR M+ NSCLC Treated with TKIEfficacy and Safety of Gefitinib for Elderly Patients with EGFR Mutation Positive NSCLC Kei Kusaka, Takashi Hirose, Atsuhisa Tamura, Satoshi Ide, Minako Saito, Masahiro Ogiya, Eri Inoue, Hiroyuki Tashimo, Akira Yamane, Hirotoshi Matsui, Ken Ohta *The Center for Pulmonary Diseases, National Hospital Organization Tokyo National Hospital, Kiyose City, Tokyo/Japan*

Background: Elderly patients with lung cancer have been increasing. Of all cases of lung cancer 47% were 70 years or older and 14% were 80 years or older. Epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) is a key drug for patients with EGFR mutation positive advanced non-small cell lung cancer (NSCLC). Although treatment of gefitinib is known to have fewer myelosuppression and gastrointestinal adverse events than cytotoxic chemotherapy, treatment of gefitinib frequently has skin rash and liver dysfunction. Until now, there have been few reports of the efficacy and

safety of gefitinib in elderly patients with advanced NSCLC. Therefore, the efficacy and safety of treatment of gefitinib in elderly patients with EGFR mutation positive advanced NSCLC have yet to be confirmed. **Methods:** We retrospectively assessed the efficacy and safety of gefitinib in 52 patients with EGFR mutation positive advanced NSCLC who were 70 years older and were treated with gefitinib. In addition, we compared the frequency and severity of adverse effects between patients 70 to 79 years and patients 80 years or older. **Results:** Of 52 patients, 35 (67%) were female and 13 (25%) were performance status of 2 or more, and the median age was 75 (range, 70-89 years). Fifteen patients (29%) were 80 years or older. All patients were adenocarcinoma. The type of EGFR mutation was as follows: 28 patients (54%) had exon 19 deletion, 23 (44%) had exon 21 L858R, and 1 (2%) had exon 18 G719A. The response rate was 73.1% (95% CI, 59.0% to 84.4%) and the disease control rate was 90.4% (95% CI, 79.0 to 96.8%). The median time to progression was 10.7 months (range, 0 to 36.2 months). The median survival time was 23.8 months (range, 0.2 to 65.6 months). The common adverse events were skin rash (52%), liver dysfunction (29%), diarrhea (25%), and interstitial lung disease (4%). Doses of gefitinib were reduced in 12 patients (23%) and discontinued in 11 patients (21%) due to toxicity, mainly skin rash and liver dysfunction. There were no differences in response rates, disease control rates, survivals, adverse events, and dose reduction rates between patients 70 to 79 years and patients 80 years or older. **Conclusion:** Treatment of gefitinib is highly effective for elderly patients with EGFR mutation positive advanced NSCLC, although dose reduction rates were more frequent in elderly patients than those in recently published trials in younger patients. **Keywords:** EGFR-TKI, elderly

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-018 Icotinib for Control of Leptomeningeal Carcinomatosis in Non-Small Cell Lung Cancer with Sensitive EGFR Mutations Yun Fan[1], Lei Gong[2], Zhiyu Huang[2], Lulu Miao[2], Yanjun Xu[2] [1]*Zhejiang Cancer Hospital,Key Laboratory Diagnosis and Treatment Technology on Thoracic Oncology , Hangzhou, China, Hangzhou/China,* [2]*Zhejiang Cancer Hospital, Hangzhou/China*

Background: The incidence rate of leptomeningeal carcinomatosis (LC) has been increased in advanced non-small cell lung cancer (NSCLC) patients, especially with *EGFR* mutations. The purpose of this study was to evaluate the efficacy of icotinib for the control of LC in NSCLC with sensitive *EGFR* mutations. **Methods:** Twenty-one NSCLC patients with sensitive *EGFR* mutations and cytologically proven LC diagnoses between 2011 and 2014 at Zhejiang Cancer Hospital were retrospectively reviewed. **Results:** Ten patients had exon 21 point mutations and eleven patients had exon 19 deletional mutations. Sixteen of 21 patients received standard dose of icotinib (125 mg/day, three times a day) after LC diagnoses. The other five patients had already used icotinib and switched to double dose of icotinib (250 mg/day, three times a day) after LC occurrence. Eight patients received intrathecal chemotherapy, and nine of them were treated with combined whole-brain radiotherapy. Eighteen of 20 patients (90.0%) showed improvement of dizziness and headache. Seventeen of 21 patients (80.9%) had an improved Eastern Cooperative Oncology Group *performance status (ECOG PS)* score after icotinib treatment. The median overall survival was 10.1 months (95% CI: 8.4–12.0). Univariate analysis showed that the poor ECOG PS score (PS > 2), coexisting parenchymal brain metastasis, and the taken of icotinib were unfavorable prognostic factors for patient survival.The ECOG PS scare was an only independently predictor for survival in the multivariable analysis. **Conclusion:** This study suggested that icotinib had efficacy for the control of LC in NSCLC with sensitive *EGFR* mutations and was well tolerated. The Further prospective study is warranted. **Keywords:** icotinib, non-small cell lung cancer, EGFR mutation, leptomeningeal carcinomatosis

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-019 Treatment and Clinical Evolution of a Cohort of 105 EGFR Mutant Patients from a Single Institution Helano C. Freitas, Augusto O. Saito, Fabio N. Santos, Izabela W. Cunha, Aldo L.A. Dettino, Mariana P. Macedo, Graziela Z. Dal Molin, Vladmir C.C. Lima *Oncologia Clínica, A C Camargo Cancer Center, Sao Paulo/Brazil*

Background: Lung cancer is among the most common malignancies in Brazil. The use of tyrosine-kinase inhibitors (TKI) is nowadays a solidly stablished treatment strategy for *EGFR* mutaion bearing NSCLC metastatic tumors. In this study we describe the clinical evolution of a cohort of 115 EGFR-mutant NSCLC patients from a single brazilian institution. **Methods:** We describe a retrospective cohort of 115 consecutive patients bearing metastatic *EGFR* mutated NSCLC, treated at A.C. Camargo Cancer Center, Sao Paulo, from August/2010 to December/2014. Patients were older than 18y and had to have a histologically confirmed NSCLC dianosis. Clinical and pathological data was extracted from their eletronical medical charts. Chi-square statistics, or Fisher's exact test when appropriate, was used to compare proportions among groups, Kaplan-Meier method was used for survival analysis and log-rank's test was performed to compare survival curves. **Results:**Median age was 64y, 62% of patients were female, 94% had adenocarcinoma and 22% were smokers/former smokers. Data about treatment and survival was available for 85/115 patients. Eighty eight percent (75/85) of them were metastatic at diagnosis, of whom 52% (39/75) received a TKI in first line, 24% (18/75) in second line, 5% (4/75) in third/later lines and 16% were never treated with a TKI. Median progression free survival (PFS) was 13.9 months (m) for first line TKI and 11.4m for TKI treatment in second line (p=0.028). Median PFS for first line platin-based chemotherapy was 9.6m as compared to 3.1m for platin-based chemotherapy in second line (p=0.001). PFS with TKI treatment was numerically superior but not statistically significant for patients bearing tumors with exon 19 deletions as compared to L858R mutantions (22.9m vs 13.4m, respectively; p=0.42). There was no difference in overal survival (OS) between patients treated with TKI in first or second line. Median OS for patients receiving first line TKI was 36.3m and was not reached for patients that received TKI in second line (p=0.61). **Conclusion:** OS survival was not different for patients bearing *EGFR* mutated NSCLC tumors treated in first or second line, despite a longer PFS for TKI given as first line therapy. **Keywords:** EGFR testing, EGFR mutation frequence, Rare EGFR mutations

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-020 Updated Data from JP28927 Study of Alectinib in ALK+ NSCLC Patients with or without History of ALK Inhibitor Treatment Katsuyuki Hotta[1], Toyoaki Hida[2], Kazuhiko Nakagawa[3], Takashi Seto[4], Miyako Satouchi[5], Makoto Nishio[6], Haruyasu Murakami[7], Yuichiro Ohe[8], Koji Takeda[9], Takuya Yoshimoto[10], Tomohiro Tanaka[10], Tomohide Tamura[11] [1]*Okayama University Hospital, Okayama/Japan,* [2]*Aichi Cancer Center, Nagoya/Japan,* [3]*Kinki University Faculty of Medicine, Osaka-Sayama/Japan,* [4]*National Kyusyu Cancer Center, Fukuoka City/Japan,* [5]*Hyogo Cancer Center, Akashi/Japan,*[6]*The Cancer Institute Hospital of Jfcr, Tokyo/Japan,* [7]*Shizuoka Cancer Center, Shizuoka/Japan,* [8]*National Cancer Center Hospital, Tokyo/Japan,* [9]*Osaka City General Hospital, Osaka/Japan,* [10]*Chugai Pharmaceutical Co., Ltd, Tokyo/Japan,*[11]*St.Luke'S International Hospital, Tokyo/Japan*

Background: Alectinib, a next generation ALK inhibitor, was granted approval in Japan 2014, since it showed good efficacy and tolerability in *ALK*+ NSCLC patients without previous ALK inhibitor treatment in Phase I/II study (AF-001JP). We also reported its promising response and good tolerability for crizotinib pre-treated patients in JP28927 study (ESMO 2014). This report describes the update of efficacy and safety result in JP28927 study. **Methods:** Patients (with/without prior ALK inhibitor treatment) who had *ALK*+ NSCLC were enrolled in JP28927. Patients received alectinib (300mg) twice daily; treatment was continued until the investigator determined lack of clinical benefit. **Results:** Thirty-five patients were enrolled into JP28927 study. Median follow-up duration was 400 days (35-457 days). The median progression free survival (PFS) of 35 patients was 13.9 months (95%CI: 11.1- NR). Among 30 patients with the target lesions at base line, the overall response rate (ORR) was 70% (95%CI: 50.6-85.3) with rapid response (the median time to response was 1.2 months [95%CI: 1.1-2.1]). Twenty-three out of 35 patients had been confirmed the progressive disease with crizotinib treatment. Their median PFS was 12.9 months (95%CI: 3.9-NR). Twenty out of 23 patients had the target lesions at base line. ORR was 65% (95%CI: 40.8-84.6) and the median time to response was 1.2 months (95%CI: 1.1-1.3). The treatment-related adverse events (AEs) observed in more than 10% of the patients were constipation (31.4%), dysgeusia (25.7%), WBC count decreased (22.9%), neutrophil count decreased (22.9%), vomiting (14.3%), rash (14.3%), blood bilirubin increased (14.3%) and AST increase (14.3%). Treatment-related Grade 3 AEs, i.e. pulmonary thrombosis, lymphocyte count decrease, hypophosphatemia, were observed in 3 patients. No treatment-related Grade 4 or 5 AEs were observed. **Conclusion:** The updated results in JP28927 study once again endorsed our previous reports which had indicated alectinib's promising response even for *ALK*+NSCLC patients who failed to crizotinib treatment. **Keywords:** Alectinib, ALK+ NSCLC, ALK Inhibitor

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-021 New Perspectives for the Patients with ALK Positive Lung Adenocarcinomas, after Failure of Crizotinib Therapy. A Single Institution Experience Milos Pesek[1], Petr Grossman[2], Marek Minarik[3], Gabriela Krakorova[1], Ondrej Fiala[4] [1]*Department of Pneumology, University Hospital Pilsen, Plzen/Czech Republic,* [2]*Deratment of Pathology, Medical School and Teaching Hospital in Pilsen, Charles University, Pilsen/Czech Republic,* [3]*Center for Applied Genomics of Solid Tumours, Genomac Research Institute, Prague, Czech Republic, Prague/Czech Republic,* [4]*Department of Oncology and Radiotherapy, University Hospital Pilsen, Pilsen/Czech Republic*

Background: Patients suffering from ALK-rearranged non-small cell lung cancer (NSCLC) should have significant benefit of ALK inhibitor targeted therapy by crizotinib. Even if high frequency of response rate to this therapy is documented, wast majority of those tumors become resistent due to overgrow of secondary resistent mutations bearing tumour cells. Such resistence should be overcome with the help of an alternative second generation ALK inhibitors. **Methods:** We present our diagnostic and therapeutic single institution experience in patients having ALK-rearranged NSCLC, as examined by FISH. We also present two case reports of patients treated by a second generation ALK inhibitor (ceritinib) after failure of the initial crizotinib therapy. **Results:** Between January 2011 and January 2015, a total of 595 tumour tissue samples were prospectively analysed for a presence of ALK rearrangements. A conclusive FISH result was obtained from a subset of 483. ALK rearranement was found in 15 patients (3.1%). The group consisted of 9 males and 6 females, with a median age of 65. 13 of the tumours were adenocarcinomas, 2 adenosquamous carcinomas. 8 patients were nonsmokers, seven were smokers. Consequently, 6 patients were treated by crizotinib while the rest did show a rapidly progressing tumours. 3 of the 6 crisotinib patients had a documented benefit from the therapy lasting for 22, 15 and 6 months.Finally, after failure of crizotinib, 2 patients reached a second partial remission on ceritinib,lasting 9 and 6 months. **Conclusion:** Targeted therapy of ALK-positive tumours is capable to prolong survival of patients quite significantly. In crizotinib - resistent tumours, second generation ALK inhibitors (such as ceritinib in this case), maybring further benefits to patients. **Keywords:** Ceritinib, NSCLC, ALK, crisotinib

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-022 A Prospective Multicenter Study for ALK IHC+ Metastasized NSCLC
Erik Thunnissen[1], Bg Skov[2], Jens Sorensen[3], Anders Mellemgaard[4], H.J.M. Groen[5], Ed Schuuring[6], Wim Timens[6], Michel V.D. Heuvel[7], J. De Jong[8], Kim Monkhorst[8], Joop De Langen[9], Miep Van Der Drift[10], Monika Looijen-Salamon[11], Anne-Marie Dingemans[12], Ernst-Jan M. Speel[13], Suzy Samii[14], F Duplaquet[15], Birgit Weynand[16], X Durando[17], Frederique Penault-Llorca[18], Patrick Pauwels[19], Keith Kerr[20], Marianne Nicolson[21], Stephen P. Finn[22], O Schildgen[23], Lukas Bubendorf[24], S Rohtschild[25], Annemieke Hiemstra[1], Birgit Witte[26], Egbert Smit[27] [1]*Department of Pathology, VU University Medical Center, Amsterdam/Netherlands,* [2]*Department of Pathology, Copenhagen University Hospital, Rigshospitalet, Copenhagen/Denmark,* [3]*Department of Oncology, Copenhagen University Hospital, Rigshospitalet, Copenhagen/Denmark,* [4]*Department of Oncology, Herlev University Hospital, Copenhagen/Denmark,* [5]*Department of Pulmonary Diseases, University of Groningen and University Medical Center Groningen, Groningen/Netherlands,* [6]*Department of Pathology and Medical Biology, University of Groningen and University Medical Center Groningen, Groningen/Netherlands,* [7]*Department of Thoracic Oncology, The Netherlands Cancer Institute – Antoni Van Leeuwenhoek Hospital, Amsterdam/Netherlands,* [8]*Department of Pathology, The Netherlands Cancer Institute – Antoni Van Leeuwenhoek Hospital, Amsterdam/Netherlands,* [9]*Department of Pulmonary Diseases, VU University Medical Center, Amsterdam/Netherlands,* [10]*Department of Pulmonary Diseases, Radboud University Medical Center, Nijmegen/Netherlands,* [11]*Department of Pathology, Radboud University Medical Center, Nijmegen/Netherlands,* [12]*Department of Pulmonary Diseases, Maastricht University Medical Center, Maastricht/Netherlands,* [13]*Department of Pathology, Maastricht University Medical Centre, Maastricht/Netherlands,* [14]*Department of Pulmonary Diseases, Deventer Hospital, Deventer/Netherlands,* [15]*Department of Pneumology, CHU Mont-Godinne, Catholic University of Louvain (Ucl), Yvoir/Belgium,* [16]*Department of Pathology, CHU Mont-Godinne, Catholic University of Louvain (Ucl), Yvoir/Belgium,* [17]*Department of Medical Oncology, Centre Jean Perrin, Clermont-Ferrand/France,* [18]*Department of Pathology, Centre Jean Perrin, Clermont-Ferrand/France,* [19]*Department of Pathology, Antwerp University Hospital, Edegem/Belgium,* [20]*Department of Pathology, Aberdeen Royal Infirmary, Aberdeen/United Kingdom,* [21]*Department of Oncology, Aberdeen Royal Infirmary, Aberdeen/United Kingdom,* [22]*Department of Pathology, University of Dublin, Trinity College and St. James'S Hospital, Dublin/Ireland,*[23]*Institute of Pathology, University Medical Center Witten/Herdecke, Cologne/Germany,* [24]*Insitute of Pathology, University Hospital Basel, Basel/Switzerland,* [25]*Department of Medical Oncology, University Hospital Basel, Basel/Switzerland,*[26]*Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam/Netherlands,* [27]*Departments of Pulmonary Diseases and Thoracic Oncology, VU University Medical Center and the Netherlands Cancer Institute - Antoni Van Leeuwenhoek, Amsterdam/Netherlands*

Background: Pulmonary adenocarcinomas may harbor driver mutations, that sensitize tumors to drugs that specifically target the genetic alteration. Metastasized NSCLC with an EML4-ALK translocation are sensitive to a range of tyrosine kinase inhibitors, of which crizotinib is most extensively studied. ALK-positive NSCLC was determined in a phase III trial with fluorescence in situ hybridisation (ALK FISH+). ALK immunohistochemistry (IHC) seems to run parallel with ALK FISH positivity. However discrepant cases occur, which include ALK IHC+ FISH-. The aim of this study is to collect cases with ALK IHC+ and compare within this group response to crizotinib treatment of ALK FISH+ cases with ALK FISH- cases. **Methods:** A prospective multicenter investigator initiated research study was started in Europe. This study is supported by Pfizer. Cases diagnosed with ALK IHC+ lung cancer (5A4 or D5F3) treated with crizotinib are collected centrally. Slides are submitted centrally for validation of ALK IHC (with ETOP and Ventana protocol), ALK FISH (with Vysis probes) and DNA analysis. **Results:** The study started on April 1 2014 and is still open. Currently 10 centers are actively participating. 1443 cases have been examined with ALK IHC of which 39 (2.7%) recorded positive. 24 cases have been submitted to the database. The validation process is still ongoing. The fraction of ALK IHC+ FISH- cases is low. Two cases with ALK IHC+ FISH- metastastatic NSCLC responded to crizotinib treatment. In two cases ALK positivity could not be confirmed (ALK IHC- and ALK FISH-). These patients had progressive disease following crizotinib treatment. **Conclusion:** A clinically relevant question what the effect of ALK inhibitor treatment is on metastatic NSCLC ALK IHC+ FISH- compared to ALK IHC+ FISH+ is examined. Other centers with interested collaborating physicians are invited to participate.
Keywords: ALK* immunohistochemistry*NSCLC* treatment

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-023 A Phase II Trial of AUY922, a Heat Shock Protein 90 (HSP90) Inhibitor, in ALK-Positive Lung Cancer Patients Previously Treated with ALK Inhibitors
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Background: Anaplastic lymphoma kinase (ALK) fusions are key oncogenic drivers in non-small cell lung cancer (NSCLC) that confer sensitivity to treatment with ALK tyrosine kinase inhibitors (TKIs), such as crizotinib. Despite this activity, ALK-positive patients ultimately develop resistance to ALK TKIs. In preclinical models, ALK fusion proteins are HSP90 clients and remain sensitive to HSP90 inhibition despite acquired resistance to ALK TKIs. We therefore designed a phase II trial of the HSP90 inhibitor AUY922 in patients with previously treated, ALK-positive NSCLC. **Methods:** In this single-arm, multicenter, open-label study, we enrolled patients with advanced, ALK-positive NSCLC who had failed at least one prior ALK inhibitor. Key eligibility criteria included ECOG PS 0-2, measurable disease based upon RECIST version 1.1, and presence of an ALK rearrangement by FISH. Participants were treated with AUY922 at a dose of 70 mg/m^2 IV once weekly until disease progression, unacceptable toxicity, or death. The primary endpoint was objective response rate (ORR) according to RECIST version 1.1. Key secondary endpoints included safety, progression-free survival (PFS), and disease control rate (DCR). The planned sample size was 20 patients. **Results:** Between December 2012 and December 2014, 6 patients were enrolled. Median age was 52.5 years (range 42-54 years). A majority of patients (83%) were female. The median number of prior lines of therapy was 3 (range 2-4). All patients had previously received at least 1 ALK TKI (crizotinib n=5, alectinib n=1), and 2 patients had received a second ALK inhibitor (ceritinib n=2). Most patients (n=4) had received an ALK inhibitor as the last line of therapy prior to enrollment. Among the 6 patients enrolled, no objective responses were observed (ORR 0%). Three patients (50%) had a best response of stable disease (SD), but none remained on therapy beyond 3 months from the time of enrollment (Table). The median PFS was 1.43 months (95% CI 1.3-2.8 months). Common adverse events (AEs) included grade 1-2 diarrhea (83%), vision disorders (50%), fatigue (50%), and constipation (33%). The only treatment-related grade 3 AE was alkaline phosphatase elevation in 1 patient. The study was closed due to poor accrual in December 2012.

Table 1

Patient	Best Response RECIST v1.1.	Progression-Free Survival (months)
1	-4.9%	2.80
2	36.5	0.73
3	5.1	1.03*
4	121.9	1.43
5	11	2.60
6	69.5	1.30
* Censored (Discontinued due to toxicity)		

Conclusion: Although limited by a small sample size and premature closure, this study suggests that AUY922 is associated with minimal anti-tumor activity in ALK-positive patients previously treated with ALK inhibitors. Combinations of ALK TKIs and HSP90 inhibitors may represent an alternative strategy, and several such studies are now ongoing.
Keywords: ALK, Heat shock protein 90, HSP90

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-024 The Effect of Pemetrexed as First Line Chemotherapy in Advanced Non-Small-Cell Lung Cancer with Anaplastic Lymphoma Kinase Gene Rearrangements
Di Ma, Junling Li, Xuezhi Hao, Puyuan Xing, Yan Wang *Medical Oncology, Cancer Institute and Hospital Chinese Academy of Medical Sciences Peking Union Medical College, Beijing/China*

Background: The efficacy of pemetrexed-based first-line chemotherapy in ALK-positive NSCLC has been documented in several studies. More data for Chinese population are still needed. **Methods:** We retrospectively reviewed the chart of 34 patients with ALK-positive advanced NSCLC. All of them had received pemetrexed as the first-line chemotherapy in our hospital from May 2011 to October 2014. We analyzed the clinical characteristics and treatment outcomes of these patients.The primary end points were response rate and progression-free survival. **Results:** The median age was 52 years (range from 34 to 76) and 58.8% (20/34) of the patients were never smokers. All tumors were adenocarcinoma. There were two cases harboring ALK translocation and EGFR mutation. Pemetrexed combined with platinum was administered in the first-line setting and the median treatment cycle was 4.5. The median progression-free survival (PFS) of ALK-positive patients was 8.8 months (95%CI 7.397-10.213). At the time of analysis, 7 with PR (20.6%), 23 with SD (67.6%), 4 with PD (11.8%) and no CR achieved. The objective response rate was 20.6% (7/34), and the disease control rate was 88.2% (30/34). Common adverse events with pemetrexed were neutropenia (52.9%), nausea (58.8%), transaminase elevation (29.4%) and fatigue (9.3%), mainly in grade 1 or 2. **Conclusion:** Pemetrexed is efficient and well tolerated as first-line treatment for ALK-positive NSCLC in Chinese population. Thus, pemetrexed might provide an alternative option for the treatment of ALK-positive lung adenocarcinoma.
Keywords: Anaplastic lymphoma kinase, lung cancer, pemetrexed, Progression-free survival

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-025 Real-Life Experience and Clinical Characterization in Patients with ALK Positive NSCLC: A Multicentre Study of the Austrian Lung Cancer Group
Maximilian J. Hochmair[1], Sophia Holzer[1], Andrea Mohn-Staudner[1], Klaus Kirchbacher[2], Ulrike Setinek[1], Irene Kapfhammer[1], Madeleine Arns[3], Arschang Valipour[1], Georg Christian Funk[1], Andreas Fazekas[1], Otto Chris Burghuber[1] [1]*Department of Respiratory and Critical Care Medicine, Otto Wagner Hospital, Vienna/Austria,* [2]*Wilhelminenspital, Vienna/Austria,* [3]*Landeskrankenhaus Hochegg, Hochegg/Austria*

Background: ALK translocations, occuring in 3-5% of patients with NSCLC (non-small

cell lung cancer), has improved the treatment for these patients. We examined the clinical characteristics, diagnosis modalities and treatment outcomes of these ALK + NSCLC patients. **Methods:** Data from patients with adenocarcinoma and NSCLC/NOS (Not Otherwise Specified) whose tumors were routinely analyzed for EML4-ALK were reviewed. Patient characteristics including age, sex, race, smoking history, localization of biopsy, response to ALK inhibitors and presence/absence of brain metastasis were collected. All data were obtained from 4 hospitals in Austria with high expertise in the management of lung cancer from August 2011 till October 2014. EML4-ALK was identified by a two-step procedure. First an immunhistochemical staining was done with the Ventana anti ALK (D5F3), Opti View DAB IHC DetectionKit and Opti View Amplifikation Kit®. Further, all positive cases (weak to strong) were tested by ALK FISH (dual colour breakapart FISH/Abbott Vysis®). **Results:** 1754 consecutive patients were tested for EML4-ALK mutation. EML4-ALK positive immunohistochemical staining was found in 226 patients (12.9 %). 37 of these patients (2.1 %) showed positive ALK FISH analysis. However 2 patients with strong immunohistochemical staining showed no rearrangement in FISH analysis. These 2 patients were also treated with an ALK Inhibitor and showed tumour shrinkage. From these EML4-ALK translocation positive 39 patients, 23 patients were women and 16 men. 24 patients (61%) were Never-Smoker, 9 were former smokers (23 %) and 6 smokers (15 %). Biopsies were taken in 24 patients from the primary tumor and in 8 patients from the lymph nodes; in 6 patients the analysis was performed by drainage of pleura effusions and in 1 patient by drainage of a pericardial effusion. 24 patients received an ALK inhibitor. 5 patients had a complete response, 18 patients a partial response, 0 patients a stable disease and 1 patient showed a progressive disease. 15 patients did not receive an ALK Inhibitor, because they were in an operable stage. Before therapy with an ALK inhibitor, 5 patients had initial brain metastasis and additional 8 patients developed brain metastasis during treatment. **Conclusion:** ALK rearrangements are observed in 2.2 % of Adenocarcinoma and NSCLC/NOS. It can be detected in all patients independent of any clinical characterization and/or smoking behavior. Therefore, reflex testing is recommended, since patients treated with an ALK inhibitor had a clear benefit from treatment. **Keywords:** EML4-ALK, Real-life experience , targeted therapy, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-026 Short-Term Efficacy of Helical Tomotherapy in the Treatment of Intracranial Multiple Brain Metastases of Lung Cancer Feng Wang, Rongqing Li, Yong Zhang *Radiotherapy, First Affiliated Hospital of Kunming Medical University, Kunming/ China*

Background: To explore the dosimetry advantages, adverse reactions and efficacy of helical tomotherapy in the treatment of intracranial multiple brain metastases of lung cancer. **Methods:** Seven patients with intracranial multiple brain metastases from Feb., 2012 to May 2014 were treated with helical tomotherapy. Whole-brain radiotherapy: the clinical target volume (CTV) was 45 Gy/25 times and gross tumor volume (GTV) was 50～58 Gy/25 times, 5 times in a week. **Results:** Both the homogeneity and shape-adaptability of radiation in 7 patients were better. The response rate came up to 78%, and the adverse reactions could be tolerated. **Conclusion:** Helical tomotherapy in the treatment of intracranial multiple brain metastases of lung cancer has better dose distribution and short-term efficacy. It provides a new therapeutic platform for the treatment of multiple brain metastases of lung cancer. **Keywords:** multiple brain metastases; helical tomotherapy; radiotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-027 Lung Adenocarcinoma in Patients from the Colombian Coffee Zone Gustavo Rojas[1], Jaime A. Echeverri F[2], Marco Kimmel[1], Jose W. Martinez[1], Paula Londno[1] [1]*Oncologos Del Occidente S.A., Pereira/Colombia,* [2]*Pulmonary Medicine, Oncologos Del Occidente, Pereira/Colombia*

Background: During 1998 and 2013 the "Colombian Coffee Zone" (conformed by Caldas, Quindio, and Risaralda states) had an increase of 105 mortality cases of Bronchi and lung malignant tumors, as reported in death certificates. **Methods:**This is an observational and descriptive study that was made in patients at Clinica Oncologos del Occidente in the year 2014 and the Information was taken from the Clinical History Administration System (SAHICO). Thereafter, pending data was collected, by phone calls to patients or patient's family, according to every case. Patients were interviewed to know their actual performance status and, in case of death, date and basic cause of death was asked. **Results:** SAHICO reported 178 patients with lung cancer. From these patients, 33 did not have a correct diagnosis. Basically, they did not have a histology report. This happens in patients that consulted with a clinical presentation compatible with a pulmonary origin neoplasia and radiology reports concluding in thorax tumors, which had a lung dependency. But such patients had a very low performance status, because they did not assist to the second consult, they never started treatment, and finally because they died. Among these 178 patients 3 had other diagnoses, which initially were unclear: one had Gastric Cancer, the second had prostate carcinoma and the last one had breast cancer. Also, 12 Patients came with the diagnosis of Adenocarcinoma or Squamous cellular lung cancer, they only went to radiation treatment with us and the rest of the clinical treatment was taken in another clinic, or they died before treatment initiates, this group was called *without following*. There were 38 patients with adenocarcinoma. The proportion between Squamous Cellular and Adenocarcinoma was 1.7 patients with squamous cellular carcinoma for every patient with Adenocarcinoma. 28 patients were tested for the EGFR mutation analysis, from these, 5 had the EGFR mutation. The average age of the patients with adenocarcinoma was 64.2 years old. The median survival time found was 167.6 days and the calculation for confidence interval of 95% ($CI_{95\%}$ 67.3 to 267.9) **Conclusion:** Of the population evaluated, proportion of lung adenocarcinoma (ratio of tumors), is different than other reports of the world. Outcome is like patients with another tumors, because they consult to late, in advance stage of disease, then mortality is higher and shorter survival. Implementation in diagnosis of detection of epidermic growth factor receptor mutation (EGFR) in the institution has been of great value to reorient pharmacological treatment. **Keywords:** Lung Neoplasms, Survival, Carcinoma Bronchogenic

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-028 Serum Levels of C-Reactive Protein Predict Poor Outcome of Patients with Advanced-Stage NSCLC Treated with Erlotinib Ondrej Fiala[1], Milos Pesek[2], Jindrich Finek[1], Ondrej Topolcan[3], Jaroslav Racek[4], Marek Minarik[5], Lucie Benesova[6], Zbynek Bortlicek[7], Tomas Buchler[8] [1]*Department of Oncology and Radiotherapy, Medical School and Teaching Hospital in Pilsen, Charles University, Pilsen/ Czech Republic,* [2]*Department of Pneumology, Medical School and Teaching Hospital in Pilsen, Charles University, Pilsen/Czech Republic,* [3]*Department of Nuclear Medicine, Medical School and Teaching Hospital in Pilsen, Charles University, Pilsen/Czech Republic,* [4]*Istitute of Clinical Biochemistry and Hematology, Medical School and Teaching Hospital in Pilsen, Charles University, Pilsen/Czech Republic,* [5]*Center for Applied Genomics of Solid Tumours, Genomac Research Institute, Prague, Czech Republic, Pilsen/Czech Republic,* [6]*Center for Applied Genomics of Solid Tumours, Genomac Research Institute, Prague/Czech Republic,* [7]*Institute of Biostatistics and Analysis, Faculty of Medicine, Masaryk University, Brno/Czech Republic,* [8]*Department of Oncology and First Faculty of Medicine, Charles University and Thomayer Hospital, Prague/Czech Republic*

Background: Erlotinib is a low-molecular weight tyrosine kinase inhibitor (TKI) directed at epidermal growth factor receptor (EGFR), widely used in the treatment of locally-advanced or metastatic stage NSCLC. Although introduction of EGFR-TKIs have significantly extended survival of advanced-stage NSCLC patients, their efficacy in the entire patient population is relatively low, especially in Caucasians. Aside from activating *EGFR* gene mutations, no reliable biochemical or molecular predictors of response to erlotinib have been established. The aim of our retrospective study was to evaluate the association of baseline serum levels of C-reactive protein (*CRP*) with outcomes in patients with advanced-stage NSCLC treated with erlotinib. **Methods:** We retrospectively analysed clinical data of 595 patients with advanced-stage NSCLC (IIIB or IV) treated with erlotinib. Serum CRP was measured using immunoturbidimetric method. **Results:** Before the treatment initiation, high baseline levels of CRP (≥ 10 mg/l) were measured in 387 (65%) patients and normal levels (< 10 mg/l) were measured in 208 (35%) patients. The median PFS and OS for patients with high CRP was 1.8 and 7.7 compared to 2.8 and 14.4 months for patients with low CRP ($p<0.001$ and $p<0.001$). The multivariate Cox proportional hazards model revealed that CRP (HR=1.57, $p<0.001$), *EGFR* status (HR=2.22, $p<0.001$), stage (HR=1.31, p=0.013) and ECOG PS (HR=1.22, p=0.024) were significantly associated with PFS and also with OS (HR=1.63, $p<0.001$; HR= 1.97, p=0.011; HR=1.44; p=0.007 and HR=1.72, p<0.001, respectively). **Conclusion:** The results of the conducted retrospective study suggest that the baseline level of CRP was independently associated with PFS and also with OS. CRP is commonly used biomarker which is simple and easy to detect and thus it is feasible for the use in the routine clinical practice. *This study is supported by Ministry of Health, Czech Republic - conceptual development of research organization Faculty Hospital in Pilsen - FNPl, 00669806 and by the project CZ.1.05/2.1.00/03.0076 from European Regional Development Fund.* **Keywords:** Erlotinib, NSCLC, C-reactive protein, biomarker

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-029 Factors Impacting Delay in Timely Care for Patients Diagnosed with Lung Cancer in Victoria Sue Evans, Arul Earnest, Meera Senthuren, Peta Mclaughlin, Rob Stirling *Epidemiology and Preventative Medicine, Monash University, Melbourne/VIC/Australia*

Background: Delay in patient management timelines in lung cancer may exceed recommended timeframes, potentially adversely impacting quality of life, curative resection rates, disease progression and survival. The aim of this study was to evaluate the contribution of health service variables to delay between referral (T0), diagnosis (T1) and treatment (T2) for lung cancer patients. **Methods:** Demographic, clinical and health service data from the Victorian Lung Cancer Registry (VLCR) was analysed to identify variables predictive of extended critical time intervals. Explanatory variables were included in multivariate models. Sub-group analysis of the magnitude of delay of each interval was also performed. **Results:** Among 1417 subjects, median T0-T1 interval was 15 days (IQR 5-38), T1-T2 was 12 days (IQR 0-34) and diagnosis to palliative care 19 days (IQR 5-48). Significant T0-T1 delay was associated with country of birth, whether English is the first language, treatment first received and health status at diagnosis (ECOG score). Significant T1-T2 delay was associated with country of birth, the type of hospital where treatment was provided, presence of major comorbidities and initial treatment type. Factors associated with T2-T3 delay included age at diagnosis, the type of hospital where treatment was provided, health status at diagnosis and initial treatment type. Multivariate analysis demonstrated that type of hospital, stage of disease at diagnosis, ethnicity and type of initial treatment were all associated with significant delay at various stages of the patient journey to initial treatment (T0, T1 and T2). **Conclusion:** Understanding factors associated with delay in patients with lung cancer receiving effective management is crucial to developing interventions to address gaps. This research has identified priority areas for action in Victoria

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-030 Multimodality Treatment for Non-Small Cell Lung Cancer with Ipsilateral Pleural Dessimination Aleksey Kurchenkov, Vyacheslav Kurchin *Thoracic Oncopathology, N.N. Alexandrov National Cancer Centre of Belarus, P. Lesnoy-/Belarus*

Background: Patients with non-small cell lung cancer (NSCLC) with ipsilateral pleural dissemination previously treated without surgery. There are few reports about sucsessful surgical treatment of these patients. Using intrapleural hyperthermochemotherapy cans improve survival patients NSCLC with pleural dissemination. The aim of our research is increasing the efficiency of the treatment of these patients. **Methods:** From january 2006 to decemder 2012 in N.N. Alexandrov National Cancer Centre of Belarus twenty one patients with non-small cell lung cancer with ipsilateral pleural dissemination was included of the study under histological examination. All patients was shared in two groups: 1) control group – 10 patients was done chemotherapy (2-6 courses: cisplatin 75-90 mg/m^2 in 1 day, vinorelbine 30 mg/m^2 in 1 and 8 days); 2) study group – 11 patients was treated by multimodality care: pleuropneumonectomy, intrapleural hyperthermochemotherapy (IHTC) and adjuvant chemotherapy. The regimen of IHTC (ThermoChem HT-1000) was 42^{0}C in 1 hour with cisplatin 120 mg/m^2 and vinorelbine 30 mg/m^2. Adjuvant chemotherapy was done 4 courses: cisplatin 90 mg/m^2 in 1 day, and vinorelbine 30 mg/m^2 in 1 and 8 days. **Results:** 4 patients was done intrapleural hyperthermochemotherapy before surgery, because of pleural dissemination was diagnosed by thoracoscopy. Radical surgery was done through 2-4 weeks after IHTC. The rest of patients intrapleural hyperthermochemotherapy was spent with surgery jointly, because pleural dissemination was seen and verified by thoracotomy. All patients of the control group was died during 24 months, while overall 3-years survival patients of the study group was 61.4±15.3% (p=0.05). **Conclusion:** Multimodality treatment is including: surgery, intrapleural hyperthermochemotherapy and adjuvant chemotherapy for non-small cell lung cancer with ipsilateral pleural dissemination, allowing to increase level of 3-years overall survival for patients from 0.0% till 61.4±15.3% (p<0.05) as compared with chemotherapy. **Keywords:** itrapleural hyperthermochemotherapy, adjuvant chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

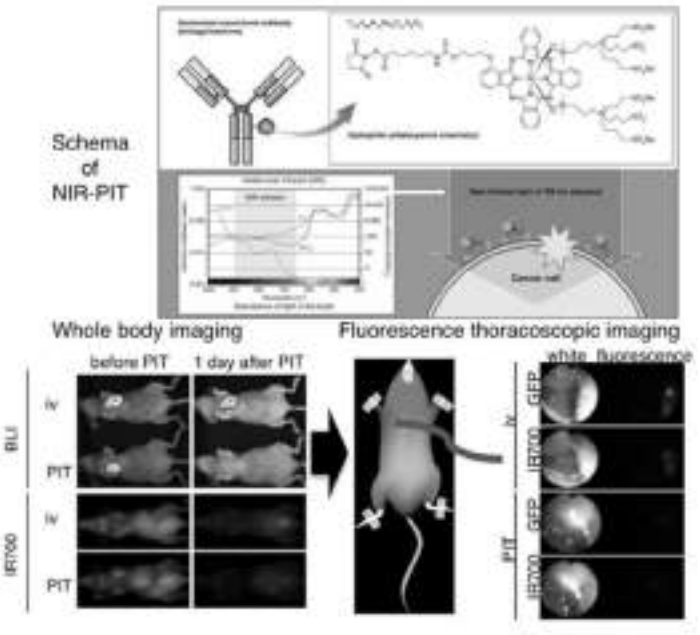
P3.01-031 Prognosis Factors in Stage IV Lung Adenocarcinoma with Single Brain Metastasis Lucian Miron[1], Marius Paduraru[2], Adela Calancea[2], Ingrith Crenguta Miron[1], Teodora Alexa[1] [1]*Medical Oncology, University of Medicine and Pharmacy Gr. T. Popa, Iasi/Romania,* [2]*Medical Oncology, Regional Institute of Oncology, Iasi/Romania*

Background: With the change of lung cancer epidemiology, the frequency of lung adenocarcinoma is steadily increasing. This histological subtype is often associated with brain metastasis, which negatively impact survival. Standard treatment for single-brain metastasis includes surgery, radiotherapy and platinum-based chemotherapy. However, this approach is often associated with acute and chronic toxicity and may negatively impact quality of life in these patients. We need simple prognosis factors to better determine which patients will benefit from this combined therapy. **Methods:** We performed a retrospective analysis of all lung cancer patients treated in the Oncology department of the Regional Oncology Institute, Iaşi, Romania between January 2012 and January 2014. Inclusion criteria: ECOG 1-2, stage IV lung adenocarcinoma with single-brain metastasis that underwent surgery and radiotherapy for the brain metastasis, followed by systemic treatment with a platinum-based regimen. Data were collected for each patient: age, sex, metastasis size and localization, neurological symptoms, the presence of other secondary lesions at diagnosis, concurrent illnesses, hemoglobin levels, white blood cells, platelets and lactate dehydrogenase (at the time of diagnosis). Data were analyzed by means of SPSS v.20 software - Cox regression. Continuous variables are expressed as mean±SE. Statistical significance was set at .05. **Results:** 31 patients met the inclusion criteria. Mean age was 58.6±1.55 years. Overall survival (OS) was 266±28.32 days. Cox regression analysis indicated that a **high white blood cell count**, **extra-cerebral metastatic sites**, **age** and **pre-existing illnesses**negatively impact OS (p<0.05). In contrast, symptoms, localization and size of the brain metastasis, as well as hemoglobin, lactate dehydrogenase and platelets had no impact on OS in this analysis. Patients with a high white blood cell count (n=13) had an average OS of 168.3±35.3 days as compared with 336±33.2 days in patients with normal white blood cell count at diagnosis (n=18). **Conclusion:** As more and more aggressive therapeutic strategies emerge, we need simple and effective parameters that can predict survival in order to select the best approach for each individual patient. High white blood cell count, extra-cerebral metastatic sites, age and pre-existing illnesses were associated with decreased OS. A future prospective study is warranted to confirm our results. **Keywords:** Brain metastasis, Prognosis, Adenocarcinoma

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-032 Near Infrared Photoimmunotherapy for Pleural Metastases: Preclinical Experience Kazuhide Sato, Peter L. Choyke, Hisataka Kobayashi *Molecular Imaging Program, Ccr, National Cancer Institute/ National Institutes of Health, Bethesda/MD/United States of America*

Background: Pleural metastases are common in patients with advanced thoracic cancers and are a cause of considerable morbidity and mortality yet they are difficult to treat. Near Infrared Photoimmunotherapy (NIR-PIT) is a new cancer treatment that utilizes the specificity of intravenously injected antibodies to target photosensitizers to specific cancers (Figure). Since one interesting property of the lung is that it transmits light better than any other organ, light therapy is a viable alternative therapy. Herein, we evaluate the efficacy of NIR-PIT in a mouse model of disseminated pleural metastases in a non-small cell lung cancer (NSCLC) model. **Methods:** *In vitro* and *in vivo* experiments were conducted with a HER2, luciferase and GFP expressing NSCLC cell line (Calu3-luc-GFP). An antibody-photosensitizer conjugate (APC) consisting of trastuzumab and a phthalocyanine dye, IRDye-700DX, was synthesized. *In vitro* NIR-PIT cytotoxicity was assessed with dead staining, luciferase activity, and GFP fluorescence intensity. *In vivo* NIR-PIT was performed in mice with tumors implanted within the intrathoracic cavity or in the flank, and assessed by tumor volume and/or bioluminescence and fluorescence thoracoscopy. Body weight was measured as an index of systemic toxicity. **Results:** *In vitro* NIR-PIT-induced cytotoxicity was light dose dependent. *In vivo* NIR-PIT led to significant reductions in both tumor volume (p = 0.002 vs. APC) and luciferase activity (p = 0.0004 vs. APC) in a flank model, and prolonged survival (p < 0.0001). Bioluminescence indicated that NIR-PIT lead to a significant reduction in the volume of pleural metastases 1 day after PIT (p = 0.0180)(Figure). Fluorescence thoracoscopy confirmed this result (Figure). Body weight ratio showed no significant reduction in NIR-PIT treated mice.



Conclusion: NIR-PIT has the ability to effectively treat pleural metastases caused by NSCLC. We foresee NIR-PIT as an adjuvant to surgery with an initial conventional debulking procedure followed by NIR-PIT to "mop up" residual disease. Moreover, it would be feasible to deliver light via thoracoscopy, bronchoscopy or even during open-surgery. Thus, although this particular animal model is not typical of NSCLC, the feasibility of treating thoracic malignancies with light therapy is demonstrated. NIR-PIT is a promising therapy for disseminated pleural tumors. **Keywords:** photoimmunotherapy, NSCLC, pleural disseminated metastases, fluorescence thoracoscopy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-033 Comparison of Symptom Score and Bronchoscopy Based Assessment with Conventional CT Based Assessment of Response to Chemotherapy in Lung Cancer Digambar Behera, Yenge L. Baburao, Ashutosh N. Aggarwal, Navneet Singh *Pulmonary Medicine, Postgraduate Institute of Medical Education and Research (Pgimer), Chandigarh/India*

Background: Computed tomographic (CT) measurements of primary tumor and/or metastatic sites are commonly used for assessment of objective responses to chemotherapy by RECIST and/or WHO criteria. Decisions regarding continuation/stopping chemotherapy are often also based upon changes in clinical symptoms. There is paucity of published literature on symptom plus bronchoscopy based decision making in routine clinical practice. This study aimed to compare reliability of response evaluation of lung cancer patients undergoing chemotherapy by symptoms, chest radiograph (CXR) and fibreoptic bronchoscopy (FOB) based assessment with conventional CT based assessment. **Methods:** Prospective, non-interventional, comparative analysis study. Treatment naïve patients with lung cancer having atleast one evaluable lesion on FOB and planned for chemotherapy were enrolled over a 1-year period. All assessments were done at baseline and after 3rd cycle of chemotherapy. Six symptoms (dyspnea, cough, chest pain, hemoptysis, anorexia and weight loss) on visual analogue scale [VAS] were noted. Respiratory symptom burden (RSB) and Total symptom burden (TSB) were calculated from first four and all six symptoms respectively. CXR responses were assessed as per WHO criteria. Bronchoscopic findings were recorded in a proforma adapted and modified from European Respiratory Society (ERS) classification for tracheobronchial stenosis. Video-recording of all bronchoscopies was preserved for objective review. CT response as per RECIST 1.1 was taken as reference standard and agreements tested using Cohen's kappa (k) statistic. **Results:** Of 87 patients enrolled, 53 completed ≥3 cycles and were included for final analysis. Mean age was 55 years, majority (81.1%)

were males, had advanced/metastatic disease [stage IV 56.6%; IIIB 37.7%] and ECOG performance status of 0-1 (52.8%) or 2 (32.1%). Squamous cell carcinoma (50.9%) and small cell (35.8%) were the commonest histological types. Mean scores of all six individual symptoms, RSB and TSB showed statistically significant improvement after chemotherapy. Mean number as well as distribution of FOB lesions decreased significantly after chemotherapy. CXR response had poor agreement with both FOB based and CT based responses. Changes in RSB and TSB categories had no/minimal agreement with CT based responses. RECIST and WHO criteria had strong agreement (k=0.872) with each other for overall response assessment. Bronchoscopic assessment had minimal agreement with both RECIST (k=0.324) and WHO (k=0.349) criteria based assessment. For differentiating responders (CR+PR) from non-responders (SD+PD), FOB based assessment had weak agreement with both RECIST (k=0.462) and WHO (k=0.501) criteria based assessment. For differentiating disease control (CR+PR+SD) from disease progression (PD), WHO criteria based CT response had perfect agreement (k=1.000) while FOB based assessment had moderate agreement (k=0.629) in comparison to RECIST. Variable combinations of FOB based assessment with symptom based assessment and/or CXR response continued to show only moderate agreement (k=0.600-0.799) with CT based assessment for detecting PD. **Conclusion:** Majority of patients have symptomatic improvement after chemotherapy. However, changes in symptom scores and CXR responses correlate poorly with CT responses. CT scan based assessment by RECIST/WHO criteria remains the reference standard for objective evaluation of response to chemotherapy in lung cancer. Bronchoscopic progression may be used as a surrogate for disease progression if CT assessment is not feasible. **Keywords:** RECIST, Response assessment, Symptom score, bronchoscopy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-034 Long-Term Survival in Metastatic Non-Small Cell Lung Cancer: Predictive Clinical Factors Leonardo A. Boente, Alexandre A.B.A. Da Costa, Augusto A.R. Pereira, Talita Gonzaga, Aline F. Fares, Daniel V. Araújo, Daniel Garcia, Daniela Lacerda, Marcello F. Fanelli, Jose A. Rinck *Cinical Oncology, Ac Camargo Cancer Center, Sao Paulo/Brazil*

Background: While most patients with non-small cell lung cancer (NSCLC) stage IV, presents an unfavorable prognosis, a small proportion presents median overall survival beyond 2 years. The aim of this study is to identify clinical factors associated with long-term survival (LTS) in patients metastatic NSCLC. **Methods:** Single-center, retrospective study performed from the selection of patients in electronic medical records with a diagnosis of NSCLC, metastatic at diagnosis, and treated at AC Camargo Cancer Center in Brazil, from January / 2007 to June / 2014. We compared the group of patients who survived more than two years, the long-term survivors (LTS), to that survived less than two years, the short-term survival (STS), regarding the clinical characteristics and treatments performed. Using the chi-square test (categorical variable), and T test (continuous variables), for univariate analysis and by binary logistic regression model for multivariate analyzes, adopting the significance level $P < 0.05$ **Results:** From 292 patients with stage IV NSCLC, there were 46 (15.7%) patients who survived beyond 2 years, and the remaining 246 patients who survived less than two years, we selected a control group of 46 patients. In the LTS group, the median overall survival (OS) was 39.7 months, and five-year-survival was 10.8%, while in the control group median OS was 9.2 months. In the univariate analysis related to clinical factors, the LTS was associated with female gender (*P:* 0.03); not smoking (*P:* 0.013); ≤ 2 metastatic sites (*P:* 0.02); ECOG of 0-1 (*P:* 0.01); absence of extra-thoracic metastasis (*P:* 0.001); absence of liver metastasis (*P:* 0.004) absence of bone metastasis (*P:* 0.001); absence of weight loss (*P:* 0.03); absence of decreased appetite (*P:* 0.001); and the presence of activating mutation in the EGFR gene (0.024). In univariate analysis regarding factors related to treatment, the LTS was associated with: two or more systemic treatment lines (*P:* 0.001); partial or complete response in first-line chemotherapy (p = 0.0001); use of tyrosine-kinase inhibitor (p = 0.0001); and maintenance chemotherapy (*P:* 0.012). In multivariate analysis of clinical factors, were considered long predictors of survival: two or fewer metastatic sites (OR: 7.1; *P:* 0.008) and ECOG 0-1 (OR: 12.2 *P:* 0.024). There was a trend for female gender (OR: 3.1 *P:* 0.057). **Conclusion:** We conclude that, in our sample, patients with stage IV NSCLC who have ECOG 0-1 and oligometastatic disease (≤ 2 sites) are more likely to long-term survival. **Keywords:** Long-term survivor, metastatic non-small cell lung cancer, prognostic fators, retrospective study

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-035 Treatment of NSCLC Patients by Community Health Practitioners: Practice Pattern and Competence Assessments Marie N. Becker, Alison Heintz, Jason Everly *Educational Concepts Group, Llc, Atlanta/GA/United States of America*

Background: The complexity of current treatment and management for patients with metastatic non-small cell lung cancer (NSCLC) continues to rise. The volume and pace of scientific advances make it challenging for the community practitioner to stay abreast of optimal patient care. Education is vital in disseminating critical information to practitioners and allows professional reflection of appropriate therapeutic decision making and peer discussion. Understanding the base knowledge, competence, and current practice patterns of practitioners is essential to identifying community needs and implementation of education that impacts patient care. **Methods:** From May through December 2014, educational outcomes assessments were gathered from 42 live independent continuing medical education (CME) activities held within community practices across the United States. Participants were asked a series of case-based questions via an audience response system to assess baseline knowledge, competence, and identify practice patterns. Assessments were repeated following the 1-hour CME certified activity. Long-term assessment was conducted electronically 6-weeks following the educational initiative. **Results:** The overall program educated 847 practitioners, including 477 physicians. Three patient scenarios were profiled during the activity: 1) non-squamous NSCLC, non-smoker, no targetable mutation, 2) non-squamous NSCLC, EGFR del19 mutation, and 3) non-squamous NSCLC, ALK rearranged. Participant responses at baseline indicated a need for further education about molecular testing, maintenance therapies, and front-line therapies. All three cases also addressed treatment options at disease progression following initial treatment. For all cases, education resulted in responses better aligned to current practice guidelines and clinical data. With respect to molecular testing there was a 28% increase in the number of participants who would recommend testing and a 17% increase in participants who would recommend sufficient biopsy specimen for testing prior to treatment. There was a large gap in knowledge about the need for a repeat biopsy after progression on EGFR TKI therapy to confirm the nature of the lesion and select the optimal targeted therapy. Education closed this gap with a 53% increase in respondents understanding this need. With respect to maintenance therapies in the different scenarios, there was 22% change in the use of pemetrexed for non-targeted NSCLC and 21% for radiotherapy after progression on crizotinib. Self-reported levels of competence to integrate biomarkers, clinical characteristics and tumor histology to provide an individualized treatment for patients increased after education. At 6-week follow-up the majority of participants reported that they were more likely to order molecular testing (80%), and were better able to select first-line (93%) and second-line therapies (93%). Participants also report increased familiarity with therapeutic options after education. Barriers to implementation included the newness of treatment data and lack of reimbursement. **Conclusion:** The results highlight baseline gaps in clinical practice. Several gaps are closed both in the short-term and the long-term through continuing education. Educational benefits appear to endure to the 6-week time point. Longer term follow-up would benefit CME educational providers and in turn drive more relevant activities that would benefit clinicians and ultimately, their patients. **Keywords:** Education, CME, educational outcomes

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-036 The Safety and Efficacy of Thoracic Reirradiation Michael W. Straza[1], Adam Currey[1], Selim Firat[1], Rafael Santana-Davila[2], Smitha Menon[3], Elizabeth Gore[4] [1]*Medical College of Wisconsin, Milwaukee/WI/United States of America,* [2]*University of Washington, Seattle/United States of America,* [3]*Hematology/Oncology, Medical College of Wisconsin, Milwaukee/WI/United States of America,* [4]*Medical College of Wisconsin, Milwaukee/AL/United States of America*

Background: Intrathoracic malignancies including lung, esophageal, and pulmonary metastases frequently recur locally or regionally after initial therapy. The existing literature on the safety and efficacy of multiple courses of thoracic irradiation is limited. The purpose of this study was to evaluate local regional control and toxicity in patients who received up to three courses of thoracic radiation. **Methods:** We conducted a retrospective review of 51 patients who had undergone at least two courses of thoracic radiation. Two patients were found to have only a previous course of whole breast irradiation and were thus excluded for a total of 49 patients. Patient age, diagnosis, courses and doses of radiation therapy, chemotherapy and surgery were extracted from the record. Time to recurrence was determined by time from last radiation treatment to pathological confirmation or radiographic progression. Six potential treatment related grade 4 or 5 toxicities were identified (5 deaths). **Results:** The median age at diagnosis was 64. Median follow up was 3 years (range 0.76-12). 43 of the patients were with primary lung malignancy, 2 with esophageal, 3 with metastases and 1 unknown. 49 patients received at least two courses of intrathoracic radiation, 5 received 3 courses. 38 patients had died at time of last follow up, 10 were alive and one lost to follow up. 46% had local-regional recurrence at time of last follow up while 24% were disease free. The median cumulative dose was 111Gy for all patients, 113 Gy in those with Grade 4 or higher toxicity (NS). Median survival after completion of the first radiation treatment was 3.2 years. Median survival after completion of the last course of radiation was 1.25 years versus 0.58 years for those without and with Grade 4-5 toxicity respectively. The median time between the first and last course of radiation was 1.7 years. Five of the six patients with severe toxicity were disease free at time of death or last follow up. Grade 5 toxicities included massive hemoptysis, tracheal erosion, cardiac arrest, and respiratory failure. Dosimetric evaluation of these patients is underway. 50% of patients with severe toxicity had previous or subsequent thoracic surgery versus 23% in those without. Median time from end of first treatment to end of last treatment was 634 days (range: 0.39 -7.5 years) versus 465 days (range: 0.6-2.3 years) for patients without and with Grade 4-5 toxicity, respectively. None of the 5 patients who received 3 courses of radiation exhibited severe toxicity. **Conclusion:** Repeat courses of thoracic irradiation appear to be generally safe and effective with a median survival of 1.26 years following the last radiation treatment with 10% Gr4-5 toxicity in this population with cancer specific mortality of 78%. Future studies will identify clinical and dosimetric parameters that predict for severe toxicity. **Keywords:** Retreatment, recurrence, radiation

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-037 Impact of Endobronchial Stents on Patients with NSCLC and Central Airway Obstruction (CAO) Nagla Abdel Karim[1], Mahmoud Shehata[1], Ahmed Mostafa[2], Shuchi Gulati[3], Michelle Kirshner[4], Changchun Xie[5], John Morris[6], Sadia Benzaquin[7] [1]*Internal Medicine/Division of Hematology/Oncology, The University of Cincinnati, Ohio/OH/United States of America,* [2]*Pulmonary Medicine, The University of Cincinnati, Ohio/United States of America,* [3]*Internal Medicine, The University of Cincinnati, Ohio/OH/United States of America,* [4]*The University of Cincinnati, Ohio/OH/United States of America,* [5]*Biostatistics,*

The University of Cincinnati, Ohio/OH/United States of America, [6]Internal Medicine-Division of Hematology/Oncology, The University of Cincinnati, Ohio/OH/United States of America, [7]Pulmonary Medicine, The University of Cincinnati, Ohio/OH/United States of America

Background: Approximately 30% of lung cancer patients develop central airway obstruction (CAO) increasing the risk of post-obstructive pneumonia and respiratory failure. Therapeutic interventional bronchoscopy including airway stenting (AS) can provide immediate and effective palliation to improve patient quality of life (QoL). Unfortunately, there is little data about the impact on OS or the risk of hospitalization in patients with CAO mandating stent placement versus patients with CAO lesions that did not require stent placement. **Methods:** Between 2011-2014, twenty five patients with advanced lung cancer were evaluated by the Interventional Pulmonary (IP) Service at the University of Cincinnati for endobronchial stent placement for CAO. We retrospectively reviewed the OS and the risk of hospitalization in patients with lung cancer with CAO mandating stent placements versus patients who did not have lesions requiring stent placement. Death was considered as the endpoint. Kaplan-Meier method was used to calculate median overall survival and 95% CI. Cox model was used to test the overall survival difference between the patients who need stent and patients who do not need stent adjusted for age and sex. Logistic regression was used to test the hospitalization rate difference between the patients who need stent and patients who do not need stent adjusted for age and sex. Data were analyzed using the SAS ® Version 9.4. **Results:** Between 2011-2014, twenty five patients with advanced lung cancer were evaluated by the Interventional Pulmonary (IP) Service at the University of Cincinnati for endobronchial stent placement for CAO. Eight patients did not require placement of a stent and 17 patients had obstructive lesions that required stenting. Age and gender did not have any impact on the risk of hospitalization or OS of both of these groups of patients. The eight patients whose lesions did not mandate stent placement had a significantly lower risk of hospitalization compared to the 17 patients with CAO requiring a stent (OR 15.9, 95%CI 1.2, 209.1; p =0.035). Patients with advanced NSCLC and CAO that required IP stent placement had a median OS of 424 days (95%CI, 119-606 days) compared to a median OS of 729 days (95%CI, 426-. days) for patients with CAO not requiring a stent. Even with a lower survival in patients with stent placement, their OS of 424 days was slightly longer than the reported one-year survival for patients with stage IV NSCLC suggestive of improved outcome of patients with advanced stage NSCLC supported by IP. **Conclusion:** Lung cancer patients with less severe CAO have a lower risk of hospitalization and have better OS compared to patients with CAO mandating stent placement; however, CAO patients with IP evaluation and management in addition, may have improved OS suggesting that IP consultation may offer both improvements in QoL and OS to patients with advanced NSCLC and CAO. **Keywords:** endobronchial, stents, central airway obstruction, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-038 Comparing Next-Generation Sequencing (NGS) Platforms in Patients with Thoracic Tumors: Tumor Tissue vs. Circulating Cell-Free DNA from Blood Melissa L. Johnson[1], Rebecca Nagy[2], Holli H. Dilks[3], Richard B. Lanman[2], Amir A. Talasaz[2], Kimberly Banks[2], Charles Swanton[3], Howard Burris[1], David R. Spigel[1] *[1]Sarah Cannon Research Institute/Tennessee Oncology, Pllc, Nashville/TN/United States of America, [2]Guardant Health, Inc, Redwood City/United States of America, [3]Sarah Cannon Research Institute, Nashville/TN/United States of America*

Background: Next-generation sequencing (NGS) from tumor tissue is used to acquire comprehensive genomic information to aid clinical decision-making for cancer patients. In order to obtain sufficient tissue for tumor-based NGS, patients must often undergo repeat biopsies after diagnosis which are invasive, associated with risk and expense, and sometimes unsuccessful because of tumor size or location. Genomic information may also be obtained by analyzing cell-free DNA (cfDNA) from plasma samples, which affords the potential for NGS testing to a greater number of patients, and offers a wide variety of cancer diagnostic and surveillance applications. We sought to compare the results of tumor based-NGS with an analysis of circulating tumor cfDNA from matched plasma samples in patients with thoracic tumors (non-small cell lung cancer, small cell lung cancer and thymic malignancies) to determine concordance between the tests. **Methods:** We compared NGS results obtained from tumor tissue analyzed by Foundation One with plasma-based analysis of cfDNA using Guardant360, a 54-gene panel covering 80,000 base pairs with high sensitivity (75-85% in most solid tumors) and ultra-high specificity (>99.9999%). Guardant360 detects single nucleotide variants (SNVs), including synonymous alterations, variants of uncertain significance, and somatic point mutations, gene amplifications (CNVs), select insertions/deletions (indels) and genomic rearrangements. Because Foundation One is a 316-gene panel, concordance was defined based on the genes covered by both panels. Only patients with cancers originating in the chest were included. **Results:** Of 56 patients with Guardant360 testing performed between 6/2014 and 2/2015, 100% were successfully assayed. Eleven had matched NGS from tumor and concordance was noted in 5/11 (45%) of patients. TP53 and KRAS were commonly found in both tumor tissue and plasma cfDNA. A total of 34 patients (61%) with successful plasma-based cfDNA analysis were unable to undergo tissue-based NGS for various reasons; fourteen patients had tumor tissue sent for NGS analysis that was deemed "insufficient", 16 had exhausted prior tumor biopsy specimen, and 4 patients were too ill to undergo a repeat biopsy. In 19 of these 34 cases where tissue NGS results were not available (56%), a genomic alternation was identified by plasma cfDNA analysis, which corresponded to targeted therapies available on clinical trials that otherwise would not have been known. **Conclusion:** Plasma-based NGS testing identified actionable genomic alternations in 23 of 56 (41%) patients tested. In most cases, this information was supplementary to that obtained from tumor-based NGS and partially concordant in matched cases. These findings support continued efforts to establish the value of cfDNA in those cases where repeat tissue biopsy is contraindicated or may pose undesirable risk of complications, or when tissue-biopsy based NGS is inadequate or uninformative. **Keywords:** cell-free DNA, next-generation sequencing, blood-based biomarkers, re-biopsy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-039 Patient Characteristics and Treatment Outcome of Advanced Non-Squamous NSCLC with over 6-Month Disease Control from Icotinib Sheng Yang, Xingsheng Hu, Junling Li, Ziping Wang, Yan Wang, Xuezhi Hao, Hongyu Wang, Jianping Xu, Bin Wang, Lin Lin, Xin Zhang, Shengyu Zhou, Peng Liu, Haiyan Wang, Puyuan Xing, Yutao Liu, Shanshan Chen, Hua Lin, Xiangru Zhang, Yan Sun, Yuankai Shi *Department of Medical Oncology, Cancer Institute and Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing Key Laboratory of Clinical Study on Anticancer Molecular Targeted Drugs, Beijing/China*

Background: Epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) has an established role in the treatment of advanced non-squamous non-small cell lung cancer (NSCLC). Icotinib is an EGFR-TKI with non-inferior efficacy but milder toxicities compared with gefitinib. Disease control for over 6 months suggests that the case is not primary resistant to the drug. The present study investigated the patient characteristics and treatment outcome of advanced non-squamous NSCLC with at least 6-month disease control from icotinib. **Methods:** Non-squamous NSCLC patients with disease control after 6-month icotinib treatment were enrolled and retrospectively analyzed. Clinical characteristics were collected from the medical records. Efficacy and outcome data were analyzed. **Results:** A total of 87 patients were enrolled onto this study in which 56 were female, 18 with brain metastasis, and 32 patients harbored known EGFR mutation. For the overall population, 42(48.3%) patients achieved partial response. Response rate were 65.6% (21/32) and 38.2% (21/55) in patients with EGFR mutation and those with unknown mutation status, respectively(P=0.014). Patients with brain metastasis appeared to have lower response rate (26.7% *vs* 56.9%, p=0.033).The median progression-free survival (PFS) after 6 months' icotinib treatment was 9.7 months (95% CI 4.1-15.4 months) for the overall population, and 5.0 months (95% CI 0.6-3.9 months) and 12.9 months (95% CI 3.4-6.2 months) for those with and without brain metastasis, respectively. Median progression-free survival in patients with PR or SD showed no statistically significant difference (15.5 months *vs* 9.3 months, P=0.477). **Conclusion:** The present study provided evidence from a relatively large single institutional study of icotinib in clinical practice. Patients with disease control for over 6 months showed similar clinical features to those with EGFR mutation. Those patients will have prolonged clinical benefits with continuous icotinib therapy after 6 months, regardless of PR or SD. Brain metastasis is a potential unfavorable predictive factor for PFS for those patients **Keywords:** Epidermal growth factor receptor tyrosine kinase inhibitor, icotinib, Brain metastasis

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-040 Prospective Evaluation of Changes in Cancer Cachexia in NSCLC in Patients given Chemotherapy by Correlating Skeletal Muscle Mass with PRO Results Ryan D. Gentzler[1], Alejandro R. Boiles[2], Jose N. Galeas[2], Louise M.-W. Man[1], Richard D. Hall[1], Patricia Hollen[3], Richard J. Gralla[2] *[1]Hematology/Oncology, University of Virginia, Charlottesville/VA/United States of America, [2]Department of Medicine, Jacobi Medical Center - Albert Einstein College of Medicine, Bronx/NY/United States of America, [3]School of Nursing, University of Virginia, Charlottesville/VA/United States of America*

Background: Cancer cachexia and sarcopenia are common in lung cancer, and are associated with poor outcomes. Several recent interventional trials in cancer cachexia in patients with lung cancer have endeavored to improve skeletal muscle mass (measured by skeletal muscle mass index – SMI - using DXA or CT) and to correlate changes with functional outcomes of benefit to the patient. While functional tests such as stair climb power and hand grip strength have been used, these measures are neither sufficiently sensitive in patients with cancer, nor do they evaluate outcomes demonstrated to be valuable to patients. Patient Reported Outcomes (PROs) such as EORTC, FACT and others, have been collected, but specific components useful to patients have not been identified as ones correlating highly with SMI. Recent large studies at baseline using the 3-Item Global Index (3IGI) of the Lung Cancer Symptoms Scale (LCSS) quality of life and functional measure found strong correlations predicting survival in non-small cell lung cancer (N = 602) and in mesothelioma (N = 444); thus the 3IGI appears to be a good factor for associating PROs with SMI changes (Symanowski ASCO 2014; Gralla ASCO 2014). Additionally, over 90% of patients with NSCLC have expressed that parameters such as activity level and quality of life (included in the 3IGI) are of great importance to them. **Methods:** The LCSS was measured every 3 weeks in patients with a minimum KPS = 60 who were receiving chemotherapy. Correlations of SMI changes with 3IGI scores were made at baseline (at the time of initiation of chemotherapy) and at a median of 14 weeks in patients with Stage IIIB or IV NSCLC. SMI was measured by CT (Slice-O-Matic software) at the L1 vertebral level. A change in SMI by ± 4% was considered a threshold change of importance. **Results:** We have analyzed 24 patients to date (50% female; medians: age 57, KPS 80%; baseline: BMI 24.3, SMI 59.9, with 38% of males < 55.4 SMI). 19 patients are evaluable at this time. 42% of patients had a change in SMI by ± 4%; of these 75% had either improvement or worsening of the 3IGI in the direction expected from the change in SMI (improved 3IGI with increased SMI; worsened 3IGI with decreased SMI). No clear relationship in SMI was observed with response to chemotherapy thus far in the analysis. **Conclusion:** These results suggest: 1) the 3IGI may be useful in identifying both positive and negative changes in SMI, when using a 4% threshold change; 2) while we continue to enlist patients in this study, a confirmatory larger evaluation should be conducted; and 3) no measure should be used in practice or clinical trials of cancer cachexia or sarcopenia unless it has demonstrated validity in patients with cancer. **Keywords:** sarcopenia, patient reported outcomes, lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-041 Treatment Beyond Second Line Chemotherapy Outside of a Clinical Trial Is Appropriate for Selected NSCLC Patients Ahmed A. Badawy[1], Sejong Bae[2], Stefan C. Grant[3] [1]*Alexandria University, Alexandria/Egypt,* [2]*University of Alabama at Birmingham, Birmingham/AL/United States of America,* [3]*Medical Oncology, Wake Forest Baptist Medical Center, Winston-Salem/NC/United States of America*

Background: Guidelines generally recommend entry into a clinical trial or best supportive care for patients with NSCLC who progress after second line chemotherapy. We sought to explore whether this strategy remains valid with newer drugs and regimens and to evaluate the benefit of additional treatment beyond second line in advanced NSCLC. **Methods:** A retrospective analysis of stage IV NSCLC patients treated at a tertiary teaching hospital from 2002-2012 was undertaken. Demographics, details of treatment and overall survival was recorded for each patient. Patients who originally received adjuvant therapy and no further treatment upon recurrence and those receiving first line treatment on a clinical trial with no further therapy were excluded from analysis. Statistical analyses was performed using SPSS software and calculated using log-rank testing. **Results:** 409 cases of NSCLC were included in this analysis. 239 (58.4%) patients received second line chemotherapy, 102 (24.9%) received third line treatment, 36 (8.8%) received fourth line treatment and 11 patients (2.7%) received fifth line therapy. The addition of second line treatment was associated with a statistically significant improvement in overall survival, with median survival for patients received second line treatment of 18.7 vs 9.1 months (p<0.001) for patients not receiving second line treatment. The most commonly used second line regimens were single agent docetaxel, single agent pemetrexed, tyrosine kinase inhibitors or combined chemotherapy doublets and there was no significant difference in overall survival based on what regimen was used as second line therapy. The addition of third line treatment also was associated with a statistically significant improvement in overall survival, with a median survival for patients receiving third line therapy of 26.1 vs 11.3 months (p<0.001) for patients not receiving third line treatment. The most common therapeutics regimens for third line treatment were single agent docetaxel, single agent pemetrexed, single agent gemcitabine, single agent vinorelbine, tyrosine kinase inhibitors or combined chemotherapy doublet, and there is no significant difference between these regimens regarding overall survival. The addition of fourth and fifth line treatment also resulted in statistically significant improvements in overall survival with median survival compared to patients not receiving this treatment of 32.7 vs 13 months (p<0.001) and 40.3 vs 13.4 months (p=0.003) respectively. **Conclusion:** Although the present analysis is limited by its retrospective nature, our data suggest that continuing treatment after progression in patients who previously responded to chemotherapy is appropriate and is likely to prolong survival, provided their performance status and functional reserve are adequate to tolerate further treatment. In addition, the sequence of chemotherapy regimens did not appear to have a major impact on survival. Analysis is ongoing. **Keywords:** chemotherapy, NSCLC, third line

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-042 Neutrophilia and Lymphopenia Can Be Prognostic Factors in Non-Small Cell Lung Cancer with Adenocarcinoma Histology Jaeheon Jeong, Jae Joon Han, Chi Hoon Maeng, Sun Kyung Baek, Hwijoong Yoon, Si-Young Kim *Internal Medicine, Kyung Hee University, Seoul/Korea*

Background: Neutrophil count is associated with prognosis in some cancers. Direct cell-cell interactions between neutrophils and tumor cells enhance tumor growth in Non-small cell lung cancer (NSCLC). We planned to identify clinical and laboratory factors including neutrophil and lymphocyte counts that can be used to estimate the overall survival. **Methods:** We retrospectively reviewed 60 patients with advanced or recurrent NSCLC with adenocarcinoma histology diagnosed between 2009 and 2013. We performed univariate and multivariate stepwise Cox regression analyses to identify survival prognostic factors. **Results:** Median survival time was 18.0 months (95% CI; 13.8 – 22.2 months). Median age was 64.5 years old. Sixteen patients (26.7%) were current smoker, sixteen patients (26.6%) were past smokers and 28 patients (46.7%) were non-smokers. Forty three patients' ECOG PS was 0 or 1 and remaining seventeen patients' ECOG PS was 2. Number of metastatic sites was less than four in the forty four patients and remaining sixteen patients have more than four metastatic sites. In univariate analysis, seven factors were identified: Loss of appetite (HR, 0.344), brain metastasis (HR, 0.444), metastasis in other organs (HR, 2.886), WBC count (HR, 3), neutrophil count (HR, 2.322), lymphocyte count (HR, 0.431), neutrophil lymphocyte ratio (HR, 2.322). In multivariate analysis, two independent prognostic factors were identified: neutrophil count (HR, 2.418), lymphocyte count (HR, 0.414). **Conclusion:** Increase of neutrophil count and decrease of lymphocyte count can be used to predict survival in advanced or recurrent non-small cell lung cancer patients with adenocarcinoma histology. **Keywords:** NEUTROPHIL, prognostic factor, LYMPHOCYTE, lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-043 Assessing Treatment Strategies for Lung Cancer in Octogenarians: Insights From a Cohort of 337 Patients Virginie Zarza[1], Bénédicte Mastroïanni[1], Lize Kiakouama[2], François Tronc[1], Maurice Perol[3], Pierre Jean Souquet[4], Nicolas Girard[1] [1]*Hôpital Louis Pradel, Hospices Civils de Lyon, Lyon/France,* [2]*Hôpital de La Croix-Rousse, Hospices Civils de Lyon, Lyon/France,* [3]*Léon Bérard Cancer Center, Lyon/France,* [4]*Centre Hospitalier Lyon Sud, Pierre Bénite/France*

Background: Aging increases the incidence of lung cancer in octogenarians. In this population, only limited data about treatment strategies and results are available, as those patients are usually not eligible for clinical trials; meanwhile, previously reported cohorts mostly focused on early-stage tumors. Our objective was then to provide a global picture of the treatment strategies for lung cancer in octogenerians, and to parallel those with available standards. **Methods:** Retrospective observational study of all consecutive patients aged 80 or more, with pathologically-confirmed lung cancer, and diagnosed at the Hospices Civils de Lyon between January 2005 and April 2014. **Results:** 337 patients were included, 298 (88%) with non-small cell lung cancer (NSCLC), and 39 (12%) with small-cell lung cancer. For NSCLC, tumor was stage I, II, III, and IV in 10%, 9%, 25% et 57% of cases, respectively. Overall survival was 8.4 months. Geriatric assessment had been done only for 11% of patients. Overall, a standard treatment strategy - i.e. based on available recommendations and guidelines - was conducted for 42% of patients, while 24% received non-standard treatment, and 34% best supportive care only. At multivariate analysis, favorable prognostic factors on overall survival were performance status 0-1 (p<0.001), stage I/II (p<0.001), adenocarcinoma histology (p=0.026), and a standard treatment strategy (p<0.001). In the setting of metastatic NSCLC, 35% of patients received chemotherapy, the most frequent regimen being carboplatine and paclitaxel. **Conclusion:** Octogenarians with lung cancer are eligible for antitumor treatment in nearly 70% of cases, consisting of standard, recommended therapy in about half of the cases. Our data provide a unique overview of the management of octogenarians with lung cancer, to foster future prospective studies dedicated to this subset of patients. **Keywords:** Surgery, chemotherapy, NSCLC, elderly

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-044 FDG-PET/CT Based Response Prediction of Stage IV NSCLC Treated with Paclitaxel-Carboplatin-Bevacizumab with or without Nitroglycerin Evelyn E.C. De Jong[1], Wouter Van Elmpt[1], Otto S. Hoekstra[2], Harry J.M. Groen[3], Egbert Smit[4], Ronald Boellaard[2], Esther G.C. Troost[1], Philippe Lambin[1], Anne-Marie C. Dingemans[5] [1]*Department of Radiation Oncology (Maastro), Grow-School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht/Netherlands,* [2]*Department of Nuclear Medicine & Pet Research, VU University Medical Center, Amsterdam/ Netherlands,* [3]*Department of Pulmonary Diseases, University Medical Center Groningen, Groningen/Netherlands,* [4]*Department of Pulmonary Diseases, VU University Medical Center, Amsterdam/Netherlands,* [5]*Department of Pulmonology, Grow-School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht/Netherlands*

Background: A prospective study in stage IV non-small cell lung cancer (NSCLC) patients was performed to assess the predictive value of early response of the primary tumor evaluated by [18F]FDG-PET/CT to bevacizumab containing combination therapy with or without nitroglycerin (NTG) patches as first line treatment. NTG is a vasodilator which is hypothesized to increase tumor blood flow thereby decrease hypoxia, and 1) leading to a decrease in [18F]FDG uptake, and 2) facilitating early response assessment using [18F]FDG to predict treatment outcome. **Methods:** In total, 223 patients were randomized between carboplatin-paclitaxel-bevacizumab (PCB) with or without NTG (day -2 to +3; NVALT12 trial, NCT01171170). 78 patients were available for image analysis having undergone an [18F]FDG-PET/CT scan prior to the first cycle of chemotherapy and a second (optional) [18F]FDG-PET/CT scan at day 1-2 after start of the second cycle. The primary gross tumor volume (GTV) was delineated on both PET/CT scans. On the [18F] FDG-PET scan, the maximum standardized uptake value (SUV), mean SUV, peak SUV and total lesion glycolysis (TLG defined as SUVmean*CTvolume) were calculated and correlated with progression-free survival (PFS) and overall survival (OS). Early response assessment was quantified using relative changes in [18F]FDG-PET uptake parameters of the GTV expressed as delta. The median of the parameter of interest was used as cut-off value for both study arms for analysis using cox regression. Furthermore response was assessed according to PERCIST and RECIST. **Results:**

Hazard ratio os SUV parameters > versus < the median for PFS and OS						
SUV parameter		median	PFS		OS	
			HR (p-value)	95% CI	HR (p-value)	95% CI
Delta PCB+NTG (%)	SUVmax	40.4	1.026 (0.408)	0.966-1.090	1.006 (0.844)	0.945-1.071
	SUVmean	39.9	1.048 (0.127)	0.987-1.113	1.034 (0.279)	0.973-1.099
	SUVpeak	42.3	1.035 (0.258)	0.975-1.100	1.016 (0.615)	0.955-1.082
	TLG	64.5	1.064 (0.043)	1.002-1.131	1.039 (0.221)	0.977-1.106
Delta PCB (%)	SUVmax	53.2	1.027 (0.454)	0.957-1.103	1.009 (0.810)	0.939-1.084
	SUVmean	51.6	1.027 (0.465)	0.957-1.102	1.011 (0.766)	0.941-1.086
	SUVpeak	53.9	1.040 (0.281)	0.969-1.116	1.018 (0.623)	0.947-1.094
	TLG	75.9	0.994 (0.873)	0.927-1.066	0.998 (0.951)	0.928-1.072

1) On average no decrease in [18F]FDG-PET uptake was observed for the experimental NTG group. However, patients in the experimental group showed a significantly larger variation in most SUV parameters of the second PET/CT scan compared to control group without NTG.2) In table 1 the hazard ratios are shown for the relative delta SUVmax, SUVmean, SUVpeak and TLG for both study arms. In the experimental group, patients with a small delta TLG (<64%) had a shorter PFS than patients with a larger change in TLG (HR:1.064; 95% CI 1.002-1.131; p=0.043). Response assessed by PERCIST and RECIST did not predict for a longer PFS or OS. **Conclusion:** Adding NTG did not result in a decrease in [18F]FDG-PET uptake compared to patients without NTG although NTG increased variability of the measured SUV parameters. Patients in the experimental NTG arm without an early response on [18F]FDG-PET/CT imaging had a worse PFS than patients with a response. For the group without NTG no difference was observed. Also, RECIST and PERCIST were not predictive. **Keywords:** response assesment, FDG-PET, NSCLC, nitroglycerine

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-045 Short-Term Outcomes of Stage IV Non-Small Cell Lung Cancer with Brain Metastasis Su Kyung Hwang, Seung Il Park, Dong Kwan Kim, Yong-Hee Kim, Se Hoon Choi, Hyeong Ryul Kim *Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul/Korea*

Background: Patients who had non-small cell lung cancer with brain metastasis at the initial diagnosis had poor prognosis and quality of life. We reviewed patients who had undergone lung resection and brain surgery. We also analyzed the characteristics of the patients and the factors affecting survival and recurrence. **Methods:** Between 2007 and 2012, 25 consecutive patients who had undergone lung resection and brain surgery because of non-small cell lung cancer with brain metastasis were retrospectively evaluated in a single-center. The non-small cell lung cancer subtype was adenocarcinoma in 23 patients, squamous cell carcinoma in 1 patient, and adenosquamous cell carcinoma in 1 patient. Twenty patients underwent Gamma Knife radiosurgery. Nodal stage was stage 0 in 9 patients, stage 1 in 9 patients, and stage 2 in 7 patients. **Results:** The median survival time after lung resection was 36.8 months. The 1-, 2-, and 3-year survival rates after lung resection were 95.8%, 79.2%, and 54.2%, respectively, and the 1-, 2-, and 3-year disease-free survival rates were 95.8%, 82.9%, and 64.2%, respectively. There were no local recurrences. Brain surgery methods did not affect disease-free survival (p=0.201) or overall survival (p=0.567). Nodal stage also did not affect disease-free survival (p=0.519) or overall survival (p=0.645). **Conclusion:** Even in cases of stage IV non-small cell lung cancer with brain metastasis, assertive lung resection and brain surgery bring improvements of survival and recurrence to patients. Brain surgery methods do not affect survival or recurrence. Therefore, Gamma Knife radiosurgery is a good choice for quality of life for patients. **Keywords:** Short-term outcomes, Brain metastasis, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-046 Pleural Photodynamic Therapy in Pleural Metastasis by Lung Cancer Ke-Cheng Chen, Yi-Shan Hsieh, Ming-Jium Shieh, Jang-Ming Lee *Institute of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University, Taipei/Taiwan*

Background: Pleural metastasis is difficult to treat in malignancies, especially in lung cancer. Currently, the options of management of pleural metastasis include chemotherapy, operation with pleurectomy, or/and photodynamic therapy. Photodynamic therapy is a method utilizing photosensitizer to locate the site of tumor, and the tumor is exposed to the light after performing pleurectomy. Literature had reported successfully treatment of malignant mesothelioma by photodynamic therapy, a new approach for pleural malignancy dissemination. However, little was known about the result when in lung cancer. **Methods:** Between 2005 and 2015, we retrospectively reviewed the clinical characteristics, operative methods, and treatment outcomes of 25 patients with lung cancer with pleural seeding. **Results:** The mean patient age was 51.6 ± 10.7 years. There is no procedure-related mortality. Using Kaplan-Meier survival analysis, 3-year survival rate and 5-year survival rate was reached 71.8% and 59.3%, respectively. We compared the PDT lung cancer patients with those receiving chemotherapy or target therapy (n=51) and found that the PDT group had better survival than non-PDT patients (mean survival time: 42.8 versus 17.6 months; P=.041). **Conclusion:** With proper patient selection, photodynamic therapy of pleural dissemination in patients with lung cancer is feasible and associated with a good survival rate **Keywords:** pleural dissemination, non-small cell lung cancer, photodynamic therapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-047 Weekly Paclitaxel plus Bevacizumab in Heavily Pre-Treated Non-Small-Cell Lung Cancer (NSCLC) Patients Andrés F. Cardona[1], Leonardo Rojas[2], Hernan Carranza[1], Carlos A. Vargas[1], Jorge M. Otero[1], Mauricio Cuello[3], Luis Corrales[4], Claudio Martin[5], Oscar Arrieta Rodriguez[6] [1]*Clinical and Translational Oncology Group, Foundation for Clinical and Applied Cancer Research - Ficmac, Bogotá/Colombia,* [2]*Centro Javeriano de Oncologia, Hospital Universitario San Ignacio, Bogota/Colombia,* [3]*Clinical Oncology, Hospital de Clinicas - Udelar, Montevideo/Uruguay,* [4]*Clinical Oncology, Hospital San Juan de Dios, San José/Costa Rica,* [5]*Clinical Oncology, Instituto Fleming, Buenos Aires/Argentina,* [6]*Unidad Funcional de Oncología Torácica Y Laboratorio de Medicina Personalizada, National Cancer Institute, Mexico City/Mexico*

Background: Combination of weekly paclitaxel and bevacizumab showed synergistic effect, anti-tumor efficacy and a good toxicity profile in patients with non small cell lung cancer (NSCLC). We retrospectively reviewed safety and efficacy of this regimen in metastatic non-squamous NSCLC as fourth-line therapy or beyond. **Methods:** Thirty nine patients were included between November 2011 and December 2014; those were bevacizumab eligible and received weekly paclitaxel (80 mg/m^2, days 1, 8 and 15 every 21 days) plus bevacizumab (7.5 mg/kg at day 1) after three prior lines of chemotherapy. Efficacy was evaluated by CT-scan every 10 to 12 weeks and treatment was continued until progression or unacceptable toxicity. Main outcomes were overall response rate (ORR), progression free survival (PFS) and overall survival (OS). **Results:** Median age 61 (44-78), female 51.3%, never smokers 53.8%, ECOG >2 25.6% and more than four previous lines 53.8%. All patients were treated with a first-line platinum-based doublet with (38.5%) or without bevacizumab (61.5%) and all of them received docetaxel as second-line (ORR 33.4/SLP 4.6 months, CI95% 2-6.7). With weekly paclitaxel/bevacizumab the ORR was 36% and 28.2% achieved stable disease for at least 3 months. Median PFS was 5.8 months (CI95% 4.6-7.1) and OS was 18.0 months (CI95% 15.2-34.2). Grade 3-4 adverse events included neutropenia (10%), onycholysis (7.6%) and infection (5%). One patient died from a massive hemoptysis and prolonged responses were observed in two patients who had received bevacizumab as part of first-line chemotherapy and in another one who harbored an ALK rearrangement. **Conclusion:** In this retrospective series, our results suggest that weekly paclitaxel/bevacizumab had_a good safety and efficacy profile in heavily pre-treated metastatic NSCLC. **Keywords:** paclitaxel, bevacizumab, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-048 Predictors of Subsequent Lines of Therapy (LOTs) in Non-Small Cell Lung Cancer (NSCLC) Eric Nadler[1], John R. Penrod[2], Janet L. Espirito[3], Thomas Wilson[3], Debra A. Patt[4], Beata Korytowsky[2] [1]*Texas Oncology, Dallas/TX/United States of America,* [2]*Bristol-Myers Squibb, Princeton/NJ/United States of America,* [3]*Mckesson Specialty Health, The Woodlands/TX/United States of America,* [4]*Texas Oncology, Austin/TX/United States of America*

Background: In recent years, the number of NSCLC treatment options has increased. The majority of patients receiving first-line therapy (1L) for locally advanced or metastatic NSCLC progress; however, fewer than half receive subsequent treatment. This analysis investigated which factors might be predictive of patients receiving subsequent LOTs within a US community network. **Methods:** A retrospective data analysis was conducted using electronic health records in the US Oncology Network for adult patients with advanced NSCLC receiving second-line therapy from 3/1/10 to 12/31/12, with follow-up through 10/31/14. Patients receiving 1L tyrosine kinase inhibitors (EGFR/ALK+), with concurrent cancer diagnoses, or in a clinical trial were excluded. Data on monotherapy/combination treatments, LOT, staging, histology, ECOG performance status (PS), metastases, comorbidities, age, gender, geography and practice size were collected. Chi-square tests examined patient and disease factors related to the receipt of subsequent treatments (2L–3L and 3L–4L). Logistic regression was used to predict the likelihood of receiving a subsequent LOT in multivariate models. Overall survival (OS) was estimated from diagnosis and from the initiation of each LOT. **Results:** Of 2,122 patients receiving 2L treatment, 963 (45%) advanced to receive 3L and 319 (15%) advanced to receive ≥4L treatment. Median age at 2L was 67 years (range, 34–94); 58% were male. PS at 2L was available for 80% of patients; 8%, 68%, and 24% were PS 0, 1, or 2+, respectively. The histology breakdown was 54% non-squamous, 25% squamous, and 21% not-specified. In univariate analysis, significance (P<0.05) for receiving a 3L/4L+ therapy was found for age, PS, histology, and treatment type. Multivariate analysis results are presented (Table).

LOT	Predictors (P<0.05)	Odds ratio	P-value
3L	PS 2+	0.58	0.005
	Squamous histology	0.54	0.004
	Pemetrexed monotherapy in 1L	0.51	<0.001
4L+	PS 2+	0.48	0.023
	Erlotinib monotherapy in 3L	0.36	0.007
	Age <53–59 years	2.6	0.013

Of patients receiving 2+ LOTs, median OS from advanced NSCLC diagnosis was 22 months (95% CI: 20, 23). Median OS from the start of 2L, 3L, and 4L was 8.9, 7.0, and 7.2 months, respectively. In 2L, median OS for patients who received a 3L compared to those who did not was 13.4 vs 5.0 months (P<0.0001); median OS in 3L for patients who received a 4L compared to those who did not was 12.9 vs 4.9 months (P<0.0001). **Conclusion:** Receiving subsequent LOTs is associated with improved OS in advanced NSCLC. Whether this represents the efficacy of therapeutic agents or an enrichment for patients capable of receiving additional therapy is unclear. Nonetheless, these data on patient and treatment predictive factors may assist in understanding how future treatments might allow more patients to advance to later LOTs.

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-049 Concomitant Chemoradiotherapy with Etoposide & Cisplatin versus Docetaxel & Cisplatin in Locally Advanced Non-Small Cell Lung Cancer Yesim Eralp[1], Fatma Sen[1], Makbule Tambas[2], Kubra Ozkaya[2], Berker Ozkan[3], Ethem N. Oral[2], Esra K. Saglam[2], Pinar Firat[4], Pinar Saip[1], Alper Toker[3], Ahmet Kizir[2], Adnan Aydiner[1] [1]*Istanbul University, Institute of Oncology, Department of Medical Oncology, Istanbul/Turkey,* [2]*Istanbul University, Institute of Oncology, Department of Radiation Oncology,*

Istanbul/Turkey, [3]Istanbul University, Istanbul Faculty of Medicine, Department of Thoracic Surgery, Istanbul/Turkey, [4]Istanbul University, Istanbul Faculty of Medicine, Department of Pathology, Istanbul/Turkey

Background: There is currently no consensus regarding which chemotherapy regimen is best to administer with radiotherapy in patients with locally advanced non–small-cell lung cancer. Here, our aim was to compare the outcome of patients treated with either etoposide-cisplatin (EP) or docetaxel-cisplatin (DP) in this curative setting. **Methods:** The patients treated with concurrent radiotherapy with either EP or DP with from 2004 to 2012 were identified. Patients whose medical records and follow up information obtained in details were included to this retrospective study. Survival rates were compared using Cox proportional hazards regression models with adjustments for confounding provided by propensity score methods. **Results:** A total of 105 patients were treated with concurrent chemoradiotherapy for locally advanced (IIB-IIIA-IIIB) non-small cell lung cancer in Istanbul University, Institute of Oncology between 2004 and 2012. Totally 50 patients (median age 54 yr; 32-70 yr) given concurrent EP and 55 patients (median age 55 yr; 37-73) given concurrent DP were enrolled to analyses. There was no statistically significant difference in baseline clinicopathological features including age, gender, performance status, and weight loss, histological subtype, primary lung side, clinical T, N and TNM stages between 2 groups. In univariate analysis, median overall survival of patients treated with EP was found to be higher than that of patients treated with DP (41 months versus 20 months, p= 0.003). Multivariate analysis further revealed survival advantage with EP as compared to DP (hazard ratio [HR], 0.46; 95% CI, 0.25 to 0.83) (p=0.009). Toxicity profile of 2 treatment groups were found to be similar except that pulmonary toxicity was higher in DP group compared to EP (grade 3-4: 0 versus 6%, p= 0.024). **Conclusion:** Concurrent chemoradiotherapy with EP may provide more favorable outcome than that of DP with acceptable safety profile.
Keywords: locally advanced non-small cell lung cancer, concomitant chemoradiotherapy, etoposide plus cisplatin, docetaxel plus cisplatin

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-050 A Interim Analysis of Randomized Phase III Trial of Nedaplatin or Cisplatin Combined with Docetaxel as First-Line Treatment for Advanced ASQC

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Background: Cisplatin combined with docetaxel is one of the stand treatment in advanced squamous cell carcinoma(ASQC) of the lung. Nedaplatin combined with docetaxel has demonstrated potent activity in ASQC in phase II study. But until now there is no randomized phase III study comparing these 2 chemotherapy regimens. The aim of this study was to evaluate and compare the efficacy and safety between the combination chemotherapy of nedaplatin or cisplatin plus docetaxel in patients with ASQC. **Methods:** This is a multicentre, open-label, randomized, phase III study in China (NCT02088515). Chemo-naive stage IIIB/IV squamous NSCLC with Eastern Cooperative Oncology Group performance status 0/1 were randomized (1:1) to four cycles of nedaplatin (80 mg/m^2) plus docetaxel(75 mg/m^2) or cisplatin(75 mg/m^2) plus docetaxel (75 mg/m^2) . The primary endpoint was progression-free survival (PFS). Secondary end points were overall survival (OS), overall response rate (ORR), disease control rate (DCR) and quality of life. **Results:** From December 2013 to January 2015, 117 patients were accrued: nedaplatin plus docetaxel (n = 57) and cisplatin plus docetaxel (n = 60). The objective response rates were 27% and 31% and the disease control rate were 78.92 % and 82.67% in nedaplatin and cisplatin groups, respectively. There is no significance difference in nausea / vomiting(21% vs 30%) , diarrhea(3% vs 5%), liver dysfunction(12% vs 15%), neutropenia(60% vs 65%), thrombocytopenia(10% vs 12%), anemia(8% vs 7%) between the 2 arms. The renal dysfunction incidence is higher in the cisplatin group(3% vs 0%). Although there is no 3/4 grade toxicities difference between 2 arms including nausea / vomiting(0% vs 0%) , diarrhea(0% vs 1%), liver dysfunction(0% vs 0%), renal dysfunction(0% vs 0%) , neutropenia(4% vs 3%), thrombocytopenia(0% vs 0%), anemia(0% vs 0%) . This is an interim analysis and we haven't got the data of survival and quality of life. **Conclusion:** There is no ORR difference between the group of nedaplatin plus docetaxel and cisplatin plus docetaxel. But the toxicity of nedaplatin regiment is less toxicities, especially in renal toxicity,as first-line treatment for patients with advanced squamous NSCLC
Keywords: squamous cell carcinoma, chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-051 Biomarker Analyses from a Phase II Trial of Nab-Paclitaxel/ Carboplatin vs Emcitabine/Carboplatin in Advanced Squamous Cell Lung Cancer

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Background: The administration of *nab*-paclitaxel/carboplatin (*nab*-PC) as first-line therapy in patients with advanced non-small-cell lung cancer (NSCLC) was efficacious and resulted in a significantly improved objective overall response rate (ORR) versus solvent-based PC in a phase Ⅲ trial. However, our phase Ⅱ trial (NCT01236716; CTONG1002), which compared the efficacy and safety of first-line *nab*-PC with gemcitabine/carboplatin (GC) in advanced squamous cell carcinoma of the lung, only showed a marginally improved ORR caused by first-line nab-PC. Meanwhile, the matricellular glycoprotein SPARC (secreted protein acidic and rich in cysteine) and caveolin-1 are potential biomarkers for advanced NSCLC patients receiving nab-PC. Therefore, we retrospectively aimed to explore their predictive and prognostic value using immunohistochemistry (IHC). **Methods:** From November 2010 to June 2013, 127 untreated patients with locally advanced and metastatic squamous cell carcinoma of the lung were randomly assigned 1:1 to receive first-line *nab*-PC (*nab*-P, 135 mg/m^2, d1, d8, q3w; C, AUC = 5, d1, q3w) or GC (G, 1,250 mg/m^2, d1, d8, q3w; C, AUC = 5, d1, q3w). There were 110 patients evaluable for ORR (nab-PC, 54; GC, 56), 119 evaluable for survival (nab-PC, 57; GC, 62) respectively. However, there were 72 patients with sufficient tissue for IHC of both SPARC and caveolin-1 proteins. Different cut-off values of IHC scoring systems were used to explore predictive and prognostic role of both biomarkers. **Results:** The last follow-up was on January 16, 2015. Considering treatment, when the maximum rank method was used for cut-off values, median progression-free survival (PFS) was 7.5 (95%CI: 2.4~12.6) months in higher SPARC-expression arm and 4.3 (95%CI: 2.2~6.3) months in lower SPARC-expression arm for patients treated with GC, HR=0.43 (95%CI: 0.19~0.94), p = 0.030; Median overall survival (OS) was 20.0 (95%CI: 14.7~25.3) months in lower SPARC-expression arm and 10.1 (95%CI: 6.2~14.0) months in higher SPARC-expression arm for patients treated with nab-PC, HR=2.41 (95%CI: 1.08~5.40), p = 0.027. When average method was used for cut-off values, median OS was 18.2 (95%CI: 9.6~26.8) months in lower SPARC-expression arm and 8.4 (95%CI: 5.1~11.7) months in higher SPARC-expression arm for patients treated with nab-PC, HR=2.46 (95%CI: 1.07~5.65), p = 0.029. Regardless of treatment, when the maximum rank method was used for cut-off values, median OS was 14.5 (95%CI: 6.8~22.1) months in lower SPARC-expression arm and 8.4 (95%CI: 5.3~11.5) months in higher SPARC-expression arm, HR=0.47 (95%CI: 0.27~0.83), p = 0.007. When average method was used for cut-off values, median OS was 14.4 (95%CI: 9.2~19.5) months in lower SPARC-expression arm and 8.4 (95%CI: 5.4~11.4) months in higher SPARC-expression arm, HR=0.48 (95%CI: 0.27~0.87), p = 0.013. ORR was not correlated with expression of SPARC, p>0.05. However, there were no significant differences in ORR, PFS and OS between higher and lower caveolin-1 expression arms, p>0.05. **Conclusion:** SPARC expression could be a negative prognostic factor for OS of patients with advanced squamous cell carcinoma of the lung, but was not a predictive factor for ORR and PFS, except for patients treated with GC. However, caveolin-1 expression had neither predictive nor prognostic value.
Keywords: Gemcitabine, Squamous cell carcinoma of the lung, biomarker, nab-paclitaxel

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-052 Randomized Phase II Individualized Chemotherapy Study Based on BRCA1 and RRM1 Message RNA Level for Advanced NSCLC (BRAVO Study)

Guanghui Gao[1], Shengxiang Ren[1], Aiwu Li[1], Xuefei Li[2], Chao Zhao[2], Wei Li[1], Yayi He[1], Chunxia Su[1], Xiaoxia Chen[1], Yan Wang[1], Jie Zhang[2], Caicun Zhou[1] [1]*Oncology, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Tongji University Cancer Institute, Shanghai/China,* [2]*Tongji University Cancer Institute, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

Background: We assessed whether BRCA1 and RRM1 message RNA(mRNA) levels could help to select chemotherapy regimen to improve objective response rate in patients with advanced NSCLC. **Methods:** Eligible patients were randomly assigned 2:1 according to stratification factors of smoking, gender and histological type. In experimental arm, gemcitabine/cisplatin(GP) were selected if both RRM1 and ERCC1 mRNA levels were low, irinotecan/cisplatin(IP) if RRM1 high and BRCA1 low, gemcitabine/vinorelbine(GN) if RRM1 low and BRCA1 high, and docetaxel(T) if both high. GP was chose in the control arm. The primary end point was objective response rate (ORR). (Registered No. NCT01424709). **Results:** 121 patients were enrolled and 120 received at least one dose of therapy. The median number of cycles given was four in both arms. In experimental arm, 36 patients treated with GP, 14 with IP, 13 with GN and 17 with T. The ORR and DCR were 33.3% and 79.5% in the experimental arm, which were not significant different from 32.5% (p=0.12) and 87.5%(p=0.18) in the control arm. When patients with both low mRNA levels of RRM1 and ERCC1 were removed, the sub-analysis showed the ORR in the experimental arm was marginally significantly higher than in the control arm (42% vs. 36.3%, p=0.06)). Survival analysis showed similar PFS in the two arms (5.1 vs. 5.3m, p=0.11), while sub-analysis revealed that PFS was marginally significantly longer in the experimental arm (5.7 vs. 5.3m p=0.09). No unexpected side effect happened in both arms. **Conclusion:** BRCA1 and RRM1 mRNA levels were potentially used for therapeutic decision making in newly diagnosed patients with advanced NSCLC.
Keywords: NSCLC; mRNA;BRCA1;RRM1

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-053 Efficacy and Safety of Extended Therapy with Endostar Combined with Chemotherapy in Patients with Advanced NSCLC: A Retrospective Study
Weiheng Hu, Fang Jian, Jun Nie, Ling Dai *Department of Thoracic Oncology Ii, Beijing Cancer Hospital, Beijing/China*

Background: It is known that the addition of endostar (recombinant human endostatin, a novel broad-spectrum inhibitor of tumor angiogenesis) to chemotherapy resulted in a significant effective benefit in the treatment of patients with advanced non–small cell lung cancer (NSCLC). Previous research showed that multicycle application of angiogenetic drug combined with chemotherapy might prolong overall survival of NSCLC. However, the optimal treatment duration of endostar and chemotherapy remains uncertain. **Methods:** A retrospective analysis of ≥ 4 cycles versus < 4 cycles of endostar combined with platinum-based doublet chemotherapy(PBDC) was performed in patients with advanced NSCLC. For efficacy assessments, patients received ≥ 4 cycles of therapy (extended group) were compared with those who received less than 4 cycles but not because of tumor progression (control group). Toxicity analyses were performed for all patients. **Results:** A total of 232 patients were enrolled, of whom 128 patients completed at least four cycles of the therapy (extended group), 64 patients ceased their therapy before 4 cycles not because of progression(control group). The median progress free survival(PFS) was 8.2 months versus 5.4 months in extended group and control group (p=0.027), and the median overall survival(OS) was 22.5 months versus 13.6 months (p=0.000), respectively. Subgroup analysis showed that, among the EGFR mutation-positive patients, the control group seemed to result in a trend toward survival benefit according to the Kaplan-Meier curves, although the differences are not statistically significant. Hematological toxicity and fatigue occurred more frequently in patients received 4 or more cycles (p<0.05), but no statistically significant difference was detected in all grade ≥3 adverse events.

Fig. 1 Kaplan-Meier curves for progression-free survival by treatment group

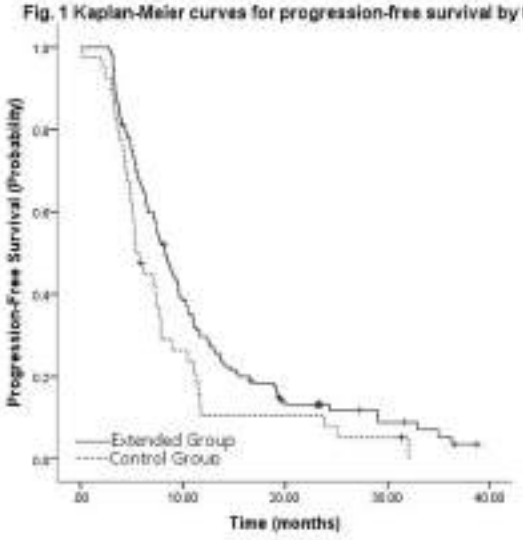
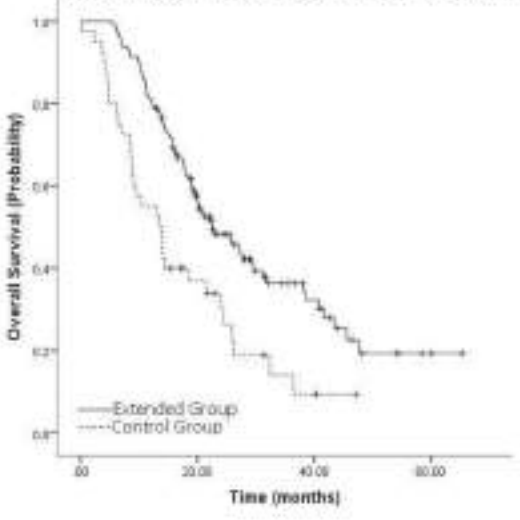


Fig. 2 Kaplan-Meier curves for overall survival by treatment group



Conclusion: Extended treatment of endostar combined with chemotherapy exhibited increased survival and acceptable toxicity in previously untreated patients with NSCLC, supporting further evaluation in larger prospective studies.
Keywords: NSCLC, Extended Therapy, chemotherapy, Endostar

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-054 Etirinotecan Pegol (NKTR-102) in the Treatment of Patients with Metastatic NSCLC after Failure of 2nd Line Treatment: A Phase II Study
Charu Aggarwal, Roger B. Cohen, Tracey Evans, Evan Alley, Joshua Bauml, Arati Desai, Kristine Mykulowycz, Hope Kushner, Mona Jacobs-Small, Corey J. Langer *University of Pennsylvania, Philadelphia/PA/United States of America*

Background: 3rd line treatment options are limited for patient (pts) with metastatic NSCLC. NKTR-102 is a long-acting topoisomerase-I inhibitor designed to concentrate in tumors and provide continuous exposure throughout the chemotherapy cycle. Based on clinical activity of irinotecan in NSCLC, we conducted a Phase II single arm trial to evaluate efficacy of NKTR-102. **Methods:** Pts >18 yrs with histologically proven NSCLC who received 2 prior systemic therapy regimens were eligible. Measurable disease, ECOG PS ≤1 and adequate end organ function were required. NKTR-102, 145mg/m2 was administered IV q3 weeks till progression. Response was assessed q6 weeks by RECIST 1.1. Primary endpoint was overall response rate. Secondary endpoints were progression free survival (PFS), overall survival (OS) and safety. Simon two-stage design was implemented; if 0/12 responses were observed in the 1st stage, the study would be terminated for futility. If there was at least 1 objective response in the 1st stage, the study would continue to stage 2, enrolling an additional 25 pts, for a total of 37. **Results:** Between 01/2013 and 01/2015, 37 pts have been enrolled. Median age 63 yrs (18-82), 45% female, ECOG PS 0=8 pts, 92% current/former smokers, 9 pts with squamous cell, 28 had adenocarcinoma. Median time from diagnosis to initiation of NKTR-102 was 18 mos (6-72). Pts received a median of 3 cycles (1-13). All pts were evaluable for response rate and toxicity. One pt in Stage I (adenocarcinoma) had a partial response. Fifteen pts had stable disease, 7 pts are still on treatment. 3 pts had Grade 3 GI toxicity attributable to NKTR-102. 6 pts required a dose reduction to 120 mg/m2 due to diarrhea. There was no hematological toxicity. Median PFS was 2.3 mos. For pts with >1 yr follow up (n=20), median OS was 5.5 mos. Complete PFS and OS data will be presented. **Conclusion:** NKTR-102 is well tolerated and leads to stabilization of disease in third line treatment of metastatic NSCLC. These clinical data combined with a favorable safety profile warrant further clinical investigation of this agent. Clinical trial information: NCT01773109.
Keywords: pegylated irinotecan, 3rd line therapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-055 Carboplatin-Pemetrexed Combination in Elderly Patients with Advanced Non-Squamous Non Small Cell Lung Cancer (NS-NSCLC)
Sergio Vazquez[1], Maria Carmen Areses[2], Natalia F. Núñez[3], Ana Alonso Herrero[4], Marta Covela Rúa[3], María J. Villanueva Silva[4], Francisco J. Afonso-Afonso[5], Gaspar Esquerdo Galiana[6], Martin Lazaro Quintela[4], Jesus Garcia Mata[2], Urbano Anido Herránz[7], Joaquin Casal Rubio[4], José L. Fírvida Pérez[2] [1]*Hospital Universitario Lucus Augusti, Lugo/ Spain,* [2]*Complejo Hospitalario Universitario de Ourense, Ourense/Spain,* [3]*Oncología Médica, Hospital Universitario Lucus Augusti, Lugo/Spain,* [4]*Oncología Médica, Complexo Hospitalario Universitario de Vigo, Vigo/Spain,* [5]*Oncología Médica, Complejo Hospitalario Universitario de Ferrol, Ferrol, A Coruña/Spain,* [6]*Oncología Medica, Hospital de Benidorm, Benidorm/ Spain,* [7]*Complexo Hospitalario Universitario de Santiago, Santiago de Compostela/Spain*

Background: The standard treatment for elderly patients in advanced NS-NSCLC is not defined. The aim of this study was to evaluate the efficacy and safety profile of the combination of carboplatin and pemetrexed in this population. **Methods:** Elegibility criteria included, histologically or citologically confirmed NS-NSCLC clinical stage IIIB vs IV, evaluable disease, no prior cytotoxic chemotherapy, an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, an adequate organ function and ³ 70 years old. Patients received carboplatin at an area under the concentration time curve (AUC) of 5 and pemetrexed 500 mg/m2 for four cycles on day 1 every 3 weeks. In non-progressing patients, maintenance therapy with pemetrexed every 3 weeks was optional to continue at the discretion of the investigator, until either disease progression or unacceptable toxicity. The primary endpoint was progression-free survival (PFS). The secundary endpoints were the response rate (RR), disease control rate (DCR), overall survival (OS) and the rates of adverse events. **Results:** A total of thirty-six patients were included in a phase II clinical trial from 6 different centers. The patients demographics were: median age 76 years (range 70-82), 8 female and 28 male; 33 patients adenocarcinoma and 3 large-cell lung carcinoma; tumor EGFR status wild type in all patients. 51% went to manteinance. Among 32 patients evaluated, the RR was 31,3%, disease stabilization 31,3%, disease progression 28,1% and non-evaluable 9,3%. The DCR was 62.5%. In non-manteinance group the PFS was 4.1 months and OS 8.6 months. In the manteinance group instead, the PFS was 9.5 months and OS 11.9 months. Most common attributable adverse events were fatigue and anemia. Each of the toxicities were controllable and there were no treatment-related deaths. **Conclusion:** These data provided that Carboplatin and pemetrexed combination is effective and well tolerated in elderly patients with advanced NS-NSCLC
Keywords: Carboplatin and pemetrexed; NS-NSCLC; elderly; effective; well tolerated

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-056 Phase II Study of Carboplatin plus Weekly Nab-Paclitaxel in Elderly Patients with NSCLC: North Japan Lung Cancer Study Group Trial 1301
Osamu Ishimoto[1], Kazuhiro Usui[2], Makoto Maemondo[3], Eisaku Miyauchi[4], Heisuke Saito[5], Yuka Fujita[6], Terufumi Kato[7], Toshiro Suzuki[8], Taku Nakagawa[9], Toshiyuki Harada[10], Hiroyuki Miura[11], Hiroshi Watanabe[12], Akira Inoue[4], Masakazu Ichinose[4] [1]*Respiratory Medicine, Sendai Kousei Hospital, Sendai/Japan,* [2]*Respirology, Ntt Medical Center Tokyo, Tokyo/*

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Background: Recent IFCT-0501 trial demonstrated that carboplatin (CBDCA) combined with weekly paclitaxel (PTX) would be advantageous compared with monotherapy. Subsequently, CA031 trial suggested that weekly nab-paclitaxel (nab-PTX) was superior in efficacy and safety compared with 3-weekly PTX when combined with CBDCA. Since the subgroup analysis for elderly patients (pts) in CA031 showed very promising data (34% of overall response rate (ORR) and 8.0 months of progression-free survival (PFS)), we conducted this multicenter, non-randomized, open label, phase II trial to evaluate the efficacy and tolerability of CBDCA plus weekly nab-PTX regimen for elderly patients with advanced non-small cell lung cancer (NSCLC) prospectively. **Methods:** Eligible pts were aged 75 years or older with newly diagnosed clinical stage IIIB, IV, and postoperative recurrence NSCLC; ECOG performance status (PS) of 0-1; adequate organ function; written informed consent. Pts received CBDCA (AUC 6) on day 1 and nab-PTX (75mg/ m^2) on day1, 8, and 15, every 4 weeks. The primary endpoint was ORR and secondary endpoints were PFS, overall survival (OS), and toxicity profile. Assuming that ORR of 40% would be potential usefulness while ORR of 20% would be the lower limit of interest, 32 pts were required. **Results:** Between March 2013 and May 2014, 35 pts were enrolled and 32 pts were eligible. Median age was 78 years (range, 75-86), 84% (27/32) were male and 56% (18/32) were stage IV. 56% (18/32) had squamous cell carcinoma and 44% (14/32) had adenocarcinoma. Median treatment cycle was 4 (range, 1-6). ORR and DCR were 50% (95%CI: 33-67) and 94% (95%CI: 85-100), respectively. With a median follow-up of 9.1 months, median PFS was 6.4 months (95%CI: 4.8-8.0). Median OS had not been reached at the data cutoff point. Grade 3 or severer toxicities were as follows: neutropenia (47%), leukopenia (38%), anemia (34%), thrombocytopenia (25%), and anorexia (9%). No febrile neutropenia and treatment-related deaths were observed. **Conclusion:** The combination of CBDCA and weekly nab-PTX demonstrated significant efficacy with acceptable toxicities in elderly patients with advanced NSCLC.
Keywords: NSCLC, elderly, nab-paclitaxel, carboplatin

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-057 Randomized Phase 2 Study of Plinabulin and Docetaxel in Patients with Advanced Non-Small Cell Lung Cancer - Mechanism-Based Efficacy Analyses Lyudmila Bazhenova[1], Osvaldo Arén Frontera[2], Alain Mita[3], Jonathan Polikoff[4], Steven Reich[5], Gloria Lee[6], William Mikrut[7], Lan Huang[6] [1]*Moores Cancer Center, University of California San Diego, La Jolla/United States of America, [2]Centro Internacional de Estudios Clinicos, Santiago/Chile, [3]Cedars Sinai Medical Center, Los Angeles/CA/United States of America, [4]Kaiser Permanente, San Diego/CA/United States of America, [5]Na, Del Mar/ CA/United States of America, [6]Beyondspring Pharmaceuticals, New York/United States of America, [7]Currently Vantage Data Designs, San Diego/AL/United States of America*

Background: Plinabulin (N), a tubulin binding agent, which depolarizes microtubules, resulting in tumor vasculature obliteration, apoptosis via JNK pathway and maturation of dendritic cells. A multicenter randomized phase 2 study was performed to compare overall survival (OS) between plinabulin/docetaxel (DN) and docetaxel (D). Results of Intent-to-treat (ITT) analyses have been presented at ASCO 2014. The primary objective of OS prolongation was not met, however, exploratory mechanism based analysis revealed improvement in outcomes in patients with large tumors. **Methods:** From November 2008 to July 2011 172 patients with advanced NSCLC who progressed after at least one chemotherapy were enrolled. Patients were treated with D 75mg/m^2 on day 1 and N 30 mg/^{2} on days 1 and 8. A second cohort of N 20 mg/m^2 was also enrolled. This exploratory analysis is based on 105 patients (50 DN arm and 55 D arm) receiving 30 mg/m^2 dose, which was selected for an ongoing Phase 3 study and explains the population chosen for future investigation. **Results:** Median OS was 8.7 months (m) (CI 6.6-12.6) in DN arm and 7.5 m (6.3-10.5) in D arm (p=0.899, HR=0.97). PFS was 2.8 m and 3.5 m and ORR was 14.0% vs 14.5% respectively. Among clinical parameters, lesion size (Table 1) and presence of pulmonary disease were identified to impact OS. The OS in patients with pulmonary disease was 11.3 m (6.7-15.1) in DN and 6.7 m (6-9.8) in D, respectively (p=0.29, HR=0.76) regardless of lesion size.

Table 1: Exploratory Analysis of Overall Survival by Tumor Size

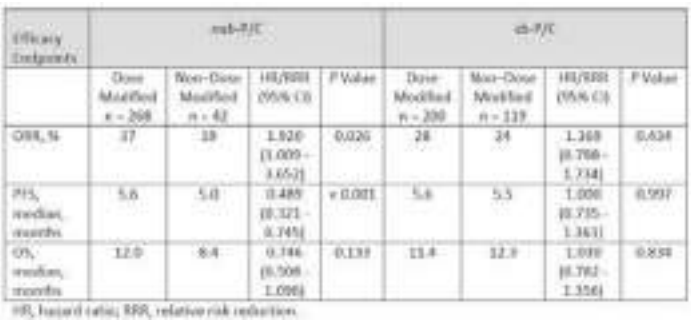
Patients	Tumor size	Median OS Months (95% CI)	Hazard Ratio	P-value	
DN (30mg/m^2)	**D**				
ITT 1 and 2 prior chemo-therapy	All	8.68 (6.33, 12.63) N=50	7.47 (6.17, 10.60) N=55	0.972	0.8993
≤ 3 cm	6.45 (3.73, NA) N=16	6.47 (5.6, 22.43) N=19	0.934	0.8687	
> 3 cm	8.98 (6.60, 12.63) N=34	7.47 (4.77, 11.60) N=36	0.967	0.8990	
> 5 cm	8.98 (4.57, 19.23) N= 20	6.70 (4.07, 12.93) N=21	0.750	0.4176	
> 7 cm	7.32 (4.57, 19.23) N= 8	5.03 (2.93, 6.70) N= 10	0.507	0.1936	

CI = confidence interval; D = docetaxel; DN, docetaxel + plinabulin; ITT = intent-to-treat; OS = overall survival (Months). **Conclusion:** Mechanism-based exploratory analyses of Phase 2 results have identified advanced NSCLC patients with lung lesion size >3 cm to have benefited from plinabulin. A Phase 3 to confirm this observation is on-going.
Keywords: metastatic, chemotherapy, lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-058 *nab*-Paclitaxel + Carboplatin in Advanced Non-Small Cell Lung Cancer NSCLC: Dose Modification Analysis Pieter E. Postmus[1], Mary E.R. O'Brien[2], Mark A. Socinski[3], Li Li[4], Teng Jin Ong[4], Cesare Gridelli[5] [1]*Clatterbridge Cancer Center, Liverpool/United Kingdom, [2]Royal Marsden Hospital, London/United Kingdom, [3]Upmc Cancer Pavilion, University of Pittsburgh, Pittsburgh/PA/United States of America, [4]Celgene Corporation, Summit/United States of America, [5]S.G. Moscati Hospital, Avellino/Italy*

Background: Chemotherapy dose modifications may impact clinical outcomes in patients with cancer. In a phase III trial, first-line treatment of patients with advanced NSCLC with *nab*-paclitaxel plus carboplatin (*nab*-P/C) significantly improved the overall response rate (ORR; primary endpoint) compared with solvent-based paclitaxel plus C (sb-P/C; 33% vs 25%; *P* = 0.005; Socinski et al. *J Clin Oncol*. 2012;30:2055-2062). This exploratory analysis examined the correlation between patients receiving protocol-specified dose modifications and clinical outcomes in the phase III trial. **Methods:** Patients with histologically or cytologically confirmed stage IIIB/IV NSCLC and no prior chemotherapy for metastatic disease received either *nab*-P 100 mg/m^2 on days 1, 8, and 15 or sb-P 200 mg/m^2 on day 1, both in combination with C AUC 6 on day 1, every 21 days (randomized 1:1). ORR and progression-free survival (PFS) were assessed by blinded, centralized review. *P* values for ORR were based on the chi-square test, and those for overall survival (OS) and PFS were based on the log-rank test. Patients who discontinued treatment before cycle 3 or remained on treatment after 6 months were excluded from this analysis unless otherwise specified. **Results:** Dose modification and clinical outcomes for patients treated for ≥ 3 cycles but ≤ 6 months are shown in the Table. In the *nab*-P/C arm, 268 of 310 patients (86%) who were treated for ≥ 3 cycles and ≤ 6 months had a dose modification compared with 200 of 319 (63%) in the sb-P/C arm. In the *nab*-P/C cohort, ORR and PFS were significantly higher in patients who received a dose modification vs those who did not (Table), possibly due to better tolerability and longer treatment duration. In the sb-P/C arm, there were no differences in efficacy outcomes between either group. As predicted, patients with a lower numerical incidence of toxicity were those that did not require dose modifications. **Conclusion:**This exploratory analysis suggested that, in this patient subset, protocol-specified dose modifications did not negatively impact the primary endpoint of ORR and in fact resulted in a greater ORR for those receiving *nab*-P/C.



Efficacy Endpoints	nab-P/C				sb-P/C			
	Dose Modified n = 268	Non-Dose Modified n = 42	HR/RRR (95% CI)	P Value	Dose Modified n = 200	Non-Dose Modified n = 119	HR/RRR (95% CI)	P Value
ORR, %	37	19	1.920 (1.009 - 3.652)	0.026	28	24	1.169 (0.766 - 1.734)	0.434
PFS, median, months	5.6	5.0	0.489 (0.321 - 0.745)	< 0.001	5.6	5.5	1.006 (0.735 - 1.361)	0.997
OS, median, months	12.9	8.4	0.746 (0.508 - 1.096)	0.133	13.4	12.3	1.039 (0.782 - 1.356)	0.858

HR, hazard ratio; RRR, relative risk reduction

Keywords: nab-paclitaxel, carboplatin, NSCLC, dose modification

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-059 Treatment Intensity and Duration in Patients Receiving First-Line Nab-paclitaxel or Paclitaxel (Weekly or Every 3 weeks) for Stage IV Non-Small Cell Lung Cancer (NSCLC): A Retrospective Analysis Utilizing Electronic Medical Records Jared Weiss[1], Rex W. Force[2], Brooke A. Pugmire[2], Teri Peterson[2], Claudio Faria[3], Sandra Margunato-Debay[3], Manish Patel[4] [1]*Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill/NC/United States of America,* [2]*Improverx, Pocatello/United States of America,* [3]*Celgene Corporation, Summit/NJ/United States of America,* [4]*Health Economics, Celgene Corporation, Summit/NJ/United States of America*

Background: In a phase III trial, weekly *nab*-paclitaxel (*nab*-P) plus carboplatin demonstrated a significantly higher response rate than paclitaxel (P) plus carboplatin every 3 weeks, with less grade ≥ 3 neuropathy, neutropenia, arthralgia, and myalgia but more thrombocytopenia and anemia in patients with advanced NSCLC (Socinski et al. *J Clin Oncol*. 2012;30:2055-2062). We hypothesized that these differences might lead to differences in the cumulative dose received and regimen duration in clinical practice. **Methods:** Fully de-identified electronic medical records (EMRs) from October 1, 2012, to September 30, 2014, from a national EMR (OncoEMR; Altos Solutions, Inc) were analyzed. Patients receiving first-line therapy with P every week (P7), P every 3 weeks (P21), or *nab*-P every week for stage IV NSCLC were identified. The majority of patients also received carboplatin. The total cumulative dose (mg/m^2), treatment duration, and database persistence (a surrogate for overall survival) for the taxane regimens were determined. Regression and Cox proportional hazards models were used to assess the 3 groups, with the inclusion of age, sex, race, platin use, bevacizumab use, histology, prior adjuvant taxane use, and comorbidities (a total of 11 degrees of freedom) to control for the potentially confounding effects of these variables. **Results:** A total of 475 patients had complete data. 208 patients with NSCLC received P7, 153 received P21, and 114 received *nab*-P. The total cumulative dose was significantly greater for *nab*-P (932 mg vs 487 mg for P7 and 695 mg for P21; $P < 0.001$ for both). The median treatment duration was 104.5 days for *nab*-P, 69.5 days for P7, and 84.0 days for P21 ($P < 0.05$ for both). The median database persistence after taxane initiation was significantly longer for *nab*-P (378 days vs 214 days for P7 and 196 days for P21; $P < 0.001$ for both). **Conclusion:** Patients with NSCLC treated with *nab*-P had a longer treatment duration, received a greater cumulative dose, and had longer database persistence than patients treated with P7 or P21. **Keywords:** NSCLC, treatment intensity, duration

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

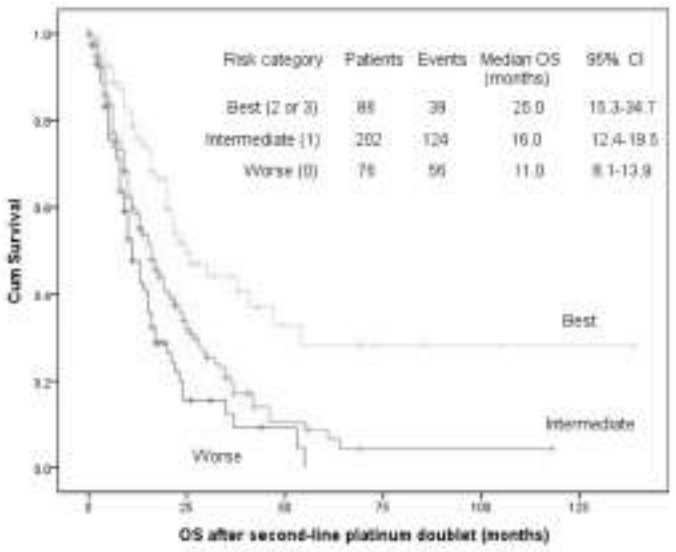
P3.01-060 Prognostic Value of Serum Proteomic Test and of Comorbidity Index in Diversified Population with Lung Cancer Arkadiusz Z. Dudek[1], Mani Keshgtarpur[2], Jack Zwanziger[3] [1]*Medicine, University of Illinois, Chicago/IL/United States of America,* [2]*Medicine, University of Illinois, Chicago/United States of America,* [3]*School of Public Health, University of Illinois, Chicago/AL/United States of America*

Background: Proteomic (VeriStrat®) serum test has prognostic and predictive value in response to erlotinib; but the relation between comorbidity index and test performance and usefulness of this test in different races has not been adequately studied yet. **Patients and Methods:** We have reviewed electronic records of lung cancer patients from 09/2009 till 07/2014who had proteomic test performed to help with therapy choice. Extracted data was analyzed for survival using SAS software 9.4. **Results:** Among 49 qualified patients, 31 had VeriStrat® test done before and 18 after the first line treatment for metastatic disease. Nineteen cases with good VeriStrat® (VSG) test received erlotinib, and 12 received chemotherapy; 4 cases with VeriStrat® poor (VSP) results received erlotinib and 12 received chemotherapy. When stratified for test results "VSG vs. VSP" overall survival did not differ between white race and other races (HR=1.005; 95%CI=0.43-2.35; p=0.99). There was a trend of better survival for combined effect of VeriStrat® good test (VSG) and African American (AA) race. Patients with VSG test had better survival than patients with VSP test in each Charlson comorbidity index (CCI) stratum. **Conclusion:** Our study shows that there is no significant impact of race on prognostic and predictive values of VeriStrat® test. Prognostic value of this test is independent of comorbidities and older age. **Keywords:** comorbidity ndex, non-smal cell lung cancer, epidermal growth factor inhibitor therapy, proteomic serum test

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-061 A Prognostic Model for Platinum-Doublet Regimens as Second-Line Chemotherapy in Advanced Non-Small-Cell Lung Cancer (NSCLC) Patients Yuankai Shi, Hongnan Mo, Xuezhi Hao, Yutao Liu, Lin Wang, Xingsheng Hu, Jianping Xu, Sheng Yang, Puyuan Xing, Youwu Shi, Bo Jia, Yan Wang, Junling Li, Hongyu Wang, Ziping Wang, Yan Sun *Department of Medical Oncology, Cancer Institute and Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing Key Laboratory of Clinical Study on Anticancer Molecular Targeted Drugs, Beijing/China*

Background: Poor prognosis of advanced non-small-cell lung cancer (NSCLC) patients and the promising therapeutic effect of platinum urge the oncologists to evaluate the role of platinum-doublet as second-line chemotherapy and establish the definition of platinum sensitivity in NSCLC. **Methods:** We retrospectively analyzed 364 advanced NSCLC patients who received platinum-doublet regimens as second-line chemotherapy after platinum-based first-line treatment. Patients were divided into four groups by their time-to-progression (TTP) after first-line chemotherapy: 0-3, 4-6, 7-12, and >12months group, respectively. Treatment efficacy of patients' overall survival (OS), progression-free survival (PFS) and response rate (RR), as well as treatment-related toxicity, were compared among the four groups. A prognosis score system was established by Cox proportional hazard model. **Results:** All patients had Eastern Cooperative Oncology Group performance status (ECOG PS) of 0-1. As part of the platinum-doublet regimen,145(39.8%) patients received taxol, 81(22.3%) received gemcitabine, 99(27.2%) received pemetrexed, 32(8.8%) received vinorelbine, 4(1.1%) received etoposide, and 3(0.8%) received irinotecan. The most frequent grade 3/4 toxicity was neutropenia (20.1%) and nausea/vomiting (3.3%).The median follow-up time was 11.0 months. Patients with TTP> 12 months had significant longer survival than the rest of the group after second-line platinum-rechallenge (HR, 0.809; 95% CI: 0.703-0.931;P=0.003).Prognostic score (TAF score) was calculated by adding 1 point each for any of the following: TTP>12 months, age≤60 years, and female, all of which were independent prognostic factors for patient survival (P=0.015, P=0.002, P=0.012, respectively). Median OS were equal to 25.0, 16.0 and 11.0 months for best (2-3 points), intermediate (1 point) and worst (0 point) category, respectively (P<0.0001, Figure 1). Figure 1 Kaplan–Meier curves of overall survival according to patients' TAF Score. After second-line platinum-based chemotherapy, patients with a TAF Score of 2-3 had significant better survival than those scored 0 or 1 (P<0.0001).



Conclusion: A TAF score of 2 or 3 points indicates a good prognosis if advanced NSCLC patients received platinum-rechallenge after disease progression. **Keywords:** Non-small-cell lung cancer, platinum rechallenge, second-line chemotherapy, prognostic model

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-062 Impact of Gender on Survival Outcome in Saudi Patients with Advanced Non-Small Cell Lung Cancer Hani Eltaani[1], Shereef Elsamany[2], Turki Al-Fayea[3] [1]*King Abdullah Medical City, Makkah/Saudi Arabia,* [2]*Oncology Center, Mansoura University, Mansoura/Egypt,* [3]*King Abdulaziz Medical City(Kamc) - Jeddah Princess Nourah Oncology Centre, Jeddah/Saudi Arabia*

Background: Different prognostic variables have been proposed in non-small cell lung cancer (NSCLC). The present study aims to evaluate the prognostic value of patients' gender in Saudi patients with advanced non-squamous NSCLC. **Methods:** In this retrospective study, patients with stage IIIB-IV non-squamous NSCLC, from 3 institutes in Saudi Arabia, were included. We examined the distribution of patients and treatment characteristics at diagnosis according to the gender.These categorical variables were compared using Chi-square test. Overall survival (OS) was assessed according to the gender in addition to age categories (≤ 60 vs. > 60 years), ECOG performance status (PS) (0-2 vs. 3-4), type of 1st line chemotherapy (pemetrexed containing vs. others) and EGFR status. Differences in survival distributions were evaluated via Log Rank test. Multivariate analysis by Cox proportional hazard model has been used to check for independent prognostic factors associated with OS. **Results:** One hundred and twenty patients were included (100 stage IV, 20 stage IIIB, 92 males, 28 females). Eighty patients had available results of EGFR testing and 26.2% of them were mutant. EGFR mutations were more common among female patients (45.4% vs.18.9%, p=0.023). Only half of EGFR-mutant patients received 1st line erlotinib, while the other half received erlotinib as a maintenance or 2nd line therapy due to delayed EGFR testing results. No difference in the distribution of other parameters according to the gender including age, PS, site (bone vs. others) and number of metastasis (single vs. multiple), type of 1st line therapy and number of cycles of chemotherapy. After a median follow up of 22 months (range 15-31 months), greater proportion of females were alive compared to males (60.7% vs. 23.9% respectively, p<0.0001). In univariate analysis, OS was improved in female patients (female; 23.0 months, 95% CI= 17.03-28.97 vs. male; 8.7 months, 95% CI= 5.16-12.24, p < 0.0001), PS 0-2 (PS 0-2;14.4 months, 95% CI= 10.66-18.14 vs. PS 3-4; 2.0 months, 95% CI= 0.50-4.99, p < 0.0001), those with pemetrexed-containing chemotherapy (pemetrexed-containing; 17.0 months, 95%

CI=12.87-21.13 vs. others; 11.0 months, 95% CI=5.90-16.10, p= 0.019) and EGFR-mutant patients (mutant; 23.0 months, 95% CI=16.41-27.39 vs. wild;11.7 months, 95% CI=8.24-15.16, p=0.006). In multivariate analysis, mutant EGFR status (HR=2.49, 95% CI=1.19-5.19, p=0.015) and female gender (HR=2.78, 95% CI= 1.30-5.95, p=0.008) were independent predictors of improved OS. **Conclusion:** Female Saudi patients with advanced non-squamous NSCLC have better survival outcome irrespective of their EGFR status. Low frequency of smoking habit among Saudi females may explain this outcome.
Keywords: gender, prognosis, advanced, lung cancer

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-063 Development of a Patient-Reported Outcome (pro) Assessment of Core Non-Small Cell Lung Cancer (NSCLC) Symptoms Kendra Debusk[1], Nathan Johnson[2], Christopher Evans[3], Adrian Jubb[4], Alan Sandler[5], Suresh S. Ramalingam[6], Alicyn K. Campbell[1] [1]*Patient Centered Outcomes Research, Genentech, South San Francisco/CA/United States of America,* [2]*Endpoint Outcomes, Boston/MA/United States of America,* [3]*Endpoint Outcomes, Boston/United States of America,* [4]*Achaogen, South San Francisco/AL/United States of America,* [5]*Genentech, South San Francisco/United States of America,* [6]*Emory University, Atlanta/United States of America*

Background: Early stage lung cancer is largely asymptomatic; however, as the disease progresses, patients experience significant distress from their lung cancer symptoms. The assessment and monitoring of changes in NSCLC symptoms is increasingly important in clinical trials when making treatment comparisons between new therapies. The objective of this study was to capture the patient perspective on core symptoms of NSCLC in order to develop a new symptom measure for use in clinical trials. **Methods:** This was a non-interventional, cross-sectional qualitative study that consisted of conducting individual interviews with patients with a diagnosis of NSCLC who were either treatment-naïve or had already received surgery, chemotherapy, radiation, or targeted therapy. Patients aged ≥18 years with stage IIB-IV NSCLC took part in concept elicitation interviews to provide descriptions of NSCLC symptoms, including severity, frequency and development over time. Data were used to develop the items constituting the Symptoms in Lung Cancer (SILC) Questionnaire. **Results:** A total of 28 patients were recruited (17 treatment-naïve, 11 post-treatment) for concept elicitation interviews. In the treatment-naïve population, the most common spontaneously reported symptoms of NSCLC were cough (58.8%), shortness of breath (47.1%), chest pain (47.1%) and fatigue (29.4%). These symptoms were included in the initial 12-item version of the SILC. An additional 10 patients participated in cognitive interviews to ensure that the items were correctly interpreted, relevant, and disease-related (i.e., not treatment-related). Following cognitive interviews and analysis of data from treatment-naïve and post-treatment patients, the fatigue items were dropped after patients indicated that attributing a specific symptom to the underlying condition or treatment was challenging. The final draft of the 9-item SILC uses a 5-point verbal response scale (higher scores indicating greater severity/frequency), a 7-day recall period, and assesses 3 core symptom concepts: chest pain (severity and frequency), cough (severity and frequency), dyspnea (while lying down/sitting, standing, walking, carrying a light load and when walking up an incline). **Conclusion:** SILC is an easy-to-use and concise tool to assess the core symptoms of disease in NSCLC patients, and is in compliance with the FDA PRO Guidance (2009) document.
Keywords: Patient-reported outcomes, PRO, Patient-centered outcomes research, symptoms

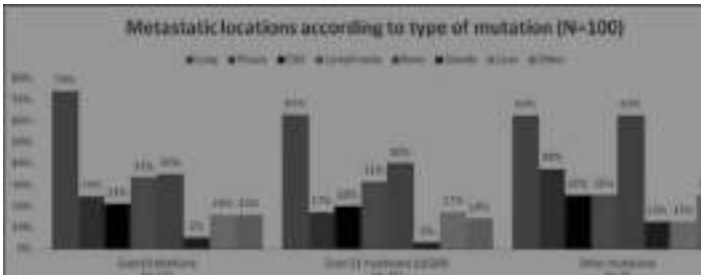
POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-064 Erlotinib in EGFR-Positive NSCLC: Efficacy, Safety and Feasibility for Rebiopsy Manuel Trigo[1], Juana Oramas[2], David Aguilar[3], Javier De Castro[4], An Laura Ortega[5], Margarita Majem[6], Emilio Esteban[7], Beatriz Esteban[8], Cristina García-Bernáldez[9], Rocio Gordo[9] [1]*Hospital Universitario Virgen de La Victoria, Málaga/ Spain,* [2]*Hospital Universitario de Canarias, Tenerife/Spain,* [3]*Hospital Universitario de Gran Canaria Doctor Negrín, Gran Canaria/Spain,* [4]*Hospital Universitario La Paz, Madrid/ Spain,*[5]*Complejo Hospitalario Ciudad de Jaén, Jaén/Spain,* [6]*Hospital de La Santa Creu I Sant Pau, Barcelona/Spain,* [7]*Hospital Universitario Central de Asturias, Asturias/Spain,* [8]*Hospital General de Segovia, Segovia/Spain,* [9]*Roche Farma S.A., Madrid/Spain*

Background: First-line Erlotinib (E) delays progression in 10-14 months in patients (p) harboring *EGFR* mutations (*EGFR*m+). Understanding the resistance mechanisms in order to personalize treatment justify the need for rebiopsy. However, undergoing this procedure could be not feasible on a daily basis. Due to different clinical courses and progression patterns, NCCN guidelines recommend strategies according to symptomatology, extent and site of metastasis in recurrent setting. Nowadays, identifying tumour recurrence patterns and evaluating the potential limitations of rebiopsy are relevant in clinical practice. **Methods:** ASPET is an ongoing, multicentre, observational study. Eligible p are chemonaïve with *EGFR*m+ advanced NSCLC treated with E (150mg/d, until unacceptable toxicity or progressive disease). Primary endpoint is to correlate PFS and tumour localization/characteristics at progression. The evaluation of potential feasibility of rebiopsy (questionnaires completed by physicians and p at diagnosis) is one of the secondary endpoints. **Results:** Baseline characteristics of 100 p included in this preliminary analysis: mean age 66 yrs; 65% female; 89% adenocarcinoma; 91% stage IV; 69% PS-ECOG 0-1; 60% never smokers; 31% central tumours; 57% Del19, 35% L858R, 8% other mutations. Different metastatic locations according to type of mutation have been reported (Figure 1). Objective Response Rate of 63.33% and Disease Control Rate of 90% (60 p evaluable). Main related grade≥3 toxicities were skin disorders (7%) and diarrhoea (2%). Questionnaires completed by 80 physicians: 81.2% considered technically feasible repeat biopsy, 66.25% believe that p would be willing to undergo rebiopsy and 72.5% would direct changes in therapy with rebiopsy results. Results from questionnaires completed by 69% of p are shown in Table 1.

Table 1: Results from patient-reported questionnaires (N=69)

Before the biopsy procedure, you thought that it would be	**N (%)**
Not uncomfortable	13 (18.84)
Uncomfortable	31 (44.93)
Painful	22 (31.88)
Insufferable	3 (4.35)
The punctures of each lesion have been	**N(%)**
Not uncomfortable	23 (33.33)
Uncomfortable	34 (49.28)
Painful	9 (13.04)
Insufferable	3 (4.35)
Overall, you consider the procedure	**N(%)**
Not uncomfortable	20 (28.99)
Uncomfortable	37 (53.62)
Painful	9 (13.04)
Insufferable	3 (4.35)
If you would have to repeat another biopsy	**N(%)**
I will do it	52 (75.36)
I will not repeat it again	4 (5.80)
I would need anesthesia	13 (18.84)



Conclusion: Rebiopsy is considered feasible for physicians in clinical practice and the majority of p would undergo a second biopsy. No new safety data have seen so far and efficacy results in terms of responses match with previously reported data.
Keywords: Erlotinib, EGFR, rebiopsy, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-065 PET Tumor Response by PERCIST Predicts Local-Regional Control in Locally Advanced NSCLC after Concurrent Chemoradiotherapy with Erlotinib Xiong Wei[1], Pamela K. Allen[1], Jeremy Erasmus Jr[2], George Blumenschein, Jr.[3], Myrna Godoy[2], Jack Lee[4], Michael S. O'Reilly[1], James W. Welsh[1], James D. Cox[1], Waun Ki Hong[5], Ritsuko U. Komaki[1] [1]*Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston/TX/United States of America,* [2]*Diagnostic Radiology, The University of Texas MD Anderson Cancer Center, Houston/TX/United States of America,* [3]*The University of Texas MD Anderson Cancer Center, Houston/United States of America,* [4]*Biostatistics, The University of Texas MD Anderson Cancer Center, Houston/TX/United States of America,* [5]*Diagnostic Radiology, The University of Texas MD Anderson Cancer Center, Houston/United States of America*

Background: Assessing response of locally advanced non-small cell lung cancer (NSCLC) after concurrent chemoradiotherapy by computed tomography (CT) can be complicated by treatment-related pneumonitis or fibrosis. Hypothesizing that measurements of tumor response by ^{18}F-fluorodeoxyglucose standardized uptake values (SUVs) on positron emission tomography (PET) are more reliably associated with treatment outcomes than those by CT, we compared outcomes and responses according to PET SUV vs. CT among patients in a phase II study of erlotinib+chemoradiation for stage III NSCLC. **Methods:** Trial 2005-1023 enrolled 46 patients in 2007–2010; patients received 63 Gy in 35 fractions over 7 weeks with daily erlotinib and weekly paclitaxel-carboplatin. Tumor response was assessed on diagnostic CT scans with contrast or CT from PET-CT and scored according to RECIST 1.1. Tumor response was also assessed by PERCIST 1.0 (based on SUV) as follows: complete response (CR), disappearance of all measurable tumors; partial response (PR), ≥30% reduction in the sum of SUVs of target lesions; progressive disease (PD), ≥30% increase in the sum of SUVs of target lesions; and stable disease (SD), insufficient change in SUV to qualify for PR or PD. The longest diameter of measurable primary lesions and the short axis of measurable lymph

nodes were measured. All non-target lesions were also measured. Two-sided Pearson's chi-square tests were used to assess frequency associations. Overall survival (OS) and local-regional control (LRC) rates were assessed from treatment start by Kaplan-Meier analysis and log-rank tests; $P \leq 0.05$ indicated significance. **Results:** One patient did not have CT and PET after treatment. For the 45 evaluable patients, best response by PET-CT at 6 months after treatment was CR for 15 patients (33%), PR for 19 (42%), SD for 0, PD for 4 (9%), and not available due to did not have baseline or post treatment PET for 7 (16%). Best response by CT at 6 months was CR for 11 (24%), PR for 27 (60), SD for 3 (7%), and PD for 4 (9%) ($P<0.001$). The 3 patients with SD by CT all died within 7 months after treatment; the 4 patients with PD had new distant metastases. Four-year OS was associated with best overall response on both PET and CT at 6 months ($P<0.05$) and at 1 year ($P<0.05$). LRC was associated with best overall response on PET ($P<0.01$) and best primary tumor response on PET ($P<0.05$) at 6 and 12 months. Lymph node response was not associated with OS or LRC by PET or CT. **Conclusion:** The CR rate was higher with PET than with CT. Tumor response at 6 months by PET or CT predicted treatment outcomes after chemoradiotherapy for stage III NSCLC. The best overall and primary tumor response by PET within 6 months after treatment was more reliably associated with LRC than was response on CT because of difficulty to assess response due to pneumonitis/lung fibrosis.
Keywords: NSCLC, Tumor response, PERCIST, RECIST

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-066 Bevacizumab Combined with Docetaxel: A Real Active Second Line Regimen in Elderly Patients with Advanced Non-Small Cell Cancer (NSCLC)
Sherif Abdelwahab, Wesam Elghamry, Mohamed Kelany, Mai Ezzdin *Clinical Oncology, Ain Shams University, Cairo/Egypt*

Background: Majority of patients with non-small cell lung cancer (NSCLC) are elderly, and age is known to be an important factor for management and treatment. Elderly are underpresented in cancer research. Therefore, we conducted this phase II study aiming at assessing the efficacy and safety of adding bevacizumab to docetaxel as a second line treatment of elderly patients with advanced non squamous NSCLC **Methods:** Twenty five previously treated elderly patients with advanced non squamous NSCLC (stage III, IV) were enrolled into this study between May 2011 and May 2014. All patients received docetaxel 60 mg/m^2 followed by bevacizumab 15mg/kg, both agents were given via I.V infusion on day 1 and the cycle was repeated every 21 days until disease progression or unacceptable toxicity developed. **Results:** The median age was 70 years old (range 65-79 years); 19 (76%) patients were men; ECOC PS was 0 in 6 (24%) patients, 1 in 12 (48%) patients and 2 in 7 (28%) patients. The objective response rate was 60%, while disease control rate was 84%.The median progression-free survival time was 7 months, while the median overall survival time was 19.8 months. Grade 3/4 neutropenia had been recorded in 18(72%) patients, and grade 3/4 fatigue had occurred in 5(20%) patients. No cases of severe bleeding nor treatment-related deaths had been reported in this study. **Conclusion:** Bevacizumab added to docetaxel showed a real activity as a second line treatment in previously treated elderly patients with advanced NSCLC and has an acceptable toxicity.
Keywords: Bevacizumab,docetaxel,elderly,NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-067 Pemetrexed (P)/Carboplatin/Bevacizumab (B) Followed by Maintenance P/B in Hispanic Patients with Non-Squamous NSCLC
Leonardo Rojas[1], Andrés F. Cardona[2], Hernan Carranza[2], Carlos A. Vargas[2], Jorge M. Otero[2], Mauricio Cuello[3], Luis Corrales[4], Claudio Martin[5], Oscar Arrieta Rodriguez[6]
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Background: The present study evaluated the efficacy and safety of pemetrexed, carboplatin and bevacizumab, followed by maintenance pemetrexed and bevacizumab, in chemotherapy-naïve patients with stage IV non-squamous non-small cell lung cancer (NSCLC). **Methods:** The patients were administered pemetrexed (500 mg/m^2), carboplatin (AUC 5.0 mg/ml/min) and bevacizumab (7.5 mg/kg) intravenously every three weeks for up to four cycles. Patients who did not experience tumor progression remained on maintenance pemetrexed and bevacizumab until disease progression or unacceptable toxicity. Primary endpoints were overall response rate (ORR), progression free survival (PFS) and overall survival (OS). **Results:** Hundred forty-four Colombian patients were included and received treatment. The median age was 64 years (range, 32-86 years), 61% was female and 55% had some history of tobacco exposure. The median follow-up was 13.8 months, and the median number of manteinance cycles was 8 (range, 1- 32). Among patients assessable for response, the ORR was 66% (95%CI, 47% to 79%). Median progression-free and overall survival rates were 7.9 months (95%CI 5.9-10.0 months) and 21.4 months (95%CI 18.3 to 24.4 months), respectively. Grade 3/4 hematologic toxicity was anemia (14%), neutropenia (8%), and thrombocytopenia (16%). Grade 3/4 nonhematologic toxicities were proteinuria (2%), venous thrombosis (4%), fatigue (11%), infection (6%), nephrotoxicity (2%), and sensory neuropathy (4%). There was no grade 3 or greater hemorrhagic events or hypertension cases. **Conclusion:** Overall, pemetrexed and carboplatin plus bevacizumab, followed by maintenance pemetrexed and bevacizumab, was effective and tolerable in hispanic patients with non-squamous NSCLC. This regimen was associated with acceptable toxicity and prolonged OS.
Keywords: First line therapy, Manteinance, bevacizumab, Adenocarcinoma

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-068 Phase II Study of S-1 plus Bevacizumab for Pretreated Patients with Non-Squamous NSCLC
Kazuhiko Yamada[1], Masao Ichiki[2], Kazuhisa Takahashi[3], Yasushi Hisamatsu[4], Koichi Azuma[1], Takaaki Tokito[1], Hidenobu Ishii[1], Hiroaki Takeoka[2], Takehito Shukuya[3], Kazuo Nishikawa[4], Tomoaki Hoshino[1] [1]*Division of Respirology, Department of Internal Medicine, Kurume University School of Medicine, Kurume Japan,* [2]*Kyushu Medical Center, Fukuoka/Japan,* [3]*Division of Respiratory Medicine, Juntendo University Faculty of Medicine & Graduate School of Medicine, Tokyo/Japan,* [4]*Department Ofmedical Oncology and Hematology, Oita University Faculty of Medicine, Oita/Japan*

Background: The additional effects of bevacizumab (B) as first-line chemotherapy for non-squamous non-small cell lung cancer (Non-sq NSCLC) have been established. However, the efficacy of B in a second-line setting or further has not been clarified. It has recently become clear that S-1 (S), an oral fluoropyrimidine, is effective for advanced NSCLC, and S is now used with platinum as one of the standard forms of first-line chemotherapy. Furthermore, preclinical findings have suggested that the combination of S plus B is a promising treatment option. **Methods:** Non-sq NSCLC patients with an ECOG performance status of 0-2, and who had undergone prior platinum-based chemotherapy regardless of the use of B, were eligible for the study. S (80 mg/m^2) was administered orally twice daily for 14 days, and B (15 mg/kg) on day 1 every 3 weeks until disease progression or unacceptable toxicity occurred. The primary endpoint was progression-free survival (PFS), and the planned sample size was 28 patients. **Results:** Between March 2012 and June 2014, 28 patients (14 males and 14 females; median age 62 years; PS 0/1/2: 21/7/0; Ad/Other: 26/2, EGFR mutation positive/wild type 12/16) were accrued from 4 centers in Japan. All 28 patients were included in analysis of efficacy and toxicity. With a median follow-up of 9.3 months, the median PFS was 3.2 months (95% CI: 2.2-4.0 months). Patients who had not received prior pemetrexed or who had shown a good response to prior chemotherapy tended to have a longer PFS (5.3 and 5.0 months, respectively), although this was not statistically significant. An objective response was observed in 4 patients (PR; 4, SD; 20, PD 4), the response rate and disease control rate being 14.3% and 85.7%, respectively. The treatment was well tolerated, the most common treatment-related side effects being anorexia (75%) and fatigue (68%). **Conclusion:** This is the first report to evaluate the efficacy and safety of SB. Although SB seems to have a higher tumor reduction effect than S alone for previously treated Non-sq NSCLC, this study failed to meet its primary endpoint. SB is well tolerated and no new toxicities were observed.
Keywords: NSCLC, S-1, bevacizumab, non-squamous

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-069 Phase II Trial of Paclitaxel, Irinotecan, and Bevacizumab for Patients with Untreated NSCLC Overexpressed ERCC1 MRNA; Evaluated by EBUS-GS
Yoichi Nakamaura[1], Ken Kitazaki[2], Takaya Ikeda[3], Hirofumi Nakano[4], Shinya Tomari[5], Seiji Nagashima[6], Shuntaro Sato[7], Katsumi Nakatomi[1], Shinnosuke Takemoto[1], Hiroyuki Yamaguchi[1], Minoru Fukuda[8] [1]*Nagasaki University Hospital, Nagasaki/Japan,* [2]*The Japanese Red Cross Nagasaki Genbaku Hospital, Nagasaki/Japan,* [3]*Sasebo General Hospital, Sasebo/Japan,* [4]*Uresino Medical Center, Uresino/Japan,* [5]*Isahaya General Hospital, Isahaya/Japan,* [6]*Nagasaki Medical Center, Omura/Japan,* [7]*Nagasaki University Hospital Clinical Research Center, Nagasaki/Japan,* [8]*Clinical Oncology Center, Nagasaki University Hospital, Nagasaki/Japan*

Background: We prospectively evaluated the efficacy and toxicity of non-platinum triplet regimen, which consist of paclitaxel, irinotecan, and bevacizumab for patients with advanced non-small cell lung cancer (NSCLC) expected to be platinum resistant. **Methods:** All patients were diagnosed with NSCLC using endobronchial ultrasonography with a guide sheath (EBUS-GS) system. We defined the EBUS-GS as a core biopsy. RNA was immediately isolated from this unfixed biopsy specimens, and quantitative real-time reverse transcriptase PCR assays were performed to determine the excision repair cross-complementing 1 (ERCC1) mRNA expression. Patients with advanced, untreated NSCLC showing high ERCC1 levels ($\Delta Ct \geqq 6.5$) were entered the phase II trial of the non-platinum triplet regimen. Paclitaxel of 180mg/m2 on day 1, irinotecan of 50mg/m2 on day 1 and 8, and bevacizumab of 15mg/kg on day 1 were administered every 4 weeks. Primary end point was the objective response rate (ORR), assuming 30% for a standard therapy and 60% for a target therapy (alpha=0.05 and beta=0.1), and the estimated required total number of patients was 28 by Simon's Optimal Two-stage Design. **Results:** Total 141 untreated patients received EBUS-GS and were evaluated the expression of ERCC1, and 30 patients were entered in this trial. The ORR was 66.7%(95% confidence interval [CI]: 47.2-82.7). Median progression-free survival was 174 days. Grade 4 thrombosis occurred one patient, but other toxicities were mild and controllable. Fifty-three patients were treated with platinum-containing regimens and 22 patients were responded (ORR was 41.5% [95% CI: 28.1-55.9]). Twenty-three of these patients were high ERCC1 levels and 6 patients were responded, and 30 patients were low ERCC1 levels and 16 patients were responded (p=0.0053, by Fisher's exact test). **Conclusion:** The triplet combination of paclitaxel, irinotecan and bevacizumab might be effective for patients with advanced, untreated NSCLC overexpressing ERCC1. ERCC1 mRNA levels extracted from unfixed lung biopsy specimens obtained by EBUS-GS also might be a predictive factor for platinum-containing regimens.
Keywords: non-small cell lung cancer, EBUS-GS, ERCC1, non-platinum regimen

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-070 Experience with Docetaxel plus Nintedanib with Previously Treated NSCLC Patients: Compassionate Use Program Single Institution in Mexico Saul Campos-Gomez, Karen A. Campos-Gomez *Dep of Medical Oncology, Centro Oncologico Estatal Issemym, Toluca/Mexico*

Background: Nintedanib is an oral, potent, tyrosine kinase inhibitor that simultaneously targets vascular endothelial growth factor receptors 1-3, platelet-derived growth factor receptors α and β, and fibroblast growth factor receptors 1-3, as well as FLT3 and Src. Currently, the molecule has proved benefit for second-line in non-small cell lung cancer patients. We report the results of a cohort of NSCLC patients receiving nintedanib within a compassionate-use program (CUP) in México. **Methods:** Patients with advanced NSCLC progressing after one line of chemotherapy were enrolled. Eligible patients received docetaxel 75 mg/m(2) (day 1) plus nintedanib 200 mg twice daily; days 2-21) in 21-day cycles. Data collection was monitored. Treatment continued until disease progression or unacceptable drug-related AEs. The intention of this CUP was to provide controlled access to nintedanib. **Results:** From February 2014 to April 2015, 17 patients (63% male; median age: 61 years [range: 29-83 years]) were enrolled. Patients received nintedanib 200mg BID (n=16). The primary analysis was done after a median follow-up of 7 months; the median overall survival was 42 months (33-52 weeks). Grade 3 or worse febrile neutropenia developed in eight patients (31 %) and neutropenia in four patients (15 %). The most frequent drug-related adverse events (all grades) were diarrhea (30%), asthenia (61.9%), nausea (23%), hand-foot syndrome (15%), and vomiting (7.6%). Drug-related adverse events all grades included neutropenia (12.5%), fatigue (18.7%), decreased appetite (18.7%), and elevations in alanine aminotransferase (37.5%) and aspartate aminotransferase (31.2%). Dose-limiting toxicities (all grade 3 hepatic enzyme elevations) occurred only in 2/16 patients (12.5%). All hepatic enzyme elevations were reversible and manageable with dose reduction. Among 16 evaluable patients, 13 (81.25%) had a partial response and 3 (18.75%) had stable disease by Response Evaluation Criteria In Solid Tumours criteria. Three of all patients died of events unrelated to disease progression; the most common of these events were sepsis and pneumonia. **Conclusion:** Based on cohort result, treatment with second-line nintedanib combined with docetaxel was well tolerated and showed efficacy in Mexican patients with advanced non-small-cell lung cancer. **Keywords:** advanced lung cancer, Secod line, nintedanib, Safety

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.01-071 RAS Inhibitor Prevent Proteinuria of NSCLC Patients Who Received Bevasizumab Chemotherapy: NJLCG 1303 Shoichi Kuyama[1], Satoru Nihei[2], Toshiyuki Harada[3], Toshiro Suzuki[4], Yoshitaka Saito[5], Satoshi Oizumi[6], Shigeki Kisara[7], Akira Inoue[8], Atsuko Yokota[9], Hiroshi Yokouchi[10], Koji Okada[11], Yoshiaki Mori[12], Masami Tsuchiya[13], Makoto Maemondo[14], Kazufumi Terui[15], Kageaki Taima[16], Yumiko Tadokoro[17], Hiroshi Watanabe[18], Junya Sato[2], Naoto Morikawa[19] [1]*Department of Respiratory Medicine, NHO Iwakuni Medical Center, Iwakuni/Japan,* [2]*Department of Pharmacy, Iwate Medical University Hospital, Iwate/Japan,* [3]*Center for Respiratory Disease, Jcho Hokkaido Hospital, Sapporo/Japan,* [4]*Respiratory Medicine, Iwate Prefectural Isawa Hospital, Oushu/ Japan,* [5]*Department of Pharmacy, Hokkaido University Hospital, Sapporo/Japan,* [6]*1St Dept of Medicine, Hokkaido University School of Medicine, Sapporo/Japan,* [7]*Department of Pharmacy, Tohoku University Hospital, Sendai/Japan,* [8]*Respiratory Medicine, Tohoku University Hospital, Sendai/Japan,* [9]*Department of Pharmacy, Fukushima Medical University Hospital, Fukushima/Japan,* [10]*Department of Pulmonary Medicine, Fukushima Medical University, Fukushima/Japan,* [11]*Department of Pharmacy, Iwate Prefectural Central Hospital, Iwate/Japan,* [12]*Iwate Prefectural Central Hospital, Iwate/Japan,* [13]*Department of Pharmacy, Miyagi Cancer Center, Sendai/Japan,* [14]*Respiratory Medicine, Miyagi Cancer Center, Natori/ Japan,* [15]*Department of Pharmacy, Hirosaki University Hospital, Hirosaki/Japan,* [16]*Hirosaki University Hospital, Hirosaki/Japan,* [17]*Saka General Hospital, Shiogama/Japan,* [18]*Respiratory Medicine, Saka General Hospital, Shiogama/Japan,* [19]*Iwate Medical University School of Medicine, Morioka/Japan*

Background: Proteinuria caused by bevacizumab (BV) often becomes an obstacle to continuation of the treatment. Renin-angiotensin system inhibitor (RASI), angiotensin receptor blocker and angiotensin converting enzyme inhibitor, has demonstrated anti-proteinuria effect in diabetic nephropathy and nondiabetic kidney disease. This retrospective observational study was conducted to evaluate the anti-proteinuria effect of RASI for NSCLC patients (pts) who received BV chemotherapy. **Methods:** We reviewed the medical records of NSCLC pts between 2008 and 2014 at 11 hospitals. Eligible pts had a treatment of BV chemotherapy, no proteinuria, and no diabetes mellitus. Clinical characteristics, use of the antihypertensive drugs, change of the blood pressure, and proteinuria generation were investigated during first 6 courses of BV chemotherapy. **Results:** A total of 211 pts were enrolled. Pts characteristics were: male/female 121/90; median age 63 (range 35-88); ECOG performance status 0-1/2-3 199/12; stage Ⅳ/recurrent 189/22; dose of BV(/kg) 7.5mg/15mg 21/190; BV cycle 1-2/3-4/5-6 18/55/138; antihypertensive drugs RASI/non-RASI/ none 59/44/108. Proteinuria was observed in 49 pts (23%) as grade 1/2/3 33/14/2. The rate of proteinuria generation was significantly lower in the RASI group than non-RASI group (17% vs. 41%, P=0.025). Multivariate analysis revealed that RASI significantly reduced proteinuria (HR=0.43, 95% CI=0.17-0.91, P=0.043). **Conclusion:** RASI demonstrated anti-proteinuria effect for NSCLC pts who received BV therapy. **Keywords:** Renin-angiotensin system inhibitor, Anti-proteinuria effect, bevacizumab

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-072 Final Efficacy and Safety Results of ECOG Performance Status (PS) Subgroup Analyses From the SQUIRE Phase III Study Mark A. Socinski[1], Alexander V. Luft[2], Aleksandra Szczesna[3], Wojciech Szafrański[4], Rinat K. Galiulin[5], Beatrix Bálint[6], Keunchil Park[7], Martin Reck[8], Henrik Depenbrock[9], Shivani Nanda[10], Nadia Chouaki[11], Nick Thatcher[12] [1]*University of Pittsburgh, Pittsburgh/PA/United States of America,* [2]*Leningrad Regional Clinical Hospital, St. Petersburg/Russian Federation,* [3]*Regional Lung Disease Hospital, Otwock/Poland,* [4]*Voivodeship Specialist Hospital, Radom/ Poland,*[5]*Omsk Regional Oncology Center, Omsk/Russian Federation,* [6]*Csongrád County Hospital of Chest Diseases, Deszk/Hungary,* [7]*Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul/ Korea,* [8]*Department of Thoracic Oncology, Lung Clinic Grosshansdorf, Airway Research Center North (Arcn), Member of the German Center for Lung Research (Dzl), Grosshansdorf/ Germany,* [9]*Lilly Deutschland Gmbh, Bad Homburg/Germany,* [10]*Eli Lilly and Company, Bridgewater/NJ/United States of America,* [11]*Eli Lilly and Company, Neuilly-Sur-Seine/ France,* [12]*The Christie Hospital, Manchester/United Kingdom*

Background: As previously reported, the SQUIRE study demonstrated that the addition of necitumumab (N) to gemcitabine-cisplatin (GC) chemotherapy significantly improved survival in patients with stage IV squamous NSCLC. Overall survival (OS), progression-free survival (PFS), and safety results are presented for Eastern Cooperative Oncology Group (ECOG) PS 0–1/2 subgroups. **Methods:** Patients with stage IV squamous NSCLC were randomized 1:1 to N (800 mg iv, days 1 and 8) plus GC (G=1250 mg/m^2 iv, days 1 and 8; C=75 mg/m^2 iv, day 1) or GC alone every 21 days for up to six cycles in this multicenter, open-label study. N+GC patients without progression continued on N alone until progressive disease or intolerable toxicity. The study was powered for OS and PFS (previously reported). Preplanned subgroup analyses were performed for ECOG PS 0–1 and 2. **Results:** Subgroups PS 0–1/2 (n=996 [91%]/n=96 [9%]) were well balanced regarding baseline characteristics (males, 83% vs 86%; median age, 62 vs 65 yrs; smoking/ex-light smoker/nonsmoker, 91/4/5% vs 89/6/5%). GC median relative dose intensity was similar between PS 0–1/2 subgroups; N (overall) was higher for the PS 0–1 than for PS 2 subgroup (94.8% and 90.0%). Post-study therapy use was generally higher in the PS 0–1 than in the PS 2 subgroup, but was balanced between both arms. The OS hazard ratio (HR) for N+GC vs. GC was 0.85 (95% CI: 0.74, 0.98; p=0.026) for PS 0–1 and 0.78 (95% CI: 0.51, 1.21; p=0.275) for PS 2. The PFS HR (N+GC vs. GC) was 0.86 (95% CI: 0.75, 0.99; p=0.035) for PS 0–1 and 0.79 (95% CI: 0.50, 1.24; p=0.292) for PS 2. Select Grade ≥3 treatment-emergent adverse events (TEAEs) are shown in the table. The percentage of patients with adverse events leading to discontinuation of any study drug was lower in the PS 0–1 subgroup (N+GC=30%; GC=23%) than the PS 2 subgroup (N+GC=42%; GC=41%). The percentage of patients hospitalized was higher in the PS 0–1 subgroup (N+GC=43%; GC=34%) than the PS2 subgroup (N+GC=25%; GC=30%). **Table. Select TEAEs**

Grade ≥3 Event*	PS 0-1 N+GC (%) N=490	PS 0-1 GC (%) N=495	PS 2 N+GC (%) N=48	PS 2 GC (%) N=46
Neutropenia	25.5	28.1	12.5	21.7
Febrile neutropenia	0.6	1.4	2.1	0
Anemia	11.2	10.3	4.2	17.4
Thrombocytopenia	10.4	10.5	8.3	13.0
Fatigue	7.1	7.1	8.3	6.5
Hypomagnesemia	9.8	1.0	4.2	2.2
Rash	7.8	0.4	0	0
Arterial thromboembolic events	3.7	1.8	6.3	4.3
Venous thromboembolic events	5.5	2.6	0	2.2

Adverse events of possible relevance to treatment, according to either composite categories or preferred terms (febrile neutropenia only)* **Conclusion: OS and PFS treatment results for N+GC were consistent and considered favorable across subgroups including ECOG PS 2 patients. Administration of N+GC was well tolerated in PS 2 patients, with no evidence of an increased safety risk in this subgroup. **Keywords:** necitumumab, ECOG PS, efficacy, safety

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.01-073 Nimotuzumab in Advanced Squamous Cell Lung Cancer: A 2 Year Comparative Indian Clinical Experience Govind Babu *Medical Oncology, Kidwai Memorial Institute of Oncology, Karnataka/India*

Background: Lung cancer is mainly a disease of modern era and probably one of the most important health problems today. Approximately 63,000 new lung cancer cases are reported each year (Ganesh et al., 2011) in India. In the series from west as well as from India, it is reported that 30% of lung cancers are of squamous cell histology (SQCLC) and 50-70% cases usually present in advanced stage (Becket, 1993; Govindan et al., 2006; Grivaux et al., 2011; Malik et al., 2013). The median overall survival observed

with the current standard of care is 9-11 months and highlights the need for targeted agents that will add to the survival and quality of life of these patients. EGFR is the most evaluated target in lung cancer. EGFR overexpression is recorded in about 75-80% of the patients and associated with a worser clinical outcome. Nimotuzumab is humanized EGFR antagonist and is being actively evaluated in the management of advanced lung cancer. This study is done to observe the safety and efficacy of nimotuzumab in combination with chemotherapy (docetaxel and carboplatin) versus chemotherapy alone in patients with stage IIIB/IV SQCLC with recorded EGFR overexpression. **Methods:** This single-center, open-label, study evaluating 20 patients to receive nimotuzumab plus chemotherapy (nimo group, n=10) or chemotherapy alone (control group, n=10), and comprised concomitant, maintenance, and follow-up phases. Nimotuzumab 200 mg was administered once weekly for 13 weeks during the first two phases with four cycles of chemotherapy and docetaxel 75 mg/m2 and carboplatin (area under the curve 5 mg/mL*min) every 3 weeks for a maximum of four cycles during the concomitant phase. The primary endpoint was objective response rate (sum of complete response and partial response). Secondary endpoints, ie, overall survival and progression-free survival, were estimated using the Kaplan–Meier method. Efficacy was evaluated on the intent-to-treat and efficacy-evaluable sets. Safety was assessed from adverse event and serious adverse event data. **Results:** The objective response rate was significantly higher in the nimotuzumab group than in the control group in the intent-to-treat population (66% versus 34.5%; P=0.04). A complete response and partial response were achieved in 15% and 50% of patients, respectively, in the nimotuzumab group, and in 4% and 30.9% of patients, respectively, in the control group. Median progression-free survival and median overall survival in nimo group and control groups were 5.9 vs 3.7 months and 12.2 vs 9.8 months respectively, both being significant for Nimotuzumab. Safety profiles were comparable between the two groups. **Conclusion:** Nimotuzumab plus chemotherapy significantly improved the tumor response, PFS and mOS as compared with chemotherapy alone. The combination was safe and well tolerated in patients with stage IIIB/IV lung cancer. **Keywords:** nimotuzumab, Targeted therapy, Advanced squmous cell lung cancer, Epidermal growth factor receptor

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-074 Phase I-II Trial of Combined PKC Iota and mTOR Inhibition for Patients with Advanced or Recurrent Lung Cancer - A Trial in Progress
Helen J. Ross[1], Harshita Paripati[2], Verline Justilien[3], Alan Fields[3] [1]*Mayo Clinic, Scottsdale/AZ/United States of America,* [2]*Mayo Clinic, Scottsdale/United States of America,* [3]*Mayo Clinic, Jacksonville/FL/United States of America*

Background: Cancer stem cells may be responsible for initiation, maintenance, progression and metastatic spread of lung cancers and native or acquired drug resistance can allow cancers to escape from conventional therapy. Eradicating cancer stem cells may improve clinical outcomes. We (APF, VJ) showed that PKCi is an oncogene for NSCLC and is amplified in most squamous lung cancer cells (LSCC). PKCι is required for LSCC cell proliferation *in vitro* and tumorigenicity *in vivo* and for maintenance of the lung cancer tumor initiating cell (TIC) phenotype. LSCC oncospheres have cancer stem cell characteristics, express stem genes, and exhibit clonal expansion, enhanced transformed growth and the ability to maintain lung tumors and metastases in vivo. The PKCi-Rac1-Ect2-MMP10 signaling axis is activated in LSCC TICs and PKCι knock down, impairs soft agar growth, clonal expansion and tumorigenicity. The gold salt auranofin (ANF) reproduces the effects of PKCι knock down on the PKCi-Rac1-Ect2-MMP10 signaling pathway and on clonal expansion and tumorigenicity. ANF potently and selectively inhibits oncogenic PKCι signaling and combined PKCι and mTOR inhibition synergistically reduces lung cancer cell proliferation and tumor growth *in vivo* and *in vitro* (Ross H, Justilien V, Hill K, Walsh M, Fields AP. Protein kinase C iota is required for maintenance of a tumor initiating cell phenotype in lung squamous cell carcinoma. Abstract 2644 WCLC 2013). A phase I/II clinical trial of oral ANF + the mTOR inhibitor sirolimus in patients with advanced or recurrent lung cancer is ongoing. **Methods:** A phase I/II clinical trial is accruing patients to test the hypothesis that combined inhibition of PKCι and mTOR is safe and effective in lung cancer patients. NCT01737502 NCI sponsored clinical trial R21 CA153000 Eligible participants are adults with confirmed diagnosis of lung cancer (squamous, RAS-mutated adenocarcinoma or small cell lung cancer), PS 0-2, adequate organ function, no significant comorbidities and who have completed at least one prior course of platinum doublet chemotherapy. Patients receive ANF + sirolimus orally daily in 28 day continuous cycles. Tumor biopsies are collected for biomarker assessment focused on the PKCi-Rac1-Ect2-MMP10 pathway. Study endpoints are safety, survival and biomarker development. **Results:** The trial has completed the phase I portion with six patients without dose limiting toxicity. The phase II portion of the trial is now accruing with doses of ANF 6 mg daily and sirolimus 5 mg daily continuously in 28 day cycles. Biomarker assessment is ongoing. **Conclusion:** The phase I portion of this trial demonstrated preliminary safety of the combination of auranofin and sirolimus at doses that were effective against NSCLC in preclinical models. Phase II accrual is ongoing. **Keywords:** Protein kinase C iota, mTOR, Phase I/II clinical trial, Cancer Stem Cells

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-075 Phase 2 Trial of Bortezomib in KRAS G12D Mutant Lung Cancers
Gregory J. Riely[1], Anya Litvak[2], Natasha Rekhtman[2], M Catherine Pietanza[2], Jamie E. Chaft[2], Kaitlin Woo[3], Paul Paik[1], Vincent Miller[4], Mark G. Kris[5], K Rodriguez[1], Alexander Drilon[2] [1]*Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [2]*Memorial Sloan Kettering Cancer Center, New York/United States of America,* [3]*Epidemiolgy and Biostatistics, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America,* [4]*Clinical Development, Foundation Medicine, Inc, Cambridge/MA/United States of America,* [5]*Thoracic Oncology, Memorial Sloan Kettering Cancer Center, New York/NY/United States of America*

Background: KRAS mutations are the most common oncogenic drivers in lung cancers without any approved targeted therapy. Preclinical evidence suggests that KRAS mutations are highly dependent on the NF-kB pathway. Bortezomib, a small molecule proteasome inhibitor, has been shown to downregulate the NF-kB pathway and lead to objective responses in patients with KRAS G12D in early phase clinical trials. In this single-institution, open label, phase II study we assessed the efficacy and safety of subcutaneous bortezomib in KRAS mutant lung cancers. **Methods:** Patients with advanced KRAS G12D mutant lung cancers were eligible. Bortezomib was administered at 1.3mg/m2/dose subcutaneously on days 1, 4, 8, and 11 of a 21 day cycle until disease progression or unacceptable toxicity. The primary objective was radiographic response rate (RECIST version 1.1). The secondary endpoints were progression free survival (PFS) and overall survival (OS) determined from the time of first bortezomib treatment. Simon two-stage minimax design was used (H0=10%, H1=30%, power=90%). **Results:** Sixteen patients with KRAS G12D mutant lung adenocarcinomas were treated on study: 44% women, 38% never smokers, 31% former smokers ≤15 pack years, and 69% with invasive mucinous adenocarcinomas. Patients received treatment for a median of 2 months (range 1-12months). One patient had a partial response with a 66% reduction in disease burden (6% observed rate, 95% CI 0.2 to 30.2%). Of the 6 patients (40%) with stable disease, 2 remained on study for over 5 months. The median PFS was 1 month (95% CI 1-6). The median OS was 13 months (95% CI 6-NA). The median OS from date of diagnosis of metastatic disease was 39 months (95% CI 35-NA). The most common treatment-related toxicities of any grade were fatigue (50%), diarrhea (38%), nausea (31%), and papulopustular rash (31%). Treatment-related peripheral neuropathy occurred in 25% of patients (3 patients with grade 1, 1 patient with grade 2). **Conclusion:** In patients with G12D KRAS mutant lung cancers, bortezomib was well tolerated and associated with modest anti-tumor activity and durable disease control in a small subset of patients. Further investigation into predictive biomarkers for the efficacy of bortezomib should be pursued. Without a clear biomarker, no further study of bortezomib in KRAS- mutant lung cancers is warranted. **Keywords:** KRAS, synthetic lethal

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-076 Efficacy and Safety of Recombinant Human Tumor Necrosis Factor Application for the Treatment of Malignant Pleural Effusion Caused by Lung Cancer
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Background: Malignant pleural effusion (MPE) is mainly caused by metastatic pleural cancer and defines malignant tumors with a poor prognosis. To achieve sufficient control of MPE and to minimize invasive interventions are the primary goals of the treating physicians. Recombinant human mutant tumor necrosis factor-alpha (rhu-TNF) has been used in the treatment of MPE. The aim of our research study, which included a total of 102 patients with MPE caused by lung cancer, was retrospectively to evaluate efficacy and safety of rhu-TNF application via ultrasound-guided chest tube for the treatment of MPE. Malignant pleural effusion (MPE) is mainly caused by metastatic pleural cancer and defines malignant tumors with a poor prognosis. To achieve sufficient control of MPE and to minimize invasive interventions are the primary goals of the treating physicians. Recombinant human mutant tumor necrosis factor-alpha (rhu-TNF) has been used in the treatment of MPE. The aim of our research study, which included a total of 102 patients with MPE caused by lung cancer, was retrospectively to evaluate efficacy and safety of rhu-TNF application via ultrasound-guided chest tube for the treatment of MPE. **Methods:**Rhu-TNF was administered as a single dose to 102 patients, and dexamethasone (Dmx, 5 mg) was administered 30 min before rhu-TNF in 35 patients in order to prevent side effects. The primary endpoint was the efficacy of the Rhu-TNF treatment (disease response rate) and side effects (pain, fever and flu-like symptoms) evaluated four weeks after instillation. **Results:** The disease response rate of Rhu-TNF treatment in 102 patients was 81.37%. Side effects included 13 (12.75%) patients complaining about flu-like symptoms, 15 (14.71%) with fever/chill, and 14 (13.73%) with chest pain. A significantly higher efficacy was observed for the treatment with three versus two million units rhu-TNF (= 0.036), while the adverse effects were similar. Although application of Dmx before the intra-pleural instillation of rhu-TNF reduced the incidence of adverse events, no significant differences were found. **Conclusion:** In conclusion, our study shows that intra-pleural instillation of rhu-TNF in MPE patients achieves sufficient control of MPE and minimizes invasive interventions. **Keywords:** lung cancer, malignant pleural effusion, Rhu-TNF, Intra-pleural instillation

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-077 A Randomized, Phase II Study of Nimotuzumab Plus Gefitinib vs Gefitinib in Advanced Non-Small Cell Lung Cancer After Platinum- Based Chemotherapy
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Background: Nimotuzumab is a humanized anti-epidermal growth factor receptor (EGFR) monoclonal antibody. We aim to evaluate the efficacy of dual inhibition of EGFR with nimotuzumab plus gefitinib in advanced non-small cell lung cancer (NSCLC) previously treated with platinum-based chemotherapy. **Methods:** An open label, randomized, phase II trial was conducted in 6 centers; 160 patients were randomized (1:1) to either nimotuzumab (200mg, IV weekly) plus gefitinib (250mg p.o. daily) or gefitinib alone until disease progression or intolerable toxicities. The primary endpoint was progression free survival (PFS) rate at 3 months. Secondary endpoints included PFS, overall survival (OS), overall response rate (ORR) and safety. **Results:** A total of 155 patients (78 in nimotuzumab plus gefitinib, 77 in gefitinib) were evaluable for efficacy and toxicity. Patient characteristics were well balanced in both groups. Majority of patients had adenocarcinoma histology (65.2%) and ECOG performance status 0 to 1 (83.5%). Among 102 patients with *EGFR* mutation results available, activating *EGFR* mutation was documented in 27 patients (12/50 in nimotuzumab plus gefitinib, 15/52 in gefitinib). With a median follow-up of 12.1 months, PFS rate at 3 months was 37.2% in nimotuzumab plus gefitinib and 48.1% in gefitinib [HR 1.03; 95% CI, 0.71–1.40; *P*=0.98]. Median PFS and OS were 2.0 months and 14.0 months in nimotuzumab plus gefitinib and 2.8 months and 13.2 months in gefitinib [HR 1.03, 95% CI 0.71-1.41, *P*=0.98 for PFS; HR 0.86, 95% CI 0.57–1.30, *P*=0.47 for OS]. The ORRs were 14.1% in nimotuzumab plus gefitinib and 22.1% in gefitinib, which was not statistically significant (*P*=0.76). As expected, patients with *EGFR* mutation showed significantly longer survival than those with wild-type *EGFR* or unknown *EGFR* mutation status (10.3 *vs.* 1.2 *vs.* 2.7 months, *P* < 0.001 for PFS; 23.5 *vs.* 13.5 *vs.* 10.5 months, *P*= 0.001 for OS). Combined treatment of nimotuzumab plus gefitinib did not show superior PFS compared to gefitinib alone in patients with *EGFR* mutation (13.5 *vs.* 10.2 months in gefitinib alone, *P*=0.30) and patients with wild-type *EGFR* (0.9 *vs.* 2.0 months in gefitinib alone, *P*=0.90). The median PFS was not significantly different between two treatment arms according to histology (2.8 *vs.* 2.9 months in gefitinib alone for adenocarcinoma, *P*=0.64; 1.2 *vs.* 2.8 months in gefitinib alone for non-adenocarcinoma, *P*=0.35). Adverse events (AEs) in both treatment arms were mostly grade 1 to 2 and easily manageable. Importantly, combined EGFR inhibition with nimotuzumab and gefitinib did not increase EGFR inhibition-related AEs, such as acneiform rash (32.4 *vs.* 30.3% in gefitinib alone, *P*=0.38), diarrhea (30.7 *vs.* 35.7% in gefitinib alone, *P*=0.32), and stomatitis (11.5 *vs.* 13.4% in gefitinib alone, *P*=0.19). There was no treatment-related death. **Conclusion:** The dual inhibition of EGFR with nimotuzumab plus gefitinib did not show superiority over gefitinib alone for second-line treatment of advanced NSCLC (NCT01498562). **Keywords:** non-small cell lung cancer, EGFR, gefitinib, EGFR monoclonal antibody

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-078 Avelumab (MSB0010718C), an Anti-PD-L1 Antibody, Evaluated in a Phase III Trial versus Docetaxel in Patients with Relapsing NSCLC Keunchil Park[1], Johan Vansteenkiste[2], Marcis Bajars[3], Christoph Helwig[4], Fabrice Barlesi[5]
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Background: The programmed death-1 receptor (PD-1) and its ligand (PD-L1) are key therapeutic targets in the reactivation of the immune response against multiple cancers. Avelumab* (MSB0010718C) is a fully human anti-PD-L1 IgG1 antibody currently being investigated in clinical trials. The phase III study (NCT02395172) is an open-label, multicenter trial of avelumab compared with docetaxel in patients with non-small-cell lung cancer (NSCLC) that has progressed after treatment with a platinum-containing doublet. **Methods:** The primary objective of this head-to-head phase III study is to demonstrate superiority defined by overall survival (OS) of avelumab versus docetaxel in patients with locally advanced unresectable, metastatic, or recurrent NSCLC whose tumors express PD-L1 and whose disease has progressed following treatment with a platinum-containing doublet. Approximately 650 eligible patients (ECOG performance status 0-1 at trial entry, tumor archival material or fresh biopsy suitable for PD-L1 expression assessment, histologically confirmed NSCLC, and known-negative ALK mutation status, among other inclusion and exclusion criteria), including 522 patients with PD-L1—positive tumors, will be randomized 1:1 to receive either avelumab at a dose of 10 mg/kg as a 1h intravenous (IV) infusion Q2W or docetaxel at a starting dose of 75 mg/m2 (per label) by IV infusion Q3W. Patients will be stratified according to PD-L1 status. NSCLC histology and EGFR mutation status will be used to define 3 stratified levels for randomization: squamous cell, non-squamous cell/EGFR wildtype, and non-squamous cell/EGFR-activating mutations. Treatment will continue until disease progression, unacceptable toxicity, or any criterion for withdrawal occurs. Responses will be evaluated according to RECIST 1.1 and adjudicated by a blinded independent review committee. In addition to the primary endpoint of OS, secondary endpoints include progression-free survival, best overall response, quality of life assessments, and safety profile. Exploratory endpoints include duration of response, tumor shrinkage in target lesions per timepoint, immunogenicity, PK profile, and evaluation of molecular, cellular, and soluble markers in peripheral blood or tumor tissue that may be relevant to the mechanism of action of, or response/resistance to, avelumab. Safety profiling of trial drugs includes incidence of adverse events (AEs), serious AEs, and other assessments according to NCI-CTCAE v4.03. Patients receiving avelumab who have achieved a complete response (CR) will be treated for a minimum of 6 months and a maximum of 12 months after confirmation. In the case of relapse following a CR, treatment with avelumab may be re-initiated once at the discretion of the investigator and in the absence of treatment-related toxicity. For patients whose disease progresses with avelumab, treatment may continue past the initial determination of disease progression per RECIST 1.1 if the patient's performance status has remained stable, other criteria are fulfilled, and the investigator's opinion supports a possible benefit of continued treatment with avelumab. Patients treated with docetaxel may not crossover to the avelumab arm as long as the primary endpoint has not been met in the planned interim or final analyses. Enrollment in this trial began in April 2015. *Proposed INN. **Results:** not applicable **Conclusion:** not applicable **Keywords:** MSB0010718C, avelumab, NSCLC, PD-L1

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-079 Addition of Hsp27 Inhibitor Apatorsen to First-Line Gemcitabine/ Carboplatin in Advanced Squamous Cell Lung Cancer: Design of the Cedar™ Trial Peter Schmid[1], Dakshinamoorthy Muthukumar[2], Fiona Blackhall[3], Jason Lester[4], Sarah Khan[5], Marianne C. Illsley[6], Joss Adams[7], Shobhit Baijal[8], Angel Garcia[9], Carey Macdonald Smith[9], Siow-Ming Lee[10], Cindy Jacobs[11], Gary Middleton[12], Christine James[13], Kelly Mousa[13], Shah-Jalal Sarker[13], Louise Lim[1] [1]*Barts Cancer Institute, London/ United Kingdom, [2]Essex County Hospital NHS Trust, Colchester/United Kingdom, [3]The Christie NHS Foundation Trust, Manchester/United Kingdom, [4]Velindre Cancer Centre, Cardiff/United Kingdom, [5]Nottingham University Hospitals NHS Trust, Nottingham/ United Kingdom, [6]Royal Surrey County Hospital NHS Foundation Trust, Guildford/United Kingdom, [7]Royal Berkshire NHS Foundation Trust, Reading/United Kingdom, [8]Heart of England NHS Foundation Trust, Birmingham/United Kingdom, [9]Betsi Cadwaladr University Health Board, Rhyl/United Kingdom, [10]University College Hospitals NHS Foundation Trust, London/United Kingdom, [11]Suite 201, Oncogenex Pharmaceuticals, Inc., Bothell/United States of America, [12]University Hospital Birmingham NHS Foundation Trust, Birmingham/ United Kingdom, [13]Queen Mary University of London, London/United Kingdom*

Background: Outcomes remain poor in patients with non-small cell lung cancer (NSCLC) of squamous origin. There are few established therapeutic targets, and benefits of chemotherapy are frequently short-lived, with rapid development of treatment resistance. More effective therapies are urgently required. Substantial preclinical data demonstrate that heat shock protein 27 (Hsp27) affects numerous pathways implicated in cancer progression and treatment resistance. Approximately 70-98% of squamous-cell tumours express Hsp27. Apatorsen (OGX-427) is a second generation antisense oligonucleotide that effectively down-regulates Hsp27 in vitro and in vivo; clinical studies are evaluating apatorsen in lung, bladder, prostate, and pancreatic cancers. **Methods:** The phase 2, UK, investigator led, randomized, open-label trial Cedar trial was initiated in July 2014. Eligible patients have confirmed Stage IIIB/IV squamous cell lung cancer and no prior chemotherapy for advanced disease, with ECOG score of 0-2 and adequate bone marrow, renal, and liver function; patients with known EGFR mutation or ALK rearrangements are excluded. Planned enrollment is 140 patients; randomization (1:1) is stratified by stage and performance status. Patients receive 21-day cycles of gemcitabine (1250 mg/m^2) and carboplatin (AUC5) or gemcitabine/carboplatin plus apatorsen (600 mg IV/wk, preceded by 3 doses during a 9-day loading period) for up to 6 cycles. Tumor evaluation occurs q6 wks. Patients randomized to apatorsen may continue weekly single agent maintenance until progressive disease (PD), unacceptable toxicity, or withdrawal of consent. The primary efficacy measure is progression-free survival. Secondary efficacy measures include objective response (OR), change in tumour size at 12 wks, clinical benefit rate, duration of OR/clinical benefit, overall survival, and proportion without PD at 12 and 24 wks. Efficacy analyses are intent-to-treat. Adverse events and laboratory results are assessed, and interim safety analyses are planned. Pre-specified subset analyses will characterize the relevance of Hsp27 expression in tumour and blood samples. **Results:** Not applicable. **Conclusion:** Not applicable. **Keywords:** Hsp27, apatorsen, squamous, gemcitabine/carboplatin

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-080 An Open-Label, Multicenter, Phase 1b/2 Study to Evaluate Necitumumab in Combination with Gemcitabine and Cisplatin in the First-Line Treatment of Patients with Advanced (Stage IV) Squamous Non-Small Cell Lung Cancer (NSCLC) Tomohide Tamura[1], Makoto Nishio[2], Nobuyuki Yamamoto[3], Yuichiro Ohe[1], Katharina Wolff[4], Mika Tsujimoto[5], Sotaro Enatsu[4], Kazuhiko Nakagawa[6]
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Background: Necitumumab (N) is a human IgG1 anti-epidermal growth factor receptor (EGFR) monoclonal antibody. Squamous (SQ) histology accounts for 25-30% of non-small cell lung cancer (NSCLC) and gemcitabine combined with cisplatin (GC) is a standard of care for advanced or metastatic SQ-NSCLC. In the previous global randomized, open-label, Phase 3 trial (SQUIRE), compared with GC, the addition of N to GC (GC+N) significantly improved overall survival (OS) (HR=0.84,*p*=0.012; median 11.5 vs 9.9 months) and progression-free survival (PFS) (HR=0.85, *p*=0.020; median 5.7 vs 5.5 months). The objective response rate (ORR) was 31% vs 29% (*p*=0.400), and the disease control rate (DCR) was 82% vs 77% (*p*=0.043), respectively. The SQUIRE results were an important advance in the search for a new treatment for patients with metastatic SQ-NSCLC, where limited progress has been made over the last two decades.

However, only 8% of patients in SQUIRE Trial were Asian and no Japanese institutions participated. We have therefore conducted this Phase 1b/2 trial to evaluate the efficacy and safety of GC+N in Japanese patients with advanced SQ-NSCLC. **Methods:** This trial consists of a Phase 1b and Phase 2 part. Patients with advanced (Stage IV) SQ-NSCLC are eligible for enrollment if they are aged≥20 years with an Eastern Cooperative Oncology Group performance status (ECOG PS) 0 or 1; measurable or nonmeasurable disease according to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.0; adequate organ function. GC+N or GC may continue for a maximum of 4 cycles; patients with at least stable disease in GC+N may continue to receive N until disease progression or emerging non-acceptable toxicity. The purpose of Phase 1b part is to determine the recommended dose of the combination of GC (G=1000 or 1250 mg/m^2 iv, Days 1 and 8; C=75 mg/m^2 iv, Day 1; 3-week cycle) and N (800 mg iv, Days 1 and 8; 3-week cycle). Patients are enrolled in 2 cohorts using a conventional 3+3 study design, with dose-escalation of gemcitabine permitted according to the incidence of dose-limiting toxicity (DLT). The Phase 2 part is an open-label, randomized trial to evaluate the efficacy and safety of addition of N to GC. Patients are randomly assigned on a 1:1 basis (Stratification factors: ECOG PS and gender) to GC+N (Arm A) or GC (Arm B). The primary endpoint is OS for which the final analysis will be performed when at least 137 events are observed. The sample size of 180 patients (137 events) has 68% power for a log-rank test at 0.2 one-sided alpha. The secondary endpoints include PFS, ORR, time to treatment failure, Pharmacokinetics, safety and patient-reported outcomes. The relationship between EGFR protein expression level by immunohistochemistry (IHC) and each of several efficacy measures will also be assessed. Translational research analyses will be performed to analyze relevant biomarkers for clinical outcomes. ClinicalTrial.gov Identifier: NCT01763788. **Results:** Not applicable **Conclusion:** Not applicable
Keywords: gemcitabine-cisplatin, necitumumab, squamous non-small cell lung cancer, trial in progress

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-081 Navotrial 3: Oral Vinorelbine + Cisplatin (P) vs Gemcitabine + P in 1st Line Advanced Squamous Non-Small-Cell Lung Cancer
Piotr Jaskiewicz[1], Eric Pichon[2], Grzegorz Czyzewicz[3], Ramon Garcia Gomez[4], Joaquim Bosch-Barrera[5], Libero Ciuffreda[6], Hervé Le Caer[7], Renan Fougeray[8], Carole Levrault[8], Marcello Riggi[8], Francesco Grossi[9] [1]*Centrum Onkologi - Instytut Im. M. Sklodowskiej-Curie, Warsaw/Poland,* [2]*Hôpital Bretonneau, Centre Hospitalier Universitaire, Tours/France,* [3]*Krakowski Szpital Specjalistyczny Im. Jana Pawla Ii, Krakow/Poland,* [4]*H.Gregorio Marañón, Girona/Spain,* [5]*Institut Català D'Oncologia, Girona/Spain,* [6]*Azienda Ospedaliera Città Della Salute E Della Scienza Di Torino, Torino/Italy,* [7]*Centre Hospitalier de La Dracenie, Draguignan/France,* [8]*Pierre Fabre Medicament, Boulogne Billancourt/France,* [9]*L'Irccs Azienda Ospedaliera Universitaria San Martino - Ist, Genova/Italy*

Background: Gemcitabine – cisplatin is one of the most frequent treatment used in patients with advanced S-NSCLC without any direct comparison with other active doublets and with superiority reported only versus pemetrexed-cisplatin (Scagliotti G., 2008). Oral vinorelbine-cisplatin is also one main standard doublet but no trial has been specifically conducted in S-NSCLC. The aim of the current study is to assess efficacy and safety of oral vinorelbine-cisplatin and gemcitabine-cisplatin in S-NSCLC patients (NAVoTRIAL 3). **Methods:** This is a phase II, international multicentre, randomised study (1:1). At baseline, patients must have stage IIIB or IV, squamous histologically or cytologically proven NSCLC, Karnofsky PS ≥70 and must not have received prior systemic CT or immunotherapy for NSCLC. Patients in arm A will receive oral vinorelbine at the dose of 60 mg/m^2 in combination with cisplatin at the dose of 80 mg/m^2 on day 1, followed by oral vinorelbine, 60 mg/m^2 on day 8 at the first cycle; the dose is increased at the second cycle to 80 mg/m^2 in absence of haematological tolerance. Both agents are repeated every 3 weeks, followed by maintenance after four cycles for patients with OR/SD: oral vinorelbine at the same dose as cycle 4, day 1, 8 every 3 weeks. Patients in arm B will receive gemcitabine at the dose of 1250 mg/m^2 in combination with cisplatin 75 mg/m^2 on day 1, followed by gemcitabine, 1250 mg/m^2 on day 8. Both agents are repeated every 3 weeks, followed by maintenance after four cycles for patients with OR/SD: Gemcitabine at the same dose as cycle 4, day 1, 8 every 3 weeks. The primary endpoint is the disease control rate (NC, CR, PR, RECIST 1.1). Enrolment began in March 2013 and 110 patients will be recruited. **Results:** Not applicable **Conclusion:** Not applicable
Keywords: NSCLC, Oral Vinorelbine, Cisplatin, Gemcitabine

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-082 Multicenter Randomized Trial Comparing Erlotinib vs. Gemcitabine or Vinorelbine as Third-Line in Advanced EGFR-Wild-Type or Unknown NSCLC
Marcello Tiseo[1], Michele Tognetto[1], Luca Boni[2], Alessandro Gamboni[3], Luigi Cavanna[4], Diego Cortinovis[5], Francesco Di Costanzo[6], Lucia Longo[7], Barbara Melotti[8], Matteo Brighenti[9], Alessandro Del Conte[10], Antonio Pazzola[11], Pier Luigi Piovano[12], Giovenzio Genestreti[13], Andrea Ardizzoni[14] [1]*Medical Oncology, University Hospital of Parma, Parma/Italy,* [2]*Clinical Trials Coordinating Center, Istituto Toscano Tumori, University Hospital Careggii, Firenze/Italy,* [3]*Medical Oncology, Faenza Hospital, Faenza/Italy,* [4]*Medical Oncology, Piacenza Hospital, Piacenza/Italy,* [5]*Medical Oncology, San Gerardo Hospital, Monza/Italy,* [6]*Medical Oncology, Istituto Toscano Tumori, University Hospital Careggii, Firenze/Italy,* [7]*Medical Oncology, Carpi Hospital, Carpi/Italy,* [8]*Medical Oncology, Sant'Orsola Hospital, Bologna/Italy,* [9]*Medical Oncology, Cremona Hospital, Cremona/Italy,* [10]*Medical Oncology, Pordenone Hospital, Pordenone/Italy,* [11]*Medical Oncology, Sassari Hospital, Sassari/Italy,* [12]*Medical Oncology, Alessandria Hospital, Alessandria/Italy,* [13]*Medical Oncology, Bellaria Hospital, Bologna/Italy,* [14]*Medical Oncology, S. Orsola-Malpighi University Hospital, Bologna/Italy*

Background: In clinical practice, approximately one third of patients with advanced non-small cell lung cancer (NSCLC) is candidate at third-line treatment. Currently, only erlotinib is licensed with this indication. Recent studies (TAILOR and DELTA trials) have questioned the role of erlotinib in second-line therapy of patients with advanced EGFR wild-type NSCLC, suggesting an inferiority in survival compared to chemotherapy with docetaxel. For this reason, the use of erlotinib is gradually shifting to the third-line. However, in this setting, chemotherapy drugs, such as gemcitabine or vinorelbine, could achieve similar survival results, with limited toxicity and lower costs than erlotinib. Therefore, the objective of this study is to evaluate the efficacy of chemotherapy (gemcitabine or vinorelbine) vs. erlotinib in the treatment of patients with advanced EGFR wild-type or unknown NSCLC progressing after two lines of chemotherapy in terms of overall survival (primary end-point). The treatments will be also compared in terms of activity, quality of life, toxicity and costs (secondary end-points). **Methods:** 538 patients will be enrolled from 40 clinical Italian centers and assigned by randomization to one of 2 treatment arms (chemotherapy vs. erlotinib) with a ratio of 1:1. As stratification factors will be considered: the center, histology (squamous vs. non-squamous), EGFR (wild type vs. unknown) and PS (0-1 vs. 2). Patients will be randomized to receive treatment with erlotinib 150 mg/day (*control arm*) or chemotherapy with gemcitabine 1000 mg/m^2 or vinorelbine 25 mg/m^2 on days 1, 8 every 21 days (*experimental arm*), according to investigator choice and previous treatment received. Treatments will be administered until disease progression, patient refusal, unacceptable toxicity, patient clinical deterioration or investigator decision. It was estimated that with 440 deaths from any cause the study would have 85% power to detect a hazard ratio of 0.75 at a two-sided significance level of 5%. If the superiority comparison will fail to detect a significant difference between treatments, the non-inferiority of the chemotherapy arm will be tested with a power equal to 65% against a prospectively defined margin for non-inferiority of the HR equal to 1.25. **Results:** not applicable **Conclusion:** If this study should be positive, it will follow a change in clinical practice with an improvement in life expectancy of patients with advanced NSCLC and savings in terms of economic resources for the NHS. This study (CONFERMER trial) is supported by NHS, Regione Emila Romagna. As to 14 April 2015, 44 patients were randomized.
Keywords: NSCLC, Third-line, Erlotinib, chemotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-083 Phase III Trial of PF-06439535 or Bevacizumab-EU plus Paclitaxel/Carboplatin in NSCLC
Bhardwaj Desai[1], Danielle Rassam[1], Patrick Ezeh[2], Leah Isakov[2], Ira Jacobs[3], Julie A. Rosenberg[4] [1]*Pfizer Inc, San Diego/CA/United States of America,* [2]*Pfizer Inc, Cambridge/MA/United States of America,* [3]*Pfizer Inc, New York/NY/United States of America,* [4]*Pfizer Inc, Groton/CT/United States of America*

Background: The recombinant, humanized, monoclonal antibody bevacizumab targets vascular endothelial growth factor (VEGF) and is approved globally, including in the United States (US) and European Union (EU), for the treatment of select solid tumors, including as a first-line therapy, in combination with platinum-based chemotherapy, for advanced non-squamous non-small cell lung cancer (NSCLC). PF06439535 is being developed as a potential biosimilar to bevacizumab and has the same primary amino acid sequence as EU- and US-sourced bevacizumab (bevacizumabEU and bevacizumabUS, respectively), with sufficiently equivalent physiochemical properties and comparable inhibition of VEGF/VEGF-receptor binding in vitro. In a nonclinical model using sexually- and skeletally-immature male cynomolgus monkeys, PF06439535 showed similar toxicokinetic parameters to bevacizumabEU and no induction of anti-drug antibodies. In a phase I trial in healthy male volunteers, PF06439535 showed pharmacokinetic similarity to bevacizumabEU and bevacizumabUS and had a comparable safety profile. These strong foundational data supported implementation of a phase III study. This phase III, multinational, double-blind, randomized, parallel-group clinical trial (NCT02364999) is evaluating the efficacy, safety, pharmacokinetics, and immunogenicity of PF06439535 versus bevacizumabEU, in combination with paclitaxel and carboplatin, in previously untreated patients with advanced non-squamous NSCLC. **Methods:** A total of 798 patients (399 per treatment arm) will be enrolled. Eligible patients are aged ≥18 years (or ≥ age of consent in the region), and have newly diagnosed stage IIIB/IV NSCLC or recurrent NSCLC with no prior chemotherapy for metastatic disease; predominantly non-squamous disease; ≥1 measureable lesion per RECIST 1.1; Eastern Cooperative Oncology Group performance status 0/1; and adequate hematologic, renal, and hepatic organ function. Patients with known sensitizing mutations in epidermal growth factor receptor (*EGFR*) or translocation positive mutations in echinoderm microtubule-associated protein-like 4-anaplastic lymphoma kinase (*EML4-ALK*) are excluded. Patients will be stratified by region, gender, and smoking status, and randomized 1:1 to receive PF06439535 or bevacizumabEU (15 mg/kg intravenously [IV]) plus paclitaxel (200 mg/m^2 IV) and carboplatin (area under the curve 6 mg·min/mL IV) on Day 1 of 21-day cycles. Following 4–6 cycles of chemotherapy, patients will continue to receive PF06439535 or bevacizumabEU as blinded monotherapy every 3 weeks until disease progression or unacceptable toxicity. Tumors will be radiographically assessed every 6 weeks according to RECIST v1.1 until Week 25, after which tumor assessments will be performed every 9 weeks. The primary objective of the study is to compare objective response rate (ORR) achieved by Week 19 between treatment arms; objective responses will be subsequently confirmed by 6 weeks thereafter. Secondary objectives include evaluation of safety, additional measures of tumor control (eg, duration of response and 1-year progression-free survival and overall survival rates), population pharmacokinetics, and immunogenicity. The main hypothesis to be tested is that the 90% confidence interval of the relative risk of ORR of PF06439535 versus that of bevacizumabEU by Week 19 is within a pre-specified margin of 76%–132%. The study is open for enrollment. **Results:** Not applicable **Conclusion:** Not applicable
Keywords: PF-06439535, bevacizumab, biosimilar, NSCLC

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-084 Avelumab (MSB0010718C), an Anti-PD-L1 Antibody, Evaluated in a Phase Ib Trial as a First-Line Treatment for Patients with Metastatic NSCLC

Claire Verschraegen[1], Sanjay Goel[2], Franklin Chen[3], David R. Spigel[4], Nicholas Iannotti[5], Marcis Bajars[6], Anja Von Heydebreck[7], Karen Kelly[8] [1]*Division of Hematology/Oncology, University of Vermont Cancer Center, Burlington/VT/United States of America,* [2]*Montefiore Medical Center, Bronx/NY/United States of America,* [3]*Novant Health Oncology Specialists, Forsyth Regional Cancer Center, Winston-Salem/NC/United States of America,* [4]*Sarah Cannon Research Institute, Tennessee Oncology, Llc, North Nashville/TN/United States of America,* [5]*Hematology Oncology Associates of the Treasure Coast, Port St. Lucie/FL/United States of America,* [6]*Global Research and Early Development - Immunooncology, Emd Serono, Inc., Billerica/MA/United States of America,* [7]*R&D Global Biostatistics, Merck Kgaa, Darmstadt/Germany,* [8]*University of California Davis Comprehensive Cancer Center, Sacramento/CA/United States of America*

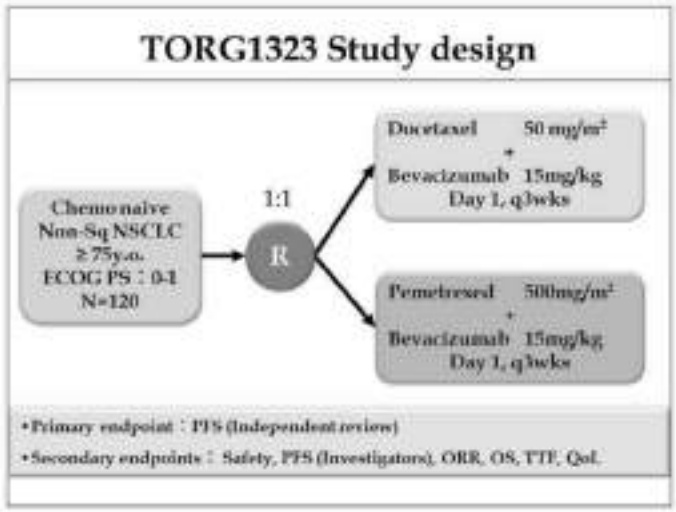
Background: The programmed death-1 receptor (PD-1) and its ligand (PD-L1) are key therapeutic targets in the reactivation of the immune response against multiple cancers. Avelumab* (MSB0010718C) is a fully human anti-PD-L1 IgG1 antibody currently being investigated in clinical trials. The phase Ib study (NCT01772004) is an open-label, parallel group expansion trial in patients with metastatic or locally advanced solid tumors that includes a cohort of patients with non-small-cell lung cancer (NSCLC) who have not been previously treated for metastatic or recurrent disease. Prior to adding this first-line cohort, this study had enrolled a separate cohort of patients with NSCLC who had received a prior platinum-containing doublet regimen. **Methods:** This trial cohort is enrolling patients with histologically confirmed stage IV (according to IASLC) or recurrent NSCLC who have not previously received treatment for metastatic or recurrent disease. In addition, this cohort is restricted to patients without an activating EGFR mutation or ALK rearrangement. Patients with unknown EGFR or ALK status will be tested during screening and are required to have negative status for inclusion. Eligible patients also must have tumor archival material or fresh biopsy, an ECOG performance status of 0 or 1 at the time of trial entry, and disease with at least 1 measurable lesion according to RECIST 1.1. Exclusion criteria include prior therapy with immune checkpoint drugs or a known history of autoimmune disease. Up to 150 eligible patients will receive avelumab at 10 mg/kg as an infusion Q2W. Treatment will continue until disease progression, unacceptable toxicity, or any criterion for withdrawal occurs. Treatment may be continued despite progression according to RECIST 1.1 if the patient's clinical status is stable and, according to investigator opinion, there is no need to start salvage therapy. The primary objective of the trial is to assess the safety and tolerability of avelumab as a first-line therapy. Select secondary objectives include: assessment of best overall response (BOR) and progression-free survival (PFS) according to RECIST 1.1; assessment of immune-related BOR and immune-related PFS (using modified Immune-Related Response Criteria); and assessment of overall survival. Association between tumor PD-L1 expression and efficacy will be evaluated. Immunomonitoring of cellular and soluble markers and intratumoral cellular surveillance will also be carried out. At each visit during the treatment phase, adverse events will be assessed and graded according to NCI-CTCAE v4.0. Tumor evaluation will be performed every 6 weeks until progression. Enrollment in this cohort began in March 2015. *Proposed INN. **Results:** not applicable **Conclusion:** not applicable
Keywords: avelumab, NSCLC, PD-L1, MSB0010718C

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-085 Randomized Phase II Study of Docetaxel plus Bevacizumab or Pemetrexed plus Bevacizumab for Elderly Non-Squamous NSCLC (TORG1323)

Toshiyuki Kozuki[1], Naoyuki Nogami[1], Natsumi Yamashita[2], Tetsu Shinkai[3], Takehito Shukuya[4], Nobuhiko Seki[5], Terufumi Kato[6], Miyako Satouchi[7], Noriyuki Masuda[8], Koshiro Watanabe[9] [1]*Dept. of Thoracic Oncology and Medicine, National Hospital Organization, Shikoku Cancer Center, Matsuyama/Japan,* [2]*Clinical Research Center, National Hospital Organization, Shikoku Cancer Center, Matsuyama/Japan,* [3]*Dept. of Internal Medicine, Shonan East General Hospital, Chigasaki/Japan,* [4]*Division of Respiratory Medicine, Juntendo University Faculty of Medicine & Graduate School of Medicine, Tokyo/Japan,* [5]*Dept. of Medical Oncology, Teikyo University School of Medicine, Tokyo/Japan,* [6]*Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Center, Yokohama/Japan,* [7]*Department of Thoracic Oncology, Hyogo Cancer Center, Akashi/Japan,* [8]*Dept. of Respiratory Medicine, Kitasato University School of Medicine, Kanagawa/Japan,* [9]*Thoracic Oncology Research Group, Yokohama/Japan*

Background: A randomized study comparing carboplatin plus weekly paclitaxel versus single-agent chemotherapy in elderly patients with non-small cell lung cancer (NSCLC) demonstrated a survival advantage for combination therapy, however, increased toxicity and treatment-related deaths were also observed. Thus, single agent approaches remain the standard of care and the improvement of treatment remains a challenge in elderly patients. The combination of bevacizumab and other platinum-based chemotherapies is the standard of care in non-elderly patients with non-squamous NSCLC. Additionally, a randomized phase II study suggested the improvement of efficacy for the combination of B plus single-agent pemetrexed or docetaxel compared with single-agent alone. Even in elderly patients, two prospective studies which we conducted demonstrated the feasibility of the combination of bevacizumab and single agent pemetrexed or docetaxel. Thus we plan this randomized phase II study (TORG1323) to select the optimal regimen for experimental arm of the future phase III study in elderly patients. **Methods:** TORG1323 is an open label multicenter randomized phase II study to compare docetaxel plus bevacizumab (DB) with pemetrexed plus bevacizumab (PB). The primary endpoint is progression free survival (PFS, assessed by independent review committee). The secondary endpoints are safety, PFS (assessed by investigators), objective response rate, overall survival, time to treatment failure and quality of life. Eligible patients are 75 years or older, have histologically or cytologically documented stage IIIb, IV or recurrent non-squamous NSCLC for which they had no received chemotherapy, ECOG performance status 0 or 1, and adequate organ function. Patients are randomly assigned to PB and DB arm (1:1). Bevacizumab is administered 15 mg/kg, pemetrexed is 500 mg/m^2 and docetaxel is 50 mg/m^2 every 3 weeks until disease progression or unacceptable toxicity. Selection design is adopted for this study. The planned sample size is 120 patients to yield 80 % power to select an optimal regimen correctly. Enrollment time is 2 years 8 months and follow-up time is 1 year. The first patient on this clinical trial was enrolled in April 2014. Further details can be found on UMIN Clinical Trials Registry (UMIN000012786).



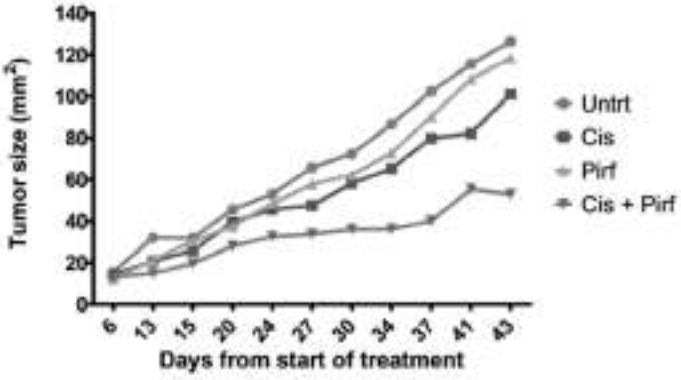
Results: not applicable **Conclusion:** not applicable
Keywords: elderly, Clinical Trial in Progress, NSCLC, bevacizumab

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-086 A Phase I Dose-Escalation Study of Pirfenidone Combined with Standard First-Line Chemotherapy in Advanced-Stage Lung NSCLC

Morganna L. Freeman-Keller[1], Jhanelle Gray[2], Scott J. Antonia[3], Melanie Mediavilla-Varela[4] [1]*Department of Graduate Medical Education, University of South Florida, Moffitt Cancer Center, Tampa/AL/United States of America,* [2]*Department of Thoracic Oncology, Moffitt Cancer Center, Tampa/FL/United States of America,* [3]*Thoracic Oncology, Moffitt Cancer Center, Tampa/FL/United States of America,* [4]*Experimental Therapeutics, Moffitt Cancer Center, Tampa/FL/United States of America*

Background: Approximately 1.6 million people are diagnosed with lung cancer annually, of which 85% of cases are NSCLC. Due to limited efficacy of current conventional chemotherapy, the majority of patients face poor prognosis; thus, combining chemotherapy with agents targeting the tumor microenvironment may be a novel approach to improving survival outcomes. Pirfenidone (5-methyl-1-phenyl-1H-pyridine-one), an agent demonstrating activity against fibroblasts and growth-promoting cytokines (TGF-β1, fibroblast growth factor [FGF], epidermal growth factor [EGF], and platelet-derived growth factor [PDGF]), has demonstrated clinical efficacy in IPF but has not yet been studied in lung cancer. We propose a proof-of-concept trial testing a novel combination of pirfenidone plus standard first-line chemotherapy in the treatment of advanced-stage NSCLC. **Pirfenidone** Pirfenidone has demonstrated activity against growth-promoting cytokines such as TGF-β1, FGF, EGF, and PDGF. A recent Phase III clinical trial of pirfenidone compared to placebo in patients with IPF demonstrated improved lung function, exercise tolerance, and progression-free survival (PFS) with an acceptable side-effect profile. To date, pirfenidone has not been studied in cancer, but its anti-fibroblast properties may play an important role in the tumor microenvironment. Our hypothesis is that pirfenidone (by targeting CAFs) in combination with standard chemotherapy will act synergistically and proffer a more potent strategy for NSCLC treatment. **Data Generated in Dr Antonia's Lab at Moffitt Cancer Center** Using low doses of pirfenidone (0.5 mg/ml), we observed a small decrease in cell proliferation (20%), also noted with low doses of cisplatin (10%). When both drugs were used, we observed a synergistic decline in proliferation (60%). An in vivo model was performed to verify this data: nude mice were inoculated with a combination of A549 cells and CAF cells at a 1:1 ratio. Treatment with pirfenidone and cisplatin began as soon as tumors were palpable. Cisplatin- or pirfenidone-treated mice had a larger tumor size than mice treated with the combination, and on the final day (43 days after start of treatment), the combination showed statistically significant improvement compared to controls. This led to our hypothesis that similar tumor regression may occur in NSCLC patients.



Methods: Phase I, single-center, dose-escalation study. Phase I trial, followed by an expansion of 20 pts with non-squamous and 10 pts with squamous cell lung cancer. **Primary Objectives:** Determine safety, tolerability, and MTD of pirfenidone plus chemotherapy in pts with advanced NSCLC, and obtain the preliminary ORR. **Secondary Objectives:** Determine OS and PFS of pts treated with pirfenidone plus standard first-line chemotherapy. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** non-small cell lung cancer (NSCLC), tumor microenvironment, Cancer-associated fibroblasts (CAFs)

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-087 A Phase I Study of Exemestane with Carboplatin and Pemetrexed in Postmenopausal Women with Metastatic, Non-Squamous Non-Small Cell Lung Cancer Richard Pietras, Jonathan W. Goldman, Diana C. Marquez-Garban, Deborah J.L. Wong, Steven Applebaum, Melody Mendenhall, Blanca A. Ledezma, Brian Wolf, Carlos R. Adame, Sarah Rosales, Jill Paroly, Sebastian Paiz, Danielle Nameth, Marshall L. Spiegel, Naomi Hecht, Meghan Brennan, Steven M. Dubinett, Edward B. Garon *David Geffen School of Medicine at University of California, Los Angeles/Translational Research in Oncology-Us Network, Santa Monica/United States of America*

Background: Lung cancer is the most common cause of cancer-related deaths in the US, with adenocarcinoma being the most common histologic subtype. Aromatase, a critical rate-limiting enzyme in estrogen biosynthesis, is notably expressed in NSCLC cells. Retrospective studies show that high NSCLC aromatase levels are associated with worse clinical outcome, particularly in postmenopausal women (Weinberg et al., Cancer Res, 2005; Mah et al., Cancer Res, 2007; Garon et al., J Thoracic Oncol, 2013). Estrogens are known survival factors in lung and promote expression of nucleotide excision repair enzyme ERCC1 that is implicated in resistance to platinum-therapy. In NSCLC cells, ERCC1 transcript expression is blocked by exemestane, an aromatase inhibitor (AI), enhancing cisplatin-induced apoptosis. In preclinical NSCLC xenograft models, exemestane exerts synergistic antitumor activity combined with cisplatin and results in prolonged tumor suppression (Marquez-Garban et al., Ann NY Acad Sci, 2009). These data provide a rationale to assess an AI in the clinic. **Methods:** Based on our preclinical studies, we are conducting a phase IB, open-label, single-center study in postmenopausal, treatment-naïve (except prior single-agent tyrosine kinase inhibitor use) women with metastatic, non-squamous NSCLC (NCT 01664754). We plan to enroll 12-15 participants divided into two dose-escalation cohorts of exemestane. All participants receive standard chemotherapy with pemetrexed (500 mg/m^2) and carboplatin (AUC 6), both given intravenously every 3 weeks. Cohort 1, which added exemestane 25 mg orally daily, has completed enrollment without any dose-limiting toxicities. Cohort 2, for which enrollment started in December of 2013, evaluates exemestane at 50 mg orally daily. Our primary aim is to evaluate safety and tolerability of the indicated regimen. Secondary objectives are tumor response rate, quality of life, pharmacokinetics/pharmacodynamics, and correlative studies of biomarkers (such as blood estrogens, tumor ERs, aromatase, and apoptosis) with tumor response. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** Estrogen, NSCLC, Post-menopausal women, Exemestane

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-088 Phase IV Study of Afatinib in Locally Advanced or Metastatic Non-Small Cell Lung Cancer Sumitra Thongprasert[1], Cosmin Boldeanu[2], Davorin Radosavljević[3], Marina Petrović[4], Hilary Jones[5], Agnieszka Cseh[6], Rabab Gaafar[7] [1]*Department of Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai/ Thailand,* [2]*Brăila County Emergency Hospital,, Brăila/Romania,* [3]*Institute for Oncology and Radiology of Serbia, Belgrade/Serbia,* [4]*Clinical Center Kragujevac, Kragujevac/ Serbia,* [5]*Oncology Department, Boehringer Ingelheim Ltd., Bracknell/United Kingdom,* [6]*Oncology Department, Boehringer Ingelheim Rcv Gmbh & Co. Kg, Vienna/ Austria,* [7]*National Cancer Institute, Cairo University, Cairo/Egypt*

Background: First-line afatinib, an oral, irreversible ErbB family blocker, improved progression-free survival (PFS), objective response rate and symptom control in patients with epidermal growth factor receptor (*EGFR*) mutation-positive locally advanced or metastatic non-small cell lung cancer (NSCLC), when compared with standard platinum-doublet chemotherapy. Afatinib also significantly prolonged overall survival in patients with Del19 mutations. Some *EGFR* mutation-positive patients still receive first-line chemotherapy and there are limited data regarding the effect of afatinib in chemotherapy pre-treated *EGFR* mutation-positive patients. This study was designed to evaluate the efficacy and safety of 40 mg/day afatinib in the second-line setting. **Methods:** Across centers in Europe, Asia and North Africa, 60 patients with locally advanced or metastatic NSCLC (stage IIIB/IV) harboring common *EGFR* mutations (Del19 and/or L858R) who have failed first-line platinum-based chemotherapy will be recruited to this ongoing, single-arm, open-label, Phase IV trial. Patients will be treated with oral afatinib 40 mg/day until the development of progressive disease or study discontinuation due to intolerable adverse events (AEs). Inclusion criteria include age ≥18 years, ECOG PS 0 or 1, documented *EGFR* Del19 and/or L858R mutation with no other known *EGFR* mutation, and adequate organ function with a life expectancy of ≥3 months. Patients are excluded from enrolling if they have received >1 line of prior therapy for disease (radiotherapy and radiosensitizers and/or intrapleural administration of anti-cancer agents is not counted as a line of therapy), or received <3 cycles of platinum-based chemotherapy due to toxicity and/or intolerance of treatment, or received previous treatment with an EGFR-targeted tyrosine kinase inhibitor or antibody. The primary endpoint is objective tumor response (complete response [CR], partial response [PR]) according to RECIST v1.1. Secondary endpoints include PFS, disease control (CR, PR, stable disease) and assessment of safety. All patients who received at least one dose of afatinib will be included in the analysis of safety, with AEs graded according to CTCAE v3.0. Efficacy and safety will be evaluated in a descriptive manner; there are no formal statistical hypotheses. This trial was initiated in October 2014 and is open for accrual. Study locations include 22 trial sites in 7 countries. Trial sites are currently open to enrollment in Egypt, Romania, and Serbia. Enrollment will soon be open in Malaysia, the Philippines, Poland, and Thailand. The estimated completion date for the primary outcome is December 2016; further details are available at ClinicalTrials.gov (NCT02208843). **Results:** Not applicable. **Conclusion:** Not applicable. **Keywords:** afatinib, NSCLC, EGFR mutated, Second-line

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-089 Nab-Paclitaxel with or without CC-486 as Second-Line Therapy for NSCLC (ABOUND.2L) Ramaswamy Govindan[1], Andrea Ardizzoni[2], Wilfried E.E. Eberhardt[3], Pilar Garrido[4], Amy Ko[5], Daniel Morgensztern[6], Petros Nikolinakos[7], Teng Jin Ong[8], Marianne Wolfsteiner[8], Martin Reck[9] [1]*Washington University School of Medicine, St. Louis/MO/United States of America,* [2]*Medical Oncology, S. Orsola-Malpighi University Hospital, Bologna/Italy,* [3]*Department of Medical Oncology, University Hospital Essen, West German Cancer Centre, Ruhrlandklinik, University Duisburg-Essen, Essen/Germany,* [4]*Irycis, Hospital Universitario Ramón Y Cajal, Madrid/Spain,* [5]*Celgene Corporation, Summit/ NJ/United States of America,* [6]*Oncology, Washington Univresity School of Medicine in St. Louis, St. Louis/MO/United States of America,* [7]*University Cancer and Blood Center, Athens/GA/United States of America,* [8]*Celgene Corporation, Summit/United States of America,* [9]*Department of Thoracic Oncology, Lungen Clinic Grosshansdorf, Airway Research Center North (Arcn), Member of the German Center for Lung Research (Dzl), Grosshansdorf/ Germany*

Background: Many patients with advanced non-small cell lung cancer (NSCLC) will experience disease progression during first-line chemotherapy. Effective and well-tolerated second-line treatment options for this patient population are limited. In a multicenter phase III trial, first-line treatment with *nab*-paclitaxel plus carboplatin (*nab*-P/C) significantly improved the primary endpoint of overall response rate (ORR) compared with solvent-based paclitaxel plus C in patients with advanced NSCLC (33% vs 25%; $P = 0.005$; Socinski et al. *J Clin Oncol*. 2012;30:2055-2062). *nab*-P combined with CC-486, an oral formulation of azacitidine, resulted in promising outcomes in a phase I trial of patients with relapsed/refractory solid tumors (LoRusso et al. *Mol Cancer Ther*. 2013;12(11 Suppl):Abstract A120). In the open-label, multicenter phase II ABOUND.2L trial, the safety and efficacy of *nab*-P with or without CC-486 will be evaluated in the second-line treatment of patients with advanced nonsquamous NSCLC. **Methods:** Approximately 160 patients who have received 1 platinum-containing chemotherapy regimen for treatment of advanced disease will be randomized 1:1 to CC-486 200 mg/day on days 1 to 14 every 21 days plus *nab*-P 100 mg/m^2 intravenously (IV; 30-minute infusion) on days 8 and 15 every 21 days or *nab*-P 100 mg/m^2 IV (30-minute infusion) on days 1 and 8 every 21 days. Key eligibility criteria include histologically or cytologically confirmed advanced nonsquamous NSCLC, ECOG performance status ≤ 1, adequate organ function, no active brain metastases, no prior taxane therapy, no known *EGFR* mutation or *EML4-ALK* translocation, and peripheral neuropathy grade < 2. Randomization will be stratified by ECOG performance status (0 vs 1), sex, and smoking status (yes vs no). ClinicalTrials.gov identifier NCT02250326.

Key Endpoints	
Primary	• Progression-free Survival
Secondary	• Disease control rate -Overall Survival -ORR -Safety
Exploratory	• Changes in quality of life -Healthcare resource utilization throughout the study -Correlation between pretreatment tumor characteristics and response to treatment

Results: Not applicable **Conclusion:** Not applicable **Keywords:** nab, CC486, NSCLC, 2nd line

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
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P3.01-090 Phase 3, Double-Blind, Placebo-Controlled Study of MEDI4736 After Chemoradiation in Stage III, Locally Advanced, Unresectable NSCLC (PACIFIC)
Byoung Chul Cho[1], Joo-Hang Kim[1], Augusto Villegas[2], Nicolas Frusch[3], Shuji Murakami[4], Kelvin Shi[5], Ramy Ibrahim[5], Marc Ballas[5], Scott J. Antonia[6] [1]*Yonsei Cancer Center, Severance Hospital, Yonsei University Health System, Seoul/Korea,* [2]*Cancer Specialists of North Florida, Jacksonville/FL/United States of America,* [3]*Centre Hospitalier de L'Ardenne, Libramont/Belgium,* [4]*Kanagawa Cancer Center, Yokohama, Kanagawa/Japan,* [5]*Astrazeneca, Gaithersburg/MD/United States of America,* [6]*H. Lee Moffitt Cancer Center and Research Institute, Tampa/FL/United States of America*

Background: Non-small cell lung cancer (NSCLC) accounts for 85–90% of all lung cancer cases. Approximately 35% of patients with NSCLC have Stage III disease at the time of diagnosis. Platinum-based, concurrent chemoradiation therapy is the standard treatment for patients with locally advanced, unresectable NSCLC. However, most patients progress despite treatment, and 5-year overall survival (OS) is only ~15%. Therefore, there is a significant unmet need for novel, effective therapeutic approaches to prolong survival. Immunotherapies that block checkpoints used by tumor cells to dampen immune responses are a promising new treatment option. Encouraging clinical activity against several tumor types has been seen for anti-PD-L1/PD-1 monoclonal antibodies (mAbs). MEDI4736 is a human IgG1 mAb that blocks programmed cell death ligand-1 (PD-L1) binding to programmed cell death-1 and CD-80 with high affinity and selectivity, preventing PD-L1-mediated inhibition of T-cell activation. It has been engineered to harbor a triple mutation in the fragment crystallizable domain, which removes antibody-dependent cell-mediated cytotoxicity and complement-dependent cytotoxicity. Evidence of clinical activity for MEDI4736 in NSCLC has been observed in a Phase 1 study (Study 1108, NCT01693562), with initial data indicating that PD-L1 expression is associated with a higher objective response rate (ORR). Chemotherapy and radiotherapy upregulate the expression of tumor PD-L1, which could increase sensitivity to PD-L1-directed therapy. Based on this rationale, the PACIFIC study (NCT02125461) will evaluate the efficacy and safety of MEDI4736 in patients with locally advanced, unresectable NSCLC (Stage III) whose disease has not progressed following platinum-based, concurrent chemoradiation therapy. **Methods:** In this Phase 3, randomized, double-blind, multicenter, international study, ~700 patients will be randomized 2:1 to receive MEDI4736 (10 mg/kg IV) or placebo every 2 weeks for up to 12 months. Eligible patients must have previously received ≥2 cycles of platinum-based concurrent chemoradiation with no subsequent disease progression, have received a total dose of radiation of ≥60 Gy, and have archival tissue available. Patients treated with sequential chemoradiation therapy for locally advanced disease and those with metastatic disease are excluded. Randomization must occur within 42 days of radiation. Co-primary endpoints are OS and progression-free survival (PFS) (RECIST v1.1). Secondary endpoints include OS at 24 months, proportion of patients alive and progression-free at 12 and 18 months, time to second progression, objective response rate, duration of response, health-related quality of life, safety/tolerability, pharmacokinetics and immunogenicity of MEDI4736. Patients who achieve and maintain disease control up to 12 months will enter follow-up. Patients will be recruited at approximately 300 sites across Australia, Asia, Europe, North and South America and South Africa. Recruitment is ongoing. **Results:** Not applicable **Conclusion:** Not applicable
Keywords: NSCLC, MEDI4736, PD-L1, Immunotherapy

POSTER SESSION/ TREATMENT OF ADVANCED DISEASES – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.01-091 Phase III Study of Front-Line Chemotherapy with TTFields for Advanced Squamous NSCLC Ori Farber[1], Uri Weinberg[2] [1]*Novocure Ltd., Haifa/Israel,* [2]*Novocure Gmbh, Lucerne/Switzerland*

Background: Tumor Treating Fields (TTFields) are a novel, non-invasive, anti-mitotic treatment modality, based on low intensity alternating electric fields. TTFields predominantly affect two phases of mitosis: metaphase – by disrupting the formation of the mitotic spindle, and cytokinesis – by dielectrophoretic dislocation of intracellular constituents. Efficacy of TTFields in non-small cell lung cancer (NSCLC) of all histologies has been demonstrated in multiple *in vitro* and *in vivo* models, as well as in a phase I/II pilot study, in combination with pemetrexed. At the time of this study, squamous histology patients were still treated with pemetrexed, and those enrolled in the trial surprisingly demonstrated a high median overall survival of 13.8 months. The promising preclinical data, high safety profile and initial clinical data in squamous histology patients have led to the design of the current study. **Methods: The LUNAR Clinical Trial** 300 patients with advanced NSCLC of squamous histology will be randomized in a ratio of 1:1 to receive either standard doublet chemotherapy alone or chemotherapy combined with TTFields. Patients will be followed-up every 6 weeks clinically and radiographically until intra-thoracic progression, then continue a follow up for vital status. **Objectives** To test the efficacy and safety of TTFields in combination with chemotherapy in this patient population. **Endpoints** Overall survival (primary), radiological response, progression free survival, in field vs. out of field time to progression, quality of life and safety (secondary). **Statistical Considerations** This is prospective, randomized, multicenter study for 300 patients. The total sample size of 300 patients (272 + 10% loss to follow up), will achieve a 80% power with an alpha of 0.05 using a two-sided log rank test to detect a hazard ratio of 0.69 for OS. Patients will be stratified based on presence of extra-thoracic disease (intra-thoracic disease only versus extra-thoracic disease), gender (male vs. female) and region. **Key Eligibility Criteria** Age > 18 years; Intra-thoracic advanced (stage IV) NSCLC with squamous histology; No prior chemotherapy or biological therapy for advanced disease; No prior intra-thoracic radiotherapy for advanced disease; ECOG performance status of 0-1; No serious co-morbidities; No contraindication for chemotherapy or TTFields; Adequate bone marrow, liver and renal functions. **Treatment** Continuous, daily TTFields Therapy at 150 kHz, applied to the thorax using the NovoTTF-100L System. The System is a portable medical device allowing normal daily life activities. The device delivers alternating electric fields to the thorax using 4 Transducer Arrays. Chemotherapy options include a taxane or gemcitabine platinum-based doublet. **Results:** not applicable **Conclusion:** not applicable
Keywords: Tumor Treating Fields, First Line, advanced NSCLC, TTFields

SESSION: POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC WEDNESDAY, SEPTEMBER 9, 2015

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-001 Factors Affecting Tumor Recurrence in Early Stage Non-Small Cell Lung Cancer Narjust Duma[1], Yulanka Castro[1], Harry D. Harper[2], Martin Gutierrez[2] [1]*Internal Medicine, Rutgers-New Jersey Medical School, Newark/NJ/United States of America,* [2]*Medical Oncology, Hackensack University Medical Center, Hackensack/NJ/United States of America*

Background: For early stage non-small cell lung cancer (NSCLC) surgery is potentially the only curative treatment. However, a proportion of lung cancer patients develop recurrence, even after complete resection. The factors affecting recurrence in these patients are largely unknown. This study aimed to identify the predictive factors for recurrence in patients with stage I/II NSCLC. **Methods:** We retrospectively reviewed all patients diagnosed with stage I/II NSCLC at our institution from 2000 to 2013. Initial diagnosis at our institution and a minimum follow up of 36 months were required. Cox regression model was used for multivariate analysis. **Results:** A total of 673 patients with stage I/II were identified, of those 175 (26%) developed local or distant recurrence, with a median time to recurrence of 18 months. Median age was 74 (range: 44-96 years), 56% were current or former smokers. Patients were more likely to have upper lobe tumors than all other tumor locations combined (58% vs 42%), adenocarcinoma was the most prevalent histologic subtype (53%) and 47% had poorly differentiated or anaplastic tumors. 152 patients (87%) received surgery with lobectomy being the most common procedure followed by wedge resection. 24% received chemotherapy and 7% radiation. Median overall survival was 26 months (95%CI: 17.2-34.5). Patients with squamous cell carcinoma had a shorter median time to recurrence when compared with adenocarcinomas (13.2 months vs. 19.7 months) ($p<0.02$). Smoking history (HR: 1.98, 95%CI: 1.62-2.82, $p<0.007$), central tumor location (HR: 1.24, 95%CI: 1.09-1.56, $p<0.01$), squamous subtype (HR: 1.46, 95%CI: 1.22-1.84, $p<0.002$) , high histologic grade (HR: 2.76, 95%CI: 1.34-5.97, $p<0.01$) and lymphovascular invasion (HR: 4.3, 95%CI: 3.32-5.00, $p<0.001$) were independent predictors of recurrence by multivariate analysis. Poorly differentiated tumors were associated with a higher frequency of distant recurrence when compared with well differentiated tumors (OR: 2.7 vs. 1.2). In 43% of the patients with recurrence lung cancer was the primary cause of death. **Conclusion:** In our cohort, we observed that patients with lymphovascular invasion have the highest recurrence risk followed by high histologic grade tumors with the former having a direct correlation with distant metastasis. Patients with these risk factors may benefit from close surveillance after surgical resection, adjuvant therapy and aggressive management of local recurrence.
Keywords: recurrence, early stage non-small cell lung cancer, Risk factors for recurrence, patients follow up

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-002 Long-Term Survival of Patients Undergoing Video Assisted Thoracoscopic Anatomical Resection for Stage I NSCLC Is Equivalent to Open Thoracotomy Diego M. Avella[1], Ujala Bokhary[2], Brittany Lapin[3], Ki W. Kim[2], John Howington[2] [1]*Surgery, University of Chicago, Chicago/IL/United States of America,* [2]*Thoracic Surgery, Northshore University Healthsystem, Evanston/IL/United States of America,* [3]*Thoracic Surgery, Northshore University Healthsystem, Evanston/United States of America*

Background: We analyze the long-term survival of patients that underwent video assisted thoracoscopic (VATS) anatomical lung resection for Stage I Non-small cell carcinoma (NSCLC) of the lung before at the Northshore University Health System **Methods:** This is a retrospective analysis of data from patients that underwent VATS lung anatomical resection before December 31st of 2010.We extracted the data through standard queries and by manual extraction from the Electronic Data Warehouse of the Northshore University Health System. The patients were selected based on surgical description of anatomical resection defined as lobectomy, bilobectomy or segmentectomy for proven NSCLC. Patients with more than one procedure performed, diagnosis of carcinoid tumor or incomplete data were excluded. The variables evaluated included demographics, preoperative workup and clinical evaluation, pathology reports, intra-operative data and post-operative outcomes and 3 and 5 years overall and disease free survival. **Results:** A total of 265 patients were included. The mean age at the time of diagnosis was 70.9 (±9.9) years, 68.5% were female, 84.3% were Caucasian with a 39.6 (±26.3) pack year smoking history. The most common comorbidities encountered were hypertension (66.3%), COPD (34.8%) and coronary artery disease (28.1%). VATS lobectomy was performed in 90% of the patients. FEV_1 data was available in 91.1% of the patients whereas DLCO data was available in 84.3% of the patients that underwent VATS anatomical resection. The mean procedure time was 151 (±59) minutes; the median length of chest drainage with tube thoracostomy was 3 days. Eighteen (20.2%) patients required admission to the Intensive Care Unit (ICU) with a median length of stay in the ICU of 2.2 days. The median length of stay in the hospital was 3.6 days. There were

no deaths within 90 days post-surgery. The overall rate of complications was 25.8% with prolonged air leak (>5 days) (11.2%) and atrial fibrillation (9.0%) being the most frequent complications. The rate of adverse events decreased over time from 27.8% in 2008 to 20% in 2010. Only one patient required a second intervention within 30 days of the first surgery for a persistent chylothorax. The median follow-up was 57 months. Recurrences occurred in 10.2% of the patients with a mean time of 1.7 (±1.0) years after surgery. Local recurrence occurred in 68.4% of the times 1.9(±1.09) years after surgery whereas distant recurrences occurred in 31.6% of the times 1.4(±0.89) years after surgery. Overall mortality was 16%. The 3- and 5-years overall survival was 86% and 76.2%. The 3 and 5-years disease-free survival was 86.8% and 82.2% **Conclusion:** VATS anatomical lung resection does not seem to affect the long-term survival in comparison with reported analysis for open thoracotomy for patients with stage I NSCLC. Our data demonstrated a decreasing rate of complications with a high rate of cure for this group of patients, which might be utilized to compare with nonsurgical therapy for NSCLC
Keywords: VATS, Stage I NSCLC

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-003 Availability of the Serum CYFRA 21-1 Level with Resected Non-Small Cell Lung Cancer: The Detectability of Recurrence and the Prognostic Impact Mikiko Suzuki, Kazuya Takamochi, Shiaki Oh, Kenji Suzuki *Department of General Thoracic Surgery, Juntendo University School of Medicine, Tokyo/Japan*

Background: The appropriate protocol of postoperative surveillance for patients with non-small cell lung cancer (NSCLC) is still controversial. The aim of this study is to evaluate the detectability of recurrence and the prognostic impact of the serum CYFRA 21-1 levels. **Methods:** We retrospectively reviewed 1076 patients who underwent surgical resection for NSCLC at Juntendo University Hospital, between January 2008 and May 2013. Patients with renal dysfunction were excluded. **Results:** Recurrence developed in 47 patients (30.5%) in high preoperative serum CYFRA 21-1 group, and 147 patients (16.0%) in normal preoperative serum CYFRA 21-1 group. High preoperative serum CYFRA 21-1 was related to the high recurrence rate (p<.0001) and the poor prognosis (p<.0001). In high preoperative serum CYFRA 21-1 group, 111 patients measured the serum CYFRA 21-1 level within the 1-3 months after surgery. Among them, 31 patients (27.9%) had an elevated serum CYFRA 21-1 level, and the poor prognosis (p<.0001) (Fig.). In 94 patients who measured the serum CYFRA 21-1 level during the follow-up period, 35 patients (37.2%) could detect recurrence by an elevated serum CYFRA 21-1 level before recurrence. Only for high preoperative serum CYFRA 21-1 group, 23 patients (67.6%) could detect recurrence. **Conclusion:** High preoperative serum CYFRA 21-1 was related to the high recurrence rate and the poor prognosis. In addition, high early-postoperative (1-3 months after surgery) serum CYFRA 21-1 was related to the poor prognosis. Measuring the serum CYFRA 21-1 level during the follow-up period is useful in the detection of recurrence, but that rate is low.
Keywords: NSCLC, CYFRA 21-1

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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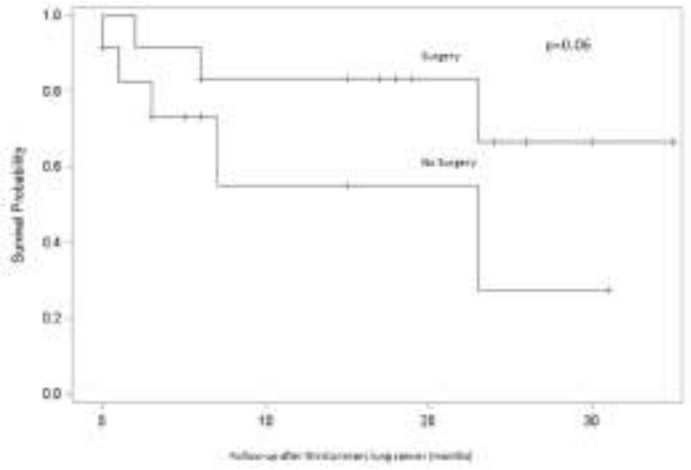
P3.02-004 PD-L1 Overexpression in NSCLC Inversely Correlated with Survival of NSCLC Patients Hua Zhong, Yan Zhou, Baohui Han, Xianxun Liu *Pulmonary Department, Shanghai Chest Hospital, Shanghai/China*

Background: Programmed cell death protein 1, also known as PD1, is a 288 amino acids cell surface protein in the immunoglobulin superfamily. [1] PD-1 is expressed on T-cells and pro-B cells, plays a pivotal role in their differentiation. [2] PD-1 has two ligands, PD-L1 and PD-L2, which are the members of a peripheral membrane protein family called B7. [3][4] PD-L1 can suppress immune system in some special events such as pregnancy and auto immune disease. Binding of PD-L1 with its receptor PD-1 on T cells delivers a signal that inhibits TCR-mediated activation of IL-2 production and T cell proliferation. [5] PD-L2's expression is more restricted compare to PD-L1 and mainly in antigen-presenting cells like Dendritic Cells and microphages. [4] Here we report a study of 139 NSCLC patients diagnosed and undergone primary surgery in Shanghai Chest Hospital. The expression of PD-L1 was exanimated by immunohistochemistry, and has a positive correlation with the stage of NSCLC. We also observed a significant correlation between PD-L1 over expression and EGFR mutation, which has the potential to be an favorable prognostic factor. High PD-L1 expression and EGFR mutation also correlated with a significant longer survival time of patients **Methods:** One pathologist examined the H&E- and IHC-stained slides and evaluated the results. The evaluation were done blinded as to the clinical pathologic characteristics and patient outcome. A series of 139 patients diagnosed with NSCLC and undergone primary surgery at Shanghai Chest Hospital (Shanghai, China) from January to December of 2008 were selected in this study. All the patients received lobectomy standard with systematic lymph node dissection. Immunohistochemistry staining for PD-L1 were performed both for tumor and tissue surrounding the tumor.PD-L1 positivity (PDL1+) was defined as 5% tumor cell membrane staining at any intensity.One pathologist examined the H&E- and IHC-stained slides and evaluated the results. The evaluation were done blinded as to the clinical pathologic characteristics and patient outcome. Overall survival data were obtained for each patient by following up visit performed on 2014. **Results:** A total of 139 tumors were examined after exclusion of uninformative slides. There were 72 patients (54.1 %) with stage II, and 61 (45.9 %) with stage III disease. For histological subtypes, there were 90 with adenocarcinoma, 43 with square carcinoma, and 6 with others. Of these, positive evaluation of PD-L1 staining was present in 81 (61.8 %) specimens, while 50 (38.2 %) specimens showed negtive/low PD-L1 staining, while the tumor adjacent tissue showed also negtive/low PD-L1 expression .We also did genotyping for the specimens and found about one third of them (50 in a total 133 specimens, 33.3%) carry EGFR mutation. Among the mutations,15 are happened on exome 19 and 33 are on exome 21. PD-L1 positively expression imply a longer survival time compared with PD-L1negatively expression. **Conclusion:** Our results suggest a prognostic value of PD-L1 expression evaluation, which can also be a potentiall immuno-target therapy for lung cancer
Keywords: lung cancer, PD-L1, Immunotherapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-005 Third Primary Lung Cancers: Incidence and Benefits of Surgical Therapy Dong-Seok Lee, Emanuela Taioli, Andrew Kaufman, Andrea Wolf, Daniel Nicastri, Faiz Y. Bhora, Fouad Lajam, Suresh Ramanathan, Raja Flores *Thoracic Surgery, Mount Sinai Health System, New York/NY/United States of America*

Background: Continued surveillance of lung cancer patients after curative surgery allows for the diagnosis of new disease. However, there is a relative paucity of data in regards to the development of third primary lung cancers. The goals of this study were to examine the incidence of third primary cancers and the results of surgical therapy. **Methods:** Surgically resected Stage 1 second primary lung cancers with complete data were identified in The Survival Epidemiology and End Results (SEER) database between 2004 and 2010. Among these 238 cases, those which developed a third primary lung cancer 6 or more months after the diagnosis of the second primary were analyzed. Statistical methods were performed using Kaplan-Meier and multivariate analysis. A p value < 0.05 was considered statistically considered significant. **Results:** Twenty-four patients (10.1%) experienced a third primary lung cancer; sixteen cases (66.7%) were diagnosed in stage I. Twelve patients (50% of cases) underwent cancer surgery. Nine patients (37.5%) were treated with beam radiation – alone (8 cases, 89%) or in combination with surgery (1 case, 11%). Surgery was performed more frequently in early stages (75% of surgical cases were stage I versus 58% of non-surgical cases). There was no difference in age between patients who underwent any treatment and those who did not. Length of follow-up in third primary cancers was 18 months if surgically treated and 8 months if not surgically treated (p < 0.02). At multivariate analysis, the only independent predictor of improved survival was treatment (Hazard ratio (HR) 0.21, 95% CI: 0.07-0.66; p=0.007). Both surgery (HR=0.02; 95% CI: 0.002-0.29) and radiation (HR= 0.04; 95% CI: 0.002-0.54) significantly improved survival.



Conclusion: The overall incidence of third primary lung cancers after a second primary is 10.1%. Surveillance and intervention at early stage results in improved survival.
Keywords: lung cancer, Third primary, Surgery, radiation

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-006 How Should We Handle Elderly Patients of the Non-Small Cell Lung Cancer? Junichi Okamoto[1], Hirotoshi Kubokura[1], Jitsuo Usuda[2] *[1]Thoracic Surgery, Nippon Medical School Musashikosugi Hospital, Kanagawa/Japan, [2]Thoracic Surgery, Nippon Medical School, Bunkyo-Ku/Japan*

Background: In Japan, the ratio of lung cancer patients of octogenarian was still increasing in 2012. Elderly patients used to have comorbidities. Thus it is more difficult to select the surgical treatment of the elderly person in the lung cancer. Therefore, we aimed to clarify the preferred surgical management in this patient group. **Methods:** A retrospective study was conducted between April 2008 and March 2015 that included patients with non-small cell lung cancer (NSCLC) aged ≥75 years. Patients were divided into those who underwent partial resection and those who underwent lobectomy. **Results:** This study included 44 patients: 28 men and 16 women. We divided into two groups; one is partial resection (P-group) and another is lobectomy group (L-group). In patient's characteristics, there were mostly no significant differences between two groups, without preoperative diabetes mellitus (p = 0.0271), tumor size on CT (p = 0.0002), operation time (p < 0.0001), post-operative hospital days (p = 0.0003), or pathological tumor size (p < 0.0001). In survival analysis, there were significant differences in overall survival (OS) between P-group and L-group (p = 0.0335). However, there was no significant difference in disease-free survival (DFS) rate among the two categories (p = 0.41), and in OS among stage I patients (p = 0.16). Postoperative complication caused poor prognosis (p =

0.0004). However, operation procedure did not correlate with postoperative morbidity. Cox regression analysis revealed statistical significance for the Brinkman Index(BI) (p = 0.0318), the ratio of the pulmonary artery diameter to the ascending aorta diameter (PA:A) (p = 0.0182), and the alveolar–arterial oxygen gradient (A-aDO2) (p = 0.0300). Only the PA:A ratio remained significant after multivariate analysis, with a higher ratio associated with better survival. Only the PA:A ratio remained significant after multivariate analysis, with a higher ratio associated with better survival, by Wilcoxon's test (p = 0.0376). **Conclusion:** In elder patients with NSCLC, surgical resection should not be denied by only age. However, operation procedure should select Partial resection, compare to Lobectomy, as much as possible, especially, with the higher patients of PA: A ratio.
Keywords: Elderly patient, NSCLC, Operation, PA: A ratio

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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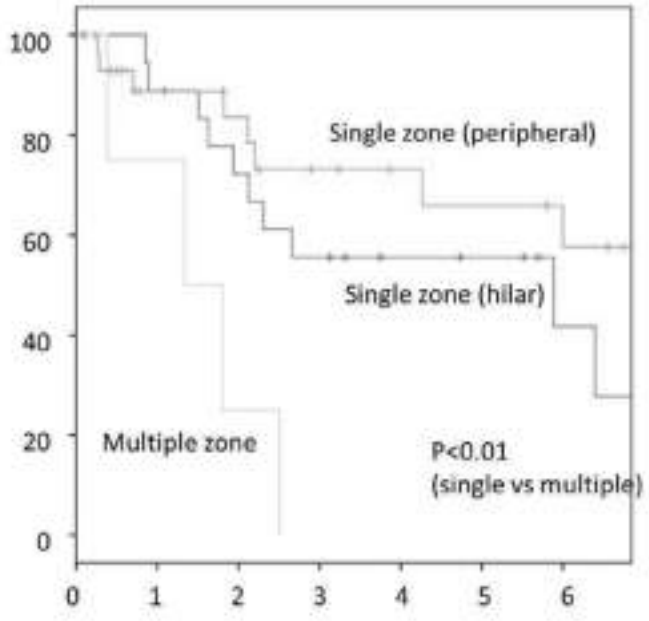
P3.02-007 Survival and Prognostic Factor in Pathological N1 Non-Small-Cell Lung Cancer
Taketsugu Yamamoto[1], Takamitsu Maehara[1], Munetaka Masuda[2]
[1]*Thoracic Surgery, Yokohama Rosai Hospital, Yokohama/Japan,* [2]*Department of Surgery, Yokohama City University Graduate School of Medicine, Yokohama/Japan*

Background: The 5-year survival rates of N1 non-small-cell lung cancer (NSCLC) were reported to be between 27% and 67%. The aim of the study was to identify common prognostic factors in NSCLC with N1 nodal involvement. **Methods:** The medical records and the follow-up data of the patients operated for NSCLC(p-N1) between January 1991 and December 2013 in Yokohama Rosai Hospital were analyzed retrospectively. Fifty-four patients with NSCLC (p-N1) who underwent lung resections with negative surgical margins were included in this study. **Results:** The subjects were 45 men and 9 women with a mean age of 67 years (range, 45-81 years). Among them 24 had adenocarcinoma, 16 had squamous cell carcinoma, 6 had large cell carcinoma, and 8 had the other histologies. T-factor of the primary tumor was T1 in 12 patients, T2 in 34, T3 in 7, and T4 in 1. Among N1 disease, peripheral zone lymph node (#12,13,14) metastasis was 18 cases, while hilar zone node(#10,11) metastasis was 30 cases, and both zone in 6 cases. The overall 5-year survival rates were 54.7 % in N1 disease. In a univariate analysis, survival was worse in case of higher T factor (T3,4) (p<0.01), multiple-N1-node involvement(p<0.01), and multiple-N1-zone involvement(p<0.01). Among patients with single-N1-zone involvement, overall survival was lower in patients with hilar zone metastasis than in those with peripheral zone metastasis, although this difference was not statistically significant (p=0.272).



Conclusion: In pN1 NSCLC patients, higher T-factor, multiple-N1-node involvement, and multiple-N1-zone involvement were worse prognostic factors.
Keywords: NSCLC, N1 disease

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-008 Clinical Characteristics of EML4-ALK Positive and Surgically Resected NSCLC Patients
Hong Tao[1], Yiran Cai[2], Zhe Liu[1], Liang Shi[1], Junfang Tang[1]
[1]*Oncology, Beijing Chest Hospital, Capital Medical University, Beijing/China,* [2]*Pathology, Beijing Chest Hospital, Capital Medical University, Beijing/China*

Background: Along with the research progress of lung cancer-related driver genes, echinoderm microtubule-associated protein-like 4- anaplastic lymphoma kinas(EML4-ALK) positive non-small cell lung cancer(NSCLC), which is a distinctive molecular subtype, has been concerned. In this study we evaluate the clinical features of EML4-ALK positive and postoperative NSCLC patients. **Methods:** Clinical data of 42 patients with EML4-ALK positive, postsurgical NSCLC were retrospectively analyzed. The organs of distant metastasis were observed. Log-rank test were used to analyse the relationship between clinical characteristics and disease free survival(DFS), overall survival(OS). **Results:** EML4-ALK positive patients are raletive young, most of them are never-smokers, peripheral type. The tumors were either moderately or poorly differentiated. The most common organ of distant metastasis was brain. Much more brain metastasis occurred in center type patients than in peripheral type patients(70.0% vs 30.0%, P=0.004).The median time from operation to brain metastasis was 17.2 months. The median post brain metastasis OS was 9.4 months. The DFS of earlier stage, peripheral type, moderately differentiated, without lymph node metastasis and with adjuvant treatment patients were significant longer than those of later stage(30.3months vs 12.8 months, P=0.016), center type(27.4months vs 7.3months, P=0.000), poorly differentiated(27.0 months vs 11.9months, P=0.048), with lymph node metastasis(30.0months vs 12.8months, P=0.027) and without adjuvant treatment(19.1months vs 1.8months, P=0.000) patients. Earlier stage, peripheral type, with adjuvant treatment patients obtained longer OS than later stage, center type, without adjuvant treatment counterparts (respectively 55.5months vs 26.2months, P=0.025; 39.2months vs 20.9 months, P=0.003; 33.4months vs 15.7months, P=0.001) . Tab 1 Clinical characteristics of paients

Characteristics	No. of patients	Percent(%)
Gender		
Male	23	54.8
Female	19	45.2
Age(yr)		
≤55	26	61.9
＞55 Median(range)	16 52(23-71)	38.1
Smoking history		
Yes	13	31.0
No	29	69.0
Stage		
Ⅰ stage	10	23.8
Ⅱ stage	3	7.1
Ⅲ stage	24	57.1
Ⅳ stage	5	11.9
Tumor location		
Center type	12	28.6
Peripheral type	30	71.4
Histology		
Adenocarcinoma	39	92.9
Squamous cell carcinoma	0	0
Adenosquamous carcinoma	1	2.4
Others	2	4.8
Differentiation degree		
Well differentiated	0	0
Moderately differentiated	26	61.9
Poorly differentiated	16	38.1

Tab 2 Relationship between clinical characteristics and DFS, OS

Group	DFS(month)	P	OS(month)	P
Gender				
Male	14.7	0.117	26.2	0.630
Female	18.8		32.8	
Age(yr)				
≤55	19.1	0.257	32.0	0.652
>55	17.4		30.0	
Stage				
Ⅰ+Ⅱ stage	30.3	0.016	55.5	0.025
Ⅲ+Ⅳ stage	12.8		26.2	
Tumor location				
Center type	7.3	0.000	20.9	0.003
Peripheral type	27.4		39.2	
Smoking history				
Yes	7.0	0.167	22.9	0.524
No	17.4		32.8	
Differentiation degree				
Moderately differentiated	27.0	0.048	39.2	0.055
Poorly differentiated	11.9		26.2	
Tumor diameter				
>3cm	12.8	0.200	32.0	0.502
≤3cm	27.0		33.4	
Lymph node metastasis				
Yes	12.8	0.027	27.8	0.071
No	30.0		45.0	
adjuvant treatment				
Yes	19.1	0.000	33.4	0.001
No	1.8		15.7	

Conclusion: EML4-ALK positive, postoperative NSCLC patients have distinctive clinical characteristics. The most common location of extrapulmonary metastasis was brain. DFS was associated with TNM stage, tumor location, differentiation degree, lymph node metastasis and adjuvant therapy. OS was related to TNM stage, tumor location and adjuvant therapy.
Keywords: postoperative, brain metastases, Lung neoplasms, EML4-ALK positive

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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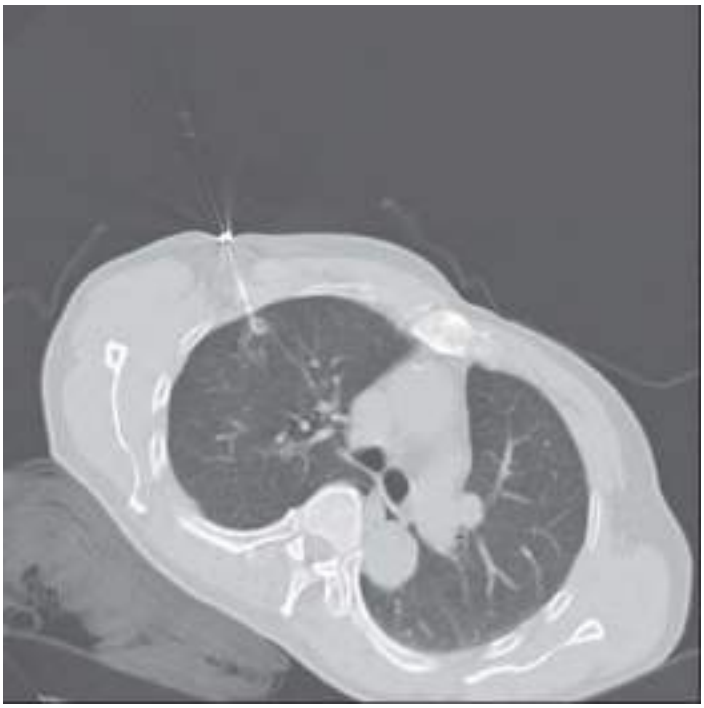
P3.02-009 Predictors of Prolonged Air Leak after Pulmonary Lobectomy Satoru Okada, Junichi Shimada, Daishiro Kato, Hiroaki Tsunezuka, Kaori Abe, Tatsuo Furuya, Narumi Ishikawa *Division of Chest Surgery, Department of Surgery, Kyoto Prefectural University of Medicine, Kyoto/Japan*

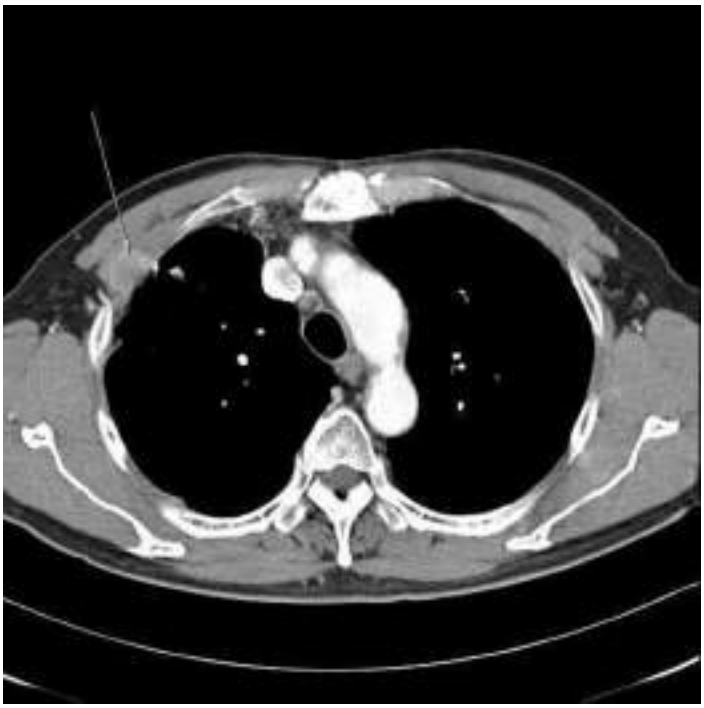
Background: Prolonged air leak (PAL) is a common complication, which occurs in 3% to 25% of patients undergoing pulmonary resection. PAL may cause severe morbidity such as pneumonia and empyema, and prolong the need for chest tube drainage and hospitalization. Thus, a careful perioperative management to decrease the risk of PAL is needed. The purpose of this study is to analyze the significance of various risk factors for postoperative PAL (air leak longer lasting more than 7 days) in patients undergoing pulmonary lobectomy for lung cancer. **Methods:** This study includes 134 patients who underwent pulmonary lobectomy for lung cancer between September 2009 and December 2014 at Kyoto Prefectural University of Medicine. We usually approached through video assisted thoracoscopic surgery that used a mini-thoracotomy and two ports. The divided interlober fissures and the small pleural defects causing minor air leak were covered with bioabsorbable sheet and/or fibrin glue. The patients with pulmonary air leak lasting until postoperative day 7 underwent pleurodesis. We retrospectively analyzed the perioperative variables in the two groups of the patients with PAL or without PAL. All results were expressed as mean ± standard error (patients with PAL vs patients without PAL). P-value <0.05 was considered statistically significant. **Results:** PAL occurred in 17 patients (12.7%), lasting an average of 8.9 days. The patients were 16 men and 1 woman with a mean age of 70.3 years old (58-79 years old). All patients underwent pleurodesis with successful closure of air leak and no patients required re-thoracotomy. Univariate analysis demonstrated significant independent predictors of PAL; a male predominance (94 vs 57% ;p=0.004), a high Brinkman index (960±580 vs 490±590; p=0.003), a preoperative low serum albumin level (4.0±0.7 vs 4.3±0.3 g/dl; p=0.003), and a long operative time (230±84 vs 184±53 min; p=0.045). A tendency toward a longer stapler length used for the interlober fissure division was also shown in the patient with PAL (109±61 vs 77±68 mm; p=0.064). PAL was not influenced by age, BMI, preoperative serum total protein level, preoperative hemoglobin, preoperative total lymphocyte count, %VC, FEV1.0%, resected lobe, and pleural adhesions. **Conclusion:** We report that a male, a long smoking history, a preoperative low albumin level, and a long operative time increased the risk of air leak lasting more than 7 days following lobectomy for primary lung cancer. Pleural adhesion, which had been reported to be a risk factor of PAL, was not related with PAL. Our analysis suggests that, for the sake of preventing PAL, we should pay attention to the preoperative nutritional status as well as well as surgical techniques, such as interlober fissure division in the cases that need multiple stapling to complete fissures.
Keywords: pulmonary air leak, lung cancer, Surgery, complication

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-010 Tumor Recurrence of the Chest Wall after Percutaneous Hook Wire Localization Hee Jong Baek[1], Jongheon Park[2], Du Hwan Choe[2], Hyungjun Yoo[2], Jae Soo Koh[2], Cheol Hyeon Kim[2], Im Il Na[2], Sung Hyun Yang[2] [1]*Thoracic Surgery, Korea Cancer Center Hospital, Seoul/Korea,* [2]*Korea Cancer Center Hospital, Seoul/Korea*

Background: Increasingly, localization of small lung nodule (solid or ground glass) is needed for thoracoscopic resection of accurate diagnostic and/or curative intent. Hook wire implantation is one of important localization techniques. Meanwhile, tumor recurrence in the chest wall of the percutaneous FNA tract is well known in thoracic malignancy, particularly lung cancer. **Methods:** We report the case of a 64-year-old-man with tumor recurrence of the chest wall. Eight months earlier, he underwent hook wire-guided thoracoscopic resection of RUL nodule and further anterior segmentectomy because of intraoperative diagnosis of NSCLC (squamous cell carcinoma, pT1aN0M0 IA). **Results:** Location of the chest wall tumor was coincident with the hook wire tract. The tumor was resected en-bloc, and reported as a metastatic squamous cell carcinoma.





Conclusion: To reduce the risk of the tumor recurrence related with localization techniques, thoracic surgeons had better know very well the topographical anatomy of lung and avoid an unnecessary localization technique, and the wire is recommended to be withdrawn through the VATS port rather than percutaneously. This is the first report of tumor recurrence related with hook wire localization in the PubMed search. **Keywords:** lung cancer, tumor recurrence, hook wire localization

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-011 Evaluation of a New Chest Tube Management Using Digital Air Leak Monitoring after Lung Resection Koichi Yoshida, Yasufumi Kato, Yoshihisa Shimada, Keishi Otani, Junichi Maeda, Masaru Hagiwara, Masatoshi Kakihana, Naohiro Kajiwara, Tatsuo Ohira, Norihiko Ikeda *Thoracic Surgery, Tokyo Medical University Hospital, Tokyo/ Japan*

Background: The use of digital drainage systems after thoracic surgery is becoming accepted as a safe method. The aim of this study was to assess the effectiveness of the digital drainage system versus traditional devices on chest tube removal and air leak duration after lung resection. We report the management of a digital drainage system in patients undergoing lung resection. **Methods:** This study is retrospective study of patients undergoing anatomical lung resection (segmentectomy, lobectomy, sleeve lobectomy, or bilobectomy).145 patients who underwent lung resections for lung cancer were evaluated. Chest tubes were removed when an air leak was not evident anymore and the drained fluid was less than 200 mL/day. **Results:** These series includes 140 lobectomies, 2 sleeve lobectomies, 1 bilobectomy and 2 anatomical segmentectomies. Patients who use digital drainage system had a significantly shorter air leak duration (0.9 versus 1.7 days; p=0.037), no significance of duration of chest tube placement (4.4 versus 5.5 days; p=0.112) and no significance of chest tube placement after the air leakage disappearance (3.5 versus 3.8 days; p=0.71). **Conclusion:** Patients managed with digital drainage system experienced a shorter duration of air leak compared with those managed with traditional devices. Digital devices appear to be safe and effective and may prove to be a useful tool in the management of lung resection. **Keywords:** digital drainage system, lung resection, Surgery, lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-012 Post-Surgical Recurrence of cN0-1 and pN2 Non-Small-Cell Lung Cancer in Postoperative Radiotherapy Candidates Haruchika Yamamoto[1], Yuji Hirami[1], Kanmei Rai[2], Ken Sato[2], Keiichi Fujiwara[2], Takuo Shibayama[2], Toshirou Yonei[2], Toshio Sato[2], Tomohiro Toji[3], Yoko Shinnou[3], Akio Andou[1] [1]*Thoracic Surgery, National Hospital Organaization Okayama Medical Center, Okayama/Japan,* [2]*Respiratory Medicine, National Hospital Organaization Okayama Medical Center, Okayama/Japan,* [3]*Pathology, National Hospital Organaization Okayama Medical Center, Okayama/Japan*

Background: Radiotherapy after initial surgery significantly improves outcomes in patients with pathological N2 non-small–cell lung cancer (NSCLC). Here, we aimed to identify best candidates for postoperative radiotherapy among patients with local recurrence. **Methods:** Among patients who underwent complete resections for NSCLC between August 2007 and December 2011 in our hospital, we enrolled all 21 patients with clinical N0–1 and pathological N2 NSCLC in this study. We assessed their age, sex, tumor size, histology, differentiation, lymphatic permeation, vessel invasion, pathological N2 location, pathological N2 number, and adjuvant chemotherapy, and classified them as the local recurrence group (recurrences limited to lymph nodes up to N3 or adjacent to the surgical margin), the distant recurrence group (in whom distant recurrence occurred within 6 months after local recurrence) and the no-recurrence group. Relationships between these clinical parameters and recurrence patterns (local or distant) were statistically assessed by Fisher's exact test. **Results:** All 21 patients underwent lobectomies and systematic mediastinal nodal dissections that included upper mediastinal nodes and subcarinal nodes. Postoperatively, 17 patients underwent chemotherapy and none underwent radiotherapy. Recurrence was seen in 15 patients: 5 local and 10 distant recurrences. Histologically, squamous cell carcinomas (SCC) were significantly more common in the local recurrence group (P=0.0358) at 3 SCC and 2 adenocarcinomas (AD), compared with the distant recurrence group: 0 SCC and 10 AD; and the no-recurrence group: 2 SCC and 4 AD. No other clinical factors were significantly associated with recurrence. Notably, vessel invasion was seen in 80% of the local recurrence group, 90% of the distant recurrence group, and 17% of the no-recurrence group. **Conclusion:** Among patients with clinical N0 or N1 and pathological N2 NSCLC, postoperative radiotherapy was most suited to those whose pathology showed SCC. **Keywords:** pN2, postoperative radiotherapy, recurrence

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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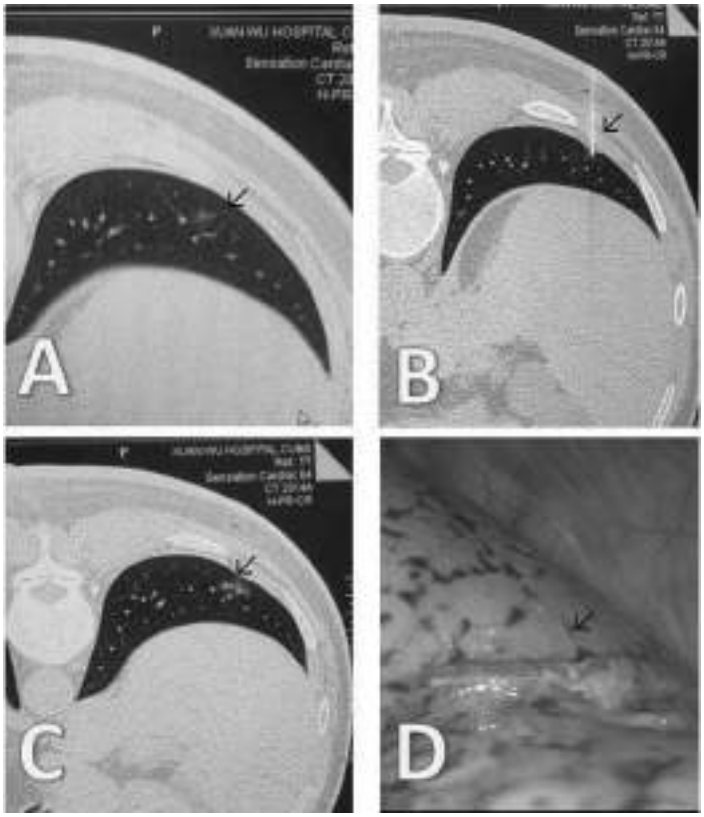
P3.02-013 Preoperative CT-Guided Percutaneous Localization of GGO with PA Injection Hu Mu *Thoracic Surgery Department, Xuanwu Hospital Capital Mediacl University, Beijing/China*

Background: Localization of ground glass nodule is a difficult challenge for thoracic surgeons, especially for those GGOs less than 10 mm in diameter. In this study we implant a new method for Preoperative localization of ground glass pulmonary opacity (GGO). **Methods:** From October 2013 to December 2014, CT-guided percutaneous Polylactic acid injection localizations were performed for 5 pulmonary nodules in 5 patients (2 men and 3 women; mean age, 59.8 years; range, 54-65 years).



Results: The injection was feasible in all patients and the localization effect was excellent, with total procedure duration 12.6 minutes (range; 10-15), Volume of Polylactic acid injected 0.38ml (Table 2). The wedge resections were easily and successfully performed in 5 cases, the cutting margin was no less than 2cm from lesion. **Conclusion:** This technique will be promising for GGO location in facilitating thoracoscopic surgery for wedge resection. **Keywords:** percutaneous localization, glass pulmonary opacity, Preoperative, Polylactic acid injection

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-014 COPD Being Misdiagnosed in Lung Cancer Patients with Thoracic Operation Guifang Wang[1], Pang Shuai[2] [1]*Department of Pulmonary Diseases, Huashan Hospital, Shanghai/China,* [2]*Department of Pulmonary Diseases, Changzheng Hospital, Shanghai/China*

Background: Chronic obstructive pulmonary disease (COPD) is a risk factor and important coexisting disease for lung cancer; at the same time, coexisting COPD owes unfavorable effect on management of lung cancer. However, the current status of management of COPD in lung cancer patients with operable sites is not fully described. This study addressed this issue in a general teaching hospital in China. **Methods:** All patients with lung cancer underwent surgery were collected retrospectively from Jan. 2002 to Dec. 2008. Medical records were reviewed about clinical information, pathological records, lung functions, etc., so as to analysis comorbidity rate about COPD and characters. The definition of COPD was according the spirometric criteria of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) document. The diagnostic rate (COPD recorded as a discharge diagnosis/spirometry-defined percentage) and conformity to GOLD treatment guidelines were investigated. The factors influencing diagnosis were analyzed. **Results:** Among all 437 undergone surgery patients aged older than 40 years old, 94 patients were diagnosed COPD, the prevalence of COPD was 21.36%(41 as GOLD 1, 52 as GOLD 2, and 1 as GOLD 3)。Among them, 89.36% was male, with average age being 63.3 years old. Only 9 patients were diagnosed as COPD, the rate of misdiagnosis was 90.4% and all of them did not receive pulmonary function test. 71.3% of those patients with COPD had smoke history; average smoke intensity was 26.7 pack-year. All surgery of pathological staging were classified as followed according to the standards of the Union International Contre le Cancer (UICC): Ⅰstage (A+B : 38+119); Ⅱ(A+B : 14+83); Ⅲ(A+B : 100+32); IV: 31; No specific: 20 cases. And patients complicated with COPD presented stages as followed: Ⅰstages (A+B : 6+23)、Ⅱ(B : 21); Ⅲ(A+B : 33+7); IV: 1; No specific: 3 cases. The rate of lung cancer complicated with COPD was 24.8%, 21.6%, 30.3% respectively. **Conclusion:** Patients of lung cancer undergone surgery have high risk morbidity of COPD. To improve the result of peri-operation period management, COPD should be pay attention to treat for these patients. **Keywords:** lung cancer, complication, copd

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-015 Impact of a Lung Multidisciplinary Team Meeting Casey Lo, Sean Galvin, Prakash Balakrishnan *Cardiothoracic Surgery, Wellington Regional Hospital, Wellington/New Zealand*

Background: Multidisciplinary team meetings (MDM) have become the standard of practice across a variety of medical disciplines. In particular, MDMs have found utility in the management of complex diseases requiring multi-modal treatment such as cancer. Advancements in information sharing technology have extended the reach of MDMs to improve care in previously remote and underserved areas. Lung cancer management is now largely directed through MDMs. However, MDMs are, by their very nature, resource intensive. In a world of increasing accountability for the distribution of limited resources, a review of the evidence for benefit of MDMs, as well as the different strategies employed in running a successful MDM, is necessary to ensure efficient provision of this care. **Methods:** A review of the existing peer-reviewed literature on MDM was conducted on Pubmed, using the broad search term of "multidisciplinary team meeting." Existing reviews and original research were included, while non-English studies and letters were excluded. **Results:** Introduction of MDMs have been attributed to a variety of positive outcomes in the management of multiple oncological diseases. While there are a handful of studies questioning the cost-benefit of MDM without adequate patient selection in colorectal cancers, the evidence for improving management in most cancers (including lung cancer) is strong. An additional benefit is the increased reach of clinical trials, with MDMs being demonstrated to improve subscription rates. However, while lung MDMs have been demonstrated to make significant improvements to the overall care of a lung cancer patient, the evidence for improved survival remains limited. The limited impact of lung MDM to overall survival may be at least partially attributable to the late-presenting nature of the disease. This may be exacerbated by geographical limitations of some healthcare networks. However, with improvements in health informatics and telemedicine, standardising early care across a vast region has been shown to be possible and improve outcomes in other cancers. **Conclusion:** While it is clear that disease management is improved with the introduction of lung MDM, further study is needed to optimise its efficacy and define its impact on survival. **Keywords:** MDM, multidisciplinary, outcomes, survival

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-016 How to Manage for Unexpected Bleeding During Thoracoscopic Anatomical Pulmonary Resection Takuro Miyazaki, Naoya Yamasaki, Tomoshi Tsuchiya, Keitaro Matsumoto, Takeshi Nagayasu *Surgical Oncology, Nagasaki Graduate School of Medicine, Nagasaki/Japan*

Background: The number of thoracoscopic pulmonary resection has been increasing due to the less invasiveness and development of endoscopic instruments and perioperative management of the patients. However, the intraoperative unexpected bleeding cases which required emergent conversion to thoracotomy were gradually reported. The aim of this retrospective study was to review our experience, management, and the outcome of unexpected bleeding during thoracoscopic surgery. **Methods:** All patients who underwent thoracoscopic anatomical pulmonary resection for primary lung cancer were analysed. Hemostatic procedures with angiorrhaphy and/or using the sealant were defined as intraoperative unexpected bleeding in this study. The location, cause, management of injured vessels, and perioperative outcome, including blood loss, hospital stay, the rate of morbidity and mortality were investigated to compare those without vessel injured. **Results:** From 2007 to 2014, a total of 241 thoracoscopic anatomical pulmonary resection was performed. 20 (8.3%) cases were required hemostatic procedures with angiorrhaphy and/or using the sealant. 15 (75%) cases of 20 were converted to thoracotomy. Injured vessels were pulmonary artery (n=13), vein (n=3), azygous vein (n=3), and superior vena cava (n=1), respectively. In pulmonary artery, the injury was seen in first branch (n=5) and small branches to right upper lobe (n=5). The main causes of injured vessels were related to the technical problems of energy devices and staplers. 16 (80%) cases were direct suture, ligation or division of injured vessels, and 3 cases were successfully controlled by TachoSil without converted to thoracotomy. Blood loss of 20 cases ranged from 150-2160 (median, 500) ml. 6 (30%) were administered with blood transfusion. Perioperative 5 comorbidities were identified in 4 patients, consisted of prolonged air leak in 2 patients and atrial fibrillation, transient recurrent laryngeal nerve palsy, and chylothorax in each patient. No mortality was identified in this study. The difference between vessel injured and non-injured patients in operation time (285 vs 235 minutes, average, p=0.003) and blood loss (804 vs 121 ml, average, p<0.001) were significant, but perioperative comorbidities including respiratory and cardiovascular complications and the duration of chest tube insertion (4.5 vs 3.5 days, average, p=0.20) and postoperative hospital stay (12.7 days vs 11.0 days, average, p=0.08) were not significant. **Conclusion:** The frequency of unexpected bleeding in this study was relatively high, but the management and the outcome of patients in this study were feasible in terms of safety. TachoSil is a useful sealant to be used next step for bleeding. For surgeons, it should be establish algorithms for this catastrophic intraoperative complication during thoracoscopic pulmonary resection. **Keywords:** Video-assisted thoracoscopic surgery, lung cancer, bleeding, pulmonary artery

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-017 Preoperative Bronchoscopy in Patients with Persistent Ground-Glass Nodule Byung Woo Jhun, Sang-Won Um, Hojoong Kim, Jhingook Kim, Kyung Soo Lee, Joungho Han *Samsung Medical Center, Seoul/Korea*

Background: There are no accurate data on the diagnostic value of preoperative flexible bronchoscopy (FB) for persistent ground-glass nodule (GGN) of the lung. We evaluated the value of preoperative FB in patients with suspected GGN-type lung cancer. **Methods:** We retrospectively searched a database for subjects who had 'ground-glass opacity', 'non-solid nodule', 'part-solid nodule', or 'sub-solid nodule' on chest computed tomography reports between February 2004 and March 2012. Patients who had infiltrative ground-glass opacity lesions, mediastinal lymphadenopathy, or pleural effusion, focal ground-glass opacity lesions >3 cm, and were lost to follow-up were excluded. We assessed the diagnostic value of preoperative FB in patients with persistent GGNs who underwent surgical resection. **Results:** In total, 296 GGNs were evaluated by FB in 264 patients with persistent GGNs who underwent preoperative FB and surgical resection. The median size of the GGNs was 18 mm; 135 (46%) were pure GGN and 161 (54%) were part-solid GGN. No visible tumor or unsuspected endobronchial metastasis was identified by preoperative FB. Only 3 (1%, 3/208) GGNs were identified preoperatively as malignant by bronchial washing cytology; all were part-solid GGNs. No other etiology was identified by FB. Of the GGNs, 271 (91%) were subsequently confirmed as malignant and 25 (9%) were confirmed as benign at surgical resection. Consequently, the overall diagnostic sensitivity and negative predictive value of preoperative FB on a per-nodule basis was 1% (3/271) and 8% (25/293), respectively. The preoperative FB did not change the surgical strategy. **Conclusion:**Preoperative FB did not add much to the evaluation of persistent GGNs of the lung. Routine preoperative FB may have limited value in surgical candidates, especially in patients with small persistent pure GGNs. **Keywords:** lung cancer, ground-glass, nodule, bronchoscopy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-018 Factors Associated with Preserved Pulmonary Function in Non-Small Cell Lung Cancer Patients after Video-Assisted Thoracic Surgery Choon-Taek Lee, Se Joong Kim, Yeon Joo Lee, Jong Sun Park, Young-Jae Cho, Ho Il Yoon, Jae Ho Lee *Internal Medicine, Seoul National University Bundang Hospital, Seongnam/Korea*

Background: Some non-small cell lung cancer (NSCLC) patients showed preserved pulmonary function after surgery. Video-assisted thoracic surgery (VATS) is currently widely performed and well known to preserve pulmonary function compared to open thoracotomy. However, it is unknown which factors are associated with the preservation of pulmonary function after VATS in NSCLC patients. **Methods:** Three hundred and fifty one patients with NSCLC who underwent VATS were enrolled. Pulmonary function tests were performed preoperatively and at 12 months postoperatively. Patients who showed preserved forced expiratory volume in 1 second (FEV_1) and diffusing capacity of carbon monoxide (DLCO) were compared with patients who did not. **Results:** FEV_1 was preserved after VATS in 65 (18.5 %) patients. They were significantly related to undertake VATS sublobar resection (P<0.001) and resect at right upper lobe (RUL) or right middle lobe (RML) (P<0.05) in multivariable analysis. DLCO showed preservation in 95 (27.1%) patients. VATS sublobar resection (P=0.005), lower baseline DLCO (P<0.001) and RUL or RML resection (P<0.05) were significantly associated with DLCO preservation in multivariable analysis. **Conclusion:** For the preservation of pulmonary function after NSCLC surgery, VATS sublobar resection was superior to VATS lobectomy and the surgical location of RUL or RML was superior to other sites. **Keywords:** VATS, Pulmonary Function, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-019 Surgery in Elderly Patients (> 70 Years or Older) with Non-Small Lung Cancer (NSCLC). Impact of Adjuvant Chemotherapy Hirsh Koyi[1], Gunnar Hillerdal[2], Karl Gustav Kölbeck[2], Olov Andersson[2], Per Bergman[3], Lotta Orre[3], Per Liv[4], Eva Brandén[1] [1]*Department of Respiratory Medicine, Gävle Hospital, Gävle/ Sweden,* [2]*Deartment of Respiratory Medicine, Karolinska University Hospital, Stockholm/ Sweden,* [3]*Deprtment of Thoracic Surgery, Karolinska University Hopsital, Stockholm/ Sweden,*[4]*Centre for Research and Development, Uppsala University/County Council of Gävleborg, Gävle/Sweden*

Background: Surgery remains the cornerstone of therapy for medically operable patients with early stage NSCLC. Differences in the frequency of surgery for patients with respect to their age, sex and socioeconomic deprivation have been described. Older patients have been found to be less likely to undergo surgery compared with younger patients even when they have similar performance status. Several randomized trials and meta-analyses have shown that adjuvant chemotherapy after resection of stages II–IIIA NSCLC improves survival. **Methods:** The medical records of all 164 patients ≥70 years, who underwent surgery for NSCLC from 2003 to 2009 at our department, were reviewed retrospectively. **Results:** One-hundred twenty-six given no adjuvant therapy. Eigthy-seven (52.4%) were male. Median mean and range of age male patients was 75.0, 74.8 and 70-85 years, while in females, these figures were 74.0, 75.5 and 70-84 years. Eighty-one (94.2%) of the males and 65 (82.3%) of the females were smoker/former-smoker. In both sexes 99% had performance status 0-1. Eighty-one (93.1%) of male patients and 71 (89.9%) of the females were stage I-II. Adenocarcinoma was the common histology in both sexes (55% of the males and 67.1% of the females). Squamous cell carcinoma came in second place, 31% respectively 20%. Lobectomi performed in 61 (84.1%) of the male patients and 62 (86.2%) female patients, left pneumonectomy in 6 (7.3%) male patients and 5 (6.9%) in female patients, right pneumonectomy in 1(1.4%) female patient. One-hundred twenty-six (77%) did not receive adjuvant therapy, mainly because of age. Median overall survival among all was 7.2 years, in the non-adjuvant group was 6.7 years and 7.6 years in the adjuvant group (p=0.5712). **Conclusion:** This single-institution series demonstrates that surgical intervention for appropriately selected elderly patients with NSCLC results in improved overall survival. Surgery should, therefore, be strongly considered for select patients ≥ 70 years of age with stage I/II and select stage IIIA NSCLC who have adequate pulmonary reserve. **Keywords:** lung cancer, elderly, Surgery, adjuvant chemotherapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-020 What Factors Affect Postoperative Respiratory Function in the Patients Performed Sleeve Lobectomy Shunki Hirayama, Kazuya Takamochi, Shiaki Oh, Kenji Suzuki *Department of General Thoracic Surgery, Juntendo University School of Medicine, Tokyo/Japan*

Background: Prediction of postoperative forced expiratory volume in 1 second (FEV1.0) is known as the basis for surgical indications of lung resection. The 0.8L or less estimated postoperative FEV1.0 has been reported an increase in surgery related deaths. In fact, there are some cases that the postoperative FEV1.0 is less than prediction of postoperative FEV1.0. The postoperative respiratory function have been reported in segmentectomy and lobectomy, but little is known in sleeve lobectomy. **Methods:** Between January 2008 and October 2014, 37 patients underwent sleeve lobectomy and evaluated respiratory function tests of preoperative and passing more than six months after surgery at the Juntendo university, Tokyo, Japan. We defined postoperative FEV1.0 / prediction of postoperative FEV1.0 ratio as postoperative FEV1.0 ratio. The patients were divided by postoperative FEV1.0 ratio into the 16 patients who evaluated postoperative FEV1.0 ratio < 1 and the 21 patients who postoperative FEV1.0 ratio ≧ 1. We investigated clinic-pathological features, postoperative complications and predictive factors in postoperative reduction of FEV1.0. **Results:** In the group of postoperative FEV1.0 ratio < 1, the median age was 63 years old (range, 35-77 years), 14 cases (88%) were male, the median postoperative FEV1.0 was 2.05L (range, 0.99-2.54) and the median prediction of postoperative FEV1.0 was 1.82L (range, 0.97-2.23). The group of postoperative FEV1.0 ratio < 1 had marginally more phrenic nerve resection (19%) and blood transfusion (50%) than the group of postoperative FEV1.0 ratio ≧ 1 (p=0.077 and p=0.072). There was no difference in the incidence of morbidity between both groups. The phrenic nerve resection was marginally risk factors of postoperative reduction of FEV1.0 in univariate analysis (p =0.053). The phrenic nerve resection and right side were risk factors of postoperative reduction of FEV1.0 in multivariate analysis (p =0.026 and p =0.048). **Conclusion:** Right side and phrenic nerve resection were independent factors to predict the postoperative FEV1.0 falls below postoperative prediction FEV1.0. **Keywords:** FEV1.0, sleeve lobectomy, phrenic nerve resection

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
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P3.02-021 Lung Cancer Surgery: A 30 Years Monocentric Experience in Tunisia Tarek Kilani[1], Sadok Boudaya[1], Adel Marghli[1], Hazem Zribi[1], Sarra Zairi[1], Tahar Mestiri[1], Faouzi Mezni[2], Hammouda Boussen[3] [1]*Thoracic and Cardiovascular Surgery, Abderrahmane Mami Hospital, Ariana/Tunisia,* [2]*Pathology, Abderrahmane Mami Hospital, Ariana/Tunisia,* [3]*Medical Oncolog, Abderrahmane Mami Hospital, Ariana/Tunisia*

Background: The results of lung cancer surgical treatment depend on several factors inherent to the tumour, the patient and the socio-economic context in which the disease is managed. Few studies have described the results of surgery for lung cancer in emerging countries, particularly in Africa. The objective of this study was to report a large monocentric experience of a North African country. **Methods:** The results of lung cancer surgical treatment depend on several factors inherent to the tumour, the patient and the socio-economic context in which the disease is managed. Few studies have described the results of surgery for lung cancer in emerging countries, particularly in Africa. The objective of this study was to report a large monocentric experience of a North African country. **Results:** There were 1485 males and 196 females (sex ratio 7.57) with a mean age of 58 (range 10-91). Clinical findings were dominated by thoracic symptoms and 176 (10.4%) were asymptomatic. Imaging findings showed a peripheral mass in 883 cases (52.5%). The mean tumour size was 5.3 cm (range, 1 – 20 cm). 48 patients received induction therapy (this treatment was not prescribed before 2009). Lobectomy or bilobectomy was performed in 1036 patients (61.6%) and pneumonectomy in 448 patients (26.6%), thoracotomy was exploratory in 153 cases (9.1%), the rate of exploratory thoracotomy has fallen at 4.5% in the last 10 years (2003 to 2012). The histology diagnoses were: squamous cell carcinoma (n=693), adenocarcinoma (n=622), carcinoid tumour (n=135). Different stages were: IA (n=167), IB (n=523), IIA (n=56), IIB (n=393), IIIA (n=244), IIIB (n=188) and IV (n=109). There were 4 operative deaths. 69 died within 1 month of surgical complications. Post operative course was uneventful in 1203 patients (71.5%) and the most frequent post operative complication was persistent air leak. Post operative mortality was 4.3% (within 30 days PO), 3.47% for lobectomies and 6.25% for pneumonectomy. Adjuvant therapy was performed in 157 patients. The median survival time was 45 months with a maximum of 276 months. The overall 5-year survival rate was at 30% and it was at 67%, 41%, 44%, 24%, 17%, 3% and 13% respectively for stages IA, IB, IIA, IIB, IIIA, IIIB and IV. Survival was influenced by sex; age over 70 years, tumour size, nodal status, tumour stage and surgical procedure. By cons, post operative radiotherapy and neoadjuvant chemotherapy did not significantly improve the prognosis of our patients. **Conclusion:** Our 30 years experience initiated in 1985 of surgery for lung cancer demonstrated that major thoracic surgery is feasible with good early results and low mortality and morbidity rates. Survival rates are lower than those of the world literature; this may be related to the more advanced stages of our series and the lack to a complete assessment of the patients: number of patients did not have CTscan in the beginning of the series, and nowadays we don't yet have PET scan in our country. **Keywords:** survival, lung cancer surgery, emerging country, results

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-022 The Digital Monitoring of Postoperative Air Leak Patterns and Air Leak Flow Is Useful for Predicting Prolonged Air Leak after Pulmonary Resection Kazuya Takamochi[1], Kota Imashimizu[1], Tatsuo Maeyashiki[2], Mikiko Suzuki[2], Takuya Ueda[2], Kenji Suzuki[1], Shiaki Oh[1] [1]*Juntendo University School of Medicine, Tokyo/ Japan,* [2]*General Thoracic Surgery, Juntendo University School of Medicine, Tokyo/Japan*

Background: The presence of prolonged air leak (PAL) after pulmonary resection sometimes results in serious complications, such as empyema. Therefore, early prediction and intervention for PAL should be performed. ThopazTM is a digital monitoring thoracic drainage system which enables the objective evaluation of air leak. This study aimed to establish the diagnostic criteria for the early prediction of PAL using the ThopazTM system. **Methods:** The postoperative data of 150 patients who underwent pulmonary resection and for whom the digital monitoring of thoracic drainage was performed using ThopazTM between December 2013 and January 2015 were prospectively collected. When the air flow level was < 20 mL/min for > 12 hours, the chest tube was removed. We examined the postoperative data, including the chest X-ray findings, the presence of postoperative complications, the duration of air leak, the duration of chest tube placement, the patterns of air leak until 72 hours after operation and the level of peak air flow until 24 hours after operation as determined by ThopazTM. The patterns of air leak were defined as Types A-E (A: No air leak was observed until the removal of the chest tube; B: Air leak flow gradually decreased; C: Although no air leak was observed immediately after operation, air leak occurred postoperatively; D: The repeated exacerbation and remission of air leak was observed; E: Air leak was observed without a trend toward improvement). **Results:** There were 100 men and 50 women; 99 smokers and 51 never-smokers; and 119 cases of lung cancer and 31 cases of other diseases. Their surgeries included 23 wedge resections, 24 segmentectomies and 103 lobectomies. Air leak at the time of the sealing test during the operation was observed in 82 (55%) patients. Air leak was observed in 31 (21%) patients, in whom the mean (± SD) duration of air leak was 3.9 (± 3.7) days. The mean (± SD) duration of chest tube placement was 3.2 (± 1.9) days in the whole study population (n = 150) and 5.2 (± 2.7) days in the 31patients with postoperative air leak. On chest X-ray films, 12 cases of subcutaneous emphysema and 4 cases of atelectasis were observed postoperatively. No complications associated with ThopazTM developed. PAL > 4 days was observed in 10 (6.7%) patients. The frequencies of PAL according to the air leak patterns were 0% (0/119) in type A, 23% (3/13) in type B, 20% (2/10) in type C, 50% (2/4) in type D and 75% (3/4) in type E. The frequencies of PAL according to the peak air flow were 11% (2/18) in < 100 ml/min, 62% (8/13) in ≥ 100 ml/min, 60% (6/10) in ≥ 200 ml/min, 83% (5/6) in ≥ 400 ml/min and 80% (4/5) in ≥ 500ml/min. **Conclusion:** The

risk of PAL was higher in patients showing type D and E air leak patterns, and a peak air flow of ≥ 400 ml/min. The results indicate that PAL after pulmonary resection may be predicted by air leak patterns and peak air flow using the ThopazTM system. **Keywords:** pulmonary resection, chest drainage, air leak, lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-023 Surgical Outcomes of Lung Cancer Combined With Interstitial Pneumonia. - Single Institutional Report - Daisuke Taniguchi[1], Naoya Yamasaki[2], Tomoshi Tsuchiya[2], Keitaro Matsumoto[2], Takuro Miyazaki[2], Takeshi Nagayasu[3]
[1]*Department of Surgical Oncology, Nagasaki University Graduate School of Medicine, Sakamoto/Japan,* [2]*Surgical Oncology, Nagasaki Graduate School of Medicine, Nagasaki/Japan,* [3]*Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Science, Nagasaki, Nagasaki/Japan*

Background: Several studies have reported that acute exacervation (AE) of idiopathic interstitial pneumonia (IIP) can occur after lung resection for patients with non-small cell lung cancer (NSCLC), though the strategy of the perioperative management is controversial. **Methods:** We examined our institutional data about the lung cancer patients from June 1994 through October 2013 at Nagasaki University Hospital in a retrospective manner. **Results:** A total of patients who underwent lung resection for NSCLC(1701 cases) was investigated, 58 had IIP, for an incidence rate of 3.8%. The majority of patients were men (52 cases, 89.6%) and ex- or current smokers (53 cases, 91.3%), and the average of Packs per year was 54.1 (range 30-150). Squamous cell carcinoma was the most common type of lung cancer (23 cases, 39.6%), and the second common type was adenocarcinoma (22 cases, 37.9%). Surgical procedure was wedge resection in 12 cases, segmentectomy in 6 cases, lobectomy in 39 cases, pneumonectomy in 1 case, respectively. 6 cases(10.3%) had AE of IIP following lung resection, 3 cases(50%) of those patient died in the hospital. The univariate analysis and multivariate analysis were carried out to identify possible risk factors for AE. The univariate analysis identified LDH and bleeding amount. Multivariate analysis further identified only LDH. As a treatment for AE, we performed steroid pulse therapy and administration of Neutrophil elastase inhibitor. In some cases that no effect was given by such treatments, we performed direct hemoperfusion with a polymyxin B immobilized fiber column and administered immunosuppressant. **Conclusion:** Patients with lung cancer combined with IIP increases the risk of chest surgery, and the prognosis of them is poor. Because the prediction of AE is often difficult, surgery and perioperative management should be done very carefully. **Keywords:** non-small cell lung cancer, Interstitial pneumonia, lung resection, acute exacervation

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-024 Lobectomy versus Stereotactic Ablative Radiotherapy (SABR) for Stage I Non Small Cell Lung Cancer (NSCLC) in 182 Patients Vieri Scotti[1], Gabriele Simontacchi[1], Ilaria Francesca Furfaro[1], Daniele Scartoni[1], Alessandro Gonfiotti[2], Domenico Viggiano[2], Carla De Luca Cardillo[1], Katia Ferrari[3], Benedetta Agresti[1], Giacomo Zei[1], Marco Perna[1], Paolo Bastiani[4], Alessio Bruni[5], Luca Voltolini[2], Lorenzo Livi[1] [1]*Oncology, Radiation Oncology Unit, Florence/Italy,* [2]*Thoracic Surgery Unit, Cardiovascular Department, Florence/Italy,* [3]*2Nd Pneumology Unit, Geriatric Department, Florence/Italy,* [4]*Radiotherapy Unit Azienda Sanitaria Firenze, Oncology Department, Florence/Italy,* [5]*Radiotherapy Unit Aou Policlinico of Modena, Oncology and Respiratory Disease Department, Modena/Italy*

Background: Data from prospective randomized clinical trials are lacking in the comparison between lobectomy (L) and SABRT in operable patients and ongoing trials have troubles in recruiting. In inoperable patients a local control of 64-95% in retrospective and 92-98% in prospective trial is reported when BED is over 100 Gy. **Methods:** From 2003 to 2013, 182 I-IIA NSCLC patients were treated at our Institution. Clinical characteristics are summarized in *table I*; cyto-histological prove of NSCLC was available in all surgical patients and in 61/88 (69%) SABRT patients. Spirometry was available in 120/182 (66%). Response was evaluated according to RECIST criteria after primary treatment. Toxicity was graduated according to CTCAE version 4 criteria.

	RT	Surg	Total	p^
	n=**88 (%)**	n=**94 (%)**	n=**182(%)**	
Gender				
Male	70(79.5)	61(64.9)	131(72.0)	**0.032**
Female	18(20.5)	33(35.1)	51(28.0)	
Age (median)				
≤72	26(29.5)	67(71.3)	93(51.1)	**0.0001**
>72	62(70.5)	27(28.7)	89(48.9)	
Hystology				
Adenocarcinoma	36(59.0)	69(73.4)	105(67.7)	0.14
SCC	23(37.7)	24(25.5)	47(30.4)	
Large Cell Carcinoma	2(3.3)	1(1.1)	33(18.1)	
Performance Status				
0	13(14.8)	62(66.0)	75(41.2)	**0.0001**
1	45(51.1)	29(30.9)	74(40.7)	
2	30(34.1)	3(3.1)	33(18.1)	
FEV1				
<1.5	35(43.8)	7(17.5)	42(35.0)	**0.005**
>1.5	45(56.2)	33(82.5)	78(65.0)	

Results: Median follow-up time was 25 months (range: 6-110). Three local relapses (LR) were observed in L and 18 in SABRT group (p=0,0001). No difference in distant metastases was observed (19 in L vs 18 in SABRT group) (p=1-data not shown). Results of univariate survival analysis are shown in *table II*. Multivariate analysis confirmed the protective effect of L on OS and of good FEV1 (>1,5L) on DFS. A subgroup comparison of SABRT patients treated with BED>100Gy vs surgical patients showed no difference in local control (LC) (p=0,60) while OS and tumor-specific survival (TSS) remain in favor of L (p=0,001 and 0,049 respectively). Moreover, comparing surgical patients with SABRT with known histology and BED>100 Gy no difference was seen in TSS (p=0.10) nor in LC (p=0,36). No grade 3-5 toxicity was observed in both group.

	Died	% OS	p^	LR	% DFS	p^
Age (median) ≤72	26	56.1	**0.001**	10	84.3	0.50
>72	50	10		11	79.9	
Hystology Adenocarcinoma	34	37.9	0.66	9	87	0.81
SCC	22	35		3	91.2	
Large Cell Carcinoma	1	66.7		0	100	
Performance Status 0	17	59.8	**0.001**	7	87.3	0.52
1	29	19		9	79.5	
2	3	18.3		5	81	
FEV1 <1.5	27	20.4	0.14	11	86.2	**0.005**
>1.5	37	14		7	80.9	
Treatment Radiotherapy	62	4.4	**0.0001**	18	67.4	**0.0001**
Surgery	14	72.9		3	95.1	
Total	**76**	**12.2**		**21**	**82.4**	

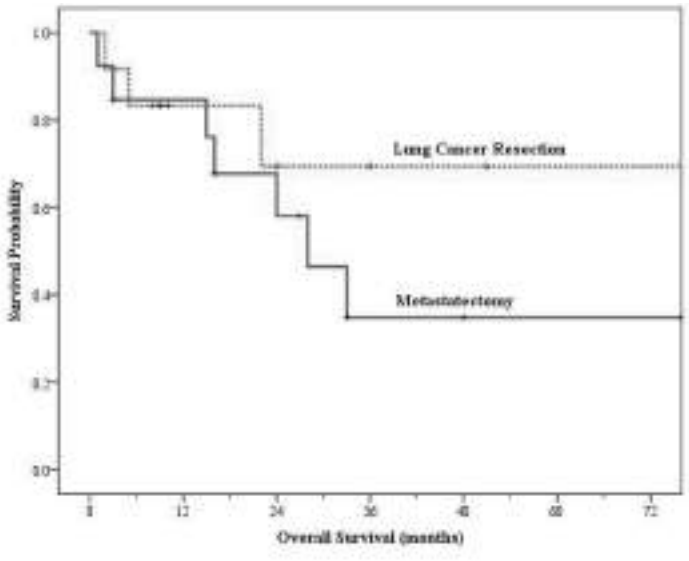
Conclusion: SABRT with adequate doses vs L in operable patients shows promising results in terms of LC and TSS with few toxicitiy. OS is mainly influenced by the selection of patients addressed to L vs SABRT. **Keywords:** biological equivalent dose (BED), lobectomy, Stereotactic ablative radiotherapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-025 Therapeutic Lung Resection in Biliopancreatic Cancer Patients Lary A. Robinson[1], Gregory Springett[2], Tawee Tanvetyanon[1], Jacques Fontaine[1], Eric M. Toloza[1], Pamela Hodul[2], Mokege Malafa[2] [1]*Thoracic Oncology, Moffitt Cancer Center, Tampa/FL/United States of America,* [2]*Gastrointestinal Oncology, Moffitt Cancer Center, Tampa/FL/United States of America*

Background: Of the major malignancies, carcinoma of the pancreas and the distal

biliary duct are the most lethal, primarily because the diagnosis is usually made at an advanced stage and the cancer is relatively resistant to therapy. Occasionally, pancreatic cancer presents as a relatively indolent disease and localized blood-borne lung metastases may be solitary and potentially resectable for therapy. As well, some lung lesions that develop may represent another disease unrelated to the pancreatic cancer and may be treated with surgical resection. Therefore we reviewed our experience with therapeutic lung resections in pancreatic cancer patients. **Methods:** We performed a retrospective, case-control study of treated pancreatic cancer patients who underwent subsequent therapeutic lung resections from 1998-2015. All clinical and pathologic data were gathered for comparison in patients undergoing pancreatic pulmonary metastasectomy and those undergoing lung resection for other diseases. Kaplan-Meier (KM) analyses of survivals were calculated. **Results:** 25 patients with treated biliopancreatic cancer underwent lung resections with curative intent. 13 patients (mean age 60.2 ± 10.7 years) had resection of isolated biliopancreatic cancer metastases. 11 patients had 12 resections of primary lung cancers (all Stage I) and 1 patient had resection of active Cryptococcus granulomas (mean age 70.8 ± 7.0 years). A smoking history was present in 77% of metastasecomy patients and 67% of lung cancer resection patients. All never-smokers with lung cancer were females. There were no surgical complications or operative mortalities. The median times from pancreatectomy to pulmonary metastasectomy was 29 months (range 0-64), and 12.5 months (range 0-108) for the lung cancer resection group. During the study period, 11/25 (44%) patients died, although only 64% of the deaths were related to pancreatic cancer recurrence. The KM median survivals after lung resection in the pulmonary metastasectomy group was 28 months (range 3-76) and 78 months (range 2-81) in the lung cancer resection group (see Figure).



Conclusion: Although biliopancreatic cancers have an overall dismal prognosis with just a 12.7 month median survival, 40% present with potentially resectable disease. The lung is the primary site of recurrence after resection of the primary biliopancreatic cancer. Based on our experience, we recommend considering pulmonary metastasectomy in highly selected patients who present with no evidence of disease elsewhere. Pulmonary resection can be done safely in this patient population. Additionally, not all new lung masses in pancreatic cancer patients are metastases, and resection should be considered, whenever feasible, for often we find a second primary lung cancer. **Keywords:** non-small cell lung cancer, biliopancreatic cancer, pulmonary metastasectomy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-026 Positive or Negative Indications for Wedge Resection of Non-Small Cell Lung Cancer Masafumi Kataoka[1], Haruyuki Kawai[2], Kazuhiko Watanabe[2], Koukichi Miyamoto[2], Izumi Togami[3], Tsuneharu Morito[3], Kotaro Yasui[3], Souichi Kojima[3], Toshinori Ohara[1] [1]*Surgery, Okayama Saiseikai General Hospital, Okyayama/Japan,* [2]*Internal Medicine, Okayama Saiseikai General Hospital, Okayama/Japan,* [3]*Radiology, Okayama Saiseikai General Hospital, Okyayama/Japan*

Background: Limited resection for non-small cell lung cancer is gaining popularity because of early detection and the increase of elderly patients. To reveal the relevant indications for wedge resection, we retrospectively investigated patients who underwent wedge resection by dividing them into positive (PW) and negative (NW) indication groups. **Methods:** Clinical N0M0 cases with tumours <1 cm or predicted lepidic pattern adenocarcinoma were labelled PW, while other wedge resection cases were labelled NW. We investigated 35 PW and 32 NW cases surgically treated at our hospital between 2002 and 2009. The mean age was 66 years in the PW group and 77 years in the NW group. All PW cases were c-stage IA, while the NW group included 21, 7, 2, and 4 cases of IA, IB, IIB, and IIIB, respectively. **Results:** The overall 5-year survival rates (OS) of the PW and NW groups were 100% and 59.4%, while the disease-specific 5-year survival rates (DS) were 100% and 82.6%, respectively. The indications for (number of) limited resections in the NW group were low respiratory function (15), other malignancies (4), cardiac disease (4), cerebral disease (3), and other (5). The OS/DS of the NW group were 57.1/85.7 for IA; 71.4/100 for IB; 0/0 for IIB; and 50/50 for IIIB. There were 9 cases of death due to other diseases. There were 6 cases of death due to lung cancer recurrence. Among the patients with c-stage I tumours, 7 died of other disease, while only 2 died of lung cancer distant metastasis recurrence (Table). Table

Death due to lung cancer	6	Death due to other diseases	9
1st recurrence site		Other malignancy	4
bone	3	Cardiovascular disease	2
pleura	2	Cerebral disease	1
brain	1	Liver failure	1
		Hemorrhagic enteritis	1

Conclusion: Wedge resection is positively indicated in PW cases. Negative wedge resection should be positively indicated in NW cases of c-stage I disease because treatment for other diseases must start as quickly as possible to maximize quality of life. **Keywords:** wedge resection, limitted resection, non-small cell lung cancer

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-027 Surgical Salvage Resection for Local Recurrence after Stereotactic Body Radiotherapy for Primary and Metastatic Lung Tumors Therezia Bokor-Billmann[1], Sonja Adebahr[2], Severin Schmid[1], Agnes Csanadi[3], Ursula Nestle[4], Bernward Passlick[1], Jussuf T. Kaifi[1] [1]*Thoracic Surgery, University of Freiburg, Freiburg/Germany,* [2]*Radiation Oncology, University of Freiburg, Freiburg/Germany,* [3]*Pathology, University of Freiburg, Freiburg/Germany,* [4]*Radiation Therapy, University Medical Center Freiburg, Freiburg/Germany*

Background: Stereotactic body radiation therapy (SBRT) is an alternative to surgery for the treatment of early stage lung cancer or solitary metastasis in high-risk individuals. The aim of the study was to identify patients that underwent surgical resection as a salvage therapy for local recurrences following SBRT. **Methods:** In a single institution prospective database patients that underwent SBRT for early-stage NSCLC or pulmonary metastatic tumors were identified over 5 years. Patients that underwent surgical salvage resection for local recurrences after SBRT were analyzed for clinicopathological data and outcome. **Results:** In 4/188 (2.1%) patients salvage surgery was performed for local recurrences after SBRT within a median period of 14.5 months. SBRT was performed with a total dosage of 35 Gy in 3 and 37.5 Gy in 1 patient. No perioperative mortality occurred after salvage resection, and complete resection was achieved in all cases. Histopathology demonstrated viable tumor cells accompanied by fibrosis and necrosis in all resected specimens. **Conclusion:** Salvage surgery should be considered in operable patients after lung SBRT for primary and metastatic tumors as viable tumor can be expected. It can be performed safely in appropriate candidates that need to be identified in a multidisciplinary setting. Further analysis of larger series could further clarify true incidence of local recurrences after SBRT and selection criteria for salvage surgery in this challenging group of patients. **Keywords:** local recurrence, non small cell lung cancer, Lung metastasis, Stereotactic body radiation

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-028 miMRST Wedge Resection Cured Aged, Cardiopulmonary Dysfunction Patients with Small Lung Cancer (≤2cm) Jun Zhang[1], Ning Chen[2], Xueshan Qiu[1] [1]*China Medical University Lung Cancer Center, The First Hospital of China Medical University, Shenyang/China,* [2]*Department of Logistic Management, College of Economics and Management, Liaoning University of Traditional Chinese Medicine, Shenyang/China*

Background: In China, lung cancer is increasing rapidly. There are more and more aged, cardiopulmonary dysfunction patients were found with peripheral small lung cancer (≤2cm); chemotherapy and radiation are usually denied because of age, cardiopulmonary dysfunction, and fear of the serious side effects of chemo-radiation; surgery was denied because they could not tolerate traditional "large-incision" posterolateral thoracotomy. Video-assisted thoracoscopic surgery (VATS) is good for them; however, most Chinese patients refuse VATS because of the high cost not covered by medical insurance. "miMRST", minimally invasive small incision, muscle- and rib-sparing thoracotomy, minimally invasive lung cancer radical surgery, was developed to help resolve these problems: helps resect the tumor, minimally invasive, not cost too much, with good prognosis, widely accepted by Chinese patients. We discussed typical cases here. **Methods:** Case1: Man, aged 80 in Nov 2007, right upper lobe suspected peripheral lung cancer 2.0cm; smoking 57 years, with years' serious chronic bronchitis, pulmonary bullae, emphysema, and diabetes mellitus, encephalatrophy; chemotherapy and radiation was denied; surgery was denied; VATS was not available then. Case2: Man, aged 68 in Oct 2007, right lower lobe suspected peripheral lung cancer or metastatic cancer 1.5cm; gastric cancer resection in 2002, lung cancer left lower lobe resection in 2006, followed by chemo-radiation; chemotherapy and radiation was denied because of sickly status, age, cardiopulmonary dysfunction, possible resistance to chemotherapy; surgery was denied because of suspected potential multi metastasis, and the heavy risk and difficulties may meet in operation, fear of single one left upper lobe could not ensure the safety of operation and anesthesia, and further resection of the lung will obviously

aggravate postoperative pulmonary dysfunction. Both patients were transferred to CMU Lung Cancer Center. "miMRST" wedge resection became the best choice for these aged, cardiopulmonary dysfunction patients with suspected peripheral small lung cancer (≤2cm). **Results:** About 10cm lateral chest incision was enough for most lung cancer resection and mediastinal lymph node dissection, with the latissimus dorsi and serratus anterior muscles were protected, no rib cut needed. Wedge resection was performed for both patients, and cutting edges of the lung were more than 2-3cm away from the tumors. No swelling lymph node was found and no dissection done. The patients recovered much better and quickly than other patients who underwent traditional "large-incision" posterolateral thoracotomy. Regular follow-up: Case 1 now alive healthily for his 8th year postoperatively, no sign of recurrence and metastasis; Case 2 lived healthily for more than 4 years, no sign of recurrence and metastasis, but died at the 5th year postoperatively due to other reason not lung cancer. **Conclusion:** miMRST, neither causes serious damage as traditional "large-incision" posterolateral thoracotomy does, nor costs too much as VATS does. miMRST wedge resection is a good choice for aged cardiopulmonary dysfunction patients with peripheral small lung cancer (≤2cm), with a good acceptable prognosis, even cure lung cancer, very suitable for lung cancer surgery in developing countries. (This study was partly supported by the Fund for Scientific Research of The First Hospital of China Medical University, No.FSFH1210). **Keywords:** lung cancer, muscle-sparing rib-sparing thoracotomy, minimally invasive lung cancer radical surgery, minimally invasive small incision

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-029 Micro- Small Lung Cancer (≤1cm) Needs Lobectomy with Systematic Lymph Node Dissection or Sublobular Limited Resection Only? Jun Zhang[1], Ning Chen[2], Xueshan Qiu[1] [1]*China Medical University Lung Cancer Center, The First Hospital of China Medical University, Shenyang/China,* [2]*Department of Logistic Management, College of Economics and Management, Liaoning University of Traditional Chinese Medicine, Shenyang/China*

Background: Lung cancer is increasing rapidly in China. More and more pulmonary ground-glass opacity (GGO) were detected, most are not malignant, but some are indeed early stage lung cancer, micro- small lung cancer (≤1cm) (mi-SLC), either adenocarcinoma in situ (AIS), or minimally invasive adenocarcinoma (MIA). Surgical resection could cure most of them, but the resection extent for mi-SLC is a dilemma. Typical cases will be discussed. **Methods:** Case 1: Woman, aged 67 in Mar 2013, left upper lobe GGO 0.8cm, not peripheral; hypertension and coronary heart disease 10 years; anti-inflammatory strategy used, GGO size increased a little one month later. Her mental stress increased greatly. Case 2: Woman, aged 59 in Nov 2013, right middle lobe pure GGO 1.0cm, peripheral; sickly status for years; anti-inflammatory strategy used, GGO size no change. Both patients were referral to China Medical University Lung Cancer Center for surgical resection, "miMRST", minimally invasive small incision, muscle- and rib-sparing thoracotomy, minimally invasive lung cancer radical surgery, was scheduled. **Results:** About 10cm lateral chest incision was enough for most lung cancer resection and mediastinal lymph node dissection, with the latissimus dorsi and serratus anterior muscles were protected, no rib cut needed. For Case 1, the lesion could not be located, left upper lobe resection was undergone as expected; frozen pathological diagnosis was AIS; swollen lymph node 3a,5,6,10,11,12 and surrounding adipose tissue were systematicly dissected. No lymph node in subcarinal and pulmonary ligament region was found. Postoperative pathology confirmed AIS, no lymph node metastasis. For Case 2, wedge resection was performed as expected; cutting edges of the lung were more than 2cm away from the tumor. The frozen pathological diagnosis was atypical adenomatous hyperplasia (AAH), cancer to be excluded by wax slide pathology. No swollen lymph node was found and no dissection done. Postoperative pathology was minimally invasive adenocarcinoma (MIA). The patients recovered much better and quickly than other patients who underwent traditional "large-incision" posterolateral thoracotomy. Regular follow-up: both patients are alive healthily, in her 3rd year postoperatively for Case 1, in her 2nd year postoperatively for Case 2; no sign of recurrence and metastasis. No adjuvant treatment used. **Conclusion:** For these micro- small lung cancer (≤1cm), wedge resection is the first choice for frozn pathological diagnosis; if the diagnosis is AAH, wedge resection should be enough; if is AIS, lobular resection, at least segment resection is to be performed; if the diagnosis is MIA or just lung cancer, thus standard lobectomy plus systematic lymph node dissection is essential. For AIS, lymph node dissection is a dilemma. For GGO not in peripheral part, if segment resection is difficult, loectomy become dilemma. But for wedge resection of AAH, it would become a bigger dilemma when the postoperative pathology become MIA. Prospective observation of more patients with long follow-up will be more helpful. (This study was partly supported by the Fund for Scientific Research of The First Hospital of China Medical University, No.FSFH1210). **Keywords:** micro- small lung cancer, GGO, AIS, MIA

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-030 Linguar-Sparing Left Upper Lobectomy for Lung Cancer in a 97 Year Old Man Henrietta Wilson, Michael Ghosh-Dastidar, Karen Harrison-Phipps *Thoracic Surgery, Guy'S Hospital, London/United Kingdom*

Background: Current trends in increased life-expectancy and lung cancer incidence have led to a growing number of elderly patients with non-small cell lung cancer. Advances in surgical techniques and perioperative care have led to improved outcomes in octogenarians undergoing pulmonary resection. There have been few reports, however, of surgical management in patients over the age of ninety years. Between 2009 and 2011 a total of 5133 new cases of lung cancer were reported in people over the age of 85 years in the UK. In view of this, clinicians will face more difficult decisions as to the management of lung cancer in elderly patients. Here we report the case of a 97 year old man with NSCLC successfully treated with anatomical pulmonary resection. To the best of our knowledge this is the oldest individual reported to have undergone this lung cancer surgery. **Methods:** A 97 year old gentleman presented with a cough and was found to have an abnormal chest x-ray. CT scan demonstrated a lesion within the apex of the left upper lobe, which was confirmed as a squamous cell carcinoma on CT guided biopsy. Further staging was carried out with a PET scan showing a T2b N0 M0 disease. At review the patient appeared to be a fit and active gentleman with a good exercise tolerance of a half mile without any shortness of breath and at least one flight of stairs. He had a past history of stroke four years ago with no significant residual neurology. He also had a history of hypertension, diabetes, raised cholesterol and chronic renal impairment. Pulmonary function tests were reasonable with an FEV1 of 1.75L (75% predicted) and an FVC of 2.5L (96% predicted). **Results:** Following counselling regarding management options and risk the patient opted for surgical resection. A left lingular-sparing upper lobectomy was performed via posterolateral thoracotomy. Lymph nodes were taken from stations 5, 7 and 10. Postoperative airleak was prolonged with drain removal on day 10. In addition, the patient developed a pseudomonas urinary tract infection which required a course of antibiotics. The postoperative course was otherwise unremarkable and he was discharged home on day 14. At follow-up in the outpatient clinic 6 weeks following surgery the patient had returned to his pre-operative exercise tolerance. **Conclusion:** Lung cancer is the leading cause of cancer death in both men and women in the UK. In the past there has been a trend towards a less aggressive approach in elderly patients. Here we present successful anatomical pulmonary resection for NSCLC in a 97 year old. A significant number of studies have demonstrated the feasibility of anatomic lung resection in carefully selected octogenarians with acceptable morbidity and mortality. Although there are only a few case reports of surgical management in patients over ninety years old it is fair to assume that similar criteria could be used for patient selection. Surgical resection remains the gold-standard of care for curative intent in early lung cancers and should not be precluded based on age alone. **Keywords:** lung cancer surgery, Nonagenarian

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-031 Patient Outcomes following Curative-Intent Lung Resection among Non-Small Cell Lung Cancer (NSCLC) Patients in China Jian Zhou[1], Eric Q. Wu[2], Fan Yang[1], Jipan Xie[3], Simeng Han[4], Xun Wang[1], Huaying Song[4], Jun Wang[1] [1]*Thoracic Surgery, Peking University People'S Hospital, Beijing/China,* [2]*Analysis Group, Inc., Boston/MA/United States of America,* [3]*Analysis Group, Inc., New York/NY/United States of America,* [4]*Analysis Group, Inc., Beijing/China*

Background: Lung resection is a common treatment for patients with non-small cell lung cancer (NSCLC), particularly those with early stage disease. This study aimed to assess patient short-term outcomes following curative-intent lung resection among patients with NSCLC. **Methods:** Data were obtained from an NSCLC surgical outcome registry, which included patients from 13 tertiary hospitals in 11 provinces in 2013 and 2014. The surgery types include thoracotomy, video-assisted thoracic surgery (VATS), conversion from thoracotomy to VATS and mini-thoracotomy under VATS. Among all patients, 1,071 were followed up for at least 6 months. Post-surgery treatment pattern and patient outcomes (surgical complication rate and rates of survival, new metastasis and recurrent at the 6-month follow-up) were described; patient outcomes were compared among different tumor stages using Fisher's exact test. **Results:** Among the 1,071 patients with ≥ 6-month follow up, the median age was 60 (range 26 to 84) years old and 68.3% were male. The most common types of cancer were adenocarcinoma (56.1%) and squamous cell carcinoma (38.3%). Based on the pathologic staging, 42.3% patients had stage I tumor; and stage II, III and IV tumor accounted for 27.5%, 27.8% and 2.4% of the patients, respectively. After surgery, 57.9% patients received further treatment: most of them received chemotherapy (78.3%), 1.2% received targeted therapy, 1.2% received radiation, 0.3% received re-operation, 7.2% received alternative medicine treatment. The overall post-surgery complication rate following surgeries was 6.0% and it did not vary significantly by stage (5.1%, 5.4%, 9.4% and 9.5% for stage I-IV, respectively; p=0.122). The overall survival rate at 6 months was 96.2% and it decreased substantially with increasing stage (98.3%, 95.4%, 92.2% and 85.7% for stage I-IV, respectively; p=0.0005). Recurrence rate was 1.5% for all patients and it was substantially higher among patients with stage IV cancer (2.2 %, 1.7%, 0.4% and 10.0% for stage I-IV, respectively; p=0.032). New metastasis occurred in 6.4% patients. Again, the rate varied significantly across different stages (4.9%, 4.2%, 10.0% and 25.0% for stage I-IV, respectively; p=0.001). **Conclusion:** Chemotherapy was the most commonly used treatment after surgery for NSCLC patients. Additionally, the NSCLC patients who underwent curative-intent lung resection surgeries had relatively high survival rate, low rates of recurrence and new metastasis at the 6-month follow up. As expected, prognosis became worse with increasing tumor stage. **Keywords:** outcome, follow up, Surgical resection, NSCLC registry

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-032 Effect of Age on Adjuvant Chemotherapy after Resection of Non-Small Cell Lung Cancer Xiaoyu Zhai, Ziping Wang *Department of Medical Oncology, Cancer Institute and Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing/China*

Background: Adjuvant chemotherapy (ACT) improves the survival for completely resected non-small cell lung cancer (NSCLC) patients. However, there are few reports to explore the effect of age on the efficacy of adjuvant chemotherapy of NSCLC after surgery. **Methods:** Patients received adjuvant chemotherapy after surgery in Cancer

Hospital, Chinese Academy of Medical Sciences from 2001-2010 were analyzed. Disease Free Survival (DFS) of the two groups of patients was compared in terms of their age. Survival analysis was performed using Kaplan–Meier estimates, log-rank tests and Cox's proportional hazards regression analysis. Propensity score matching (PSM) was used, and a survival analysis of the match data was carried out. **Results:** The data of 256 patients with stage I to stage Ⅲ NSCLC who underwent completely resection was analyzed. Those two groups,patients aged≤65 years (27~65, n=206) and patients aged>65 years (66~72, n=50) ,were compared. Figure 1 shows the baseline characteristics of the two groups of patients before and after PSM. There was no significant difference in DFS between the two groups (mDFS: 594 days vs. 554 days, P=0.951) (Figure 2), and the age was not associated with DFS in multivariable analysis (P =0.602). DFS was continually not significant difference in 40 PSM pairs (mDFS: 600 days vs. 554 days, P=0.731) (Figure 2).

Characteristic	Before PSM			After PSM		
	Age ≤65 years (n=206)	Age >65 years (n=50)	P value	Age ≤65 years (n=40)	Age >65 years (n=40)	P value
Gender, n(%)						
Male	128 (61.2%)	39 (78.0%)	0.47	32 (80.0%)	29 (72.5%)	0.439
Smoking history, n(%)						
No	98 (47.6%)	24 (48.0%)	1	19 (47.5%)	17 (42.5%)	0.82
Histology subtype, n(%)			0.458			0.442
squamous carcinoma	77 (37.4%)	12 (24.0%)		13 (32.5%)	15 (37.5%)	
adenocarcinoma	124 (60.2%)	33 (66.0%)		22 (55.0%)	25 (62.5%)	
other	5 (2.4%)	5		5	5	
Differentiation, n(%)			0.349			0.799
poorly	58 (28.2%)	12 (24%)		14 (35.0%)	10 (25.0%)	
poorly-moderately	52 (25.2%)	17 (34%)		10 (25.0%)	13 (32.5%)	
moderately	83 (40.3%)	18 (36%)		14 (35.0%)	13 (32.5%)	
moderately-well	10 (4.9%)	3 (6%)		4 (10.0%)	3 (7.5%)	
well	3 (1.4%)	0		0	0	
Lymphatic involvement stage, n(%)			0.833			0.378
N0	98 (48.3%)	9 (18.0%)		17 (42.5%)	13 (32.5%)	
N1	62 (30.0%)	22 (44.0%)		14 (35.0%)	20 (50.0%)	
N2	46 (22.3%)	19 (38.0%)		9 (22.5%)	7 (17.5%)	
Clinical stage, n(%)			0.803			0.319
I	32 (15.5%)	7 (14.0%)		6 (15.0%)	3 (7.5%)	
II	52 (25.2%)	14 (28.0%)		14 (35.0%)	17 (42.5%)	
III	122 (59.2%)	29 (58.0%)		20 (50.0%)	20 (50.0%)	
Performance status(ECOG), n(%)			0.999			0.339
0	2 (1.0%)	1 (2.0%)		2 (5.0%)	0	
1	189 (91.7%)	46 (92.0%)		36 (90.0%)	40 (100%)	
2	15 (7.3%)	3 (6.0%)		2 (5.0%)	0	
Adjuvant radiotherapy, n(%)						
No	173 (84.0%)	46 (92.0%)	0.223	36 (90.0%)	36 (90.0%)	1

PSM, propensity score matching.

Figure 1. Patients demographic characteristics and propensity score-matched characteristics between two groups.

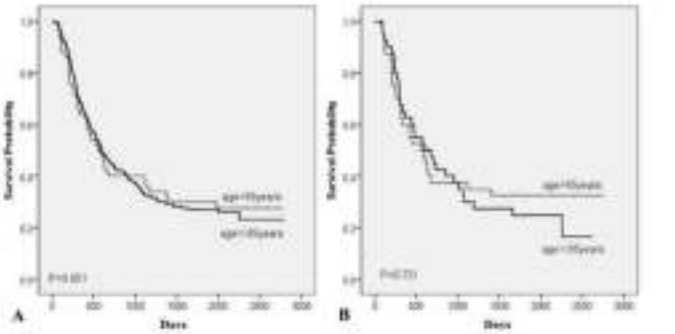


Figure 2. Kaplan-Meier plot for NSCLC disease-free survival(DFS) according to age. A. In all patients,there was no significant difference in the DFS between younger patients (age≤65 years) and older patients(age>65 years) (P=0.951). B.In propensity score-matched pairs, DFS was not significant difference between the 2 groups(P=0.731).

Conclusion: The results suggest that older patients do not appear a shorter DFS than younger. Thus, elderly patients should not be denied adjuvant chemotherapy based merely on age. The conclusion was limited by the small sample size; moreover, the number of patients between the groups was not close. Larger sample of cases should be warranted in future. **Keywords:** non-small cell lung cancer, adjuvant chemotherapy, disease free survival

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-033 Analysis of Factors That Have Impact on Adjuvant Chemotherapy Application in Operated Stage IIA-IV Non-Small Cell Lung Cancer Patients

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Background: Surgery is the only potentially curative treatment in early stage non-small cell lung cancer (NSCLC). Even though relapse occurred in the majority of operated patients. Adjuvant chemotherapy is a standard management of an operable IIA –IV NSCLC, in order to reduce cancer recurrence and prolong overall survival. The aim of the study was to define the factors that reduce delivery of adjuvant chemotherapy. **Methods:** We performed a retrospective analysis of prospectively collected data of 498 IIA-IV NSCLC patients operated with radical intent between 2007 and 2013. Age, type and extension of surgery, presence of surgical complications, Charlson Comorbidity Index, forced vital capacity (FVC), forced expiratory volume in one second (FEV1), 6-minutes walk test (6MWT), marital status, distance between home to the hospital, duration of smoking habit, number of cigarettes smoked daily, number of packyears were considered in uni- and multivariate analysis for identification of factors that have potential influence the application adjuvant chemotherapy. **Results:** In univariate analysis age (p<0.001), 6MWT distance (p=0.007), FEV1 [dm3] (p<0.001), FEV1 (%) (p=0.006), FVC [dm3] (p<0.001), FVC (%) (p<0.001), complications after surgery (p=0.005), and type of surgery (p=0.036) were identified as factors that have impact on delivery of adjuvant chemotherapy. In the multivariate analysis, FVC [dm3] (p=0.043) and FEV1 [dm3] (p=0.013) were found as independent factors. **Conclusion:** Low pulmonary function tests limits delivery of complete adjuvant chemotherapy while age, comorbidity, type and extension of surgery has no impact in this regard. **Keywords:** non-small cell lung cancer, adjuvant chemotherapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-034 Utilization of Adjuvant Therapy Among Completely Resected Non-Small Cell Lung Cancer (NSCLC) Patients at Charleston Area Medical Center

Steven J. Jubelirer[1], Seth B. Larson[2], Christine A. Welch[3], Zelia R. Budhan[1]
[1]*Hematology Oncology, Charleston Area Medical Center,/ West Virginia University, Charleston Division, Charleston/WV/United States of America,* [2]*Hematology Oncology, Charleston Area Medical Center, Charleston/WV/United States of America,*[3]*Outcomes Research, Charleston Area Medical Center, Charleston/WV/United States of America*

Background: Recently, adjuvant chemotherapy has become the standard of care for completely resected (R0) stage II and IIIA NSCLC patients; up for debate is the use of adjuvant therapy for stage IB. This retrospective study examined the therapies used in completely resected NSCLC patients. **Methods:** Information was initially gathered from the CAMC Cancer Registry which recorded nearly 2,500 occurrences of lung cancer during the study period (2005-2012). Those with completely resected (R0) stage IB (tumor size ≥ 4 cm) through IIIA (R0) NSCLC were selected for further review. Patients who did not receive preoperative therapy were included. **Results:** Meeting inclusion criteria were 171 patients, 96% Caucasian, with an average age of 66 ± 10 years (range 40-86). The majority were male (66%), 63% were married, and 55% had Medicare/Medicaid and most underwent a lobectomy (82%) Stages included IB (26%), IIA (23%), IIB (35%), and IIIA (16%), with 46% adenocarcinoma and 42% squamous cell. Adjuvant treatment type by stage is presented in Table 1. The majority of those not receiving treatment refused or elected observation (52%), while 16% were not treated due to comorbidities and 12% expired within 2 months of surgery. Logistic regression revealed that those who were treated were age < 65 years (odds ratio 3.3, CI 1.6-7.1, p = .002), stage IIIA (odd ratio 2.0, CI 1.3-2.9, p < .0005) and stage IIB (odd ratio 1.3, CI 1.0-1.7, p < .03).

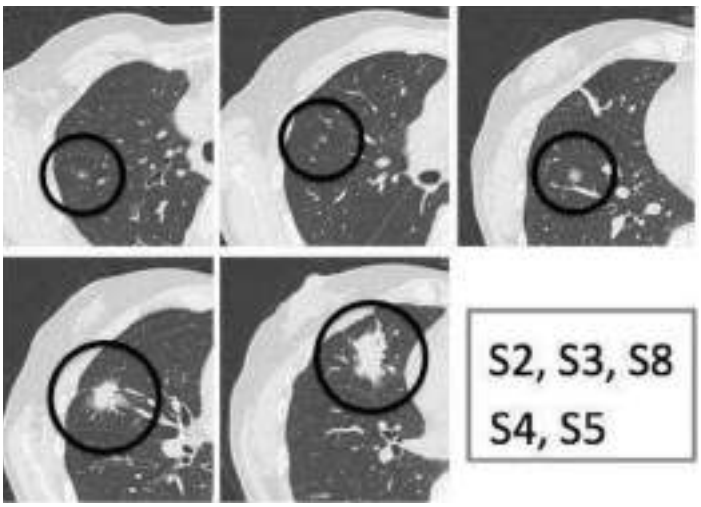
Treatment by stage for completely resected NSCLC				
	Stage			
	IB	IIA	IIB	IIIA
	n(%)			
Treatment				
No Treatment	33(73.3)	24(60)	31(52.5)	6(22.2)
Chemotherapy				
Cisplatin-based	7(15)	9(22.5)	12(20.3)	9(33.3)
Carboplatin-based	4(8.9)	6(15)	9(15.3)	2(7.4)
Sequential chemo/RT	0(0)	1(2.5)	1(1.7)	0(0)
Concurrent chemo/RT	0(0)	0(0)	6(10.2)	7(25.9)
RT alone	1(2.2)	0(0)	0(0)	3(11.1)

Conclusion: Adjuvant therapy was seen more in stages IIB and IIIA. Stage IIIA received the highest rate of radiation. Of the patients who underwent treatment the majority received treatment that is compliant with NCCN guidelines. Unfortunately only 2 of the patients who received treatment were part of a clinical trial. The proportion of patients treated, was similar to the NCCN Outcomes Data Project of Zornosa C, et al. **Keywords:** non-small cell lung cancer, Adjuvant therapy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-035 A Case of Synchronous Quintuple Lung Cancers Treated with Salvage Surgery after Treatment with Erlotinib Kaori Abe, Junichi Shimada, Daishiro Kato, Hiroaki Tsunezuka, Satoru Okada, Tatsuo Huruya, Narumi Ishikwa
Division of Chest Surgery, Department of Surgery, Kyoto Prefectural University of Medicine, Kyoto/Japan

Background: The detection of multiple ground glass nodules(GGNs) is increasing with improvement in the computed tomography (CT) technique. Indelible GGNs are very often indicative of atypical adenomatous hyperplasia or relatively early stage lung adenocarcinoma, so its detection and accurate diagnosis are required for appropriate treatment. **Methods:**



A 64-year-old woman with no significant medical history was referred to our hospital after an abnormal shadow was detected on chest radiograph. CT showed two part-solid GGNs in the right upper lobe(diameter: S2,9mm;S3, 5mm), two solid nodules surrounded slightly part of GGN in the right middle lobe (S4, 27mm;S5, 38mm), and one part-solid GGN in the right lower lobe(S8, 8mm).Fluorine-18-fluorodeoxyglucose positron emission tomography showed abnormal uptake in the two nodules in the middle lobe. Biopsy of the nodule in S4 was performed using a bronchoscope, and the results indicated adenocarcinoma with an EGFR exon21 (L858R) substitution mutation. The two solid nodules in the middle lobe were diagnosed as intrapulmonary metastasis in the same lobe(cT3N0M0,stageIIB). Because the patient refused surgery, two courses of combination chemotherapy with cisplatin, pemetrexed, and bevacizumab were administered, which was discontinued because of the adverse effects. Therefore, oral administration of erlotinib was started, and she showed a partial response. Fourteen months after initiation of treatment with erlotinib, salvage surgery was performed. Salvage surgery involved right middle lobe resection with preoperative lipiodol marking for GGNs, upper lobe wedge resection, and lower lobe wedge resection. **Results:** The five nodules could be resected completely with adequate resection margin. Histopathologically, all nodules were diagnosed as adenocarcinoma of the lung, with a lepidic pattern and no vascular invasion. Since the histopathological features differed slightly between nodules, the lung cancers were not diagnosed as intrapulmonary metastases but synchronous quintuple lung cancers. The final histopathological diagnosis was pT2aN0M0, stage IB lung cancer. **Conclusion:** Our findings indicate that synchronous lung cancers as well as lung intrapulmonary metastasis need to be considered in patients presenting with multiple lung nodules with even a minor GGN component, and that complete resection after treatment with erlotinib could be the appropriate treatment in such cases. EGFR tyrosine kinase inhibitor (TKI) often leads lung cancers with EGFR mutations to good response, but most tumors acquire resistance to EGFR-TKI after less than 12 months treatment. There is a possibility that salvage operation is useful after treatment of EGFR-TKI.
Keywords: synchronous multiple lung cancers, salvage operation, Erlotinib, ground glass nodule

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-036 Predictors of Lung Fibrosis after Stereotactic Body Radiation Therapy (SBRT) for Stage I-II Non-Small Cell Lung Cancer (NSCLC) Norman Yeh[1], Quentin Diot[1], Basel Altoos[1], Brian Kavanagh[2], Laurie Gaspar[1] [1]*University of Colorado-Denver, Aurora/CO/United States of America,* [2]*University of Colorado-Denver, Aurora/United States of America*

Background: Radiographic lung injury, fibrosis, occurs in over 50% of patients after SBRT. The purpose of this study was to evaluate clinical and dosimetric predictors of lung fibrosis after SBRT for stage I-II NSCLC **Methods:** A retrospective single institution database was examined for patients with Stage I-II NSCLC, T1-2N0, and lesions less than 5 cm treated with SBRT to 45-54 Gy in 3-5 fractions from 2010 to 2013. 4D CT imaging was used to assist with target localization and CT scans with at least 9 months of followup were rigidly registered to the planning CT scan based on common anatomical landmarks. Fibrosis volume was manually contoured. Simple and multiple linear regression were used to assess clinical and dosimetric variables under univariate and multivariate analyses. **Results:** We identified 26 patients and 27 lesions that met inclusion criteria. On UVA, increasing PTV volume, V20, and intermediate dose spillage (maximum total dose to any point 2 cm from PTV divided by dose prescribed) were significantly associated with increasing fibrosis ($p<0.05$). Non-significant predictors of fibrosis included patient age, pack years of smoking, COPD GOLD stage, use of ACE-I, and radiation dose to the PTV. On MVA accounting for factors significant for fibrosis (PTV volume, V20, intermediate dose spillage), only PTV volume remained significantly correlated with fibrosis volume (0.43 cm^3 increase in fibrosis for every 1 cm^3 increase in PTV, 95% CI, 0.08-0.77, $p=0.02$). **Conclusion:** In this analysis of predictors of fibrosis after SBRT, only increasing PTV volume was associated with increased fibrosis. We plan to utilize these results for future studies using pharmacologic strategies to decrease lung fibrosis.
Keywords: fibrosis, PTV, SBRT

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-037 Robotic SBRT with Fiducial Tracking for Inoperable Peripheral Stage I NSCLC: Mature Survival and Toxicity Outcomes Nima Aghdam[1], Richa Bhasin[1], Ryan Malik[1], Shaan Kataria[1], Simeng Suy[1], Sean Collins[1], Thomas Chang[2], Filip Benovac[2], Eric Anderson[3], Brian Collins[1] [1]*Department of Radiation Medicine, Georgetown University Hospital, Washington Dc/United States of America,* [2]*Department of Radiology, Georgetown University Hospital, Washington Dc/United States of America,* [3]*Division of Pulmonary, Critical Care and Sleep Medicine, Georgetown University Hospital, Washington/ DC/United States of America*

Background: Surgery is not an option for many patients with stage I non-small-cell lung cancer (NSCLC). Here we report mature robotic stereotactic body radiation therapy (SBRT) with fiducial tracking outcomes for inoperable patients with peripheral clinical stage I NSCLC. **Methods:** Inoperable patients with biopsy-proven peripheral clinical stage I NSCLC were treated. PET/CT imaging was completed for staging. Three-to-five gold fiducial markers were implanted in or near tumors to serve as targeting references. Gross tumor volumes (GTVs) were contoured using lung windows. The margins were expanded by 5 mm circumferentially to establish the planning treatment volume (PTV). Doses delivered to the PTV ranged from 45 to 60 Gy in 3 or 5 fractions (BED Gy_{10} >100 Gy). **Results:** Forty patients ranging in age from 62-94 years (median age 76 years) with a median percent predicted FEV1 of 61% (range, 21-107%) were treated over a 6-year period extending from August 2005 to August 2011 and followed for a minimum of 40 months or until death. The median maximum tumor diameter was 2.6 cm (range, 1.4-5.0 cm). A median dose of 50 Gy was delivered over a 3 to 13 day period (median, 7 days). At a median potential follow-up of 56 months, the 5-year Kaplan-Meier locoregional and distant control estimates were 95% and 82%. The 5-year cancer-specific and overall survival estimates were 75% and 40%. There was no change in percent predicted FEV1 one year following robotic SBRT; there was a small but statistically significant 8% decline in percent predicted DLCO at one year. Radiation induced rib fracture (RIRF) was identified on surveillance CT imaging in 17 patients. The estimated cumulative incidence of RIRF at 3 years was 40%. The median time to rib fracture was 24 months (range, 7-38 months). **Conclusion:** Robotic SBRT with fiducial tracking outcomes for inoperable peripheral stage I NSCLC are comparable to conventional SBRT outcomes. Additional research will be required to determine the optimal SBRT technique.
Keywords: Rib Fracture, Robotic SBRT, NSCLC, Inoperable

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-038 Survival outcomes of Stereotactic body radiotherapy for early-staged non-small cell lung cancer: a comparison between different doses Yin Kwan Chik, Ka Man Cheung, Ho Ching Lam, Chung Kong Kwan, Joseph S K Au
Clinical Oncology, Queen Elizabeth Hospital, Hong Kong/Hong Kong

Background: Stereotactic body radiotherapy (SBRT) is a definitive local treatment option for patients with early stage non-small cell lung cancer (NSCLC) who are considered unfit for surgical treatment either due to poor lung function or medical comorbidities. The purpose of this work is to report on the outcomes of stage I and II non-small cell lung cancers treated with SBRT in a tertiary oncology centre in Hong Kong. **Methods:** One hundred and five patients diagnosed with Stage I-II NSCLC underwent treatment with SBRT between January 2006 and December 2014. Data were collected and analyzed retrospectively. Overall survival (OS) and local control (LC) were calculated using the Kaplan-Meier method. **Results:** Median follow-up was 28 months (range 5-100 months) with a median age of 77 years. The median size of treated lesion was 2.7cm (range 1.2-7cm). The median SBRT dose was 50Gy (range 40-60 Gy) delievered in a median of 4 fractions (range 4-10). The median biological equivalent dose (BED10) was 105.6 Gy (range 39 -180Gy). The overall median OS was 28 months. The overall LC was 86.5% and 43.7% at 1 and 3 years, the overall OS was 91% and 51.3% at 1 and 3 years, respectively. Patients with stage T1 (n=60) disease had better LC and OS when compared with T2 (n=42). Median OS was 30.5 months (T1) and 18 months (T2; P=0.006). 1-year LC was 89% (T1) and 83% (T2; p=0.45), 1-year OS was 96.3% (T1) and 83.8% (T2; p=0.006), 3-year LC was 57.8% (T1) and 37.5% (T2; p=0.045), 3-year OS was 60.4% (T1) and 38.7% (T2; p=0.006). A higher BED10 of more than 105Gy was associated with improvement in OS and LC. For tumors treated with BED10<105 Gy and BED10>=105 Gy, overall LC at 2 year was 71.8% and 86% (p= 0.017), 2-year OS was 69.4% and 79%, respectively (p=0.026). T2, but not T1 tumors was associated with improved LC with higher BED10. 2-year LC at 2 years for T2 tumors treated with BED10<105 Gy and BED10>=105 Gy were 40 % and 75% respectively (p=0.002). Median OS for T2 tumors treated with BED10<105 Gy and BED10>=105 Gy were 28 months and 31 months respectively (p=0.14). Toxicity was graded based on Common

Terminology Criteria for Adverse Events (CTCAE v4.02). Two patients (1.9%) developed grade 3 toxicity of esophagus. There were no grade 4 or above toxicity. Eight patients developed asymptomatic rib fracture, all of these patients had peripheral lesions (defined as < 2.5cm from chest wall), of which three patients had lesions touching chest wall, median time to development of rib fracture was 19 months (range 9-40 months). **Conclusion:** SBRT is an effective treatment option for early-stage-non-small cell lung cancer with limited toxicity. Overall survival and local control were greater for patients with T1 tumors compared to T2 tumors. Higher doses (BED10>105 Gy) were associated with improvement in local control and overall survival. Significant improvement in local control was observed in patients with T2 tumors treated with BED10>105 Gy. **Keywords:** lung cancer, non-small cell lung cancer, stereotactic body radiotherapy, Biologically effective dose

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-039 Is Volumetric Rapid Arc Irradiation Superior in the Treatment of Non Small Cell Lung Cancer? Evy Bossuyt[1], Christel M. De Pooter[2], Katrien Erven[1], Yasmine Geussens[1], Rita Reymen[1], Philippe Huget[1] [1]*Az St Augustinus, Wilrijk/Belgium,* [2]*Radiotherapy, Az St Augustinus, Wilrijk/Belgium*

Background: To make an irradiation plan for a patient with non small cell lung cancer without compromising myelum and healthy lung tissue, is often a challenging task. The purpose of this study was to investigate if Volumetric Rapid Arc irradiation would be superior in doing so. **Methods:** Patients were simulated with regular breathing on a lung support. The target alignation and definitions were standard. Dose optimalisation and calculation were performed in Eclipse using AAA version 10.0.28. 82 Different approaches in planning were made for different patients: conventional beams, and rapid arc plans with half arcs, full arcs, arcs with avoidance sectors and hybrid solutions. Calculations were made for a dose of 33 x 2Gy , with 98% coverage of PTV (planning target volume) with 95% of the dose , taking into account the mean lung dose, V20 and V5. **Results:** There is no class solution for the best treatment approach. The best technique depents on tumor size, lung size, tumor localisation and patient anatomy. Especially for small tumors, the conventional beams often give the best results in terms of lung dose, especially when myelum can be avoided without irradiating the contralateral lung. Half arcs were mostly not interesting, probably because both sides of oblique posterior fields are often needed for good PTV coverage. Using avoidance sectors was a better approach to spare more healthy lung tissue. Choosing the angles of the avoidance sectors is important, like choosing angles for conventional fields. Making a simple conventional plan first, gives a good idea of feasible lung and PTV dose and about angles for the avoidance sectors. The use of avoidance sectors generally gives a better solution in terms of lung dose, but if PTV is not fully covered and a lot of overdosage appears, one has to use smaller avoidance sectors or even work without. If the proposed constraints are not reached with these tools, it is possible to work with a hybrid solution. This is in practice more complicated, therefore we did not introduce this as a standard planning technique in our clinic. **Conclusion:** For small tumors, conventional beams are often better than rapid arc. If the tumorvolume is larger (> 300cc) and reaching different sides of the body (from left to right or from cranial to caudal), rapid arc gives better results. Avoidance sectors have to be chosen wisely to optain the constraints without turning to hybrid techniques. **Keywords:** hybrid irradiation, Radiotherapy, rapid arc irradiation, NSCLC

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-040 PEARL: Pathologic Effect of NeoAdjuvant Stereotactic Ablative Body Radiotherapy (SABR) in Operable Early Stage Lung Cancer Jan P. Van Meerbeeck[1], Katrien Vandecasteele[2], Kurt Tournoy[3], Karim Y. Vermaelen[4], Frederic De Ryck[5], Veerle F. Surmont[4] [1]*Thoracic Oncology, University Hospital, Edegem/ Belgium,* [2]*Radiation Oncology, University Hospital, Gent/Belgium,* [3]*Pulmonology, Onze Lieve Vrouwe Ziekenhuis, Aalst/Belgium,* [4]*Pulmonology, University Hospital, Gent/ Belgium,* [5]*Thoracic Surgery, University Hospital, Gent/Belgium*

Background: SABR is considered a valid alternative to surgical resection in stage IA NSCLC (*Senan, TLO 2013*). However, doubts persists regarding the risk of local recurrence as lymph node staging is suboptimal and the completeness of pathological response is not verified (*Van Schil, TLO 2013*). **Methods:** We conducted a prospective phase 2 trial in functionally operable patients with NSCLC, staged cIA after PET/CT and endosonographic staging, who provided informed consent for neoadjuvant SABR, followed by VATS resection of primary tumour and draining lymph nodes. **Results:** We report on 1 patient, after which the trial was prematurely closed. This 57 year old smoker was incidentally diagnosed with a cT1bN0M0 adenocarcinoma in the middle lobe (2.9 x 2.1 cm) and EBUS-confirmed tumour-free ipsilateral hilar and mediastinal lymphnodes. 3 weeks after receiving 20 Gray on the tumour bed on days 1/4/7 each, he underwent a VATS middle lobectomy with systematic lymph node sampling. The resection specimen showed a completely resected 2.5 cm vital adenocarcinoma with invasion of 1/3 hilar lymph nodes (ypT1bpN1M0R0PI0). 4 cycles of adjuvant cisplatin-based chemotherapy were uneventfully administered and patient remains in complete remission 4 years after resection. **Conclusion:** This prospective case report challenges the completeness of pathological response and of lymph node staging with SABR. Comprehensive bio-imaging will be presented at the meeting. **Keywords:** lymph node staging, SABR, stage IA NSCLC, lobectomy

POSTER SESSION/ TREATMENT OF LOCALIZED DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.02-041 Stereotactic Body Radiation Therapy Associated with Erlotinib for Localized Clonal Progression of Metastatic Non Small Cell Lung Cancer Lisa K. Morikawa[1], Guilherme M. Gondin[2], Ernani Anderson[1], Helio A. Salmon[1], Clarissa Baldotto[3], Juliana Panichella[1], Carlos G. Ferreira[4] [1]*Radiation Oncology, Clinicas Oncologicas Integradas (Coi), Rio de Janeiro/Brazil,* [2]*Radiation Oncology, Ac Camargo Hospital, Sao Paulo/Brazil,* [3]*Medical Oncology, Clinicas Oncologicas Integradas (Coi), Rio de Janeiro/Brazil,* [4]*Medical Oncology, Oncologistas Associados, Rio de Janeiro/Brazil*

Background: Stereotactic Body Radiation Therapy (SBRT) has been widely used in early stage Non-Small-Cell Lung Cancer (NSCLC) with low toxicity and local control rates above 90%. Experience with this technique in the treatment of metastatic tumors is limited. EGFR receptor antagonist Erlotinib acts as a radiosensitizer and increases the overall survival of patients with metastatic NSCLC harboring mutations of this receptor. Temporary suspension of this drug may cause a quick progression of the disease known as "disease flare." Reports about the combination of this drug with SBRT are rare and the toxicity of this treatment is practically unknown. **Methods:** We present an 80 years-old, female patient with metastatic NSCLC who was treated with Erlotinib and had her disease controlled for 3 years. The patient underwent SBRT in a small lung lesion of 22mm representing the isolated progression of the disease. Treatment with Erlotinib was briefly suspended for the SBRT to avoid "disease flare." The patient was treated with a dose of 5000 cGy in 5 fractions delivered by Volumetric Modulated Arc Therapy (VMAT) without using an accessory for rigid immobilization. Treatment was performed by a linear accelerator with 6 MV photon beam and a 2.5mm micro-multileaf collimator. Margins of 5mm from Internal Target Volume (ITV) were applied, which included the tumor and its movements during the breathing cycle, without safety margin for microscopic disease. IGRT was performed daily with Cone Beam kV computed tomography. **Results:** Before undergoing SBRT, the patient had a Carcinoembryonic Antigen (CEA) level of 8 ng/mL. This tumor marker dropped to 3.5 ng/mL immediately and 1.7 ng/mL three months after the procedure. PET-CT 6 months after SBRT showed a reduction from 9.0 to 3.6 in the SUVmax of the lung lesion. Approximately 60 days after SBRT, the patient developed cough and was diagnosed with actinic pneumonitis. Prednisone was started and kept for about a month with complete resolution of the condition. It has been more than 1 year after she underwent SBRT and more than 3 years since she started chemotherapy with Erlotinib. The patient still shows no evidence of new metastatic lesions and remains with good tolerance to chemotherapy. **Conclusion:** Actinic pneumonitis is uncommon after SBRT of lesions with these small dimensions. A dose of 5000 cGy in 5 fractions is considered a conservative approach and all normal tissue constraints were respected in the present case. We believe this side effect to be a result of the radiosensitizer action of Erlotinib when associated with SBRT. We recommend caution when applying SBRT after a recent suspension of chemotherapy with this drug. **Keywords:** NSCLC, SBRT, Erlotinib, pneumonitis

SESSION: POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC WEDNESDAY, SEPTEMBER 9, 2015

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-001 Comparison of Adjuvant Therapy Modes Following Resection in Lung Cancer Patients with Clinically (-) but Pathologically (+) N2 Disease Hyojung Park[1], Dongryul Oh[1], Yong Chan Ahn[1], Hongryull Pyo[1], Jong-Mu Sun[2], Jin Seok Ahn[2], Myung-Ju Ahn[2], Keunchil Park[2], Yong Soo Choi[3], Hong Kwan Kim[3], Jhingook Kim[3], Jae Ill Zo[3], Young Mog Shim[3] [1]*Radiation Oncology, Samsung Medical Center, Seoul/ Korea,* [2]*Medicine, Samsung Medical Center, Seoul/Korea,* [3]*Thoracic & Cardiovascular Surgery, Samsung Medical Center, Seoul/Korea*

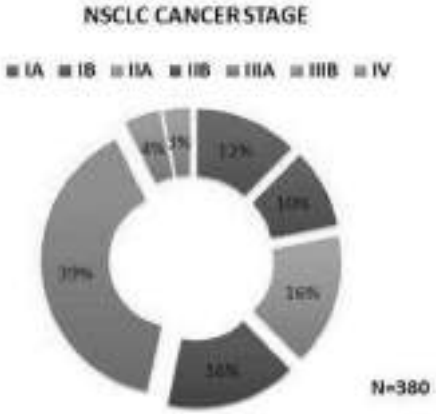
Background: Mediastinal nodal staging is very important before recommending surgical resection in newly diagnosed non-small cell lung cancer patients. Following curative resection for having apparently clinically uninvolved mediastinal node (cN0-1), some proportion of patients, however, turns out to have pathologically involved mediastinal node (pN2). There have been controversies on optimal adjuvant therapy during past 2 decades in this clinical setting. Systemic chemotherapy, either followed by or concurrent with radiation therapy, has remained most important modality. This study is to evaluate clinical outcomes following similar, but different, 3 adjuvant therapy modalities, in all of which included systemic chemotherapy, at authors' institute. **Methods:** Between 2006 and 2012, authors identified 240 cN0-1/pN2 patients who received adjuvant systemic chemotherapy following curative resection: chemotherapy alone in 85 patients (Group A); chemotherapy concurrent with thoracic radiation therapy (CCRT) in 68 (Group B); and CCRT followed by consolidation chemotherapy in 87 (Group C), respectively. Chemotherapy dose intensity was lower in CCRT setting than in upfront or consolidation chemotherapy settings, while thoracic radiation therapy dose schedule was the same (50 Gy/25 fractions). Clinical outcomes of loco-regional control (LRC), distant-metastasis free survival (DMFS) and overall survival (OS) were compared among Groups. **Results:** Median follow-up duration was 30 (5~93) months. Median age of all patients was 60 years and 149 patients (62.1%) were male. Majority of patients (224 patients, 93.3%) underwent lobectomy, while 16 (6.7%) did pneumonectomy. Adenocarcinoma was most common in 165 patients (68.8%) followed by squamous cell carcinoma in 53 (22.1%), and others in 22 (9.2%). There was no difference among Groups with respects to pretreatment and treatment characteristics except median age (Group A was older: 63 years vs. 58 years vs. 58 years, p=0.022). LRC, DMFS and OS rates at 5 years in all patients were 75.1%, 38.0% and 76.2%, respectively.

Though no significant difference in OS at 5 years among Groups (76.8% vs. 68.4% vs. 82.5%, p=0.096), LRC rate at 5 years was significantly improved by addition of thoracic radiation therapy (62.9% vs. 78.9% vs. 82.9%, p=0.011), while DMFS rate at 5 years was significantly improved by delivering full dose chemotherapy (40.6% vs. 19.4% vs. 28.6%, p=0.018). **Conclusion:** Although in retrospective nature having potential selection bias, current observations support that maximal benefit could be achieved by thoracic radiation therapy concurrent with chemotherapy and consolidation full dose chemotherapy with respects to LRC and DMFS. Further prospective clinical trial would be desired. **Keywords:** Stage IIIA, non-small cell lung cancer, concurrent chemoradiotherapy

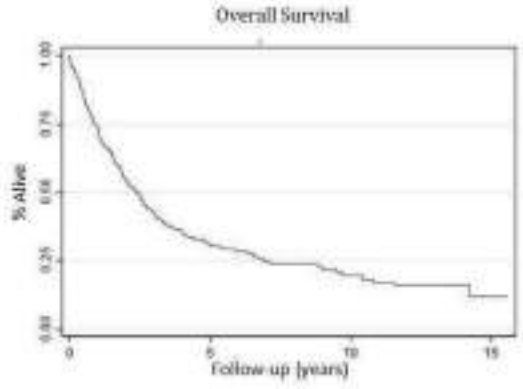
POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-002 Risk Factors and Outcomes of Pneumonectomy in Patients with Lung Cancer Manuel Wong Jaen, Joan Solé Montserrat, Laura Romero Vielva, María Deu Martin, Alberto Jauregui Abularach, Irene Bello Rodriguez, Mercedes Canela Cardona *Thoracic Surgery, Vall D'Hebron University Hospital, Barcelona/Spain*

Background: Pneumonectomy has been associated with high morbidity and mortality. The aim of this study is to evaluate complications, risk factors of mortality and overall survival of patients undergoing pneumonectomy for lung cancer. **Methods:**Retrospective study of 380 consecutive patients operated between January 2004 and December 2014. The majority were male (87, 4%), with a mean age of 60.7 years (r: 29-81) and a mean follow-up of 31.7 months. **Results:** Right pneumonectomy was the most frequent procedure (58.2%). Most of the patients were diagnosed with squamous cell carcinoma (56.1%). Half of the patients received neoadjuvant chemotherapy (50.5%) and 18 (4.7%) concomitant radiotherapy. N2 disease was present in 125 patients (32.9%).



The most frequent complication was atrial fibrillation (14%). Twenty-seven patients (7.1%) required reoperation for postoperative bleeding. Bronchopleural fistula appeared in 54 patients (14.21%). Twenty-five patients (6.6%) died within 30-days after surgery. Overall survival was 36.6% months with rates at 1, 3 and 5 years of 73.2%, 42.5% and 31,2% respectively.



Survival according to tumor size showed significant differences (T1: 33.1 months, T2: 21.1 months, T3: 11.4 months and T4:10.3 months). Survival was lower in patients with N2 disease(10.8 vs 30 months, p=0.0000). Overall survival was higher for left pneumonectomy (17.6 vs 24.8 months).There were significant differences in survival when analyzing lung function parameters, histological type, cancer stage, neoadjuvant treatment, pulmonary or cardiac complications, and reoperation for postoperative bleeding. **Conclusion:** In our series, age, side of resection, lung capacity, tumor extension, extent of surgical resection, comorbidities and postoperative complications are associated with decreased survival. **Keywords:** overall survival, pneumonectomy, risk factors, morbidity

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-003 Pilot introduction of the IASLC nodal classification system across EBUS-TBNA, CT and PET in staging of Non Small Cell Lung Cancer Lorena F. Zhang[1], Louise Emmett[2], Brad Milner[2], Natalia Belousova[3], Liam Clifford[4], Adrian Havryk[2], Emily Stone[2] [1]*The Kinghorn Cancer Centre, Sydney/NSW/Australia,* [2]*St Vincent'S Hospital, Sydney/NSW/Australia,* [3]*Port Macquarie Hospital, Port Macquarie/NSW/ Australia,* [4]*The University of New South Wales, Sydney/NSW/Australia*

Background: The accurate reporting of lymph node status is important in the staging and subsequent management of primary non small cell (NSCLC) lung cancer. However, lymph node nomenclature varies widely across staging modalities and between operators. Nodal stage may therefore be lost in translation when interpreting reports, compromising accuracy and possibly patient care. The International Association for the Study of Lung Cancer (IASLC) system of lymph node classification facilitates standardized, accurate identification of mediastinal lymph node groups. Preliminary work at our institution indicates a low uptake of this classification system in staging modalities, particularly CT and PET/CT. Application of this classification system across staging modalities may improve consistency of staging in primary NSCLC.

Aim
To determine the feasibility and impact of prospectively introducing the IASLC nodal classification system in a retrospectively identified series of NSCLC cases **Methods:** A series of cases of NSCLC (n=54) with IASLC classification at EBUS-TBNA identified in preliminary work will be reviewed. A sub-group will be selected that have had both other key staging modalities (CT and PET/CT) at our institution. IASLC classification will be applied retrospectively to two other key staging modalities, CT and PET/CT, by study investigators. **Results:** The primary endpoint for analysis is change in final nodal stage before and after the application of IASLC classification. Secondary endpoints include (i) change in IASLC classification between PET/CT and EBUS-TBNA, (ii) change in IASLC classification between CT and PET/CT, (iii) change in IASLC classification between CT and EBUS-TBNA. **Conclusion:** The effect of introducing IASLC lymph node classification across three staging modalities in NSLC (CT, PET/CT and EBUS-TBNA) will be presented. **Keywords:** Nodal classification, EBUS-TBNA, Mountain-Dresler, NSCLC

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-004 Clinicopathological Factors Associated With Postoperative Survival in Patients With Pathological Stage IB Non-Small-Cell Lung Cancer Masanori Shimomura, Shunta Ishihara *Department of General Thoracic Surgery, Ayabe City Hospital, Ayabe, Kyoto/Japan*

Background: The treatment outcomes of patients with non-small-cell lung cancer have improved because of advances in diagnostic imaging and multidisciplinary therapies. However, the reported 5-year survival rate of patients with pathological stage IB non-small-cell lung cancer is approximately only 60%. We evaluated the clinicopathological factors associated with postoperative survival in patients with pathological stage IB non-small-cell lung cancer. **Methods:** From July 2006 through July 2014, 56 patients with pathological stage IB non-small-cell lung cancer underwent lung resection. We retrospectively evaluated the factors of age, sex, preoperative carcinoembryonic antigen level, pathological classification, tumor diameter,*EGFR* mutation, and pleural, lymph duct, and venous invasion. **Results:** The 5-year survival rates of the overall cohort and of patient subsets with squamous and non-squamous cell carcinoma were 60.8%, 22.7%, and 83.2%, respectively. A survival analysis revealed that both squamous cell carcinoma and v1 venous invasion were associated with poor prognosis. Further analysis revealed that the 5-year survival rates of patients with v1 and v0 invasion were 24.6% and 73.9%, respectively. **Conclusion:** Patients with pathological stage IB non-small-cell lung cancer classified as squamous cell carcinoma and those with v1 invasion have a higher risk of recurrence. **Keywords:** Non-small-cell lung cancer, Surgery, stage IB, Prognosis

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-005 Review of the Impact of Robotic Surgery on Pulmonary Resections Performed at a Comprehensive Cancer Center Patrick Ross[1], Patsy Skabla[2], Priyal Shah[1], Thomas Williams[2] [1]*The Ohio State University Wexner Medical Center, Columbus/ OH/United States of America,* [2]*The Ohio State University Wexner Medical Center, Columbus/ United States of America*

Background: Minimally invasive surgical techniques have emerged as potential platforms for improving surgical outcomes. Thoracoscopic pulmonary resection was developed in the mid 1990's but has yet to achieved dominance as the resection approach of choice. Robotic-assisted pulmonary resection has been developed in a number of institutions. In this report we will review the impact of the robotic platform on pulmonary resections at a comprehensive cancer center. **Methods:** All robotic cases were entered prospectively into an IRB outcomes database. Comparable data for open and thoracoscopic procedures was retrieved from our STS database submissions. We limited the review to the procedures performed by a single surgeon to eliminate the impact of multiple learning curves on the robotic resections. We reviewed 330 robotic pulmonary resections culled from the total robotic experience of 503 between 2010 through March, 2015. Single-surgeon data for open cases was retrieved for the same time frame through the STS database. We evaluated percentage of minimally invasive cases annually, length of stay, length of procedure, complications, duration of air leak, readmissions and mortality. **Results:**Between 2010 and 2015 the percentage

of minimally invasive lobectomies performed annually increased from 23 % to 94%. Conversions from robotic approach to open decreased from 8% in the first 100 cases to 4% in the last 100 cases. Mortality for robotic lobectomy was 0.8% compared to open lobectomy 2.0%. Readmission rate for robotic resections was 9.7 % compared to 16% for open cases. Only a single robotic case was readmitted for pain management. There was a trend to lower post-operative pneumonia incidence in the minimally invasive group. **Conclusion:** In our single institution, single surgeon experience, adding the robotic platform quadrupled the percentage of lobectomies accomplished with a minimally invasive approach. There was a continued decrease in length of procedure as team experience accumulated. The outcomes measures of mortality, readmission, length of stay and pneumonia demonstrated advantage to the robotic platform. Robotic pulmonary resection may be the platform for increasing minimally invasive resections. Throughput metrics of operating time, length of stay and readmission are favored in the robotically performed procedures with an experienced team. **Keywords:** Thoracic Surgery, Robot, lobectomy, lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-006 Wide Wedge Resection with Adequate Surgical Margin for Pure GGO Lesion after Marking the Position near the Tumor with Lipiodol under a CT Scan Guide Katsuo Kojima[1], Ken Takahashi[1], Yasunori Arai[2] [1]*Thoracic Surgery, Musashino Red-Cross Hospital, Musashino-Shi, Tokyo/Japan,* [2]*Division of Radiology, Musashino Red-Cross Hospital, Musashino-Shi, Tokyo/Japan*

Background: It is said that wide wedge resection of lung is suitable for the surgical method for adenocarcinoma in situ (=AIS) in lung cancer in case that surgical margin is gotten enough. If the tumor shadow in high resolution CT scan is pure ground glass opacity (=pure GGO), we can suppose the tumor to be AIS. But pure GGO lesion is often too difficult for us to recognize the localization and the border of a tumor at surgery. We had once undergone segmentectomy or lobectomy after the pure GGO lesion had progressed so as to include consolidation in the tumor as a result of several follow-up CT examinations. The technique of the lipiodol marking to lung under a CT scan guide was developed and a small lesion of lung came to be able to be marked safely. Therefore we have undergone wide wedge resection in which the surgical margin was gotten enough for expected AIS with the following modified technique of the marking. **Methods:** We have performed this technique for the pure GGO lesions which is increasing in size or in concentrations but do not have occurrence of consolidations in periodic high resolution CT scan examination. Marking technique is following. Marking is performed under local anesthesia in a CT room one day before surgery. We stab the skin at slightly remote diagonal position from right above tumor with 22G needle and push forward needlepoint to the central near side of tumor while confirming it by real-time CT scan before we inject 0.3ml of lipiodol at the central near side of tumor. The operation of marking is finished after confirming whether pneumothorax exists. Surgical technique is following. We perform this surgery by three port thoracoscopic surgery. We grasp the marked position of the lung with ring forceps under thoracoscope while confirming the lesion marked by lipiodol is located in the center of the ring by real time fluoroscopy (Mobile C-arms). Then we cut the lung along ring circumference of the forceps with automatic suture instruments. After taking out a specimen outside the body, we confirmed that the surgical margin was gotten enough by measuring the distance between the resection stump and the position of marking under fluoroscopy. **Results:** We performed wide wedge resection to 19 cases (22 lesions) with this technique between 2011 and 2014. Tumor diameter was an average of 9mm (6-13mm). Surgical margin was an average of 17mm (11-28mm). Pathological diagnosis was AIS in 19 lesions, minimally invasive adenocarcinoma in 1 lesion, atypical adenomatous hyperplasia in 1 lesion and mucinous adenocarcinoma in 1 lesion. There was one complication before surgery (pneumothorax which needed drainage after marking). We underwent left S9 segmental resection with lymph node dissection in addition for a case of mucinous adenocarcinoma. **Conclusion:** This technique is an extremely useful method when we perform the most minimally invasive surgery such as wide wedge resection for very early lung cancer before progressing because it is easy to get surgical margin enough. **Keywords:** pure GGO, lipiodol marking under a CT scan guide, wide wedge resection, surgical margin

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-007 Salvage Surgery for Local Recurrence after Cryoablation for Non-Small Cell Lung Cancer: Importance of Diagnosis of Recurrence without Delay Shinsaksu Matsuda[1], Takashi Ohtsuka[1], Hideaki Yashiro[2], Seishi Nakatsuka[2], Keisuke Asakura[1], Tai Hato[1], Ikuo Kamiyama[1], Katsura Emoto[3], Yuichiro Hayashi[3], Hisao Asamura[1] [1]*Division of General Thoracic Surgery, Department of Surgery,, School of Medicine, Keio University, Shinjuku-Ku, Tokyo/Japan,* [2]*Department of Diagnostic Radiology, Keio University, School of Medicine, Tokyo/Japan,* [3]*Division of Pathology, School of Medicine, Keio University, Shinjuku-Ku, Tokyo/Japan*

Background: Non-surgical treatment for lung cancer, such as stereotactic body radiation therapy (SBRT), radiofrequency ablation (RFA), and percutaneous cryoablation have been performed as alternatives to surgery for lung cancer in patients with comorbidities, limited pulmonary reserve, or early diseases. Not many, but the significant portion of patients with such local modalities experience the local failures. The salvage surgery for such recurrence might have been attempted with considerable technical and oncological difficulties. Two cases with salvage resection for local failure after cryoablation are described. **Methods:** We reviewed two patients who had previously undergone cryoablation, in whom local recurrences were treated with salvage surgery. We evaluated perioperative parameters and histological findings, which indicated the local failure. **Results:** Case1: A woman was underwent cryoablation treatment for second primary T1aN0M0 lung adenocarcinoma in left lower lobe after 6 years of right lower lobectomy for lung adenocarcinoma. 4 years after the cryoablation, CT scan showed a tumor increasing in size in the area of treatment and local recurrence was suspected. Recurrence of adenocarcinoma was confirmed by CT guided biopsy. Segmentectomy of posterior segment of left lower lobe was performed. Operation time was 155minutes and blood loss was 72 ml. This patient is alive without any sign of recurrence after 8 years from surgery. Case2: A woman was underwent cryoablation for clinical stage T1aN0M0 lung adenocarcinoma in right lower lobe after 20 years of right upper lobectomy for lung cancer. 3 years after the cryoablation, CT scan showed a tumor growing in size in the area of treatment and local recurrence was suspected. Local recurrence of adenocarcinoma was proved by CT guided biopsy. Segmentectomy of superior segment of right lower lobe was performed. Operation time was 291minues and blood loss was 230 ml. This patient is alive without any sign of recurrence after 22 months from surgery. In both cases, salvage surgeries were performed without any difficulties. Pathological examinations showed viable cancer cells with necrotic tissue and fibrosis around which was consistent with the local recurrence after cryoablation. **Conclusion:** The salvage surgery for the local failures after non-surgical treatment modalities might be indicated in selected cases. The difficulties in diagnosis of local recurrence might cause the optimal timing of surgery. **Keywords:** salvage surgery, lung cancer, local recurrence, cryoablation

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-008 Lung Resections: Limited Resection for Operable Lung Cancer Swamyvelu Krishnamurthy, Durgesh Kumar *Surgical Oncology, Kidwai Memorial Institute of Oncology, Bangalore/India*

Background: Lung cancer is the commonest cancer worldwide and the leading cause of cancer related deaths. Most common etiology is smoking which includes both active and passive. Surgery ,chemotherapy and radiation therapy ,are treatment options available . In india presentation of the lung cancer is usually in advanced stages because of various socioeconomic conditions. **Methods:** It is a retrospective study. Data were collected from the hospital database which includes no of patients who underwent lung resection for carcinoma lung between a period of January 2011 to December 2014. Data was analysed regarding number of patients who underwent surgery, surgery related complications, adjuvant treatment , and survival **Results:** Total number of cases seen in this time period was 360 with a sex ratio of 2:1 out of which 45 underwent surgery (12.5 %),rest underwent palliative chemotherapy due to advance disease .Out of 45 cases 28 were diagnosed as adenocarcinoma, 16 squamous cell and 1 case of limited stage small cell lung cancer .Most cases were stage IIA (17/45) followed by (IB 9/45), 6 cases were diagnosed as stage IIB , 4 cases stage IA and 9 out of 45 cases were stage IIIA .39 out of 45 underwent lung resection and rest 6 cases were found locally advanced on exploration ,biopsy taken and closed .Lobectomy done in 23 patients (60 %) followed by bilobectomy (30.7 %) pneumonectomy in 3 cases only and 1 patient underwent bilobectomy with excision of the ribs with chest wall reconstruction .Post operative pneumonia was the most common complication found in 3 patients ,followed by wound infection (1/39) , prolonged air leak(2/39) and chest wall recurrence (1/39).All patients with stage IB and above underwent cisplatin based adjuvant chemotherapy and six patients underwent adjuvant radiotherapy . Average survival in our study was 2 years for stage IA – IIB and 6 months for stage IIIA . **Conclusion:** The incidence of lung cancer is rising dramatically and it is now the most common cause of cancer related mortality and morbidity not only in industrialised nations,but also in developing countries like India as well.In our study we found only 13 % operable lung cancer despite of huge incidence and we were able to do less than pnemonectomy in majority of the patients .The survival is moderate for the lung cancer patients in view of our inability to detect early lung cancer patients.The ideal screening tools for early detection of the lung cancerhas still not found so drastic measures amied at discouraging people from smoking and early encouraging high risk population to undergo regular screening to reduce the morbidity and mortality.

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-009 A Case of Completion Pneumonectomy Performed Through Mid-Sternal Incision and Posterolateral Incision Masato Watanabe, Shozo Fujino, Takehiro Okumura *Department of Surgery, University Hospital Mizonokuchi, Teikyo University School of Medicine, Kawasaki, Kanagawa/Japan*

Background: We report a case of completion pneumonectomy (CP) for recurrent lung cancer in which we resected the residual left lower lobe through posterolateral incision following confirmation of resectability of residual lung and no mediastinal lymph node metastasis through mid-sternal incision. **Methods:** [Case] A 71 year-old-man who underwent left upper sleeve lobectomy 2 years ago (squamous cell carcinoma, pT2bN1M0 2B) complained chronic coughing and sputum. Bronchofibroscope and chest computed tomography (CT) revealed a local recurrence at the left main bronchus and surrounding tissue of left pulmonary artery. No distant metastasis was pointed out by CT and other examinations. The patient's pulmonary function was good (VC 3.29L, FEV1 .0 2.05L) and the predictive FEV1 .0 was 1.94L by the ventilation-perfusion scintigraphy. [Surgery] We added a mid-sternal incision in the supine position and confirmed no mediastinal lymph node metastasis and the resectability of left main pulmonary artery, then we cut the left main pulmonary artery in the pericardial cavity with exposing trachea, tracheal bifurcation and left main bronchus. After closing mid-sternal incision, the patient was converted into the right decubitus position and added posterolateral incision. After having separated the lower pulmonary vein and the stump of upper pulmonary vein in a pericardium, we exfoliated and cut left main bronchus and removed the residual left lower lobe. The operation time was 13 hours and 7 minutes

and total blood loss was 2.23L. Postoperative course was almost uneventful and he left our hospital on the 30th postoperative day. He has no recurrence or metastasis 12-months after surgery. **Results:** [Discussion] It is said that the incidence of serious complications after CP extends to 18.4~40.7% and the incidence of bronchial fistula is over 10 percent. Because the survival rate is reported with 38.9~48.3% at 3-year and 16.9~48% at 5-year, careful adaptation decision is necessary. **Conclusion:** [Concluding remarks] Our approach to confirm the resectability and no mediastinal lymph node metastasis through mid-sternal incision is useful to make final decision of indication for CP. In addition, there is an advantage that intrathoracic operation is easy to perform because hilar region is handled beforehand through mid-sternal incision. **Keywords:** completion pneumonectomy, mid-sternal incision, posterolateral incision

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-010 Usefulness of Vessel Sealing Devices in Thoracoscopic Lobectomy for Lung Cancer Masayuki Toishi, Kazuo Yoshida, Hiroyuki Agatsuma, Takao Sakaizawa, Takashi Eguchi, Gaku Saito, Akira Hyogotani, Kazutoshi Hamanaka, Takayuki Shiina *Department of Thoracic Surgery, Shinshu University School of Medicine, Matsumoto/Japan*

Background: Vessel sealing devices (VSD) are widely used for various surgical procedures. They are regarded as useful in thoracoscopic surgery, but few reports have substantiated this belief by comparison with non-use of VSD in human thoracoscopic lobectomy. Aiming to establish a simpler and safer thoracoscopic lobectomy, we examined the usefulness of VSDs. **Methods:** Primary lung cancer patients for whom a thoracoscopic lobectomy involving mediastinal lymph node dissection was planned in our department from April 2011 to June 2013 were recruited for the study. Patients were randomly allocated to a control group (n=15) or a VSD group (n=46), which constituted of three subgroups, namely, EnSeal (n=17), LigaSure (n=15), and Harmonic (n=14). The control group comprised of patients undergoing surgery solely with ligation and conventional electrocautery. EnSeal, LigaSure, and Harmonic were chosen because they are the 3 most popular disposable VSDs used in Japan. Primary endpoints were burst pressure of the pulmonary artery stump (measured using resected specimens), operative time, intraoperative blood loss, instances of endostapler use, intraoperative surgeon stress (assessed by visual analog scale), and postoperative drainage volume and duration. As a secondary objective, the individual VSD groups were also compared with each other. **Results:** The burst pressure of ligation-treated pulmonary artery stumps was higher than that of VSD-treated stumps (P<0.0001). The burst pressure of < 5-mm wide VSD-treated stumps was higher than that of ≥ 5 mm wide stumps (P=0.0359). However, burst pressure for all groups and all vessel diameters was sufficient to withstand physiological pulmonary artery pressure. The VSD group demonstrated reduced intraoperative blood loss (P=0.0174), surgeon stress (P=0.0001), postoperative drainage volume (P=0.0270), and shortened postoperative drainage duration (P=0.0330). Operative time and the instances of endostapler use did not significantly differ. Comparison between each of the VSD groups revealed no significant differences. None of the patients experienced serious perioperative complications or died because of surgery. **Conclusion:** VSD is simple and safe to use in thoracoscopic lobectomy involving mediastinal lymph node dissection for primary lung cancer. Further, none of the VSDs used in this study presented any observable differences in quality that could lead to clinical problems. **Keywords:** vessel sealing, burst pressure, mediastinal lymph node dissection, thoracoscopic lobectomy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-011 General Anesthesia Is Not Required for Safe, Accurate Endoscopic Diagnosis of Malignant and Non-Malignant Disease in the Mediastinum John D. Doty[1], Jaspal Singh[2], H J. Norton[3] [1]*Thoracic Oncology, Levine Cancer Institute, Charlotte/NC/United States of America,* [2]*Thoracic Oncology, Levine Cancer Institute, Charlotte/United States of America,* [3]*Department of Biostatistics, Carolinashealthcare System, Charlotte/NC/United States of America*

Background: Since its introduction in the early to mid 2000's, endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) of mediastinal lymph nodes has been shown to be superior to "blind" TBNA for the diagnosis of malignancy and sarcoidosis in multiple studies. There is no consensus, however, regarding the optimal method of procedural sedation for EBUS. The purpose of this retrospective study was to determine differences in sampling accuracy and safety between a group of patients undergoing EBUS with moderate sedation and a group with general anesthesia. **Methods:** A retrospective chart review was performed of 51 consecutive patients undergoing convex probe EBUS-guided TBNA over a six-month period at a large, community-based referral hospital. Fifteen procedures were performed under general anesthesia and 36 with moderate sedation using midazolam and fentanyl after topical preparation of the upper airway with lidocaine. Twenty nodal biopsies were performed on the 15 general anesthesia patients, and 47 biopsies were performed on the 36 patients from the moderate sedation group. Rapid on-site cytologic evaluation (ROSE) was used for most cases. **Results:** No statistically significant difference was found in any measured variable between the two groups, specifically sample adequacy (85% in the general anesthesia [GA] group vs. 83% in the moderate sedation [MS] group; p = 1.0; 95% confidence interval (CI), -17.0 to 21.0%) or frequency of adverse events (6.7% GA vs. 5.6% MS; p = 1.0; 95% confidence interval (CI), -13.6 to 15.8%). There was no significant difference in the mean size of lymph nodes biopsied (16.4 mm GA vs. 18.3 mm MS; p = 0.28). Additionally, there was no difference in the proportion of biopsies taken from individual nodal stations or in the numbers and types of diagnoses made between the two groups. Adverse events were mild and included self-limited, non-cardiac chest pain in a patient receiving GA, and two episodes of desaturation in the MS group that resolved with temporary interruption of the procedure. **Conclusion:** As payor scrutiny and emphasis on quality, cost-effective health care increases, convex probe EBUS-guided biopsy utilizing moderate sedation remains an effective, accurate method of diagnosing malignant and non-malignant disease in the mediastinum without the added cost of general anesthesia and without compromising patient safety. Certainly general anesthesia can be an invaluable resource for bronchoscopic procedures in high-risk patients with morbid obesity, sleep apnea, heavy home narcotic or sedative use and other complex comorbidities, but healthcare facilities without anesthesia services can acquire and effectively employ convex EBUS technology with confidence. **Keywords:** TBNA, EBUS, general anesthesia

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-012 Prediction of Occult Lymph Node Metastasis Using Metabolic PET Parameters in Small Size Peripheral Non-Small Cell Lung Cancer Joonho Jung[1], Seong Yong Park[1], Su Jin Lee[2] [1]*Department of Thoracic and Cardiovascular Surgery, Ajou University School of Medicine, Suwon/Korea,* [2]*Department of Nuclear Medicine & Molecular Imaging, Ajou University School of Medicine, Suwon/Korea*

Background: Small size peripheral non-small cell lung cancer (NSCLC) patients without lymph node metastasis may be the optimal candidates for sublobar resection. We aimed to identify the predictors of occult lymph node metastasis using F-18 fluorodeoxyglucose positron emission positron emission tomography/computer tomography (PET/CT) in small size NSCLC patients who were clinically node negative. **Methods:** One hundred fifty three patients with small size NSCLC (less than 3cm in diameter) who underwent surgical resection with mediastinal lymph node dissection were evaluated. The maximum standardized uptake value (SUVmax), metabolic total volume (MTV), and total lesion glycolysis (TLG) of primary tumor were measured on pretreatment PET/CT. These metabolic parameters and pathological variables were analyzed for lymph node metastasis. **Results:** The mean tumor size was 2.11 ± 0.55 cm and the mean numbers of dissected lymph nodes were 16.33 ± 9.81. The adenocarcinoma was 103 (67.3%). Thirty patients (19.6%) had lymph node metastasis. The mean SUVmax, MTV and TLG were 4.85 ± 4.02 (0.5 ~ 16.4), 3.39 ± 5.54 (0 ~27.2) and 14.99 ± 27.78 (0 ~155.9), respectively. On receiver operating characteristic curve analysis, area under the curve (AUC) of SUVmax, MTV, TLG for node metastasis were 0.744, 0.750 and 0.745, respectively. On multivariate analysis, SUVmax (Odds ratio [OR] = 1.172, p=0.006), MTV (OR = 1.153, p=0.002) and TLG (OR=1.024, p=0.08) were risk factors for node metastasis after adjusting the tumor size and cell type. The concordance index of MTV was 0.722, which was slightly higher than those of SUVmax and TLG.

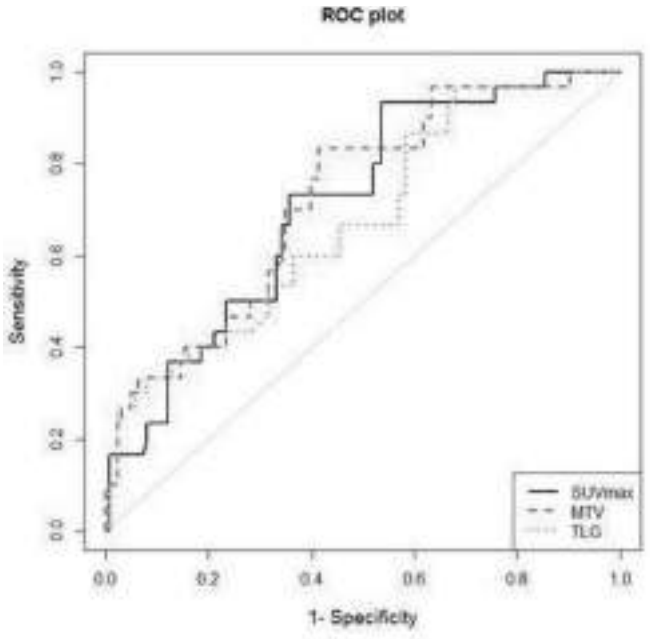


Figure. ROC curve of each volume parameters of positron emission tomography/computer tomography for predicting the node metastasis **Conclusion:** SUVmax and volume-dependent parameters of primary lesion were significant risk factors for node metastasis in small peripheral NSCLC. MTV showed better predictive performance than other PET parameters, therefore MTV may be the possible indicator for sublobar resection in clinically node-negative small size NSCLC. **Keywords:** NSCLC, lymph node metastasis, PET/CT

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-013 Predictive Factors for Survival in Stage IIIA (N2) NSCLC Patients Treated with Neoadjuvant Chemotherapy Followed by Surgery Yaping Xu, Jinshi Liu, Xinmin Yu, Qiang Zhao, Youhua Jiang, Qixun Chen, Xinming Zhou, Weimin Mao
Zhejiang Cancer Hospital, Zhejiang/China

Background: For locally advanced non-small cell lung cancer (NSCLC) patients, although the evidence level for induction chemo (chemoradio) therapy is low, the incorporation of chemotherapy, radiotherapy, and surgery will greatly impact the strategy of future treatment. The objective of this study was to evaluate the risks of recurrence and overall survival (OS) in stage IIIA (N2) NSCLC patients undergoing definitive resection after neoadjuvant chemotherapy. **Methods:** A retrospective analysis of 106 consecutive patients with stage IIIA (N2) NSCLC who received neoadjuvant chemotherapy followed by surgery between January 2008 and October 2013. While reviewing the clinical and surgical data, we also assessed histopathologic and imaging (chest CT scan) factors. Disease-free survival (DFS) and OS were estimated with predictors for recurrence and survival. The Kaplan–Meier method was used to evaluate patient DFS and OS. Univariate analysis of patient clinical characteristics and treatment response were conducted using the Chi-square and Fisher's exact test. **Results:** Median age was 60, 96 (90.5%) patients were male, 85 (80.2%) patients were squamous cell carcinoma and 21 (19.8%) patients were non-squamous cell carcinoma, 93 (87.7%) patients had a lobectomy. The 3-year OS for patients with and without recurrence was 33.1 and 56.7 %, respectively ($p < 0.001$). Size decrease of target lesion(s) ≥30 % on post-neoadjuvant chemotherapy chest CT scan ($p = 0.040$), primary tumor size on surgical specimen <10 mm ($p = 0.047$), and pathological complete remission in the mediastinal lymph nodes were related to longer OS. Larger tumor size on post-neoadjuvant chemotherapy chest CT scan ($p = 0.038$), male gender ($p = 0.043$), squamous cell carcinoma ($p = 0.048$), larger primary tumor size on surgical specimen ($p = 0.041$), pathological non-complete remission in the mediastinal lymph nodes ($p = 0.031$) were related to shorter DFS significantly. **Conclusion:** OS is prolonged with greater extent of size decrease of target lesion(s) on post-neoadjuvant chemotherapy chest CT scan, smaller tumor size on surgical specimen and pathological complete remission in the mediastinal lymph nodes. Larger tumor size on post-neoadjuvant chemotherapy chest CT scan, male gender, squamous cell carcinoma, larger primary tumor size on surgical specimen, pathological non-complete remission in the mediastinal lymph nodes may prone to the higher probability of recurrence. **Keywords:** Mediastinal nodal involvement, N2 non-small-cell lung cancer, predictive factors, neoadjuvant therapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-014 The Impact of Post-Operative Adjuvant Chemotherapy for Resected NSCLC in the Real-World Setting: Single Center Experience Wenhua Liang[1], Qihua He[2], Jianrong Zhang[1], Jianxing He[1] [1]*The First Affiliated Hospital of Guangzhou Medical University, Guangzhou/China,* [2]*Department of Thoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou/China*

Background: Recent evidence argues against the benefits from adjuvant chemotherapy (ad-chemo) for resected NSCLC in the real world setting. We sought to examine the impact of ad-chemo based on the data from our center. **Methods:** A consecutive cohort of 681 patients who underwent radical resection for stage I to III NSCLC in our center between Sep 2009 and Dec 2011 was collected. Patients who received adjuvant EGFR-TKIs were excluded. Patients lost follow-up upon discharge (uncertain history of ad-chemo) were included in sensitivity analyses. The primary endpoint was disease-free survival (DFS). **Results:** 372 patients received ad-chemo whereas 224 did not, and the remaining 85 had no certain record of ad-chemo. There were 222 events (175 recurrence and 47 deaths). Univariate analysis showed that patients who received ad-chemo had shorter DFS than those who did not (HR 1.94, 95%CI 1.40 to 2.67; P<0.001). Incorporation of those without certain record of ad-chemo (HR 1.88; P<0.001) or excluding patients with stage I disease (HR 1.36; P=0.17) did not alter the trend. After adjusting for some important prognostic factors, such as stage, histology, visceral-pleural invasion, the inferiority of ad-chemo remained. In ad-chemo arm, we observed potentially better DFS in patients receiving platinum-based regimen (HR 0.64, 95% CI 0.38 to 1.07; P=0.09) and patients complete 4 or more cycles of ad-chemo (HR 0.73, 95% CI 0.52 to 1.01; P=0.05). **Conclusion:** Current results suggested that applying adjuvant chemotherapy should be based on strict patient selection. Establishment of selection criteria regarding recurrence risk and physical status is highly encouraged. **Keywords:** NSCLC, adjuvant chemotherapy, Real world

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-015 Outcomes of Chemoradiotherapy for Stage III Non-Small Cell Lung Cancer in South of Brazil Juliano Cé Coelho[1], Mariane Araújo Branco[2], Rafaela Pirolli[2], Carolina Beatriz Muller[3], Luis Felipe Carissimi Schmidt[1], Fábio Klamt[3], Guilherme Geib[1], Gilberto Schwartsmann[1] [1]*Medical Oncology, Hospital de Clínicas de Porto Alegre, Porto Alegre/Brazil,* [2]*Universidade Federal Do Rio Grande Do Sul, Porto Alegre/Brazil,* [3]*Department of Biochemistry, Universidade Federal Do Rio Grande Do Sul, Porto Alegre/Brazil*

Background: Patient with stage III lung cancer are commonly treated with chemotherapy and radiation. The concurrent treatment improves local control and overall survival, but also increase toxicity. A meta-analysis study with more than 1800 patients found a 30% reduction in 2-years mortality in who received a platinum-based chemotherapy. Trials populations are selected and usually are not representative of Brazil lung cancer population. **Methods:** From January 2005 to December 2013, all patients diagnosed with locally advanced non-small cell lung cancer (IIIA or IIIB) treated with etoposide/cisplatin (EP) with concurrent radiotherapy at an University Hospital in South of Brazil were identified from electronic database. Medical records were revised and demographic data, tumor and treatment characteristics were collected. Overall survival and progression freen survival were estimated by Kaplan-Meier curves. Multivariate analysis (Log-Rank tests) was performed to identify factors associated with survival. Statistical analysis was performed with SPSS 22.0. **Results:** Seventy-three patients were identified and included in analysis. Patients characteristics revealed a mean age of 59.2 ± 10,7 years, male sex in 63%, Caucasian ethnicity in 90%, smoking history in 86%, good performance status (0-1) 89% and stage IIIA and IIIB in 52% and 48%, respectively. Thirty-eight (52%) patients had adenocarcinoma, 24 (34%) squamous cell and 10 (13%) other histologies. All patients were treated with EP concurrent to radiation and 20% received two consolidation cycles of chemotherapy. Fifty-three (72%) completed all the treatment and 34 (45%) achieved complete or partial response. In the observational period 64 patients (88%) had died, with progression free survival of 10,1 months (95% IC, 6.97 to 13.17) and overall survival of 15.9 months (95% IC, 9.83 to 22.10). In multivariable analysis, clinical stage (IIIA vs IIIB) and performance status (0-1 vs ≥ 2) were independently associated with survival, HR 2.23 (95% IC, 1.16 to 4.29) and HR 6.39 (95% IC, 2.09 to 19.54), respectively. **Conclusion:** To our knowledge, this is the first Brazilian report of concurrent chemoradiation of locally advanced non small cell lung patients. Our outcomes are similar to previously reported clinical trials of concurrent treatment. Stage IIIB and performance status ≥ 2 were predictors of worst outcomes in our population. **Keywords:** non-small cell lung cancer, chemoradiation, EP

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-016 Randomized ph II Trial of Cyclophosphamide with Allogeneic DPV-001 Cancer Vaccine Alone or with Adjuvant for Curatively-Treated Stage III NSCLC Rachel E. Sanborn[1], Brian Boulmay[2], Rui Li[1], Kyle T. Happel[2], Helen J. Ross[3], Sachin Puri[1], Christopher Paustian[1], Christopher Dubay[1], Helena Hoen[1], Sandra Aung[4], Brenda Fisher[1], Carlo Bifulco[1], Keith Bahjat[1], Augusto C. Ochoa[2], Hong-Ming Hu[1], Traci L. Hilton[4], Bernard A. Fox[1], Walter J. Urba[1] [1]*Providence Cancer Center, Earle A. Chiles Research Institute, Portland/OR/United States of America,* [2]*School of Medicine, Louisiana State University Health Science Center, Stanley S. Scott Cancer Center, New Orleans/United States of America,*[3]*Mayo Clinic Arizona, Phoenix/AZ/United States of America,* [4]*Ubivac, Portland/OR/United States of America*

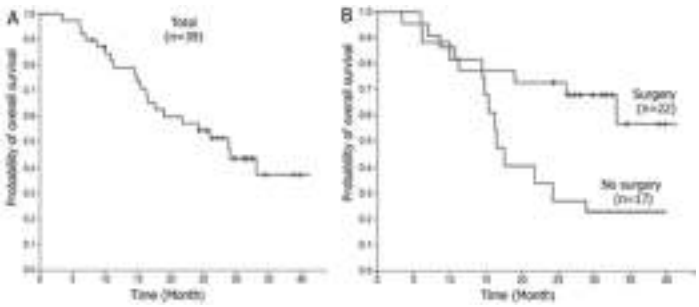
Background: Tumor-derived autophagosomes (DRibbles) are a novel dendritic cell-targeted cancer immunotherapy that preclinically provides cross-protection against related tumors and efficacy against established tumors. We hypothesize DRibbles' efficacy is due to presentation of stabilized tumor-derived short-lived proteins (SLiPs) and defective ribosomal products (DRiPs) normally not processed or presented by antigen presenting cells (APCs). SLiPs and DRiPs provide a potential pool of tumor antigen to which the host may not be not tolerant. This DRibble DPV-001 vaccine packages several hundred putative cancer antigens, including 13 antigens from the NCI list of priority antigens and agonist activity for TLR 2, 3, 4, 7 and 9 into stable double membrane microvesicles which have surface molecules targeting DRibbles to CLEC9A+ APCs (the most effective APC at cross-priming immunity). DPV-001 contains an average of 176 proteins from genes overexpressed in NSCLC patient tumors. Many of these putative cancer antigens have single amino acid variants that may serve as mimetopes, or altered peptide ligands, and thereby increase immunogenicity. **Methods:** Pts are eligible after completion of standard curative-intent therapy for stage III NSCLC. Pts receive induction cyclophosphamide, then 7 DPV-001 vaccines at 3-week intervals. The first vaccine is given intranodally; subsequent vaccines intradermally. Pts are randomized to receive DRibble alone, or with adjuvant imiquimod or GM-CSF. Peripheral blood mononuclear cells and serum are collected at baseline and at each vaccination. Serum from baseline and week 12 is analyzed for antibody response to >9000 human proteins (ProtoArray). When available, multispectral Immunoprofiling is performed on tumor to evaluate pre-existing immunity and Human Exome Capture and Next Generation Sequencing is done on tumor (100x coverage) and matched normal tissue. Tumor somatic mutations are compared to DPV-001 to identify shared non-synonymous single nucleotide variations (nsSNVs) with the vaccine, including mutations with potential increased immunogenicity. Pts will be analyzed comparatively for strong antibody responses (>15 fold increase in titer). 11 pts will be randomized to each arm, with 15 more enrolled on the arm with greatest number of strong antibody response. 8 pts have been enrolled, and accrual is ongoing. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** non-small cell lung cancer, Vaccine, Immunotherapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-017 Interim Overall Survival of Neoadjuvant Erlotinib Intercalated with Gemcitabine/Cisplatin for IIIA N2 NSCLC Patients: A Phase II Study Zhiwei Chen[1], Gening Jiang[2], Xin Wang[3], Qingquan Luo[1], Shun Lu[1] [1]*Lung Cancer Center, Shanghai Chest Hospital, Shanghai/China,* [2]*Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China,* [3]*Sun Yat-Sen University Cancer Center, Guangzhou/China*

Background: The optimal treatment for locally advanced stage IIIA non-small cell lung cancer (NSCLC) disease is not well established although neoadjuvant chemotherapy showed active results in stage IIIA N2 pts. A few case reports also indicate the advantages of neoadjuvant erlotinib. FASTACT II study showed that the regimen of erlotinib intercalated with chemotherapy improved PFS and OS in an unselected advanced NSCLC population of east Asian patients. Here we report the interim overall survival (OS) results of a phase II study which was to assess the efficacy and safety

profile of erlotinib intercalated with gemcitabine/cisplatin as neoadjuvant treatment in stage IIIA N2 NSCLC pts. **Methods:** Patients with untreated stage IIIA bulky N2 NSCLC and ECOG PS 0/1 were enrolled to received up to 2 cycles of gemcitabine 1,000 mg/m^2 on days 1 and 8 and cisplatin 75 mg/m^2 on day 1 or carboplatin AUC=5 d1, followed by oral erlotinib (150 mg, once a day) on days 15 to 28 as neoadjuvant therapy. A repeat computed tomography (CT) scan evaluated the response after induction therapy and eligible patients would undergo surgical resection. The primary endpoint was ORR which was reported in 2013 WCLC. The secondary endpoints included pCR, resection rate, DFS (disease free survival) and OS (overall survival), safety, QoL and biomarker analyses. **Results:** Between March 2011 and December 2012, a total of 39 patients (29 male, median age 59.0 years; range 34.0 to 74.0 years) were enrolled in the study, in which 36 patients (92.3%) had completed 2-cycle erlotinib neoadjuvant treatment. For pathologic type, 13 pts were adenocarcinoma, 18 pts were squamous carcinoma, and 8 pts were other types. One patient withdrew from the study and one patient was lost in the follow-up. Twenty-two (56.4%, 22/39) patients underwent surgical resection after erlotinib neoadjuvant treatment. Till Jan 15, 2015, the median follow up duration was 24.4 mo (range 5.5 to 43.7 mo). To the cut-off date, 22 patients (56.4%) died. The median OS for total 39 patients was 29.0 mo (Figure 1A, range 3.4 to 43.7 mo). The median OS for those no surgery pts was 17.0 mo (range 6.1 to 39.8 mo) while the median OS is not matured ye for those pts who received surgery (Figure 1B).



Conclusion: Neoadjuvant erlotinib intercalated with gemcitabine/cisplatin brought clinical benefits by extending overall survival for stage IIIA N2 NSCLC pts. **Keywords:** intercalated chemotherapy, IIIA N2 NSCLC, Erlotinib, noadjuvant treatment

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-018 Intercalated TKI and Chemotherapy Induction in EGFR mt+ NSCLC Stage IIIA and IIIB: 3 Cases with Complete Remission in Mediastinal Lymph Nodes Frank Griesinger[1], Anne C. Lueers[1], Markus Falk[2], Imme Conradi[1], Michael Reinhardt[3], Alexander Kluge[4], Kay Wilborn[5], Regina Prenzel[6], Douglas Scriba[7], R.-P. Henke[8], Wilfried E.E. Eberhardt[9], Cora Hallas[2], Markus Tiemann[2] [1]*Oncology, Pius-Hospital, Oldenburg/Germany,* [2]*Haematopathology Hamburg, Hamburg/Germany,* [3]*Nuclear Medicine, Pius-Hospital, Oldenburg/Germany,* [4]*Diagnostic Radiology, Pius-Hospital, Oldenburg/Germany,* [5]*Department of Radiation Oncology, Pius-Hospital, Oldenburg/Germany,* [6]*Pulmonary Medicine, Pius-Hospital, Oldenburg/Germany,* [7]*Thoracic Surgery, Pius-Hospital, Oldenburg/Germany,* [8]*Pathology Oldenburg, Oldenburg/Germany,* [9]*University Hospital Essen, West German Cancer Centre, Ruhrlandklinik, University Duisburg-Essen, Essen/Germany*

Background: EGFR TKI treatment is standard of care in patients with metastasized NSCLC carrying an activating EGFR mutation. However, induction concepts in locally advanced NSCLC with EGFR mutation including TKI have not been studied extensively. Recently new focus has been shed on intercalated regimens of chemotherapy and TKI, showing improved PFS as well as OS. This concept was used as induction regimen in 3 patients with activating EGFR mutation in stages IIIA and IIIB. **Methods:** Patients were diagnosed and worked up according to standard imaging, histology and immunohistology methods. EGFR, KRAS, BRAF, ALK and P53 mutation analysis were performed with standard procedures as described by Halbfass et al. 2013. Remission induction was measured by RECIST 1.1, regression grading by Junker criteria. **Results:** 2 female never smokers (pt #1 and 3), 62 and 59 y.o. and 1 male light smoker (pt#2) (5 packyear), 58 y.o . were diagnosed with with TTF1+ adenocarcinoma of the lung, 2 with exon 21 L858R (#2,3) and 1 with Exon 19 deletion (#1). All patients carried a p53 mutation, exon 6 (#2,3), exon 8 (#1). Tumor stage was T (extension to mediastinal pleura) N2 (2R, 4R) M0, IIIA4 (#1), T2aN3(4L,7,2R)M0 IIIB (#2) and T2N3M0. Induction therapy was started with erlotinib 150 mg/die p.o. days -12 to -1 (#1,2) and gefitinib (#3) in order to prove responsiveness of the tumor to EGFR-TKI. On day 0 partial response or no progression was achieved in all 3 patients. Therapy was continued with 3 cycles of docetaxel 75 mg/m2 d1 and cisplatin 50 mg/m2 d1 and 2 qd22 in combination with erlotinib d4-19 (#1), 1 cycle of docetaxel and cisplatin followed by 2 cycles of paclitaxel and carboplatin (#2) and switch from erlotinib to gefitinib with cycle 2 (#2) because of diarrhea) and 3 cycles of docetaxel and cisplatin with gefinitib 250 mg d4-19 (#3). PR was was achieved after 2 cycles in all patients. All three patients were resected and regression grade IIB was remarked in mediastinal lymph nodes (#1-3), regression IIA was remarked in the primary tumor in 2 patients (#2,3), regression grade III in 1 patient (#1). All three patients received adjuvant radiotherapy. Patients #1 and 3 are in CR, patient 2 developed one isolated CNS metastasis which has been stereotactically irradiated. No additional therapy, including TKI was administered postoperatively. **Conclusion:** Intercalated TKI treatment is a promising treatment choice in patients with EGFR mt+ locally advanced NSCLC. A phase II trial (NeoIntercal) trial is currently under way in 9 German centers in stages II and III using gefitinib in combination with induction taxane based chemotherapy, supported by ASTRA Zeneca. **Keywords:** Intercalated therapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-019 Salvage Surgery after Definitive Chemoradiotherapy in NSCLC Patients Oleg Pikin[1], Andrey Ryabov[2], Vladimir Glushko[1], Konstantin Kolbanov[1], Ali Amiraliev[1], Dmitriy Vursol[1], Vladimir Bagrov[1], Vitaliy Barmin[1], Roman Rudakov[1] [1]*Thoracic Surgery, Hertzen Research Institute of Oncology, Moscow/Russian Federation,* [2]*Thoraco-Abdominal Surgery, Hertzen Research Institute of Oncology, Moscow/Russian Federation*

Background: The benefits of salvage resection for lung cancer recurrence following high-dose curative-intent chemoradiation therapy are unclear. The study was aimed to assess postoperative morbidity and survival after salvage lung resection following definitive chemoradiation. **Methods:** In this retrospective study, medical records of 14 patients undergoing lung cancer resections at our institution following definitive chemoradiation therapy were reviewed from June 2008 to December 2013. There were 10 (71,4%) males and 4 (28,6%) females, median age - 52,6 years. The most common histologic type of lung cancer was squamous cell carcinoma (64,3%). Pretreatment lung cancer stage was IIB - in 2, IIIA - in 11 and IIIB - in one patient. Definitive radiation treatment varied from 45 to 70 Gy (median - 58Gy). Mean number of chemotherapy cycles was 3,8 per patient. Surgery included pneumonectomy in all patients, except one, whom left-lower lobectomy was performed. In all cases bronchial stump was reinforced with a pedicled muscle flap. Postoperative complications were registered according to the Thoracic Morbidity and Mortality System (TMM). **Results:** Postoperative complications were registered in 7 (50,0%) patients: grade II complications were detected in 2, grade IIIA – in 1, grade IVA – in 3 and grade V (mortality) – in one patient (7,1%). Pathologic stage was IB – in 2, IIA – in 1, IIB – in 5, IIIA – in 4 and IIIB – in 2 patients. Overall 1, 2 and 3-year survival was 89,1%, 82,0% and 48,0% with median survival 35 months. Disease-free 1, 2 and 3-year survival was 84,2%, 72,0% and 24,8% respectively, median – 28 months. Overall and recurrence-free 5-year survival was 10,8%. Recurrence in the chest was diagnosed in one patient, distant relapse – in 6. No variables were found to be associated with improved post-chemoradiation survival from the time of definitive treatment or postoperative survival. **Conclusion:** Salvage lung resection for recurrent lung cancer following definitive chemoradiation therapy is feasible and is associated with postoperative survival and complication rates that are reasonable. **Keywords:** lung cancer, salvage surgery, definitive chemoradiotherapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-020 Outcomes of Concurrent Chemoradiotherapy in Elderly Patients with Stage III Non-Small Cell Lung Cancer Seok Ho Lee[1], Seung Heon Lee[1], Ho-Jin Heo[1], Kihoon Sung[1], Kyu Chan Lee[1], Sung Hwan Jung[2], Jeong Woong Park[2], Eun Kyung Cho[3], Hee Kyung Ahn[3] [1]*Radiation Oncology, Gachon University Gil Medical Center, Incheon/Korea,* [2]*Internal Medicine, Gachon University Gil Medical Center, Incheon/Korea,* [3]*Division of Hematology and Oncology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon/Korea*

Background: The aim of this study was to assess the outcomes of concurrent chemoradiotherapy(CCRT) in elderly patients with stage III non-small cell lung cancer(NSCLC), focusing on the survival outcomes, prognostic factors and toxicities. **Methods:** From January 2006 to May 2012, 39 elderly patients older than 60 years (median 68 years; range 62~78 years) with stage III NSCLC were enrolled in this study. Radiotherapy (RT) was administered to the primary tumor and regional lymph nodes with concomitant administration of chemotherapy. The total RT dose was 46.8-79 Gy in daily 1.8-2.5 Gy fractions (median 66.6 Gy). Overall survival (OS) and progression free survival (PFS) were estimated with the Kaplan-Meyer method. Prognostic factors (gender, age, smoking, pathology, ECOG performance status, body weight, RT dose and tumor response) were analyzed by the log-rank test and Cox regression model. Acute toxicities were assessed according to Radiation therapy oncology group(RTOG) criteria. **Results:** The median follow-up period was 18.4 months. The 1, 2 and 3-year overall survival(OS) rates were 61.5%, 41.0% and 30.8%, respectively. The 1, 2 and 3-year progression free survival(PFS) rates were 51.7%, 30.0% and 21.8%, respectively. Multivariable analysis showed that ECOG performance status(p=0.002) and tumor response(p=0.001) significantly influenced OS. The tumor response(p=0.013) was a significant prognostic factor for PFS in multivariable analysis. The grade 3 or higher radiation pneumonitis and esophagitis were developed in 9 (23.1%) and 4 (10.3%) patients. Neutropenia with grade 3 or higher was developed in 8 patients (20.8%). **Conclusion:** Survival (OS and PFS) of elderly patients with stage III NSCLC treated with CCRT is significantly affected by tumor response. However, the survival outcomes for elderly patients with stage III NSCLC treated with CCRT showed comparable results with previous reports. The CCRT related toxicity such as pneumonitis and neutropenia were relatively higher. These results means that CCRT is effective in increasing survival, however, the careful selection of elderly NSCLC patients for CCRT is also required. **Keywords:** Elderly patients, Non-small cell lung cancer, Chemoradiotherapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-021 Neoadjuvant Chemotherapy for Locally Advanced Non-Small Cell Lung Cancer (NSCLC) Patients Taku Nakagawa[1], Yoshihiro Minamiya[2], Hajime Saito[2], Kazuhiro Imai[2], Hayato Konno[2], Satoshi Kudo[1], Yoshitaro Saito[2], Nobuyasu Kurihara[2], Shinnosuke Watanabe[1] [1]*General Thoracic Surgery, Omagari Kosei Medical Center, Daisen, Akita/Japan,* [2]*Thoracic Surgery, Akita University Graduate School of Medicine, Akita/Japan*

Background: Neoadjuvant chemotherapy (NAC) has gained popularity in recent years, becoming a standard treatment for locally advanced non-small cell lung cancer (NSCLC) to improve resectability and downstage nodal disease, which have clear impacts on

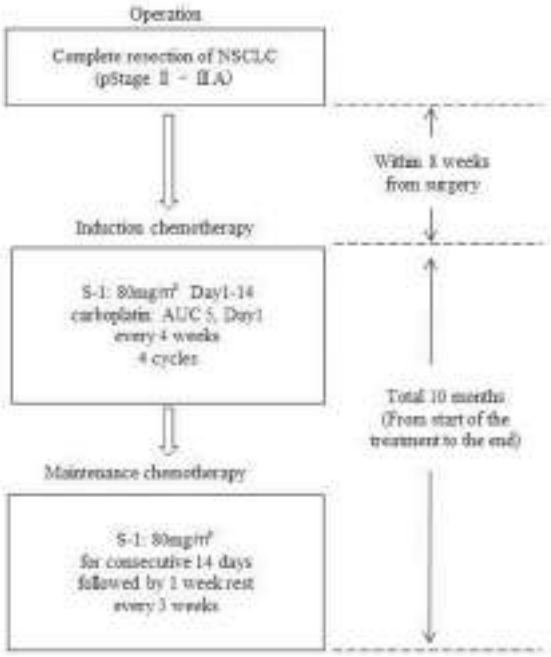
prognosis. Potential disadvantages are increased morbidity and/or mortality after surgery and risk of progression of disease that could have been initially resected. The purpose of this study was to evaluate outcomes in a series of patients with locally advanced NSCLC receiving NAC followed by surgery. **Methods:** A total of 12 patients (66.7% males; median age, 71 years) affected by NSCLC in clinical stage IIA-IIIB underwent platinum-based NAC followed by surgery between 2008 and 2014. The clinical stage was IIA in 3 patients, IIIA in 8 (4 of which were IIIAN2), and IIIB in 1. Histology was adenocarcinoma in 8, squamous cell carcinoma in 3, and adenosquamous carcinoma in 1. **Results:** All patients received platinum-based chemotherapy (median, 4 cycles). The NAC regimen was weekly paclitaxel-carboplatin in 6 patients, pemetrexed-carboplatin in 3, paclitaxel-carboplatin-bevacizumab in 2, and gemcitabine-cisplatin in 1. Radiologic response to NAC was complete in 1 patient (8.3%), partial in 8 (66.7%) and stable disease in 3 (25.0%). Overall response rate was 75.0% (95% confidence interval, 51-100%). Grade 3 or 4 hematological toxicities were common, including neutropenia (50%) and anemia (8.3%), but were transient and manageable. Non-hematological toxicities were moderate and no treatment-related deaths were encountered. Eleven patients (91.7%) underwent complete surgical resection after induction. Surgical procedures comprised lobectomy in 10 patients, bilobectomy in 1 and pneumonectomy in 1. No severe intraoperative complications or 30-/90-day mortality were seen. At pathological evaluation, 8 patients (66.7%) showed downstaging of disease, with complete in 1 (8.3%), major in 3 (25.0%) and minor in 7 (58.3%). With a median follow-up of 12.7 months (range, 5.2-50.8 months), the 1-year relapse-free survival rate was 56.6%. Four of the 12 patients developed metastasis (at 4.7, 6.0, 8.4, and 9.2 months), and 2 patients died at 14.7 and 23.9 months. **Conclusion:** NAC using platinum-based chemotherapy with new-generation cytotoxic agents for locally advanced NSCLC seems justified by low morbidity and mortality, good response rates, and high resectability. Although the evidence level for induction chemotherapy is low, incorporation of chemotherapy and surgery will greatly impact strategies for future lung cancer treatment. **Keywords:** neoadjuvant chemotherapy, Locally advanced NSCLC, Platinum, NAC

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

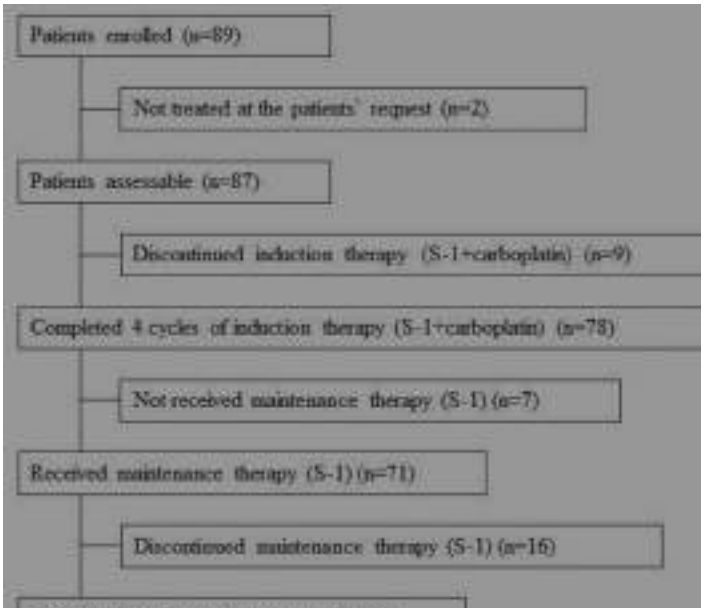
P3.03-022 Feasibility of Adjuvant Therapy with S-1 plus Carboplatin Followed by Maintenance Therapy with S-1 for Resected Non-Small-Cell Lung Cancer

Norihito Okumura[1], Makoto Sonobe[2], Kazunori Okabe[3], Hiroshige Nakamura[4], Masafumi Kataoka[5], Motohiro Yamashita[6], Masao Nakata[7], Kazuhiko Kataoka[8], Yoshinori Yamashita[9], Junichi Soh[10], Hiroshige Yoshioka[1], Katsuyuki Hotta[10], Keitaro Matsuo[11], Junichi Sakamoto[12], Shinichi Toyooka[10], Hiroshi Date[2] [1]*Kurashiki Central Hospital, Kurashiki/Japan,* [2]*Kyoto University Graduate School of Medicine, Kyoto/Japan,* [3]*Yamaguchi Ube Medical Center, Ube/Japan,* [4]*Tottori University Faculty of Medicine, Yonago/Japan,* [5]*Okayama Saiseikai General Hospital, Okayama/Japan,* [6]*Shikoku Cancer Center, Matsuyama/Japan,* [7]*Kawasaki Medical School, Kurashiki/Japan,* [8]*Iwakuni Clinical Center, Iwakuni/Japan,* [9]*Kure Medical Center/Chugoku Cancer Center, Hiroshima/Japan,* [10]*Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama/Japan,* [11]*Kyushu University Faculty of Medical Sciences, Fukuoka/Japan,* [12]*Tokai Central Hospital, Kakamigahara/Japan*

Background: The prognosis of patients with locally-advanced stages (II or IIIA) non-small-cell lung cancer (NSCLC) is unsatisfactory, even after complete resection, and the 5-year survival rate is <50%, indicating the need for further improvements in postoperative survival. This multicenter study (the Setouchi Lung Cancer Group Study 0701) aimed to evaluate the feasibility of novel adjuvant chemotherapy with S-1 plus carboplatin followed by single-agent, long-term maintenance with S-1 in patients with completely-resected stage II–IIIA NSCLC. **Methods:**



Patients received four cycles of S-1 (80 mg/m2/day for 2 weeks, followed by 2 weeks' rest) plus carboplatin (area under the curve 5, day 1) followed by S-1 (80 mg/m2/day for 2 weeks, followed by 1 week's rest). Patients unable to continue S-1 plus carboplatin because of severe toxicity converted to single-agent S-1 maintenance. The duration of adjuvant chemotherapy was 10 months in both situations. The primary endpoint was feasibility, defined as the proportion of patients who completed four cycles of S-1 plus carboplatin and single-agent S-1 maintenance for 10 months. The treatment-completion rate was determined and treatment was considered feasible if the lower 90% confidence interval (CI) was ≥50%. **Results:**



Eighty-nine patients were enrolled, of whom 87 were eligible and assessable. Seventy-eight patients (89.7%) completed four cycles of S-1 plus carboplatin and 55 (63.2%) completed the following S-1 maintenance therapy for a total of 10 months. The treatment-completion rate was 63.2% (90% CI: 54.4–71.2%), indicating feasibility. There were no treatment-related deaths. Grade 3/4 toxicities included neutropenia (11.5%), thrombocytopenia (10.3%), and anorexia (2.3%). The 2-year relapse-free survival rate was 59.8%. **Conclusion:** We concluded that novel adjuvant chemotherapy with S-1 plus carboplatin followed by single-agent maintenance therapy with S-1 was feasible and tolerable in patients with completely-resected NSCLC. **Keywords:** Non-small-cell lung cancer, adjuvant chemotherapy, S-1, maintenance therapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-023 Phase III Study of Accelerated Hypofraction in CCRT of Unresectable Stage III NSCLC: Interim Analysis of KROG 0903

Sung-Ja Ahn[1], Kwan-Ho Cho[2], Young-Chul Kim[3], In-Jae Oh[3], Jae-Uk Jeong[1], Sung Ho Moon[4], Jin Hee Kim[5], Mee Sun Yoon[1], Joo Young Song[1], Taek-Keun Nam[1] [1]*Radiation Oncology, Chonnam National University Hwasun Hospital, Jeonnam/Korea,* [2]*Radiation Oncology, National Cancer Center, Ilsan/Korea,* [3]*Lung and Esophageal Cancer Clinic, Chonnam National University Hwasun Hospital, Jeonnam/Korea,* [4]*National Cancer Center, Goyang/Korea,* [5]*Keimyung University, School of Medicine, Taegu/Korea*

Background: KROG 0301 prospective phase I & II study of the modified hypofractionation using concomitant boost to the gross tumor volume (GTV) simultaneously in the patients with unresectable NSCLC showed outstanding results comparing to the previous ones. So, we designed phase III prospective clinical trial comparing it with the standard 2 Gy fractionation. **Methods:** Eligibility criteria were histologically proven unresectable stage III NSCLC determined by thoracic surgeon and more than one lesion measurable with CT scan according to the criteria of RECIST (version 1.1). Exclusion criteria were supraclavicular nodal metastasis, superior vena cava syndrome, atelectasia obscuring GTV contouring, and disease suspected to extend the major vessels and bronchus and to be at the risk of hemorrhage after concurrent chemoradiation (CCRT). In conventional fractionated RT group (Arm-1), a dose of 2Gy was delivered daily to the PTV and total cumulative dose was 44Gy to the PTV in 22 fractions and field was reduced and 2Gy was delivered to GTV and proceeded to 60Gy to the GTV in 30 fractions. In hypofractionated RT group (Arm-2), a dose of 1.8Gy was delivered daily to the PTV with a synchronous boost of 0.6Gy to the GTV to bring its daily dose to 2.4Gy per fraction. Total cumulative doses were 60Gy to the GTV and 45Gy to PTV in 25 fractions over 5 weeks. All patients received concurrent weekly chemotherapy consisting of paclitaxel first (50mg/m^{2}intravenously over 1 hour) and cisplatin (20mg/m^2 intravenously over 1 hour) on days 1,8,15,22,29, and (36). Chemotherapy was performed before radiotherapy in a day. Dose modification of chemotherapy was guided according to the severity of toxicity. **Results:** One-hundred twelve patients who were followed more than 6 months after completion of planned treatment were included in this analysis. Median F-U was 14 months. Median age was 67 years(45-75) and male to female was 112/8. Stage IIIA was 81(72%) and IIIB 31(28%). Sixty and fifty-two patients were allocated in Arm-1 and 2, respectively. Patient's characteristics

were evenly distributed between two groups. Overall survival, local progression free, and disease progression free survival of all patients was median 30 months, 15months, and 12 months, respectively. Two- and 3-year survival rates were 53.6% vs. 54.1% and 50.4% vs. 44.6% in Arm-1 and Arm-2 (p=0.95), respectively. Two-year local tumor control rates were 58.3% and 50.0% (p=0.977) and 2-year progression free survival rates were 41.4% and 34.2% (p=0.704) in Arm-1 and Arm-2, respectively. Radiation esophagitis (≥ grade 2) was 15(25%) and 10(20%) and radiation pneumonitis (≥ grade 2) was 8(13.3%) and 7(13.5%) in Arm-1 and Arm-2, respectively. **Conclusion:** Interim analysis did not show any statistically significant toxicity or survival differences between two groups. This on-going clinical study needs to continue for the confirmative results. **Keywords:** Unresectable stage III, non-small cell lung cancer, Hypofractionation, Concurrent Chemoradiation

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.03-024 Efficacy of 18 F-FDG PET/CT as Response Predictor in Locally Advanced Non-Small Cell Lung Cancer Soumyajit Roy[1], Sushmita Pathy[1], Rakesh Kumar[2], Bidhu K. Mohanti[1], Vinod Raina[3], Anand Jaiswal[4], Sameer Taywade[2], Arun Malhotra[2], Sanjay Thulkar[5], Anant Mohan[6], Sandeep Mathur[7], Digamber Behera[4]
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Background: The study was aimed to assess the role of ^{18}F-FDG PET/CT in response assessment of patients with locally advanced non-small cell lung cancer (NSCLC) and in evaluating the predictive value of metabolic response for progression-free survival (PFS) and overall survival (OS). **Methods:** Thirty patients of locally advanced NSCLC were enrolled in this randomized controlled study and were allocated to one of the two treatment arms. Patients in Arm A (n=15) received neoadjuvant chemotherapy (NACT) and external beam radiotherapy (EBRT) while arm B (n=15) received NACT and EBRT with concomitant chemotherapy. ^{18}F-FDG PET/CT was carried out at baseline and after 6-weeks of completion of intended treatment. Pre and post-treatment maximum standardized uptake value (SUVmax) was noted. A reduction of SUVmax> 50% (ΔSUVmax) were considered to be metabolic responders (MR) and ≤ 50% as non-responders (MNR). The difference in SUVmax parameters were compared by Wilcoxon signed rank test and Mann-Whitney U test for paired and unpaired samples. The significance of difference in the number of MR and MNR between two arms was computed using Fisher's exact test. Survival time was estimated by Kaplan–Meier survival analysis. Survival pattern was compared using the log-rank test. Factors which had p value <0.25 in univariate analysis were subjected to multivariate analysis using Cox regression analysis. Statistical analysis was carried out using Stata software version 12.0. **Results:** Twenty one patients completed the intended treatment. The median pre and post-treatment SUVmax were 14, 6.4 for arm A and 15.3, 3.5 for arm B. There was no statistically significant difference between pre and post treatment SUVmax among the two treatment arms. Significant decrease in SUVmax was observed in both arms (median ΔSUVmax of 50% and 74% in arm A and B; p=0.618). Twelve patients achieved metabolic response. Metabolic response rate in arm A and B was 50% and 64% respectively (p=0.783). At median follow-up of 18.98 months the median PFS and OS of the MR were 22.31, 24.73 months and of MNR were 7.83, 8.26 months The Cox proportional hazard ratio for PFS and OS in MNR group was 2.33 (95% confidence interval i.e. C.I: 0.78-6.91) and 2.12 (95% C.I: 0.65-6.97). No significant difference in OS and PFS was observed between MR and MNR subpopulation of two arms (table-1).

Group	Median PFS (in months)	P value (Log rank test)	Median OS (in months)	P value (Log rank test)
Total cohort:	17.02 (95% C.I:7.44-22.31)	-	24.73	-
MR: MNR:	22.31 7.83	0.09	24.73 8.26	0.12
Arm A Arm B	18.7 9.12	0.59	24.73 15.4	0.27
MR of Arm A MR of arm B	10.5 22.3	0.34	15.4 Not achieved	0.27
MNR of arm A MNR of Arm B	7.44 7.83	0.71	7.47 8.26	0.71

Conclusion: PET/CT distinguishes responders to treatment based on metabolic activity in patients with locally advanced NSCLC, but did not provide any prognostic significance. **Keywords:** locally advanced NSCLC; 18F-FDG PET/CT; response assessment; SUVmax

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-025 Fatal and near Fatal Radiation Lung Injury after Lung Cancer Treatment Choonhee Son[1], Mee Sook Roh[2], Soo-Jung Um[2] [1]*Pulmonology, Dong-A University Hospital, Busan/Korea,* [2]*Dong-A University Hospital, Busan/Korea*

Background: Radiotherapy is important, and potentially curative method of treatment in lung cancer. Radiation pneumonitis and fibrosis is very frequent complication of radiotherapy, but usually asymptomatic or mild. Sometimes, however, it is fulminant and fatal. We reviewed clinical characteristics of fatal and near fatal form of radiation lung injury after lung cancer treatment. **Methods:** We retrospectively reviewed medical records of patients with lung cancer who received radiation on thorax greater than 50 Gy from January 2006 to December 2014, and clinical, radiologic, and pathologic characteristics were assessed. **Results:** Three hundred forty two patients were received thoracic radiation greater than 50 Gy. Radiation lung injury was observed in 284 patients(74.3%), and in 177 patients(62.3%) those lung injury was asymptomatic and mild fibrosis confined in directly radiated lung field. Fatal and near fatal radiation pneumonitis were developed in 39 patients(11.4%), of them 25 patients(7.3%) died of respiratory failure. In 25 patients, 13 patients(52.0%) had pre-existing interstitial lung disease, 16 patients(64.0%) received chemotherapy concurrently. All the fatal lung injuries were extensive consolidation and ground glass opacity out of radiation field. **Conclusion:** Radiation lung injury is usually mild and asymptomatic, however extensive radiation pneumonitis out of radiation field is fatal and near fatal. Concurrent chemoradiation and pre-existing interstitial lung disease were risk factors of this fulminant lung injury. **Keywords:** Radiation pneumonitis, interstitial lung disease

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-026 Analysis of Clinical and Dosimetric Factors Influencing Radiation-Induced Lung Injury in Patients with Lung Cancer Han Shuiyun[1], Feiying Gu[1], Gang Lin[1], Xiaojiang Sun[1], Yuezhen Wang[1], Zhun Wang[1], Qingren Lin[1], Denghu Weng[1], Yaping Xu[1], Weimin Mao[2] [1]*Department of Radiation Oncology, Zhejiang Cancer Hospital, Hangzhou/China,* [2]*Department of Thoracic Surgery, Zhejiang Cancer Hospital, Zhejiang/China*

Background: Dose escalation of thoracic radiation is limited by the occurrence of radiation-induced lung injury (RILI). This study investigated the clinical and dosimetric factors influencing RILI in lung-cancer patients receiving chemoradiotherapy. **Methods:** A retrospective analysis was carried out on 161 patients with non-small-cell or small-cell lung cancer (NSCLC and SCLC, respectively), who underwent chemoradiotherapy between April 2010 and May 2011 with a median follow-up time of 545 days (range: 39–1453). Chemotherapy regimens were based on the histological type (squamous cell carcinoma, adenocarcinoma, or SCLC), and radiotherapy was delivered in 1.8–3.0 Gy fractions, once daily, to a total of 39–66 Gy (median, 60). Univariate analysis was performed to analyze clinical and dosimetric factors associated with RILI. Multivariate analysis using logistic regression identified independent risk factors correlated to RILI. **Results:** The incidence of symptomatic RILI (≥grade 2) was 31.7%. Univariate analysis showed that V5, V20, and mean lung dose (MLD) were significantly associated with RILI incidence (P=0.029, 0.048, and 0.041, respectively). The association was not statistically significant for histological type (NSCLC vs. SCLC, P = .092) or radiation technology (IMRT vs. 3DCRT, P = .095). Multivariate analysis identified MLD as an independent risk factor for symptomatic RILI (OR=1.249, 95%CI=1.055–1.48, P= .01). The incidence of bilateral RILI in cases where the tumor was located unilaterally was 22.7% (32/141) and all dosimetric-parameter values were higher (P< .05) for bilateral versus ipsilateral injury, but only for grade-1 (low) RILI. The RILI grade was higher in cases of ipsilateral lung injury than in bilateral cases (Mann-Whitney U test, z=8.216, P< .001). **Conclusion:** The dosimetric parameter, MLD, was found to be an independent predictive factor for RILI. Contralateral injury does not seem to be correlated with increased RILI grade under the condition of conventional radiotherapy treatment planning. **Keywords:** radiation induced lung injury, lung cancer, mean lung dose

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-027 Lung Cancer: Doses to Mediastinal Structures Can Be Reduced with Volumetric Modulated Arc Therapy and Deep Inspiration Breath-Hold Radiotherapy Gitte F. Persson[1], Jonas S. Rydhög[1], Marianne C. Aznar[1], Maja V. Maraldo[1], Lotte Nygård[1], Junia Costa[2], Anne K. Berthelsen[2], Lena Specht[1], Mirjana Josipovic[1] [1]*Department of Oncology, Rigshospitalet Copenhagen University Hospital, Copenhagen/Denmark,* [2]*Department of Clinical Physiology, Nuclear Medicine and Pet, Rigshospitalet Copenhagen University Hospital, Copenhagen/Denmark*

Background: When thoracic radiotherapy (RT) doses are escalated, toxicity from mediastinal structures are a limiting factor (Cannon et al. JCO 2013). In this study we examined, if deep inspiration breath-hold (DIBH) combined with volumetric modulated arc therapy (VMAT) can decrease the dose to lungs, heart, central bronchi and esophagus compared to free breathing (FB) RT. **Methods:** 17 patients with stage III NSCLC were CT scanned in both FB (4DCT) and visually guided voluntary DIBH before radical RT. Lungs, heart, central bronchi, trachea, esophagus and heart subvolumes (coronary arteries and valves) were contoured. Three dimensional conformal (3DC) and VMAT plans were computed on FB and DIBH images. VMAT plans were optimized using constraints for target and lungs. DIBH plans were compared to FB plans. Friedman signed rank test with post-hoc Nemenyi test was applied. **Results:** GTV sizes were slightly smaller in DIBH (mean 119 vs. 132 ml, p=0.01). Lung volume increased in DIBH by median 60% (range 35-108%, p<0.0001) compared to FB. Median and range of dose parameters are listed in the table together with Friedman signed rank test p-values. Mean lung dose was in DIBH reduced with a median 3.2 Gy (p=0.002) with 3DC and 3.5 Gy (p<0.001) with VMAT. DIBH alone did not significantly alter heart, esophagus and trachea-bronchial dose parameters, but VMAT did. The largest differences were found between FB 3DC and DIBH VMAT. Mean doses to coronary arteries, tricuspid and pulmonary valves were significantly reduced with DIBH VMAT compared to FB 3DC (P=0.002-0.04). No differences were found for aortic and mitral valves.

	FB 3DC	DIBH 3DC	FB VMAT	DIBH VMAT	P-value
Lung:					
V5 (%)	55 (29-79)	43 (25-72)	68 (40-89)	56 (34-74)	<0.0001
V20 (%)	27 (17-40)	23 (13-34)	26 (15-39)	21 (11-31)	<0.0001
Mean dose (Gy)	18 (9-22)	14 (7-21)	16 (9-20)	12 (7-19)	<0.0001
Heart:					
V5 (%)	31 (2-100)	21 (0-93)	37 (2-100)	26 (0-100)	0.0858
V30 (%)	4 (0-29)	4 (0-29)	1 (0-9)	1 (0-10)	<0.0001
Mean dose (Gy)	10 (1-29)	8 (1-29)	9 (1-20)	6 (1-21)	<0.0001
Esophagus:					
V50 (%)	38 (0-55)	32 (10-52)	20 (0-34)	13 (0-29)	<0.0001
Mean dose (Gy)	31 (12-40)	26 (15-38)	23 (10-30)	20 (11-27)	<0.0001
Trachea:					
Mean dose (Gy)	41 (1-49)	38 (1-55)	33 (1-45)	29 (1-40)	<0.0001
Bronchi:					
V60 (%)	68 (15-98)	62 (18-96)	60 (3-85)	51 (7-74)	<0.0001
Mean dose (Gy)	53 (29-66)	52 (25-65)	54 (19-63)	49 (21-60)	<0.0001

Median (range)

Conclusion: DIBH VMAT decreased the estimated mean doses to heart, lungs, esophagus and bronchii compared to FB 3DC. Possibly, the dose to these structures could be further reduced, had the mediastinal structures been included in the VMAT optimization process. Combining DIBH and VMAT may facilitate dose escalation to target volumes or subvolumes, without decreasing mediastinal toxicity compared to current standard, FB RT. **Keywords:** Breathhold, VMAT, Radiotherapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-028 High Dose Rate (HDR) Dual Intraluminal Brachytherapy Catheter in Treatment of Bilateral Endobronchial Tumor Progression: A Case Report
Larry Ladi[1], John Grecula[2], Eric Allan[2], Shaheen Islam[1] [1]*Pulmonary, Allergy, Critical Care, and Sleep Medicine, The Ohio State University-Wexner Medical Center, Columbus/OH/United States of America,* [2]*Radiation Oncology, The Ohio State University-Wexner Medical Center, Columbus/United States of America*

Background: While radiation therapy is used for locoregional disease with a curative intent, the use of brachytherapy is one method of delivering a higher radiation dose to endobronchial tumor while sparing the surrounding normal tissues. Although commonly done with a single catheter we report on the simultaneous use of dual HDR-intraluminal brachytherapy catheters **Methods:** CASE PRESENTATION: We report a case of a 71-year-old gentleman with history of squamous cell carcinoma of left lung, status post left upper lobe resection in March, 2012. He developed biopsy proven,left mainstem recurrence in April, 2014 which was treated with concurrent chemoradiation (63 Gy/ 35 tx). In January, 2015, he was referred to interventional pulmonary clinic for bronchoscopy revealing extension of tumor involving carina and proximal 2 cm of both left and right mainstem bronchi (Fig.1) Biopsy demonstrated squamous cell carcinoma. He underwent rigid bronchoscopy with tumor debulking using Nd:YAG laser. He was than referred to radiation oncology for HDR-brachytherapy. Since both main stem bronchi were involved a decision was made to place two catheter to radiate both sides simultaneously. The patient was intubated with an 8.0 endotracheal tube and two brachytherapy catheters were placed into the left and right mainstem bronchus respectively under general anesthesia (Fig.2). The length and patency of the catheters were manually checked. The guidewire was removed from the catheters and replaced with the dummy source cables (Fig.3). A dose plan was then created to irradiate the proximal 5 cm of both the right and left mainstem bronchi and carina with a dose of 750cGy prescribed at 1 cm from the source. The computer was programmed to irradiate the above area (Fig.4). The catheters were connected to the high dose rate afterloader. A dose of 750 cGy at 1 cm from the source was delivered over actual time 466.2 seconds with the high activity (4.33 Ci) Ir-192 source (nominal treatment time = 201.6 seconds). Two additional weekly treatments of 750 cGy to the above area is planned. **Results:** DISCUSSION: Central airway obstruction worsens the quality of life in lung cancer patients. When surgical resection is not plausible, HDR-brachytherapy is effective in palliating dyspnea. Hennequin C, et al treated 106 patients with endobronchial lung cancer with HDR-bachytherapy which consisted of six fractions of 5 or 7 Gy, who were not eligible for surgery or external beam radiotherapy, and had relapse after surgery or external beam radiotherapy or respiratory insufficiency. The histologic response rate, evaluated at 3 months after HDR-brachytherapy, was 59.4% [1]. In our patient, given the bilaterality of tumor progression, routine HDR-intraluminal brachytherapy would have required our patient to undergo unilateral treatment separately in multiple sessions and may have resulted in overlap of the brachytherapy isodoses. By planning the bilateral HDR-intraluminal brachytherapy catheters simultaneous, the risk of future overlap is avoided, and the overall treatment interval is reduced in half **Conclusion:** CONCLUSION: Here we demonstrate the concomitant use of two intraluminal brachytherapy catheters placed in separate bronchi decreased the overall treatment interval. Future studies need to be conducted to evaluate efficacy. **Keywords:** lung cancer, brachytherapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-029 No Inferior Outcomes after Stereotactic Radiotherapy for Stage I and II NSCLC Compared with Surgery
Elisabeth A. Kastelijn[1], Sherif El Sharouni[2], Frederik Hofman[3], Bart Van Putte[3], Evelyn Monninkhof[4], Marco Van Vulpen[2], Franz Schramel[1] [1]*Department of Pulmonology, St. Antonius Hospital, Nieuwegein/ Netherlands,* [2]*Department of Radiotherapy, University Medical Centre Utrecht, Utrecht/ Netherlands,* [3]*Department of Cardiothoracic Surgery, St. Antonius Hospital, Nieuwegein/ Netherlands,* [4]*Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht/ Netherlands*

Background: Surgical resection is the treatment of first choice for patients who are diagnosed with stage I and II non-small cell lung cancer (NSCLC). However, last years, stereotactic body radiotherapy (SBRT) has shown to be a good alternative treatment, especially for the elderly or for patients with a poor pulmonary function. We compared the overall survival (OS), progression free survival (PFS) and locoregional and distant recurrence between patients with stage I and II NSCLC treated with SBRT or surgery. **Methods:** Patients who were diagnosed with stage I and II NSCLC between 2008 and 2011 and treated with SBRT or surgery were included. Crude survival and recurrence rates in both groups were evaluated and compared by Kaplan-Meier survival and Cox proportional hazard analyses. Since the selection of treatment is influenced by patients characteristics, we used the propensity score method to account for this bias. Propensity scores were estimated by a logistic regression model that included treatment as dependent variable and age, gender, performance status, FEV_1, DLCO, nodule diameter and clinical TNM classification as independent variable. The propensity score was added as covariate to Cox proportional hazard analyses to adjust the outcome for patient characteristics. **Results:** The cohort treated with SBRT and surgery consisted of 53 and 175 patients, respectively. Before adjustment for the propensity score, the OS at 1 and 3 years after SBRT was 87% and 43% and after surgery 89% and 70% (HR = 2.42, 95% CI 1.65 – 3.56; p = 0.0001). The PFS at 1 and 3 years was 72% and 39% after SBRT and 80% and 60% after surgery (HR = 2.07; 95% CI 1.43 – 2.99; p = 0.0001). The locoregional recurrence rates at 1 year after SBRT and surgery were 94% and 95% and at 3 years for both 85% (HR = 1.43 ; 95% CI = 0.60 – 3.43; p = 0.42). The distant recurrence rates at 1 and 3 years after SBRT were 73% and 62% and after surgery 88% and 74% (HR = 1.67; 95% CI = 0.96 – 3.92; p = 0.07). After adjustment for the propensity score, the OS and PFS after SBRT were not significantly different compared with surgery (HR = 1.71, 95% CI 0.87 – 3.35; p = 0.12 respectively HR = 1.56; 95% CI 0.83 – 2.93; p = 0.17). The locoregional and distant recurrence rates between SBRT and surgery were also not significantly different (HR = 2.11; 95% CI = 0.56 – 7.75; p = 0.26 respectively HR = 1.24; 95% CI = 0.48 – 3.20; p = 0.65). **Conclusion:** This study shows that, after adjustment for the propensity score, the OS, PFS and recurrence rates after SBRT are not inferior compared with surgery in patients with stage I and II NSCLC. Although, we used the propensity score to reduce the effects of confounding by indication, randomized clinical trials are desired. Due to the lack of these trials, a thorough discussion of the patient individual merits and drawbacks of surgery and SBRT should be the cornerstone of the treatment. **Keywords:** NSCLC, stereotactic radiotherapy, Surgery, outcome

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-030 Evaluation of the Functional Heart Condition During Radiotherapy for Lung Cancer
Yury Ragulin[1], Vladimir Parshin[2], Elena Kozlova[2], Nina Dvuchsherstnova[2] [1]*Thoracic Department, Medical Radiological Research Center, Obninsk/ Russian Federation,* [2]*Diagnostic Department, Medical Radiological Research Center, Obninsk/Russian Federation*

Background: Alterations in cardiac function appearing immediately during radiation therapy for lung cancer are insufficiently studied. It is necessary to continue studying alterations in left ventricular systolic and diastolic function arising during radiotherapy for lung cancer to prevent other complications. We aimed to study the functional state of the left ventricle during radiotherapy for lung cancer. **Methods:** The study included 39 patients with lung cancer. Irradiation was performed with a total radiation dose (TRD) of 60 Gy and a single radiation dose (SRD) of 1+1.5 Gy delivered from two different treatment fields. Initial echocardiographic examinations were carried out before starting radiotherapy in order to assess the functional state of the heart. Subsequently, the patients were followed up during radiotherapy with TRD of 20 Gy, 40 Gy, and 60 Gy. The following parameters were evaluated: left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV), stroke volume (SV), ejection fraction (EF), ratio of early and late diastolic filling rates of the left ventricle (E/A), motion rate of the lateral part of the fibrous ring of the mitral valve in early diastole (E a), motion rate of the lateral part of the fibrous ring of the mitral valve in late diastole (A a), ratio of motion rates of the lateral part of the fibrous ring of the mitral valve in early and late diastole (E a/ A a). **Results:** At dose 20 Gy, left ventricular end diastolic volume decreased by 13%, and at TRD of 60 Gy – by 20%. At TRD of 20 Gy, left ventricular end systolic volume was altered by 9%, and at TRD of 60 Gy – by 14%. At TRD of 20 Gy, stroke volume decreased by 16%, and at TRD of 60 Gy – by 32% compared to the initial level. At TRD of 20 Gy, the ejection fraction decreased by 9 %, and at TRD of 60 Gy – by 23%. The parameters of left ventricular diastolic function were found to be reduced as well. At TRD of 20 Gy, the ratio of filling rates of the left ventricle in early and late diastole decreased by 4% and at TRD of 60 Gy – by 18%. At TRD of 20 Gy, the motion rate of the lateral part of the fibrous ring of the mitral valve in early diastole decreased by 10% and at TRD of 60 Gy – by 20%. At TRD of 20 Gy, the ratio of motion rates of the lateral part of the fibrous ring of the mitral valve in early and late diastoles decreased by 12%, and at TRD of 60 Gy – by 21%. Thus, an increase in radiation dose led to a decrease in left ventricular systolic and diastolic function. **Conclusion:** Radiation therapy for lung cancer significantly alters left

ventricular systolic and diastolic function. Increased radiation doses cause the growth in the number of altered parameters. **Keywords:** echocardiography, lung cancer, Radiotherapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-031 Predictors of Radiation Pneumonitis and Associated Changes of Pulmonary Function After Definitive Concurrent Chemoradiotherapy in NSCLC
Jae-Sung Kim[1], Young Hee Park[2] [1]*Radiation Oncology, Seoul National University Bundang Hospital, Seongnam/Korea,* [2]*Radiation Oncology, Seoul National University Hospital, Seoul/Korea*

Background: To evaluate the predictive factors of radiation pneumonitis (RP) and associated changes of pulmonary function after definitive concurrent chemoradiotherapy (CCRT) in patients with NSCLC **Methods:** Medical records of 61 patients with NSCLC who received definitive CCRT at Seoul National University Bundang Hospital were retrospectively reviewed. Dose volumetric parameters, clinical factors, pulmonary function test (PFT) data were analyzed. RP was graded according to the Common Terminology Criteria for Adverse Events v3.0. Percentage of lung volume that received a dose of 10 Gy or more (V10), 20 Gy or more (V20), 30 Gy or more (V30), mean lung dose (MLD) were analyzed for potential dose volumetric (DV) parameters. PFT changes were calculated as the difference between pre-RT and post-RT values compared to the pre-RT values at 3, 6, 12 months after RT. Tumor location was categorized two groups, upper (including middle) and lower lobe. **Results:** The overall and progression-free survival time were 21.9 month and 10.6 months. Twenty-three patients (38%) developed grade≥2 RP. Among clinical factors, underlying chronic obstructive pulmonary disease was associated with RP (p=0.050) but not with grade ≥2 RP (p=0.871). Tumor located at lower lobe was associated with grade ≥2 RP (p=0.002). Among the DV parameters, only MLD > 15 Gy was associated with grade ≥2 RP (p=0.009). There were statistically significant decreases in PFT values at all points compared with pre-RT values. MLD was associated with magnitude of forced vital capacity (FVC) changes at 6/12 months (p=0.006/0.016) and forced expiratory volume in 1 s (FEV1) changes at 6 months (p=0.005). V10 and V20 were associated with FVC changes at 12 months (p=0.048/0.025) and V30 was associated with diffusion capacity for carbon monoxide changes at 6 months (p=0.023). **Conclusion:** MLD > 15 Gy and lower lobe tumor were predictors of grade ≥2 RP. Pulmonary functions were decreased after CCRT and the magnitude of change was associated with DV parameters. **Keywords:** Non-small cell lung cancer, Radiation pneumonitis, Dose volumetric parameter, Pulmonary function

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.03-032 MD Anderson Oncology Expert Advisor™: A Cognitive Clinical Decision Support Tool for Evidence-Based Multi-Disciplinary Lung Cancer Care
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Background: The majority of patients diagnosed with non-small cell lung cancer (NSCLC) receive care in the community setting with limited access to multidisciplinary management common in tertiary care centers. The availability of genomics allows tailored treatments for patients; and with novel, rapidly emerging therapeutic options, it is challenging for busy clinicians to maintain familiarity with current therapy recommendations. Therefore, to empower practicing oncologists in community settings to offer the optimal management at the first intervention, we have developed the MD Anderson Oncology Expert Advisor™ (OEA) application for multi-disciplinary management of lung cancer patients. As the first multi-disciplinary solution for providing comprehensive management of lung cancer, the objective of OEA™ Lung is to leverage cognitive analytics on vast and ever evolving clinical care information and patient big data to disseminate knowledge and expertise, thus enabling physicians to provide evidence-based care and management tailored for the individual patient, similar to consulting an expert. Further, we aimed to create a system for sharing knowledge from more experienced experts to provide care pathways and management recommendations for physicians globally. **Methods:** Using cognitive computing, our cancer center partnered with IBM Watson to develop an expert system designed to provide physicians with the tools needed to process high-volume patient and medical information and to stay up-to-date with the latest treatment and management options, so that they can make the best evidence-based treatment decisions for their lung cancer patients. The OEA™ application for lung was built upon core capabilities of the OEA™ applications for leukemia and molecular/targeted therapies. Experts in multiple disciplines including thoracic surgery, medical oncology, and radiation oncology met regularly to design and provide specialized input to the IBM technical team in an agile development cycle. This system was powered to utilize both structured and unstructured data from validated sources; to thoroughly evaluate and stage patients; and to offer eligible clinical trials and personalized therapeutic options. In addition to delivering evidence-based, weighted therapy recommendations, OEA™ Lung provides care pathways for management of toxicities for each treatment modality (surgery, radiation, and medical oncology). **Results:** The OEA™ Lung application supports three core functions: 1) dynamic patient summary assimilating complete (structured and unstructured) data to show demographics, labs, genotype, treatment history, and previous treatment responses; 2) weighted evidence-based, multimodality treatment options, with recommendations based on literature support which is provided, along with screening for relevant trials; 3) care pathway advisories, to manage treatment related toxicities for each modality. Further, this product improves quality of care by optimizing outcomes with access to trials and care pathways. **Conclusion:** The OEA™ application for lung is a cognitive expert system designed to assimilate multidisciplinary recommendations for care and management of lung cancer patients based on current consensus guidelines and expert recommendations from a quaternary referral cancer center to the community practice setting. By democratizing knowledge from our specialty cancer center, we have taken steps toward achieving an important goal of ending cancer for all, by providing global access to optimal cancer care for patients with this disease. Further evaluation of outcomes following implementation are warranted. **Keywords:** NSCLC, Multidisciplinary Care, Cognitive Computing, care pathways

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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P3.03-033 Management of Clinical T3-4 Locally Advanced Non-Small-Cell Lung Cancer
Naoya Yamasaki, Tomoshi Tsuchiya, Keitaro Matsumoto, Takuro Miyazaki, Daisuke Taniguchi, Katsunori Takagi, Tomohiro Obata, Koichiro Shimoyama, Takeshi Nagayasu *Surgical Oncology, Nagasaki University, Nagasaki/Japan*

Background: Several studies of trimodality therapy for locally advanced lung cancer invvasing neighboring structures including SST were reported. They resulted in high rates of pathological complete response and better survival than previous reports. The aim of this study was to retrospectively review our experience of patients for clinical T3-T4 lung cancer. **Methods:** Between January 2000 and March 2014, 52 patients underwent surgical complete resection for locally advanced clinical T3-T4 non-small cell lung cancer. Also, we are conducting a phase II trial from 2011 to evaluate induction chemoradiotherapy using cisplatin and TS-1 combined concurrent radiotherapy (40Gy) followed by surgery would improve the survival of these patients. The extent of chest wall involvement was limited to the parietal pleura, pm1 (T3 in the same lobe) and pm2 (T4 in another lobe beyond the interlobe) were excluded in this study. Patients were divided into three groups. In the initial surgery group (IS group, n=35), patients underwent surgery without induction therapy. In the chemotherapy group (CT group, n=4), patients were received chemotherapy followed by surgery, and in chemoradiotehrapy group (CRT group, n=13), patient were received chemoradiotherapy followed by surgery. **Results:** The median age was 64 years old (range, 41-83). Patients with T3 were in 42 (chest wall: n=30, pericardium: n=5, diaphragm: n=4, main bronchus: n=3), and with T4 were in 10 (left atrium: n=2, carina: n=2, vertebra: n=2, esophagus: n=1, subclavian artery: n=1, superior vena cava: n=1, mediastinal fat: n=1), respectively. The histological types included 21 squamous cell carcinoma, 16 adenocarcinoma, 4 large cell carcinoma, 4 pleomorphic carcinoma, and 7 other types. All patients underwent complete resection. The 3- and 5-year overall survival rate was 61.5% and 17.5%, respectively in this series. The 3-and 5-year survival rate in patients with T3 was 65.3%, 20.8%, while that with T4 was 48.0%, 0%, respectively. There was no significant difference in survival rate between them (p=0.1454). The prognosis in the N0 disease was significant better than N1-2 disease (p=0.0073). Multivariate analysis showed N0 disease was independent factor of a favorable prognosis (p=0.046). In the CRT group, patients with T3 disease was in 9, and T4 in 4. Induction therapy was completed in all 13 candidates (100%), and 5 (38%) had a complete response, 8(62%) had a partial response in the pathological examinations. The 3-year survival rate in the CRT group was 69.2%. The prognosis in the CRT group was better than the IS plus CT group, but there was no significant difference between the group. Although there were no locoregional recurrences after surgery in the CRT group, 4 patients experienced major postoperative complications and 1 patient who underwent combined resection of both chest wall and superior vena cava with reconstruction by artificial materials died of septic shock. **Conclusion:** Multimodality therapy consisted of 2 cycle chemotherapy with concurrent 40 Gy of radiation for clinical T3-4 locally advanced lung cancer showed be feasible and good local control. However, the criteria for selecting patients should be mature, especially patients using artificial material. **Keywords:** locally advanced non-small cell lung cancer, Surgery, induction therapy

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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P3.03-034 Utility of Surveillance Imaging in Detection of Recurrence in Treated Stage III NSCLC Patients
Omid S. Tehrani[1], Antoinette Wozniak[2], Peter Paximadis[2], Laura Mantha[2], Judith Abrams[2], Ann G. Schwartz[2], Michele L. Cote[2], Gerold Bepler[2], Shirish Gadgeel[2] [1]*University of California San Francisco, Fresno/CA/United States of America,* [2]*Wayne State University/Karmanos Cancer Institute, Detroit/MI/United States of America*

Background: About a third of newly diagnosed NSCLC patients have stage III disease at diagnosis, of whom, a quarter achieve long term survival. The current recommendation of National Comprehensive Cancer Network (NCCN) for surveillance following completion of therapy is to perform CT scan of the chest every 6-12 months for 2 years. However, it is unclear if strategy of surveillance scans is superior in detecting recurrences as compared to the strategy of scans done for symptoms suggestive of disease progression. We conducted a retrospective analysis of stage III NSCLC at our institution to estimate the rate of detection of recurrence in scans performed for symptomatic worsening, in patients on surveillance scans. **Methods:** This study is a

single institutional, retrospective, review utilizing the Karmanos Cancer Institute lung cancer database established in 2010. Inclusion criteria: stage III lung cancer patients who had completed therapy and who were treated between 2011 and 2013. Exclusion criteria: inadequate documentation and those who were not eligible for treatment based on clinician or patient preference. Patients were followed until progression or last assessment. The primary objective was to estimate the percentage of patients who had documented tumor recurrence on a surveillance scan. **Results:** Fifty four patients met the eligibility criteria. Mean age was 61 years (40-80), 34% were males; 44% were Caucasians and 39% were African-Americans; 85% were current or former smokers. Histology at diagnosis was adenocarcinoma in 67% and squamous cell in 31%, the remaining were large cell and poorly differentiated. Thirty-seven (69%) patients received chemotherapy and radiation, 12 (22%) received surgery with chemotherapy and radiation, and 5 (9%) received surgery and chemotherapy. The median follow up following completion of treatment was 18 months. Eighteen (33%) patients have had disease recurrence, with 11 (20%) recurrences within 1 year following completion of therapy. Of all 18 patients with recurrences, 17 (98%) were detected on surveillance scans. Only 1 (2%; 95% CI: 0-10%) recurrence was detected on scans obtained for worsening symptoms. **Conclusion:** In this retrospective analysis in stage III NSCLC patients who had completed therapy, except one case, all of the recurrences were detected on surveillance scans, strongly suggesting that routine surveillance scans provide clinical utility. **Keywords:** Stage-III NSCLC, lung cancer, follow up imaging, follow up post treatment

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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P3.03-035 Unclear Clinical Course and Treatment Options for Clear Cell Lung Cancer: A Case Series Muhammad K. Riaz, David Mosko, Jiang Wang, Nagla A. Karim
University of Cincinnati Medical Center, Cincinnati/OH/United States of America

Background: Clear cell lung cancer (CCLC) is an extremely rare variant of lung tumors which was first described by Liebow and Castleman in 1963. It has vague natural history with slight female predominance and is most often seen in elderly. The clear appearance results from intracellular accumulation of glycogen in absence of mucus production. Because of the rarity of this disease, clinical course and treatment options are not well established. Here we describe a case series of 4 patients of clear cell adenocarcinoma and highlight these aspects. **Methods:** We reviewed the charts, pathological diagnosis and imaging studies of 4 rare cases of clear cell adenocarcinoma of the lung that were encountered over the past 5 years at the University of Cincinnati Medical Center. **Case1:** 61 yo F smoker presented with new onset hemoptysis and unintentional weight loss. CT scan revealed 7.2cm lung mass with endobronchial extension. This was followed by biopsy and the pathology revealed poorly differentiated CCLC. She was started on definitive chemoradiotherapy but, just after a month of completing treatment, she developed brain metastasis. **Case2:** 52 yo F smoker had workup for unintentional weight loss and CT scan revealed 1.4cm spiculated nodule. She underwent Video-assisted thoracoscopic surgery (VATS) and pathology confirmed high grade CCLC without lymphovascular or perineural invasion. She was managed conservatively. **Case3:** 71 yo F smoker had CT chest which showed a 2.2cm nodule. Because FNA was equivocal she underwent VATS and pathology showed clear cell adenocarcinoma without evidence of metastasis. No adjuvant therapy was offered. **Case4:** 74 yo F with history of Orthotopic heart transplantation had a CT scan which incidentally showed 4cm nodule which turned out to be an adenocarcinoma on biopsy. She underwent VATS and pathology was consistent with clear cell adenocarcinoma without evidence of infiltration. Her post-op course was complicated by infection and she passed away. **Results:** Clear cell features are cytologic changes that occur in association with adenocarcinoma or large cell carcinoma per WHO classification. Our 4 cases were all clear cell adenocarcinoma of the lung confirmed by immunohistochemistry. Immunostains were positive for CAM5.2, TTF-1 and CK7 and negative for CK20, p63, S-100 and PAX-8. Case1 and case2 highlights the lack of established treatment guidelines for CCLC. Currently, same chemotherapy regimens are used as for non-clear cell adenocarcinoma. One study reported KRAS as driver mutation, which, if established, could lead to future therapeutic options. Case3 showed that small biopsies could be insufficient for diagnosis of CCLC. Case4 questions if these lesions could be followed without surgery in high-risk patients to avoid unnecessary morbidity and mortality. Finally, clear cell carcinoma of renal, endometrium and ovarian origin should be considered before making the final diagnosis of CCLC. **Conclusion:** CCLC is a rare tumor and more studies are needed to establish management and guidelines. Genetic mutations could be potential therapeutic targets. Risks and benefits of treatment should be considered in high-risk patients. **Keywords:** Clear cell, Adenocarcinoma, lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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P3.03-036 PET for Prognostic Assessment in Patients with Unresectable Stage III Non-Small Cell Lung Cancer Treated with Concurrent Chemoradiotherapy Ufuk Yilmaz[1], Zehra Asuk[2], Hakan Koparal[3], Engin Ozbilek[3], Esra Korkmaz[4], Burcu Yalcın[1], Hasan Yilmaz[4] [1]*Pulmonary Medicine, Izmir, Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital, Izmir/Turkey,* [2]*Pulmonary Medicine, Abant Izzet Baysal University School of Medicine, Bolu/Turkey,* [3]*Nuclear Medicine, Izmir, Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital, Izmir/Turkey,* [4]*Radiation Oncology, Izmir, Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital, Izmir/Turkey*

Background: Concurrent chemoradiotherapy is the standard of care for locally advanced, unresectable non-small cell lung carcinoma(NSCLC). The study purpose was to assess the prognostic value of maximum standardized uptake values (SUV max) from FDG PET/CT for stage III NSCLC. **Methods:** This study included 61 patients with unresectable stage III NSCLC treated with concurrent thoracic radiotherapy (63Gy) given with cisplatin and etoposide. 18F-FDG PET/CT scans were obtained from all patients within 45 days before treatment. The prognostic value of SUVmax of the primary tumors were analyzed with univariate Cox regression. Survival was estimated using the Kaplan–Meier method **Results:** The median age of the patients was 56 years (range 40–71). The median follow-up time was 20 months (range 1.4–81 months). The median SUVmax of the tumor (15.0) was decided as the cutoff value, and the impact of the SUVmax on survival was statistically evaluated according to this cutoff value. There was no a statistically significant difference in overall survival (OS) between the low (≤15) and high (>15) SUVmax groups (p = 0.006) upon univariate analysis (p=0.403). **Conclusion:** SUV max of the primary tumor did not predicted overall survival in patients with unresectable stage III NSCLC treated with concurrent chemotherapy and radiotherapy **Keywords:** SUV, PET/CT, lung cancer, Prognosis

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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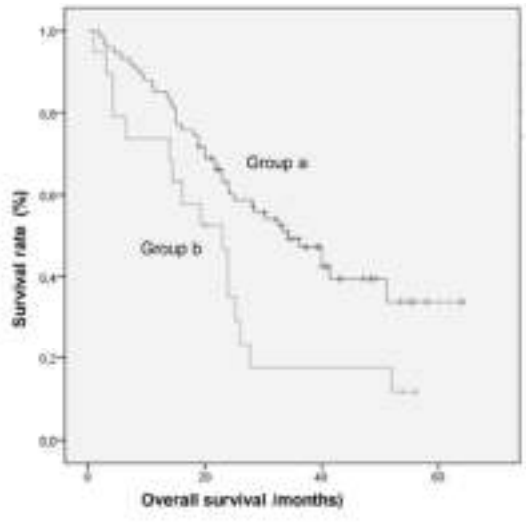
P3.03-037 High Pretreatment Neutrophil-Lymphocyte Ratio: A Poor Prognostic Factor for Stage III Non-Small Cell Lung Cancer Patients Ahmet T. Sumbul[1], Celal Batmacı[2], Edip Ucar[2], Fatih Kose[1], Ali M. Sedef[1], Berna Yildirim[3], Huseyin Mertsoylu[1], Ahmet Sezer[1], Ozgur Ozyilkan[1] [1]*Medical Oncology, Baskent University, Adana,/ Turkey,* [2]*Mustafa Kemal University, Hatay/Turkey,* [3]*Radiation Oncology, Baskent University, Adana,/Turkey*

Background: Smoldering inflammation induced by tumor tissue form cytokine enrich environment which increase tumor growth potential significantly. Neutrophil-Lymphocyte ratio (N/L) has been reported as a valuable indicator for tumor induced systemic inflammation in literature. With this study, we aimed to evaluate potential prognostic role of pretreatment N/L ratio in locally advanced NSCLC patients those who were treated with curative chemoradiotherapy. **Methods:** Stage III 97 NSCLC patients were included into this study. Demographic characteristics of patients and well defined clinic and histopathological prognostic factors of their tumors were recorded. There is no clear delineated cut off value for N/L ratio in literature; first, we performed ROC curve statistical analysis. Our statistical analysis showed cut off level of 4.26 ED with high sensitivity and specifity. We used Kaplan-Meier survival curve and log-rank test (p<0.05) for survival analysis. **Results:**



Median age was 58 years old (range 39-75), and 87 (89.7%) of the patients were men. ECOG performance score was 0-1 in 93 patients (95.9%). Squamous histology, most common histology, was diagnosed in 46 patients (47.4%). Number of Stage IIIA and IIIB patients 41(42.3%) and were 56 (57.7%), respectively. Objective response rate (CR+PR) and clinical benefit rate (CR+PR+SD) were 75.3% and 83.5%, respectively. Median follow-up time was 23.8 months (range 0.9-60). Median PFS and OS were 10.3 ([(95%CIs), 9.2-11.5) and 17.8 months ([(95%CIs), 11.4-24.4]. When we evaluate 61 (62.8%) patients those who relapsed, distant and local relapse rate were found as 57.1 and 42.9 %, respectively. When the patients were grouped through N/L ratio, below (group a) or upper (group b) the cut-off value (4.26 ED), there was a statistically significant difference between these groups, group a and group b, PFS and OS; 15.2 vs 8.1, 34 vs 23 months, respectively (p<0.005). **Conclusion:** Prognostic and predictive markers are major tools for oncologist to make decision making process. With this study, our results proved that pretreatment N/L ratio, marker for the systemic inflammation, may be used as a prognostic marker for the local advanced stage III NSCLC patients. **Keywords:** neutrophil/lymphocyte ratio, inflammation, prognosis, lung cancer

POSTER SESSION/ TREATMENT OF LOCOREGIONAL DISEASE – NSCLC
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P3.03-038 A Multi-Center Trial Comparing Standard 22-Gauge and 22-Gauge Bibevel (ProCore) Needles for Endobronchial Ultrasound Nichole T. Tanner[1], Paul Nietert[2], Jason Akulian[3], Lonny Yarmus[4], Jack Yang[5], Leslie Dodd[6], Peter B. Illei[7], Arnold Schwartz[8], Gerard Silvestri[1] [1]*Medicine, Medical University of South Carolina, Charleston/SC/United States of America,* [2]*Public Health Sciences, Medical University of South Carolina, Charleston/SC/United States of America,* [3]*University of North Carolina, Chapel Hill/NC/United States of America,* [4]*Johns Hopkins University, Baltimore/MD/ United States of America,* [5]*Pathology, Medical University of South Carolina, Charleston/ SC/United States of America,* [6]*Pathology, University of North Carolina, Chapel Hill/NC/ United States of America,* [7]*Pathology, Johns Hopkins University, Baltimore/United States of America,* [8]*Pathology, George Washington University, Washington Dc/DC/United States of America*

Background: Endobronchial ultrasound fine needle aspiration (EBUS-FNA) is recommended as the first tissue sampling procedure for the staging and diagnosis of known or suspected lung cancer. With the advent of targeted agents for lung cancer therapy, there is an increasing demand to extend EBUS-FNA samples for molecular testing. While it has been shown to be adequate for EGFR mutational analysis in 77-96% of samples, as new discoveries are made the challenge is to obtain enough quality tissue via EBUS-FNA. Bibevel (ProCore) needle technology used during endoscopic ultrasound (EUS) procedures has been shown to provide larger samples of tissue for histologic diagnosis of gastrointestinal malignancies. This same needle technology may also provide more tissue during EBUS to allow for better histologic and molecular analysis than standard EBUS-FNA. The goal of this study is to determine the utility of the 22-gauge (G) ProCore EBUS needle by comparing it to standard single bevel 22G EBUS needles. **Methods:** This multicenter randomized trial will enroll 200 patients with known or suspected lung cancer during standard of care diagnostic/staging EBUS. A maximum of two lymph nodes (pathologic in size (>1cm) and/or hypermetabolic on PET/CT) will be included in the comparison. A total of 8 passes will be taken from each node (4 from the bibevel needle, 4 from standard) and cell blocks compared by a blinded pathologist . The primary outcome is tumor cells per mm^2. Descriptive statistics will be used to characterize the study subjects and their outcomes with the 2 different needles. For the within-subject (i.e. between needle) comparisons of tumor quantity and ability to perform commercially available immunohistochemical stains and mutational analysis, non-parametric Wilcoxon signed rank tests will be used. Since cell block quality will be quantified as simply which needle's sample provided the better sample, the non-parametric sign test will be used. All hypothesis testing will be 2-sided, using an alpha level of 0.05 **Results:** Forty-one patients from three centers have been enrolled, with 48 lymph nodes sampled. There is an even gender distribution (22 (54%) male, 19 (46%) female). The majority are non-Hispanic white (n=30, 73%). 22 patients have (54%) have a malignant diagnosis, 12 (30%) a benign diagnosis, and 2 (5%) have been non-diagnostic. Minor complications include bleeding at the site in 7 (17%). There have been no major complications. **Conclusion:** Data for the primary outcomes have yet to be analyzed, however the trial design is feasible and thus far the use of two separate needles during EBUS has shown to be safe. **Keywords:** endobronchial ultrasound, molecular analysis, tissue aquisition

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POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-001 Exosomal RNA Based Liquid Biopsy Detection of EML4-ALK in Plasma from NSCLC Patients Kay Brinkmann[1], David P. Carbone[2], Daniel Enderle[1], Tina Koestler[1], Stefan Bentink[1], Jennifer Emenegger[1], Alexandra Spiel[1], Romy Mueller[1], Vince O'Neill[3], Johan Skog[3], Mikkel Noerholm[1] [1]*Exosome Diagnostics Gmbh, Martinsried/ Germany,* [2]*The Ohio State University Medical Center, Columbus/OH/United States of America,* [3]*Exosome Diagnostics Inc., Ma/MA/United States of America*

Background: Molecular profiling to direct targeted therapy has revolutionized cancer treatment. For instance, the tailored therapy of NSCLC patients carrying somatic EML4-ALK rearrangements with ALK inhibitors has shown to be associated with substantial clinical response. A prerequisite of this approach is highly sensitive and specific diagnostics to detect and monitor the prognostic biomarker. Today's tissue-based diagnostics like FISH are limited by complications of biopsy and technical challenges. Therefore, biomarker assessment in plasma circulation would be a valuable alternative to tissue based testing and provide a simple new option for identifying and monitoring EML4-ALK positive NSCLC patients. We previously demonstrated the feasibility of detecting EML4-ALK fusion transcripts in 6 plasma samples from patients known to be positive by tissue FISH testing (the gold standard). Here we present more comprehensive performance characteristics of this diagnostic test analyzing the exosomal expression of EML4-ALK in plasma of NSCLC patients. **Methods:** We developed a diagnostic test to monitor the expression of EML4-ALK fusion transcripts in low-volume plasma samples of lung cancer patients. The Exosome Diagnostics ALK assay comprises column-based isolation of total vesicular RNA from 0.5 – 2.0 ml patient plasma, followed by discrete detection of EML4-ALK variants v1, v2 and v3 via qPCR. Assay quality is confirmed by inclusion of internal and external controls. Following validation on both synthetic and human samples, we monitored variant-specific expression of EML4-ALK in a cohort of more than 20 plasma samples from NSCLC patients. The data was analyzed for concordance with time-matched tissue and aligned with patient's response data. **Results:** Applying our diagnostic test for EML4-ALK fusion variants, we were able to identify the predictive biomarker in exosomal RNA transcripts isolated from patient plasma. We determined the variant-specific expression profile of EML4-ALK fusion transcripts in a cohort of NSCLC patients with high sensitivity and specificity. We observed high concordance of the qPCR-based plasma results with FISH-based tissue information. **Conclusion:** Liquid biopsies represent a low-risk and viable approach to testing for predictive cancer markers in NSCLC patients. Here, we demonstrate the capability of our validated diagnostic test to determine expression of rare EML4-ALK fusion transcripts in plasma as a sensitive alternative to repeat biopsy. Monitoring discrete EML4-ALK fusion variants would enable effective personalized treatment and has clear clinical application. **Keywords:** EML4-ALK, liquid biopsy, RT-qPCR, extracellular vesicles

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-002 Correlation of ALK Status Between FISH and Immunohistochemistry in Lung Cancer: A Multicenter Study of 738 Cases in Argentina Maria Jose Labanca[1], Pablo D. Roitman[1], Erica Rojas Bilbao[2], Lina Marino[3], Gabriel Casas[4], Mercedes L. Dalurzo[1], Paola X. De La Iglesia[1] [1]*Pathology, Hospital Italiano de Buenos Aires, Ciudad Autonoma de Buenos Aires/Argentina,* [2]*Pathology, Instituto de Oncología Angel Roffo Y Hospital Alemán, Ciudad Autónoma de Buenos Aires/ Argentina,* [3]*Pathology, Instituto de Oncología Angel Roffo, Ciudad Autónoma de Buenos Aires/Argentina,* [4]*Pathology, Hospital Alemán, Ciudad Autónoma de Buenos Aires/Argentina*

Background: Anaplastic lymphoma receptor tyrosine kinase (ALK) gene rearrangements are infrequent alterations in lung cancer occurring in approximately 3-6% of non small cell lung carcinomas (NSCLC). ALK status is an important predictive factor in NSCLC, as ALK rearranged tumors have shown sensitivity to Crizotinib treatment. Even though FISH remains the gold standard for assessment of ALK status, it bears some disadvantages such as availability, need for trained personnel and difficult evaluation in some cases. Currently, this tool is the only approved diagnostic test by the FDA to detect ALK rearrangement. Detection of ALK protein by immunohistochemistry (IHC) is a much more affordable and widespread method. The use of new clones and highly sensitive methods have improved the sensitivity, specificity and predictive values of IHC in the assessment of ALK status. **Methods:** We compared ALK rearrangement in 738 consecutive cases from three Reference center's surgical pathology laboratories (Hospital Italiano de Buenos Aires, Instituto de Oncología Angel H. Roffo and Hospital Alemán). They were evaluated by FISH and ultra sensitive IHC. FISH was performed on unstained 4 um formalin-fixed paraffin embedded tumor tissue sections using an ALK break-apart probe set (Vysis LSI ALK Dual Color, Break Apart Rearrangement Probe; Abbott Molecular) and paraffin pretreatment IV reagent kit (Vysis, Abbott Molecular). Assays were performed following the manufacturer's instructions. Positive and negative controls were present in each run. Sections were analyzed by a trained observer under a fluorescence microscope, using appropriate filters. Cases were considered ALK-FISH positive if ≥15% tumor cells showed split red and green signals (separation of 2 diameters or more) and/or single red signals. IHC was performed on an automated Benchmark XT slide stainers, using Ventana anti-ALK D5F3 monoclonal antibody on previously deparaffinized 4um tissue sections. For detection, OptiView DAB IHC Detection Kit and OptiView amplification Kit (Ventana, AZ) was used. Positive and negative controls were present in each run. IHC staining results were interpreted as either negative (weak or no staining present) or positive (strong granular cytoplasmic staining in tumor cells). **Results:** Of 738 cases, 709 were FISH negative and 29 FISH positive (prevalence of ALK rearranged cases 3.92%). Of FISH negative cases, two cases had IHC positive results, and 29 out of 29 FISH positive cases were also IHC positive. For IHC testing, sensitivity was 100%, specificity was 99,71% with a positive predictive value of 93,54% and a negative predictive value of 100%. **Conclusion:** Our results show that IHC has a high sensitivity and specificity to detect ALK rearrangements. Discordant results were unusual, agreeing with the values reported in the literature. While several studies have shown good response to crizotinib in cases with negative FISH and positive IHC, larger studies are needed to validate this association. So far, international guidelines have accepted the use of properly validated IHC as a screening tool in assessing ALK status. **Keywords:** Non small cell lung carcinomas (NSCLC), Fluorescence in situ hybridization (FISH), Anaplastic lymphoma receptor tyrosine kinase (ALK), Immunohistochemistry (IHC)

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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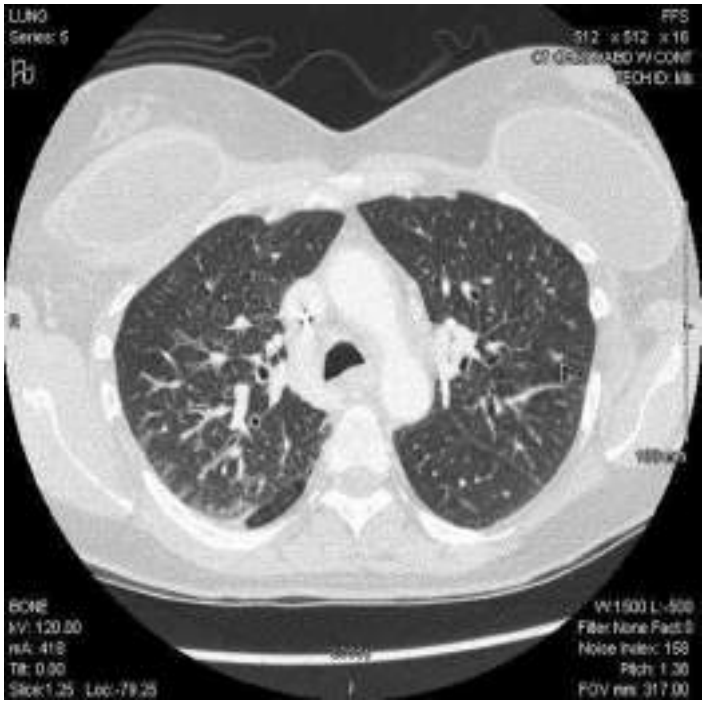
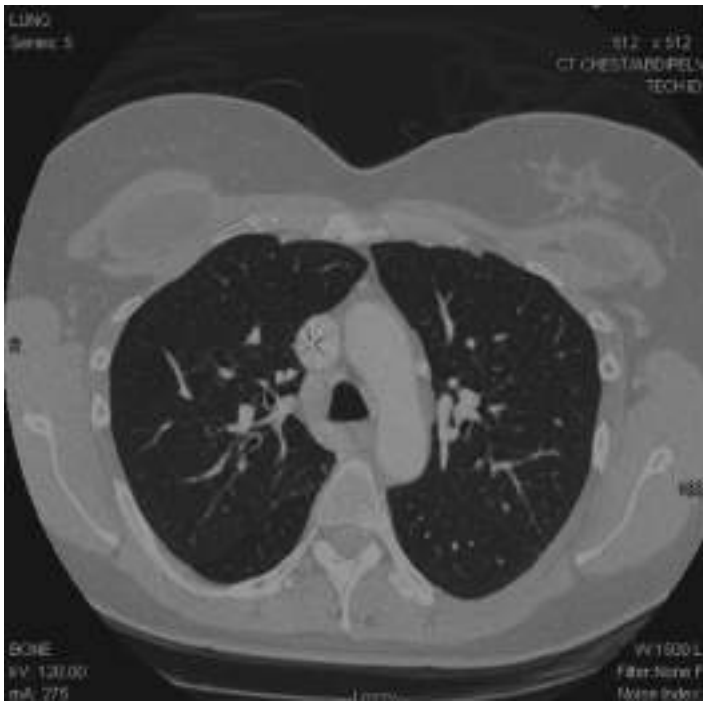
P3.04-003 Novel Fusion Protein ALK-MPRIP Exhibits ALK Activation and Sensitivity to Crizotinib Namrata Shah, Kristina Teso, Katie Zilli, Smitha Menon *Hematology/Oncology, Medical College of Wisconsin, Milwaukee/WI/United States of America*

Background: Rearrangement of the ALK gene is an important therapeutic pathway in NSCLC. EML4 is the partner gene in the vast majority of ALK driven cancers, with other variants rarely reported. The clinical characteristics and sensitivity to ALK targeted agents in patients with non-EML4 variants are unknown. **Methods:** We report a patient case with a novel fusion of ALK-MPRIP (myosin phosphatase-Rho-interacting protein gene). A 49-year-old Caucasian female with less than 10 pack-year smoking history presented with chest pain and dyspnea on exertion. Chest x-ray showed mild CHF. An echocardiogram demonstrated a large pericardial effusion with tamponade physiology. She underwent a pericardial window with cytology of the pericardial fluid demonstrating adenocarcinoma, positive for TTF1 and napsin, consistent with lung primary. CT imaging revealed cervical and mediastinal adenopathy, bilateral pleural effusions, small lung nodules. She was staged as TxN3M1a. She was negative for EGFR and ALK by FISH. Tissue was sent for next generation sequencing due to her light smoking history, which revealed a never before characterized ALK-MPRIP fusion. As the functional significance of this

alteration was unknown, she continued Carboplatin/Pemetrexed/Bevacizumab therapy for 4 cycles followed by 6 cycles of maintenance Pemetrexed/Bevacizumab before documented progression. She was subsequently started on Crizotinib. **Results:** Two months after starting Crizotinib, CT scans demonstrated decreased lung nodules, lymphadenopathy and improved interstitial thickening. After 5 months of treatment CT scans demonstrated new ground glass opacities with increasing bilateral interlobular septal thickening concerning for either Crizotinib-induced lung toxicity or lymphangitic carcinomatosis. Bronchoscopy with transbronchial biopsy demonstrated lymphangitic spread suggestive of progression on Crizotinib within 6 months of therapy. The average PFS of Crizotinib treated EML4-ALK translocated patients is 7.7 months.





Conclusion: ALK-MPRIP is a novel fusion gene causing ALK activation. Our patient responded to Crizotinib but had a shorter than average PFS compared to EML4-ALK mutated patients.
Keywords: non-small cell lung cancer, novel ALK fusion, crizotinib

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-004 Utility of Cytology Specimens for ALK Fusion Detected by qRT-PCR in Patients of Advanced Non Small Cell Lung Cancer Yan Wang[1], Guanghui Gao[2], Yayi He[2], Xuefei Li[2], Chao Zhao[2], Chunyan Wu[2], Shengxiang Ren[2], Caicun Zhou[2]
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Background: Tumor tissue is the essential specimen for anaplastic lymphoma kinase (ALK) rearrangements detection by the methods of fluorescence in situ hybridization assay(FISH) and immunohistochemistry(IHC). However, a lot of patients could just provide cytological samples but not tumor tissue in clinical practice. The aim of this study was to evaluate the feasibility of cytology as an alternative specimen for ALK detection in patients with advanced non small cell lung cancer (NSCLC). **Methods:** Advanced NSCLC patients with cytology specimens or tumor tissue who had their ALK fusion status detected by qRT-PCR in Shanghai Pulmonary Hospital, Tongji University were included into this analysis. The efficacy was evaluated in those with ALK fusion and treated with crizotinib. **Results:** From December 10th 2010 to March 20th 2015, 1386 patients entered into this study with 1144 cytology specimens and 242 tumor tissue. Among them, 110 of 1144(9.6%) patients were ALK qRT-PCR positive using cytology specimens to perform detection and 26 of 242(10.7%) patients with tumor tissue were ALK fusion positive. Totally, 69 patients received the treatment of crizotinib. The overall response rate (ORR) of the 50 patients with cytology specimens was 62.0%, which was similar as 52.6% in 19 patients with tissue (p=0.479). Median progression free survival (mPFS) was 8.3 months (95% CI 6.91-9.75) in the cytology specimens group, which was also similar as 5.2 months (95% CI 2.58-7.82) (p=0.604) in the tissue group. **Conclusion:** Cytology specimens showed a high feasibility to perform ALK fusion status detection by qRT-PCR and a similar response to ALK inhibitor as tissue specimens, which might be regarded as alternative specimens for ALK detection in patients of advanced NSCLC.
Keywords: qRT-PCR, NSCLC, ALK, cytology specimens

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-005 Discrepancies between ALK FISH and Capture Based NGS Test NEOplus and Clinical Outcome with ALK TKI Therapy Rafal Dziadziuszko[1], Martin Reck[2], Sylvie Lantuejoul[3], Frank Griesinger[4], Federico Cappuzzo[5], Wilfried E.E. Eberhardt[6], Markus Tiemann[7], Roopika Menon[8], Lukas C. Heukamp[8], Johannes Heuckmann[8] [1]*Medical University of Gdansk, Gdansk/Poland,* [2]*Lungenclinic Grosshansdorf, Grosshansdorf/Germany,* [3]*CHU de Grenoble, Grenoble/France,* [4]*Pius-Hospital Oldenburg, Oldenburg/Germany,* [5]*Istituto Toscano Tumori, Livorno/Italy,* [6]*University Hospital Essen, West German Cancer Centre, Ruhrlandklinik, University Duisburg-Essen, Essen/Germany,* [7]*Haematopathology Hamburg, Hamburg/Germany,* [8]*Neo New Oncology, Cologne/Germany*

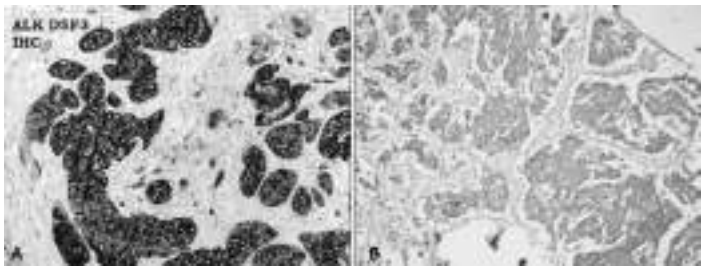
Background: Research in recent years has unraveled several gene fusions driving tumor development in lung cancer. Especially adenocarcinomas of the lung harboring *ALK* and *ROS1* gene fusions exhibit striking sensitivity to ALK and ROS1 kinase inhibitors respectively, translating to dramatic responses in the clinic. Several different technologies are available to detect aberrant genomic structures. The most frequently used technologies include fluorescent in situ hybridization (FISH), currently considered as the "gold standard", immunohistochemistry (IHC), RT-PCR based approaches and hybrid capture based NGS sequencing. **Methods:** Here, we describe a selection of tumor samples showing discrepant results between fluorescent in situ hybridization and hybrid capture based NGS sequencing. These included samples with positive FISH but negative NEOplus as well as negative FISH and positive NEOplus results. In addition, we used response data of targeted therapies to evaluate the true genetic phenotype of the tumor. **Results:** Overall, several lung adenocarcinomas showed discrepant results when FISH and NEOplus data were compared. First, one sample was tested positive for ALK rearrangement using FISH which was not confirmed using NEOplus. In line with this finding, the tumor did not respond to ALK TKI treatment. Second, a total of 4 cases were fusion negative by FISH but positive by NEOplus. Three out of 4 ALK positive cases showed clinical response to ALK kinase inhibition, the clinical results for case number 4 are pending. Interestingly, one of these responding tumors was also negative for ALK expression using IHC. **Conclusion:** In summary, we describe a selection of tumor samples with discrepant results for fusion detecting using FISH and NEOplus. Overall, in all of the cases for which clinical response data was available, tumor sensitivity was in line with the initial diagnosis generated by the NEOplus assay.
Keywords: ALK, FISH, NGS, outcome

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-006 ALK Immunohistochemistry in NSCLC: Evaluation of Performance of D5F3-IHC without Using Automated Ventana System Deepali Jain[1], Kirti Jangra[1], Prabhat Malik[2], Mehar C. Sharma[1] [1]*Pathology, All India Institute of Medical Sciences, New Delhi/India,* [2]*Medical Oncology, All India Institute of Medical Sciences, New Delhi/India*

Background: Since the advent of targeted therapy, molecular testing for common mutations has become vital in the diagnostic algorithm of non- small cell lung cancer (NSCLCs). *ALK-EML4* fusion is a rare abnormality detected in 3–13% patients of adenocarcinomas (ADC). Although Fluorescent In-Situ Hybridization (FISH) is a gold standard technique for detection of ALK rearrangement, it is expensive, time-consuming and requires specialized equipment and expertise for interpretation. Immunohistochemistry (IHC) with *ALK* rearrangement-specific antibodies is considered as a more economical method for routine diagnostic practice. Ultrasensitive automated

Ventana D5F3-IHC revealed a very high correlation with FISH and approved by China FDA for targeted therapy; however, the automated IHC apparatus are not widely used in most general laboratories. In this study, we evaluated performance of *ALK* IHC using manual semiquantitative method in a cohort of 133 adenocarcinomas, to achieve the frequency of *ALK* positivity in Indian patients and correlation with automated Ventana D5F3-IHC. **Methods:** We tested 133 cases of primary lung ADCs, which were negative for EGFR mutation, for *ALK*rearrangement by D5F3-IHC.Thirty three of them were tested by both automated Ventana (D5F3) and manual methods (Cell Signaling Technology, Danvers, MA, USA). The intensity of cytoplasmic staining was classified as 0 (negative) or 1+/2+/3+ (weak/medium/strong). Binary score of positive (strong granular cytoplasmic staining in any percentage of tumor cells) and negative (absence of strong granular cytoplasmic staining) was used for Ventana IHC which was taken as gold standard. A comparison analysis and clinicopathological features were recorded. **Results:** Male to female ratio of the patient population was 2.3:1. *ALK* rearrangement was positive in 10 (7.5%) cases, out of which 7 were men and 50% were non- smokers. Median age for all ADCs was 55 years and for *ALK* rearrangement positive cases was 47 years. Three of 10 *ALK* IHC positive cases showed signet ring cell morphology. On comparison, all cases positive by Ventana (10 cases) **(Figure 1A)** showed positive results by manual method. Six cases showed 3+ **(Figure1B)** whereas 2+ (Three cases) and 1+ (one case) staining intensity was observed. The latter 4 cases were positive by FISH. All negative cases by Ventana system were negative by manual method.



Conclusion: Mutation specific IHC serves as a rapid tool for detection of *ALK* rearrangement in low resource settings. Manual IHC is equally effective in detection of *ALK* rearranged cases as automated methods. IHC positive cases may subsequently be analyzed by FISH thus reducing the cost of automated systems. **Keywords:** NSCLC, ALK immunohistochemistry, Ventana, automated IHC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-007 EML4/ALK Status in Lung Cancer - A 2 Year Experience from a Tertiary Care Cancer Centre in India Sudha S. Murthy[1], Senthil J. Rajappa[2], Sandhya D. Gundimeda[1], Krishna M. Mallavarapu[2], Santa Ayyagari[2], K V. Raju[3], Thamineedi S. Rao[3], Daphne Fonseca[1], Veeraiah Koppula[4] [1]*Pathology & Laboratory Medicine, Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad/India,* [2]*Medical Oncology, Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad/India,* [3]*Surgical Oncology, Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad/India,* [4]*Diagnostic Radiology, Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad/India*

Background: Detection of EML4-ALK rearrangement in lung cancers has influenced the diagnosis and management of a subset of patients with advanced adenocarcinoma. It has become pertinent that all ethnic groups are evaluated for ALK status. Since there is only one published study of EML4/ALK status (Desai et al, 2013) from India, we sought to analyse the frequency of ALK positivity and correlation of this gene rearrangement with different parameters (age, gender and morphologic subtypes etc.). **Methods:** A retrospective analysis of data on ALK gene rearrangement status in lung cancer patients from the archives of the Department of Pathology & Laboratory Medicine was done over a period of 2 years(between March 2013 to March 2015) as per the ASCO / CAP/ IASLC guidelines 2013. Majority of the assays were done by Fluorescence in situ hybridization (FISH) using the Vysis ALK Breakapart rearrangement probe (Abbott Molecular Inc). Immunohistochemistry was done with ALK D5F3 clone (Ventana). The morphology was reviewed by two pathologists trained in pulmonary pathology. Statistical analysis was performed to assess the impact of age, gender and morphologic subtypes on ALK positivity. **Results:** Of the 217 cases of adenocarcinoma of lung diagnosed in the Pathology department, 16 patients were excluded from the study. Two hundred and one patients underwent assay for ALK gene rearrangement. The assay was done by FISH in 181 patients(90%) and IHC in 20 patients(9.95%). The male to female ratio was 1.25:1. The tissue submitted for analysis comprised of lung tissue in 138 patients (68.7 %) and tissue from metastatic sites in 63 patients (31.34%). The most common metastatic siteswere lymph nodes 30 (47.61) and skeletal metastases 10 (15.87%). Of these, ALK was positive in 16 cases (7.96%) and negative in 185 patients(92.03%). All cases detected to be positive for ALK by either method (FISH/IHC) were confirmed by the other methodology inhouse.The major morphologic subtypes included acinar predominant 99 (49.25%),solid predominant 36 (17.91%),mucinous 16 (7.96%) and lepidic predominant 15(7.46%). Of the 99 (47.76%) cases, TTF 1 expression was seen in 89 cases (92.07%). ALK positivity was seen in 10 female patients (62.5%) as opposed to 79(42.7%) females lacking ALK rearrangement. ALK positive patients were younger (median 41 years) among females when compared to ALK negative women (median 54.5 years). ALK positive males were also younger(median 50 years) when compared to negative cases (median 60 years). Stratifying the ALK status in relation to age groups in increments of 10 years showed that 68.7% of the ALK positive patients were below the age of fifty years when compared to 27% of ALK negative cases. Statistical analysis showed that younger age (p= 0.0143) and female preponderance (p=0.0251) were statistically significant in the ALK positive subset. A specific predilection towards morphology could not be established. Acinar subtype constituted the majority of all subtypes 8/16 (50%) **Conclusion:** Increased frequency of ALK positivity in lung adenocarcinoma (7.96%) was noted in comparison to earlier published data .ALK D5F3 assessment by IHC may prove to be a cost effective alternative for analysis **Keywords:** ALK,FISH,Immunohistochemistry ,Lung

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-008 Detection of EML4-ALK Fusion Gene by Using Nested Long-Ranged Polymerase Chain Reaction Shinnosuke Takemoto[1], Hiroaki Senju[1], Yoichi Nakamura[1], Hiroshi Gyotoku[1], Takaya Ikeda[2], Hiroyuki Yamaguchi[1], Takeshi Kitazaki[3], Katsumi Nakatomi[1], Minoru Fukuda[4], Junji Tsurutani[5], Kazuhiro Tsukamoto[6], Shigeru Kohno[1] [1]*Second Department of Internal Medicine, Nagasaki University Hospital, Nagasaki City/Japan,* [2]*Division of Respiratory Medicine, Sasebo City General Hospital, Sasebo/Japan,* [3]*Division of Respiratory Medicine, Japanese Red Cross Nagasaki Genbaku Hospital, Nagasaki/Japan,* [4]*Clinical Oncology Center, Nagasaki University Hospital, Nagasaki/Japan,* [5]*Department of Medical Oncology, Kinki University, Sayamashi/Japan,* [6]*Department of Pharmacotherapeutics, Unit of Medical Pharmacy, Nagasaki University, Nagasaki City/Japan*

Background: The fusion of the anaplastic lymphoma kinase (*ALK*) with the echinoderm microtubule-associated protein-like 4 (*EML4*) was identified in Non-small cell lung cancer (NSCLC). ALK tyrosine kinase inhibitors were proved to be superior to standard chemotherapies and it is important to detect *EML4-ALK* fusion gene accurately. Reverse transcriptase-polymerase chain reaction (RT-PCR), Fluorescence in situ hybridization (FISH) and Immunohistochemical (IHC) stain are performed clinically to detect the fusion gene. However, there are discrepancies among these methods for detection of *EML4-ALK* fusion gene and the best detection method remain unknown. The purpose of this study was to evaluate the new method for detection of the *EML4-ALK* fusion gene. **Methods:** The combination of nested polymerase chain reaction (PCR) and long-ranged PCR (Nested long-ranged PCR) was used to detect *EML4-ALK* fusion gene. Genomic deoxyribonucleic acid (gDNA) was extracted from *EML4-ALK* positive lung cancer cell lines (NCI-H2228,NCI-H3122,ALKSFA8). It was verified whether the fusion gene was amplified. We evaluated the sensitivity of Nested long-ranged PCR for *EML4-ALK* fusion gene in various ratios. It was confirmed whether the amplification products were *EML4-ALK* fusion gene by using PCR direct Sequencing. **Results:** *EML4-ALK* fusion genes were detectable successfully in each of *EML4-ALK* positive lung cancer cell lines.NCI-H3122 had *EML4-ALK* variant 1. ALK-SFA8 and NCI-H2228 had *EML4-ALK* variant 3a/b. One fusion gene in the presence of 1×10^2 wild type genes was detectable in each cell line. Each PCR product was confirmed by sequencing from both ends. **Conclusion:** In this study, we were able to detect the fusion gene in vitro by Nested long-ranged PCR. This may become a new diagnostic method for *EML4-ALK* fusion gene. **Keywords:** genomic DNA, PCR, EML4-ALK, NSCLC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-009 Evaluation of RT-PCR Methodology for ALK Assessment in Patients with NSCLC in Europe: Results from the ETOP Lungscape Project Igor Letovanec[1], Solange Peters[2], Zoi Tsourti[3], Stephen P. Finn[4], Alex Soltermann[5], Lukas Bubendorf[6], Ernst-Jan M. Speel[7], Antonio Marchetti[8], Daisuke Nonaka[9], Henrik Hager[10], Miguel Martorell[11], Kim Monkhorst[12], Aleksandra Sejda[13], Richard Cheney[14], Irene Sansano[15], Eric K. Verbeken[16], Verena Tischler[17], Spasenija Savic[18], Alessia Di Lorito[8], Maria Consuelo Calabuig[19], Enriqueta Felip[20], Alex Adjei[21], Arne Warth[22], Paul Baas[23], Peter Meldgaard[24], Fiona Blackhall[25], Anne-Marie Dingemans[26], Hendrik Dienemann[27], Rafal Dziadziuszko[28], Johan Vansteenkiste[29], Rosita Kammler[30], Urania Dafni[31], Keith Kerr[32], Erik Thunnissen[33], Rolf Stahel[34] [1]*Co-First Author, Department of Pathology, Centre Hospitalier Universitaire Vaudois - Chuv, Lausanne/Switzerland,* [2]*Co-First Author, Department of Oncology, Etop and Centre Hospitalier Universitaire Vaudois (Chuv), Lausanne/Switzerland,* [3]*Frontier Science Foundation-Hellas, Athens/Greece,* [4]*Department of Pathology, University of Dublin, Trinity College and St. James'S Hospital, Dublin/Ireland,* [5]*Institute of Surgical Pathology, University Hospital Zurich, Zurich/Switzerland,* [6]*Institute of Pathology, University Hospital Basel, Basel/Switzerland,* [7]*Department of Pathology, Maastricht University Medical Centre, Maastricht/Netherlands,* [8]*Anatomia Patologica, Ospedale Clinicizzato, Chieti/Italy,* [9]*The Christie Hospital and Institute of Cancer Sciences University of Manchester, Manchester/United Kingdom,* [10]*Department of Pathology, Aarhus University Hospital, Aarhus/Denmark,* [11]*Department of Pathology, Consorcio Hospital General Universitario, Valencia/Spain,* [12]*Department of Pathology, Netherlands Cancer Institute, Amsterdam/Netherlands,* [13]*Department of Pathology, Medical University of Gdansk, Gdansk/Poland,* [14]*Department of Pathology and Laboratory Medicine, Roswell Park Cancer Institute, Buffalo/NY/United States of America,* [15]*Department of Pathology, Hospital Universitari Vall D'Hebron, Barcelona/Spain,* [16]*Department of Pathology, University Hospital Leuven, Leuven/Belgium,* [17]*Institute of Clinical Pathology, University Hospital Zurich, Zurich/Switzerland,* [18]*Insitute of Pathology, University Hospital Basel, Basel/Switzerland,* [19]*Consorcio Hospital General Universitario, Valencia/Spain,* [20]*Vall D'Hebron University Hospital and Vall D'Hebron Institute of Oncology (Vhio), Barcelona/Spain,* [21]*Medicine, Roswell Park Cancer Institute, Buffalo/NY/United States of America,* [22]*Department of Pathology, University Hospital Heidelberg, Heidelberg/Germany,* [23]*Department of Thoracic Oncology, Netherlands Cancer Institute, Amsterdam/Netherlands,* [24]*Department of Oncology, Aarhus University Hospital, Aarhus C/Denmark,* [25]*Manchester University and the Christie NHS Foundation Trust, Manchester/United Kingdom,* [26]*Department of Pulmonary Diseases, Maastricht University Medical Center, Maastricht/Netherlands,* [27]*Department of Thoracic Surgery, Thoraxklinik at University of Heidelberg and TLRC, Heidelberg/Germany,* [28]*Department of Oncology and Radiotherapy, Medical University of Gdansk, Gdansk/Poland,* [29]*Respiratory Oncology,*

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Background: ALK rearrangement is documented in 2%-7% of NSCLC, depending on the population studied and detection method used. Although the reverse transcriptase-polymerase chain reaction (RT-PCR) was the first used and published method, fluorescence in situ hybridization (FISH) has become the primary standard diagnostic method. Recently, immunohistochemistry (IHC) has also proven to be a reproducible, faster and sensitive technique. This is one of the first studies concurrently comparing all three techniques in resected lung adenocarcinomas from the large ETOP Lungscape cohort. **Methods:** 95 cases from the ETOP Lungscape iBiobank, selected based on any degree of IHC staining (clone 5A4 antibody, Novocastra, UK), were examined by ALK FISH (Abbott Molecular, Inc.; Blackhall, JCO 2014) and central RT-PCR. For the latter, formalin-fixed, paraffin-embedded (FFPE) unstained slides were collected from participating centers. Slides were de-paraffinized, Toluidine Blue stained, and tumors macro-dissected. Tissue digestion and RNA extraction were performed (Qiagen RNeasy FFPE Kit). Using primers described in the literature covering most of ALK known translocations, RT-PCR (Superscript One-Step RT-PCR with Platinum Taq – 40 loops) was performed, followed by capillary electrophoresis in two separate mixes. Co-amplification of B-actin was done to validate the procedure and RNA quality. All tests were duplicated. **Results:** 76 of 95 RT-PCR had adequate RNA quality (B-actin co-amplification present). Among these, 18 were FISH positive, 16 were RT-PCR positive, including EML4-ALK V3a/b in 7, V1 in 5, V2 in one, and undetermined variants in 3 cases. 53 of 54 FISH negative cases were also RT-PCR negative (98%). 15 of 18 FISH positives harbored a translocation by RT-PCR (83%). Among the 4 discrepant cases, 2 FISH+/ RT-PCR- cases had IHC H-scores of 180 and 260, and 98.3% and 95% of rearranged cells by FISH, probably corresponding to variants not covered by the RT-PCR. One had an IHC H-score of 5, and 16% cells rearranged on FISH, most probably corresponding to a FISH false positive case. The last had an IHC H-score of 200, 13% rearranged cells by FISH, and, thus is defined as a false negative FISH result. Provided IHC is defined as positive by an H-score above 120, all but one case (H-Score 20, FISH and RT-PCR positive) gave concordant results by a combination of FISH and RT-PCR. Overall, using as true negative or true positive the concordant result of two of the methods, the third method is characterized by high specificity and sensitivity with corresponding values of 100/98/100% and 94/94/89% for IHC/FISH/RT-PCR, respectively. **Conclusion:** RT-PCR is a very good tool for sorting discordant IHC/FISH cases, however, we do not recommend using this technique as single method due to the lower sensitivity of RT-PCR, as not all variants are covered, and also due to the limitations with RNA preservation.
Keywords: NSCLC, ETOP, RT-PCR, ALK

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-010 EML4-ALK Fusion Detected by qRT-PCR Confers Similar Response to Crizotinib as Detected by FISH in Patients with Advanced NSCLC Shengxiang Ren[1], Yan Wang[2], Guanghui Gao[1], Xuefei Li[3], Chao Zhao[4], Chunxia Su[5], Xiaoxia Chen[3], Yayi He[5], Caicun Zhou[6] *[1]Oncology, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Tongji University Cancer Institute, Shanghai/China, [2]Shanghai Pulmonay Hospital, Shanghai/China, [3]Lung Cancer and Immunity Laboratory, Shanghai Pulmonary Hospital, Tongji University; Tongji University Medical School Pulmonary Cancer Institute, Shanghai/ China, [4]Medical Oncology, Shanghai Pulmonary Hospital, Shanghai/China, [5]Shanghai Pulmonary Hospital, Shanghai/China, [6]Department of Medical Oncology, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

Background: Quantitative reverse transcriptase polymerase chain reaction assay (qRT-PCR) has been proved to have high sensitivity and specificity to detect anaplastic lymphoma kinase (ALK) rearrangements. The aim of this study was to investigate the response to crizotinib in patients of advanced non-small-cell lung cancer (NSCLC) with ALK rearrangements detected by qRT-PCR. **Methods:** Patients with advanced NSCLC who had their ALK rearrangement status detected by qRT-PCR were included in this analysis. The utility of qRT-PCR and fluorescence in situ hybridization assay (FISH) were compared in patients who were treated with crizotinib based on their positive ALK rearrangements. **Results:** 1010 patients were included in this study. Among them, 104 patients were ALK qRT-PCR positive and 53 of them received crizotinib treatment. Among 255 tumors simultaneously analyzed by FISH and RT-PCR, the latter successfully detected all the 25 tumors with arrangements, including two cases which were missed by FISH. The overall response rate (ORR) and median progression free survival (mPFS) of the 53 patients with ALK rearrangements who received crizotinib treatment were 60.4% (95%CI, 47.2-73.6) and 8.4 months (95% CI 6.75-10.05) respectively, which were similar to the 21 patients detected by FISH with ORR of 57.1% (95% CI 33.3-76.2) (p=0.799) and mPFS of 7.4 months (95% CI 4.43-10.38) (p=0.833) after crizotinib treatment. Interestingly, there were 2 patients responded to crizotinib had their ALK rearrangement detected by qRT-PCR but not FISH. **Conclusion:** qRT-PCR should be considered as an alternative assay to detect ALK fusion oncogene in NSCLC patients who might be benefit from crizotinib treatment.
Keywords: ALK, RT-PCR, FISH, NSCLC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-011 A Validation Study for the Use of ROS-1 Immunohistochemistry in Screening for ROS-1 Translocations in Lung Cancer Patrizia Viola[1], Manisha Maurya[2], James Croud[1], Jana Gazdova[2], Nadia Suleman[1], Eric Lim[3], Sanjay Popat[4], Alexandra Rice[1], Angeles Montero Fernandez[1], David Gonzalez De Castro[2], Andrew G. Nicholson[5] *[1]Histopathology, Royal Brompton Hospital, London/United Kingdom, [2]Centre for Molecular Pathology, Royal Marsedn Hospital, Sutton/United Kingdom, [3]Department of Thoracic Surgery, Royal Brompton and Harefield NHS Trust, London/United Kingdom, [4]Medical Oncology, Royal Marsden Hospital, London/United Kingdom, [5]Pathology, Royal Brompton and Harefield NHS Foundation Trust and National Heart and Lung Institute, London/United Kingdom*

Background: ROS-1 translocations are a rare genetic abnormality in lung cancers that, when identified, are a target for personalised therapy. The current test of choice is FISH, although with a rate of no more than 1-2%, screening using FISH is an expensive proposition. A further possibility is using immunohistochemistry (IHC) as a screening tool and commercial antibodies are now available that identify the ROS-1 protein in tumour cells. We present our data in undertaking a validation study for potential diagnostic usage. **Methods:** Given the relative rarity of the translocation and the fact the most driver mutations occur in isolation, a test cohort of cases was selected from patients recruited to phase 1 of the Cancer Research UK-Stratified Medicine Project (CRUK-SMP), who were identified as negative for EGFR, KRAS and/or BRAF mutations, as well as ALK translocations. Negative cases were then screened with an antibody for ROS-1 (D4D6, Cell Signalling, 1 in 300 dilution) and scored as negative, weakly positive or moderately positive, along with the percentage of positive cells. Cases were then sent for FISH analysis for the ROS-1 translocation, with a cut-off of > or = to15%, and the sensitivity and specificity of positive staining for ROS-1 was generated. **Results:** From 170 patients recruited from our institution into CRUK-SMP phase 1, a total of 103 patients were wild type for the above mutations (90 for all 4 genetic abnormalities. 9 further cases had failed tests for one and 4 for two mutations (6 carcinoids, 38 squamous cell carcinomas, 5 small cell carcinoma, 2 adenosquamous carcinoma, 1 pleomorphic carcinoma, 3 large cell carcinoma, 2 large cell neuroendocrine cell carcinoma, 7 non-small cell carcinoma (on biopsy) and 39 adenocarcinomas). 39 cases were tested (adenocarcinoma = 37, adenosquamous carcinoma = 2) with FISH, and one case was positive (78% positive cells). FISH testing was negative in 35 cases with scores of 1-8%, and three cases failed. The one positive case was positive on IHC (>90% of cells, moderate staining). In the 35 cases negative for FISH, four cases showed variable positivity on IHC (20, 40,50, 90%, moderate staining) and five cases showed weak focal staining (<5, <5, 10, 20, 30%, weak staining). The remainder were negative on IHC. All non-adenocarcinomas were negative on IHC. Several cases show positive staining of entrapped background pneumocytes and alveolar macrophages, making scoring problematic in some adenocarcinomas. **Conclusion:** Moderate staining for ROS-1 using IHC, independent of percentage positive cells, showed high sensitivity (100%) for tumours that contained a high level of translocated cells. However, specificity was at best 50%, even if a cut-off of 50% positive cells was applied. Pathologists also need to be aware of background staining so cases are not interpreted as false positives.
Keywords: lung cancer, ROS-1 immunohistochemistry, FISH, ROS-1 translocations

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-012 Transition of HSP90-Dependent Client Proteins in ALK Rearranged Non-Small Cell Lung Cancer Ryohei Yoshida, Shunsuke Okumura, Takaaki Sasaki, Yoshinobu Ohsaki *Asahikawa Medical University, Asahikawa/Japan*

Background: Heat Shock Protein (HSP) 90 is one of the major intracellular molecular chaperones, the protein expression is increased in the cell stress conditions, is one of the proteins most present in the cytoplasm in normal condition. HSP90 plays a role for the correct folding of proteins in the correct conformation, and function by interacting with various intracellular proteins. The client proteins that interact with HSP90 contains many important role signaling molecules for cell proliferation and differentiation, such as protein kinase and steroid hormone receptors. Luminespib (AUY922) is a specific HSP90 inhibitor bound to the ATP-binding pocket, leading inactivation, destabilization and degradation of HSP90-dependent client protein. In Non-small cell lung cancer, ALK rearranged cancers are reported as highly sensitive to luminespib, which supposed to ALK fusion proteins are the client proteins of HSP90. By comparing the expression changes in intracellular proteins after treatment of luminespib, we determined the significant pathways in the ALK rearranged cancer cells both sensitive to ALK tyrosine kinase inhibitors (TKIs) and resistant to ALK-TKIs.

Methods: HSP90 inhibitor luminespib (AUY922, Novartis Pharm.) and ALK-TKIs, alectinib (CH5424802, Chugai Pharm.) and were used in this study. Alectinib resistant cell lines were established by exposing increased dose of alectinib to ALK rearranged H3122 cell line (AFR). To study the protein expression screening after treatment of luminespib, protein lysate from H3122 and AFR with or without luminespib were collected, and submitted for mass-spectrometry using iTRAQ. We also determined the protein expression of HSP90-dependent client protein and signaling proteins by Western Blotting. **Results:** The iTRAQ data analysis and protein identifications were done with ProteinPilot version 4.5. We observed 1118 proteins/peptides in each cell lines. At first we focused on changes in the protein expression of HSP family after treatment of luminespib. The HSP90A after treatment of luminespib was increased in H3122 and the HSP90B after treatment of luminespib was decreased in AFR. The protein expression of HSP70 after treatment of luminespib was increased in H3122 and in AFR. These results suggested that the role of HSP90-dependent client proteins have changed in ALK-TKIs acquired resistant cells. Secondly, we studied the HSP90-dependent client proteins by

intracellular pathway analysis. We suggested that the focal adhesion pathway such as paxilin/crkII revealed significant HSP90-dependent client proteins. **Conclusion:** The focal adhesion molecules are one of the significant signaling pathways in the ALK rearranged NSCLC both sensitive and resistant to ALK-TKIs, and that proteins in the focal adhesion pathway could be a potential target of a ALK-rearranged NSCLC.
Keywords: HSP90 inhibitor, Resistance, mass spectrometry, ALK-rearranged NSCLC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-013 Clinicopathological Data's of Advanced NSCLC Patients with ROS1 Gene Rearrangement and of Clinical Responses to Crizotinib in TURKEY
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Background: The ROS1 oncogene encodes an orphan receptor tyrosine kinase related to anaplastic lymphoma kinase (ALK), leukocyte receptor tyrosine kinase, and members of the insulin receptor family. Chromosomal rearrangement of ROS1 occurs in a variety of human cancers, including non-small cell lung cancer (NSCLC). Crizotinib (XALKORI®) is , first-in-class, small molecule tyrosine kinase inhibitor of ALK, ROS1, and c-MET. It has been approved in several countries for the treatment of advanced ALK-positive NSCLC. A global phase I study of crizotinib includes expansion cohorts for patients with molecularly defined tumors, including a cohort of patients with advanced NSCLC harboring ROS1 fusions. **Methods:**Between January 2014 and January 2015, a total of 542 patients with advanced NSCLC was enrolled. They were all negative for EGFR mutation and also ALK rearrangement. All of the cases of ROS1 rearrangement were identified through a break-apart ROS1 fluorescence in-situ hybridization (FISH) assay together with immunohistocemical ROS1 (D4D6 clone) positivity. **Treatment** All patients received at least one prior line of standard therapy for advanced NSCLC. After that Crizotinib was administered orally at the standard dose of 250 mg twice daily in continuous 28-day cycles. **Results:** ROS1 rearrangements were found in 5 cases of 542 lung cancer samples, the total incidence was 0,9%. All the tumors of the positive cases were adenocarcinoma. The ROS-1 rearrangements were more frequent in female patients (80%) than male ones. They were all young patients median age 39 years old. The majority of patients had never smoked (60%) and the others were light-smoker. The first patient has been receiving Crizotinib therapy for thirteen months and all patients are still alive. Two patients (40%) achieved a complete response, 2 patients (40%) achieved a partial response. Last patient was started Crizotinib therapy in the March of 2015. **Conclusion:** Patients with *ROS1*-positive NSCLC have similar demographic characteristics to those with *ALK*-positive NSCLC. ROS1 rearrangement test is recommended for all patients whose tumors were negative EGFR and ALK. ROS1 rearrangement defines a second molecular subset of NSCLC for which crizotinib is a highly active treatment. This is the first report presenting clinico-pathological data of the patients harboring ROS1 rearrangement in TURKEY.
Keywords: ros1 rearrangement, nonsmall cell lung cancer, crizotinib treatment

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-014 High concordance of ALK fusion between primary tumor and paired metastatic lymph node in patients with adenocarcinoma
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Background: Anaplastic lymphoma kinase gene (*ALK*) rearrangement represents a novel oncogenic gene in NSCLC patients which show response to crizotinib, an ALK inhibitor. Lung cancer is a heterogeneous tumor. It remains unclear whether ALK rearrangement was distributed heterogeneously in tumor from different anatomic site of the same patient. To address this issue, we compared the concordance of ALK gene fusion status between primary tumor and paired lymphatic metastasis. Meanwhile, we evaluated the effectiveness of crizotinib treatment of advanced NSCLC patients with ALK rearrangement detected on biopsy or cytology from primary tumors or metastatic lymph nodes by RT-PCR. **Methods:** A total of 101 NSCLC patients with metastatic lymph nodes by surgical resection were enrolled from September 2013 to Auguast 2014, including 33 patients with N1 and N2 lymphatic metastasis. We performed immuohistochemical(IHC) staining for the ALK protein with Ventana D5F3 antibody on primary tumor and paired metastatic lymph nodes. Reverse transcriptase-polymerase chain reaction (RT-PCR) was used to confirm ALK fusion status. Discordance of ALK fusion gene status between primary tumor and paired metastatic lymph nodes was further confirmed by fluorescence in Situ hybridization (FISH). Progression-free survival (PFS) was evaluated in 13 ALK positive advanced adenocarcinoma patients with crizotinib treatment including 7 patients who harbored ALK rearrangement detected on primary tumor and 6 patients detected on metastatic lymph nodes. **Results:** The concordance rate of ALK rearrangement between primary tumor and paired metastatic lymph nodes was 98%. ALK fusion gene status between different groups of metastatic lymph nodes in the same patient showed totally concordant. PFS (11.1 months) was similar in patients with ALK rearrangement detected on primary tumor and patients (PFS, 10.8 months, $P=0.2$) detected on metastatic lymph nodes by RT-PCR. **Conclusion:** The current results indicated that ALK rearrangement showed a high concordance between primary tumor and lymphatic metastasis and successfully predict response to ALK inhibitor. RT-PCR detecting ALK rearrangement on biopsy or cytology with limited tissue from primary tumors and metastatic lymph nodes can be important for ALK inhibitor treatment in advanced NSCLC patients.
Keywords: ALK rearrangement, primary tumor and metastasis, crizotinib, RT-PCR

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P3.04-015 Immunohistochemistry With 3 ALK Antibodies and Thymidylate Synthase Evaluation of FISH-Positive ALK-Rearranged Lung Adenocarcinomas
Paolo Bironzo[1], Valentina Monica[1], Paolo Graziano[2], Luisella Righi[1], Evaristo Maiello[3], Marcello Tiseo[4], Maria R. Migliorino[5], Lucio Buffoni[6], Fausto Barbieri[7], Alessandra Lombardi[8], Giulio Rossi[9], Silvia Novello[1] [1]*University of Turin, Department of Oncology, Turin/Italy,* [2]*Unit of Pathology, Scientific Institute for Research and Health Care "Casa Sollievo Della Sofferenza", S. Giovanni Rotondo/Italy,* [3]*Oncology Unit, Scientific Institute for Research and Health Care "Casa Sollievo Della Sofferenza", S. Giovanni Rotondo/Italy,* [4]*Medical Oncology Unit, University Hospital of Parma, Parma/Italy,* [5]*1St Oncological Pulmonary Unit, San Camillo-Forlanini High Specialization Hospitals, Rome/Italy,* [6]*Medical Oncology, Città Della Salute E Della Scienza - Molinette Hospital, Turin/Italy,* [7]*Department of Oncology, University Hospital Policlinico of Modena, Modena/Italy,* [8]*16Th Oncological Pulmonary Unit, San Camillo-Forlanini High Specialization Hospitals, Rome/Italy,* [9]*Unit of Pathology, University Hospital Policlinico of Modena, Modena/Italy*

Background: ALK-rearranged lung tumors represent approximately 2-7% of all Non-Small-Cell Lung Cancers (NSCLCs). Young age, never/light smoking habit, adenocarcinoma (ADK) histology and good response to chemotherapy with pemetrexed characterize ALK-positive patients (pts). Current treatment strategies in this molecular setting are based on ALK-kinase inhibition with small molecules including first (crizotinib/CZT) and second generation TKIs. The FDA-approved companion diagnostic test for CZT treatment is the Vysis break-apart FISH probe, but several works support the immunohistochemistry (IHC) as a sensitive and specific test. The European Medical Agency (EMA) recently approved CZT for second-line treatment of ALK-rearranged NSCLC as detected by "an accurate and validated ALK assay", thus endorsing IHC for eligibility purposes. Here, we retrospectively assessed ALK status in 28 pts with known FISH-positive ALK-rearranged NSCLC performing IHC with 3 different antibodies in order to assess their diagnostic accuracy as compared to the FISH assay. Moreover, we evaluated thymidylate synthase (TS) expression using real-time polymerase chain reaction (RT-PCR) given the conflicting literature data on pemetrexed sensitivity in those tumors. As a secondary end point we will compare molecular and clinical outcomes. **Methods:** FISH was performed with Vysis break-apart FISH probe. IHC was performed with 3 different antibodies: ALK1 (DAKO), 5A4 (Novocastra) and D5F3 (Ventana/Cell Signaling Technology). For ALK1 and 5A4 an IHC scoring value between 0+ and 3+ was used, as previously proposed, while a positive or negative score was used with D5F3 and Ventana KIT. TS gene expression was measured through Real Time PCR, TaqMan method. **Results:** 28 specimens of ALK-rearranged ADK diagnosed between 2010 and 2013 from 7 different Italian Oncology Centres were evaluated. Pts median age at diagnosis was 55 (range: 25-78), 9 pts were female. 25/28 (89.3%) specimens were D5F3 positive. 13/28 (46.4%) had 5A4 3+ positivity, 12 (42.8%) showed 2+ positivity while the remaining 3 were negative. 3/28 specimens (10.7%) had ALK1 3+ score, 9 (32.1%) 2+, 13 (46.5%) 1+ and the remaining 3 (10.7%) were negative. Among the 3 FISH-positive and IHC-negative cases, 2 pts underwent CZT treatment, both progressing within 2 weeks and with low percentage of rearranged tumor cells at FISH testing (16-20%) When considering 3+ and 2+ scores as positive, 12 specimens (42.8%) resulted to be positive with all the 3 antibodies, while score 1+ was observed only with ALK1 in 13 (46.4%). Only 3 cases resulted strongly positive with all clones. TS gene expression median value on 25 cases was 6.27 (range 2,8-14-94). 65% of cases had low expression as compared to a population of ALK-negative lung ADK (personal data). **Conclusion:** IHC proved to be a reliable tool to diagnose ALK-rearranged lung tumors, especially with D5F3 and 5A4 antibodies. As the two IHC negative and FISH positive patients who received CZT didn't respond to treatment, IHC should be used as screening tool or a confirmatory test in case of low-rearranged FISH-positive cases. TS expression appeared to be lower in ALK-positive lung tumors as compared to ALK-negative lung ADK. Further comparisons between clinical and molecular data are ongoing.
Keywords: FISH, Immunohistochemistry, Thymidilate Synthase, ALK

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P3.04-016 EML4-ALK Fusion in a NSCLC Patient Detected by High Sensitivity Circulating Tumor DNA Assay Empowers Targeted Therapy Decisions
Nisha Mohindra[1], Becky Nagy[2], Bahram Kermani[2], Stefanie Mortimer[2], Richard B. Lanman[2], Helmy Eltoukhy[2], Amir A. Talasaz[2], Jyoti Patel[1] [1]*Medical Oncology, Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago/IL/United States of America,* [2]*Guardant Health, Inc, Redwood City/CA/United States of America*

Background: The National Comprehensive Cancer Network (NCCN) non-small cell lung cancer (NSCLC) guidelines recommend genomic testing of seven genes in order to determine appropriate targeted therapy, including fusions in the anaplastic lymphoma kinase (*ALK*) gene which may be highly responsive to matched therapies. Tissue-based approaches to determine the tumor's genetic status are often hampered by patient intolerance to repeat biopsy or insufficient tissue. Novel digital sequencing technology of plasma cell free circulating tumor DNA (ctDNA) allows assessment of these biomarkers without an invasive tissue biopsy. **Methods:** A 58 year-old woman was diagnosed with metastatic lung adenocarcinoma with bone predominant metastatic disease in February 2013. Despite histologic confirmation of adenocarcinoma, tissue was insufficient for genotyping despite multiple attempts at biopsy. She was treated empirically with carboplatin/pemetrexed with initial response, suffered from symptomatic progression in bone and underwent cell free circulating tumor DNA testing. Assessment of ctDNA levels using a comprehensive 68-gene digital sequencingTM panel (Guardant360) with high sensitivity (detection of single nucleotid variants, focal gene amplifications in 16

genes, *EGFR* indels and fusions in *ALK*, *ROS1*, *RET* and *NTRK1*) in 87%+ of advanced cancer patients) and ultra-high specificity (>99.9999%) was performed on a blood sample from the patient. **Results:** Analysis of the patient's ctDNA revealed an *EML4-ALK* fusion at 0.06% mutant allele fraction, which is equivalent to a single mutant molecule in a 10 mL tube of blood. This result was repeated in a second tube of blood, and two DNA fragments with the *EML4-ALK* fusion breakpoint were found. The patient also had a single nucleotide variant (R386G) in the *AR* gene at 0.25% and *JAK2* V617F variant at 0.93% concentration. Crizotinib therapy was initiated on the basis of the *EML4-ALK* fusion and clinical improvement has already been noted. Repeat ctDNA measurements are planned and will be correlated with clinical response parameters based on RECIST criteria and protein-based tumor marker levels. This information will be reported at the time of presentation. **Conclusion:** To our knowledge, this is the first case report of *EML4-ALK* fusion identified in the clinical setting via biopsy-free circulating tumor DNA analysis. With single molecule sensitivity, this simple blood test was able to identify a therapeutic option in a patient who was unable to undergo tissue-based NGS. **Keywords:** EML4-ALK, personalized medicine, cell free DNA, Circulating Tumor DNA

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P3.04-017 Acinar Subtype of Lung Adenocarcinoma Is Significantly Related to EML4-ALK Translocation in Eastern European Patients Bojan Zaric, Branislav Perin, Vladimir Stojsic, Milana Panjkovic, Dragana Tegeltija, Vanesa Stepanov, Tomi Kovacevic *Clinic for Thoracic Oncology, Institute for Pulmonary Diseases of Vojvodina, Faculty of Medicine, University of Novi Sad, Sremska Kamenica/Serbia*

Background: The incidence of echinoderm microtubule-associated protein-like4-anaplastic lymphoma kinase (EML4-ALK) translocation among surgically treated patients with adenocarcinoma of the lung of the Eastern European ethnicity is underreported. The aim of this trial was the determination of EML4-ALK translocation frequency in investigated population, and the evaluation of correlations between lung adenocarcinoma subtype and clinical characteristics with mutation status. **Methods:** This was a prospective trial which included 195 patients with adenocarcinoma of the lung who underwent surgical treatment. ALK mutation screening was performed by immunohistochemistry (IHC). IHC scores of 2+ and 3+ were regarded as positive. Confirmatory FISH was performed in all IHC positive and in 2:1 ratio in negative patients. **Results:** Overall ALK mutation rate established by IHC was 6.2%, while FISH confirmed rate of 5.1%. The FISH confirmed ALK positivity in 7.6% Hungarians, 5.5% Serbians, and 6.6% Slovakians. Acinar subtype of adenocarcinoma of the lung was significantly (p=0.02) related to EML4-ALK positive mutation status. Most of the patients were males (56.9%), smokers (50.8%), or former smokers (28.7%) with acinar (55.4%) or solid (35.9%) adenocarcinoma of the lung. Sensitivity and specificity of IHC were 100% and 98.9% respectively. **Conclusion:** ALK mutation rate in surgically treated patients with adenocarcinoma of the lung was found to be 6.2% by IHC and 5.1% by FISH. Acinar subtype of the adenocarcinoma of the lung was significantly related to ALK positive mutation. **Keywords:** adenocarcinoma of the lung; anaplastic lymphoma kinase (ALK); EML4-ALK translocation; non-small cell

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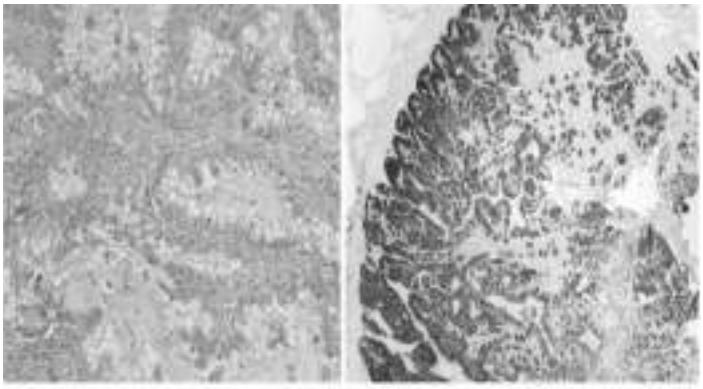
P3.04-018 Expression of Protein Kinase EML4-ALK Gene in Non-Small Cell Lung Cancer (NSCLC) in a University Hospital of Reference in Latin America Luz F. Sua[1], Liliana Fernandez[2], Carlos A. Muñoz[3], Juan G. Restrepo[4] [1]*Department of Pathology and Laboratory Medicine and Phd Biomedical Sciences, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [2]*Interventional Pulmonology, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [3]*Medical Research, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia,* [4]*Hemato-Oncology Clinic, Fundacion Valle Del Lili, Universidad ICESI, Cali/Colombia*

Background: Lung cancer, the leading cause of cancer deaths worldwide, exists in two distinct entities: small and non-small cell lung cancer, representing 85% of lung cancers, and generally presents at diagnosis with locally advanced or metastatic disease. The rare genetic changes, anaplastic lymphoma kinase (ALK) gene rearrangements, most often consisting in a chromosome 2 inversion leading to a fusion with the echinoderm microtubule-associated protein like 4 (EML4) gene, results in the abnormal expression and activation of this tyrosine kinase in the cytoplasm of cancer cells. This rearrangement occurs in 2–5% of NSCLC, predominantly in young patients (50 years or younger), in non-smokers or former smokers with adenocarcinoma. This aberration most commonly occurs independent of EGFR and KRAS gene mutations. Inmunohistochemical analysis is a cost-effective alternative for the detection of ALK gene rearrangements and recent guidelines from the College of American Pathologists, International Association of the Study of Lung Cancer, and The Association for Molecular Pathology supports the use of IHC screening as long as it has been appropriately validated. **Methods:**Between November 2014 and March 2015, 20 tumor samples were obtained in the Fundacion Valle del Lili, Cali-Colombia. The Ventana anti-ALK (D5F3) assay was performed using OptiView DAB IHC detection kit and OptiView Amplification Kit, with external controls rated with positive and negative cell lines (H2228 and CALU-3 respectively), with appropriate expression. **Results:** We analyzed samples from 20 patients with NSCLC using immunohistochemistry. We found tumor cells in 100% of the samples. The average age was 62.8 years ± SD, 45% (9) women and 55% (11) men. The protein kinase expression of EML4-ALK gene was found in 20% of the cases (4),which included 3 females. Thirteen cases were adenocarcinoma and fourteen patients were diagnosed in stage IV. Fourteen of twenty patients received chemotherapy. At this time in our hospital began the Phase Three study of the molecule specific for this tumor rearrangement. The mortality in this group of patients was 3 of 20. **Conclusion:** Knowledge of cancer biology and oncogenic drivers has led to a better understanding of lung cancer and the development of very active targeted therapies. ALK rearrangements have been identified as oncogenic drivers for a subgroup of lung adenocarcinoma. The clinical benefit gained by targeted therapies has led to transition from a standardized therapeutic approach to a personalized approach based on molecular tumor characteristics in current clinical practice.



A. Mucinous adenocarcinoma histological variant (H & E) B. Positive expression for the detection of protein kinase gene of EML4-ALK (IHC)

Keywords: NSCLC, IHC, EML4-ALK

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P3.04-019 A Retrospective Analysis of Frequency of ALK Gene Rearrangement in Saudi Lung Patients Fouad H. Al Dayel[1], Hamad Al Husaini[2], Shamayel Mohammed[1], Asma Tulbah[1], Khawla Al Kuraya[3] [1]*Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh/Saudi Arabia,* [2]*Oncology, King Faisal Specialist Hospital and Research Centre, Riyadh/Saudi Arabia,* [3]*Research Centre, King Faisal Specialist Hospital and Research Centre, Riyadh/Saudi Arabia*

Background: Lung carcinoma represents 2.6% of cancer seen at King Faisal Specialist Hospital and Research Centre (KFSH&RC) and 4.5% of cancers in Saudi Arabia as per Saudi Cancer Registry. *EML4-ALK* re-arrangements are found to play an oncogenic driver role in lung adenocarcinoma tumor genesis in 3-6% of cases. ALK gene rearrangement testing can identify patients with adenocarcinoma who are sensitive to ALK kinase inhibitors. However, no data are available on the prevalence of ALK rearrangements changes in Middle Eastern population. Therefore, we carried out this study to evaluate the prevalence of ALK gene rearrangements in lung adenocarcinoma of Saudi patients. **Methods:** ALK gene rearrangements were studied using fluorescence in situ hybridization (FISH) on 97 adenocarcinoma samples utilizing tissue microarray format. ALK gene rearrangements tested using break-apart probes from Vysis (Abott Molecular, Il, USA). **Results:** One hundred ninety eight (198) lung adenocarcinoma cases were evaluated. Eleven (11) cases exhibited ALK gene rearrangement (5.5%). Seven (7) of these cases were metastatic lung adenocarcinoma (stage IV). Mean age of the patient is 51 years (21-79 years). History of smoking was available on only four (4) cases (2 smokers and 2 non-smokers). All cases were moderately to poorly differentiated adenocarcinoma. None of our cases showed signet cells or abundant intracellular mucin. **Conclusion:** The findings of this retrospective study show that the incidence of ALK gene rearrangements positive adenocarcinoma in Saudi patients is 5.5%. This is similar to the published data. **Keywords:** ALK rearrangement, FISH, lung tumors, Adenocarcinoma

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P3.04-020 ALK Rearrangements Epidemiology in Latin America (CLICaP) Oscar Arrieta Rodriguez[1], Andrés F. Cardona[2], Guillermo Bramuglia[3], Graciela Cruz-Rico[1], Claudio Martin[4], Alejandro Aviles-Salas[5], Luis Corrales[6], Omar Castillo[7], Hernan Carranza[2], Erica Rojas Bilbao[8], Carlos A. Vargas[2], Leonardo Rojas[9], Hernán Lupera[10], Horacio Astudillo[11] [1]*Unidad Funcional de Oncología Torácica Y Laboratorio de Medicina Personalizada, National Cancer Institute, Mexico City/Mexico,* [2]*Clinical and Translational Oncology Group, Foundation for Clinical and Applied Cancer Research - Ficmac, Bogotá/Colombia,* [3]*Argenomics, Buenos Aires/Argentina,* [4]*Clinical Oncology, Instituto Fleming, Buenos Aires/Argentina,* [5]*Pathology, National Cancer Institute, Mexico, Df/Mexico,* [6]*Clinical Oncology, Hospital San Juan de Dios, San José/Costa Rica,* [7]*Oncology, Hospital Santa Fe, Panama, Panama/Panama,* [8]*Pathology, Instituto de Oncología Angel Roffo Y Hospital Alemán, Ciudad Autónoma de Buenos Aires/Argentina,* [9]*Centro Javeriano de Oncología, Hospital Universitario San Ignacio, Bogotá/Colombia,* [10]*Medical Oncology, Hospital Metropolitano, Quito/Ecuador,* [11]*Laboratory of Translational Cancer Research and Cellular Therapy, Oncology Hospital,, Medical Center Xxi Century, Mexican Institute of Social Security (Imss), Mexico/Mexico*

Background: Latin American countries are heterogeneous in terms of lung cancer incidence, ethnicity, and exposure to potential carcinogens. The discovery of the echinoderm microtubule-associated protein like 4-anaplastic lymphoma kinase (EML4-ALK) translocation as an oncogenic driver has led to the development of novel therapies with activity *in vitro* and in the clinic. In this study we evaluated the frequency and clinical characteristics of ALK rearrangements in six Latin-American

countries. **Methods:** A total of 2799 biopsies of advanced NSCLC patients from 6 countries of Latin America (Argentina, Colombia, Costa Rica, Panama, Ecuador, and Mexico) were evaluated by the method fluorescence *in situ* hybridization (**FISH**) for detection of ALK-rearrangements. Demographic and clinicopathologic characteristics were analyzed. **Results:** The FISH analyses showed positive ALK fusion gene status in **6.55%** (181/2761) of the total sample from all participating countries. ALK+ for each country was a follows: **Argentina 6.08%** (105/1726), **Colombia 4.83%** (10/207), **Costa Rica 4.83%** (2/49), **Mexico 8.57%** (64/746), and **Panama 0%** (0/33). Ecuador only used immunohistochemistry for ALK detection rearrangement; therefore, these samples were excluded from FISH technique analysis. **Conclusion:** The frequency of ALK rearrangement in Latin America is higher than previously reported for the Caucasian and Japanese populations. In addition, there is significant continental variability. Until now, FISH for ALK testing is not widely available in Latin America due to its high cost, time-consumption and result interpretation. There is an increased need to develop a common platform for genomic evaluation in developing countries. **Keywords:** Non-small-cell lung cancer, Rearrangements ALK, FISH, Latin America

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P3.04-021 Mutation Profiling by Targeted Next-Generation Sequencing for Diagnostics and Patient Cohort Screening in FFPE NSCLC Samples Linnea La Fleur[1], Lotte Moens[1], Elin Falk-Sörqvist[1], Magnus Sundström[1], Johanna S.M. Mattsson[1], Hirsh Koyi[2], Eva Branden[2], Hans Brunnström[3], Simon Ekman[1], Martin Sandelin[4], Johan Isaksson[2], Karin Jirström[3], Patrick Micke[1], Mats Nilsson[5], Johan Botling[1] [1]*Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala/Sweden,* [2]*Department of Respiratory Medicine, Gävle Hospital, Gävle/Sweden,* [3]*Department of Clinical Sciences Lund, Division of Oncology and Pathology, Lund University, Lund/Sweden,* [4]*Department of Medical Sciences, Uppsala University, Uppsala/Sweden,* [5]*Department of Biochemistry and Biophysics, Stockholm University, Stockholm/Sweden*

Background: Recent discovery of the landscape of somatic mutations in non-small cell lung cancer (NSCLC), and introduction of new therapeutics have raised the demands for multiplex mutation assays. In exploratory research, mutation profiling has largely been performed on fresh-frozen tissue from surgical specimens. However, for patients with advanced disease the assays need to be adapted to small formalin-fixed paraffin embedded (FFPE) biopsies and cytology preparations. Targeted next-generation sequencing (NGS) techniques are now being developed to address these challenges and have now reached the point where they are more cost efficient than previously used methods, hence there is a need to optimize and validate these techniques to determine if they are robust enough to work in clinical diagnostics. **Methods:** Here we have developed and evaluated Haloplex gene panels in comparison to pyrosequencing and quantitative PCR(qPCR), i.e. the current standard methods for molecular diagnostics of solid tumours in Sweden. The target enrichment was focused on short DNA fragments and included independent capture of complementary strands, "two strand capture", to address fragmentation and base damage induced by formalin fixation. The panels include all exons of 18-32 genes (for lung cancer and other solid tumors respectively) with known clinical relevance. Seventy-one clinical samples (NSCLC, colorectal carcinoma and melanoma), with known mutational status of hotspots in KRAS, BRAF, NRAS, PIK3CA and EGFR, were selected for analysis. DNA was prepared from FFPE tissues and used for library preparation using the panels and subsequently sequenced on an Illumina MiSeq instrument. **Results:** A complete concordance was seen between the previously defined pyrosequencing and qPCR genotypes and the corresponding variants detected using the gene panels. Both point mutations and smaller indels (<25bp) could be detected by this technique using an in-house bioinformatic pipeline. False positive FFPE-induced mutation artefacts could reliably be identified by the two-strand filter. The technical sensitivity of mutation detection was determined to 2%, and we have decided to use a 5% variant allele frequency threshold for clinical reporting. In addition, clonality and subclonality could be discovered in patients with complex tumour disease (mixed or multiple tumour lesions) by analysis of the mutation patterns. An extended 85 gene panel has also been designed to screen for mutations in NSCLC patient cohorts for clinical molecular research. **Conclusion:** We believe that the established lung cancer gene panels for targeted enrichment and NGS can replace pyrosequencing and qPCR for molecular diagnostics in NSCLC, and will be useful for screening of unselected population-based prospective and retrospective lung cancer patient cohorts in clinical research. **Keywords:** target enrichment, formalin-fixed paraffin embedded, next-generation sequencing, non-small cell lung cancer

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P3.04-022 The Johns Hopkins University TCGA Experience Candace Griffin[1], Beverly Lee[2], Kristen Rodgers[1], Andrew Yang[1], Vincent Battafarano[1], Craig Hooker[1], Alicia Hulbert[2], Peter B. Illei[3], Dante Trusty[3], James Shin[3], Richard Battafarano[1], Daniela Molena[1], Stephen Yang[1], Malcolm Brock[1] [1]*Department of Thoracic Surgery, Johns Hopkins University School of Medicine, Baltimore/MD/United States of America,* [2]*Department of Oncology, Johns Hopkins Medical Institution, Baltimore/MD/United States of America,* [3]*Department of Pathology, Johns Hopkins University, Baltimore/United States of America*

Background: The Cancer Genome Atlas (TCGA) is a genomic mapping effort that characterizes and analyzes the major types of cancer. Specimens have to meet strict tissue criteria to become eligible for shipment to TCGA and used for genomic analysis. Johns Hopkins University (JHU) is a part of the TCGA network and we have sent numerous biospecimens for analysis. Our experience is catalogued over 3 different shipments and may be unique only to JHU. This paper will analyze if the JHU samples that have qualified for TCGA are representative of the overall selected lung cancer samples. **Methods:** We analyzed the JHU cohort using TCGA's shipment qualification reports in addition to our biospecimen data pre-selected for TCGA. Specimens with at least 60% tumor qualified for TCGA and those that disqualified were because of lack of RNA. Specimens that were not eligible for shipment had less than 60% tumor. **Results:** There is a trend in older specimens being disqualified throughout the TCGA shipments. In contrast, those specimens that were cut but deemed ineligible to be sent to TCGA tended to be older, male, adenocarcinoma (p=0.003), and earlier stage (p=0.010) than those that were actually shipped. The majority of the specimens that were shipped were sent during shipment 1 (p<0.001) and the proportion of specimens sent were older (long surgery to cut duration) than younger comparing specimens with durations of 0 years, 1-10 years, and 11-21 years (p<0.001).

Table 1. Comparison of Patient Demographic Distributions for Johns Hopkins Lung Cancer Specimens Sent to TCGA (N=120)

	"Disqualified" 91 (75.8%)		"Qualified" 29 (24.2%)		
Characteristics	#	%	#	%	p value
Median Age, yrs (IQR)	66	(60-72)	68	(62-72)	0.523
Gender					0.752
Male	44	48.3	15	51.7	
Female	47	51.7	14	48.3	
Race					0.061
White	70	76.9	27	93.1	
Black	21	23.1	2	6.9	
Histology					0.165
Adenocarcinoma	43	47.3	18	62.1	
Squamous cell	48	52.7	11	37.9	
Stage*					0.538
I	46	49.4	10	38.4	
II	37	41.6	14	53.9	
III	8	9.0	2	7.7	
Cut for TCGA†					0.065
First (2010)	82	77.4	24	22.6	
Second (2011)	1	25.0	3	75.0	
Third (2012)	8	80.0	2	20.0	
Years from Surgery to Cut†					0.115
0	7	58.3	5	41.7	
1-10	28	70.0	12	30.0	
11-21	56	82.4	12	17.6	

* Five observations missing stage, disqualified (2(2%)) and qualified (3(10%)).
† Percentages are presented by row.

Table 2. Comparison of Patient Demographic Distributions for Johns Hopkins Lung Cancer Specimens – Sent vs. Not Sent to TCGA (N=167)

	Not Sent 47 (28.1%)		Sent 120 (71.9%)		
Characteristics	#	%	#	%	p value
Median Age, yrs (IQR)	69	(61-73)	66	(60-72)	0.392
Gender					0.474
Male	26	55.3	59	49.2	
Female	21	44.7	61	50.8	
Race					0.326
White	41	87.2	97	80.8	
Black	6	12.8	23	19.2	
Histology					0.003
Adenocarcinoma	35	76.1	61	50.8	
Squamous cell	11	23.9	59	49.2	
Stage*					0.010
I	28	60.3	54	47.0	
II	10	22.2	51	44.3	
III	5	11.1	10	8.7	
IV	2	4.4	0	0.0	
Cut for TCGA†					<0.001
First (2010)	14	11.7	106	88.3	
Second (2011)	7	63.6	4	36.4	
Third (2012)	26	72.2	10	27.8	
Years from Surgery to Cut†					<0.001
0	22	64.7	12	35.3	
1-10	12	23.1	40	76.9	
11-21	13	16.1	68	83.9	

* Seven observations missing stage, not sent (3(4%)) and sent (5(4%)).
† Percentages are presented by row.

Conclusion: Our data suggests that older specimens were the most likely to be disqualified when shipped to the TCGA as well as those that were not sent but were cut for shipment. Future research should focus on developing more advanced technology that will allow the inclusion of a wide range of specimens that do not exclude a large part of the lung cancer population. **Keywords:** biospecimen, lung cancer, TCGA

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-023 Exosomes and Their Potential for Detection of Lung Cancer Birgitte Sandfeld Paulsen[1], Kristine R. Jakobsen[1], Rikke Bæk[2], Peter Meldgaard[3], Kim Varming[2], Malene Jørgensen[2], Boe S. Sorensen[1] [1]*Dept. of Clinical Biochemistry, Aarhus University Hospital, Aarhus C/Denmark,* [2]*Dept of Immunology, Aalborg University Hospital, Aalborg/ Denmark,* [3]*Dept. of Oncology, Aarhus University Hospital, Aarhus C/Denmark*

Background: A recent study showed that advanced lung adenocarcinoma patients have a distinct exosomal protein-profile compared to a matched group without cancer (Jakobsen et al., 2015, JEV). To improve the overall survival, it is however crucial to develop tools capable of detecting early stages of lung cancer as well. In addition, it is unsettled if different histologic subclasses result in distinct exosomal protein profiles. The aim of this study is to explore the potential of using exosomal proteins as biomarkers in lung cancer patients of all stages and of different histology histology. **Methods:** Plasma was isolated from patients suspected of having lung cancer. Patients diagnosed to be cancer free were defined as controls. Based on previous experiments a panel of 47 antibodies were selected for exosome-capture using a highly sensitive extracellular vesicle protein array (EV Array). 10 µl unpurified plasma was applied to the EV Array and captured exosomes were visualised by binding of biotin-conjugated CD9, CD63 and CD81 antibodies. The information from all 47 markers was investigated by multivariate analysis by partial least squares discriminant analysis (PLS-DA). **Results:** The study included 504 patients; 153 control patients and 351 patients with NSCLC (adenocarcinoma 70%, squamous cell 24%, other 6%). 51% had locally advanced or advanced disease and 49% had local disease. Multivariate analysis produced a combined marker model separating cancer patients from controls regardless of stage and histology. Area under the curve (AUC) was for each stage: I: 0.74 (0.68-0.82), II: 0.68 (0.57-0.79), III: 0.77 (0.62-0.91) and IV 0.79 (0.73-0.83). For all stages AUC was 0.755, CI (0.72-0.81) with sensitivity 0.70 and specificity 0.66. The accuracy of the test was 0.69. **Conclusion:** We demonstrate that the EV array is able to lung cancer in advanced as well as low stages regardless of histology.
Keywords: exosomes, EV Array, NSCLC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-024 Lung Adenocarcinoma with Neuroendocrine Feature Revealed by Transcriptome Profiling Takeshi Fujiwara, Yuichi Ishikawa *Japanese Foundation for Cancer Research, Tokyo/Japan*

Background: Although our previous transcriptomic analyses revealed that a subgroup in lung adenocarcinoma with a neuroendocrine feature exhibits poor prognosis, the link of the phenotype with patient outcomes has been limited only to two populations derived from a Japanese and a US institution. Here we performed additional transcriptomic profiling analyses to elucidate whether our method was useful also to other populations. **Methods:** Seven independent web-based datasets of lung adenocarcinoma, either on expression microarrays or on an RNA-seq platform, were examined. The expression level of the *ASCL1* geneset (100 probes closely correlated with *ASCL1* expression) was used to define the neuroendocrine character based on the method we previously reported. Subtyping was performed by consensus clustering with non-negative matrix factorization. Correlation of overall survival was analyzed with the Kaplan-Meier method. **Results:** The neuroendocrine subtype was identified from each of seven independent cohorts with 45, 90, 117, 183,196, 443 and 548 lung adenocarcinoma samples. Among them, three datasets showed statistically significant association with patient survival ($p<0.05$). The neuroendocrine subtype was inversely correlated with expression of ubiquitination genes. Somatic mutations identified in the neuroendocrine subtype with the TCGA data were common ones such as *TP53*, *STK11* and *KRAS*. **Conclusion:** Transcriptomic profiling partially reproduced the neuroendocrine subtype in lung adenocarcinoma samples derived from the independent datasets.
Keywords: transcriptome

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-025 DNA Extraction of Lung Cancer Samples for Advanced Diagnostic Testing Jeffrey Conroy[1], Hanchun T. Defedericis[1], Angela Stout[2], Kiersten Marie Miles[2], Blake C. Burgher[1], Antonios Papanicolau-Sengos[1], Carl D. Morrison[1] [1]*Center for Personalized Medicine, Roswell Park Cancer Institute, Buffalo/NY/United States of America,* [2]*Molecular Pathology, Roswell Park Cancer Institute, Buffalo/NY/United States of America*

Background: Tumor specimens are routinely formalin fixed and paraffin embedded (FFPE) prior to histologic evaluation. This process preserves the morphology and cellular features required for proper staining and microscopic review. However, this practice presents numerous challenges for the extraction of high quality DNA for advanced diagnostic testing that include nanoString and Next-Generation Sequencing (NGS) technologies. An extraction process that consistently produces sufficient DNA yield and fragment size from these difficult but most precious tissue samples is a requirement for any Molecular Pathology laboratory utilizing these platforms. The data presented here will compare the quantity and quality of DNA extracted using two methods, QIAGEN and Covaris, and success of downstream testing. **Methods:** FFPE tumor samples from a variety of tumor types, including lung, were macro-dissected using 14-guage needles, with 1 core extracted using the Covaris truXtract FFPE DNA isolation method and the other matched core using the QIAGEN DNeasy tissue kit. All samples were processed using manufacturer's recommended instructions. DNA metrics were measured using Qubit (picogreen) and NanoDrop for yield and purity, followed by fragment size estimation on a 2100 BioAnalyzer (Agilent Technologies). A subset of matched DNA sample pairs were used as template for PGM AmpliSeq and MiSeq TSCA library preparation, followed by NGS. A subset of DNA sample pairs were also analyzed for copy number using the nanoString nCounter system. **Results:** DNA yields and fragment lengths were substantially higher for truXtract samples as compared to DNeasy when measured by picogreen quantitation and Bioanalyzer electrophoresis (Figure 1). A higher degree of successful advanced molecular diagnostic test results was also observed for the truXtract DNA samples, especially for the Illumina NGS system (improved clustering and coverage) and nCounter platform (improved counts) that prefer longer fragment lengths than Ion Torrent NGS.

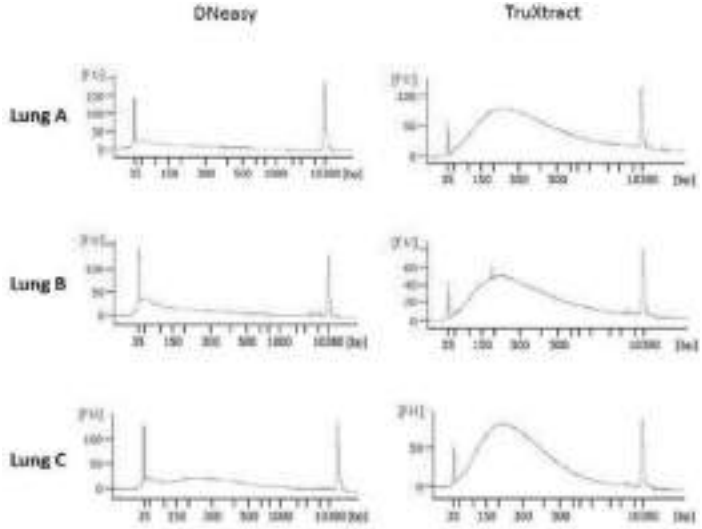

Figure 1: 2100 Bioanalyzer traces of DNA prepared from three lung cancer FFPE samples; DNeasy (left) and TruXtract (right). Conclusion: FFPE tumor samples prepared using the truXtract FFPE DNA isolation kit provides an efficient system for generating high quality DNA samples from even the most difficult lung cancer specimens. The combination of improved yield and fragment size measured for nearly every sample tested suggests that even smaller biopsies can now be collected for advanced diagnostic testing.
Keywords: DNA extraction, molecular diagnostics, FFPE tissue, NGS

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-026 Reflex Testing of EGFR and ALK in Non-Squamous Non-Small Cell Lung Cancer Jonan Z.-E. Tan[1], Whee-Sze Ong[2], Daniel S.-W. Tan[3], Angela Takano[4], Tony Kiat-Hon Lim[4], Kian-Sing Chan[4], Lynette Lin-Ean Oon[4], Alvin Soon-Tiong Lim[4], Amit Jain[5], Chee-Keong Toh[5], Mei-Kim Ang[5], Quan-Sing Ng[5], Ravindran Kanesvaran[5], Anantham Devanand[6], Chong-Hee Lim[7], Tina Puay-Theng Koh[8], Wan-Teck Lim[5], Eng Huat Tan[5] [1]*Bristol University, Bristol/United Kingdom,* [2]*Division of Clinical Trials and Epidemiological Sciences, National Cancer Centre, Singapore, Singapore/Singapore,* [3]*National Cancer Centre, Singapore, Singapore/Singapore,* [4]*Pathology, Singapore General Hospital, Singapore/Singapore,* [5]*Medical Oncology, National Cancer Centre, Singapore, Singapore/ Singapore,* [6]*Respiratory and Critical Care Medicine, Singapore General Hospital, Singapore/ Singapore,* [7]*Cardiothoracic Surgery, National Heart Centre, Singapore, Singapore/ Singapore,* [8]*Surgical Oncology, National Cancer Centre, Singapore, Singapore/Singapore*

Background: Reflex molecular testing has affirmed the paradigm shift in the classification of tumors by genetic profile, in addition to conventional histopathology. It plays a critical role in identifying actionable targets and prompt allocation of patients to the appropriate treatment. We sought to compare the clinical characteristics and treatment outcomes between patients with genetic alterations against wild-type (WT) tumors for both EGFR and ALK in non-squamous non-small cell lung cancer (NSCLC) to examine the impact of reflex testing which was recently implemented in the National Cancer Centre Singapore. **Methods:** We analyzed all NSCLC patients diagnosed between Jan 2010 and Mar 2014 from a prospective database maintained by the Lung Cancer Consortium Singapore. Patients underwent reflex Sanger-based EGFR analysis from 2010 and ALK-FISH analysis from 2012. These analyses were undertaken upon histological diagnosis, regardless of the AJCC stage at presentation. Clinical characteristics of the mutant and WT groups were compared using chi-squared and Mann Whitney U tests. Overall survival(OS) was estimated using Kaplan-Meier method. Survivals were compared using log-rank test, and prognostic factors were determined using multivariate cox regression. **Results:** The overall EGFR mutation rate in our cohort (n=1308) was 51.4%. The corresponding rates in adenocarcinoma and non-adenocarcinoma groups were 52.5% and 34.9% respectively. EGFR mutants were more prevalent among females, never-smokers, and less symptomatic. A higher proportion had better ECOG status, well to moderately differentiated histology, more sites of distant metastases especially in the lungs and bones, presented with Stage IV, , and received more lines of palliative treatment (all $p<0.05$). The median OS(months) for the mutant group was 24.8 versus 13.3 for the WT group ($p<0.001$). Prognostic factors included ethnicity, smoking status, stage, histology, number of symptoms, ECOG status, number of metastatic sites, treatment intention and EGFR tyrosine kinase inhibitor (TKI) treatment (all $p<0.02$). The overall ALK alteration rate (n=405) was 12.6%, 12.4% in adenocarcinoma and 15.2% in non-adenocarcinoma. Contrary to prior reports, there were no differences in gender,

diagnosis age, and smoking status between fusion and WT groups. The percentage of ALK fusion among Malays was higher (26.3% vs 7.9%; p=0.031). While ALK fusion had more lines of palliative treatment than WT, there was no significant difference in OS between both groups. Prognostic factors include gender, ethnicity, ECOG status, treatment intent, and number of palliative treatment and metastatic sites (all p<0.02). **Conclusion:** This study demonstrated significant differences in clinical features, management and subsequent response to treatment between genetically altered and WT patients for both EGFR and ALK profiles, reiterating the importance of reflex testing in patient management. While significant survival benefit was demonstrated with EGFR TKI therapy in EGFR cohort, this was not demonstrated for the ALK cohort, which can be attributed to the relative lack of access to ALK TKI (93% treated with EGFR TKI compared to 46.6% treated with ALK TKI). Finally, the considerable rate of EGFR and ALK mutations in non-adenocarcinoma groups reflects the need to extend reflex testing to these patient groups, and not just in patients with adenocarcinoma or adenocarcinoma components.
Keywords: Reflex testing, EGFR mutations, ALK fusion

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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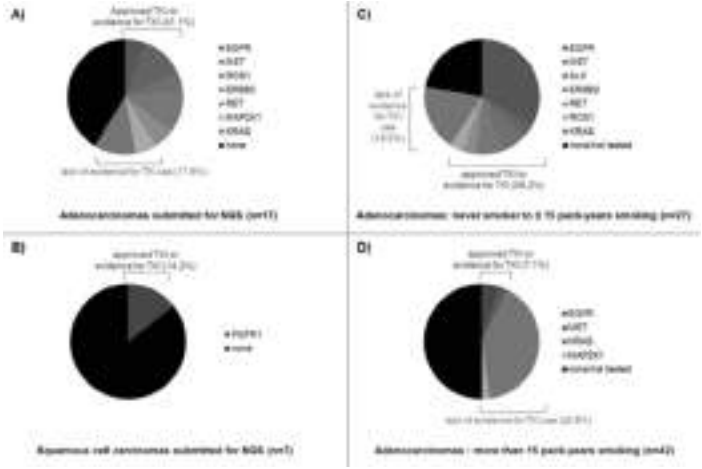
P3.04-027 Targeted next Generation Sequencing in Lung Cancer: Genomic Oncology in Daily Practice Deepa Rangachari[1], Paul Vanderlaan[2], Xiuning Le[3], Erik Folch[4], Michael S. Kent[5], Sidhartha P. Gangadharan[6], Adnan Majid[4], Richard L. Haspel[2], Loren J. Joseph[2], Mark S. Huberman[1], Daniel B. Costa[1] [1]*Division of Hematology/Oncology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston/MA/United States of America,* [2]*Department of Pathology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston/MA/United States of America,* [3]*Division of Hematology/Oncology, Beth Israel Deaconess Medical Center, Boston/United States of America,* [4]*Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston/MA/United States of America,* [5]*Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston/MA/United States of America,* [6]*Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston/United States of America*

Background: Tumor genotyping using single gene assays (SGAs) is a standard approach in the management of advanced NSCLC. We evaluated how therapeutic decision-making was altered by the introduction of next generation sequencing (NGS) into routine clinical practice. **Methods:** Clinicopathologic data, tumor genotype, and clinical decisions were retrospectively compiled over 6 months following introduction of NGS assay use at our institution. **Results:** 82 tumors were genotyped: 75 by SGAs, 7 by NGS alone, and 22 by SGAs and NGS. SGAs identified 10 EGFR-mutated, 3 ALK-rearranged, and 21 KRAS-mutated tumors. Sequential testing with SGAs followed by NGS was more common for patients with EGFR/ALK/KRAS-negative tumors (22/29 or 75.9%) and adenocarcinomas (ACs) (21/22 or 95.5%). Most EGFR/ALK/KRAS-negative tumors were sent for NGS (21/35 or 60%). Of 17 ACs, 10 harbored abnormalities in a known driver oncogene (1-EGFR, 2-ERBB2, 1-ROS1, 1-RET, 2-MET, 2-KRAS and 1-MAP2K1). Primary NGS was used mainly in squamous cell cancers (SCCAs) (6/7 or 85.7%). In 7 SCCAs, 1 sample had a driver aberration (FGFR1); 6 had other genomic events (all with TP53 mutations). NGS was successful in 24/29 (82.7%) tumors overall. There was a trend toward increased assay failure in those samples undergoing sequential SGAs followed by NGS as compared to primary NGS alone. All patients with EGFR-mutated or ALK-rearranged tumors received approved tyrosine kinase inhibitors (TKIs) or were consented for clinical trials. Clinical decisions were impacted by NGS results in 8/17 (47.0%) ACs (trial consideration in 6, off-label TKI use in 2). Therapeutic decisions were influenced by NGS results in 0/7 SCCAs (p=0.0538 when compared to ACs). Actionable therapeutic targets were significantly more frequent in patients with a ≤15 pack-year tobacco history vs. those with >15 pack-years of tobacco use (17/27 or 62.9% vs. 3/42 or 7.1%, respectively; p<0.0001). Only 1/9 (11%) of oncologists demonstrated a detailed understanding of the genomic technologies being used.



Conclusion: Targeted NGS can identify a significant number of driver events in lung ACs—particularly in never/light smokers—for which targeted therapies are available or in development. However, for SCCAs, NGS results are less likely to alter standard practice, barring participation in biomarker-driven studies. Future research into the cost effectiveness and optimal use of NGS in NSCLC is warranted, as well as continued efforts to improve provider awareness and application of genomic technologies.
Keywords: lung cancer, EGFR, ALK, next generation sequencing

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

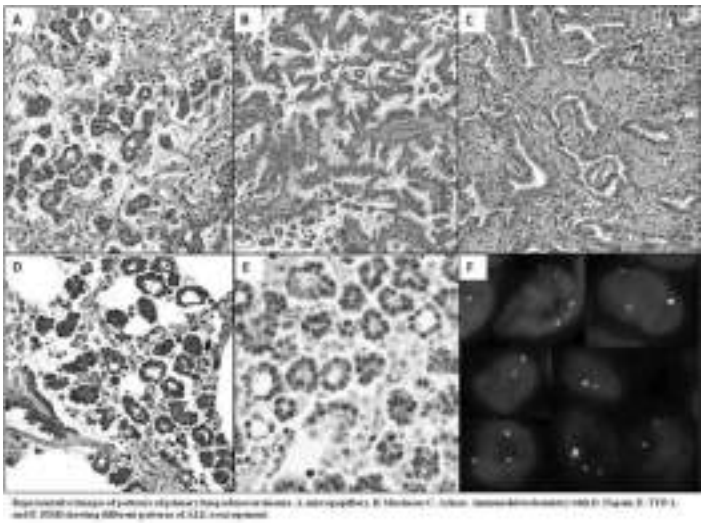
P3.04-028 Defining the Molecular Profile of Non-Small Cell Lung Carcinoma in a Comprehensive Cancer Center in Mexico City Cesar Octavio Lara-Torres[1], Diana E. Aguilar-Leon[2], Guadalupe Canchola-Aguilar[2], Laura García-Alanís[2], María De Los Angeles Ibarra-Meneses[2], Gabriel Herrera-Maya[2], Raquel Gerson-Cwilich[3], Alberto Villalobos Prieto[3], Carlos Ortiz Hidalgo[2] [1]*Molecular Pathology Laboratory, The American British Cowdray Medical Center, Mexico City/Mexico,* [2]*Molecular Pathology Laboratory, The American British Cowdray Medical Center, Mexico/Mexico,* [3]*Cancer Center Oncology Department, The American British Cowdray Medical Center, Mexico/Mexico*

Background: Molecular characterization of lung cancer is of paramount importance. Although genetic drivers such as EGFR,KRAS and ALK mutation are routine, they represent 30-40% of all mutations identified. The relative frequency vary according to the population studied and scarce data exist on Mexican population. The aim of the study is to describe the clinicopathologic characteristics and molecular profile of the population of NSCLC patients studied in a recent molecular pathology laboratory. **Methods:** Cases diagnosed with NSCLC from January 2012 to March 2015 seen at the department of surgical and molecular pathology of TheAmerican-BritishCowdrayMedical Center in Mexico City were retrieved. Medical records were reviewed for data on clinicopathologic characteristics (age, sex, biopsy site, histological parameters, and mutational status of EGFR, KRAS and ALK. DNA extraction was done using QIAampDNAFFPE Tissue Kit(Qiagen). EGFR and KRAS determination was performed using scorpion-ARMS technique(Therascreen/ Qiagen) in Rotor-GeneQThermalcycler(Qiagen). ALK rearrangement was determined using ALK-LSI probes(Abbott Molecular), and evaluated with OlympusBX53 fluorescence microscope. All the procedures were carried out according to manufacturer instructions. **Results:** 90 cases were retrieved, 77(85.6%) adenocarcinoma, 6(6.7%) squamous cell carcinoma, 3(3.3%)large cell carcinoma and 4(4.4%) mixed cells types (2 adenosquamous carcinoma, 1 adenocarcinoma with neuroendocrine component, and 1 sarcomatoid carcinoma). Histologic subclassification showed predominant acinar in 56%, solid 20%, lepidic 15%, and 9% micropapillary pattern. Lung biopsies were the tissue specimen in 58 cases(64.4), metastatic site in 28(31.1)(lymph node 9, bone 8, pleura 3, skin 2, soft tissue 2, mediastinal tumor 1, ovary 1, parotid 1 and CNS 1), and non-specified 4(4.5%). Demographic variables and mutational status of EGFR/KRAS/ALK are shown in table 1

TABLE 1. Comparison of Clinical Characteristics of Lung NSCLC Patients and Driver Mutations

Characteristics	Total (n=90)	EGFR mutation (n=86)*	KRAS mutation (n= 64)*	ALK fusion (n=74)*	Triple Negative (n=67)**
Overall, *n* (%)		17 (19.5)	18 (28.1)	1 (1.4)	32 (47.7)
Age, median (range)	67 (28-88)	64 (46-82)	64.5 (51-79)	86 (86)	71 (38-88)
Gender					
Men, *n* (%)	39 (43.3)	3 (3.4)	8 (12.5)	1 (1.4)	17 (25.4)
Women, *n* (%)	51 (56.4)	14 (16.1)	10 (15.6)	0	15 (22.3)
Primary, *n* (%)	58 (64.4)	12 (13.8)	16 (25)	1 (2.0)	19 (28.4)
Age, median (range)	64 (35-88)	68 (46-82)	63 (51-79)	86 (86)	72(47-88)
Gender					
Men, *n* (%)	16 (44.8)	2 (16.6)	7 (38.8)	1 (4.5)	9 (47.4)
Women, *n* (%)	12 (55.2)	10 (83.4)	9 (50)	0	10 (52.6)
Metastasis, *n* (%)	28 (31.1)	5 (5.7)	2 (3.1)	0	12 (17.9)
Age, median (range)	64.5 (28-84)	64 (28-84)	68.5 (65-72)	-------	71 (38-84)
Gender					
Men, *n* (%)	12 (42.8)	1 (20)	1 (50)	-------	8 (66.6)
Women, *n* (%)	16 (57.2)	4 (80)	1 (50)	-------	4 (33.3)

* Number of cases assessed
**Number of cases with the three mutations verified



Conclusion: We corroborate in our population the higher frequency of

EGFR mutation in female patients, with a percentage between Caucasian and Asian populations. KRAS is the most frequent mutation and mutually exclusive with EGFR and ALK. Triple negative cases represent half of NSCLC. **Keywords:** non-small cell lung cancer, EGFR/KRAS/ALK, demography, Mexican population

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-029 Development of Lung Cancer Diagnosis Panel Based on the Target Sequencing Technology: A Validation Result Yoohwa Hwang[1], Hyeri Kim[2], Won-Chul Lee[2], Ahreum Seong[2], Nak-Jung Kwon[2], Jae Sook Sung[3], Chang Won Park[2], Kap-Seok Yang[2], Yoo Jin Jung[4], Sae Bom Lee[4], Yun Ho Kim[4], In Kyu Park[1], Chang Hyun Kang[1], Yeul Hong Kim[3], Jeong-Sun Seong[5], Young Tae Kim[1] [1]*Thoracic and Cardiovascular Surgery, Seoul National University Hospital, Seoul/Korea,* [2]*Macrogen, Seoul/Korea,* [3]*Cancer Research Institute, Korea University, Seoul/Korea,* [4]*Cancer Research Institute, Seoul National University, Seoul/Korea,*[5]*Genomic Medicine Institute (Gmi), Seoul National University, Seoul/Korea*

Background: Recent development of next generation sequencing technologies enabled the accumulation of a lot of information about genomic variants in cancer. However, the price of whole genome / exome sequencing is still high to be used as a diagnostic testing for treatment decision-making. **Methods:** To develop a clinically useful diagnostic kit, we designed a lung cancer diagnostics (LCDx) panel to discover all coding mutations on 42 genes, *MET* exon14 skipping and fusion genes involving 4 genes (*ALK, RET, ROS1* and *AXL*). The performance of the panel was tested by using 100 lung cancer tissues and compared the results to those of three different diagnostic platforms, including Sanger sequencing, Ion AmpliSeq Cancer Hotspot Panel (Thermo-Life Technologies) and fluorescence in situ hybridization (FISH). **Results:** For the detection of *EGFR* and *KRAS* mutations, LCDx panel showed 100% sensitivity and specificity. For fusion discovery, the specificity reached 93% but the sensitivity was only 35%, which suggested a novel design of fusion detection method should be addressed for future development.

EML4-ALK				
	FISH+	**FISH-**		
LCDx+	8	8	Sensitivity	42.1%
LCDx-	11	62	Specificity	88.6%

KIF5B-RET				
	FISH+	**FISH-**		
LCDx+	1	2	Sensitivity	14.3%
LCDx-	6	78	Specificity	97.5%

Conclusion: In our result, we confirmed all the lung cancer mutations currently being examined by multiple clinical assays could be identified by one target sequencing method more accurately and conveniently using LCDx. Our results suggest that, with improvement of fusion discovery, cancer panel such as our LCDx panel, can be used for clinical diagnostics and treatment decision making of non-small cell lung cancer patients. **Keywords:** mutation, fusion, Adenocarcinoma, cancer panel

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-030 Are Experienced Physicians More Likely to Acquire Adequate Tissue Material for EGFR-Testing? Janna Berg[1], Pål Suhrke[1], Lars Fjellbirkeland[2], Odd Terje Brustugun[3], Åslaug Helland[3] [1]*Dept. of Medicine, Vestfold Hospital Trust, Tønsberg/ Norway,* [2]*Dept.Of Pulmonology, Oslo University Hospital-Rikshospitalet, Oslo/Norway,* [3]*Dept of Oncology, Oslo University Hospital-Radiumhospitalet, Oslo/Norway*

Background: Epidermal Growth Factor Receptor (EGFR) mutation testing is now recommended practice for non-squamous non-small cell lung cancer. The patients with activating EGFR mutations are eligible for targeted personalized treatment offering better survival and quality of life, often with low toxicity. However, little is known about how the physician's level of experience influences the quality of samples taken for EGFR-analysis and if complicated interventions result in more inadequate samples. We therefore performed a retrospective analysis on correlation between doctors' experience and tissue quality at a moderately-sized community hospital. **Methods:** The Norwegian Lung Cancer Group (NLCG) recommended EGFR- testing of all patients with non-small cell lung carcinoma from June 2010. In March 2013 squamous cell carcinomas were excluded. Basic demographic data, sample type, test results and procedure related complications were recorded for the period June 2010 to December 2013, and the level of experience (measured as inexperienced physicians having less than 10 procedures per year) of the involved physicians was recorded. **Results:** Material was sent for EGFR analysis for 256 of the 304 eligible patients diagnosed in the period. For a total of 34 patients (13%) the first biopsy was not analyzed at department of molecular pathology due to inadequate tumor material. The tissue collected by experienced physicians was sufficient for EGFR analyses in 91-97.2% (median 93%), compared to 50-90% (median 86.7%) for the less experienced physicians. For image supervised biopsies, non-analyzable samples were more frequent when puncturing small (<3 cm) peripheral tumors than when taken from large central tumors. Of 14 image guided biopsies that were returned because of inadequate tumor tissue, only two had complications: one with bleeding and the other with pneumothorax. Both tumors were peripheral. Of three bronchoscopical biopsies that were returned due to inadequate tumor tissue, one was complicated by major bleeding, in another the patient was very restless during the procedure. The last was uncomplicated. **Conclusion:** Our results show that the quality of image guided biopsies taken by more experienced physicians is better than those taken by doctors with less experience. For small peripheral tumors, the frequency of non-analyzable samples were higher than for large central tumors taken by image guided biopsy. **Keywords:** EGFR mutation, Pathology, lung cancer

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P3.04-031 Combining CT Texture Analysis with Semantic Imaging Descriptions for the Radiogenomic Detection of EGFR and KRAS Mutations in NSCLC James Sorensen[1], Jeremy Erasmus Jr[1], Girish Shroff[1], Arvind Rao[1], Francesco Stingo[1], Laurence Court[1], Kathryn A. Gold[2], Jack Lee[3], John V. Heymach[4], Stephen Swisher[5], Myrna Godoy[1] [1]*Thoracic Radiology, University of Texas MD Anderson Cancer Center, Houston/United States of America,* [2]*Thoracic/Head & Neck Medical Oncology, University of Texas MD Anderson Cancer Center, Houston/TX/United States of America,*[3]*Biostatistics, MD Anderson, Houston/TX/United States of America,* [4]*Thoracic/Head and Neck Medical Oncology, MD Anderson, Houston/TX/United States of America,* [5]*Thoracic and Cardiovascular Surgery, MD Anderson, Houston/AL/United States of America*

Background: Existing literature suggests quantitative texture features derived from CT imaging can differentiate tumor genotypes and phenotypes. We combined CT texture analysis with semantic imaging descriptions provided by radiologists, and evaluated their ability to identify EGFR and KRAS mutation status in NSCLC. **Methods:** We retrospectively reviewed CT images from 628 patients from the GEMINI (Genomic Marker-Guided Therapy Initiative) cohort. Included were NSCLC patients whose biopsies included genetic testing for EGFR or KRAS mutations, and who underwent contrast-enhanced CT imaging within 90 days of biopsy. Excluded were patients who had undergone therapy or biopsy of their primary tumor before imaging, or whose tumors weren't segmentable. All CT images were contrast-enhanced, with body kernel reconstruction, and slice thicknesses of 1.25-5mm. Tumor segmentation was done in 3DSlicer (Harvard University, Cambridge MA) using a semi-automatic segmentation algorithm. Image pre-processing and textural feature extraction was performed using IBEX (MDACC, Houston TX). Semantic descriptions of the tumors were recorded by a thoracic radiology fellow and a board-certified thoracic radiologist in consensus. For each patient a set of textural features was calculated, based on the GreyLevel Co-Occurrence Matrix, Run-Length Matrix, voxel intensity histogram, and geometric properties of the tumor. Feature selection was based on existing literature, prior research experience, and excluded those features previously found to be poorly reproducible in lung tissue. These were combined with semantic descriptions (e.g. presence or absence of features such as spiculations, air bronchograms, and pleural effusions), for a total of 51 textural and geometric features, and 11 semantic features. When available, the SUVmax for the tumor was also included. To detect correlations with genetic mutations, these features were combined to train a Random Forest machine learning algorithm. This algorithm output a prediction for the mutation status of each tumor, and the predictive accuracy was assessed based on 10-fold cross-validation. **Results:**Included were 121 patients, 113 tested for KRAS mutations (26 positive) and 118 tested for EGFR mutations (31 positive). Maximum tumor dimensions ranged from 1.2–15.5cm (mean 5.6cm). Individual semantic features found to correlate with mutation status included tumor cavitation, pleural effusion, presence of ground glass opacity, and the nature of tumor margins (all p-values <0.05). Used collectively in a Random Forest classifier, textural features alone showed a sensitivity and specificity for KRAS detection of 50% and 81% respectively, with 74% overall accuracy. This increased modestly to a sensitivity and specificity of 50% and 84% respectively when semantic features were added, with accuracy increasing to 77%. For EGFR detection, textural features had sensitivity and specificity of 48% and 77% respectively, giving 69% accuracy. Detection of EGFR did not improve with inclusion of semantic features. **Conclusion:** Texture analysis correctly identified EGFR and KRAS mutation status in most patients. Although some semantic features correlated with mutation status, when combined with textural features they provided little or no improvement in predictive accuracy. One possible explanation is that textural features may already be capturing the information contained in the semantic features. Our results suggest oncogenic drivers of NSCLC are associated with distinct imaging features that can be detected radiographically. **Keywords:** CT, radiogenomics, texture, NSCLC

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P3.04-032 Clinical Applications of Next Generation Sequencing on Therapeutic Decision-Making in Lung Cancer Masayuki Takeda[1], Kazuko Sakai[2], Masato Terashima[2], Hiroyasu Kaneda[1], Hidetoshi Hayashi[1], Kaoru Tanaka[1], Tsutomu Iwasa[1], Takeshi Yoshida[1], Takayuki Takahama[1], Kazuto Nishio[2], Kazuhiko Nakagawa[1] [1]*Medical Oncology, Kinki University Faculty of Medicine, Osaka-Sayama/Japan,* [2]*Department of Genome Biology, Kinki University Faculty of Medicine, Osaka-Sayama/Japan*

Background: The identification of driver mutations, such as epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK), have already been successfully translated into clinical practice. The clinical implementation of genomic profiling for NSCLC with high-throughput and multiplex genotyping tests is thus warranted in order to prioritize appropriate therapies for individual patients. **Methods:** The present study has recruited lung cancer patients at Kinki University Hospital from June 2013. To screen patients with lung cancer for genetic alterations relevant to novel

molecular-targeted therapeutics, we have applied a Ion AmpliSeq RNA Fusion Lung Cancer Research Panel to detect known fusion transcripts such as ALK, ROS1, RET, and NTRK1 rearrangements simultaneously in a RNA sample obtained from FFPE lung cancer tissues. Deep sequencing was also performed using the Ion AmpliSeq Colon and Lung Cancer Panel. There were two co-primary endpoints for this study. First, we assessed the percentage of patients with additional therapy options uncovered by detecting potentially actionable genetic alterations. Second, we evaluated the percentage of patients who actually received genotype-directed therapy. **Results:** From June 2013, one hundred ten patient tumor samples were sequenced with these assays, and 104 (95%) patients received the results of Ion AmpliSeq Colon and Lung Cancer Panel and 106 (96%) patients received the results of the Ion AmpliSeq RNA Fusion Lung Cancer Research Panel with a >90% success rate for genotyping. An actionable driver alteration was detected in 43 (39%) of tumors from patients, leading to use of a targeted therapy in 23 (21%). **Conclusion:** Multiplexed genomic testing can aid physicians in matching patients with targeted treatments and appropriate clinical trials. **Keywords:** lung cancer, NGS, Driver mutation

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P3.04-033 Screening for Driver Mutations in Caucasian Patients with Central Nervous System Metastases of Non-Small-Cell Lung Cancer

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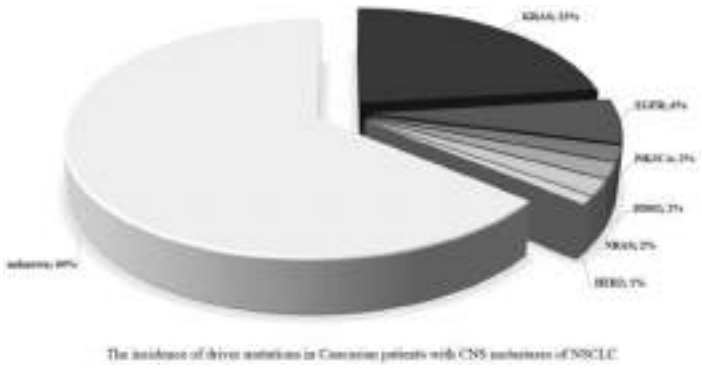
Background: The knowledge about molecular profile of advanced NSCLC may increase the possibility and effectiveness of cancer treatment. According to data of LCMC, FNN and CRUK, driver mutations are reported in 50-60% of non-small cell lung cancer (NSCLC) patients, especially in adenocarcinoma subtype. Unfortunately, we have limited information concerning the incidence of driver mutations in metastatic lesions of NSCLC. The main aim of the study was characterize the molecular background of central nervous system (CNS) metastatic lesions of NSCLC. It was performed by estimation the frequency of selected driver mutations in Caucasian chemotherapy and molecularly targeted therapy naïve patients. **Methods:** The studied group included 145 patients (45 females, 100 males, age: 60±8,8 years) with CNS metastases of NSCLC.The studied group included 80 adenocarcinomas, 29 squamous-cell carcinomas, 22 large-cell carcinomas and 14 not otherwise specified patients. 36 patients were non-smokers. In 30 patients the material was simultaneously available from primary and metastatic NSCLC tumors. The molecular profile of driver mutations was determined in *EGFR*, *KRAS, NRAS, BRAF, PIK3CA*, *HER2*, and *DDR2* genes. Mutations were screened in DNA isolated from formalin-fixed paraffin-embedded tissue samples using the quantitative real-time PCR technique with commercially available molecular kits. The driver mutations presence was confirmed by DNA sequencing, multiple single-strand conformation polymorphism (MSCCP) and other PCR techniques. **Results:** The driver mutations were identified in 52/145 (36%) of patients with CNS metastases (Fig.1), significantly more frequent in adenocarcinoma (p= 0.05, χ^2= 3.817), patients and non-smokers (p= 0.004, χ^2= 8.131). Only one patient had doublet mutations in *DDR2* and *KRAS* genes. In corresponding primary tumors we detected 10/30 (33%) mutations in *KRAS* gene (7/30, 23%) and *EGFR* gene (3/30, 10%). However, 5 KRAS mutations were identified both in primary and metastatic lesions, while 1 mutation was detected only in primary tumor and 1 mutation - only in the metastatic tumor. **Conclusion:** Analysis of molecular profile confirmed assumptions that driver mutations could be detected both in primary and CNS metastatic tumors of NSCLC. Therefore, both primary and metastatic tumor samples could be considered as a representative for molecular testing in patients with metastatic cancer.



Keywords: NSCLC, CNS-metastases, driver mutations

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-034 Molecular Subtyping in Advanced Non-Small Cell Lung Cancer, a Minimally Invasive Strategy with Small Volume Fine Needle Aspirates

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Background: Lung cancer is the leading cause of cancer related deaths worldwide. Non-small cell lung cancer (NSCLC) accounts for the vast majority representing approximately 85-90% of cases. NSCLC is further divided into histological subtypes including adenocarcinoma (AC) and squamous cell (SCC). Significant treatment implications exist according to histological classification which can be difficult due to scarcity of tissue or poor cellular differentiation. Patients often present with advanced disease thus making small volume, minimally invasive biopsy techniques ideal. Small volume biopsies, however, present an inherent challenge in obtaining sufficient amounts of high quality cancer cell-specific genomic material for testing and diagnostics. Here we tested the RNA yields from several minimally invasive techniques. We utilized two separate platforms to test a previously determined adeno-squam signature. We hypothesized that RNA yields would be sufficient for molecular histologic classification from a single needle biopsy. We sought to compare the yields of small volume biopsy techniques to RNA extracted from larger volume fresh frozen surgical specimens. **Methods:** Forty-eight individuals with suspected lung cancer underwent diagnostic biopsy with the standard approaches utilizing trans-thoracic needle biopsy (n=22) and transbronchial needle aspiration (n=26). RNA was extracted from a single pass specimen after the diagnostic biopsies were obtained (multiple passes). The total mass (ug), RNA integrity number (RIN) and % mass equal to or above 300 base pairs were recorded for all specimens. Statistical t-test analysis was performed on subgroups with focus on yield and quality. RNA from both FNA specimens as well as fresh frozen surgical specimens (n=44) obtained from a tumor bank at our institution were analyzed using Nanostring technology with the previously identified specific gene panel (A/S signature) obtained on the Quantigene platform. **Results:** Histological classification of FNA samples included adenocarcinoma (n=24), squamous cell (n=16) and NSC-NOS (n=8). Mean values for all FNA specimens included total mass of 1.58 ug, RIN of 4.0, and 85.4% mass equal to or above 300 base pairs. Fresh frozen surgical specimens including adenocarcinoma (n=21) and squamous cell (n=23) underwent successful RNA isolation with mean total mass of 45.2 ug, RIN of 6.1, and 68.8% mass equal to or above 300 base pairs. Differential histological gene expression occurred for both FNA and fresh frozen surgical specimens on the Nanostring platform. **Conclusion:** RNA isolation from NSCLC related small volume tissue biopsies is possible among several minimally invasive FNA techniques. Small volume tissue biopsy RNA yields are a sufficient means for molecular analysis and histological subtyping. We have successfully validated differential histological expression on two separate platforms from both single pass FNA techniques and frozen tumor samples. Given the increasing prevalence of such techniques and evolution of molecular analysis this may prove to be a powerful research and diagnostic tool. **Keywords:** NSCLC, Fine Needle Aspirates, Genetic Expression Analysis, Molecular Subtyping

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P3.04-035 Genetic Heterogeneity of Actionable Genes between Primary and Metastatic Tumor in Lung Adenocarcinoma

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Background: Because procedures obtaining lung cancer tissues involve high probability of critical complication, biopsies are usually done at a site of easy access. Authors questioned whether genetic information obtained at one biopsy site represent that of other lesion and is sufficient for therapeutic decision. **Methods:** Forty-one matched non-small cell lung cancer (NSCLC) samples of primary tumor and metastatic lymph node (L/N) were randomly selected from institutional tissue archives. non-synonymous mutation and ins-del of 16 genes that contain actionable mutations, intron 2 deletion polymorphism of *Bcl2-like11*, and copy number variation (CNV) of *MET* and *FGFR1* were analyzed by NGS based technique. **Results:**A total 251 mutations, including 217 non-synonymous mutations, 30 deletions, and 4 insertions were discovered in this study. There were higher chances to discover non-synonymous mutations in the primary tumor than in the metastatic L/N (140 (64.5 %) *vs.* 77 (35.5%)). In the primary tumor, 106 G>A: C>T transitions (75.7%) out of 140 non-synonymous mutation were detected, whereas in the metastatic L/N 44 (57.1%) out of 77 were discovered, showing decrease of G>A: C>T transition in the L/N metastatic lesion. The proportion of C>G: G>C and C>T: G>A was 80.7% in the primary tumor and 67.5% in the metastatic L/N, showing APOBEC activity in the metastatic L/N was not prominent in this study model. When the mutation profile between primary and metastatic lesion were compared, 28 out of 41 (68.3%) cases showed identical mutation profiles whereas 13 (31.7%) showed discrepancy. Fifty out of 82 tested samples showed CNV of either *FGFR1* or *MET* and 24 out of 41 cases showed discrepancy of copy numbers of tested genes between primary tumor and metastatic L/N. **Conclusion:** The genetic heterogeneity between the primary tumor and lymph node metastatic lesions are significant findings to consider when designing a therapeutic plan

from a result of one site inspection. A large prospective study is needed to evaluate the impact of genetic heterogeneity on the clinical outcome of NSCLC patients. **Keywords:** co-mutation, next generation sequencing, copy number variation, lung adenocarcinoma

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P3.04-036 Rare Discrepancies in a Driving Gene Alteration within Histologically Heterogeneous Primary Lung Cancers Wen-Zhao Zhong[1], Jian Su[1], Fang-Ping Xu[2], Hao-Ran Zhai[3], Xu-Chao Zhang[1], Xue-Ning Yang[1], Zhi-Yong Chen[1], Zhi-Hong Chen[1], Wei Li[3], Song Dong[1], Qing Zhou[1], Jin-Ji Yang[1], Yi-Long Wu[4] [1]*Department of Pulmonary Oncology; Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou/China,* [2]*Department of Pathology and Laboratory Medicine; Guangdong Lung Cancer Institute, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou/China,* [3]*Department of Pulmonary Oncology; Guangdong General Hospital & Guangdong Academy of Medical Sciences; Southern Medical University, Guangzhou/China,*[4]*Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhgou/China*

Background: Most lung adenocarcinomas consist of a mixture of histological subtypes among which driving gene mutations occurred with different frequencies. However, little is known about intratumoral heterogeneity within histologically heterogeneous primary lung cancers. Investigating key driver genes in respective morphological pattern is crucial to clinical practice and personalized treatment. **Methods:** Morphologically different tumor areas within the same surgically resected primary tumors were extracted from tissue sections and the gene status in each growth pattern was analyzed. Driving genes, epidermal growth factor receptor (*EGFR*), *KRAS*, and rearrangements in echinoderm microtubule-associated protein-like 4-anaplastic lymphoma kinase (*EML4-ALK*), were assessed by assays of different sensitivity. **Results:** Seventy-nine consecutive, surgically resected, adenocarcinomas or adeno-squamouse cell carcinomas harboring a driving gene mutation or rearrangement (*EGFR*, n = 65; *KARS*, n = 10; *EML4-ALK*, n = 4) were selected. For *EGFR* mutations in adenocarcinomas, ITH occurred in 13.3% (8/60) as determined by direct sequencing, but in only 1.7% (1/60) by ARMS(*P*= 0.016). A consistent intratumoral *EGFR* mutation status was found within 5 histologically heterogeneous adeno-squamous cell carcinomas, as shown with ARMS. ITH among *KRAS* mutations were detected in 20% (2/10) of regions examined by direct sequencing ,whereas a consistent status (10/10) was obtained with HRM. There were no discrepancies in EML4-ALK rearrangements according to FISH for four tumors. **Conclusion:** Rare ITHs deriving from *EGFR/KRAS/EML4-ALK* alterations within histologically heterogeneous primary lung adenocarcinomas were found with methods of high sensitivity. Discrepancies might be due to the abundance of cells harboring driving gene and detection assays. **Keywords:** Intratumor heterogeneity, Epidermal growth factor receptor, KRAS/EML4-ALK, lung cancer

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P3.04-037 Prevalence of NRG1 fusions in Caucasian NSCLC patients determined by fluorescence in situ hybridisation Andreas H. Scheel[1], Katja Schmitz[2], Lea Wilsberg[2], Rieke N. Fischer[3], Sabine Merkelbach-Bruse[1], Elke Binot[1], Dennis Plenker[4], Jürgen Wolf[3], Koji Tsuta[5], Takashi Kohno[6], Roman K. Thomas[4], Hans-Ulrich Schildhaus[2], Reinhard Büttner[1] [1]*Institute of Pathology, University Hospital of Cologne, Cologne/Germany,* [2]*Pathology, University Hospital Göttingen, Göttingen/ Germany,* [3]*Lung Cancer Group Cologne, Department I of Internal Medicine, University Hospital of Cologne, Cologne/Germany,* [4]*Department of Translational Genomics, Center for Integrated Oncology Cologne/Bonn, University of Cologne, Cologne/Germany,* [5]*Pathology, National Cancer Center Hospital, Tokyo/Japan,* [6]*Genome Biology, National Cancer Center Research Institute, Tokyo/Japan*

Background: Fusions of the gene *Neuregulin1* (*NRG1*) have been described to activate PI3K-AKT signaling in NSCLC via NRG1 overexpression and binding to Her2/Neu-Her3. *NRG1* fusions were detected in pulmonary mucinous adenocarcinoma of Asian non-smokers lacking other known oncogenic driver mutations. The incidence in such patients has been described to be between 17.6% (6/34) and 44.4% (4/9). *NRG1* fusions might be targeted by Her2/Her3-inhibitors and clinical trials are planned. Here we describe for the first time the systematic analysis of *NRG1* in Caucasian patients by Fluorescence in situ hybridization (FISH). **Methods:** A ZytoLight®-based FISH assay (ZytoVision, Bremerhaven, Germany) was developed and verified on nine published clinical cases with known *NRG1* fusions. A total of 160 Caucasian NSCLC patients were screened. 25 of the cases were mucinous adenocarcinoma lacking a known oncogenic driver mutation as determined by deep-sequencing and FISH tests. 135 cases were pulmonary adenocarcinoma of various subtypes including 35 cases that lacked a driver mutation and 100 cases that were *EGFR*, *ALK* and *ROS1* wildtype. The smoking-status was not evaluated. Statistics were calculated using R 3.1.0 . **Results:** The *NRG1* fusions in the published cases were easily detected by the FISH assay. However, none of the screened cases harbored a *NRG1* fusion. The result is significant compared to published reference values of 17.6% (p=0.041) and 44.4% (p<0.001). The theoretical maximum incidence of *NRG1* fusions among Caucasian NSCLC patients not stratified by smoking-status was calculated to be <16.6% for mucinous adenocarcinomas lacking driver mutations, <7.5% for adenocarcinoma of all morphological subtypes lacking driver mutations and <3% for *EGFR*, *ALK*, *ROS1* negative pulmonary adenocarcinoma (95% confidence intervals). **Conclusion:** FISH is a suitable technique to screen for *NRG1* fusions in pulmonary adenocarcinoma. Among 160 Caucasian patients including 25 mucinous carcinomas lacking a driver mutation none were *NRG1* positive. Thus, the incidence among Caucasian patients appears to be low and should be evaluated in studies of large NSCLC cohorts. **Keywords:** fusion gene, NRG1, FISH, Mucinous Adenocarcinoma

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P3.04-038 Molecular Topography of Early-Stage Lung Adenocarcinomas Esther Conde[1], Barbara Angulo[1], Rebeca Martinez[1], Luis Madrigal[2], Luis Jimenez[2], Elena Piñeiro-Yañez[3], Fatima Al-Shahrour[3], Victor Reyes[4], Susana Hernandez[1], Fernando Lopez-Rios[1] [1]*Pathology-Laboratorio de Dianas Terapeuticas, Hospital Universitario Hm Sanchinarro, Madrid/Spain,* [2]*Thoracic Surgery, Hospital Universitario Hm Sanchinarro, Madrid/Spain,* [3]*Translational Bioinformatics Unit, Cnio, Madrid/Spain,* [4]*Pathology-Laboratorio de Dianas Terapeuticas, Hospital Universitario Hm Puerta Del Sur, Madrid/Spain*

Background: Intratumor heterogeneity may have implications for targeted therapies. Despite the well known morphologic intratumor heterogeneity of lung adenocarcinomas (ACs), the heterogeneity of druggable alterations throughout individual primary tumors is still controversial and has remained poorly defined. The purpose of our work was to comprehensively characterize histological intratumor heterogeneity in primary lung ACs. **Methods:** A total of 83 consecutive patients with stage I-IIIA primary lung AC who underwent surgery at HM Sanchinarro University Hospital were considered. All tumors were always included *in toto* for histological analysis, regardless of size, by the same pathologists. We carefully reviewed all slides to identify and quantify (with the help of digital pathology, [iScan, Ventana Medical Systems, USA]) the different histological patterns according to the revised International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society (IASLC/ATS/ERS) classification of lung ACs. Every pattern from each specimen was macrodissected, and a new paraffin block per pattern was constructed. Afterwards, we performed targeted next-generation sequencing (Ion AmpliSeqTM Cancer Hotspot Panel v2, Life Technologies, USA) to detect actionable somatic mutations and copy number variations (CNVs) in 50 genes in every different histological pattern of each tumor. The raw data were processed using the RUbioSeq and MuTect softwares. After a filtering process, the detected variants were then annotated with the Ensembl Variant Effect Predictor. The annotations were used to compute a variant score and rank the mutations according to their clinical significance. **Results:** All 83 tumors were primary invasive ACs. Detailed histological analysis revealed that 63 tumors (76%) had more than one histological pattern. Among them, 52 (82,5%) exhibited two patterns, and 11 (17,5%) showed three components. An initial pilot study of 20 cases showed that 45% of the tumors had heterogeneous results regarding the presence of somatic mutations and CNVs between different histological patterns within a given tumor. We observed intratumor heterogeneity predominantly regarding the mutational status of several genes (e.g. 2 out of 11 *TP53* mutated tumors, 1 out of 6 *KRAS* positive tumors, 1 out of 3 *STK11* mutated cases, and 3 out of 3 *CDKN2A* mutated tumors). Solid patterns accumulated more molecular alterations than other patterns, and also showed events not present in other components (i.e. *CDKN2A* or *NOTCH1* mutations, copy number gain of *ALK*, *HER2, FGFR2* or *NOTCH1). RET* and *GNAS* mutations were exclusively observed in papillary patterns. *EGFR* and *HER2* mutations were not heterogeneous. **Conclusion:** In early stage lung ACs there is a significant degree of intratumor heterogeneity. Our preliminary results indicated a trend towards a high somatic events rate in solid patterns. The comprehensive approach presented herein links routine pathology practice with targeted clinical molecular annotation of lung ACs. Therefore, it could be used prospectively to assess the implications of studying single tumor regions. Acknowledgements This study was partially funded by Instituto de Salud Carlos III (ISCIII), Fondo de Investigaciones Sanitarias (FIS) [Fondos FEDER, Plan Nacional de I+D+I 2008-2011 (PI11-02866) and Plan Estatal de I+D+I 2013-2016 (PI14-01176)]. **Keywords:** lung adenocarcinoma, Heterogeneity, next generation sequencing, fluorescence in situ hybridization

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P3.04-039 Characterization of RNA Splicing Factor Mutations in Lung Adenocarcinoma Peter S. Choi, Angela N. Brooks, Matthew Meyerson *Medical Oncology, Dana-Farber Cancer Institute, Boston/United States of America*

Background: Large-scale genomic surveys of lung adenocarcinoma have revealed unexpected mutations in RNA splicing factors such as *U2AF1* and *RBM10*, and it remains unknown how changes in splicing are involved in promoting cancer. Somatic alterations in the RNA-binding protein *RBM10* occur at a frequency of approximately 7% and consist predominantly of loss-of-function mutations. In this study, we sought to investigate the functional impact of *RBM10* mutations in lung cancer. **Methods:** *RBM10* mutant non-small cell lung cancer (NSCLC) cell lines were identified by analysis of Cancer Cell Line Encyclopedia gene expression data and Sanger sequencing of *RBM10* coding exons. Ectopic expression of wildtype RBM10 or a control protein (BFP) was induced using the tetracycline-regulatory system. RNA–sequencing and JuncBASE software were used to identify differentially spliced transcripts between *RBM10* wildtype and mutant cells. Changes in individual splicing events were validated by RT-PCR. **Results:** We have identified several NSCLC cell lines harboring loss-of-function mutations in *RBM10*. Restoring expression of wildtype *RBM10* in these *RBM10*-mutant cell lines resulted in significant growth suppression and inhibition of anchorage-independent growth. These phenotypic effects were associated with a variety of splicing changes and expression of wildtype *RBM10* frequently increased skipping of cassette exons. Expression of *RBM10* variants with either deletion of an RNA recognition motif (RRM), or containing a cancer-associated missense mutation in the RRM, were significantly diminished in their ability to promote exon skipping and suppress cellular proliferation. **Conclusion:** Our results suggest that *RBM10* functions as a novel tumor suppressor in lung adenocarcinoma through its effects on RNA splicing. Further work is needed to better understand how changes in specific splicing events may be directly contributing to lung tumorigenesis. **Keywords:** RNA splicing, splice factor mutations, RBM10

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P3.04-040 Comparison of Histology with Genome-Wide Copy Number Profiling in Patients with Metachronous or Synchronous Tumors Erik Thunnissen[1], Julien Vincenten[1], Hf Van Essen[1], Nicole Bulkmans[1], Katrien Grunberg[1], Egbert Smit[2], Birgit Witte[3], Bauke YIstra[1] [1]*Department of Pathology, VU University Medical Center,, Amsterdam/ Netherlands,* [2]*Dept. of Thoracic Oncology, Netherlands Cancer Institute, Amsterdam/ Netherlands,* [3]*Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam/Netherlands*

Background: Multiple synchronous and metachronous lung tumors are frequently encountered in patients with lung cancer. In addition, tumors of head and neck (usually squamous cell carcinoma) have a chance for a second primary malignancy in the lung. For treatment purposes it is important to know whether tumors are related (clonal = metastases) or not (multiple primaries). Histopathological comparison of the synchronous or metachronous tumors has been associated with molecular analysis. The purpose of this study is to examine the value of histopathological scoring with genome-wide copy number profiling for determination of clonality. **Methods:** From cases in which array CGH for clonality analysis performed between 2006 and 2012 were selected if at least one intrathoracic tumor was present. In the first years genome-wide copy number profiling was performed with arrayCGH and later with shallow sequencing. Results of the genome-wide copy number profiling were compared to histological (sub)typing. **Results:** 100 tumor pairs from 59 patients were examined. 32 pairs were discovered simultaneously (synchronous), the other 68 were metachronous. The histopathological diagnosis was similar in 74 cases (74%). genome-wide copy number profiling revealed evidence for clonality in 55% of the pairs, no-clonality in 28% and was undetermined in 17%. Comparing of histology with genome-wide copy number profiling revealed concordancy in 54 pairs (74%; 44 clonal en 10 non-clonal). In 18 of the 62 pairs where histology was similar the genome-wide copy number profiling revealed a non-clonal pattern. In 11 out of 21 pairs where histology differed between the pairs, genome-wide copy number profiling revealed a clonal pattern. Thus histology was not prognostic in 29/83 pairs (35%). **Conclusion:** For the determination of clonality in lung cancer histological examination is discordant with genome-wide copy number profiling in 35% of the comparisons. As histology is a poor predictor of clonality, genome-wide copy number profiling is preferred for clonality analysis between tumors.
Keywords: multiple primary tumors*lung*molecular analysis*histology

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-041 Identification of the Functional Significance of Mutations in Lung Cancer Using the Novel Precision Cancer Analysis System Nir Peled[1], Gabi Tarcic[2], Mariusz Adamek[3], Naama Barabash-Katzir[2], Zohar Barabash[2], Shlomo Yaakobi[2], Eli Besser[2], Hani Nevo[2], Michael Vidne[2], Yaniv Tocker[2], Damian Czyzewski[3], Yakov Fellig[4], Karen Meir[4], Keith Mostov[5], Erez Chimovits[6], Yoram Altschuler[2] [1]*Tel Aviv University Sackler School of Medicine, Tel Aviv/Israel,* [2]*Novellusdx, Jerusalem/Israel,* [3]*Medical University of Silesia, Zabrze/Poland,* [4]*Hadassah-Hebrew-University-Medical-Center, Jerusalem/Israel,* [5]*University of California School of Medicine, San Francisco/CA/United States of America,* [6]*Orbimed, Herzliya/Israel*

Background: Mounting evidence indicates that growth of pathologically identical lung cancers in each individual patient is fueled by different sets of driving mutations. The need to identify these drivers stems from the recognized necessity for tailoring therapy and scheduling future surveillance. This personalized medical approach has been shown to result in better treatment outcomes. We present a novel Precision Cancer Analysis system (PCAS) capable of identifying activated signaling pathways by means of a transfected cell-based fluorescent reporter assay yielding a quantitative output of particular pathway activation levels. Being a functional platform PCAS reveals activated pathways regardless of the type of mutation behind it, i.e. whether it is already a known mutation or a variant of unknown significance (VOUS) mutation. **Methods:** In 10 patients with lung cancer next generation sequencing (NGS) was employed to sequence a set of 37 genes relevant in lung carcinogenesis. These genes were sequenced with 90 -100 % coverage. According to the prevalence of mutations in the analyzed cohort 3 major genes were selected for the current study: EGFR, PIK3CA and KRAS. These genes were then mapped to their major signaling pathways, and the reporters that best account for their activation were selected. Four major signaling pathways were found to be relevant for these genes - MAPK, STAT, NFkB and AKT. **Results:** In analyzed samples of 10 patients 14 mutations were identified, among them 3 in the tested genes: 2 in KRAS and 1 complex mutation in EGFR. The remaining mutations were found in STK11, CDKN2A, NF1, RB1 and TP53 genes. Of mutations found in KRAS 1 was known mutation (K117N) and 1 was VOUS (G60R). The former caused activation via MAPK/ERK but not via AKT pathway. The latter, never so far reported in cancer, significantly activated both pathways: MAPK/ ERK and AKT. Interestingly the VOUS KRAS mutation was identified in carcinoid, whereas 2 carcinoid samples from other individuals displayed no mutations in the 37-gene panel. Additionally, 1 VOUS in RB1 and 2 mutations in STK11 were found to be associated with cancer cells aggressiveness evidenced by vessel and nerve tissue invasion. Measuring the functional mechanism behind known mutations and VOUS provides another layer of critical information to the physician. **Conclusion:** The study produced a comprehensive delineation of the oncogenic activity of each patients' individual mutations demonstrating the ability of the PCAS to:

- Accurately deliver comparable actionable information as found by NGS
- Functionally characterize mutations annotated as VOUS.
- Monitor oncogenic activity of signaling pathways induced by different mutations and mutation-combinations enabling informed treatment decisions.

Keywords: NGS profiling, onconege activity map

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-042 Evaluation of Texture Analysis Parameters in EGFR Mutated or ALK-Positive Advanced Non-Small Cell Lung Cancer (NSCLC) Maria V. Bluthgen[1], Caroline Caramella[2], Silvia Rosellini[3], Charlotte Leduc[4], Francesco Facchinetti[1], Eva Haspinger[1], Charles Ferte[1], Stefan Michiels[3], Jean C. Soria[1], Benjamin Besse[1] [1]*Cancer Medicine, Gustave Roussy, Villejuif/France,* [2]*Radiology, Gustave Roussy, Villejuif/ France,* [3]*Biostatistics and Epidemiology, Gustave Roussy, Villejuif/France,* [4]*Chest Diseases, Strasbourg University Hospital, Strasbourg,/France*

Background: The quantitative assessment of heterogeneity in tumor images through Texture Analysis is an emerging tool that can potentially provide a non-invasive prognostic biomarker. We investigated if Texture Analysis parameters derived from contrast-enhanced CT (CTTA) were associated with EGFR/ALK status and have a prognostic value in NSCLC patients treated with tyrosine-kinase inhibitors. **Methods:** The CT images of patients with EGFR mutated or ALK rearranged advanced NSCLC treated with tyrosine-kinase inhibitors were retrospectively reviewed. CTTA using the filtration-histogram method was applied to the region of interest (ROI) in the primary tumor of the enhanced-CT by two independent operators to examine the inter-individual reproducibility. A wilcoxon test was used to correlate CTTA with EGFR / ALK status and a Cox model to evaluate the prognostic value of CTTA for overall survival. A p-value cutoff of 0.01 was used to adjust for multiple testing. **Results:** CTTA parameters were evaluated in CT scan from 68 patients recruited in 2 centers between 2008 and 2013, of them, 80.9% (n=55) were EGFR mutated and 19.1 % (n=13) ALK+ NSCLC, 48.5% received treatment with gefitinib (n=33), 33.8% with erlotinib (n=23) and 17.7% with crizotinib (n=12). The CTTA measures were highly reproducible between the 2 operators as indicated by Bland-Altman plots and correlation values. The skewness of the distribution was significantly different between EGFR mutated and ALK+ tumors for coarse texture with spatial filter value 3.3 (p= 0.002), filter value 2.8 (p=0.001) and medium texture with spatial filter value 2.2 (p=0.004). The median follow-up time was 35 months; 39 deaths occurred. The A unit increase in skewness in coarse texture (2.8 spatial filter) was significantly associated with better survival with an univariate cox analysis (HR: 0.36 [0.2-0.69] p=0.002). A multivariate analysis adjusted by prognostic factors (PS, lymphocyte count, hepatic and adrenal metastasis) indicate a similar trend for better survival (HR: 0.40 [0.2-0.8] p=0.01). **Conclusion:** CTTA parameters were reproducible between the 2 operators. The skewness was significantly different between EGFR mutated and ALK rearranged advanced NSCLC and may have a prognostic value.
Keywords: Texture analysis, non small cell lung cancer, EGFR mutated, ALK rearranged, computed tomography

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-043 Driver Mutations in Non-Small Cell Lung Cancer in Western Pennsylvania: Prevalence and Barriers to Testing Rohit Rao[1], Zachary D. Otaibi[2], Blair Jobe[3], Ali Zaidi[3], Rodney Landreneau[3], Gene G. Finley[1] [1]*Medical Oncology and Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh/PA/United States of America,* [2]*Internal Medicine and Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh/PA/United States of America,*[3]*Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh/United States of America*

Background: EGFR gene mutations and EML4-ALK rearrangements are key therapeutic targets in nonsquamous non-small cell lung carcinoma (nsNSCLC). Therapy targeted towards these mutations has been shown to improve tumor response, progression-free survival, and quality of life. Current guidelines recommend testing all advanced (Stage IIIB and IV) nsNSCLC patients for these genetic aberrations. Despite this recommendation, not all patients eligible for mutation analysis are tested. In our institution, preliminary observations suggest the percentage of patients being tested and the frequency of driver mutations are significantly lower compared to published data. The purpose of the study was to review tumor registry data in order to determine the rate of testing and the frequency of driver mutations in Western Pennsylvania. Our secondary aim was to evaluate whether biopsy size impacts the frequency of EGFR and ALK testing. **Methods:** From the tumor registry, 167 cases of advanced nsNSCLC were identified (2011-2013). The testing rates for driver mutations, frequency of driver mutations, and the tissue procurement technique were determined by individual chart review. Surgical specimens, core biopsies, and large volume thoracentesis specimens were categorized as large tissue biopsies and samples obtained by fine needle aspiration, bronchial washing, and bronchial brushing were considered small tissue biopsies. Using a Chi-square analysis, mutation testing rates were compared between the large and small biopsy groups. Frequency of driver mutations was determined, excluding unknown or inadequate samples. **Results:** Of the 167 cases, there were 120 (71.9%) large and 47 (28.1%) small biopsy specimens. 61 (50.8%) large sample biopsies and 17 (36.2%) small sample biopsies were submitted for EGFR analysis. 39 (32.5%) large sample biopsies and 10 (21.3%) small sample biopsies were tested for ALK rearrangements. It was found that large tissue biopsies were more likely to be analyzed for EGFR mutations and ALK rearrangements although the results did not reach statistical significance (p=0.088 and p=0.150, respectively). Across all samples, a total of 7 EGFR mutations and 0 ALK rearrangements were identified representing a frequency of 10.0% and 0.0% respectively. **Conclusion:** Despite current guidelines for testing driver mutations in advanced nsNSCLC, we are testing less than 50% of our patients. There are several barriers that continue to thwart this recommendation, including failure to integrate driver mutation testing into routine pathology practice (i.e., reflex testing), lack of care coordination with relevant clinical specialties beyond medical oncology and pathology, and insufficient tissue obtained from biopsy. More

importantly, these trends are not isolated to our institution and reflect a significant challenge within the oncology community. In the coming months, we will be initiating a Lean Six Sigma approach to modify our current clinical practice and improve our testing rate. In addition, we have begun using a blood based assay (liquid biopsy) to interrogate advanced nsNSCLC for driver mutations. We have also demonstrated that the frequency of driver mutations in Western Pennsylvania is lower than published data. Accession of additional patients to this data set continues and a final analysis will be presented. **Keywords:** testing rate, non-small cell lung cancer, EGFR, EML4-ALK

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-044 EGFR and ALK Status Influence Health Utility and Global Quality of Life Scores in Patients with Metastatic Lung Cancer Catherine Labbe[1], Erin Stewart[1], Catherine Brown[1], Andrea Perez Cosio[1], Ashlee Vennettilli[1], Devalben Patel[1], Nicholas Cheng[1], Mindy Liang[1], Gursharan Gill[1], Yvonne Leung[1], Hiten Naik[1], Nicole Mittmann[2], Natasha Leighl[1], Ronald Feld[1], Penelope Bradbury[1], Frances Shepherd[1], Doris Howell[1], Geoffrey Liu[1] [1]*Princess Margaret Cancer Centre, Toronto/Canada,* [2]*Health Outcomes and Pharmacoeconomics (Hope) Research Centre, Sunnybrook Research Institute, Toronto/ON/Canada*

Background: *EGFR* mutations and *EML4-ALK* rearrangements play important roles in prognosis and response to treatment. While extending survival is a main goal of treatment, improving symptoms, well-being, and quality of life is an equally important priority. **Methods:** At Princess Margaret Cancer Centre, a cross-sectional study evaluated 224 outpatients with metastatic lung cancer who completed demographic and EQ5D-3L questionnaires generating health utility scores (HUS, 0-1) and a visual analogue scale (VAS) slider (0-100). Patients rated their ECOG performance status (0-4), and described their health over the last month from 1 (excellent) to 5 (poor). Results were correlated with clinical and demographic data. Our objective was to compare HUS and global quality of life by mutational status. Patients with *EGFR* mutations and *ALK* rearrangements were enriched through targeted enrolment, while patients with neither alteration were selected randomly from the same outpatient clinics. **Results:** 94 patients (42%) had an *EGFR* mutation, 23 (10%) an *ALK* rearrangement and 107 (48%) had neither ("wildtype") in their tumor. Participation rate was 87%. Characteristics of the populations were as expected, with higher rates of never smokers in patients with *EGFR* or *ALK* alterations ($p<0.0001$), greater proportion of Asians ($p=0.0004$), and higher proportion of adenocarcinoma ($p<0.0001$). Current systemic treatment differed among groups, as the majority of patients with driver mutations were receiving targeted agents at the time of assessment (77% *EGFR* and 65% *ALK* vs 7% wildtype). Conversely, wildtype patients were more likely on chemotherapy (6% vs 17% vs 38%) or not on treatment (17% vs 17% vs 47%, $p<0.0001$). Patients filled questionnaires on average 25 months after initial diagnosis of lung cancer. Patients with *EGFR* mutations (97%) or *ALK* rearrangements (100%) were more often ECOG performance status 0-1 at the time of diagnosis of stage IV disease than wildtype individuals (86%, $p=0.02$). For quality of life analysis, we regrouped the patients with *EGFR/ALK* alterations (n=117). Their mean HUS was better than for wildtype patients (0.80 vs 0.71, $p=0.0003$), their mean VAS slider was higher (66.9 vs 60.8, $p=0.0381$) and their mean self-rated ECOG scores was better (0.90 vs 1.26, $p=0.022$). **Conclusion:** In a clinical population, patients with metastatic lung cancer harboring *EGFR* and *ALK*alterations report superior HUS and global quality of life scores when compared with patients without these molecular changes, during the course of their therapy. This is reflected in higher proportion of patients on active therapy, particularly with molecularly targeted agents, and with improved self-reported performance scores. Health utility values used in economic analyses of metastatic lung cancer patients in clinical practice should be specific for different mutations. **Keywords:** health utility scores, metastatic lung cancer, EGFR mutation, ALK rearrangement

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-045 Insights into NSCLC Molecular Testing in Central and Eastern European Countries Ales Ryska[1], Peter Berzinec[2], Tanja Cufer[3], Rafal Dziadziuszko[4], Maya Gottfried[5], Włodzimierz Olszewski[6], Buge Oz[7], Lukas Plank[8], Jozsef Timar[9] [1]*Fingerland Institute of Pathology, Hradec Králové/Czech Republic,* [2]*Oncology, Specialised Hospital of St Zoerardus Zobor, Nitra/Slovak Republic,* [3]*University Clinic Golnik, Ljubljana/Slovenia,* [4]*Medical University of Gdansk, Gdansk/Poland,* [5]*Meir Medical Center, Kfar Saba/Israel,* [6]*Institute of Oncology, Warsaw/Poland,* [7]*Cerrahpasa Medical Faculty, Istanbul/Turkey,* [8]*Comenius University Jessenius Medical Faculty, Martin/Slovak Republic,* [9]*Semmelweis University, Budapest/Hungary*

Background: Information is lacking about molecular testing practices for NSCLC in Central and Eastern Europe; identification of the challenges for personalized lung cancer treatment within this region might facilitate strategies to overcome these and to improve patient care. **Methods:** A Working Group of oncologists, pulmonologists and pathologists from Central and Eastern Europe was established in order to get more information about NSCLC molecular testing used in these countries, technologies, patient selection, availability and other questions, and to raise greater awareness of the current issues around personalized medicine for lung cancer in this region. As a first step, a questionnaire including 37 questions about issues connected with NSCLC molecular testing and other aspects of NSCLC management was distributed in 2014 to 59 specialists in different areas of NSCLC, including epidemiologists, oncologists, pulmonologists and pathologists. **Results:** In all, 25 experts from 9 countries (Bulgaria, Croatia, Czech Republic, Hungary, Israel, Poland, Slovakia, Slovenia, Turkey) responded. The responses show that there are some differences between the countries in the region and also between centers within countries with regard to NSCLC molecular testing. Some are minor, e.g. for EGFR mutation testing real-time PCR is used in all countries, direct sequencing in 5, and other methods are used in addition in only 2 countries. Up to one-quarter of samples are inadequate for testing. For ALK testing, IHC followed by FISH and/or FISH alone are currently used in all 7 countries with responses; in Israel, other methods including DNA sequencing are also used. However, some of the differences are quite large, such as the proportion of eligible patients tested for EGFR mutations and ALK rearrangements, and the proportion of NSCLC patients discussed at multidisciplinary tumor boards. There is also wide variation in funding sources for EGFR and ALK testing. **Conclusion:** NSCLC molecular testing is available in all Central and Eastern European countries participating in this survey. For the future, ensuring adequate NSCLC samples, solving sustainable financing of molecular testing and enabling wide access of eligible patients to molecular testing resulting in raising the number of patients reviewed by multidisciplinary boards are among the key challenges. **Keywords:** NSCLC, molecular testing

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-046 Prevalence of ROS1, HER2, and BRAF Alterations in a Cohort of Advanced Non-Small Cell Lung Cancer (NSCLC) Patients (P) Triple Negative (TN) Teresa Morán[1], Enric Carcereny[1], Josefa Terrasa[2], Raquel Marse[2], Ana Estival[1], Monica Guillot[2], Laia Vila[1], Maria De Los Llanos Gil[1], Max Hardy-Weber[1], Iris Teruel[1] [1]*Medical Oncology, Catalan Institute of Oncology-Hospital Germans Trias I Pujol, Badalona/ Spain,* [2]*Medical Oncology, Hospital Universitari Son Espases, Palma de Mallorca/Spain*

Background: During the last years, new predictive and less frequent biomarkers have emerged in NSCLC, such as ROS1 translocation (ROS1t), HER2 mutations (HER2m) and BRAF mutations (BRAFm). We analyze retrospectively the frequency, clinical and tumor characteristics of NSCLC p TN(EGFR, KRAS and ALK wild-type). **Methods:** The study included data from all consecutive non-squamous and non-smokers squamous TN advanced NSCLC p diagnosed at our hospital from December 2008 to July 2014 **Results:** 101 p were included. The table below summarizes p characteristics. ROS1t were found in 4.9% p and were found more in female gender (100%), non-smokers(100%), stage IV (100%), adenocarcinoma histology (100%) and p had more lung metastasis(50% vs 34.2%), brain metastasis (50%vs 38.5%) and pleural/pericardial effusions (50% vs 12.8%). HER2m was found in 1 p (1.25%). Female, non-smoker and adenocarcinoma histology. BRAFm were found in 2 p (3.2%), one male and one female, smokers and adenocarcinoma histology. Valid results range from 85.6% to 96.2% for biopsy samples and from 78.2% to 81.4% for citology samples.

		TO-TAL(N101)	ROS1(N81)	BRAF(N80)	HER2(N80)
Mean age		61	58	63	63
Gender	Male Female	65(64,3%) 36(35,6%)	57(70,3%) 24(29,6%)	52 (65%) 28(35%)	52(65%) 28(35%)
Smok-ing history	Current Former Never	38(37,6%) 41(40,5%) 22(21,7%)	32(39,5%) 37(45,6%) 12(14,8%)	33(41,2%) 31(38,7%) 16(20%)	33(41,2%) 31(38,7%) 16(20%)
Histol-ogy	Adeno-carci-noma Squa-mous NOS LCC	88(87,1%) 5(4,9%) 6(5,9%) 2(1,9%)	72(88,8%) 3(3,7%) 6(7,4%) 0	71(88,7%) 2(2,5%) 5(6,2%) 2(2,5%)	71(88,7%) 2(2,5%) 5(6,2%) 2(2,5%)
Sample	CItology Biopsy	29(28,7%) 72(71,2%)	27(33,3%) 54(66,6%)	23 (28,7%) 57 (71,2%)	23 (28,7%) 57 (71,2%)
Site metas-tasis	Lung Bone Brain Liver	33(32,6%) 28(27,7%) 30(29,7%) 9(8,9%)	28(34,5%) 21(25,9%) 25(30,8%) 5(6,1%)	25(31,2%) 22(27,5%) 27(33,7%) 7(8,7%)	25(31,2%) 22(27,5%) 27(33,7%) 7(8,7%)

Conclusion: ROS1t, HER2m and BRAFm have emerged as targetable oncogenic drivers in NSCLC. Although the prevalence is low (1%–2%), could be increased selecting by clinical and molecular characteristics. Citology samples could be useful to detect these molecular alterations. **Keywords:** ROS1 translocation, HER2 mutations, BRAF mutations, molecular alterations

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-047 Prospective Study of Molecular Markers in Patients with Advanced Lung Adenocarcinoma in CEMIC. Argentina Gonzalo Recondo[1], Valeria Denninhoff[2], Gonzalo Recondo Jr[1], Constanza Lorente[2], Martin Greco[1], Maria T. Cuello[2], Maximo De La Vega[1], Enrique A. Diaz Canton[1], Mariana Dos Santos[2], Florencia Perazzo[1], Silvana Nieto[2], Jorge Nazar[3], Matias Lescano[3], Alejandro Garcia[2], Pablo Rodriguez[4], Shigeru Kozima[5], Alejandra Avagnina[2] [1]*Medical Oncology, Cemic, Buenos Aires/ Argentina,* [2]*Pathology, Cemic, Buenos Aires/Argentina,* [3]*Thoracic Surgery, Cemic, Buenos Aires/Argentina,* [4]*Neumonology, Cemic, Buenos Aires/Argentina,* [5]*Imaging, Cemic, Buenos Aires/Argentina*

Background: Lung Cancer is the first cause of cancer related death in Argentina being Adenocarcinoma the most frequent histology. The incidence of EGFR mutations is 13% but there isn't data regarding other molecular abnormalities. The objective is to study the prevalence of EGFR, BRAF and KRAS mutations together with ALK and MET overexpression in consecutive adult patients with advanced lung adenocarcinoma. **Methods:** Pts with tumor biopsy and candidates for treatment who consented were included. Specific sites regarding each gene were analyzed with PCR and Sanger sequencing: KRAS exon2 (G12V/S/D/A/C/R, G13D, V14X, G15X); EGFR exons 18 (G719C/S/A, V689M, E709K/Q, S720P), 19 (deletions and insetions 746-759), 20 (T790M, D700_N771, V769L, S768I,V765A, T783A) and 21 (L858R,L884Q, G863D,N826S, A839T, K864R) and BRAF exon 15 (V600E, D594M,N709K/Q and S720P) and 11 . IH for ALK was performed with 5A4 Mo Ab and CMET with C-12-sc-10 Mo Ab. CMET 2+/3+ and ALK 3+ were considered positive, ALK positive samples were confirmed by FISH. **Results:** From May 2012 to December 2014 119 patients signed the informed consent, 107 pts with at least one mutational and/or IH analysis were included and 12 pts were excluded due to other histologies or inadequate material. Median age was 63 years (32-82), male/female 61/46, smoker/former/never 37 (34%)/50 (47%)/20 (19%). Complete mutational and IH analysis was performed in 85 pts(79,5 %), 3 had incomplete analysis (3,75 %) , and 19 only IH (17,75%). Complete molecular testing was achieved in 90% of surgical and 36% of imaging guided biopsies. KRAS was mutated in 18/85 pts (21%): 12 in codon 12 and 6 in codon 13. EGFR was mutated in 15 pts (15%), 11 (13%) harbored EGFR tki responding mutations: 1 exon 18 (E709K), 1 exon 20 (V765A), 4 in exon 21 (3 L858R and 1 G863D) and 5 have exon 19 deletions. Exon 20 insertions (D770_N771 and V774_c775) conferring EGFR tki resistance were detected in 2 patients (2%). One BRAF mutations were detected in exon 11 (G469A). ALK IH was 3+ in 2/107 (2%) and CMET were positive in 57 % (43% 2+ and 14% 3+) of 106 samples tested. In the 85 patiens where all test were performed the prevalence of KRAS mutations was 21 %, EGFR 15 %, BRAF 1,2 % and ALK 2,4 %. **Conclusion:** The molecular analysis of multiple molecular markers in lung adenocarcinoma in an academic center in Argetnina is feasible. The amount of tumor obtained from non surgical biopsies is frequently inadequate for full evaluation by this methods. The prevalence of *BRAF*, *KRAS*, *EGFR* mutations and *ALK* IHC is similar to larger series in other western countries **Keywords:** Adenoarcinoma, Molecular analysis.

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-048 Rare Gene Mutations in Japanese Surgically Resected Non-Small-Cell Lung Cancer Patients Teppei Nishii[1], Tomoyuki Yokose[2], Yohei Miyagi[3], Yataro Daigo[4], Tomohiko Matsuzaki[1], Masashi Nagata[1], Tetsuya Isaka[1], Hideyuki Furumoto[1], Hiroyuki Ito[1], Saki Manabe[1], Shuji Murakami[1], Tetsuro Kondo[1], Haruhiro Saito[1], Kouzo Yamada[1], Munetaka Masuda[5], Haruhiko Nakayama[1] [1]*Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama/Japan,* [2]*Department of Pathology, Kanagawa Cancer Center Hospital, Yokohama/Japan,* [3]*Molecular Pathology and Genetics Division, Kanagawa Cancer Center, Yokohama/Japan,* [4]*Department of Medical Oncology and Cancer Center, Shiga University of Medical Science Hospital, Otsu/Japan,* [5]*Department of Surgery, Yokohama City University Graduate School of Medicine, Yokohama/Japan*

Background: Driver gene mutations except for *EGFR* are rare in Japanese population. In this study, we investigated *EGFR*, *KRAS*, *BRAF* and *PIK-3* mutations in surgically resected non-small-cell lung cancer (NSCLC). **Methods:** A total of 388 consecutive patients with NSCLC who underwent complete tumor resection in our hospital from 2006 through 2008 were studied retrospectively. Formalin-fixed, paraffin-embedded tissue sections were used to isolate DNA from carcinoma lesions. Mutational analyses of *EGFR, KRAS, BRAF and PIK-3* were performed by loop-hybrid mobility shift assay, a highly sensitive polymerase chain reaction-based method. **Results:** We identified 185 *EGFR* mutations (47.7%), 33 *KRAS* mutations (8.5%), 3 *BRAF* mutations (0.77%), and 4 *PIK-3* mutations (1.03%). In patients with *BRAF* mutation, all three patients were adenocarcinomas and smokers. There was no mutual mutation with *EGFR* and *KRAS*. *PIK-3* mutations include 2 adenocarcinomas and 2 squamous cell carcinomas. Three of 4 patients were smoker. We found one *PIK-3* and *EGFR* double mutation case. **Conclusion:** In Japanese surgically resected NSCLC, there are a lot of *EGFR* mutations, but there was little *KRAS* mutation. Although new molecular targeted therapy is expected, *BRAF* and *PIK-3* mutations were very rare. Highly smoking rate in patients with *KRAS* and *BRAF* mutations was not different from past reports, but we could not find other clinical characteristics. Histopathologically, correlation between *PIK-3* mutation and small cell carcinoma is attracting attention recently. In this study, histological types of cases with *PIK-3* mutation were various. **Keywords:** PIK-3, Non-small-cell lung cancer, BRAF

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-049 HER-2 Mutations in Chinese Lung Adenocarcinoma Patients with Negative EGFR Mutations Caicun Zhou[1], Xuefei Li[2], Chao Zhao[2], Shengxiang Ren[1], Chunxia Su[1] [1]*Department of Medical Oncology, Shanghai Pulmonary Hospital, Tongji University; Tongji University Medical School Pulmonary Cancer Institute, Shanghai/China,* [2]*Lung Cancer and Immunity Laboratory, Shanghai Pulmonary Hospital, Tongji University; Tongji University Medical School Pulmonary Cancer Institute, Shanghai/China*

Background: To determine the prevalence and clinicopathological features of epidermal growth factor receptor 2 (*HER-2*) mutations in Chinese lung adenocarcinoma patients with negative *EGFR* mutations. **Methods:** Formalin-fixed and paraffin-embedded (FFPE) tissue sections from 398 lung adenocarcinoma patients with wild-type *EGFR* were screened for *HER-2* mutations by amplification refractory mutation system (ARMS) assay and all *HER-2* mutations were validated by direct sequencing. The protein expression of HER-2 was evaluated by immunohistochemistry (IHC). Of the 398 samples, 331 were also detected *ALK* and *ROS1* fusions by multiplex RT-PCR, and all fusions positive were verified by direct sequencing. The relationship between *HER-2* mutations and clincopathological features and the prognostic effect of its status on disease free survival (DFS) were analyzed. **Results:** 21 of 398 (5.3%) harbored *HER-2* mutations; 7.6% of 278 samples with triple-negative lung adenocarcinoma (*EGFR-*, *ALK-*, *ROS1-*) were found to have *HER-2* mutations. 17 samples (81.0%) were A775_G776insYVMA, two with G776>VC, one with V777_G778insGSP and the last one with 2340_2341ins12 in-frame insertions of exon 20. 59 of 398 (14.8%) were positive of HER-2 expression. No association was found between HER-2 mutations and expression, only two patients coexisted the positive in mutation and expression. There was no statistically significant difference in age, sex, smoking history, and pathological stage between patients with *HER-2* mutations and those with negative patients. The DFS of patients with HER-2 mutations have no significant difference compared with those patients with negative mutations. **Conclusion:** 5.3% of Chinese lung adenocarcinoma with wild-type *EGFR* harbored *HER-2* mutations. The *HER-2* mutations had no association with HER-2 expression. **Keywords:** lung adenocarcinoma, HER-2 mutation, HER-2 overexpression, EGFR mutation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-050 Detection of PIK3CA Mutations, including a Novel Mutation of V344G in Exon 4, in Metastatic NSCLC: A Retrospective Study of 139 FNA Cases Derek B. Allison, Mohammed T. Lilo, Susan Geddes, Ming-Tseh Lin, Edward Gabrielson, Frederic Askin, Qing Kay Li *Pathology, Johns Hopkins Medical Institutions, Baltimore/MD/United States of America*

Background: Several molecular alterations of *PIK3CA* (phosphatidylinositol-4,5-biphosphate 3-kinases, catalytic subunit alpha) signaling pathways have been detected in primary non-small cell lung carcinoma (NSCLC). These include genomic amplifications of the regulatory subunit p85 and the catalytic subunit p110 alpha, as well as mutations of the helical binding domain on exon 9 and the catalytic subunit on exon 20. A mutation in the *PIK3CA* gene is a much rarer event than amplification in NSCLCs (approximately 2% in primary NSCLCs). The clinical significance of *PIK3CA* mutations in carcinoma is still not fully understood and is controversial. For example, some have suggested that *PIK3CA* mutations are associated with a favorable prognosis in breast cancer, while others have found *PIK3CA* mutations to be associated with a poor prognosis in primary lung cancers. Additionally, *PIK3CA* alterations have been associated with *EGFR*, *KRAS* and *AKT*mutations in primary NSCLC. In this study, we have collected FNA specimens of metastatic NSCLCs, investigated *PIK3CA* mutations, and correlated the findings with other molecular results. **Methods:** We identified 139 fine needle aspiration (FNA) cases of metastatic NSCLC with targeted next-generation sequencing (NGS) analyses of *AKT*, *BRAF*, *EGFR*, *ERBB2*, *KRAS*, *NRAS*, and *PIK3CA* genes, as well as testing for *ALK* gene rearrangements by fluorescence in situ hybridization (FISH) at the Johns Hopkins Medical Institute. **Results:**

Age	Sex	Location	Diagnosis	*PIK3CA*Mutation (exon #)	*EGFR* Mutation	*BRAF*-Mutation	*KRAS*-Mutation
63	F	LN	ADC	R88Q (1)	(-)	V600E	(-)
69	M	LN	ADC	V344G(4)	E709A G719C	(-)	(-)
53	F	PL	ADC	V344G(4)	T790M E746_A750del	(-)	(-)
68	M	LN	NSCLC	E542K(9)	(-)	(-)	(-)
58	M	PL	ADC	E542K (9)	T790M L747_A750delinsP S768_V769delinsIL (S768I + V769L)	(-)	(-)
55	F	Pelvic Bone	SqCC	E545K(9)	(-)	(-)	(-)
74	F	LN	ADC	P539R(9)	(-)	(-)	G12C
60	M	PR	ADC	H1047R(20)	T790M L858R K860I	(-)	(-)

LN: Lymph node; PL: Pleural fluid; PR Peritoneal fluid. (-): not detected. **Conclusion:** *PIK3CA* mutation was detected in 5.8% of metastatic NSCLCs. The majority of the mutations were located on exon 9 or exon 20; however, a rare mutation in exon 1 was seen in one case. Further, a novel mutation, to our knowledge, for NSCLC was detected (V344G) in exon 4 in two cases. Among *PIK3CA* mutations, 50.0%, 12.5%, and 12% were associated with *EGFR*, *BRAF*, and *KRAS* mutations,

respectively. In contrast to primary NSCLC, we did not find any metastatic cases to contain both *PIK3CA* and *AKT* mutations. The unique role of *PIK3CA* mutation in metastatic NSCLC and its clinical implications need to be further investigated. **Keywords:** metastatic non-small cell lung cancer, molecular testing, PIK3CA mutation, fine needle aspiration

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P3.04-051 Molecular Testing on Cell Blocks Formed From Bronchial Brush Tip Washing Asha Bonney[1], Michael Christie[2], Anne Beaty[2], Louis B. Irving[1], Daniel P. Steinfort[1] [1]*Respiratory Medicine, Royal Melbourne Hospital, Melbourne/VIC/ Australia,* [2]*Anatomical Pathology, Royal Melbourne Hospital, Melbourne/VIC/Australia*

Background: With the rapid growth of genotype guided targeted therapies, molecular testing is increasingly important for the routine work up in lung cancer. This testing is traditionally performed on biopsy specimens. Bronchoscopy is commonly performed for diagnosis of suspected lung cancer; and multiple sampling modalities are often combined to maximize diagnostic yield. Bronchial brushings are frequently reported to have the highest sensitivity, though the cytology smears generated from these brushings are rarely used for molecular analysis. The aim of this study was to assess the feasibility and accuracy of molecular testing performed on cell blocks (CB) formed from a brush tip wash (BTW). **Methods:** We retrospectively reviewed molecular testing performed on CB from BTW in patients undergoing investigation of peripheral lung lesions between January 2014 and March 2015. During bronchoscopy, brushings were performed and smears created. Following this, the brush tip was then washed in normal saline. This was repeated each time the peripheral lesion was sampled with the bronchial cytology brush. The fluid from the BTW was then processed into a formalin fixed paraffin embedded CB. Patients were included in the study cohort if molecular testing was attempted on the CB created from BTW. The CB specimens underwent molecular testing targeting regions on BRAF (exon 15), KRAS (exon 2,3,4), NRAS (exon 2,3,4), PIK3CA (exon 9. 20) and EGFR (exon 18, 19, 20, 21) genes by amplicon-based parallel sequencing using an Illumina MiSeq. **Results:** There were 22 patients in whom BTW CB was subjected to molecular testing. Results are summarized in figure 1

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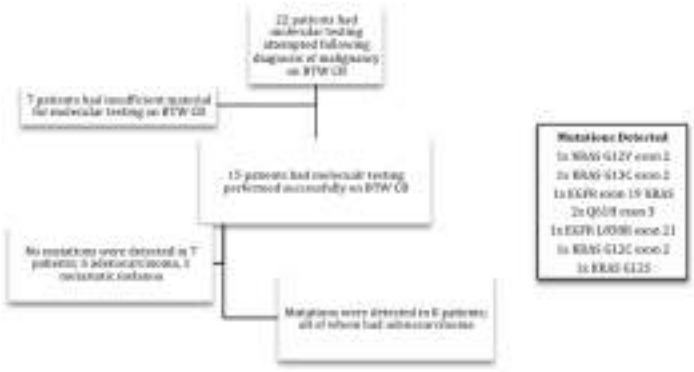

Figure 1. Results of molecular analysis In fifteen cases (68%) a CB was generated, and was successfully subject to molecular testing. Fourteen of these were adenocarcinomas, in which the frequency of detecting a mutation in any of the five assayed genes was 57% (8/14). This is similar to previous reports of molecular testing on adenocarcinoma from other sampling modalities, and suggests that BTW CB generally contain adequate tumour cells for testing. In seven cases, there was no diagnosis obtained from transbronchial lung biopsy, meaning BTW was the sole specimen available for molecular testing. **Conclusion:** Our results demonstrate that molecular studies can successfully be performed on cell blocks obtained from brush tip wash and that this may be the only sample that has adequate material for analysis. We suggest that brush tip washings be routinely created during bronchoscopy to maximize the likelihood of successful molecular testing. **Keywords:** molecular testing, brush tip wash, cell block, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-052 Next Generation Exome Sequencing of Archival Lung Cancer Resection Specimens Chad M. Vanderbilt[1], Kenneth Jones[2], Mark W. Geraci[3], Bifeng Gao[3], John Mitchell[4], Michael Weyant[4], Wilbur A. Franklin[1] [1]*Department of Pathology, University of Colorado Som, Aurora/United States of America,* [2]*Biochemistry and Molecular Genetics, University of Colorado Som, Aurora/CO/United States of America,* [3]*Department of Medicine, University of Colorado Som, Aurora/CO/United States of America,* [4]*Department of Surgery, University of Colorado Som, Aurora/CO/United States of America*

Background: Genetic testing of non-small cell lung cancer has grown rapidly in recent years to accommodate expansion of the number of agents with molecular targets. Whole exome sequencing (WES) has been proposed as a method to comprehensively assess tumor mutation status that could replace current piecemeal approaches to predictive testing. The feasibility of WES for formalin fixed paraffin embedded (FFPE) clinical samples has recently been documented. However, several issues remain to be resolved before this platform can be adopted for routine clinical use. The purpose of the present study is to evaluate tissue coring as a method for obtaining DNA from FFPE tumor tissue, to assess the gene coverage of libraries prepared from FFPE, to determine how best to identify specific validated treatment targets, and to determine mutation load in clinical samples. **Methods:** We extracted DNA from 0.6 mm tissue cores selected both from tumor rich regions of paraffin blocks and normal lung tissue. DNA quality was assessed by Bioanalyzer and Qbit testing. A sequencing library was prepared using the Agilent Sure Select XT5 (v5) library kit. DNA was sequenced using an Illumina Hiseq 2500 ultrahigh throughput sequencing system. We used two flow cells for each of 4 samples to obtain a high level of coverage and to determine the effect of reducing coverage on mutation detection by computational methods. We used the DNA from non-tumoral regions to identify genomic polymorphisms and to then compile lists of mutations that were suspected of have a deleterious effect on the host. As a control, we tested DNA from each tumor by a clinically validated multiplexed panel (Illumina True Site panel). We compared our sequencing results with the TCGA database for the respective tumors. **Results:** DNA yield was 13 and 17 micrograms for the SCC and adenocarcinoma respectively. After shearing to 200 base pairs and library preparation, excellent quality DNA was obtained for sequencing. All of the mutations detected by Miseq analysis were detected by WES. Several mutations identified by WES have not been documented in TCGA. The mutations of the two tumors are sumarized below, including mutation load.

WES Mutations	SCC	Adenocarcinoma
Nonsynonomous SNV	247	51
Stopgain SNV	16	1
Fs deletion	10	1
Non-fs substitution	9	7
Fs insertion	2	2
Non-fs deletion	1	3
Non-fs insertion	1	0
Stoploss SNV	1	0
Splice region abnormality	9	0
Not present in TCGA	37	7
Present in TCGA	265	59
Mutations detected by Miseq	TP53 (p.G245R)	EGFR exon19 del CTNNB1 (p.S45C)
Total (Mutation Load)	**302**	**66**

Conclusion: This study confirms that WES is feasible on FFPE tissue and that the two tumors sequenced fall into the two categories, high and low mutation loads. The mutations identified include several that have not previously been reported. All mutations identified by high coverage clinical platforms were also detected by WES. WES may be suitbable for clinical application. **Keywords:** next generation sequencing, Mutation load, Whole exome sequencing (WES), Sequencing archival tissue

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P3.04-053 SPECTAlung: Screening Patients with Thoracic Tumors for Efficient Clinical Trial Access Benjamin Besse[1], Jessica Menis[2], Julien Adam[3], Thierry Berghmans[4], Tanja Cufer[5], Rafal Dziadziuszko[6], Enriqueta Felip[7], Stephen P. Finn[8], Ludovic Lacroix[3], Julien Mazières[9], Peter Melgaard[10], Silvia Novello[11], Solange Peters[12], Sanjay Popat[13], Martin Reck[14], Egbert Smit[15], Johan Vansteenkiste[16], Baktiar Hasan[17], Jonathan Steuve[18], Emilie Varin[18], Denis Lacombe[18], Rolf Stahel[19] [1]*Gustave Roussy Cancer Campus, Villejuif/France,* [2]*Medical Department, Eortc Headquarters, Brussels/ Belgium,* [3]*Department of Medical Biology and Pathology, Gustave Roussy Cancer Campus, Villejuif/France,* [4]*Intensive Care and Thoracic Oncology, Institut Jules Bordet, Brussels/ Belgium,* [5]*Medical Faculty, University Clinic Golnik, Lubjana/Slovenia,* [6]*Department of Oncology and Radiotherapy, Medical University of Gdansk, Gdansk/Poland,* [7]*Vall D'Hebron University Hospital and Vall D'Hebron Institute of Oncology (Vhio), Barcelona/ Spain,* [8]*University of Dublin, Trinity College and St. James'S Hospital, Dublin/Ireland,* [9]*Hôpital Larrey, Centre Hospitalier Universitaire de Toulouse, Toulouse/France,* [10]*Medical Oncology, Aarhus University Hospital, Aarhus/Denmark,* [11]*Department of Oncology, University of Turin, Aou San Luigi, Orbassano/Italy,* [12]*Department of Oncology, Centre Hospitalier Universitaire Vaudois (Chuv), Lausanne/Switzerland,* [13]*Department of Medicine - Lung, Royal Marsden NHS Foundation Trust, Surrey/United Kingdom,* [14]*Lungclinic Grosshansdorf, Grosshansdorf/ Germany,* [15]*VU University Medical Center,, Amsterdam/Netherlands,* [16]*Department of Pneumology University Hospital Gasthuisberg, Kul Leuven, Leuven/Belgium,* [17]*Statistical Department, Eortc Headquarters, Brussels/Belgium,* [18]*Eortc Headquarters, Brussels/ Belgium,* [19]*University Hospital Zürich, Zurich/Switzerland*

Background: The identification of molecular alteration and its targeting has completely changed the treatment and prognosis of lung cancer. However, designing and implementing clinical trials in small subsets of patients with a particular molecular alteration is challenging because of lack of uniform screening program. Across Europe, screening for molecular alterations is center or country dependent and, generally limited to a small subset of genes. SPECTAlung is the first European standardized, quality-assured molecular screening program of the European Organization for the Research and Treatment of Cancer (EORTC) in collaboration with the European Thoracic Oncology Platform (ETOP) to

facilitate clinical trial access for patients with thoracic tumors. It is expected to test 500 to 1000 patients each year with the overall goal of offering patients clinical trials with targeted agents. **Methods:** Patients sign the informed consent for their tumor tissue to be collected, centralized and processed according to defined international quality control standards at Gustave Roussy Biobank (Villejuif, France). Next Generation Sequencing (NGS) is performed at Sanger Institute (Cambridge, UK) where a panel of about 360 genes is analyzed for mutation, rearrangements and gene copy number. Eligible patients will be those having a pathological diagnosis of any thoracic tumor (lung cancer, malignant pleural mesothelioma and thymic malignancies) at any stage of disease, availability of tumor tissue, age at least 18 years, PS 0-2, life expectancy > 3 months, no active malignancy in the 5 years before study entry and absence of any exclusion criteria that may prevent inclusion into clinical trials. A molecular report will be released to the investigator highlighting identified molecular alterations and also the trials for which the patients might be eligible. The study has been submitted to ethical committees of 15 selected highly specialized and qualified thoracic centres in 12 countries in Europe. EORTC and ETOP will promote the implementation of clinical trials in molecularly selected groups of patients at the SPECTAlung centers. SPECTAlung offers innovative and attractive models of collaboration with commercial and research organizations, by improving patient access to novel therapeutic clinical trial and support the development of personalized medicine. Clinical trial registry number NCT02214134. **Results:** Not applicable **Conclusion:** Not applicable
Keywords: clinical trial, biomarker, thoracic tumor, Screening

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P3.04-054 Validation of PTEN and c-MET Status in Small Biopsy Material and Cytology for Pulmonary Adenocarcinoma Dimple Pandya, Achim Jungbluth, Natasha Rekhtman, Andre Moreira *Pathology, Memorial Sloan-Kettering Cancer Center, New York/NY/United States of America*

Background: Targeted therapy in lung cancer is an expanding field. Molecular alterations in phosphatase and tensin homolog (PTEN) and c-MET (mesenchymal epithelial transition proto-oncogene) are potential therapeutic targets. Loss of PTEN expression has been associated with activation of *PIK3CA/AKT/mTOR* pathway and is associated with sensitivity to mTOR inhibitors. Amplification or overexpression of c-MET is associated with resistance to tyrosine kinase inhibitors and/or poor prognosis. Both PTEN and c-MET can be detected by immunohistochemistry. In this study we evaluated the concordance rate of both antibodies in biopsy material and subsequent excision of the same tumor, since small biopsy and cytology material are the only tissue available for diagnosis in patients with advanced stage. In addition since biopsy material is collected in different fixatives, we also compared the antibody expression in alcohol versus formalin fixed tumors. **Methods:**Pathology database was queried for concurrent biopsy and surgical specimens from 12/2010-7/2014. Surgical core biopsies (n=44) and cytology aspiration biopsies (n=10) with surgical specimens were reviewed to evaluate tumor histology and specimen cellularity. In addition, 8 cases of NSCLC were scrapped and collected in formalin and alcohol fixative. Immunohistochemistry with PTEN antibody (clone 138G6) and c-MET antibody (clone sp44) were performed according to manufactures' instruction following a rigorous validation using positive and negative controls. PTEN staining was evaluated for complete loss of expression or retention (any cytoplasmic or nuclear stain). c-MET staining was evaluated for the intensityand extent of the staining. Positivity is defined as a strong membranous staining (2-3+) in more than 50% of the tumor cells. **Results:** There was a 90% (19/21) concordance for PTEN expression between biopsy and resection (k=0.76). 6 cases showed loss of expression in the biopsy, among these cases 2 were classified as retained PTEN in the excision. In both cases the excision specimen had partial loss of PTEN. Partial loss of PTEN was seen in 3 other cases with retained PTEN in biopsy. There is a 95.2% (20/21) concordance in c-MET staining (k=0.89). In the discrepant case, the biopsy was deemed positive (2+ > 50% of tumor cells), with a negative excision (1+ >70% of tumor cells). For the cases that were fixed in alcohol and formalin there was a 62% (5/8) concordance for PTEN (k=0.37). 3 cases showed loss of expression in alcohol fixed tissue but retention in formalin fixed material. There was a 37% (3/8) concordance for c-MET between the two fixatives (k=0.21). In the 5 discordant cases, c-MET expression was interpreted as negative in alcohol fixed but was considered positive in formalin fixed tissue due to variability in the intensity of staining. **Conclusion:** Despite a good correlation between biopsy and resection for both markers, our results show there is a greater possibility of discrepant results for PTEN than c-MET because of geographic heterogenetic of expression and scoring criteria. The type of fixative (alcohol vs. formalin) is associated with variability in antibody expression. Therefore evaluation of PTEN and c-MET staining in biopsy material and alcohol fixed tissue should be interpreted with caution, especially when designing clinical trials for potential therapy.
Keywords: c-Met, Immunohistochemistry, Adenocarcinoma, PTEN

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P3.04-055 Accurate Strategies to Detect Clinical Important Long Indels from RNA-Seq Data: EGFR as Example Zhifu Sun[1], Naresh Prodduturi[1], Aditya Bhagwate[1], Jinsung Jang[2], Jin Jen[2], Ping Yang[1], Jean-Pierre Kocher[1] [1]*Health Sciences Research, Mayo Clinic, Rochester/MN/United States of America,* [2]*Medical Genome Facility, Mayo Clinic, Rochester/United States of America*

Background: Somatic mutations are driver for tumor development and tumor characteristics that can be used for diagnosis and targeted therapy. These mutations are mostly detected from tumor DNA. As dynamic molecules of gene activities, transcriptome by RNA-seq is increasingly popular, which not only measures gene expression but also structural variants such as alternative splicing, fusion products or mutations. The full utilization of the multi-level information will facilitate personalized medicine. Although single nucleotide mutations (SNVs) can be more easily identified from RNA-seq, intermediate insertions/deletions (indels) exert significant bioinformatics challenges as RNA-seq data is much more complex as a result splicing and most RNA-seq alignment programs do not align reads with gap well and variant callers designed for DNA-seq are not adequate for RNA-seq, which leaves most of important indels undetected. **Methods:** We evaluated commonly used RNA-seq analysis programs TopHat, BWA, BWA-MEM, STAR, and GSNAP along with single sample variant and paired tumor/normal somatic mutation callers GATK, VarScan, MuTect, JointSNVmix, SomaticSniper in a set of lung adenocarcinomas with known single nucleotide and indel (from 15 to 19 bases) mutations from exome-seq data. We aimed to develop highly sensitive and specific strategies for both single nucleotide and longer indel mutations that are important to clinical actions. **Results:** The alignment is the critical step for longer indel identification and the evaluated programs had a wide range of sensitivity to map sequence reads with indels, ranging from not at all (TopHat with either Bowtie 1 or 2) to a decent number of reads mapped if sequence reads are long (GSNAP). The sensitivity was significantly impacted by sequence lengths (50bp vs 100bp) or if gapped alignment was explicitly used. When sufficient reads with indels were aligned, most variant calling programs were able to detect the indels with varied sensitivities except MuTect which only single nucleotide mutations were reported. Specificity was highly filtering criteria dependent. We implemented and recommended different strategies for the indel detection depending upon which alignment program was used. For TopHat alignment, unmapped reads were realigned with BWA-MEM; alignments from STAR or GSNAP were further processed following RNA-seq variant detection best practice. With these strategies, we demonstrated high accuracy in SNV or somatic mutation detections in RNA-seq data compared with exome-seq data and known mutations validated from other technologies in lung adenocarcinoma datasets. With the information, a more comprehensive genomic aberration characterization can be made to each individual tumor for clinical decision making. **Conclusion:** With careful modifications and customization to bioinformatics algorithms, RNA-seq data can be reliably used for both single nucleotide and long indel detection that can be used for treatment selection and outcome prediction.
Keywords: Bioinformatics, RNA sequencing, long insertion deletion, EGFR

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-056 Some Lung Cancer Patients End up without an EGFR-Mutation Analysis Janna Berg[1], Pål Suhrke[1], Lars Fjellbirkeland[2], Odd Terje Brustugun[3], Åslaug Helland[3] [1]*Dept. of Medicine, Vestfold Hospital Trust, Tønsberg/Norway,* [2]*Dept. Of Pulmonology, Oslo University Hospital-Rikshospitalet, Oslo/Norway,* [3]*Dept of Oncology, 3Oslo University Hospital-Radiumhospitalet, Oslo/Norway*

Background: Lung cancer patients with activating mutations in the EGFR-gene are eligible for targeted therapy with tyrosine kinase inhibitors, and clinicians strive for acquiring enough tumor tissue for the needed diagnostic analyses. However, not all patients have an EGFR-test, and little is known about the subsequent steps for patients with inadequate first biopsy. **Methods:** Data on the diagnostic work-up on all NSCLC patients eligible for EGFR-testing was collected at a medium-sized Norwegian hospital for the period June 2010 to December 2013. For samples without successful EGFR-mutation results, we recorded possible explanations. **Results:** Material was sent for EGFR analysis for 256 of the 304 eligible patients diagnosed in the period. For a total of 34 patients (13%) the first biopsy was not analyzed at the department of molecular pathology due to inadequate tumor material. Of these 34 patients, 23 (65%) had no new sample submitted for analysis. 13 of the 23 (57%) were in stage IV, and of these, three did not want active treatment and one was not a candidate for active treatment because of poor general condition. One patient was not re-biopsied due to rapid disease progression. Eigth patients were for no obvious reason never considered for re-biopsies, including a younger patient who had brain metastases at the time of diagnosis, but who lived for 19 months after diagnosis. One of the 11 sent was diagnosed with activating EGFR mutation in the second sample sent for analyses. For patients with rejected samples, EGFR results were available after 17 - 69 days (median 38) from rejection of the first sampling. **Conclusion:** For 65% of the rejected samples, no new samples were submitted for analysis. 57% of the patients with no new sample taken, were in stage IV. When a new biopsy was planned, our study shows that EGFR results from the new sampling were available after median 38 days. For this patient group, with poor prognosis and often rapid disease progression, one should strive for a new sampling and a quicker turn-around time.
Keywords: Pathology, lung cancer, EGFR mutation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-057 Pyrosequencing VS NGS KRAS and EGFR Mutation Detection: A Head to Head Comparison in Lung Adenocarcinomas Antonios Papanicolau-Sengos, Jeffrey Conroy, Hanchun T. Defedericis, Carl D. Morrison *Pathology, Roswell Park Cancer Institute, Buffalo/United States of America*

Background: Pyrosequencing is a popular method for detecting actionable somatic mutations. Most labs use pyrosequencing at an analytical sensitivity of 10%, potentially missing actionable mutations that have a low variant allele frequency (VAF) due to low neoplastic nuclear content or due to neoplastic heterogeneity. Furthermore, the cost-effectiveness of pyrosequencing rapidly decreases when numerous hotspots are interrogated simultaneously and scaleability is limited. Next-generation sequencing (NGS) is scaleable and has the capacity to detect mutations at VAFs less than 10%. The goals of this study were to perform NGS on a series of KRAS and EGFR cases that were "mutation negative" but had suspicious pyrosequencing peaks which were

insufficient for a definite determination, and to review EGFR exon 19 deletion cases that were detected by NGS but missed by pyrosequencing. **Methods:** All the KRAS and EGFR pyrosequencing runs performed at Roswell Park Cancer Institute between July 2011 and November 2014 were manually reviewed. All actionable KRAS and EGFR variants that were found at a VAF of 4% or more and less than 10% and had remnant DNA were tested by a dual MiSeq/PGM platform NGS pipeline with a 3.6% VAF analytic sensitivity for FFPE tissues. We also included EGFR exon 19 cases that had discrepant findings between NGS and pyrosequencing. **Results:** Six lung adenocarcinomas with suspicious KRAS pyrograms were reviewed. By NGS, 4/6 were found to have activating codon 12 and 13 KRAS mutations (NGS VAF range 6-14%). Twelve lung adenocarcinomas with suspicious EGFR pyrograms or discrepant EGFR exon 19 pyrosequencing/NGS results were reviewed. By NGS, 4/12 were found to have actionable mutations, including 3 exon 19 deletions (NGS VAF range 5-24%) and 2 T790M resistance mutations (NGS VAF range 4-5%). **Conclusion:** Pyrosequencing lacks the analytic sensitivity to detect actionable KRAS and EGFR mutations with very low VAF and can entirely miss EGFR exon 19 deletions, even at a high VAF. NGS and can be optimized to detect single nucleotide alterations with a VAF less than 5% and can reliably detect EGFR exon 19 deletions. The capabilities of NGS can translate into improved clinical validity and clinical utility. **Keywords:** NGS, pyrosequencing, EGFR, KRAS

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-058 Is Targeted next Generation Sequencing Superior to Older Methods at Identifying Actionable Mutations in Selected NSCLC Patients? Wendy Cooper[1], Spiridoula Kraitsek[2], Christina Selinger[1], Thang Tran[1], Maija Kohonen-Corish[3], Steven Kao[4], Sandra O'Toole[1], Bing Yu[2] [1]*Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital, Camperdown/NSW/Australia,* [2]*Medical Genomics, Royal Prince Alfred Hospital, Camperdown/NSW/Australia,* [3]*Kinghorn Cancer Centre and Garvan Institute of Medical Research, Darlinghurst/NSW/Australia,* [4]*Medical Oncology, Chris O'Brien Lifehouse, Sydney/NSW/Australia*

Background: Mutation testing for clinically actionable somatic mutations is standard of care for patients with lung adenocarcinoma. Multiplex cancer panels that simultaneously assess for a range of possible mutations are available for next generation sequencing (NGS) platforms covering a wider range of genes than previously available, but it is uncertain if these provide more clinically useful information than older multiplex systems. **Methods:** We undertook targeted next generation sequencing (NGS) of paraffin embedded tumour tissue from a cohort of 13 never smokers and 18 unselected patients who underwent surgical resection of lung adenocarcinoma using the Truseq Amplicon Cancer Panel that assesses hot spots in 48 genes using the Illumina platform. Control normal tissue was obtained from non-involved lymph nodes or normal lung parenchyma obtained from the resection specimens. Results were compared to those obtained using OncoCarta™ v1.0 panel that assesses hot spots in 19 genes using mass spectrometry. **Results:** 3 of the samples from the never smokers were unsuitable for NGS analysis as they failed quality control. Of the 10 samples that could be assessed, 6 (60%) had *EGFR*mutations (3 L858R and 3 exon 19 deletions), 1 (10%) had a *KRAS* G12D mutation and 5 (50%) had *T53* mutations (3 in association with an *EGFR* mutation). Other mutations identified were *ATM*, *PTEN* and *PDGFRA* mutations in one of the patients that also had an *EGFR* mutation. All of the *EGFR* and *KRAS* mutations were also identified using the OncoCarta™ panel. Of the 3 samples that could not be assessed by NGS, 1 had an exon 19 deletion in *EGFR* and 1 had a *BRAF* V600M mutation. In the unselected patient population all of the samples passed quality control and were suitable for both NGS and mass spectrometry. Using NGS, 10/18 (55.6%) had a *KRAS* mutation, 3 (16.7%) had an *EGFR* mutation, 7 (38.9%) had a*TP53* mutation, 2 (11.1%) had *PIK3CA* mutations and 1 (5.6%) each had a BRAF *AF, ERBB4*, *MET*, *HRAS*, *STK11*, *HRAS*, *PDGFRA*, *CTNNB1*, *NOTCH1* or *SMARCB1* mutation. Using the OncoCarta™ panel, all of the *EGFR* and *KRAS* mutations were identified along with only 1 of the *PIK3CA* mutations. The *BRAF* G469S mutation was not identified by mass spectrometry. **Conclusion:** NGS using a targeted cancer panel identifies more mutations than older generation multiplex mutation testing but has a higher failure rate. In the never-smoker patient group, no additional clinically actionable mutations were identified by NGS that were not found by the OncoCarta™ panel. In patient populations with a high rate of *EGFR* mutations, such as never smokers, there may not be much advantage to using more expensive broader NGS cancer mutation panels. **Keywords:** next generation sequencing, never-smoker, lung adenocarcinoma, mutation

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P3.04-059 Non-Small Cell Lung Cancer Mutation Analysis in Purely Caucasian Croatian Population Marko Jakopovic[1], Luka Brcic[2], Marija Misic[3], Fran Seiwerth[1], Gordana Drpa[1], Branka Cucevic[1], Sanja Plestina[1], Suzana Kukulj[1], Mihovil Roglic[1], Silvana Smojver-Jezek[1], Nabil Chalfe[1], Sven Seiwerth[3], Zoran Janevski[1], Miroslav Samarzija[1] [1]*University Hospital Centre Zagreb, Zagreb/Croatia,* [2]*Institute of Pathology, Medical University Graz, Graz/Austria,* [3]*Department for Pathology, Zagreb Medical School, Zagreb/Croatia*

Background: Molecular profiling in lung cancer patients is crucial before starting treatment. Driver mutations in EGFR and ALK genes are targets for tyrosine kinase inhibitors. Mutation rate in domain of EGFR, ALK and KRAS genes varies between populations of lung cancer patients. The aim of the study was to analyze rates of mutation in these genes in purely Caucasian Croatian population. **Methods:** Reflex testing was performed on all non-squamous NSCLC in a period of 6 months, regardless of staging and received therapy. There were altogether 387 patients with adequate (histological and cytological) material for testing. EGFR mutations were tested first (cobas® EGFR Mutation Test, Roche), all negative were than tested for KRAS mutations (cobas® KRAS Mutation Test, Roche), and double negative samples were than tested for ALK mutation using immunohistochemistry (IHC) (clone D5F3, Ventana). **Results:** Out of 387 samples 57 had EGFR mutation (14.72%). Most common mutation was exon 19 deletion (23/57, 40.35%), while 8/57 (14.04%) had two simultaneous mutations. KRAS mutations were present in 158 samples out of 330 samples that were tested (47.88%). ALK immunohistochemistry was performed on 172 double negative samples, resulting in 12 positive cases (6.98%). When calculating with the whole cohort, we had 14.72% of EGFR positive cases, 40.82% with KRAS mutations and 3.10% of ALK IHC positive cases. **Conclusion:**gene changes rates in EGFR and ALG gene are in Croatian lung cancer patients in concordance with previously reported rates in Caucasian population, while KRAS rates are higher than previously reported. For the first time, rates of genetic changes are reported for representative sample of purely Caucasian Croatian population. **Keywords:** EGFR, ALK, KRAS, Croatia

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P3.04-060 Non Small Cell Lung Cancer in Women: Identification of Molecular Biomarkers Towards Sex Specific Tailored Treatments Tiziana Vavala, Valentina Monica, Marco Lo Iacono, Teresa Mele, Elisa Gobbini, Luisella Righi, Mauro Papotti, Giorgio V.V. Scagliotti, Silvia Novello *Department of Oncology - University of Turin, Thoracic Oncology Unit, Orbassano/Italy*

Background: Lung cancer is the leading cause of cancer mortality in both men and women in more developed countries, with a four-fold increase in lung cancer in women in US over the past 30 years. This was confirmed in Europe where, in the last 5 years, lung cancer mortality fell in men (–6%) and increased in women (+7%). Several studies documented sex differences in lung cancer in terms of clinical presentation, survival, pathological patterns and treatment related toxicities; younger age at diagnosis, higher frequency of adenocarcinoma histology, different metabolism of tobacco-related carcinogens, differential gene expression are commonly seen in women. Furthermore, previous studies showed in female gender the expression of functional aromatase enzyme in lung tumor tissues as well as the interaction between Estrogen Receptors (ERs) and Epidermal Growth factor Receptor (EGFR) pathways in lung cancer cells. The aim of this study is to collect a prospective series of advanced stage non small cell lung cancers (NSCLC), to identify, through the Next Generation Sequencing (NGS) technology, potential gender sex differences of selected tumor-associated genes, assessing their both mutational status and gene expression levels. **Methods:** One hundred patients, including 50 women and 50 men, with newly diagnosed stage IV NSCLC will be prospectively enrolled. Smoking history, clinical and anamnestical data will be collected for all patients. Female patients will also provide obstetrical-gynecological anamnesis, while men will provide urological one, if present. Formalin fixed, paraffin embedded diagnostic sample of each patient will be collected and sectioned to obtain: a DNA genomic library to define the mutational profile of a selected panel including 50 tumor-associated genes, a mRNA library to obtain gene expression levels of the corresponding transcripts and protein expression of estrogen receptor Beta (ERß) and DNA repair enzyme ERCC1. Immunohistochemistry reaction, for both ERCC1 and ERβ, will be scored according to the H-score method. NGS analyses will be performed by means of the Ion Torrent Personal Genome Machine (PGM, Life Technologies, Grand Island, NE). Tumor tissues will be tested with commercial library kits: Ion AmpliSeq Cancer Hotspot Panel v.2 to investigate 50 cancer-associated genes and significant gene variations will be further confirmed using Sanger Sequencing method; Ion AmpliSeq™ RNA Cancer Panel to define also gene expression of the same 50 cancer-associated genes (Life Technologies). Correlations among mutational profile, transcriptional pattern, protein levels and clinico-pathological characteristics will be assessed. **Results:** Not Applicable **Conclusion:** Lung cancer incidence in women is increasing worldwide and genetic predisposition, sex hormones or specific molecular features could all account for the clinical differences observed between females and males. Up to the current date, the clinical approach to lung cancer treatment does not rely on gender. The identification of differential status of specific biomarkers can deepen knowledge on the molecular basis of this disease, guiding clinicians towards sex-based treatments. **Keywords:** NSCLC, Women, Gender differences, lung cancer

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P3.04-061 Thoracic Oncology Clinic: Our First 200 Cases, San Jose, Costa Rica Raquel Rojas Vigott, Luis Ugalde Gamboa, Luis Corrales-Rodríguez *Oncology, CCSS, Cartago/Costa Rica*

Background: Lung Cancer has been gaining interest in our country, because there is a higher number of cases and the capacity to make diagnosis and give opportunities of treatment t the patiens. As we give opportunities of treatment to th patients.As we realized, this is a complex pathology, and heterogeneous disease. For that reason, we decided three years ago, to orgnize a multidisciplinary approach for lung cancer patients and to obtain our own statistis. **Methods:** We reviewed 200 cases (files) and followed the patients during the last 3 years. (Retrospective study) **Results:** We attended 200 cases with teh diagnosis of lung cancer. The average age was 63 years old. 62% of patients were female. 68% patients had an adenocarcinoma histology, 17% squamus cell and 10% Small Cell Lung cancer. 59% of patients were people who used to smoke, 41% never smoke. 69% were patients inn stage IV disease, 16% stage III (A,B) and 15% Stage I. From patients in stage IV, 73% received some medical treatment. We tested 100 patients who hat adenocarcinoma for EGFR mutation. 26% of the patients with adenocarcinoma had EGFR (+) ; 53% exon 19, 7% exon 20 and 34% exon 21. 9 patients have received treatment with Erlotinib. 6 of them have accomplished al least 10 months of PFS, and

least 1.5 years of OS. **Conclusion:** We understand taht lung cancer is a complex disease and we are getting our first results of the multidisciplinary work in our hospital. We are so motivated to continue working in this paticular cancer and to understand the profile of our patients. The majority of our patients are in stage IV, nevertheless tha major part of them have the opportunity to receive some medical treatment. Testing for EGFR is now a routine exam, and the analisys of new targets (ALK) is our concern.In Costa Rica the incidence of EGFR positive is around 26%. We are analizing actual data in relation to OS and PFS. **Keywords:** Lung Cancer, Costa Rica, EGFR, 200 cases

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P3.04-062 Application of Molecular Detection of Lung Cancer in Developing Countries Aimin Zang, Youchao Jia, Yanhong Shang *Department of Oncology, Affiliated Hospital of Hebei University, Baoding/China*

Background: The era of personalized medicine of non-small cell lung cancer (NSCLC) has arrived. Gene detection plays a key role in the decision of clinical treatment for patients with adenocarcinoma at least. Access to those tests is still very limited in the developing countries, such as quality control, expenditure/cost and popularization. **Methods:** Individualized treatment of lung cancer, application of molecular detection in developing countries and challenges that high-quality molecular detection faces were all retrospectively reviewed. **Results:** The strategies certainly vary from country to country due to the differences of national conditions in developing countries. Individualized treatment based on molecular detection kits and targeted drugs has been a reality, and the subtypes of lung adenocarcinoma will emerge rapidly. **Conclusion:** Molecular epidemiology data generated by developing countries, as well as application of their emerging scientific and technologic capacities to generate and validate novel biomarkers and diagnostic kits, will certainly contribute to better treatment of patients with lung cancer worldwide. **Keywords:** carcinoma; non-small cell lung cancer; genes; developing countries

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P3.04-063 The Mutational Landscape of Pulmonary Premalignancy in the Context of Lung Adenocarcinoma Kostyantyn Krysan[1], Linh Tran[1], Atsuko Seki[2], Tonya Walser[1], Avrum Spira[3], Michael Fishbein[2], W. Dean Wallace[4], Steven M. Dubinett[1] [1]*Medicine, David Geffen School of Medicine at UCLA, Los Angeles/CA/United States of America,* [2]*Pathology, David Geffen School of Medicine at UCLA, Los Angeles/CA/United States of America,* [3]*Boston University, Boston/United States of America,* [4]*Pathology, David Geffen School of Medicine at UCLA, Los Angeles/United States of America*

Background: While genomic alterations in lung cancer are being actively investigated, the early mutational events that occur within the pulmonary field of cancerization that subsequently drive early carcinogenesis are poorly understood. As a result, the clinical importance of premalignant lesions remains enigmatic. Epithelial cells in the field of lung injury can give rise to distinct premalignant lesions that may bear unique genetic aberrations. A subset of these lesions may progress to invasive cancer, however the mutational landscape that may predict progression has not been determined. In the present study we performed whole exome DNA sequencing to measure the incidence of somatic DNA alterations in matched sets of primary tumor, premalignant lesions and adjacent normal lung tissues. **Methods:** FFPE tissue blocks from 41 patients were obtained from the UCLA Lung Cancer SPORE Tissue Repository. The following regions were dissected from distal airways utilizing Laser Capture Microdissection: a) normal airway epithelial cells (1-3 regions), b) premalignant atypical adenomatous hyperplasia (AAH, 2-4 regions), c) adenocarcinoma *in situ* (AIS, 1-3 regions) and, d) adenocarcinoma (ADC, 1-3 regions). DNA was extracted and sequencing libraries were constructed followed by exome capture. Sequencing was performed on an Illumina HiSeq2000 with a mean coverage of ~50x per base. **Results:** Data analysis included analyses for germline and somatic variants, loss of heterozygosity and copy number alternations. Within each case, position-specific missense and nonsense mutations were compared. Different cases were compared for the mutations at a gene-specific level. Mutations found only in AAH lesions were defined as premalignant, in ADC as malignant, and in both AAH and ADC as progression-associated mutations. The analysis demonstrated that AAH lesions from the same patient often have different mutational profiles. We identified novel recurring progression-associated mutations in 33 genes, most of which have not been previously described as key drivers for lung cancer. Interestingly, recurring mutations were found in genes involved in calcium signaling and extracellular matrix/receptor interaction. The data was compared to the TCGA and COSMIC databases. Among affected proteins, only 3% overlapped with the COSMIC and approximately 6% with the TCGA database. Interestingly, all of the mutations overlapping with the COSMIC, were found to be common mutations in AAH. Furthermore, pathways affected by the mutated genes were identified utilizing Gene Ontology and pathways from the KEGG, Biocarta or Reactome databases. The observation that few genes mutated in both AAH and ADC are known as key drivers, indicates that: a) progression-associated mutations might facilitate malignant transformation by mutated key driver(s), or b) a combination of two or more progression-associated mutations that are not oncogenic alone, might drive malignant transformation. These hypotheses will be further tested by mapping progression- and malignant-associated genes in the context of pathways. **Conclusion:** Our data indicate that premalignant lesions from the same patient may have different mutational profiles. This inter-lesion heterogeneity suggests that a progression-associated mutational landscape could be defined in longitudinal studies of pulmonary premalignancy. These results could help identify targets for the development of targeted chemopreventive strategies for lung cancer. Supported by EDRN (U01CA152751-AS). **Keywords:** Somatic mutations, Premalignancy, progression, Whole exome sequencing

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P3.04-064 A 24h-Single Highthroughput Assay to Identify ALK or ROS-1 Gene Fusions and EGFR Mutations in DNA from FFPE Tumor Samples or Free Circulating DNA Raphael Saffroy[1], Jean-Francois Morere[2], Nelly Bosselut[1], Pasquale Innominato[2], Catherine Guettier[3], Antoinette Lemoine[1] [1]*Oncogenetics, Aphp Hups Paul Brousse Hospital, Villejuif/France,* [2]*Medical Oncology, Hôpital Paul Brousse, Villejuif/France,* [3]*Pathology, Aphp Hups Paul Brousse Hospital, Villejuif/France*

Background: The diagnosis of metastatic lung adenocarcinoma to decide tyrosine kinase inhibitors (TKI) targeting either EGFR mutations or ALK or ROS translocations requires the combination of several techniques and different biological or pathological expertises. These are DNA sequence analysis, immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) that are performed independently and require time and DNA materials. Importantly, to our knowledge no diagnostic can be performed on extracted DNA from FFPE tumors for the identification of ALK or ROS translocations except FISH. FISH is considered as the gold standard technique for gene translocations but time-consumable and not applicable to highthoughput diagnosis. Some unsuccessful attempts have been made using RNA extracted from FFPE. **Methods:** We have developed and patented an assay using the i-plex technology and mass spectrometry detection (Sequenom-Agena Bioscience, CA, USA) allowing the concomitant identification of 20 targeted EGFR exon 18-21 gene sequence abnormalities as well as variants of EML4-ALK (variants 1-2-3a-3b) or ROS1-SLC34A2/EZR/CD74 gene fusions on extracted DNA samples in a single 24h experiment. DNA has been extracted eitherfrom either FFPE tumor samples or plasma free circulating DNA. **Results:** DNA samples from 6 different patient can be analyzed on the same 96 wells-assay (more if a 384 well-assay). As low as 16ng DNA per sample from FFPE biopsies (10 slices) or plama can be used. We have applied this new panel to a cohort of 90 lung adenocarcinoma samples positive for EGFR mutations (n=30), ALK (n=30) or ROS (n=30) translocations; one third being extracted DNA from circulating plasma samples. The limit of detection of the assay is as low as 1 to 5% depending on the gene abnormality. When compared to IHC (EML4-ALK 5A4 clone; ROS1 D4D6 clone, Cell Signalling) / FISH techniques (Vysis LSI ALK Break Apart Rearrangement Probe Kit, Abbott; ROS1 Split FISH Probe, Abnova), the specificity of the identification of ALK or ROS gene rearrangements is 97%. **Conclusion:** In conclusion, we have developed a promising and performant assay based on an innovative methodology that we have patented for the identification in a single experiment of both gene mutations and gene translocations using very low amounts of DNA extracted from FFPE tumor biopsies or plasma samples. **Keywords:** FFPE tumor or free circulating DNA, Diagnostics, ALK or ROS rearrangments on extracted DNA, highthroughput assay

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P3.04-065 Use of next Generation Sequencing to Distinguish Origin of Poorly Differentiated Carcinomas in the Lung from Carcinomas in Other Organs Jens B. Sørensen[1], Morten Grauslund[2], Linea Melchior[2], Edyta Urbanska[1], Eric Santoni-Rugiu[2] [1]*Dept. Oncology, Finsen Centre/National University Hospital, Copenhagen, Copenhagen/Denmark,* [2]*Pathology, National University Hospital, Copenhagen, Copenhagen/Denmark*

Background: Next generation sequencing (NGS) is a molecular analysis for concomitantly assessing several genes for mutations and other abnormalities. Thus, NGS can diminish costs and labour time compared to multiple analyses for individual mutations in Non Small Cell Lung Cancer (NSCLC), such as *EGFR, ALK* or *ROS1* mutations. Another important use may be in diagnostic cases, in which it may be difficult to establish whether a tumor is a primary NSCLC, or represents a metastasis from another organ. Molecular[EMU1] events in every compared sample are assessed in order to find a possible gene constellation matching best the primary origin of the disease. This study describes experience with NGS used in this differential diagnostic process **Methods:** The NGS was performed on genomic DNA purified from formalin-fixed paraffin-embedded tumor tissue using the Ion Torrent PGM NGS sequenator and the Ion AmpliSeq Cancer Hotspot Panel version 2 covering the most common hotspot mutations in 50 cancer relevant genes. The sensitivity is 5% tumor cell nuclei and >500 reads for each amplicon was obtained. **Results:** The use of NGS technique as differential diagnostic tool is exemplified in a 77 year male who in 2010 had left renal R0 resection due to papillary urothelial cancer. In January 2015 he subsequently had right lung upper lobectomy for a 22-mm tumor (primary pulmonary adenocarcinoma, CK7- and TTF1-positive, no EGFR- and ALK-mutations) and right lower lobe wedge resection of a 33 mm tumor (undifferentiated carcinoma of uncertain origin, CK7-positive, TTF1-negative). The clinical dilemma was concerning the possible postoperative treatment indication for this patient. Regarding these two lung tumours as an entire disease, it will be T4N0 and thus IIIA stage of NSCLC with strong indication for adjuvant treatment, despite of the age and one-kidney status. However, if these two resected lung tumours represent different cancers, the tumour in the upper lobe will be staged as IB (T2aN0) and possible benefit of adjuvant chemotherapy for this patient will be limited. NGS showed that each of these three tumors had one unique hotspot mutation, i.e. the urological tumor had BRAF mutation (c.1405_1406GG>TC, p.G469S), the right lung upper lobe tumor had KRAS mutation (c.35G>C, p.G12A), and the right lower lobe tumor had HRAS mutation (c.182A>G, p.Q61R). Thus, the theoretic possibility that the right lower lobe tumor was a metastasis from the urological tumor was not supported and the patient accordingly not considered as having metastatic relapse of the urological cancer, but two primary NSCLCs. Thus, the results did not provide a justification to recommend the adjuvant treatment for this patient. A series of NGS uses in the differential diagnostic process will be presented. **Conclusion:** NGS can examine simultaneously several DNA abnormalities such as *EGFR* mutations, *ALK*- and *ROS1*-rearrangements, which all are of interest for treatment possibilities of NSCLC. However, in patients with NSCLC and a carcinoma in another organ, NGS may also be

a valuable diagnostic tool for distinguishing poorly differentiated primary NSCLC from metastasis derived from another organ. A series of such cases will be presented. **Keywords:** next generation sequencing, non small cell lung cancer, poorly differentiated carcinoma, differential diagnoses

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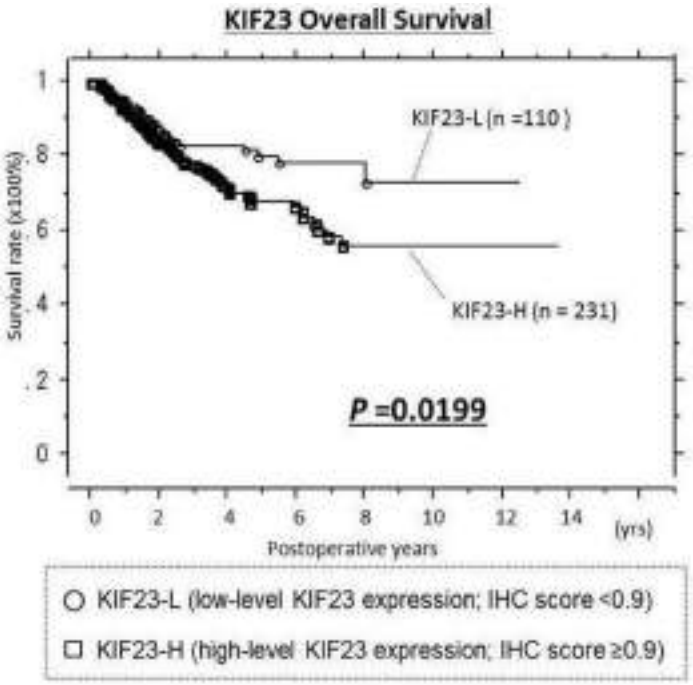
P3.04-066 Overexpression of KIF23 Predicts Clinical Outcome in Primary Lung Cancer Patients Tatsuya Kato[1], Hironobu Wada[1], Priya Patel[1], Daiyoon Lee[1], Spencer Hu[1], Kentaro Hirohashi[1], Takahiro Nakajima[1], Mitsuhito Kaji[2], Kichizo Kaga[3], Yoshiro Matsui[3], Ming S. Tsao[4], Kazuhiro Yasufuku[1] [1]*Division of Thoracic Surgery, Toronto General Hospital, University Health Network, Toronto/ON/Canada,* [2]*Department of Thoracic Surgery, Sapporo Minami-Sanjo Hospital, Sapporo/Japan,* [3]*Department of Cardiovascular and Thoracic Surgery, Hokkaido University, Sapporo/Japan,* [4]*Departments of Laboratory Medicine and Pathobiology, University of Toronto, University Health Network, Toronto/ Canada*

Background: Lung cancer is the leading cause of cancer-related mortality worldwide. To improve the survival rate, it is important to examine or analyze metastatic lymph node samples taken from advanced lung cancer patients, especially using minimally invasive techniques like endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA). We have been attempting to isolate potential molecular targets for lung cancer by analyzing expression profiles of our microarray and various types of database. Throughout these screenings, we identified kinesin family member 23 (KIF23) as a promising molecular target gene for the treatment of lung cancer. High-level expression of KIF23, a member of microtubule-dependent molecular motors that transport organelles within cells and move chromosomes during cell division, has been observed in a variety of human malignancies. The aims of the present study were to observe the expression of KIF23 in human lung cancer, examine the role of KIF23 in lung cancer cell growth and/or survival by small interfering RNA experiments, and explore its clinicopathologic significance and evaluate KIF23 expression as a prognostic marker. **Methods:**Quantitative reverse transcription-polymerase chain reaction (RT-PCR) analysis was performed to detect the expression of KIF23 mRNA using metastatic lymph nodes from patients with advanced lung cancer obtained by EBUS-TBNA and normal human organs. A role of KIF23 in cancer cell growth and/or survival was examined by small interfering RNA experiments. A total of 341 lung cancers were analyzed immunohistochemically on tissue microarrays to examine the expression of KIF23 protein in archival lung cancer samples and its clinicopathologic significance. **Results:** KIF23 transcript was extremely higher in the great majority of metastatic lymph nodes from advanced lung cancers with higher frequency compared with the average expression of normal lung tissues as determined by quantitative RT-PCR. KIF23 was more highly expressed only in the testis and the thymus compared to other human organs. Inhibiting KIF23 expression effectively suppressed non-small cell lung cancer (NSCLC) cell growth, and KIF23 siRNA-treated lung cancer cells more frequently exhibited large cell bodies with two or more nuclei. High-level KIF23 expression was observed in 67.7% of the 341 cases, and this only correlated with pathological T classification (P=0.0269). Lung adenocarcinoma patients with tumors displaying a high-level of KIF23 expression was also identified as an independent prognostic factor by multivariate analysis (P=0.0042).



Conclusion: KIF23 not only provides additional prognostic information for surgical treatment of lung cancer, but may also be a novel therapeutic target for these patients. **Keywords:** kinesin motor protein, prognostic factor, lung cancer, KIF23 (MKLP1)

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P3.04-067 Inflammatory Cytokines Are Associated with the Development of Fatigue in Patients with NSCLC Treated with Definitive Radiotherapy Shulian Wang[1], Jeff Campbell[2], Ramses Sadek[2], Paul Stanton[3], Jing Zhao[4], Ping Ye[5], Matthew Stenmark[6], Martha M. Matuszak[7], James Hayman[7], Randall Ten Haken Haken[6], Theodore S. Lawrence[7], Feng-Ming (Spring) Kong[8] [1]*Department of Radiation Oncology, Georgia Regents University, Cancer Hospital and Institute, Chinese Academy of Medical Sciences and Peking Union Medical College, Augusta/GA/United States of America,* [2]*Department of Biostatistics and Epidemiolog, Gru Cancer Research Center and Medical College of Georgia, Augusta/GA/United States of America,* [3]*Department of Radiation Oncology, Gru Cancer Research Center and Medical College of Georgia, Augusta/ United States of America,* [4]*Georgia Regents University, Augusta/GA/United States of America,* [5]*Gru-Cancer Center, Georgia Regents University, Augusta/GA/United States of America,* [6]*Department of Radiation Oncology, University of Michigan Health System, Ann Arbor/United States of America,* [7]*University of Michigan, Ann Arbor/AL/United States of America,* [8]*Department of Radiation Oncology, Gru Cancer Center/Medical College of Georgia, Georgia Regents University, Augusta/GA/United States of America*

Background: Fatigue is one of the most common symptoms in cancer patients at baseline and or treatment which affects cancer patients' quality of life. This study is to evaluate the association of inflammatory cytokines with the development of fatigue in patients with NSCLC treated with definitive radiation therapy (RT). **Methods:** 109 patients with stage I-IIINSCLC and ECOG 0-2 treated with definitive RT from prospective studies were included. The median age was 66 years (range 43-85), and 84 patients (77.1%) had stage IIIdisease. The median RT dose was 70 Gy (range 34-87.9) at 1.8~2.9 Gy/fx for 103 patients and 6 (5.5%) received stereotactic body RT (SBRT) to a total dose of 50-55Gy at 10-11 Gy/fx. Seventy-six (69.7%) received concurrent and 31 (28.4%) consolidated chemotherapy. Thirty inflammatory, pro-inflammatory, immunomodulation cytokines were measured in plasma samples before RT, using ELISA. Fatigue was evaluated and scored according to CTCAE 3.0 before, 2, 4, 6 weeks during- and 3, 6, 9, 12, 18, 24 months after RT. The fatigue scores from all time points are averaged for each person to create a composite score, which is the endpoint of this analysis. Spearman's rho test was used to check the association of cytokine levels and other clinical factors with fatigue. The p-value of the cytokines are adjusted using the Benjamini-Hochberg procedure. **Results:** 109 patients had fatigue information available before, 2, 4 and 6 weeks during RT, and 106, 101, 98, 97, 92 and 88 had fatigue information available at 3, 6, 9, 12, 18, 24 months after RT, respectively. The incidence of grade 1-3 fatigue was 37.6% before RT, 52.3%, 60.6%, 65.1% at 2, 4, 6 weeks during RT, and 62.3%, 50.5%, 33.7%, 28.9%, 14.1%, 13.6% at 3, 6, 9, 12, 18, 24 months after RT, respectively. Grade 3 fatigue was rare, less than 1% and no grade 4-5 fatigue occurred. Among 30 cytokines, IL-10 (p=0.019) and IP-10 (p=0.054) were significantly associated with fatigue. Lower level of IL-10 and higher level of IP-10 were associated with less fatigue score. SBRT (p=0.002), and consolidated chemotherapy (p=0.049) were significantly associated with fatigue. Patients treated with SBRT had lower fatigue score, but those with consolidated chemotherapy had higher fatigue score. IL-10 was not related with the use of SBRT (p=0.26) or consolidated chemotherapy (p=0.11). IP-10 was not related with the use of consolidated chemotherapy (p=0.76), but it is significantly related with the use of SBRT (p=0.01) and SBRT individuals had higher IP-10 levels. By excluding the 6 SBRT patients, IP-10 was significantly associated with fatigue for non-SBRT patients (p=0.02). Age (p=0.09), gender (p=0.59), histology (p=0.56), ECOG (p=0.16), weight loss (p=0.85), COPD (p=0.16), smoking (p=0.99), stage (p=0.89), biological equivalent RT dose for non-SBRT patients (p=0.12), and concurrent chemotherapy (p=0.59), were not associated with fatigue. **Conclusion:** For patients with NSCLC treated with definitive RT, fatigue increases during RT and decreases over time after completion of RT, with peak severity at 6 weeks during RT. Plasma level of IL-10 and IP-10 before RT, SBRT and consolidated chemotherapy play important roles in the development of fatigue. **Keywords:** non-small cell lung cancer; fatigue; cytokines; radiation therapy

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P3.04-068 A Genetic Variation in a microRNA Target Site of ETS2 Gene Is Associated with Clinical Outcome of Chemotherapy in Non-Small Cell Lung Cancer Shin Yup Lee[1], Mi Jeong Hong[2], Jin Eun Choi[2], Chengcheng Jin[2], Sook Kyung Do[2], Deuk Kju Jung[2], Hyo-Gyoung Kang[2], Seung Soo Yoo[1], Jae Yong Park[1] [1]*Internal Medicine, School of Medicine, Kyungpook National University, Daegu/Korea,* [2]*Biochemistry and Cell Biology, School of Medicine, Kyungpook National University, Daegu/Korea*

Background: Genetic polymorphisms in miRNAs or their target sites may affect miRNA-mRNA interactions, leading to altered expression of target genes. Recently, crosslinking, ligation, and sequencing of hybrids (CLASH) provided direct observation of transcriptome-wide miRNA-target pairs. The present study was performed to investigate the association of single nucleotide polymorphisms (SNPs) located in the miRNA target sites, which were experimentally verified by CLASH, with the clinical outcome of chemotherapy in advanced non–small cell lung cancer (NSCLC). **Methods:** Ninety eight SNPs in miRNA target sites of cancer related genes were selected from 18,500 miRNA:target interactions in CLASH data, and investigated in 384 advanced NSCLC patients who received first-line paclitaxel-cisplatin chemotherapy, using a sequenom mass spectrometry-based genotype assay. **Results:** Of the 98 SNPs analyzed, 17 SNPs were significantly associated with the clinical outcome after chemotherapy. Among these, *ANAPC1* rs3814026C>T, *ETS2* rs461155A>G, and *SORBS1* rs7081076C>A were found to be associated with both chemotherapy response and survival. Notably, the relative expression level of *ETS2* was significantly associated with rs461155A>G genotypes in both tumor and paired normal lung tissues (*Ptrend* = 4 x 10^{-7}, and 0.0003, respectively). **Conclusion:** These findings suggest that the three SNPs,

especially *ETS2*rs461155A>G, could be used as biomarkers predicting the response and survival of NSCLC patients treated with first-line paclitaxel-cisplatin chemotherapy. **Keywords:** NSCLC, chemotherapy, miRNA target site, polymorphism

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-069 Exportin-5 (XPO5) in Lung Adenocarcinoma: A New Biomarker of Invasion in Pathology Specimens Amy M. Coffey[1], Pierre P. Massion[2], Charles A. Powell[3], Yong Zou[2], Jun Zhu[3], Seungyeul Yoo[3], Alain C. Borczuk[4] [1]*Department of Pathology and Cell Biology, Columbia University Medical Center, New York/United States of America,* [2]*Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt-Ingram Cancer Center, Nashville/TN/United States of America,* [3]*Icahn School of Medicine at Mount Sinai, New York/NY/United States of America,* [4]*Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York/NY/United States of America*

Background: The WHO/IASLC classification of lung adenocarcinoma (LADC) emphasizes the distinction of adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA) from their invasive counterparts. The distinction between lepidic-pattern lesions, in particular AIS/MIA and lepidic-predominant adenocarcinoma (LPA), is difficult in small biopsies and cytology specimens. Currently, there are no biomarkers of lung invasion in this setting. **Methods:** The WHO/IASLC classification of LADC was used for all components of this study. Gene expression (GE) data from 58 LADC samples including 33 samples of AIS/MIA and LPA identified two predominant clusters of 553 differentially expressed genes (p<0.01, FDR<0.06). The 317 genes upregulated in LPA localized to 6 regions on chromosomes 1, 2, 6 and 17 (Gene Set Enrichment Analysis). Expression data was compared to copy number (CN) data of AIS/MIA and LPA pooled from a re-annotated Cancer Genome Atlas data set along with prior annotated Affy 6.0 SNP array data (total 1086 LADC samples including 43 AIS/MIA and 26 LPA). Two regions (6p and 17q) contained genes with increased expression and CN increase in LPA. The*XPO5* gene at 6p21 was selected for further study. Immunohistochemistry (IHC) for the *XPO5* protein product Exportin-5 (XPO5, Sigma-Aldrich, St. Louis, USA) was performed on 686 lung cancers (NSCLC), on tissue microarrays and read independently by two pathologists. Nuclear (N) and cytoplasmic (C) positivity was scored for intensity (0-3) and percentage; an H-score was calculated for each (0-300, N-score and C-score). A total score (T-score) was calculated from the sum of the N-and C-scores (0 to 600). Statistical analysis was performed using the independent-samples Kruskal-Wallis test and pairwise analysis. Cox regression was used for survival analysis (continuous variable and quartile regressions), as well as Kaplan-Meier curves, logrank statistic. **Results:** *XPO5* at 6p21 showed upregulation in LPAs by CN, GE and IHC. High XPO5 IHC T-scores correlated with CN, with a median T-score of 300 in tumors with CN gain vs. 50 in tumors without gain. High T-scores were seen in the following invasive patterns of NSCLCs as compared to AIS/MIA: acinar-ADC, solid-ADC, papillary-ADC, large cell carcinoma and squamous cell carcinoma; mean T-scores ranged from 144.7-251.4 in these groups vs. 48.3 and 72.1 in AIS and MIA, respectively. Importantly, T-scores correlated with overall survival for all-stage (n=686) and stage I (n=307) analyses, with higher scores predicting inferior survival. While IHC scores did not show statistically significant staining in LPA as compared to AIS/MIA, a qualitative difference was noted in some cases with acquisition of cytoplasmic positivity in the invasive component of LPAs. **Conclusion:** XPO5 is a candidate biomarker of invasion in LADC. GE and CN data along with IHC staining patterns in 686 NSCLC samples show upregulation of XPO5 in invasive tumors and in tumors with poor survival. In addition to its application in small biopsies, this marker may be of particular use in cytology specimens, where there is significant morphologic overlap between lepidic-pattern tumors and well-differentiated invasive patterns of LADC. **Keywords:** lung adenocarcinoma, XPO5, Exportin-5, Pathology

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-070 Early Prognostic Significance of Circulating Laminin γ2-Chain Fragment in Non-Small-Cell Lung Cancer Yu Teng, Wentao Yue, Li Ma, Xiaoting Zhao, Lina Zhang, Yue Wang, Meng Gu *Beijing Chest Hospital, Capital Medical University/ Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing/China*

Background: Laminin γ2-chain (LN-γ2), a distinctive subunit of heterotrimeric laminin-332, is frequently up-regulated in various types of carcinomas, and is of great importance in the biological processes including cell migration and tumor invasion. Despite of this, the status of circulating LN-γ2 fragment in lung cancer patients is still uncertain. **Methods:** In this study, serum samples from 538 all-stage (stage I-IV) patients of non-small-cell lung cancer (NSCLC) and 94 age-matched normal volunteers were determined by enzyme-linked immunosorbent assay. Data were statistically analyzed in combination with clinicopathological information. **Results:** Compared to the normal controls, serum LN-γ2 concentration is drastically increased in NSCLC patients (P < 0.001), even in early cases of stage I patients (P < 0.001). Furthermore, our data suggested that serum LN-γ2 level was in close correlation to male gender (P < 0.001) and smoking status (P < 0.001) with a higher positive rate relative to each counterpart, but was not significant between adenocarcinoma and squamous cell carcinoma histologies (P = 0.879). We also found that circulating LN-γ2 could reflect the progression of lung cancer with higher serum levels or positive rates in higher tumor-node-metastasis (TNM) stages. Survival analysis on 370 eligible patients who underwent a follow-up examination up to 4 years indicated that patients of serum LN-γ2 positive group survived markedly shorter compared with those in the negative group (P = 0.028), and it was especially the case for clinical stage I (N = 72, P < 0.001) and stage T1 (N = 67, P = 0.001), even for stage N0 patients (N = 148, P = 0.038), which all represent groups of early cases. As for the patients of advanced stages, however, it was not the case that the overall survival rates between LN-γ2 positive and negative patients were not significantly different among clinical stages II-IV (P = 0.830), stages T2-4 (P = 0.575), stages N1-3 (P = 0.669), and stage M1 (P = 0.849) groups, respectively. Subsequently, Cox regression analysis was performed to define serum LN-γ2 as an independent prognostic indicator in the all-stage NSCLC cases (N = 370, univariate, P = 0.035; multivariate, P = 0.007). Worthy of note, however, in the multivariate analysis on those more advanced cases (stage II-IV), no statistical significance was observed on the serum levels of Ln-γ2 (N = 298, P = 0.234). **Conclusion:** In summary, our study suggests circulating LN-γ2 to be a promising diagnostic biomarker for early-stage NSCLC and an effective indicator of tumor progression. It is proposed that circulating LN-γ2 might be important and applicable for the prognosis of early-stage NSCLC patients, rather than that of advanced cases. **Keywords:** Laminin gamma2, Circulating, Early prognosis, Non-small-cell lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-071 High Id1 Expression in Lung Cancer: A Favorable Predictor after Adjuvant Chemotherapy Yu-Jen Cheng[1], Jen-Wei Tsai[2], Shyng-Shiou F. Yuan[3] [1]*Surgery, E-Da Cancer Treatment Hospital, Kaohsiung/Taiwan,* [2]*Pathology, E-Da Hospital, Kaohsiung/Taiwan,* [3]*Obstetric and Gynecology, Kaohsiung Medical University Hosiptal, Kaohsiung/Taiwan*

Background: Overexpression of Id family proteins inhibits cell differentiation and enhances cell proliferation and invasiveness. An elevated Id1 expression was observed in lung cancer cell lines as well as lung cancer tissues. Nude mice study further confirmed an increased tumor growth in Id1-overexpressing cells and a decreased tumor growth in Id1-knockdowned cells. Id1 protein may provide a pivot role in non-small cell lung cancer (NSCLC) development. **Methods:** Effects of Id1 expression on cytotoxicity of paclitaxel and cisplatin, and the mechanisms underlying these effects, were analyzed in A549, H460 and H520 cells in vitro. The influence of Id1 expression on xenograft lung tumor growth was investigated in nude mice, following treatment with paclitaxel and cisplatin. Eighty-three surgically-treated NSCLC patients receiving adjuvant paclitaxel and cisplatin were included for clinical analysis. Id1 expression in tumor and normal lung tissues was examined by immunohistochemistry, and associations for Id1 with clinicopathological characteristics and patient survival were assessed using Cox regression models and Kaplan Meier survival curves. **Results:** NSCLC cells with high Id1 protein expression were observed to be vulnerable to the treatment of paclitaxel and cisplatin. In the nude mice xenograft model, the tumor growth was reduced to a large degree in the Id1-overexpressing group upon treatment with paclitaxel and cisplatin. There were 60 patients with adenocarcinoma (Ade) and 23 patients with squamous cell carcinoma (SqCC). After surgery followed by adjuvant chemotherapy, the Ade patients with high Id1 expression had an increased disease free survival (DFS) and overall survival (OS) compared to the patients with low Id1, whereas there was no difference in DFS or OS for SqCC patients. The pooled trends of DFS and OS were similar to those of the analyses for Ade patients only. **Conclusion:** In summary, our current data suggest that Id1, a generally negative prognostic factor, predicts a favorable prognosis in the cases of surgically treated NSCLC patients receiving the definitive adjuvant chemotherapy. **Keywords:** non-small cell lung cancer, Id1 protein, paclitaxel, adjuvant chemotherapy

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-072 Overexpression of CADM1 Is Associated with Poor Prognosis in Small Cell Lung Cancer Shinji Kikuchi[1], Yuko Minami[2], Yusuke Saeki[1], Masatoshi Yamaoka[1], Naohiro Kobayashi[1], Yukinobu Goto[1], Mitsuaki Sakai[1], Masataka Onizuka[1], Hideo Ichimura[1], Yukio Sato[1] [1]*Department of Surgery (Thoracic Surgery), University of Tsukuba, Tsukuba Ibaraki/Japan,* [2]*Department of Diagnostic Pathology, University of Tsukuba, Tsukuba Ibaraki/Japan*

Background: CADM1, a member of the immunoglobulin superfamily cell adhesion molecules, acts as a tumor suppressor in a various cancers, including non-small cell lung cancer (NSCLC). In contrast, CADM1 also acts as an oncoprotein that promotes invasion in ATL and small cell lung cancer (SCLC) cells. Here, we investigate the possible association of CADM1 expression and splicing variant with the clinical characteristics of surgically treated patients with primary lung cancer. **Methods:** Expression and splicing variant of CADM1 was examined by RT-PCR, Western blotting, immunohistochemistry, and SSCP, respectively. We studied splicing variant of CADM1 in 5 primary NSCLC tumors and a primary SCLC tumor, as well as 16 SCLC and 10 NSCLC cell lines. Immunohistochemical expression of CADM1 was analyzed in 34 primary SCLC tumors and 25 primary NSCLC tumors. Statistical analysis was performed to determine significant predictor for overall survival and recurrence-free survival. **Results:** Western blotting and RT-PCR analyses have revealed that CADM1 is significantly expressed in 11 of 14 SCLC cells growing in suspension cultures but in neither of 2 SCLC cells showing attached growth to plastic dishes, suggesting that CADM1 is involved in anchorage-independent growth in SCLC. Then, we demonstrate that SCLC expresses a unique splicing variant of CADM1 (variant 8/9) containing additional extracellular fragments corresponding to exon 9 in addition to variant 8, a common isoform in epithelia. Variant 8/9 of CADM1 is almost exclusively observed in SCLC and testis, although this variant protein localizes along the membrane and shows similar cell aggregation activity to variant 8. Interestingly, both variant 8/9 and variant 8 of CADM1 show enhanced tumorigenicity in nude mice when transfected into SBC5, a SCLC cell lacking CADM1. Inversely, suppression of CADM1 expression by shRNA reduced spheroid-like cell aggregation of NCI-H69, a SCLC cell expressing a high amount of CADM1. These findings suggest that CADM1 enhances the malignant features of SCLC, as is observed in ATL. Immunohistochemistry demonstrates that CADM1 is strongly expressed in 24 of 34 (71%) SCLC and 2 of 25 (8%) NSCLC, weakly expressed in 7of 34 (21%) SCLC and 10 of 25 (40%) NSCLC, and negative in 3 of 34 (9%) SCLC and 7 of 16 (44%). In NSCLC, loss of

CADM1 expression was preferentially observed in heavy smokers (smoking index ≥ 800). In SCLC, overexpression of CADM1 was significantly associated with poor prognosis in surgical patients. **Conclusion:** SCLC represents high recurrence rates and poor clinical outcome. Surgical treatment can achieve satisfactory results in selected cases. Overexpression of CADM1 could be an indicator of poor prognosis and could influence the decision for adjuvant therapy or follow up intervals in surgical patients with SCLC. **Keywords:** CADM1, SCLC, splicing variant

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-073 CXCR4 Expression Is Associated with Poor Survival in Early, Resected NSCLC Shannon Otsuka[1], Alexander Klimowicz[1], Karen Kopciuk[1], Michelle Dean[1], Yukun Zhang[2], Don Morris[1], D. G. Bebb[1] [1]*Tom Baker Cancer Centre/University of Calgary, Calgary/Canada,* [2]*University of Calgary, Calgary/AB/Canada*

Background: CXCR4, a G protein coupled chemokine receptor, and its ligand, stromal cell derived factor-1 (SDF-1), play a critical role in organ specific tumor metastasis. In vitro, CXCR4 expression has been shown to correlate with migration, invasion and adhesion in various cancer cell lines including lung, breast and colon, among others. In clinical studies, patients whose tumors exhibit high CXCR4 expression tend to have a poorer clinical outcome. We previously demonstrated that high expression of CXCR4 by quantitative IHC in a cohort of 170 stage IV NSCLC specimens was associated with significantly decreased overall survival, particularly in the female patients. We subsequently investigated whether CXCR4 also conferred a poorer prognosis in our early stage NSCLC patients with resected disease, to validate our previous findings. **Methods:** After ethical approval was obtained, demographic details, clinical variables and outcome data were gathered on patients diagnosed at the Tom Baker Cancer Centre (TBCC) from 2003 to 2006. Formalin-fixed paraffin embedded tumor specimens were obtained from those patients diagnosed with resected stage I, II or III NSCLC and tissue micro arrays (TMAs) were generated. CXCR4 expression in NSCLC cells was analyzed by immunohistochemistry using anti CXCR4 mAb and the HistoRx PM-2000 platform, then correlated with clinical outcome. Statistical analysis was performed using the Kaplan-Meier method, multivariate analysis and a multi-state model to account for the competing risks of disease free and overall survival. **Results:** Of 1502 patients diagnosed with NSCLC at the TBCC in 2003-2006, 166 had resected (pneumonectomy, lobectomy or wedge resection) stage I (63%), II (30.7%) or III (9.6%) disease. 37.3% of the patients received adjuvant treatment (combined chemoradiotherapy or radical radiotherapy alone) after their surgery. 46.4% of the patients were still alive at the time of analysis. The mean CXCR4 AQUA scores were significantly lower for the early stage patients than those obtained for the advanced stage IV patients (1715.90 vs 2512.44 $p< 0.0001$). High CXCR4 expression was associated with worse overall survival ($p = 0.026$) but had no significant effect on disease free survival after resection ($p = 0.376$). Subgroup analysis showed no significant differences between genders in the association between high CXCR4 expression and clinical outcome. **Conclusion:** CXCR4 is expressed in early stage resected NSCLC tumors and appears to increase significantly from stage I-III to stage IV NSCLC. High CXCR4 expression is associated with significantly poorer overall survival in early stage resected patients, validating our previous findings in stage IV NSCLC using the same method. CXCR4 does not seem to be associated with disease free survival in this cohort of patients, nor does there seem to be any association between gender and the effect of CXCR4 on poor outcome unlike that seen in our stage IV NSCLC patients. **Keywords:** NSCLC, CXCR4, survival, resected

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-074 Prognostic Multi-Gene Molecular Assay Might Improve Identification of Pathologic Stage IB Lung Adenocarcinoma Patients at Risk for Recurrence Daniel Oh[1], Kraig Yager[2], Brent Evans[2], Jonathan Nelson[2], Alison Sibley[2], Thaylon Davis[2], Kristen Rushton[2], Kathryn A. Kolquist[2], John Kidd[2], Anne-Renee Hartman[2] [1]*Keck School Ofmedicine, University of Southern California, Los Angeles/CA/United States of America,* [2]*Myriad Genetic Laboratories, Inc., Salt Lake City/UT/United States of America*

Background: Adjuvant chemotherapy improves survival for some patients with NSCLC and is recommended for consideration by NCCN guidelines for pathologic stage IB patients presenting certain high risk features. A validated, 46-gene RNA expression assay has been shown to stratify lung cancer specific, post-resection mortality risk in pathologic stage I and II NSCLC adenocarcinoma independently of pathologic staging and high risk features. The aim of this study was to compare Stage IB patient risk as assessed by cell cycle progression (CCP) and prognostic score, a combination of CCP score and pathologic stage, versus NCCN high risk features. **Methods:** Formalin-fixed paraffin-embedded surgical tumor samples from 92 stage IB lung adenocarcinoma patients, who underwent definitive surgical treatment and complete lymph node evaluation, were stratified to high or low risk groups by analysis of the molecular assay and the remaining NCCN high risk features of wedge resection, tumor size >4 cm, poorly differentiated tumor, lymphovascular invasion, and visceral pleural invasion. **Results:** Of the 92 Stage IB patients, 63 (68.5%) were designated high risk by the 46-gene molecular assay. Of these molecularly designated high risk patients, 5 (7.9%) presented no NCCN high risk features, 23 (36.5%) presented only 1 high risk feature, 22 (34.9%) presented 2 high risk features, 11 (17.5%) presented 3 high risk features, and 2 (3.2%) presented 4 high risk features. No patients presented with all 5 high risk features. **Conclusion:** This study demonstrates that a validated measure of recurrence in Stage IB adenocarcinoma patients can identify high risk patients that would have been otherwise designated as low risk according to pathological features. Significantly, in the Stage IB population, prognostic score provide quantitative risk information above that captured by current NCCN high risk features. Patients with resected Stage I lung adenocarcinoma and a high prognostic score may be candidates for adjuvant therapy to reduce cancer related mortality. **Keywords:** recurrence, proliferation, 46-gene, stage IB

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-075 The Biological and Clinical Significance of Alpha-1 Antitrypsin in Non-Small Cell Lung Cancer Adam Szpechcinski[1], Joanna Chorostowska-Wynimko[1], Renata Langfort[2], Emilia Debek[1], Wlodzimierz Kupis[3], Piotr Rudzinski[3], Jolanta Zaleska[4], Beata Poplawska-Wisniewska[1], Radoslaw Struniawski[1], Dorota Giedronowicz[2], Tadeusz Orlowski[3], Kazimierz Roszkowski-Sliz[4] [1]*Department of Genetics and Clinical Immunology, National Institute of Tuberculosis and Lung Diseases, Warsaw/Poland,* [2]*Department of Pathomorphology, National Institute of Tuberculosis and Lung Diseases, Warsaw/Poland,* [3]*Department of Thoracic Surgery, National Institute of Tuberculosis and Lung Diseases, Warsaw/Poland,* [4]*Iii Department of Lung Diseases, National Institute of Tuberculosis and Lung Diseases, Warsaw/Poland*

Background: Lung cancer progression is generally associated with extensive tissue remodeling to provide a suitable environment for tumor growth, invasion and metastasis, and it is known that proteinases expressed by cancer cells and/or host cells play a key role in this process. However, the biological role of alpha-1 antitrypsin (AAT) in lung carcinogenesis is not clear. **Methods:** Serum and FFPE tissue samples from 206 NSCLC patients (stages I-IV) were analyzed for AAT and CRP blood concentration, AAT phenotype and AAT protein expression in tumor cells. Reference groups consisted of 183 PiMM COPD patients and 23 PiMM patients with benign lung nodules (positive chest radiograph). **Results:** Only 10/206 (5%) NSCLC patients carried deficient AAT allele (mean AAT blood concentration 150 mg/dl). In the PiMM NSCLC patients mean AAT serum concentration (195.5 mg/dl) was significantly higher than in the PiMM COPD group (171 mg/dl) and the patients with benign lung nodules (154 mg/dl; $p<0.0001$). AAT concentration was significantly higher in SQC type (202 mg/dl) than ADC (175 mg/dl; $p<0.029$) patients, and in advanced (IIIb-IV, 247 mg/dl) versus early stage disease (I-IIIa, 190 mg/dl, $p<0.0001$). The AAT levels significantly correlated with CRP ($R=0.6$; $p<0.0001$), however CRP level did not differentiate NSCLC from COPD. Importantly, the strong AAT expression observed in tumor tissue was positively associated with the higher AAT blood levels, while weak or no AAT expression directly correlated with the lower AAT blood levels. **Conclusion:** Our results evidenced that local production of AAT by tumor cells significantly contribute to high levels of AAT in blood of NSCLC patients reflecting an active role of this anti-protease in lung carcinogenesis. The study is on-going. **Keywords:** non-small cell lung cancer (NSCLC), serum concentration by nephelometry, AAT expression in lung cancer FFPE tissue by IHC, alpha-1 antitrypsin (AAT)

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-076 The Crux of Molecular Prognostications in NSCLC: An Optimized Biomarker Panel Fails to Outperform Clinical Parameters Dijana Djureinovic[1], Marianna Grinberg[2], Johanna Sofia Margareta Mattsson[1], Karolina Edlund[3], Jörg Rahnenführer[2], Jan Hengstler[3], Linnea La Fleur[1], Simon Ekman[1], Hans Brunnström[4], Hirsh Koyi[5], Eva Brandén[5], Mats Lambe[6], Karin Jirström[4], Fredrik Pontén[1], Johan Botling[1], Patrick Micke[1] [1]*Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala/Sweden,* [2]*Department of Statistics, Tu Dortmund University, Dortmund/Germany,* [3]*Leibniz Research Centre for Working Environment and Human Factors, Tu Dortmund University, Dortmund/Germany,* [4]*Division of Pathology, Lund University, Lund University, Lund/Sweden,* [5]*Dept. of Pneumology, Gävle Hospital, Gävle/Sweden,* [6]*Regional Cancer Center Uppsala-Örebro, Regional Cancer Center Uppsala-Örebro, Uppsala/Sweden*

Background: The best known prognostic factors for non-small cell lung cancer (NSCLC) patients are age, tumor stage and performance status. Numerous proteins have been analyzed to improve the traditional prognostication. Even though some proteins have shown prognostic value, the performance is not sufficient to be introduced in the clinical routine. The aim of this study was to generate a prognostic classifier based on proteins that previously have shown reproducible prognostic value and represent different aspects of tumorigenesis. **Methods:** The selection of proteins was based on literature search, meta-analysis of gene expression data sets and availability of reliable antibodies towards these proteins. Finally, five proteins (Ki67, EZH2, SLC2A1, TTF1 and CADM1) were chosen and analyzed by immunohistochemistry on tissue microarrays comprising NSCLC tissue patients (n=673), divided into a training and a validation cohort. For each patient, one score was obtained for each of the five antibodies, integrating the staining intensity and the fraction of stained tumor cells. Analyses were performed using all possible combinations of proteins and tested with or without clinical parameters. The C-index was used to develop the best prediction model on a training cohort (n=326) and the model was subsequently validated in the validation cohort (n=347). **Results:** All five proteins showed a significant prognostic impact in the univariate and the multivariate Cox analyses. Using a combination of the protein scores, the model was then fitted to provide the best prognostic performance (C-index=0.60). This did, however, not outperform the use of clinical parameters alone (C-index=0.62). The same was true when the analyses were performed separately for the adenocarcinoma (C-index=0.60) and the squamous cell carcinoma subgroup, respectively (C-index=0.60). More importantly, the addition of protein data to the clinical information (C-index=0.62) did not improve the prognostic value of the clinical parameters alone (C-index=0.60). To substantiate the results of our test cohort, we transferred the best prognostic model for all NSCLC, only adenocarcinomas and only squamous cell carcinomas respectively to a validation cohort. Again, all proteins showed prognostic relevance in the univariate analysis but did not perform better, alone or in combination, than the clinical parameters. **Conclusion:** Here we have performed a comprehensive analysis in order to obtain the best survival prediction model by using clinical parameters and the expression of five proteins.

Although we chose strict criteria for protein marker selection, the prognostic power of these proteins was inferior to the traditional clinical parameters. Our findings question the general concept of using protein markers for prognostication in NSCLC but stress the value of careful assessment of traditional parameters in clinical practice.
Keywords: NSCLC;prognostication;IHC;protein panel;

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P3.04-077 Diagnosis and Prognosis of Non-Small Cell Lung Cancer Based on Metabolic Profiles of Mediastinal Lymph Node Aspirates
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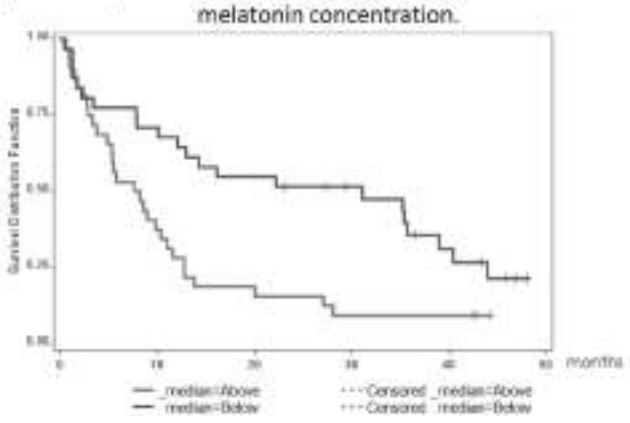
Background: Non-small cell lung cancer (NSCLC) has a high mortality. TNM staging has prognostic implications, but there is a paucity of biomarkers to predict prognosis. The aim of this study was to evaluate the metabolomic profiles of mediastinal and hilar lymph nodes of NSCLC patients and to determine the prognostic implications of different metabolites. **Methods:** Endobronchial ultrasound-guided fine needle aspirates of hilar and mediastinal nodes from patients with NSCLC were collected from January 2011 to February 2013. Metabolomic profiles were generated using liquid chromatography mass spectrometry. Electronic medical records were reviewed for histologic diagnoses and survival status. T-testing was used to compare metabolite differences between groups. Metabolites dichotomized at their median values were assessed for prognostic potential via Cox regressions. P<0.05 was regarded as statistically significant. **Results:** A total of 79 lymph node aspirates were collected. 50 were positive for NSCLC, 13 were negative for NSCLC in patients with biopsy-proven NSCLC at the primary site, and 16 were from patients with non-malignant lung disease. The histologic subtypes of patients with NSCLC were 38 (60.3%) adenocarcinoma (AD) and 25 (39.7%) squamous cell carcinoma (SCC). TNM staging for the patients with NSCLC was as follows: 8 (12.7%) stage I, 10 (15.9%) stage II, 23 (36.5%) III, and 22 (34.9%) IV. Concentrations of alanine, alpha-ketoglutarate, glutathione (reduced and oxidized states), homocysteine, malate, melatonin, malonyl-carnitine, S-adenosyl homocysteine, and S-adenosylmethionine were statistically significantly higher in NSCLC patients than in patients with benign disease. In contrast, citruline, cysteine, glutamine, isoleucine, L-carnitine, leucine, ornithine, tryptophan, and valine were lower in the NSCLC group than in the benign group. Metabolite concentrations were different for different cancer sub-types; SCC patients had a 4.92-fold higher concentration of succinate than AD (p<0.0001), whereas AD had a 1.52-fold higher concentration of homocysteine than SCC (p=0.041). Elevated concentrations of the following metabolites were associated with shorter overall survival: melatonin (HR=2.24, 95% CI: 1.27-3.97; p=0.0057) Figure 1, malate (HR=1.91, 95% CI: 1.08-3.35; p=0.025), cystathionine (HR=1.84, 95% CI: 1.03-3.28; p=0.039), and glutamate (HR=1.77, 95% CI: 1.01-3.09; p=0.045).

Figure 1.- Kaplan Meier survival curve for above and below median melatonin concentration.



Conclusion: Metabolomic data demonstrate differences between different NSCLC subtypes. In addition, metabolomic data may have prognostic potential that is independent from that associated with TNM stage. Metabolites associated with worsened prognosis offer an avenue for research; they may allow us to identify specific pathways that correlate with prognosis.
Keywords: Metabolomic profile, mediastinal lymph nodes, prognostic factor, non-small cell lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-078 Adverse Effect of Smoking on the Intratumoral Expression of Thymidylate Synthase in Lung Cancer
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Background: Cigarette smoke is a risk factor for lung cancer. A recent study showed that lung tumors exhibited distinct epidemiological, clinical, pathological, and molecular features depending on the smoking status. Thymidylate synthase (TS) is an essential enzyme for *de novo* DNA synthesis. TS expression has been associated with the proliferative activity of cancer cells, and low TS expression was associated with better outcomes for non-small cell lung cancer patients treated with TS-targeted drugs. The aim of the present study was to investigate the relationship between TS expression in lung cancer and the smoking status. **Methods:**

		Adenocarcinoma		Squamous cell carcinoma	
Smoking status No.		Non-Smoker 32	Smoker 35	Non-Smoker 3	Smoker 43
Gender	M	9	31	0	41
	F	23	4	3	2
Age	Mean ± SD (Median, Range)	66.7±1.70 (67,50-79)	64.2±1.62 (63,39-83)	63.3±15.6 (65,47-78)	66.4±9.09 (68,42-84)
P-stage	1A	11	8	0	5
	1B	16	9	1	7
	2A	4	5	1	5
	2B	2	4	0	6
	3A	2	9	0	8
	3B	4	0	0	2
	4	2	0	0	2
Tumor size (mm)	Mean ± SD (Median, Range)	32.2±13.6 (31,12-75)	37.5±20.7 (35,10-130)	37.0±11.4 (42,24-45)	43.4±19.0 (45,10-80)

Table 1. Patient's clinical and pathological characteristics according to the smoking status

The subjects were 113 patients who underwent surgical resection of lung cancer in at one of our three hospitals. Table 1 shows the patient's clinical and pathological characteristics accoding to the smoking status. We measured the intratumoral mRNA expression for TS, in manually microdissected tumor specimens using RT-PCR, and we normalized the values considering the gene for to β-actin as the reference. We analyzed the expression level of TS considering the cumulative dose of smoking in a patient's life.
Results:

		Smoking dose (No.)	TS expression value	P value
Ad	Non Smoker	(12)	2.17±2.92 (1.47,0.26-16.8)	p=0.9750
	Smoker	<45 pack-years (16)	1.56±1.75 (1.01,0.40-7.08)	p=0.0187*
		≥45 pack-years (14)	3.14±3.2 (1.68,0.85-12.8)	p=0.0153*
Sq	Non smoker	(3)	3.05±1.09 (3.47,1.19-3.87)	
	Smoker	<50 pack-years (21)	2.62±2.66 (2.01,0.38-12.6)	p=0.3038
		≥50 pack years (22)	2.46±1.27 (2.40,0.68-5.25)	p=0.5270

Table 2. The relationship between TS expression and the smoking dose. The level of significance was set at P < 0.050.

Table 2 shows the relationship between TS expression and the smoking dose. Among smokers, the median of smoking dose was 45 pack-years in patients with adenocarcinoma (Ad) and 50 pack-years in squamous cell carcinoma (Sq). TS expression was significantly higher in patients with Sq than in those with Ad (p = 0.0153). Among smokers with Ad, TS expression was significantly higher in patients with a smoking status of more than 45 pack-years compared to those with a smoking status of less than 45 pack-years (p = 0.0187). **Conclusion:** Our results indicate that it may be possible to predict high TS levels in patients with Ad by considering smoking dose.
Keywords: Thymidylate Synthase, smoking dose, non-small cell lung cancer, predictive factor

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-079 A Panel of Genetic Polymorphism Can Predict Prognosis in Lung Cancer Shin Yup Lee[1], Jin Eun Choi[2], Eungbae Lee[3], Seung Soo Yoo[1], Jae Yong Park[2]
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Background: This study was conducted to investigate whether a panel of 8 genetic polymorphisms can predict the prognosis of patients with early stage non-small cell lung cancer (NSCLC) after surgical resection. **Methods:** We selected 8 single nucleotide polymorphisms (SNPs) which have been associated with the prognosis of lung cancer patients after surgery in our previous studies. A total of 814 patients with early stage NSCLC who underwent curative surgical resection were enrolled. The association of the 8 SNPs with overall survival (OS) and disease-free survival (DFS) was analyzed. **Results:** The 8 SNPs (*CD3EAP* rs967591, *TNFRSF10B* rs1047266, *AKT1* rs3803300, *C3* rs2287845, *HOMER2* rs1256428, *GNB2L1*rs3756585, *ADAMTSL3* rs11259927, and *CD3D* rs3181259) were significantly associated with OS and/or DFS. Combining those 8 SNPs, we designed a prognostic index to predict the prognosis of patients. According to relative risk of death, a score value was assigned to each genotype of the SNPs in the genetic model which best explains the association between genotypes and prognosis for each SNP. When we categorized the patients into two groups based on the prognostic index, high risk group was significantly associated with worse OS and DFS compared to low risk group (aHR for OS = 2.21, 95% CI = 1.69-2.88, P = 8.0 x 10^{-9}, and aHR for DFS = 1.58, 95% CI = 1.29-1.94, P = 1.0 x 10^{-5}). **Conclusion:** Prognostic index using 8 genetic polymorphisms may be useful for the prognostication of patients with surgically resected NSCLC. **Keywords:** Cancer-Related Gene polymorphism, Lung cancer survival

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-080 Combination of BMI and OLR1 in Prognosis Prediction of Patients with Squamous Non-Small Cell Lung Cancer Shanshan Jiang[1], Long Jiang[2], Jianchuan Xia[1] [1]*Sun Yat-Sen University Cancer Center, Guangzhou/China,* [2]*Department of Surgery, University of California, San Francisco (Ucsf), San Francisco/United States of America*

Background: Lung cancer, especially non-small cell lung cancer (NSCLC), represents enormous challenges in continuously achieving treatment improvements. Besides cancer, obesity is becoming more and more prevalent. Obesity is increasingly recognized as a major risk factor for several types of common cancers. Significant mechanisms overlap in the pathobiology of obesity and tumorigenesis. One of these mechanisms involves oxidized low density lipoprotein receptor 1 (OLR1), as link between obesity and cancer. Additionally, body mass index (BMI) has been widely used in exploiting the role of obesity on a series of diseases, including cancer. Significantly, squamous NSCLC revealed to be divergent clinical and molecular phenotypes compared with non-squamous NSCLC. **Methods:** Chart review was performed on 1286 consecutive patients who suffered from squamous NSCLC with between November 2004 and March 2008. 131 of the 1286 patients were enrolled in the final analysis. These 131 patients were randomly assigned (2:1) centrally by computer into training group (n=87) and validation group (n=44). BMI was calculated as follow: BMI (kg/m2) = weight (kg)/height (m2). Surgically resected or biopsied specimens were fixed in formalin and embedded in paraffin for routine histopathological diagnosis and immunohistochemical analysis. Then, PFS was defined as the time from the first documentation to the time of tumor progression or death. The total OLR1 immunostaining score was calculated as the sum of the positively stained tumor cells and staining intensity. OLR1 immunostaining score and BMI were assessed by Fisher's linear discriminant analysis to discriminate if progression-free survival (PFS) would exceeding 2 years. **Results:** The mean follow-up for survivors as of December 2014 was 47.23 months. Mean PFS was 724 days and the overall 1-, 2- and 3-year PFS rates were 87.8%, 47.3% and 39.7%, respectively. OLR1 expressed on tumor cells. There was no significant difference between the training (n=87) and validation (n=44) cohorts (P > 0.1). The clinical classifying model was described by the following equation: Y = -5.811 + 1.285 ×OLR1 immunostaining score + 0.152 ×BMI (eigenvalue 1.272, canonical correlation 0.748, P < 0.001). Group centroids for PFS <= 2 years and PFS > 2 years were 0.914 and - 1.359, respectively. Next, a cut score halfway between the two centroids was determined: cut score= (–1.359 + 0.914)/2 = -0.2225. For the training set of 87 leave-one-out-cross-validated cases, 49 of 52 PFS > 2 years (94.2% sensitivity) and 30 of 35 PFS <= 2 years (85.7% specificity) were correctly classified with an overall accuracy of 90.8% (79 of 87) and an area under the curve (AUC) of 0.938. In the validation set, survival prediction for 40 of the 44 patients (90.9%) with an AUC of 0.979was achieved. **Conclusion:** The analysis of combination of BMI and OLR1 could effectively and reproducibly classify patients with squamous NCSLC according to their PFS. Further prospective validation in larger independent cohorts of patients with similar or different regimens is warranted to fully assess its predictive power. However, the combinational model offers a novel tool for survival prediction and could provide a framework for future individualized therapy in patients with squamous NCSLC. **Keywords:** Squamous non-small cell lung cancer, Oxidized low density lipoprotein receptor 1, Body mass index, Prediction model

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-081 Molecular Evidence of Viral DNA in Non-Small Cell Lung Cancer (NSCLC) and Normal Lung Lary A. Robinson[1], Crystal J. Jaing[2], Anna R. Giuliano[3], Christine M. Pierce Campbell[3], Sean J. Yoder[4], Jamie K. Teer[5], Scott J. Antonia[1]
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Background: Although 20% of human cancers are caused by infections, only suspicion exists for a microbial cause of lung cancer. This study investigated potential infectious agents in the etiology of non-small cell lung cancer (NSCLC) in both frozen tumor of the major cell types and non-neoplastic lung using several molecular methods. **Methods:** Nucleic acids were extracted from 30 frozen NSCLC [10 squamous cell (SCC), 10 adenocarcinomas (ADC), 10 bronchioloalveolar (BAC)] and 10 non-neoplastic lung tissue specimens. All specimens were screened for microbial DNA on a pan-microbial detection array containing 135,000 DNA probes and controls to detect all sequenced viral and bacterial pathogen species. Additionally, SCC specimens were evaluated by PCR for the presence of 27 subtypes of human papillomavirus (HPV) and an independent panel of 17 known or suspected oncoviruses. **Results:** RESULTS: Using the pan-microbial microarray, several species of retroviral DNA were observed in 100% of SCC, 60% of ADC, and 10% of BAC (Table 1). Among the SCC specimens, HPV DNA was found in 60%, with 30% containing one or more high-risk HPV types, but the oncovirus panel was negative. No consistent viral DNA was detected in non-neoplastic lung specimens by the pan-microbial microarray.

Lung cancer cell type	HPV (human papillo-mavirus, type 57)	HBV (hepatitis B virus)	HTLV-2 (human T- lym-photropic virus 2), a Delta-ret-rovirus	Bovine leukemia virus (a Delta-ret-rovirus, similar to HTLV-1)	Y53 Sarcoma virus (an Alpha-ret-rovirus)	STLV-1, 2, or 6 (simian T-cell leukemia viruses, Delta-ret-roviruses)
Squa-mous cell ca. n=10	6 (60%)	9 (90%)	7 (70%)	8 (80%)	0	8 (80%)
Adeno-ca. n=10	1 (10%)	2 (20%)	0	0	6 (60%)	1 (10%)
Bronchi-oloalve-olar ca. n=10	0	0	0	0	1 (10%)	0
Normal lung, n=10	0	0	0	0	0	0

Table 1. Viral DNA Found in Human Lung Cancer Specimens: Pan-Microbial Array

Results Conclusion: High-risk HPV types were detected in many squamous cell lung cancers and, retroviral DNA was found in the majority of NSCLC but not in non-neoplastic lung. Of the 24 naturally-occurring animal cancers with a known etiology including lung adenocarcinoma in sheep, *all* are induced by retroviruses. Results from this initial discovery trial encourage further study of the viral contribution to human lung oncogenesis. **Keywords:** lung cancer, virus, DNA, carcinogenesis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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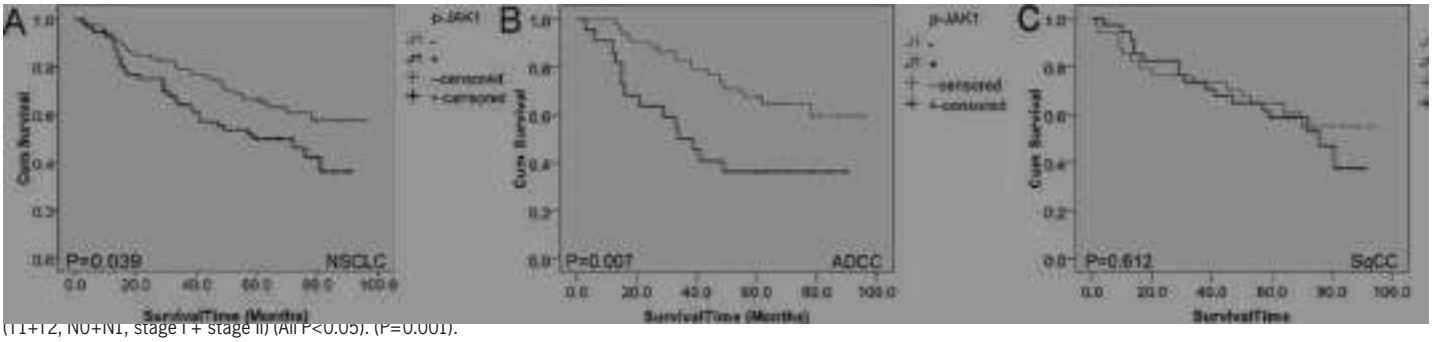
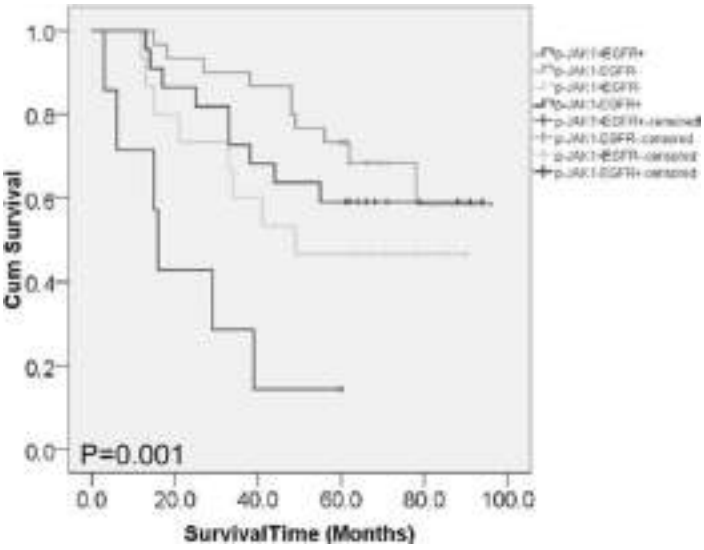
P3.04-082 Activation of JAK1 Confers Poor Prognosis in Chinese Patients with Lung Adenocarcinoma Dan Liu[1], Yi Huang[2], Weimin Li[1] [1]*Respiratory Medicine Department, West China Hospital of Sichuan University, Chengdu/China,* [2]*Clinical Laboratory Department, Sichuan Academy of Medical Sciences and Sichuan Provincial People'S Hospital, Chengdu/China*

Background: Janus kinase 1 (JAK1) has been reported to activate the JAK/STAT cascade in non-small cell lung cancers (NSCLC), among which most lung adenocarcinoma (ADCC) is associated with somatic epidermal growth factor receptor (EGFR) tyrosine kinase mutations. STAT3 is considered to be one of both JAK1 and EGFR downstream pathways promoting oncogenesis. However, the association between JAK1 activation, EGFR mutations and their prognostic value on NSCLC remains unclear. This study explored relations between the activated form, p-JAK1 and prognosis in patients with NSCLC and EGFR mutations status with ADCC subjects. **Methods:** a cohort of 142 resected primary NSCLC cases including 74 ADCC and 68 squamous carcinoma (SqCC) were collected and analyzed, p-JAK1 expression was determined by immunohistolchemical (IHC) assay. EGFR FISH status was analyzed in 74 ADCC subjects. The prognostic significances of p-JAK1 and EGFR expression status were evaluated with univariate and multivariate survival analysis. **Results:** Compared with normal lung tissues, p-JAK1 expression level significantly increased in NSCLC (P=0.000). Positive p-JAK1 expression indicated poor prognosis in NSCLC, especially in early stage subjects



(T1+T2, N0+N1, stage I + stage II) (All P<0.05). (P=0.001).

p-JAK1 is an independent predictor for poor prognosis (P=0.022). Further analysis showed that significance existed only in ADCC cases but not in SqCC. Survival time for p-JAK1(+)/EGFR(+) subjects was drastically shortened than the other 3 combinations



Conclusion: Our results provided clinical evidence that activation of JAK1 is an independent prognostic factor in early stage NSCLC, especially in ADCC. EGFR and p-JAK1 combination could be a new target for selecting individual therapy strategies and predicting therapeutic effect for NSCLC. **Keywords:** NSCLC, JAK1, EGFR, Prognosis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-083 FGFR1, 2 and 3 Expression in Early Stage Non-Small-Cell Lung Cancer Willemijn Engelsman-Theelen[1], Michel V.D. Heuvel[1], Stefan Willems[2], Lorenza Mittempergher[3], Astrid J. Bosma[3], Dennis D. Peters[4], Hans J. Blaauwgeers[5], Eva J. Japenga[6], Carel J. Van Noesel[7], Rene Bernards[3] [1]*Thoracic Oncology, NKI-AVL, Amsterdam/Netherlands,* [2]*Pathology, Umcu, Utrecht/Netherlands,* [3]*Division of Molecular Carcinogenesis, NKI-AVL, Amsterdam/Netherlands,* [4]*Molecular Pathology, NKI-AVL, Amsterdam/Netherlands,* [5]*Pathology, Olvg, Amsterdam/Netherlands,* [6]*Pulmonology, Olvg, Amsterdam/Netherlands,* [7]*Pathology, Academic Medical Center, Amsterdam/Netherlands*

Background: The aim of this study was to identify the protein expression levels of Fibroblast Growth Factor Receptors (FGFR) 1, 2 and 3 in early-stage non-small-cell lung carcinoma (NSCLC). Additionally, we performed a screen to define the frequency of FGFR3-TACC3 translocation and FGFR3 amplification. **Methods:** Archived tissue from 653 NSCLC samples (adenocarcinoma (AC), squamous cell carcinoma (SCC) and large cell carcinoma (LCC)) was analyzed with immunohistochemistry (IHC) for expression of FGFR1, 2 and 3. Expression levels of FGFR1, 2 and 3 were then correlated with clinicopathological features. The presence of FGFR3-TACC3 translocation was detected with RT-PCR and FGFR3 amplification was detected with FISH. **Results:** High protein expression of FGFR1, 2 and 3 was shown in 65 (10.5%), 78 (12.9%) and 20 (3.2%) of NSCLC tumor samples, respectively. Expression of FGFR1 was associated with light smoking ($p = 0.007$), AC ($p < 0.000$) and worse overall survival ($p < 0.04$). Expression of FGFR2 was associated with female sex ($p < 0.001$), younger age ($p = 0.01$) and AC ($p < 0.000$). Expression of FGFR3 was associated with male sex ($p = 0.047$), older patients ($p = 0.01$) and SCC ($p < 0.000$). FGFR3-TACC3 fusion was shown in 2.8% (6/210). In 45 FGFR3 IHC positive samples, two samples were FGFR3 amplified (4.4%) and one showed gain (2.2%). **Conclusion:** We show that FGFR1, 2 and 3 proteins are expressed in a significant number of NSCLC and identify some of the underlying molecular mechanisms. FGFR1 (but not FGFR2 and 3) protein overexpression is correlated with significant worse overall survival. FGFR1, 2 and 3 protein overexpression may become a new target of treatment in patients with NSCLC. **Keywords:** FGFR3-TACC3, FGFR, NSCLC, IHC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-084 Analytical Validation of a Proliferation-Based Molecular Signature Used as a Prognostic Marker in Early Stage Lung Adenocarcinoma M Bryan Warf[1], Placede G. Fosso[1], Elisha Hughes[1], Michael Perry[1], Krystal Brown[2], Julia E. Reid[1], Kathryn A. Kolquist[2], Susanne Wagner[1], Alexander Gutin[1], Benjamin Roa[1] [1]*Myriad Genetics, Inc., Salt Lake City/UT/United States of America,* [2]*Myriad Genetic Laboratories, Inc., Salt Lake City/UT/United States of America*

Background: We have developed a gene expression signature that provides prognostic information for patients with early stage lung adenocarcinoma that would benefit from adjuvant chemotherapy. This signature uses quantitative reverse transcription PCR to measure RNA expression of 31 cell-cycle progression (CCP) genes normalized to 15 housekeeping genes to provide a quantitative CCP score. The signature can identify aggressive early stage tumors that might be suitable for post-surgical therapy. The aim of these studies was to validate the analytical performance of the CCP gene signature. **Methods:** The analytical performance of the CCP gene signature was evaluated using formalin-fixed, paraffin-embedded lung resections by assessing parameters such as precision, dynamic range, and RNA input requirements. **Results:** The signature had a standard deviation (SD) of 0.06 score units, which is 1% of the clinical range of scores. The dynamic range of CCP scores in this signature was from -13 and 14 score units. The average amplicon efficiencies for target and housekeeper genes were comparable at 107% and 105%, respectively. All but one amplicon had a SD <0.5 CT. The gene signature reproducibly generated a consistent CCP score with RNA input concentrations between 0.12 and 62.5 ng/μL, which is considerably larger than the concentration ranges used for clinical testing (2–40 ng/μL). **Conclusion:** These studies demonstrate that the gene signature is robust and reproducible, making it suitable for use in a clinical setting. **Keywords:** Gene Expression, Cell-Cycle Progression, quantitative RT-PCR, Early Stage Lung Adenocarcinoma

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-085 Anti-Glycan Antibody Profiling in De-Novo Stage IV Non-Small Cell Lung Cancer: A Pilot Study Nagashree Seetharamu[1], Marko Vuskovic[2], Abraham Chachoua[3], Geraldine Brusca-Augello[4], Anna-Maria Barbuti[5], Jennifer E. Thomson[5], Ingrid Gills[5], Jordan Preiss[5], Sasha Joseph[3], Hilary Ma[3], William N. Rom[6], Margaret E. Huflejt[5] [1]*Medical Oncology, Hofstra Northshore-Lij School of Medicine, New Hyde Park/NY/United States of America,* [2]*Department of Computer Science, San Diego State University, San Diego/CA/United States of America,* [3]*Department of Medical Oncology, New York University Langone Medical Center, New York/United States of America,* [4]*Department of Radiology, New York University Langone Medical Center, New York/NY/United States of America,* [5]*Department of Cardiothoracic Surgery, New York University Langone Medical Center, New York/NY/United States of America,* [6]*Division of Pulmonary Medicine, New York University School of Medicine, New York/NY/United States of America*

Background: NSCLC is a heterogeneous disease with marked molecular and genomic variability that usually presents in advanced stage. Aberrant glycosylation occurs early during malignant transformation producing tumor-associated carbohydrate antigens (TACAs). Immune response to TACAs can be evaluated by immunoprofiling serum anti-glycan antibodies (AGAs) using printed glycan arrays (PGA), a new biomarker-discovery platform. Control and stage I NSCLC immunoprofiles were evaluated in a parallel study involving 70 subjects with high risk for developing lung cancer enrolled in low-dose CT lung cancer screening trial, 20 of who subsequently developed stage I NSCLC and a putative signature for early stage NSCLC has been obtained. The objective of this study was to obtain a putative signature of *de-novo* stage IV NSCLC patients using serum AGA immunoprofiles. **Methods:** 18 patients were enrolled in this prospective study. Data collected included demographics, tumor histology, EGFR mutational status, and cancer treatment details. Blood sample was collected at each visit. Response was assessed after every two cycles of first-line chemotherapy regimen by a radiologist using RECIST 1.1 and the best overall response and time-to-progression (TTP) were recorded. Patients were dichotomized as "good" or "poor" responders by median TTP. AGAs were immunoprofiled in 30 microliters of serum using PGA with 382 glycans. The raw PGA data were screened to remove glycans with critically low signal intensities, low Intra-array Correlation Coefficient (ICC) and high coefficient of variation (CV) of on-slide replicates. The raw data were normalized with intra-slide linear normalization, and log-transformed. The putative glycan signature was obtained by our novel Compound ImmunoRuler (CIR) algorithm based on bootstrap aggregation of multiple signatures derived from correlation-

adjusted Wilcoxon ranking using projections based on multivariate logistic regression. The training of CIR was performed on the baseline immunoprofiles of *de novo* stage IV samples with control immunoprofiles from the screening trial. **Results:** Study population included 11 males and 7 females. Mean age was 62 years (range 47-80). 15 patients (83%) had adenocarcinoma, two squamous, and one poorly differentiated. Two had EGFR mutation. Most common regimen was platinum/pemetrexed (n=14) followed by platinum/gemcitabine (n=2) and erlotinib (n=2). One patient had a complete response (CR); 6 PR and 4 had stable disease while 7 progressed. The median TTP was 140 days (41-387). For PGA data analyses, 278 glycans with ICC>80% were used for downstream analysis which delivered 3 glycans-based putative signature of Stage IV *de novo* NSCLC with AUC value 0.956; *specificity* 86%, and *sensitivity* 88.9%. Glycans in signatures of stage I and *de-novo* stage IV NSCLC were distinctly different. When immunoprofiles of stage IV NSCLC were projected on stage I ImmunoRuler, 13 out of 18 (72%) stage IV patients were accurately recognized as malignant. AGA binding to 4 glycans was significantly different between the sub-groups of "poor" vs. "good" responders. **Conclusion:** Uniquely different serum AGA-signatures of early stage and *de novo* stage IV lung cancer may provide basis for minimally-invasive test for early detection of risk for these malignancies and for better understanding their underlying pathologies. Further study in a larger population should help validate these findings. **Keywords:** non-small cell lung cancer, anti-glycan antibody profiling, ImmunoRuler

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-086 REQUITE: Validating Predictive Models and Biomarkers of RT Toxicity to Reduce Side Effects and Improve QOL Dirk De Ruysscher[1], David Azria[2], Jenny Chang-Claude[3], Susan Davidson[4], Alison Dunning[5], Philippe Lambin[6], Barry Rosenstein[7], Chris Talbot[8], Hubert Thierens[9], Riccardo Valdagni[10], Ana Vega[11], Catharine West[12] [1]*Experimental Radiation Oncology, Ku Leuven, Leuven/Belgium,* [2]*Radiation Oncology, University of Montpellier, Montpellier/France,* [3]*Radiation Oncology, 3German Cancer Research Centre (Dkfz), Heidelberg/Germany,* [4]*The Christie Hospital NHS Trust, Manchester/United Kingdom,* [5]*University of Cambridge, Cambridge/United Kingdom,* [6]*Department of Radiation Oncology (Maastro), Grow-School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht/Netherlands,* [7]*7Mount Sinai School of Medicine, New York, New York/AL/United States of America,* [8]*University of Leicester, Leicester/United Kingdom,* [9]*Universiteit Gent, Gent/Belgium,* [10]*Fondazione Irccs Istituto Nazionale Dei Tumori, Milano/Italy,* [11]*Fundación Pública Galega Medicina Xenómica, Santiago de Compostela/Spain,* [12]*University of Manchester, Manchester/United Kingdom*

Background: Recently the first replicated genetic associations for radiotherapy-induced adverse reactions were reported. These should improve the power of toxicity prediction models, opening the way to an optimised radiotherapy delivery and interventions to alleviate the side effects. The European Union funded REQUITE consortium aims to validate known predictors of adverse reactions and to develop statistical models resulting in clinically useful models. The focus of the project is on breast, prostate and lung cancer. As the barrier to clinical impact is the lack of validated statistical models incorporating genetic predictors, and the barrier to validation is the lack of standardised data collection, the main objectives of the REQUITE project are the following:

- Perform a multi-centre cohort study collecting blood samples, epidemiology and treatment data, longitudinal side effect and quality of life (QOL) data (before and after treatment: years 1 and 2 for breast and prostate cancer; with additional 3 and 6 month timepoints for lung cancer).
- Produce a centralized database and biobank of DNA for 5300 patients.
- Validate published biomarkers of radiosensitivity.
- Validate clinical predictors of radiotherapy toxicity in breast, prostate and lung cancer and incorporate biomarker data.
- Design interventional trials to reduce long-term side effects.
- Provide a resource for dissemination and exploitation to the radiotherapy community.

Methods: The central activity of the project is a multi-centre, observational study organized through WP2. Enrolment will proceed for two years in nine centres (eight in Europe and one in the United States), with another two years of follow-up. The primary endpoints are change in breast appearance at two years (breast), rectal bleeding at two years (prostate) and pneumonitis at 6 months (lung). An integrated study database is designed. Blood samples are collected before radiotherapy. Tracking, biobanking and DNA extraction is handled in WP3. Validation of biomarkers (genetic markers and apoptosis assays) as predictive factors is carried out in WP4. Some clinical factors have suggested predictive value for radiotherapy side effects, but there is no consensus. In WP5 these will be validated in existing cohorts. Finally, in WP6, predictive models will be used to design clinical interventional trials and produce protocols that seek to lower radiotherapy side effects, in those individuals at high risk of developing them, without affecting tumour control. Patient advocates will play an essential role in this effort. **Results:** Standardised data collection forms were generated. Questionnaires for collecting patient reported toxicity according to Common Toxicity Criteria for Adverse Events were developed in different languages. These forms and questionnaires are available at http://www.requite.eu/. A centralised database for electronic data capture and storage was developed. Ethical approval for the observational study was obtained in all centres. More than 1300 patients were enrolled in the REQUITE study to this date. **Conclusion:** Centralised collection of standardised data and biobanking is practical for lung cancer patients undergoing radiotherapy in routine clinical practice in a multi-centre, multi-national setting. **Keywords:** radiotherapy toxicity, biomarkers, predictive models, multi-centre cohort study

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-087 NUT Expression in Surgically Treated Small Cell, Non-Small Cell and Carcinoid Tumors of the Lung Marius Lund-Iversen[1], Krystyna K. Groholt[1], Odd Terje Brustugun[2], Elin Borgen[1] [1]*Pathology, Oslo University Hospital, Radiumhospitalet, Oslo/Norway,* [2]*Oncology, Oslo University Hosital,The Norwegian Radium Hospital, Oslo/Norwa, Oslo/Norway*

Background: NUT midline carcinoma (NMT) is a rare, highly aggressive carcinoma defined by rearrangement of nuclear protein gene in testis (NUT) on chromosome 15; in most cases to bromodomain-containing protein 4 (BRD4) on chromosome 19. Although the majority of cases occur in midline structures above the diaphragm there are reports regarding cases in non-midline solid organs. There is an increased need to identify tumors with targetable mutations, and NUT-BRD4 translocations are potential goals for bromodomain and extra terminal (BET) inhibitors. The putative incidence among lung carcinomas low, but the true incidence is unknown. **Methods:** In a tissue micro array (TMA) set we investigated samples from 483 surgically resected lung tumors for the expression of the NUT protein using immunohistochemistry with monoclonal anti-NUT antibody (clone C52B1, Cell Signaling). 278 were adenocarcinomas, 140 squamous cell carcinomas, 30 large cell carcinomas, 7 small cell carcinoma, 18 carcinoid tumours and 10 carcinoma not otherwise specified. The median age were 66.3 [33.9 – 87.0], 247 were males and 236 were females. Testis and two previously confirmed NMT served as positive controls. Lymph nodes and normal lung tissue served as negative controls. **Results:** The positive controls had distinct nuclear staining without any unspecific background. The negative controls and all tumours were completely negative for the anti-NUT staining. **Conclusion:** We did not find any NUT expression in the investigated set of tumors. The golden standard for showing NUT rearrangement are fluorescence in situ hybridization (FISH), but the sensitivity and specificity for immunohistochemistry are high, 87% and 100% respectively (Haack et al. Am J Surg Pathol 2010). Although we cannot exclude a minority to be false negative, NUT translocations does not seem to be a relevant differential diagnostic issue in unselected early stage lung carcinomas. **Keywords:** Pathology, NUT midline carcinoma, Predictive testing, Diagnostics

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-088 Matrix Proteoglycans Gene Expression Predicts Lung Cancer Patients Outcome Maristela P. Rangel[1], Tabatha Prieto[2], Eloisa R. Olivieri[3], Dirce M. Carraro[3], Vera L. Capelozzi[4] [1]*Pathology, Faculty of Medicine; University of Sao Paulo, São Paulo/Brazil,* [2]*Pathology, Faculty of Medicine, University of Sao Paulo, São Paulo/Brazil,* [3]*Pathology, Ac Camargo Cancer Center, São Paulo/Brazil,* [4]*Pathology, Faculdade de Medicina Da Usp, São Paulo/Brazil*

Background: The relationship between the extracellular matrix (ECM) components and cancer cells have an important role on cancer development and progression. Between the most important molecules present on the ECM are the glycosaminoglycans(GAGs) and their respective proteoglycans (PGs). Studies have reported that they have different behaviours when in the presence of malignant tissues.The aim of this study was to analyse PGs gene expression in normal and tumoral areas of patients with lung cancer (LC) and to explore its association with GAGs concentration. **Methods:** Eighty-seven lung specimens were evaluated. Biglycan, glypican, perlecan, syndecan and versican gene expression were analysed by qRT-PCR and sulfated GAG chains(heparan, dermatan and chondroitin sulfate - HS, DS and CS)were obtained after incubation with a proteolytic enzyme.GAGs were precipitated with ethanol and the pellet was centrifugated, dried and dissolved in DNAse(5 l/mg).The different types of sulfated GAGs and their concentration in the lung samples were identified after gel electrophoresis in diaminopropane buffer. Statistical analyses included ANOVA, Paired-samples T Test, Spearman correlation, and logistic regression. **Results:** A significant increase of biglycan was found in tumor tissue compared to normal (52.30 ± 21.2 vs 11.28 ± 3.77; p=0.04). A significant association was found between biglycan vs glypican (R= 0.64; P<0.01), biglycan vs perlecan (R=0.70; P<0.01) and biglycan vs versican (R=0.68; P<0.01). Univariate analysis demonstrated that high expression of tumoral biglycan significantly related to squamous cell carcinoma histologic type (P=0.02) and death (P=0.03). Equally significant was the association between high syndecan expression, tobacco history (P<0.01) and tumoral recurrence (P=0.04). Logistic regression analysis controlled for age, gender, Tstage, Nstage, histologic types and proteoglycans expression showed that higher biglycan expression was and independent predictor of death [OR= 1.44 (0.88-2.36)]. Those with higher relative expression of biglycan had a high risk for death. In addition, we found that biglycan and glypican gene expression related significantly to tumoral heparan sulphate concentration in tumoral tissue (R=0.38; P=0.04 and R=0.41; P=0.03). **Conclusion:** Different expression of PGs in lung cancer samples, its relationship with histologic types and death suggest a possible role of these PGs in this malignancy, but more importantly provide a potential biomolecular marker to predict outcome.The correlation between the histologic types and the expression of biglycan provide a possible role of this PG on the development of tumor agressiveness considering that one of its functions is to bind itself to growth factors and regulate their action. Moreover, the relationship between heparan sulphate concentration, biglycan and glypican gene expression might indicate what sort of PGs are produced by tumoral tissue considering that heparan sulphate is the GAG chain in these PGs. Further studies are needed to determine whether or not these PGs gene expression are able to be predict prognosis and tumoral aggressiveness. **Keywords:** proteoglycans, lung cancer outcome, extracellular matrix, biglycan

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-089 Prospective Use of Prognostic Molecular Assay Identifies Patients at Risk for Recurrence and Changes Clinical Management in Early-Stage NSCLC

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Background: Adjuvant chemotherapy recommendations depend on identification of early-stage non-small-cell lung cancer (NSCLC) patients at high-risk of recurrence. Current National Comprehensive Cancer Network (NCCN) guidelines use certain clinicopathologic features to make this recommendation for stage Ib-IIa patients. An internationally validated, 14-gene expression assay has been shown retrospectively to better stratify mortality risk in non-squamous NSCLC than conventional staging. **Methods:** Following up on a previously reported cohort of 52 patients, prospective molecular risk-stratification by the 14-gene test was performed in 66 patients with a mean follow up of 20.7 ±14.1 months. Disease-free survival and lung cancer mortality rates were compared between high- and low-risk patients by both molecular risk-stratification and NCCN "high-risk" characteristics. **Results:** Patients with low-, intermediate-, and high-risk based on molecular testing had recurrence rates of 4%, 8%, and 28% (p=.031, Fisher's exact test) and lung cancer mortalities of 0%, 0%, and 16% (p=.039), respectively. Molecular high-risk was associated with shorter disease-free survival (p=.043, Kaplan-Meier log-rank). Molecular risk assessment was discordant from NCCN "high-risk" features in 15 of 25 stage Ib-IIa patients (60%). NCCN criteria failed to significantly predict either recurrence or mortality with recurrence rates of 8% and 23% (p=.077, Fisher's exact test) and lung cancer related mortality of 3% and 12% (p=.165) among patients with NCCN low- and high-risk features respectively. Molecular high-risk scores changed adjuvant chemotherapy recommendations in 3 of 10 (30%) patients who otherwise did not meet NCCN criteria for adjuvant chemotherapy. **Conclusion:** This study demonstrates that prospective application of a 14-gene prognostic assay significantly predicts differences in disease-free survival. This prognostic information differs from NCCN high-risk clinicopathologic features and has clinical utility in better informing adjuvant chemotherapy recommendations.
Keywords: Recurrence predictors, Prognostic molecular assay, adjuvant chemotherapy, Genetic signature

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-090 Association of Nuclear Expression of RAR Beta and YY1 with Prognosis in Advance Non-Small Cell Lung Cancer

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Background: Lung cancer is the most common cause of cancer-related death worldwide and it is responsible for approximately 1.4 million deceases per year. In Mexico, the NSCLC cause more than 6,697 deaths annually. Approximately, 85% of all lung cancer corresponds to NSCLC and unfortunately at diagnosis 60% patients have advanced unresectable disease with a very poor prognosis. The standard of care treatment for advanced disease is platinum-based doublet chemotherapy, this present an objective response rates of 19% to 37% with a 7 to 10 months of median survival. The identification of molecular alteration in NSCLC has transformed the clinical management of this disease, increasing the survival and improves the response in patients. The genetic alterations affect a common group of oncogenic signaling pathways such as retinoid receptors (RR) and yin and yang 1 (YY1) resulting in lung cancer development and progression. The nuclear RR may play a critical role in the process of lung carcinogenesis. In NSCLC, reduction in the levels of mRNA RARβ and RARα have associated with lack of response to treatment and progression. As the same manner, YY1 is a key regulator of multiple signaling pathways involved in differentiation, replication, cellular proliferation and oncogenic transformation. The role of YY1 in development of cancer depend upon the context in which it binds. It could activate a variety of oncoproteins attenuates the stability of the tumor suppressor such as p53 or mediates the activation of genes with tumor-suppressive functions. The aim of this study was to analyze the expression of RARα, RARβ and YY1 and its relationship with overall survival in patients with advanced NSCLC. **Methods:** This was an observational study, where patients with advanced NSCLC at the National Cancer Institute of Mexico City from July 2005 to December 2011 were enrolled. The expression of RARα, RARβ and YY1, was determinate with immunohistochemistry by mean digital pathology and analyzed by Image-Pro Plus. **Results:** Eighty-five patients were included for the analysis. The mean and standard deviation of the nuclei expression of RARα, RARβ and YY1 were (106.7±97), (14±13) and (13±12). Patients with a high RARβ total expression have a better ECOG 0-1 vs 2-3 performance status (92.9 vs 74.4%). Non-smokers had a high nuclei expression of YY1 (61.9 vs <40.5%) and better median OS 15.6 (4.5-26.7 months). Nuclei expression of RAR-β was associated with the nuclei expression of YY-1 (R2 = 0.28; p-Value <0.0001). Also, the higher nuclei expression of RARβ was associated with a higher OS (27.5 vs 8.7 months) in both, the univariate analysis and multivariate analysis (p=0.016; p=0.037). **Conclusion:** The nuclei expression of both RARβ and YY1, could be used as biomarkers to NSCLC prognosis, specifically YY1 predicted a better response in patient that had never smoke.
Keywords: RETINOIC ACID RECEPTOR BETA, YING-YANG 1, ADVANCE NON-SMALL CELL LUNG CANCER, Biomarkers

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P3.04-091 Expression of Cytoplasmic ECT2 as a New Prognostic Marker for Early-Stage Lung Adenocarcinoma

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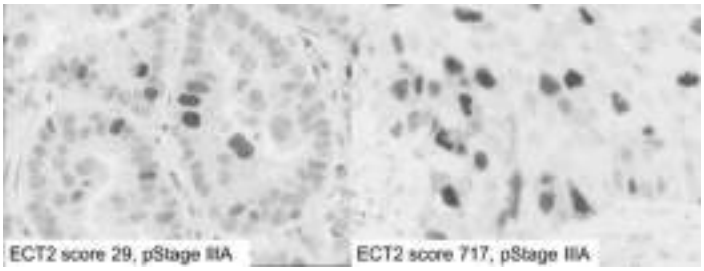
Background: We have examined genetic abnormalities in early-stage lung adenocarcinoma (LAd) using array-comparative genomic hybridization (array-CGH) and found that ECT2 amplification and overexpression can be a new prognostic marker (Cancer Science, 2014). In normal cells, ECT2 is localized in the nucleus, and its function is associated with cytokinesis. In cancer cells, however, ECT2 is thought to exist in the cytoplasm as well as the nucleus. In the cytoplasm, ECT2 is reported to bind to PKCi-Par6a and activate the Rac1 and MAPK pathway. Therefore, cytoplasmic ECT2 is thought to be associated with tumor growth and invasion. In the present study, we examined the clinicopathological implication of cytoplasmic ECT2 in terms of patient outcome, and also the biological significance of cytoplasmic ECT2 using lung adenocarcinoma cell lines. **Methods:** To examine the clinicopathological implication of cytoplasmic ECT2, 66 cases of various types of lung adenocarcinoma were examined using immunohistochemistry (IHC). Nine lung adenocarcinoma cell lines – A549, Calu-3, HCC827, LC-2/ad, NCI-H23, NCI-H1650, NCI-H1975, PC-9 and RERF-LC-KJ – were genetically examined for ECT2 amplification using FISH and for intracellular localization of ECT2 by Western blotting. **Results:** Overexpression of ECT2 in the nucleus was closely associated with the MIB-1 index (r=0.76) and was a strong prognostic factor of lung adenocarcinoma (OS; *P*=0.0096, DFS; *P*=0.019). On the other hand, cytoplasmic ECT2 was also associated with patient outcome (OS; *P*=0.02, DFS; *P*=0.023). Two of the nine lung adenocarcinoma cell lines, Calu-3 and A549, expressed ECT2 in the cytoplasm as well as the nucleus.



Conclusion: Cytoplasmic ECT2 is a prognostic factor of lung adenocarcinoma, and some lung adenocarcinoma cell lines show localization of ECT2 in the cytoplasm as well as the nucleus.

Keywords: Cytoplasmic ECT2, lung adenocarcinoma, prognostic marker, Immunohistochemistry

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-092 HNF4α Is a Marker for Invasive Mucinous Adenocarcinoma (IMA) and a Prognostic Factor in Stage I Lung Adenocarcinoma (LADC)

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Background: According to the 2015 WHO classification, invasive LADC with prominent apical intra-cytoplasmic mucin and small basally oriented nuclei, formerly referred to as mucinous bronchioloalveolar carcinoma, is classified as IMA. Hepatocyte nuclear factor 4 alpha (HNF4α) is a recently recognized marker for IMA although it is also infrequently positive for other subtypes of LADC. However, the prognostic significance of HNF4α is not known. We investigated the frequency of HNF4α expression in IMA as well as non-IMA subtypes, and the prognostic significance of HNF4α in Stage I LADC. **Methods:** Slides from patients with therapy-naive, surgically resected solitary stage I LADC (1995-2009) were subtyped according to the 2015 WHO classification. Tissue microarrays were constructed from each tumor (n=793), and stained for HNF4α. HNF4α expression intensity (0-3) and distribution (1, 1%-50%; 2, 51%-100%) were summed into a total score (0-5) and dichotomized as negative (score <2) or positive (score ≥2). Comparisons were made with TTF-1 expression. Recurrence-free probability (RFP) was estimated using the Kaplan-Meier method, and multivariate analyses were performed using the Cox proportional hazards model. **Results:** 32 cases were identified as IMA. Of all LADC, HNF4α was positive in 68 cases (9%) including72% (n = 23) of IMA, 6% (n = 45) of tumors with non-IMA subtypes (P < 0.001). Among non-IMA subtypes, HNF4α was positive in 6% of lepidic, 4% of papillary, 2% of micropapillary, 7% of solid, and 29% of colloid tumors. HNF4α was positive in 12% of *KRAS* mutant tumors while it was negative in all *EGFR* mutant tumors (P < 0.001). HNF4α was more frequently positive in TTF-1 negative tumors (40%) than TTF-1 positive tumors (5%; P < 0.001). The RFP for patients with HNF4α-positive tumors was significantly lower than that for patients with HNF4α-negative tumors (P = 0.002) in the entire cohort. This finding was confirmed in subgroup analysis of patients with non-IMA

subtypes (P = 0.009). In multivariate analysis, HNF4α was an independent prognostic factor for recurrence (HR=1.61, 95%CI =1.27-2.02, p<0.001). **Conclusion:**HNF4α expression was significantly associated with IMA histology, negative EGFR mutation status, and TTF-1 negativity. Furthermore HNF4α was also expressed infrequently in non-IMA subtypes, however in these patients it was a significant prognostic factor. **Keywords:** invasive mucinous adenocarcinoma, HNF4-alpha, lung adenocarcinoma, prognostic marker

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P3.04-093 Neutrophil/Lymphocyte Ratios Inversely Related to Weight Change, Overall Survival; ALI Inversely Related to OS in NSCLC Pts. Marta Batus[1], Jason Macklis[2], Mary Fidler[3], Sanjib Basu[4], Jeffrey A. Borgia[4], Mohammed Azeem[3], David Sher[3], Philip Bonomi[4] [1]*Hematology, Oncology and Cell Therapy, Rush University Medical Center, Chicago/AL/United States of America,* [2]*Rush University Medical Center, Chicago/AL/United States of America,* [3]*Rush University Medical Center, Chicago/United States of America,* [4]*Hematology, Oncology and Cell Therapy, Rush University Medical Center, Chicago/United States of America*

Background: A high neutrophil/lymphocyte ratio (NLR) at baseline and at follow-up is associated with shorter survival in cancer patients and may be a surrogate for ongoing inflammation which is implicated in promoting cancer cachexia and tumor progression. The objective of this study is to explore potential relationships between OS, serial weights, and serial NLRs and ALI (Advanced Lung cancer Inflammatory) index in advanced NSCLC patients receiving chemotherapy. **Methods:** 139 stage III/IV NSCLC pts were treated with first-line platinum doublets from June, 2011 to August, 2012. NLR and body weight were recorded at baseline, 6, and 12 weeks from initiation of therapy and correlated with OS. The association between NLR and OS was assessed using Cox PH analysis, and the association between NLR and weight change was assessed using a simple regression analysis. ALI index was defined as BMI (Body Mass Index) x (Albumin)/NLR. ALI was calculated at baseline, 6, and 12 weeks from initiation of therapy and correlated with OS for some pts. **Results:** 139 pts with median age 68, PS 0-1/2 = 83/17%, male/ female = 48%/52%. NLR at baseline median 3.6, range 0.1898 to 30.910; at 6wks median 3.11, range 0.2703 to 42.11; at 12wks median 3.52 range 0.2147 to 42.93. Increase in the NLR at baseline, 6, and 12 weeks were associated with a decrease in OS (baseline HR 1.06, p < 0.001; 6 wks HR 1.07, p = 0.001; 12wks HR 1.05, p < 0.001). The effect of NLR on hazard is multiplicative (i.e. a change of 5 in baseline NLR results in a HR of 1.065). Initial weight and NLR were negatively correlated (cor = -0.267, p = 0.001), and weight change and NLR were also negatively correlated at 12wks (cor = -0.371, p < 0.001; weight change -13.17kg to +16.61kg, median -0.5kg, mean -0.89kg). 96, 93 and 84 pts had ALI score available at baseline, 6wks, and 12 wks respectively. 38 pts with baseline ALI score <= 18 had significantly lower OS (median OS=9.63 mos) compared to 58 pts with ALI > 18 (median not reached, p = 0.001). 41 pts with 6 week ALI <= 18 had significantly lower OS (median OS=11.4 mos) compared to 52 pts with ALI > 18 (median not reached, p = 0.03). 30 pts with 12 week ALI <= 18 had significantly lower OS (median OS=9 mos) compared to 54 pts with ALI > 18 (median not reached, p < 0.001). **Conclusion:** High baseline and progressive increase in NLRs are associated with inferior OS and weight loss in advanced NSCLC patients. In addition to having prognostic significance, these observations suggest that studying molecular mediators of cachexia/inflammation and their relationships to tumor progression may identify new therapeutic targets in the large subset of NSCLC patients who have cancer cachexia. We also confirmed findings by Jafri at all 2013, that ALI score <=18 is associated with lower OS at any time before or during treatment. **Keywords:** NEUTROPHIL, inflammation, Cachexia, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-094 Hyperphosphorylation of Ribosomal Protein S6 Predicts Unfavorable Clinical Survival in Non-Small Cell Lung Cancer Bojiang Chen, Weimin Li *Department of Respiratory Medicine, China Hospital of Sichuan University, Chengdu/China*

Background: Ribosomal protein S6 (rpS6), a component of the 40S ribosomal subunit, is involved in multiple cellular bioactivities. However, its clinicopathological significance in non-small cell lung cancer (NSCLC) is poorly understood. **Methods:**Expressions of total rpS6 (t-rpS6) and phosphorylated rpS6 (Ser235/236, p-rpS6) were detected immunohistochemically in 316 NSCLC tissues and 82 adjacent controls, followed by statistical evaluation of the relationship between proteins expressions and patients' survivals to identify their prognostic values. Cytological experiments with overexpressing or silencing rpS6 by lentivirus in human bronchial epithelial (HBE) or NSCLC cell lines were performed to explore potential mechanisms by which rpS6 affects the clinical development of NSCLC. Additionally, RNA interference for Akt1, Akt2 and Akt3 were performed as well to investigate the upstream regulation of rpS6. **Results:** Positive rates of t-rpS6 and p-rpS6 were both significantly increased in NSCLC tissues, compared with controls (82.9% vs 62.2% for t-rpS6; 52.2% vs 22.0% for p-rpS6; both P < 0.001). However, only hyperphosphorylation of rpS6, expressed as either elevated p-rpS6 alone or the ratio of p-rpS6 to t-rpS6 (p-rpS6/t-rpS6) no less than 0.67, was greatly associated with the unfavorable survival of NSCLC patients, especially for cases at stage I (all P < 0.001). The independent adverse prognostic value of hyperphosphorylated rpS6 was confirmed by multivariate Cox regression analysis (hazard ratios for elevated p-rpS6 alone and p-rpS6/t-rpS6 no less than 0.67 were 2.403, 4.311 respectively, both P < 0.001). Overexpression or knockdown of rpS6, along with parallel alterations of p-rpS6, led to increased or decreased cells proliferations respectively, which were dependent on redistributions of cell cycles (all P < 0.05). Cells migration and invasion also changed with rpS6 interference (all P < 0.05). Furthermore, upstream overexpression or knockdown of Akt2, rather than Akt1 or Akt3, resulted in striking hyperphosphorylation or dephosphorylation of mTOR, p70S6K and rpS6 (all P < 0.05). These might be the underlying mechanisms in which rpS6 overactivation promotes the development of NSCLC. **Conclusion:** Hyperphosphorylation of rpS6, probably regulated by the Akt2/mTOR/p70S6K signaling pathway, is closely relevant to the progression of NSCLC and it might be served as a promising therapeutic target for NSCLC treatment. **Keywords:** non-small cell lung cancer (NSCLC), Hyperphosphorylation, survival, Ribosomal protein S6 (rpS6)

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P3.04-095 Intensity Expression of DOK2 as a Prognostic Marker in Patients with Advanced Stage of Lung Adenocarcinoma Huang-Chih Chang[1], Yung-Che Chen[1], Chang-Chun Hsiao[2], Meng-Chih Lin[1] [1]*Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine,, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung/Taiwan,* [2]*Graduate Institute of Clinical Medical Sciences,, Chang Gung University College of Medicine, Kaohsiung/Taiwan*

Background: DOK family is an adaptor proteins that function in feedback loops to modulate tyrosine kinase signaling, including epidermal growth factor receptor, c-Kit and platelet-derived growth factor receptor. Our previous study has shown that DOK2 was up-regulated in PBMC of NSCLC patients, and partially reversed after chemotherapy. We speculated that DOK2 levels in tumor tissue may be used to predict outcome of non-small cell lung cancer. The aim of this study is to determine the significance of DOK2 in advanced stage of lung adenocarcinoma. **Methods:** We retrospectively reviewed the data of 87 advanced stage of lung adenocarcinoma patients from Kaohsiung Chang Gung Memorial Hospital, Taiwan between Jan 2008 and Dec 2009. Tumor tissue was analyzed for DOK2 protein expressions detected via immunohistochemistry and specimens were classified into high or low DOK2 expression groups. Correlation with survival and clinicopathological parameters were undertaken. **Results:** DOK2 expression was confirmed in the advanced stage of lung adenocarcinoma tissue. Considerable differences in the protein expression were noted among the lung adenocarcinoma tissue. Patients were classified to high intensity DOK2 stained expression (n=53, 60.9%) or low intensity stained DOK2 expression (n=34, 39.1%), There were no significant correlation was found between DOK2 expression and clinicopathologic factor such as TNM stage, tumor size, performance status, comorbidity and treatment. Patients with low intensity DOK2 expression were significant and independent determinants of poor progressive free survival (9.5ms vs 4.3ms, P= 0.018) and overall survival (19.9ms vs 6.8ms, P= 0.013). **Conclusion:** Our study suggests the potential usefulness of DOK2 as a clinical marker for evaluating the advanced stage of lung adenocarcinoma progression and prognostic value. Prospective survey and mechanism studies are needed for further confirmation. **Keywords:** DOK2, non small cell lung cancer, biomarker

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P3.04-096 A Feasibility Pilot Study Testing Six DNA Methylation Markers to Improve Detection of Malignant Pleural Effusions in Lung Cancer Joshua A. Boys, Stephanie G. Worrell, Mihaela Campan, Victoria A. Scala, James M. Tatum, Jeffrey A. Hagen, Ite Laird-Offringa, Daniel S. Oh *Department of Surgery, Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles/CA/United States of America*

Background: Patients presenting with pleural effusion and suspected primary lung cancer raise suspicion for pleural metastasis. Accurate diagnosis is critical; metastatic pleural effusion indicates stage IV disease with significantly different treatment and prognosis. Currently diagnosis is obtained by cytology, however the mean sensitivity of cytology is only 60%. Lung cancer-specific DNA methylation markers may improve sensitivity. Here we determine whether six previously identified DNA methylation markers can detect malignancy in pleural effusions of lung cancer patients. **Methods:** Pleural effusions were collected from one small cell lung cancer (SCLC), 5 non-small cell lung cancer (NSCLC) and 3 patients with benign conditions not suspicious for cancer, presenting to USC Keck Hospital and Los Angeles County Hospital (June 2013 to March 2015). The 6 lung cancer patients underwent drainage and pleural fluid cytology. Samples were centrifuged (3000g, 10 minutes) to remove cellular material. DNA was extracted from 1 ml of pleural fluid and bisulfite converted. MethyLight was used to quantitate the methylation levels of the markers. The preliminary specificity and sensitivity were calculated. **Results:** Percent of methylated reference (PMR, a measure of methylation levels compared to enzymatically fully methylated DNA) is shown in Table 1. Markers LuCa-1 and LuCa-2 had 100% sensitivity and 100% specificity (Table 2). Two patients (5 and 6) had negative cytology but positive malignancy based on markers. Pathologic confirmation of malignant involvement of the pleura was obtained in both cases, one with a different cytology specimen and the other by thoracoscopic exploration.

Table 1 DNA Methylation Markers by Percentage of Methylated Reference

Patient	LuCA-1	LuCa-2	LuCa-3	LuCa-4	LuCa-5	LuCa-6	Cytology Result	Control Malignant
1	60%	22%	50%	30%	60%	55%	Malignant	Malignant
2	28%	20%	34%	10%	35%	25%	Malignant	Malignant
3	39%	15%	39%	5%	40%	9%	Malignant	Malignant
4	7%	11%	16%	3%	8%	26%	Malignant	Malignant
5	3%	8%	2%	7%	26%	18%	Benign	Malignant
6	4%	9%	2%	4%	9%	11%	Benign	Malignant
7	0%	0%	0%	0%	0%	2%	NA	Control
8	0%	0%	0%	2%	4%	13%	NA	Control
9	0%	0%	1%	1%	1%	0%	NA	Control

Table 2 DNA Methylation Marker Sensitivity & Specificity

Marker	Sensitivity	Specificity
LuCa-1	100%	100%
LuCa-2	100%	100%
LuCa-3	100%	67%
LuCa-4	100%	33%
LuCa-5	100%	33%
LuCa-6	100%	33%

Conclusion: This pilot study indicates that DNA methylation markers can detect lung cancer in pleural effusions, potentially with sensitivity and specificity that exceed routine cytology. Further analysis of these 6 markers, used separately or in combination as a multiplexed panel to detect pleural malignancy is warranted. **Keywords:** lung cancer, malignant pleural effusion, DNA methylation, Detection

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P3.04-097 Expression of GM2 Activator Protein as a Potential Biomarker for Lung Cancer Laddawan Pottprommanee[1], Kongsak Boonyapranai[2], Padchanee Sangthong[1], Busyamas Chewaskulyong[3], Shui-Tein Chen[4], Lalida Shank[5] [1]*Of Chemistry, Chiangmai University, Chiangmai/Thailand,* [2]*Department of Science, Nakornrathasima College, Nakornratchasima/Thailand,* [3]*Of Medicine, Chiang Mai University, Chiang Mai/ Thailand,* [4]*Department of Biological Chemistry, National Taiwan University, Taipei/ Taiwan,* [5]*Department of Chemistry, Chiangmai University, Chiangmai/Thailand*

Background: Lung cancer is a leading cause of cancer-related worldwide. Finding effective biomarkers for early diagnosis would be useful for potential curative treatment. GM2activator protein (GM2AP) is a glycoprotein acting as a cofactor for ganglioside GM2 degradation. GM2AP also associated with the changing levels of ganglioside which has role in tumor invasion, progression and metastases. This study aims to investigate and validate the potential of GM2AP as a lung cancer biomarker. **Methods:** The study was done from September 2011 to June 2013. Serum and urine samples were obtained from lung cancers patients and healthy volunteers from Thailand and Taiwan. The expression level of GM2AP was using two-dimensional gel electrophoresi (2-DE), Western blotting and enzyme linked immunosorbine ent assay (ELISA). This studly was approved by the local research ethics committee . Statistical analysis was performed using SPSS version 17.0. Paired samples t-test and one-way analysis of variance (ANOVA) were used to analyze in different groups. A confidential level of 95% ($P<0.05$) was consider statistically significant. **Results:** Thailand data There were total 48 lung cancer patients (male 33, female 15) and 44 healthy volunteers . The mean age of study cases and controlled group were 53.3 years (range 2-74) and 42.1 years (range 25-74) respectively. The mean of GM2AP level in lung cancer patiens was 1.60+/-1.21 ng/mL, whereas in healthy controls the levels was 0.21+/-0.14 ng/mLThe expression levels of urine and serum GM2AP were significantly increased when compared to those from healthy controls ($P<0.05$). The urine GM2AP level of lung cancer patients was 7.62+/-1.06 fold on the median. Moreover the urinary GM2AP level in the male patients (1.16+/-1.07 ng/ mL) was higher than in female patients (1.13 +/-1.05 ng/mL). According to histologic subtype, the urinary GM2AP level measured in patents with adenocarinoma, small cell carcinoma and sqaumous cell carcinoma were 1.25+/-1.12, 1.48+/-1.35 and 2.27+/- 2.20 ng.ml, respectively. From ROC curve of urinary GM2AP showed sensitivity of 90.91% and specificity of 91.67%.The expression levels of GM2AP of all patiens were included in the statistical analysis and significant correlation ($P<0.05$) was found with histology cancer types, whereas gender and pathological stage were not correlated. Taiwan data There were 133 lung cancer patients (male 60,female 73) with a mean age of 62 (range 30-81 years). The mean urinary GM2AP level in lung cancer patients was 1.46+/-1.55 ng/mL where as in controlled group was 0.18+/-0.19 ng/mL. There was a 8.03 +/- 1.36 fold increase of GM2AP level in urine and a 5.41+/-0.73 ng/mL. increase in the serum compared to the controlled group. From ROC curve provides 88.46% sensivity and 85.71% specificity in urine G2AP. The mean seum GM2AP level was 0.92+/- 0.27 and controlled group was 0.17+/-0.07 ng/mL. The ROC curve from serum G2AP provides 100% sensitivity and 82.71% specificity. No difference was shown in urinary or serum GM2AP levels when stratified by gender, smoking status , EGFR status or histology subtypes except for the pathology stage. **Conclusion:** Our data suggest that the GM2AP may be useflul as a biomarker for early diagnostic and prognostic in lung cancer. **Keywords:** GM2 activator protein, lung cancer, biomarker

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P3.04-098 Bis Expression in Patients with Surgically Resected Lung Cancer and Its Clinical Significance Chang Dong Yeo[1], Seung Joon Kim[2] [1]*Uijeongbu St. Mary'S Hospital, Uijeongbu/Korea,* [2]*Department of Internal Medicine, The Catholic University of Korea, Seoul/Korea*

Background: Bis, also known as BAG3, has been identified as a Bcl-2-interacting protein that enhances cellular anti-apoptotic activity. It is involved in cellular differentiation, angiogenesis, migration, and invasion in various tumors. The purpose of this study was to investigate the Bis expression pattern, and the clinical significance thereof, in patients with resected lung cancer. **Methods:** We studied 121 lung cancer patients who underwent curative surgical resection. Patient clinicopathological characteristics were reviewed retrospectively from medical records, including tumor recurrence and survival. The expression of Bis protein in lung cancer tissues was evaluated by immunohistochemical staining and was assessed using a four-tiered intensity score system (negative, weak, moderate, strong). Enhanced Bis expression at the periphery of a tumor facing the adjacent non-tumor region was referred as 'marginal activity.' **Results:** Although Bis expression was higher in squamous cell carcinoma than in adenocarcinoma, marginal activity was higher in adenocarcinoma than in squamous cell carcinoma. All of the small cell carcinomas and lung cancer with neuroendocrine differentiation examined were negative for Bis expression. Compared with stage I lung cancer, patients with stage II and IIIA lung cancer exhibited higher Bis protein levels in lung tissues. Recurrence and survival rates did not differ significantly according to Bis expression intensity score or marginal activity. **Conclusion:** Our study demonstrated that Bis expression differed according to the histological type and pathological stage of the lung cancer. Further studies are needed to assess its use as a biomarker and its role in the molecular pathogenesis of lung cancer. **Keywords:** Bis, lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-099 Proteome Signatures with Prognostic Impact Distinguish Non-Small Cell Lung Cancer Histology Subtypes and Metabolic States Wen Zhang[1], Shingo Sakashita[2], Paul Taylor[3], Jiefei Tong[3], Nhu-An Pham[2], Vladimir Ignatchenko[2], Melania Pintilie[2], Thomas Kislinger[2], Ming S. Tsao[2], Michael Moran[3] [1]*University of Toronto, Toronto/Canada,* [2]*Princess Margaret Cancer Centre, Toronto/ON/Canada,* [3]*The Hospital for Sick Children Research Institute, Toronto/ON/Canada*

Background: We showed that the ability to establish a primary tumorderived xenograft (PDX) is an independent predictor of shorter disease-free survival in early stage non-small cell lung carcinoma (NSCLC). Hence, NSCLC engraftment may select for critical, aggressive aspects of the cancer phenotype linked to disease progression. More recently we reported dramatic remodeling of NSCLC proteomes not predicted by genomics analyses, and which distinguish between the major histological subtypes of NSCLC. Herein we report details on NSCLC proteome remodeling as a major determinant of the expression of the metabolism proteome, engraftment, and related to patient outcome. **Methods:** Omics platforms were used to comprehensively characterize the genomes and proteomes of non-engrafting, engrafting, and derived PDX tumors associated with NSCLC. To facilitate proteome quantification by mass spectrometry, tumor samples were spiked with stable-isotope-labeled proteomes from a mixture of representative NSCLC cell lines as an internal standard. **Results:** Proteome remodeling in NSCLC is extensive and largely unpredicted by gene copy number variation, and not highly correlated with mRNA-based expression. Analysis of the proteomes of cognate engrafting primary and PDX tumor pairs revealed signatures comprising sets of metabolism proteins that distinguished between the major histological subtypes, and which were particularly highly recapitulated in PDX tumors. Interrogation of The Cancer Genome Atlas showed that the genes encoding the highly recapitulated metabolism protein signatures are for the most part not highly mutated in cancers. However, when the signature-encoding genes are considered as a singular polygene, then patients with mutations are recognized as having significantly different overall survival compared to patients without mutations. The proteomes of non-engrafting NSCLC tumors were generally more similar to normal lung than were engrafting tumor proteomes. Hence, proteome remodeling affects metabolic states associated with NSCLC outcome. **Conclusion:** NSCLC is characterized by significant proteome remodeling that is invisible to genomics platforms. The proteomes of engrafting and non-engrafting NSCLC primary tumors are different, suggesting the potential to develop proteome signatures as prognostic biomarkers. Moreover, proteome signatures associated with PDX engraftment and poor outcome may be a source of new drivers and targets in NSCLC. **Keywords:** non-small cell lung cancer, proteomics, Metabolism, Prognosis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-100 Chaperonin (HSP60) and Annexin 2 Are Candidate Biomarkers for Early Diagnosis of Non Small Cell Lung Carcinoma Ismail Agababaoglu, Banu Demir, Pınar Ercetin, Ayca Pamukoglu, Safiye Aktas, Zekiye Altun, Atila Akkoclu
Dokuz Eylul University Faculty of Medicine, Izmir/Turkey

Background: Lung cancer is responsible of 12.4% and 17.6% of all newly diagnosed cancer cases and mortality due to cancer respectively and 5-year survival rate despite all improved treatment options is 15%. This survival rate reaches 66% in the Stage 1 and surgically treated patients. Early diagnosis which could not be definitely and commonly achieved yet is extremely critical in obtaining high survival rate in this disease. For this reason; proteomic differences were evaluated using MALDI TOF/TOF mass spectrometry in the subgroups of lung adenocarcinoma and squamous cell carcinoma. **Methods:** Fresh

tissue samples of 36 malignant cases involving 83.3% (n=30) male and 16.7% (n=6) female patients were distributed into two groups as early and end stage lung cancer and each group were composed of subgroups including 18 squamous cell carcinoma (9 early stage cases, 9 end stage cases) and 18 adenocarcinoma cases (9 early stage cases, 9 end stage cases). Of the malignant cases, 41.7%, 7.3%, 44.4% and 5.6% were at Stage 1, Stage 2, Stage 3 and Stage 4, respectively. 50.0% (n=18) and 50.0% (n=18) were classified as early and final stage cases, respectively. The fresh tissues obtained from the tumoral and matched normal sites after surgical intervention. The differences in protein expression levels were determined by comparing proteomic changes in the tumoral tissues with normal tissues in each patient. The results obtained following two dimensional gel electrophoresis and MALDI TOF/TOF mass spectrometry were detected with respect to differences in protein densities of the subgroups identified by Decodon two dimensional gel analysis system. **Results:** In the subgroups of advanced stage adenocarcinoma; tumoral tissue revealed differences in expression of 2 proteins compared with normal parenchymal tissue. Of those; difference in protein expression in HSP60 (heat shock protein 60) was found statistically significant (p=0.0001). On the other side, subgroups of early and advanced stage squamous cell carcinoma revealed differences in expression of 20 particular proteins. Of those, increased protein expression level of only annexin-2 protein was found statistically significant (p=0.002). No significant difference was detected in early and advanced stage protein expressions of the tumoral tissues in the subgroups of adenocarcinoma and squamous cell carcinoma. **Conclusion:** n the light of these results; we conclude that with respect to early diagnosis of lung cancer that HSP60 and annexin-2 proteins are the important biomarkers in the subgroups of adenocarcinoma and squamous cell carcinoma. We also consider that these two proteins are molecules which may provide critical contribution in evaluation of prognosis, metastatic potential, response to treatment and in establishment of differential diagnosis between adenocarcinoma and squamous cell carcinoma. **Keywords:** Non Small Cell Lung Carcinoma, Chaperonin, Annexin 2, early diagnosis

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P3.04-101 Expression of the Endoplasmic Reticulum Stress Sensor BiP/GRP78 in Lung Adenocarcinoma: Correlations and Prognostic Significance Hisao Imai[1], Kyoichi Kaira[2], Tomohiro Yazawa[3], Akira Shimizu[4], Toshiteru Nagashima[3], Yoichi Ohtaki[3], Takayuki Asao[2], Koichi Minato[1], Tetsunari Oyama[5], Izumi Takeyoshi[3], Kimihiro Shimizu[3]
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Background: Endoplasmic Reticulum (ER) Stress Sensor, BiP/glucose-related protein 78 (GRP78) is an important member of the heat shock protein family 70 (HSPs70) that plays an essential role in the tumor growth and progression. It is localized to the endoplasmic reticulum. Although GRP78/BiP is highly expressed in various cancer cells, the clinicopathological significance of its expression in non-small cell lung cancer (NSCLC) remains unclear. The aim of the present study was to investigate the expression of the GRP78/BiP in patients with lung adenocarcinoma. **Methods:** Two hundred and twenty patients with surgically resected lung adenocarcinoma were evaluated as one institutional cohort. Tumor sections were stained by immunohistochemistry for GRP78/BiP, PERK, Ki-67, p-mTOR, and CD34 to assess the microvessel density. The correlation between GRP78/BiP and the other factors was assessed using the Spearman correlation analysis. **Results:** GRP78/BiP was highly expressed in 41% of patients, and was significantly associated with pleural invasion, lymphatic permeation, vascular invasion, cell proliferation, and p-mTOR phosphorylation. Multivaritate analysis confirmed that GRP78/BiP expression was an independent factor for predicting poor progression-free survival and overall survival in patients with stage I disease. **Conclusion:** The increased GRP78/BiP expression is an independent prognostic factor for early stage lung adenocarcinoma patients. Our study suggests that the expression of GRP78/BiP as ER stress marker plays a crucial role in the pathogenesis and development of lung adenocarcinoma. **Keywords:** Endoplasmic reticulum stress, Glucose-related protein 78, Immunohistochemistry, non-small cell lung cancer

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P3.04-102 CC Chemokine Ligand 18 as a Biomarker for the Prediction of Radiation Induced Lung Disease (RILD) Eleni Gkika[1], Sonja Adebahr[1], Tanja Schimek-Jasch[1], Antje Prasse[2], Gernot Zissel[3], Anca-Ligia Grosu[1], Ursula Nestle[1] [1]*Radiation Therapy, University Medical Center Freiburg, Freiburg/Germany,* [2]*Pneumology, Hannover Medical School, Hannover/Germany,* [3]*Pneumology, University Medical Center Freiburg, Freiburg/Germany*

Background: In patients with fibrosing lung disease the CC Chemokine Ligand 18 (CCL18) is abundantly produced by alveolar macrophages and its concentration is increased in various inflammatory and fibrotic lung diseases. In this study we aimed to analyze the role of CCL18 as a prognostic biomarker for the development of radiation induced lung disease (RILD) after thoracic irradiation. **Methods:** Between August 2011 and February 2012, 60 patients were enrolled prospectively in the study. Forty-six patients were treated for lung cancer, thirteen had an esophageal cancer and one a thymoma. Patients were treated either with conventionally fractionated (n=47) or hypo-fractionated (n=13) radiotherapy. The CCL18 levels in serum were quantified with ELISA (enzyme-linked immunosorbent assay) at predefined time points; before treatment, after 30 Gy, after 60 Gy (for conventional fractionation), at 6 weeks after completion of treatment and 3 months after therapy. These results were then correlated with routinely performed computed tomographies at 6 weeks and 3 months after the last treatment. **Results:** Twenty three patients developed radiologic signs of RILD but only three of them developed symptoms. The mean CCL18 levels, for the whole group of patients, were, before treatment, 110 ng/ml (standard deviation, SD: 53) and at the end of treatment 85 ng/ml (SD: 73). During the first (6 weeks after treatment) and second follow-up (3 months after treatment) the mean CCL18 levels were 93 ng/ml (SD: 57) and 104 ng/ml (SD: 49), respectively. The CCL18 concentrations in serum were not significantly elevated in the group of patients who developed a RILD. The mean CCL18 levels, at six weeks and three months after treatment, were in the RILD-group 94 ng/ml (SD: 62) and 104 ng/ml (SD: 61) and in the non-RILD-group 93 ng/ml (SD: 54) and 103 ng/ml (SD: 39). Furthermore there was no statistical significant correlation between CCL18 levels or decreasing serum CCL18 concentrations and RILD, fibrosis, tumor volume, T-stage, histology, adjuvant therapy, dosimetric parameters such as V20, response after treatment and overall survival. **Conclusion:** These findings do not suggest that the chemokine CCL18 is involved in the development of RILD in patients undergoing radiotherapy for chest tumors. **Keywords:** CCL18, RILD, Radiotherapy

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P3.04-103 Evaluation of the TGF Beta Superfamily Member Activin-A as a Novel Circulating Prognostic Marker in Lung Cancer Mir A. Hoda[1], Anita Rozsas[1], Thomas Klikovits[1], Elisabeth Lang[2], Zoltan Lohinai[3], Yawen Dong[1], Paul Stockhammer[1], Judit Ozsvar[1], Barbara Dekan[1], Marko Jakopovic[4], Miroslav Samarzija[4], Walter Berger[5], Walter Klepetko[1], Balazs Dome[1], Balazs Hegedus[1], Michael Grusch[2], Viktoria Laszlo[1]
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Background: Identification of biomarkers that can facilitate early detection and therapeutic decision making in lung cancer (LC) is urgently needed. Growth factors of the activin family are deregulated in a number of malignancies including thoracic tumors. Recent studies provided data regarding the tumor tissue expression levels of activin-A in lung adenocarcinoma (ADC): High activin-A expression was associated with poor prognosis, enhanced metastasis and shorter progression-free survival in stage I ADC. Since activin-A is secreted to the circulation and can be detected in plasma, this study aims to determine, for the first time, the value of circulating activin-A as a biomarker in LC patients. **Methods:** Plasma samples from patients with small cell lung cancer (SCLC, n= 79), ADC (n=87) and squamous cell carcinoma (n=36) were collected between 2009 and 2013 at the time of diagnosis or before surgical resection. Additional samples, serving as age- and sex-matched controls, consisted of individuals without malignancies (n=66). Measurement of samples was performed using the Quantikine activin-A Elisa kit (R&D Systems) and all statistical analyses were performed using the PASW Statistics 20.0 package and GraphPad Prism 6.0. **Results:** Mean plasma activin-A levels (PAL) (pg/ml) were the following: 628,8±38,42 (ADC, range: 112,4-1875), 613,5±68,22 (SCC, range: 194-2076), 771±77,06 (SCLC, range: 174,1-3627) and 433,3±16,27 (controls, range: 194,1-808,8). A gender-related variation in the PAL of controls (female (n=31, mean PAL 469,5±24,54 (range 212,95-808,79)) vs. male (n=35; mean PAL 401,3±20,49 (range 194,1-759,02)), p= 0.0319) was observed. PAL was significantly increased in patients with ADC (p=0.0009), SCC (p=0.0061) and SCLC (p<0.0001) compared to controls. There was no difference in PAL with regard to patients´ age, gender, BMI, smoking status or other co-morbidities in all 3 LC types. A significant TNM stage-dependent increase of PAL was observed in all 3 LC types. PAL was elevated in T3 SCC, in T4 ADC and in T3 and T4 SCLC. PAL was also clearly associated with N status and metastatic disease in all 3 LC types. Importantly, in case of SCLC, PAL was associated with extensive disease and showed metastatic site specificity. In ADC patients, elevated PAL was associated with significantly worse overall survival (OS) (p<0.0001). Of note, in locally advanced ADC, elevated PAL also proved to be a significant negative prognosticator (p=0.048). Moreover, elevated PAL was associated with a poor OS in SCLC patients (p=0.0009). Multivariate analysis revealed that PAL was an independent prognostic factor in ADC and SCLC patients. Survival and multivariate analysis data of the SCC cohort will be presented at the conference. ROC curve analysis showed an AUC of 0.691 in SCLC and an AUC of 0,657 in ADC for PAL. **Conclusion:** Our findings suggest that PAL is significantly elevated in a disease stage-dependent manner in LC patients. Moreover, elevated PAL is associated with poor prognosis in ADC and SCLC patients. **Keywords:** SCLC, biomarker, growth factor, NSCLC

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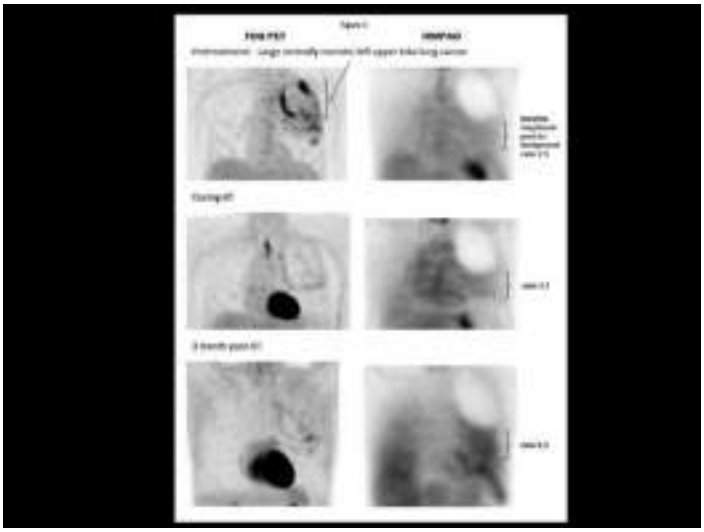
P3.04-104 Radiation Pneumonitis: Assessment by Inflammation Imaging with Tc-99m HMPAO - Clinical Trial in Progress Hadyn Williams[1], Jing Zhao[2], Zonglin Hao[2], Feng-Ming (Spring) Kong[3] [1]*Department of Radiology, Gru Cancer Center/Medical College of Georgia, Georgia Regents University, Augusta/GA/United States of America,* [2]*Gru-Cancer Center, Medical College of Georgia, Georgia Regents University, Augusta/GA/United States of America,* [3]*Department of Radiation Oncology, Gru Cancer Center/Medical College of Georgia, Georgia Regents University, Augusta/United States of America*

Background: Background: Over 60% of patients with non-small-cell lung carcinoma (NSCLC) require radiation treatment, with an overall cure rate < 10-15% and moderate toxicity in 10-30% of treated patients. While high-dose radiation improves survival, concern over radiation-induced toxicities including radiation pneumonitis (RP) have limited its use. Predicting probability of tumor control and lung toxicity offers a promising strategy for individualized radiation therapy (RT), such as giving higher dose radiation to

resistant tumors when probability of toxicity is low, improving the therapeutic ratio. Technetium-99m (Tc-99m) hexamethylpropylene amine oxime (HMPAO) imaging is an established method for evaluation of brain perfusion, tissue inflammation, infection, and abscess localization. Tc-99m HMPAO, a lipophilic biogenic amine that easily crosses the cell membrane into the endothelial cytoplasm, is a sensitive indicator of endothelial cell damage and microvascular injury, penetrating into the alveolar macrophage reflecting impaired alveolar integrity proportional to inflammation and lung toxicity. Once intracellular, it is retained by conversion to hydrophilic nondiffusable form mediated by glutathione oxidation/reduction within the epithelial lining and bronchoalveolar cell, and has been used for non-invasive detection of lung injury proportional to severity. We used Tc-99m HMPAO scintigraphy to semiquantitatively document the presence and severity of lung toxicity in 4 patients undergoing RT for NSCLC. **Methods:** Methods: Four patients with NSCLC (3 Stage IIIB receiving concurrent RT and carboplatin/paclitaxel chemotherapy, 1 Stage IB RT alone) underwent lung computed tomography (CT), positron emission tomography (PET)/CT with 2-deoxy-2-[fluorine-18]fluoro-D-glucose (FDG), ventilation (V)/perfusion (Q) lung imaging with Tc-99m diethylene triamine pentaacetic acid/Tc-99m macroaggregated albumin, and inflammation imaging with Tc-99m HMPAO; at baseline prior to treatment, during RT after 36-50 Gray, and at 3 months following radiation completion. **Results:** Results: All patients had matching V/Q lung abnormalities in the areas of tumor and RT, and tumor-positive baseline FDG PET/CT imaging that showed response to therapy. Three patients without RP had HMPAO imaging that mimicked Q lung imaging on all 3 sequential imaging studies. No patient experienced RP during RT, while one patient experienced grade 1 RP at 3 months, showing progressive increase in HMPAO inflammatory uptake in adjacent lung from baseline to during-RT to 3 months post-RT imaging, not appreciated on FDG PET/CT imaging (Figure 1). **Conclusion:** Conclusion: Tc-99m HMPAO nuclear imaging may provide more sensitive evaluation of the presence and severity of RP. In this case, uptake on during-RT imaging predated, predicted, and confirmed development of grade 1 RP at 3 months.



Keywords: radiation toxicity, Radiation pneumonitis, molecular imaging, glutathione

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P3.04-105 SPARC, a Possible Predictive Marker to Albumin-Bound Paclitaxel (Nab-Paclitaxel) in Non-Small Cell Lung Cancer Kazutoshi Komiya[1], Tomomi Nakamura[1], Hironori Sadamatsu[1], Chiho Nakashima[1], Koichiro Takahashi[1], Hitomi Umeguchi[2], Naomi Kobayashi[1], Akemi Sato[1], Yuji Takeda[1], Shinya Kimura[1], Naoko Sueoka-Aragane[1] [1]*Saga University, Saga/Japan,* [2]*Japanese Red Cross Karatsu Hospital, Karatsu/Japan*

Background: Anti-cancer agents to lung squamous cell carcinoma are limited compared to adenocarcinoma, and most novel therapeutic agents including molecular targeted therapy are indicated for adenocarcinoma not squamous cell carcinoma. Recently, it is reported that carboplatin plus albumin-bound paclitaxel (*nab*-paclitaxel) as first-line therapy in patients with advanced non-small cell lung cancer demonstrated a significantly higher overall response rate than carboplatin plus solvent-based paclitaxel (33% vs 25%, p=0.005) and in patients with squamous histology compared to non-squamous (41% vs 24%, p<0.001) . Secreted protein acidic and rich in cysteine (SPARC) plays a crucial role in cell growth and angiogenesis through an interaction with extracellular matrix or cytokines. SPARC bound to albumin and they co-localized in cancer tissues, suggesting that SPARC plays an important role on higher tumor uptake of *nab*-paclitaxel. Expression of SPARC was correlated with prognosis in breast cancers and high SPARC stromal reactivity was correlated with tumor response to *nab*-paclitaxel in pancreatic cancers. *nab*-paclitaxel showed a good tumor response to lung squamous cell carcinoma, which is one of the most difficult cancers to be treated. In this study, we investigated the possibility of SPARC as a predictive marker for *nab*-paclitaxel. **Methods:** We studied the stromal SPARC reactivity and the association with clinicopathological characteristics in 200 non-small cell lung cancers using custom tissue microarray fabricated in our laboratory by immunohistochemical staining. SPARC stromal reactivity was defined as the percentage of reactive stromal area among the optical fields and scored as − (less than 10%), + (10%<, 50%≧) or ++ (more than 50%). We also investigated the relationship between stromal SPARC reactivity and tumor response to *nab*-paclitaxel using small or surgical specimens obtained from advanced or recurrent lung cancer patients. **Results:** One hundred forty-five patients (72.5%) showed positive staining for stromal SPARC immunohistochemistry. The positivity of immunostaining was significantly higher in patients with Brinkman index (B.I) ≧ 400 (80/98, 82%) compared with in those with < 400 (65/102, 64%) (p = 0.01), in squamous cell carcinoma (26/29, 90%) compared with adenocarcinoma (107/155, 69%) (p = 0.03), and in vessel invasion positive (45/53, 85%) compared with vessel invasion negative (95/140, 68%) (p = 0.03). In contrast, positive staining of cytoplasmic or nucleus SPARC in cancer cells was rare (5 cases). We found that patients in stage I with high SPARC stromal reactivity had significantly shorter survival than patients with low SPARC stromal reactivity (log-rank p = 0.05). We also found that patients with high expression of stromal SPARC in small specimens such as TBLB or surgical specimens tend to response to *nab*-paclitaxel. **Conclusion:** Positive immunostaining of the stromal SPARC was more frequently observed in male smokers with squamous cell carcinoma , and good tumor response to *nab*-paclitaxel was correlated with high stromal SPARC reactivity. SPARC is a possible useful predictive marker for selecting *nab*-paclitaxel treatment. **Keywords:** SPARC, nab-paclitaxel, predictive marker, Squamous cell carcinoma

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P3.04-106 ATG7-Dependent Autophagy May Not Be Involved in Prognosis of Human NSCLC Shaoxing Sun, Zhihao Wang, Fang Tang, Chunxu Yang, Conghua Xie *Department of Radiation and Medical Oncology, Zhongnan Hospital of Wuhan University, Wuhan/China*

Background: Autophagy, one of two major intracellular degradation pathways, plays a critical role in energy homeostasis and the quality control of macromolecules and intracellular organelles. Autophagy plays a role in the various stages of tumorigenesis. However, the role of autophagy in cancer seems complex. Autophagy confers both pro- and anti-tumourigenic roles, depending on the cellular and environmental context. Autophagy related gene 7 (ATG7) is an essential autophagy gene. Previous studies showed that ATG7-dependent autophagy represses early oncogenesis but accelerating tumour progression in mouse lung cancer models. However, the expression of ATG7 and its correlation with prognosis of human lung cancer have not been reported. **Methods:** In Cohort 1, we analyzed 41 patients with non-small-cell-lung cancer who had undergone surgery from June 2013 through December 2013. Expression levels of ATG7 in the tumor tissues and the adjacent normal tissues were examined by immunohistochemistry. We then sought to find the relationship between the expression of ATG7 and the overall survival of NSCLC. In Cohort 2, we screened surgery sample library in Department of pathology, Zhongnan Hospital of Wuhan University for NSCLC patients sample from 2010 to 2011. None of the patients underwent radiotherapy or chemotherapy before surgery. Tissue samples of 76 included patients were obtained with the assistant of work staff in that department. Baseline characteristics were collected mainly by consulting archived medical records and the same staging system was referred to anew classify stage. Follow-up was completed within 2 months mainly through telephone contact. 13 patients were excluded from this study because of contact loss. The samples of the rest with a median age of 60 (range 37-79) were submitted for further immunohistochemical analysis and survival data analysis were conducted. Immunohistochemistry was performed by a well-trained pathological technicist. **Results:** In Cohort 1, ATG7 protein was detected mainly in the cytoplasm of tumor cells. Positive staining was identified in 26 (63.4%) tumor tissue samples while only 9 (9.8%) normal lung tissue samples were considered as positive. Chi-square test revealed a significant difference (p<0.01). In Cohort 2, Patients with no ATG7 expression had a median survival time of 17.5 months (95%CI, 11.9-23.1 months) while patients with positive ATG7 expression had the same survival time of 17.5 months (95% CI, 11.3-23.7 months). No significant difference was noticed (p=0.199). **Conclusion:** Differential expression of ATG7 between cancer cells and normal tissues indicates that ATG7 is related to early oncogenesis of NSCLC. However, different from the results obstained from mouse models, ATG7 expression is not correlated with prognosis of human NSCLC. **Keywords:** Immunohistochemistry, Autophagy, ATG7, Prognosis

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P3.04-107 MicroRNA Expression in Epithelial and Stromal Components of Early-Stage Non-Small Cell Lung Tumors Santosh K. Patnaik[1], Reema Mallick[2], Eric Kannisto[1], Wiam Bshara[3], Sai Yendamuri[1] [1]*Thoracic Surgery, Roswell Park Cancer Institute, Buffalo/United States of America,* [2]*University of Minnesota, Minneapolis/MN/United States of America,* [3]*Pathology, Roswell Park Cancer Institute, Buffalo/United States of America*

Background: MicroRNAs are ultra-short, non-coding RNAs that play important roles in the biology of lung cancer. In addition, biomarker utility of lung cancer tumor microRNAs for diagnosis, histological sub-typing, prognosis and prediction of response to therapy has been demonstrated in a large number of studies. Like all tumors, those of non-small cell lung cancer contain both cancerous epithelial and non-cancerous stromal cells. To facilitate our understanding of the role of microRNAs in lung cancer biology as well as their application as biomarkers, we examined microRNA expression in epithelial and stromal components of early-stage non-small cell lung tumors. **Methods:** Laser capture microdissection of 8 µm-thick, hematoxylin-eosin-stained sections of formalin-fixed specimens was used to separately collect epithelial and stromal components of 77 resected pathologic stage I non-small cell lung cancer tumors. Total RNA was extracted from the dissectates with the Norgen Biotek® FFPE Tissue RNA Isolation kit and quantified with Ribogreen™ assay (Invitrogen®). MiRCURY™ microarrays (Exiqon®) with locked nucleic acid hybridization probes were used to quantify microRNAs in 350 ng of each RNA isolate. For validating the microarray data, 10 microRNAs in the RNA isolates were also quantified using Taqman™

microRNA reverse transcription (RT)-PCR assays (ABI®). **Results:** Microdissection was performed for 35 adenocarcinoma, 16 bronchioloalveolar carcinoma and 26 squamous cell carcinoma tumors. Of the 1936 human mature microRNAs detectable with the microarray platform, 595 (31%) were identified as expressed and reliably quantified among the RNA samples. Microarray-based quantification of 10 microRNAs in the samples was validated by RT-PCR. Significant differences for microRNA expression between tumor epithelia and stroma, and between cancer of different histologies was noted. **Conclusion:** Our study provides information on microRNA expression in epithelial and stromal components of early-stage non-small cell lung tumors. **Keywords:** microRNA, tumor stroma, biomarker, NSCLC

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-108 Differential Cellular and Molecular Response to Ablative Radiation in Non-Small Cell Lung Cancer Based on Molecular Subtype Ayman Oweida[1], Zeinab Sharifi[1], Mojgan Ebrahimi[2], Richard Fraser[2], Siham Sabri[1], Russell Ruo[3], Jan Seuntjens[3], Bassam Abdulkarim[4] [1]*Centre for Translational Biology, Research Institute of the Mcgill University Health Centre, Montreal/QC/Canada,* [2]*Department of Pathology, Montreal General Hospital, Montreal/QC/Canada,* [3]*Medical Physics Unit, Montreal General Hospital, Montreal/QC/Canada,* [4]*Division of Radiation Oncology, Montreal General Hospital, Montreal/QC/Canada*

Background: Ablative radiotherapy (ART) is increasingly used in the management and treatment of early-stage inoperable non-small cell lung cancer (NSCLC). Clinical studies show response rates of 80-90% in NSCLC patients treated with ART. However, the cellular and molecular determinants of the response to ART have not been investigated and recent analysis of patterns of failure in patients treated with ART show increased distant metastatic recurrence. **Methods:** Human NSCLC adenocarcinoma cell lines with different molecular subtypes (EGFR, K-RAS and p53 status) were chosen for this study including, A549, HCC827 and H1975 cells. To assess the cellular response to ART, several cellular assays were used after exposure to a single dose of 12Gy. Western blotting was performed to analyze expression and phosphorylation levels of molecular determinants involved in proliferation and invasion after exposure to ART. An *In vivo* study was performed using a novel orthotopic primary NSCLC animal model. When lung tumors reached a size of 0.2 cm^3, animals were treated with a dose of 34Gy using a Varian Novalis system equipped with cone-beam CT for accurate positioning. Treated animals were sacrificed at 10days, 30days and 60days after treatment and assessed for the presence of local and distant metastasis. In addition, immunohistochemistry was performed to assess tumor markers for proliferation, invasiveness, and metastasis. **Results:** Our results show that ART significantly reduced cell proliferation compared to FRT in A549 cells only. HCC827 and H1975 cells were equally inhibited by ablative and fractionated radiation. In A549 cells, ART significantly increased the invasive phenotype of the cells while in HCC827 and H1975 cell invasion was significantly reduced compared to FRT. Molecular analysis of proteins involved in invasion and migration revealed that ART upregulated c-MET expression in A549 cells without inducing epithelial-to-mesenchymal transition (EMT). In tumor-bearing rats, 50% had complete response, 25% partial response and 25% had local progression or distant metastasis after 34Gy. Consistent with *in-vitro* data, the tumor invasive profile was independent of EMT. **Conclusion:** Our results demonstrate that there is a differential response to ablative and fractionated radiation that is cell-type dependent. A549 cells exposed to ablative doses acquired a pro-invasive and migratory phenotype, which was independent of EMT. These findings can have significant implications for NSCLC patients undergoing ART and underscore the importance of understanding the underlying biology for effective disease management and treatment. **Keywords:** invasion, ablative radiotherapy, non-small cell lung cancer, cMET

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-109 Validating ECOG Performance Status as a Prognostic Factor in Brazilian Patients with Pulmonary Adenocarcinoma Rafael C. Bitton[1], Luiz G.C.A. De Lima[2], Felipe S.R. Roitberg[1], Cristiane Mesquita[1], Renata E. Martins[1], Cheng T. Yen[1], Ricardo M. Terra[3], Evandro S. Mello[2], Gilberto De Castro Jr[1] [1]*Medical Oncology, Instituto Do Câncer Do Estado de São Paulo - Icesp, Sao Paulo/Brazil,* [2]*Pathology, Instituto Do Câncer Do Estado de São Paulo - Icesp, Sao Paulo/Brazil,* [3]*Thoracic Surgery, Instituto Do Câncer Do Estado de São Paulo - Icesp, Sao Paulo/Brazil*

Background: ECOG performance status scale (ECOG) is a score used in clinical practice to estimate cancer patients´ functionality, and its value as a prognostic factor has been extensively demonstrated. Patients (pts) harboring EGFR mutations have been experiencing substantial improvements in their functionality and ECOG after receiving targeted therapies with tyrosine kinase inhibitors (TKIs). Recently, with the availability of TKIs for the treatment of pts harboring EGFR mutations, a treatment capable of inducing marked improvements in patients´ functionality, it is pertinent to access the prognostic value of ECOG (at the moment of the diagnosis of cancer) for these pts. In this scenario, we aimed to validate ECOG as a prognostic factor in a population of Brazilian pts with pulmonary adenocarcinoma, including those harboring EGFR mutations who received treatment with TKIs. **Methods:** This is a retrospective, uniinstitutional study of all consecutively tested tissue samples from 417 pts diagnosed with pulmonary adenocarcinoma treated at our Institution. All samples were formalin-fixed and paraffin-embedded. Tumor areas were selected and macrodissected, followed by whole DNA extraction and amplification by PCR. EGFR genotyping was performed through DNA sequencing (exons 18, 19, 20 and 21) by Sanger´s methodology. Pts were treated according to their clinician´s choice: TKIs (Erlotinib or Gefitinib) were available for pts harboring EGFR mutations, and those harboring wild type EGFR were treated with chemotherapy. **Results:** 417 pts had tumor samples genotyped between Aug/2011 and Sep/2015. Median age was 62 y (17-91), and 237 (57%) were female. According to ethnicity, 357 pts were Caucasian (86%), 37 African-American (9%) and 21 Asian (5%); 140 pts were classified as never-smokers (34%), 37 (9%) as light-smokers (≤ 10 packs/year.) and 238 (57%) as current smokers (> 10 packs/year). EGFR activating mutations were identified in 103 out of 417 samples (24.7%). Among patients harboring EGFR mutations, median survival, in months (m), according to ECOG performance status was: 25.1m for ECOG 0, 19.5m for ECOG 1, 10.5m for ECOG 2, 5.9m for ECOG 3, and <1m for ECOG 4. Among patients with wild-type EGFR, median survival, in months, according to ECOG was: 112.8m for ECOG 0, 20.1m for ECOG 1, 8.8m for ECOG 2, 5.7m for ECOG 3, and 2m for ECOG 4. Among those pts with stage IV adenocarcinoma and ECOG-PS 0-1, with a median follow-up of 12 months, the median overall survival rate was 16.3 months for pts harboring EGFR-activating mutations, and 14.5 months for those with EGFR-wild-type tumors (HR 0.99, p=0.93, 95%CI 0.73-1.33). On multivariate analysis, ECOG-PS > 1 increased 1.59 times the risk of death (HR 1.59, 95%CI 1.41-1.78) regardless of EGFR-mutational status. **Conclusion:** Our data has validated ECOG performance status as a prognostic factor in this Brazilian population of pulmonary adenocarcinoma pts, independent of EGFR mutational status. As a practical and reproducible scale, ECOG remains a valuable tool to guide clinical decisions and estimate cancer patients´ prognosis, even with the advent of Tyrosine kinase inhibitors. **Keywords:** pulmonary adenocarcinoma, lung cancer, EGFR, ECOG

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P3.04-110 PTPRH Hypomethylation as a Prognostic Factor in Non-Small Cell Lung Cancer Takashi Sato[1], Kenzo Soejima[1], Eri Arai[2], Junko Hamamoto[1], Hiroyuki Yasuda[1], Daisuke Arai[1], Kota Ishioka[1], Keiko Ohgino[1], Katsuhiko Naoki[1], Takashi Kohno[3], Koji Tsuta[4], Shun-Ichi Watanabe[5], Yae Kanai[2], Tomoko Betsuyaku[1] [1]*Pulmonary Medicine, Keio University School of Medicine, Tokyo/Japan,* [2]*Molecular Pathology, National Cancer Center Research Institute, Tokyo/Japan,* [3]*Genome Biology, National Cancer Center Research Institute, Tokyo/Japan,* [4]*Pathology, National Cancer Center Hospital, Tokyo/Japan,* [5]*Thoracic Surgery, National Cancer Center Hospital, Tokyo/Japan*

Background: Tyrosine phosphorylation is an important signaling mechanism in cancer. PTPRH is a receptor-type protein tyrosine phosphatase thought to be a potential regulator of tumorigenesis. The aim of this study is to clarify the significance of*PTPRH* expression and its regulation by DNA methylation in non-small cell lung cancer (NSCLC), especially in lung adenocarcinoma. **Methods:** *PTPRH* mRNA expression was examined in 89 NSCLC and corresponding non-cancerous tissues. The correlation between DNA methylation and *PTPRH* gene expression was investigated in another cohort that consisted of 145 patients with lung adnocarcinoma. Gene regulation by DNA methylation was assessed using a DNA methylation inhibitor. Statistic analysis was performed to clarify whether the DNA methylation status of *PTPRH* is a prognostic factor for patients with lung adenocarcinoma. **Results:** *PTPRH* mRNA expression was significantly up-regulated in NSCLC. *PTPRH*DNA methylation was reduced in lung ademocarcinomas and inversely correlated with mRNA expression. 5-aza-2'-deoxycytidine treatment of lung cancer cell lines with low *PTPRH* expression, restored mRNA *PTPRH* expression levels. Furthermore, low *PTPRH* methylation was associated with shorter recurrence-free survival ($P < 0.0002$) and overall survival ($P < 0.0001$). Multivariate analysis revealed that *PTPRH* DNA methylation was an independent prognostic factor ($P < 0.01$). **Conclusion:** We confirmed that *PTPRH* is overexpressed in NSCLC. In addition, we determined that hypomethylation of *PTPRH* is a poor prognostic factor in lung adenocarcinoma. **Keywords:** non-small cell lung cancer, PTPRH, DNA methylation, prognostic factor

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P3.04-111 Gene Polymorphisms in Thoracic Tumors Receiving Cisplatin-Pemetrexed Nicolas Simon[1], Eric Dansin[2], Brigitte Baldeyrou[3], Marie-Christine Etienne-Grimaldi[4], Gérard Milano[4], Jean-François Goossens[1], Christine Bobin-Dubigeon[5], Sophie Salingue[3], Radj Gervais[6], Hélène Senellart[5], Amélie Lansiaux[7], Samuel Meignan[8] [1]*University of Lille, Lille/France,* [2]*Département de Cancérologie Générale, Centre Oscar Lambret, Lille/France,* [3]*Centre Oscar Lambret, Lille/France,* [4]*Centre Antoine Lacassagne, Nice/France,* [5]*Institut Du Cancer de L'Ouest, Nantes/France,*[6]*Centre François Baclesse, Caen/France,* [7]*Institut Catholique de Lille, Lille/France,* [8]*Tumorigenesis and Resistance To Treatment Unit - Inserm U908, Lille/France*

Background: **C**hemotherary combining cisplatin and the multitarget antifolate pemetrexed (ALIMTA®) is widely used in mesothelioma and metastatic non-squamous non-small cell lung cancer (n-sq NSCLC). Thymidylate synthase (TYMS) expression is recognized as a predictive marker of pemetrexed efficacy. Polymorphisms in TYMS and Excision repair cross-complementing (ERCC) genes have been associated with decreased tumour response to pemetrexed, and 5-10 Methylenetetrahydrofolate reductase (MTHFR) polymorphisms have been linked to increased toxicity to pemetrexed. The objective of this pilot study was to examine the feasibility and usefulness of testing gene polymorphisms for predicting pharmacodynamics of cisplatin-pemetrexed. **Methods:** This ancillary study (ALIMESO trial) was conducted on 21 patients (mean age 61, 15 men, 6 women) with malignant pleural mesothelioma (8 epithelioid, 2 sarcomatoid, 2 biphasic, 1 desmoplastic) or n-sq NSCLC (3 adenocarcinoma, 5 large-cell carcinoma) treated by cisplatin (75 mg/m^2) plus pemetrexed (500 mg/m^2) for 6 cycles (day 1 = day 22). Response to treatment was evaluated after 3 cycles (RECIST criteria). Toxicity was recorded according to CTC-AE classification. Gene polymorphisms were analyzed in all patients (blood DNA). TYMS polymorphisms in 5'UTR (28 bp repeats rs34743033 along with G>C mutation on 3R allele, rs11540151) were analyzed by PCR-RFLP and 6 bp deletion in 3'UTR (rs11280056) by PCR-electrophoresis. MTHFR C677T (rs1801133) and A1298C (rs1801131) were analyzed by sequencing. ERCC1 AAT118AAC (rs11615), ERCC2 Lys751Gln (rs13181), GSTP1 Ile105Val (rs1695) and Ala114Val (rs1138272)

were analyzed by PCR-RFLP. **Results:** 13 patients (62%) were evaluable for response (8 patients not assessable due to either no chemo or <3 cycles). ORR was 46% (6PR, no CR) and DCR was 100%. 20 patients (95%) were evaluable for toxicity. 78 chemotherapy-related adverse events were reported with 17 (22%) grade 3/4 (2 anemia, 7 neutropenia, 5 thrombocytopenia, 1 renal failure, 1 asthenia, 1 nausea). There was no toxic death. Chemotherapy was stopped after 3 cycles for 2 patients. Homozygous and heterozygous deletion in 3'UTR of TYMS was observed in 1 and 9 patients, respectively. For TYMS 5'UTR, 13 patients belong to class 2 (2R/2R, 2R/3RC or 3RC/3RC), 6 belong to class 3 (2R/3RG or 3RG/3RC) and one belong to class 4 (3RG/3RG). Other genotypes were as follows. GSTP1 codon 105: 10 Ile/Val and 4 Val/Val; GSTP1 codon 114: 1 Ala/Val; ERCC1 codon 118: 10 C/T and 4 C/C; ERCC2 codon 751: 12 Lys/Gln and one Gln/Gln; MTHFR C677T: 10 C/T and 3 T/T; MTHFR A1298C: 8 A/C and 3 C/C. There was no correlation between any gene polymorphisms and response or G3-4 toxicity. Of note, among the 6 patients homozygous for rare MTHFR alleles (i.e. 677TT or 1298CC), 4 exhibited a high-grade (grade 3/4) haematological toxicity. **Conclusion:** Present results suggest that gene polymorpshism analysis is feasible in the context of pharmacodynamics predictivity. From this limited number of patients, a trend was observed between MTHFR genotype and haematological toxicity. These preliminary data need to be confirmed on a larger set of patients with thoracic tumors treated by cisplatin/pemetrexed. **Keywords:** pharmacogenetics, Lung cancers, Cisplatin, pemetrexed

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P3.04-112 Repeated Observation of Immune Gene Sets Enrichment in Women with Non-Small Cell Lung Cancer Jhajaira Araujo[1], Joseph A. Pinto[1], Zaida Morante[2], Alfredo Aguilar[2], Silvia Neciosup[2], Luis Mas[2], Henry Gomez[2], Carlos Vallejos[2] [1]*Basic and Translational Research, Oncosalud, Lima/Peru,* [2]*Medical Oncology Department, Oncosalud, Lima/Peru*

Background: There are different patterns of lung cancer (LC) characteristics between men and women. Females tend to present LC at a younger age and with more advanced stages than males; however, the prognostic is better in women. In despite of the great advances in the knowledge of the genomic landscape of lung cancer, it is not explored the molecular differences regarding to gender. Our aim was to evaluate differentially enriched gene sets between women and men. **Methods:** We evaluated 05 public databases containing gene expression values from NSCLC patients: GSE50081 (HG-U133_Plus_2; n=81 samples), GSE47115 (Illumina HumanHT-12 WG-DASL V4.0 R2; 16 samples), GSE10072 (HG-U133A; n=71 samples), GSE32863 (Illumina HumanWG-6 v3.0; 116 samples), GSE7670 (HG-U133A; n=52 samples). In each dataset, expression levels were log2 transformed and median centered. We performed the Gene Set Enrichment Analysis (GSEA) to find differences between the two genders. Each dataset was analyzed individually. Since the smoking status is the main confounding factor, datasets were divided in cohorts of smokers and non-smokers (and healthy tissues by smoking status when it was included in the dataset). Cases with unknown smoking status and former smokers were excluded from the analysis. We use the Gene ontology biological process terms to find similar enriched pathways between cohorts, 1454 gene sets named by gene ontology terms were examined. We consider a gene set enriched when at least a cohort had a p-value<0.05 and also the observation was repeated in other datasets with a p-values <0.08 (statistical trends). **Results:** The analysis showed repeated observation of immune genes enrichment in women; defense response to virus was enriched in four data sets; cytokine biosynthetic process, innate immune response, positive regulation of cytokine biosynthetic process, regulation of cytokine biosynthetic process and response to other organism were enriched in three dataset; adaptive immune response, B cell activation, cellular defense response, chemokine activity, innate immune response, interferon gamma biosynthetic process, interleukin 8 production and others were enriched in at least two data sets. On the other hand, aminoacid transport, cellular protein catabolic process, maintenance of protein localization, regulation of GTPase activity, regulation of protein polymerization, regulation of Rho GTPase cctivity and others were enriched in three datasets in men. **Conclusion:** The analysis of global gene expression showed that Immune genes sets are frequently enriched in women compared to men. Differences on enrichment pathways between men and women should be deeply explored. **Keywords:** non-small cell lung cancer, GSEA, smoking status, Immune genes

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P3.04-113 Neutrophil to Lymphocyte Ratio (NLR) at Diagnosis as a Prognostic Marker in Patients with Stage IV Non-Small Cell Lung Cancer Eliza D. Ricardo[1], Alexandre A.B.A. Da Costa[2], Vladmir C.C. De Lima[1] [1]*Clinical Oncology, A.C. Camargo Cancer Center, São Paulo/Brazil,* [2]*Cinical Oncology, Ac Camargo Cancer Center, Sao Paulo/Brazil*

Background: Systemic inflammation has been linked with cancer development, cancer cachexia and poor outcome. Neutrophil to lymphocyte ratio (NLR), an index of systemic inflammation, has been associated with worse survival for many types of cancer. The aim of this study is to investigate the clinical significance of the blood NLR as a prognostic factor in non-small cell lung cancer (NSCLC) patients. **Methods:** We retrospectively reviewed the medical charts of patients with metastatic NSCLC, diagnosed between Jan 1st 2011 and July 30th 2014, from a single Brazilian institution. Data on prognostic factors such as histology, gender, performance status, comorbidities and type of treatment were collected. The baseline NLR was assessed just before chemotherapy treatment initiation. NLR was defined as the ratio between the absolute neutrophil and lymphocyte counts. Associations between clinical variables and NLR were tested with Chi-square or exact Fisher´s test. Overall survival (OS) was calculated by the Kaplan–Meier method. Curves were compared using the log-rank test. Multivariate analysis was performed using Cox regression to assess independent patient characteristics associated with OS, and included in the model all variables with $p < 0.05$ on univariate analysis. All analysis were considered statistically significant when $p < 0.05$. **Results:** A total of 170 patients were included in the study. Median age was 63.4 years, 54.1% were male, 80.6% had adenocarcinoma, 17.6% had mutated EGFR, 47.6% were former smoker, and 78.2% had ECOG ≤ 1. Median NLR was 4.6. NLR > 4.6 was associated with SNC metastasis. Median follow-up time was 19.64 months and median overall survival was 13.7 months. Patients with NLR > 4.6 had a worse survival. OS was 22.27 months versus 7.03 months ($p < 0.001$) for patients with NLR ≤ 4.6 and NLR > 4.6, respectively. In multivariate analysis, the NLR remained as an independent prognostic factor for worse OS after adjusting for sex, histology, tumor size and performance status. **Conclusion:** Elevated NLR at diagnosis is an independent predictor of poor OS in patients with advanced NSCLC **Keywords:** metastatic, Neutrophil to lymphocyte ratio, prognostic marker, non-small cell lung cancer

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P3.04-114 IASLC and WHO 2004 Grading System as Prognostic Factors in 492 Cases of Pulmonary Adenocarcinoma Luca Ampollini[1], Letizia Gnetti[2], Matteo Goldoni[3], Carlotta Rossi[2], Luigi Rolli[1], Michela Solinas[1], Luigi Ventura[1], Marcello Tiseo[4], Michele Rusca[1], Antonio Mutti[3], Paolo Carbognani[1], Enrico Maria Silini[2] [1]*Thoracic Surgery, University of Parma, Parma/Italy,* [2]*Pathology, University of Parma, Parma/Italy,* [3]*Departement of Clinical and Experimental Medicine, University of Parma, Parma/Italy,* [4]*Medical Oncology, University Hospital of Parma, Parma/Italy*

Background: Primary aim of the study was to evaluate the prognostic value of the IASLC grading system and the WHO 2004 classification on a consecutive series of resected primary pulmonary adenocarcinomas. Secondary aim was to identify new prognostic histological features. **Methods:** All consecutive patients undergoing radical resection with a pathological diagnosis of primary lung adenocarcinoma were considered. All histological slides were reviewed for the study. Tumor-specific survival was considered as primary outcome. Statistical analysis included Kaplan-Meyer analysis and Cox regression to identify variables with significant Hazard Ratios (HR). **Results:** 492 patients were considered between January 2002 and December 2013. 67.7% were male, mean age was 67.4 years, mean follow-up was 55 months. In a first multivariate Cox Regression Model the WHO 2004 grading was considered; gender [males *vs* females HR=1.7 95% CI (1.2-2.3), p=0.002], stage (p-trend <0.001), lymphoplasmacellular infiltrate [yes *vs* no HR=0.5 95% CI (0.3-0.8), p=0.001], and WHO 2004 grade (p-trend = 0.002) were independent prognostic factors of survival. In a second model the IASLC grading was considered; gender [HR=1.7 95% CI (1.2-2.4), p=0.002], stage (p-trend<0.001), lymphoplasmacellular infiltrate [HR=0.5 95% CI (0.3-0.8), p=0.001], and combined grading score according to Sica (p-trend=0.011) were maintained as independent prognostic factors. **Conclusion:** Tumor grading was an independent prognostic factor of survival in patients with adenocarcinoma undergoing lung resection both considering IASLC and WHO 2004 classifications. Lymphoplasmacellular infiltrate was significantly and favorably related to survival. **Keywords:** Tumour grading, IASLC grading system, WHO 2004 classification, pulmonary adenocarcinoma

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P3.04-115 A New Prognostic Index in Chinese Patients With Metastatic Non-Small Cell Lung Cancer Receiving First-Line Chemotherapy Hui Yu[1], Jialei Wang[1], Fang Liu[2], Benoît Sansas[3], Xavier Preville[3], Xianghua Wu[1], Xia Meng[2], Jianhua Chang[1], Romain Micol[3] [1]*Department of Medical Oncology, Fudan University Shanghai Cancer Center, Shanghai/China,* [2]*Institut Merieux Laboratory, Fudan University Shanghai Cancer Center, Shanghai/China,* [3]*Transgene S.A., Illkirch-Graffenstaden Cedex/France*

Background: Non-small cell lung cancer (NSCLC) is the leading cause of cancer deaths worldwide. Platinum-based duplet therapy is current standard first-line therapy for metastatic NSCLC although its influence on overall survival is modest. The response to chemotherapy and prognosis of patients with metastatic NSCLC is variable due to the heterogeneity. The purpose of the present study was to develop a new prognostic index to predict the clinical outcome of patients with metastatic NSCLC and then improve the clinical management for these patients. **Methods:** This prospective single-institutional study included 70 patients with metastatic NSCLC receiving platinum-based first-line chemotherapy. Plasma levels of 27 cytokines before chemotherapy were measured using multiplex immune assays. Receiver operating characteristics (ROC) curves were adopted to select the cut-off values for survival and chemotherapy response analyses. The Kaplan–Meier method, univariate and multivariate Cox regression analyses were used to evaluate the associations between each cytokine, ratio or clinical variable and progression-free survival (PFS) and overall survival (OS). Prognostic index (PI) was calculated by parameters estimates and PI subgroups were created using tertiles. The performance of the PI was calculated using PSEP method and validated by a bootstrap approach. **Results:** Five variables were identified as statistical significant independent prognostic factors by multivariate Cox model: three cytokines/cytokine ratios including IP-10/Eotaxin (HR, 1.578; *P*=0.018), MCP-1 (HR, 1.138; *P*=0.032) and MIP-1a (HR, 0.464; P=0.007) as well as CRP (HR, 5.948; *P*<0.001) and histology (HR, 5.372; *P*<0.001). Using these five variables, a new PI was developed to distinguish the patients into high-risk group and low-risk group according to the outcome (*P*<0.001). Internal validation showed that the mean optimism over 1000 iterations was 0.17 and an unbiased estimate of PSEP was 0.40. **Conclusion:** The new PI including cytokine and clinical variables can efficiently predict the survival outcome of patients with metastatic NSCLC. This finding may serve as the basis for further

development of biomarkers for the prognosis and treatment of metastatic NSCLC. **Keywords:** clinical factors, non-small cell lung cancer, prognostic index, cytokines

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P3.04-116 Prognostic Role of fox-p3 Positive T-Regulatory Cells in Curatively Resected NSCLC Other than Stage IA Fatih Kose[1], Ayberk Besen[1], Alper Findikcioglu[2], Tuba Canbolat[3], Yurday Ozdemir[3], Ali M. Sedef[1], Huseyin Mertsoylu[1], Ahmet T. Sumbul[1], Ozgur Ozyilkan[1], Huseyin Abali[1] [1]*Medical Oncology, Baskent University, Adana,/Turkey,* [2]*Thoracic Surgery, Baskent University, Adana,/Turkey,* [3]*Baskent University, Adana,/Turkey*

Background: Curative surgical excision accompanied by adjuvan chemotherapy for those stage II, III and high risk stage IB patients for completely resected early stage Non-small cell lung cancer is the widely accepted. However, over 50 % of cases in this early stage group recur and die after this aggressive treatment strategy. Currently used prognostic markers are imperfect to estimate the patients with high risk of relapse. Biologic agents which increase the immune system activity recently approved in the treatment of advanced NSCLC. Main aim of this study is to explore the prognostic role T-regulatory cells, which has essential role in decreasing effect of cytotoxic cells on tumor tissue, in early stage NSCLC. **Methods:** A total 48 patients those who were resected with R0 resection in baskent university between 2005-2009. Stage IA patients were excluded. İmmunohistochemical staining made on the parffin embedded tissue. Kaplan meier survival curve and log-rank test used for the stattistical evaluation. The values of p below the <0.05 was accepted as statistical signifcant. **Results:** A total 48 patients, 40 (83.3%) male and 8 (16.7%) female, were included. ECOG 0, 1, 2 scale were found in 32(66.7%), 14(29.2%), and 2 (4.2%) patients, accordingly. Mean follow-up time for whole group was 49 months (6-128). Adjuvant chemotherapy were given to 16 patients (33.3%) at physician discretion. There were 21(43.8%), 14(29.2%), and 13 (27.2%) patients with stage of IB, II, and III, respectively. Grade 0, 1, 2, 3 IHC staining intensity for CD 3 and FOX-P3 were found in 0-25 (52.1%), 11(22.9%)-21(43.8%), 16(33.3%)-2(4.2%), and 21(43.8%)-0 patients, respectively. We build a risk score based on the rate of FOXP3/CD3 grades. Low risk, intermediate risk, and high risk score were detected in 22 (45.8%), 17 (35.4%), and 9 (18.8%) patients, respectively. Disease relapse rate were 88.9, 76.5, and 18.8% in high, intermediate, and low risk group. (p:0.005). Disease free survival and overall survival were 30 (14.7-45.6) and 49 months (20.6-77.7). In univariate analyses, ECOG performance (p=0.025) scale, pathological stage (p=0.029), and grade of FOX-P3 (p=0,032) had statistically significant effects on disease free survival (DFS). In univariate analyses, ECOG performance (p=0.008) scale, pathological stage (p=0.03), and IHC staining intensity of FOX-P3 (p=0,018) had statistically significant effects on overall survival (OS). The statistical analysis failed to show statistically significant effects of formed risk groups (p>0.005) on DFS and OS. **Conclusion:** In conclusion, results of the present study showed that increase the IHC staining of T-reg cells in tumor tissue significantly related with tumor relapse (higher the intensity-higher the relapse rate). Univariate analysis showed that IHC staining intensity had negative prognostic factor and statistically significant effect on both DFS and OS. **Keywords:** lung cancer, Tregulatory cell, prognosis,

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P3.04-117 Clinical Characteristics and Survival Outcome of Non-Small Cell Lung Cancer According to Age Young Sik Park[1], Sun Mi Choi[2], Jinwoo Lee[2], Chang-Hoon Lee[2], Sang-Min Lee[2], Jae-Joon Yim[2], Chul-Gyu Yoo[2], Sung Koo Han[2], Young Tae Kim[2], Dae Seog Heo[2], Young Whan Kim[2] [1]*Internal Medicine, Seoul National University Hospital, Seoul/Korea,* [2]*Seoul National University Hospital, Seoul/Korea*

Background: Clinical characteristics of non-small cell lung cancer (NSCLC) in young age are different from those of older patients. The aim of this study was to compare the survival according to age with adjustment for major confounding factors including major drugable mutations (EGFR and ALK). **Methods:** From June 2011 to December 2014, 1860 consecutive newly diagnosed NSCLC patients were recruited. Among them, we divided 4 groups according to age; group I (age<40), group II (40≤age<60), group III (60≤age<80), and group IV (age>80). We compared survival using 3 different Cox proportional hazard model; unadjusted model, model 1 (adjusted for sex, smoking, BMI, ECOG performance status, histology of adenocarcinoma, initial stage), and model 2 (model 1 + drugable mutations). **Results:** Among 1860 patients, mean age was 66.1 years old, and 64.7% was male. Never smokers were 38.0% and adenocarcinoma observed in 62.0%. EGFR and ALK mutations were detected in 40.3% and 5.1%, respectively. The numbers of patients were 29 in group I, 436 in group II, 1276 in group III, and 119 in group IV. In Cox proportional hazard model, survival differences between age groups were significant in unadjusted model and model 1. But after adjustment for drugable mutations (model 2), the survival difference was not significant. **Conclusion:** Survival on NSCLC in young age was not different from that older patients, after adjustment for sex, smoking, BMI, ECOG performance status, histology of adenocarcinoma, initial stage and major drugable mutations (EGFR and ALK). **Keywords:** age, NSCLC, survival

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-118 Expression of TS and DPD in Primary Lung Cancer Takayuki Shiina, Takao Sakaizawa, Hiroyuki Agatsuma, Takashi Eguchi, Gaku Saito, Akira Hyogotani, Masayuki Toishi, Kazuo Yoshida *Thoracic Surgery, Shinshu University Hospital, Matsumoto/ Japan*

Background: Chemotherapy with 5-fluorouracil (5-FU) preparations is widely used to treat gastrointestinal cancer, head and neck cancer, and breast cancer. 5-FU acts by inhibiting thymidylate synthase (TS), the rate-controlling enzyme of pyrimidine synthesis, and its anticancer activity is related to the rate of TS inhibition in gastrointestinal cancer and other tumors. Dihydropyrimidine dehydrogenase (DPD) is the rate-limiting enzyme for the catabolism and inactivation 5-FU. As one biochemical modulation strategy, uracil–tegafur (UFT) has been developed to improve the bioavailability of 5-FU by inhibiting DPD. Expression levels of TS and DPD in resected lung cancer samples are generally determined quantitatively by reverse-transcription polymerase chain reaction (RT-PCR) or qualitatively by immunohistochemical analysis. However, no study has employed enzyme-linked immunosorbent assay (ELISA) to measure TS and DPD expression in lung cancer, although this technique is often used for gastrointestinal, colorectal, and breast cancers. **Methods:** From April 2004 through December 2007, we studied tissue samples from 168 of 280 patients with primary lung cancer in which both TS and DPD could be measured. TS and DPD in normal and tumor tissues were quantified by ELISA and compared according to expression level, gender, histological type, and clinicopathological characteristics. *Patient Characteristics*: Of the 168 patients, 110 were men (65.4%), and 58 were women (34.6%). The median age was 69.6 (range, 35-89) years; 107 patients were former or current smokers and 61 were nonsmokers.The pathologic disease stage was IA in 59 patients, IB in 34, IIA in 8, IIB in 23, IIIA in 33, IIIB in 7, and IV in 4. The patients with stage IV disease had brain metastasis. The most common histological type was adenocarcinoma (107 cases), followed by squamous cell carcinoma (39), adenosquamous carcinoma (2), large cell carcinoma (9), small cell carcinoma (5), pleomorphic carcinoma (3), and carcinoid (3). **Results:** Expression levels of TS and DPD were significantly higher in lung cancer tissue than in noncancerous tissue. As for patient characteristics, TS expression in tumors was significantly lower in women and nonsmokers. According to histological type, tumor TS expression was significantly lower in adenocarcinoma and squamous cell carcinoma than in other types of lung cancer, whereas DPD expression did not differ significantly among histological types. Median tumor TS expression was significantly lower in well-differentiated tumors than in moderately/poorly-differentiated tumors. Among patients with adenocarcinoma (n=107), median tumor TS expression was significantly lower in women and nonsmokers. **Conclusion:** The present study suggested that tumor TS and DPD levels are useful predictors of chemosensitivity to UFT in patients with primary lung cancer who receive postoperative adjuvant chemotherapy. The expression level of TS in tumors may be useful for selecting postoperative treatment for individual patients with lung cancer, particularly those who are women or nonsmokers or who have adenocarcinoma. **Keywords:** lung cancer, Thymidylate Synthase, Dihydropyrimidine Dehydrogenase

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-119 The Decreased Serum Dopamine Level Is Associated with Poor Prognosis in Non-Small Cell Lung Cancer and Contributes to Cancer Cell Stemness Xiaoyuan Wu, Bin Zhang, Wei Zhao *Central Laboratory, Nanjing Chest Hospital, Nanjing/China*

Background: Lung cancer ranks the first cancer related mortality worldwide. Dysregulation of dopamine-related pathways have been implicated in tumor development/angiogenesis. **Methods:** In this study, we detected dopamine in 63 non-small cell lung cancer (NSCLC) patients, and 70 healthy control serum by Elisa kit. The associations between serum dopamine level with patient's prognosis and survival were analyzed by SPSS 17.0 statistical software. Add dopamine into NSCLC cancer cell medium and FACS detected the effects on cancer cells stemness. **Results:** The serum dopamine level is significantly down-regulated in NSCLC samples, compared to the healthy control ($P < 0.0001$). In addition, low level of serum dopamine was correlated with tumor size ($P = 0.0207$) and N stage ($P = 0.007$). Kaplan-Meier analysis indicated that patients with low serum dopamine had a poor overall survival ($P = 0.0144$). Additional dopamine inhibited the stemness and proliferation of NSCLC cell line A549. **Conclusion:** Our data indicates that dopamine negatively regulates NSCLC cell stemness and might be a novel therapeutic target in NSCLC patients. **Keywords:** Dopamine, non-small cell lung cancer, Cancer stemness

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-120 Quantitative Immunofluorescence Based Expression Analysis in NSCLC Reveals Nuclear EZH2 as Poor Prognostic Biomarker Vamsidhar Velcheti[1], Sijin Wen[2], Kurt Schalper[3], Veronique Neumeister[4], Hashim Abbas[1], Wei Zhang[2], Lihong Yin[1], Patrick C. Ma[2] [1]*Cleveland Clinic, Pepper Pike/United States of America,* [2]*Mary Babb Randolph Cancer Center., West Virginia University., Morgantown/ United States of America,* [3]*Pathology, Yale University, New Haven/CT/United States of America,* [4]*Pathology, Yale University, New Haven/United States of America*

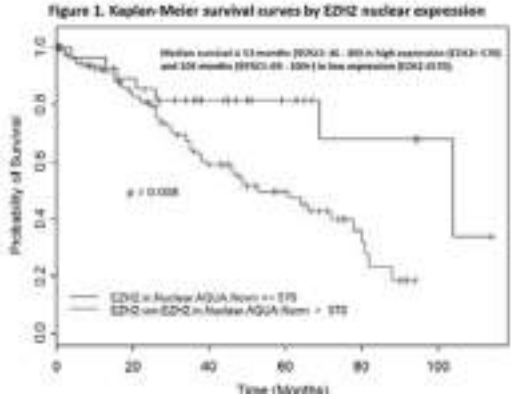
Background: EZH2 is a histone-lysine N-methyltransferase enzyme and the key functional enzymatic component of the polycomb repressive complex 2 (PRC2), which is a crucial epigenetic regulator in cancer cell survival. EZH2 methylates histone 3 at lysine 27 (H3K27me/me2/me3) and has been associated with the heterochromatin state, transcriptional repression and activation, hematopoiesis, development, and

cell differentiation. Activating EZH2 mutations has been identified in lymphoma, and EZH2 overexpression has recently been reported in solid tumors including melanoma, breast, prostate, and lung cancer. Inhibition of EZH2 is a promising therapeutic strategy and a number of EZH2 targeting drugs are currently in clinical development. **Methods:** Multiplexed QIF assay was used to evaluate EZH2 expression using monoclonal antibody (clone D2C9, cell signaling technology) against human EZH2, and cytokeratin (AE1/AE3, Dako) in a retrospective cohort of 298 stages I-IV NSCLC represented in tissue microarray (TMA) format. H3122 NSCLC xenografts and control patient samples were used to determine staining specificity and optimal titer. The association between EZH2 level, clinico-pathological characteristics and survival were studied. The classification and regression tree (CART) analysis was used to determine the optimal cutoff of EZH2 expression to predict survival. Kaplan-Meier and log-rank test were used in statistical analysis of overall survival. Chi-square test was used for clinic-pathologic correlation statistical analysis. **Results:** EZH2 protein was detected predominantly in the tumor compartment with nuclear staining pattern. A high EZH2 level was detected in 82% of cases and was correlated with active smoking (92% vs. 64%, P=0.005) and squamous cell histology (94% vs 76%, P=0.013) (Table 1). Elevated tumor nuclear EZH2 expression was significantly associated with worse survival (median survival 53 vs. 104 months; log-rank P=0.002) (Figure 1).

Table 1: Clinical Correlations of EZH2 expression in NSCLC

		EZH2.in.Nuclear.AQUA.Norm> 570	Chi-square test	
	All (%)	**No (%)**	**Yes (%)**	**p-value**
Age				
<70	120 (56.1)	22(18)	98(82)	0.864
≥70	94 (43.9)	19(20)	75(80)	
Gender				
Female	130 (60.7)	25(19)	105(81)	0.885
Male	84 (39.3)	16(19)	68(81)	
Tobacco. history				
Current Smoker	49 (22.9)	4(8)	45(92)	0.005
Former	113 (52.8)	21(19)	92(81)	
Never	39 (18.2)	14(36)	25(64)	
unknown	13 (6.1)			
Histology				
Adenocarcinoma	134 (62.6)	32(24)	102(76)	0.013
Others	26 (12.1)	6(23)	20(77)	
Squamous Cell	54 (25.3)	3(6)	51(94)	
Tumor Size				
<3cm	115 (53.7)	23(20)	92(80)	0.778
≥3cm	97(45.3)	17(18)	80(82)	
unknown	2 (1)			

Figure 1. Kaplan-Meier survival curves by EZH2 nuclear expression



Conclusion: Our study shows that high nuclear EZH2 protein expression is a poor prognostic biomarker in NSCLC, and is correlated with smoking status and squamous cell histology.

Keywords: lung cancer, biomarker, Prognostic, epigenetics

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-121 Testicular Orphan Receptor 4 (TR4) Is a Marker for Metastasis and Poor Prognosis in Non-Small Cell Lung Cancer That Drives the EMT Phenotype
Liyi Zhang, Jianzhi Zhang, Yuanyuan Ma *Department of Thoracic Surgery Ii, Peking University Cancer Hospital & Institute, Beijing/China*

Background: Aberrant expression of Testicular orphan receptor 4 (TR4) has been shown to regulate biologic processes around solid tumors. However, it is not clear the role of TR4 in prognosis for non small cell lung cancer (NSCLC) patients and the development of NSCLC cells. **Methods:** Immunohistochemical was used to evaluate the correlation between TR4 expression and clinicolpathological characteristics in 35 paired of tumor and counterpart normal tissues and 291 cases of specimens. Knock-down assay was performed to suppress the TR4 expression level. Transwell and colony formation assays were done to investigate metastatic and proliferative abilities. Quantitative real-time PCR , western blotting and immunofluorescence staining were carried out to analyze the EMT phenotype. **Results:** Immunohistochemical evaluation of clinical samples disclosed most of the lung cancer tissues were positive for TR4, while weakly positive or negative for TR4 expression in the counterpart normal tissues. Moreover, higher levels of TR4 expression were significantly associated with higher lymph node metastases, TNM stages, tumor thrombus in vana and poor prognosis with significant difference. We observed that downregulation of TR4 with stable cell transfection significantly reduced the proliferation, invasive and metastatic abilities of NSCLC cell lines A549 and PC-9. In addition, aberrant TR4 expression could modulate the expression levels of several epithelial-to-mesenchymal transition (EMT) related markers. **Conclusion:** Collectively, our results show TR4 expression in NSCLC samples is significantly associated with poor clinicopathological features and an important role in metastatic capacity of NSCLC cells by EMT regulation.
Keywords: Testicular orphan receptor 4, Prognosis, metastasis, EMT

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-122 The Prognostic Significance of Galectin-3 Expression in Non-Small Cell Lung Carcinoma
Saraswati Pokharel[1], Sharmeen Mansoor[1], Umesh Sharma[2], Richard Cheney[3] [1]*Pathology, Roswell Park Cancer Institute, Buffalo/United States of America,* [2]*Cardiology, University of Buffalo, Buffalo/AL/United States of America,* [3]*Pathology, Roswell Park Cancer Institute, Buffalo/AL/United States of America*

Background: Galectin-3 (gal-3) is a beta-galactoside binding protein expressed by various cells and is overexpressed in several malignancies, including lung cancer. Preclinical cancer models have shown gal-3 to be associated with tumor cell transformation, invasive behavior, and metastasis. The role of gal-3 in lung cancer has not been well studied. The aim of this study is to examine the prognostic significance of gal-3 overexpression in non-small cell lung carcinoma (NSCLC). **Methods:** Using pathology archives from our cancer center, tissue microarray (TMA) were constructed of 248 resected NSCLC and matching normal lung tissue. Gal-3 protein expression was assessed by immunohistochemical analysis (IHC). The staining pattern of triplicate tumor cores spread in to 3 TMAs were scored semi- quantitatively as: 0, negative, 1 weak, 2, moderate, and 3 strong. Average score was calculated and the score up to 1 was regarded as low expression and 2 and 3 were regarded as high expression. One or less cores were available for 24 cases and they were excluded from the study. The association between gal-3 score and 5-year survival, nodal metastasis, and cancer stage were analyzed using chi-square test. **Results:** Of the 224 patients included, 217 were squamous cell carcinoma and 7 were other types of NSCLC. Normal lung tissues had mean gal-3 score of 0 (median score 0, range 0-2). Tumor samples had mean gal-3 score of 2 (range 0-3) with 62% of the samples having gal-3 score of ≥ 2. In this data set, high gal-3 score was associated with less than 5-year survival rate (p=0.04) but not associated with nodal metastasis, nor higher stage (stage II-IV) in NSCLC patients. **Conclusion:** Gal-3 expression is increased in more than 60% of NSCLC, particularly squamous cell carcinoma. Higher gal-3 protein expression is associated with poorer prognosis in this cohort. Larger studies are necessary to evaluate gal-3 as prognostic factor in NSCLC.
Keywords: Galectin-3, lung cancer, survival

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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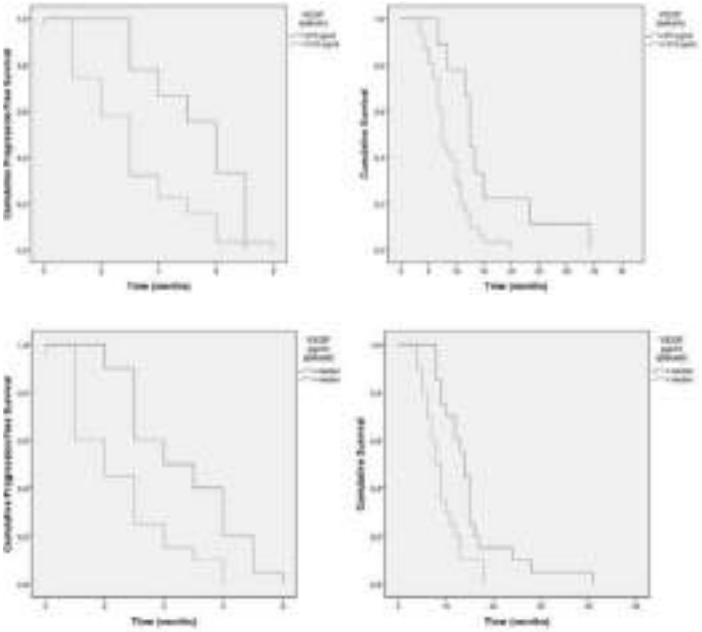
P3.04-123 Serum and Pleural Fluid VEGF Levels in Advanced NSCLC
Ioannis Gkiozos, Sofia Tsagouli, Andriani Charpidou, Dimitra Grapsa, Elias Kainis, Christina Gratziou, Konstantinos Syrigos *University of Athens, Athens/Greece*

Background: Although most previous studies have suggested that higher pretreatment serum vascular endothelial factor (VEGF) levels may be associated with reduced survival in patients with non-small cell lung cancer (NSCLC), the independent prognostic value of this biomarker remains largely controversial. The primary aim of this study was to evaluate the prognostic significance of pretreatment serum and pleural fluid VEGF levels in NSCLC patients presenting with malignant pleural effusion (MPE). **Methods:** Forty consecutive newly diagnosed NSCLC patients with MPE at presentation but without distant metastases were prospectively enrolled. Serum and pleural fluid VEGF levels were assayed by enzyme-linked immunoassay (ELISA). ROC curve analysis was used to determine the optimal cut-off value for serum VEGF to discriminate between patients and healthy subjects. Serum and pleural fluid VEGF levels were correlated with standard clinicopathological parameters, including gender, age, smoking history, performance

status (PS), histological type of tumor and treatment response. The prognostic value of each variable for overall survival (OS) and progression-free survival (PFS) was assessed by Cox regression analysis. **Results:** The median serum VEGF levels were significantly higher in patients as compared to healthy controls (p<0.001), while the optimal cut-off of serum VEGF was 375 pg/ml, with a sensitivity and specificity of 76.9% and 98.0%, respectively. Serum VEGF more than 375 pg/ml, pleural fluid VEGF over the median value and the presence of progressive disease, were all significantly associated with reduced OS and PFS, both in univariate and multivariate analysis (Figures 1 and 2). A statistically significant correlation was also observed between serum and pleural fluid VEGF levels (p<0.001).



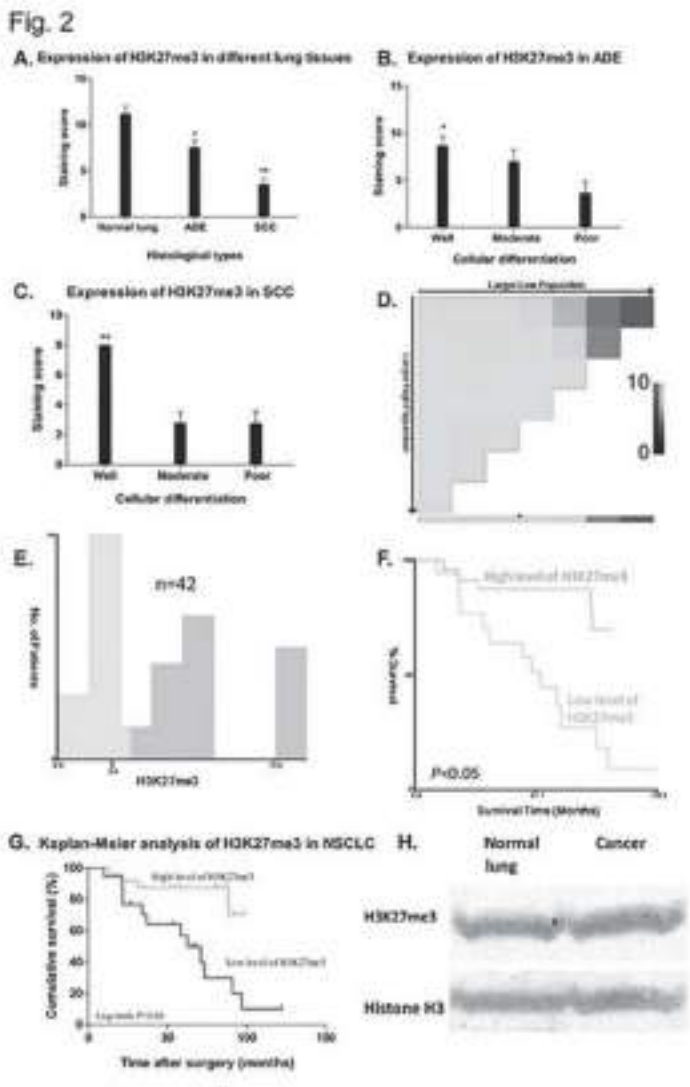
Conclusion: Our results suggest that increased pretreatment serum and pleural fluid levels of VEGF may be independent predictors of a worse survival in advanced-stage NSCLC patients. Furthermore, pretreatment serum VEGF levels may be useful in discriminating between NSCLC patients and healthy subjects. **Keywords:** vascular endothelial growth factor, non-small cell lung cancer, pleural fluid, serum

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-124 High Expression of Trimethylated Histone H3 at Lysine 27 Predicts Better Prognosis in Non-Small Cell Lung Cancer Xiaohui Chen[1], Ning Song[2], Keitaro Matsumoto[3], Takeshi Nagayasu[3], Hayashi Tomayoshi[4], Mingang Ying[1], Takehiko Koji[2] [1]*Thoracic Surgery, Fujian Provincial Cancer Hospital, Fuzhou/China,* [2]*Department of Histology and Cell Biology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, Nagasaki/Japan,* [3]*Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Science, Nagasaki, Nagasaki/Japan,* [4]*Department of Pathology, Nagasaki University Hospital, Nagasaki, Nagasaki/Japan*

Background: Lung cancer is still the leading cause of cancer death in both sexes throughout the world. The alterations in epigenomes such as DNA methylation and histone modifications play pivotal roles in carcinogenesis. It has been reported that DNA methylation level and global histone modification patterns may be possible predictors of cancer recurrence and prognosis in a large variety of cancer entities. One such repressive modification, the trimethylation of lysine 27 on histone H3 (H3K27me3), seemed to be an epigenetic label mediating gene silencing; and a mark for *de novo* DNA methylation in cancer cells by recruitment of DNA methyltransferase (DNMTs) , contributing to tumor progression through suppression of a certain gene expression. In fact, many recent studies have revealed that H3K27me3 may be involved in the characterization of various types of human cancers, excluding NSCLC. Interestingly, reports of H3K27me3 levels in different cancer samples are somewhat contradictory. It's demonstrated that low H3K27me3 levels predicted poor outcome in breast, ovarian and pancreatic cancers while high levels predicted poor outcome in hepatocellular carcinoma and esophageal squamous cell carcinoma. Moreover, H3K27 methylation is catalyzed by its specific methyltransferase, EZH2. Overexpression of EZH2 was also found in a variety of cancers, resulting in worse clinical outcome. Although many reports on the role of H3K27me3 in carcinogenesis were available, its carcinogenic role in NSCLC and how it interacts with EZH2 and DNA methylation remain unclear. **Methods:** Expressions of H3K27me3 and its methyltransferase, enhancer of zeste homolog 2 (EZH2) together with proliferating cell nuclear antigen (PCNA) were evaluated by immunohistochemistry in normal lung tissue (n=5) and resected NSCLC patients (n=42). In addition, the specificity of antibody for H3K27me3 were testified by western blotting. The optimal cut-point of H3K27me3 expression for prognosis was determined by the X-tile program. The prognostic significance was determined by means of Kaplan-Meier survival estimates and log-rank tests.

Results:



Enhanced trimethylation of H3K27me3 was correlated with longer OS and better prognosis (P<0.05). Both univariate and multivariate analyses indicated that H3K27me3 level was a significant and independent predictor of better survival (hazard ratio, 0.187; 95% confidence interval, 0.066-0.531, *P*=0.002). Furthermore, H3K27me3 expression was positively correlated with DNA methylation level at CCGG sites while reversely related to EZH2 expression (P<0.05) **Conclusion:** H3K27me3 level defines unrecognized subgroups of NSCLC patients with distinct epigenetic phenotype and clinical outcome, and can probably be used as a novel predictor for better prognosis in NSCLC patients. **Keywords:** non-small cell lung cancer, H3K27me3, epigenetics, EZH2, DNA methylation

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.04-125 Cytokine Profiles in Non-Small Cell Lung Cancer Patients Undergoing Palliative Thoracic Radiotherapy; Predictor of Response? Hanne A. Eide[1], Ann R. Halvorsen[1], Anne Fåne[2], Jon A. Kyte[2], Odd Terje Brustugun[3], Åslaug Helland[4] [1]*Department of Cancer Genetics, Oslo University Hospital - the Norwegian Radium Hospital, Oslo/Norway,* [2]*Departement for Cell Therapy, Oslo University Hospital - the Norwegian Radium Hospital, Oslo/Norway,* [3]*Department of Oncology, Oslo University Hospital-The Norwegian Radium Hospital, Oslo/Norway,* [4]*Department of Oncology, The Norwegian Radium Hospital, Oslo/Norwa, Oslo/Norway*

Background: A majority of patients with non-small cell lung cancer are diagnosed in later stages of disease where no curative treatment is currently available. The prognosis for these patients is poor. Median survival from diagnosis in stage IV is approximately 9 months. Many patients will benefit from external radiotherapy to the thorax for alleviation of symptoms due to advanced lung cancer. Despite adequate radiotherapy, however, many tumors progress locally in the radiation field. Here, we investigate whether the kinetics of cytokines in serum can be utilized as predictors for tumor response to radiotherapy and/or predictors of lung toxicity. **Methods:** Patients with histologically confirmed non-small cell lung cancer, eligible for palliative radiotherapy to the hilus-mediastinum, were included in a randomized phase II clinical trial; the ThoRaT-study. Patients were randomised to 1 of 2 study arms undergoing thoracic radiotherapy, 3 Gy

x 10, with or without the addition of erlotinib concomitant with radiotherapy treatment. Side effects were recorded and graded according to CTC version 4.0. Clinical response in the radiation field was evaluated by CT or PET-CT scans. Blood serum was sampled at different time points; prior to treatment, at mid-therapy, at the end of therapy and 6 week following treatment completion. Multiplex immunoassays were used to measure serum concentration of 52 cytokines and 9 MMPs on all collected samples. Serum samples from COPD patients were included as controls. **Results:** Cytokine analyses of serum samples are ongoing and have to date been performed on 43 non-small cell lung cancer patients. Pre-treatment and follow up CT/PET-CT scans are currently under revision. Preliminary investigations show considerable variation in cytokine patterns between the patients and between different time points for some of the cytokines. Analyses of possible predictors for radiotherapy response and toxicity, as well as comparison with normal controls are currently ongoing and will be presented. **Conclusion:** We hypothesize that pre-treatment cytokine values and/or kinetics of concentration changes may provide information on the probability of clinical response and side effects from radiotherapy. **Keywords:** cytokines, non-small cell lung cancer, Radiotherapy

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-126 Expression of Notch1 and Notch2 in Xuanwei Female Patients with Lung Cancer and Its Clinical Significance Yunchao Huang, Huatao Niu, Guangqiang Zhao, Yujie Lei *Thoracic Surgery, The Third Affiliated Hospital of Kunming Medical University, Kunming/China*

Background: To explore the expression of Notch1 and Notch2 in Xuanwei female patients with lung cancer and its clinical significance. **Methods:** The expression of Notch1 and Notch2 in the cancer tissue and distant normal tissue from 54 Xuanwei female patients with lung cancer was detected using immunohistochemical SP method. By combining with the clinicopathological characteristics and follow-up files, the functions of Notch1 and Notch2 in Xuanwei female patients with lung cancer for pathological and prognostic assessment were investigated. **Results:** Both Notch-1 and Notch-2 proteins were mainly expressed in cytoplasm. The positive rates of Notch-1 and Notch-2 expression in the lung cancer tissue of Xuanwei females were dramatically higher than in distant normal tissue ($P<0.05$). There was statistical significance by comparison to the expression of Notch-1 and Notch-2 in patients with different clinical stagings, differentiated degrees and presence or absence of lymph node metastasis ($P<0.05$). The expression of Notch-1 and Notch-2 proteins was positively correlated in Xuanwei female patients with lung cancer. **Conclusion:** The expression of Notch-1 and Notch-2 proteins goes up abnormally in the lung cancer tissue of Xuanwei females, and their expression levels combined with clinical staging has a certain clinical significance for prognostic assessment in Xuanwei female patients with lung cancer. **Keywords:** Notch1; Notch2; Female; Lung cancer, Xuanwei

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-127 Correlation Between ApoA-I and Prognosis of Advanced NSCLC Patients Chong Bai, Hui Shi, Qin Y. Sun, Yu C. Dong *Respiratory Department, Changhai Hospital, Shanghai/China*

Background: To investigate the correlation between apolipoprotein A-I(ApoA-I) and clinicopathological features, as well as the effect of ApoA-I on the prognosis of advanced non-small cell lung cancer (NSCLC) patients. **Methods:** Retrospective analysis was performed for 117 cases with histologically confirmed IIIB and IV stage NSCLC patients in Changhai Hospital from January 2009 to December 2014. All patients were classified into two groups based on the value of baseline serum ApoA-I before treatment. The relationship between ApoA-I and clinicopathological features was studied. Univariate and multivariate analyses were performed to assess the prognostic effect of ApoA-I. **Results:** All patients were divided into two groups: low serum ApoA-I levels before treatment (≤1.2g/L, n=50,42.7%) and high serum ApoA-I levels before treatment (>1.2g/L, n=67,57.3%).ApoA-I was correlated with greatest tumor diameter (P=0.013), clinical stage(P=0.012),serum C-reactive protein before treatment (P=0.018),serum albumin(P<0.0001)and ECOG PS(P=0.024).The median survival time of low and high ApoA-I levels patients were10.1months and15.1 months, respectively,which indicated a statistically significant difference ($\chi 2$=7.027,P=0.008) between the two groups.Univariate analysis showed that smoking status (P=0.029), serum C-reactive protein before treatment (P=0.024),serum albumin (P=0.013),clinical stage(P=0.014),N stage (P=0.037) ,ECOG PS (P=0.001)and serum ApoA-I levels before treatment (P=0.008).Multivariate analysis by using COX regression identified serum C-reactive protein before treatment (HR1.650, P=0.033),clinical stage (HR2.165 , P=0.001), ECOG PS (HR0.451,P=0.008)and serum ApoA-I levels before treatment (HR0.487,P=0.005) as independent prognostic factors of all the patients.In addition, stratified analysis showed that the one-year survival rate of the low ApoA-I group was lower than that of the high ApoA-I group with or without distant metastasis, and the differences were statistically significant ($\chi 2$=12.053, P=0.001). **Conclusion:** An decreased serum ApoA-I levels before treatment indicates poor prognosis in advanced NSCLC patients. ApoA-I could be a potential biological marker for advanced NSCLC patients. **Keywords:** apolipoprotein A-I, Prognosis, non-small cell lung cancer

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-128 Does the Amount of Malignant Pleural Effusion Affect the Survival in Patients with Non-Small Cell Lung Cancer? Shota Nakamura, Toshiki Okasaka, Koji Kawaguchi, Takayuki Fukui, Koichi Fukumoto, Kohei Yokoi *Thoracic Surgery, Nagoya University, Nagoya/Japan*

Background: Malignant pleuritis in non-small cell lung cancer (NSCLC) is uniformly classified as M1a/stage IV disease according to the 7th TNM classification irrespective of its amount of malignant pleural effusion (MPE) and is considered as an incurable disease condition. Although it has been reported that small amount of MPE might be an early phase of malignant pleuritis, its clinical relevance has rarely been studied. Therefore, we examined an impact of the amount of MPE on the survival in patients with NSCLC. **Methods:** Sixty NSCLC patients with malignant pleuritis were treated in our institution between 2005 and 2012. By the amount of MPE on chest high resolution computed tomography (HRCT) scans, the patients were classified into the three groups: no MPE (E0, n=21), small amount of MPE (<1.0 cm thick on HRCT) (E1, n=19), and large amount of MPE (≥1.0 cm thick on HRCT) (E2, n=20). Clinicopathological factors including the amount of MPE were investigated for the association between the amount of MPE with the survival regardless of the treatment. **Results:** The E2 group correlated significantly with shorter survival than did the E0 and the E1 groups (median survival time, 16, 31 and 20 months, respectively; log-rank $P<.01$), but there was no significant difference between the E0 and E1 groups. In the univariate analysis, the amount of MPE (E0 + E1 vs E2), histopathological type (adenocarcinoma vs others), treatment (chemotherapy or surgery vs best supportive care) and EGFR mutation (positive vs negative) were significant prognostic factors. After full adjustment with other variables, the amount of MPE, histopathological type and EGFR mutation remained as significant prognostic factors. **Conclusion:** The amount of MPE in NSCLC might be an important prognostic factor and affect the patients' survivals. We suppose the present TNM classification, which uniformly define MPE as M1a/IV status irrespective of the amount of MPE, is necessary to be reconsidered. **Keywords:** non-small cell lung cancer, TNM classification, malignant pleural effusion, malignant pleuritis

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-129 Prognostic Factors and Biomarkers in Large Cell Carcinoma and Neuroendocrine Tumors of the Lung in the Thai Population Phannin Tiraswasdichai[1], Narumol Trachu[1], Noppadol Larbcharoensub[2], Nanamon Monnamo[1], Kiattipong Kamprerasart[2], Ekaphop Sirachainan[1], Thanyanan Reungwetwattana[1] [1]*Department of Medicine, Ramathibodi Hospital, Bangkok/ Thailand,* [2]*Department of Pathology, Ramathibodi Hospital, Bangkok/Thailand*

Background: There are limited data on prognostic factors and biomarkers of large cell carcinoma and neuroendocrine tumors of the lung (LCC/NETs) due to decreasing prevalence and the lack of large epidemiological studies. This study describes the natural history and clinical behavior of the disease including exploration of molecular alterations of LCC/NETs in the Thai population. **Methods:** Patients who had a diagnosis of LCC/ NETs of the lung from January 2000 to August 2014 were identified from the tumor registry of Ramathibodi Hospital. Data on the natural history and clinical behavior of the disease were collected. The association and predictive ability of patient and tumor characteristics with overall survival (OS) and recurrence-free survival (RFS) outcomes were examined, respectively. In 46 patients with adequate tumor tissue, Ki-67, neuroendocrine markers, CD117, HER-2, PDL-1, ALK, and IGF1-R were evaluated by immunohistochemistry staining (IHC). In addition, *EGFR, PIK3CA* and *BRAF V600E* mutations were evaluated by real time PCR. **Results:** Medical records of 191 patients were reviewed. OS rates at 1 year for small cell lung cancer (SCLC), neuroendocrine carcinoma (NEC) and LCC were 39.7%, 63.6% and 32.6%, respectively. The RFS rates at 1 year for SCLC, NEC and LCC were 25.4%, 10.6% and 14.0%, respectively. There were 3 significant factors predicting for better survival outcomes. These included age, ECOG performance status, and receiving chemotherapy. There was no difference in Ki-67 expression between the SCLC and LCC/ NEC groups. In the molecular analysis, 10.8% of patients expressed ALK, 41.3% expressed CD117 (c-KIT), 23.9% expressed PDL1, and 78.3% expressed IGF1-R. In the mutational analysis, 4.9% of patients had a *PIK3CA* mutation, and 9.8% had an *EGFR* mutation. 19 out of 46 patients (41.3%) who had positive CD117 expression had better 1-year survival rate than the negative group (68.4% vs 29.6%, $P=0.018$). No *c-kit* mutation was found in exons 9 and 11

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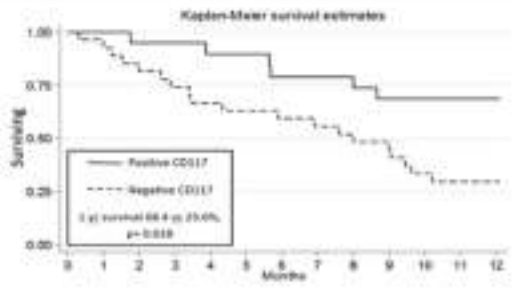
Figure 4: Kaplan-Meier curve of overall survival at 1 year according to CD117 expression (n=46)



Conclusion: Our study provided strong evidence for clinical features (age, ECOG performance status, receiving chemotherapy) as prognostic factors for LCC/NETs of the lung. CD117 expression is a useful biomarker to predict OS. While earlier studies with Imatinib in both SCLC and NSCLC were negative, further mechanistic studies in the role of CD117 in LCC/NETs may yield therapeutic insights. Finally, larger studies to further explore the molecular alterations of LCC/NETs of the lung are needed.
Keywords: neuroendocrine tumor of the lung, small cell lung cancer, large cell carcinoma, large cell neuroendocrine carcinoma

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-130 Frequency of GST Polymorphisms in Lung Cancer and Healthy Individuals from Turkey
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Background: Glutathione S-transferases play an important role in detoxification of a wide range of human carcinogens. Functional polymorphisms have been identified in the GSTM1, GSTT1, GSTP1 genes, which may alter the risk of lung cancer among individuals exposed to coal, wood, and biomass smoke, and cooking oil fumes. **Methods:** We have evaluated the association between the GSTM1, GSTT1, GSTP1 Ile105Val and GSTP1 Ala114Val polymorphisms and lung cancer risk. All genotypes were detected by reverse hibridization method. Demographics datas, genotypes and allele frequencies are evaluated. **Results:** Prospectively 351 lung cancer and 103 control cases included to the study from 7 centers in Turkey. Mean age was 60 years and 76.4% of them were male. Subgroups of the cases are shown in table 1. All genotypes of four polymorphisms are found similar between the cancer and control group (table 2). Although we found no statisticaly significant correlation between the polymorphisms and occupational risk, smoke cessation, living area, biomass exposure and familial cancer history (*p>0,05*). GSTP1 *105 and *114 compaund heterozygote genotypes increase the lung cancer risk approximately 2,5 folds (*OR=2,463;p=0,051*). Moreover GST *105 and *114 compaund heterozygote genotypes increase squamous cell cancer risk 3 folds (*OR=2,992;p=0,028*) and undiferantial carcinoma risk 4 folds (*OR=4.015;p=0.016*). **Table 1.**Lung cancer subgroups

	n	%
Squamous cell carcinoma	133	37,9
Adenocarsinoma	98	27,9
Undifferentiated carcinoma	55	15,7
Small cell carcinoma	47	13,4
Large cell carcinoma	10	2,8
Adenosquamous carcinoma	8	2,3

Table 2.GSTM1/T1/*105/*114 Genotype Distributions in Lung Cancer and Control Cases

Genotypes		**Lung cancer**	**Lung cancer**	**Control**	**Control**	**p**
		n	%	n	%	
GSTP1 **Ile105Val**	AA	169	48,1	56	54,4	
GSTP1 **Ile105Val**	AG	158	45,0	39	37,9	0,437
GSTP1 **Ile105Val**	GG	24	6,8	8	7,7	
GSTP1 **Ala114Val**	CC	289	82,3	88	85,4	
GSTP1 **Ala114Val**	CT	60	17,1	15	14,6	0,610
GSTP1 **Ala114Val**	TT	2	0,6	0	0,0	
GSTM1	**(+)**	187	53,3	52	50,5	0,654
	(-)	164	46,7	51	49,5	
GSTT1	**(+)**	253	72,1	75	72,8	1,00
	(-)	98	27,9	28	27,2	
Total		351	100,0	103	100,0	

Conclusion: In order to the most frequent lung cancer type is adenocarcinoma in world wide, our study indicate that epidermoid carcinoma was the most frequent type in our country. Recent studies showed that GST genes are expressed at human epitelial tissues including lungs. GST gene expressions are overexpressed expecially tumor tissues. Our results indicate that GST polymorphisims may play an important role at tumor pathogenesis. Therefore GSTP1 Ile105Val and Ala114Val functional polymorphisims' mutant genotypes are more relevant for Squamous cell and Undifferentiated carcinoma pathogenesis.
Keywords: lung cancer, GST genes, polymorphisim

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-131 Relationship between Peripheral Basophil Count and Non Small Cell Lung Cancer
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Background: Lung cancer is the second most common cancer diagnosed in men and women after prostate and breast respectively. Basophils are the novel targets in cancer directed immunotherapy. We propose to study co-relationship between absolute counts of peripheral basophils in patients with NSCLC. **Methods:** The study was conducted at 651 bedded tertiary care teaching hospital in Northern New Jersey, USA. The protocol was classified as "exempt" by the hospital's institutional review board. The study included 561 patients with a primary diagnosis of NSCLC registered with the hospital's tumor registry from January 2001 to June 2011. Medical records were reviewed for these patients and Age, sex, race, WBC count, absolute basophilic count, histological type and TNM staging of all patients was noted at the time of diagnosis. The exclusion criteria were: 1. Patients whose biopsy reports were unavailable in the medical records or 2. Patients whose TNM Stage or Absolute Basophil Counts were unavailable at the time of diagnosis or 3. 18 years or less in age at the time of diagnosis. Data analysis was done using Microsoft Office Excel, 2007. **Results:** Mean age for the diagnosis was 67.6±11.1 year. Adenocarcinoma (49.1%) was the most common diagnosis followed SCC (40.9%). Caucasians (61%) were more commonly diagnosed adenocarcinoma and SCC then African Americans (25.7%) & other races (13.2%). Males (64.2%) were more commonly diagnosed than females. Most of the cancers were diagnosed in the late stages (Stage III; 25.7% & Stage IV; 32.9%) accounting for 58.6% of the tumor burden. Mean White blood cell (WBC) count was 9.34±5.56 (*10^3/mm^3). There were no statistically significant differences noticed in WBC counts based on histology for Adenocarcinoma: 8.66±4.16 (p=0.103) and SCC: 9.71±5.69 (p=0.453) except other cancers: 11.20±9.26 (p=0.046). Mean peripheral basophil count (PBC) was 0.0959±0.099 (*10^3/mm^3). Based on histological types, there were no statistically significant differences noticed in PBC counts for Adenocarcinoma: 0.0897±0.0851 (p=0.418) and SCC: 0.0961±0.1048 (p=0.976) other cancers: 0.1253±0.1283 (p=0.06). Further, we assumed PBC of stage1 as baseline for all the cancers subtypes and compared PBC with stage II, III & IV using student t-test (table 2). There was no statistical difference between PBC with any stages and histological subtypes. With the p-value trending towards significance in other cancers group. Mean PBC was statistically higher for the Undifferentiated cancers (p= 0.0359; 95% CI ±0.048). NSCLC weakly correlated with absolute basophils (Adjusted R^2 = -0.000228, p = 0.70). Median interval change did not vary significantly between stages of adenocarcinoma and SCC (Kruskal-Wallis p value: 0.8702, 0.5798 respectively). **Conclusion:** Though, the study was unable to demonstrate any relationship between peripheral basophil count and adenocarcinoma or SCC of lung. But surprisingly, there is a positive relationship between Undifferenciated lung cancer and PBC. But

to translate this result in clinical significance will be difficult as absolute PBC may be very small. The mean age of diagnosis and male sex being predominantly affected corroborates with the current literature. We recommend further studies to compare the PBC in NSCLC patients with age, gender and ethnicity matched population controls
Keywords: basophill count, non small cell lung cancer, peripheral basophill count, cancer immunotherapy

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P3.04-132 Expression of nm23 and CD44v6 Proteins in Non-Small Cell Lung Cancer and Their Clinical Significance Patiguli Aerxiding, Guoqing Zhang, Ling Ma
First Department of Medical Oncology, Cancer Hospital Affiliated To Xinjiang Medical University, Urumqi/China

Background: To investigate the expression of nm23 and CD44v6 proteins in non-small cell lung cancer (NSCLC) and their clinical significance. **Methods:** The expression of nm23 and CD44v6 proteins was detected in 58 NSCLC samples using two-step immunohistochemistry. **Results:** The overall positive rate of nm23 was 87.9% (51/58), and significant difference was presented between T1～T2 groups and T3～T4 groups ($P<0.05$). The overall positive rate of CD44v6 was 55.2% (32/58), in which that of squamous cell carcinoma was dramatically higher than that of adenocarcinoma (85.7% *vs.* 24%, $P<0.05$). The positive rate of moderately-differentiated group was higher than that of poorly-differentiated group (71.9% *vs.* 44.4%,$P<0.05$). The expression of nm23 and CD44v6 was not associated with pTNM staging, lymph node metastasis and survival rate ($P>0.05$). **Conclusion:** The expression of nm23 and CD44v6 proteins is correlated with the tumor size (T), pathological types and differentiated degrees of NSCLC instead of pTNM staging and lymph node metastasis.
Keywords: genes; nm23, non-small cell lung cancer; gene expression; antigens; CD44

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P3.04-133 ADAM9 and EGFR Correlated With Lymph Node Metastasis Predicts Worse Prognosis in Surgically Resected Non-Small Cell Lung Cancer Jun Zhang[1], Ning Chen[2], Juan Qi[3], Baosen Zhou[1], Xueshan Qiu[1] [1]*China Medical University Lung Cancer Center, The First Hospital of China Medical University, Shenyang/China,* [2]*Department of Logistic Management, College of Economics and Management, Liaoning University of Traditional Chinese Medicine, Shenyang/China,* [3]*Department of Molecular Targeted Therapeutics, The First Hospital of China Medical University, Shenyang/China*

Background: Recently we first reported that a disintegrin and metalloproteinase-9 (ADAM9) was highly expressed in resected non-small cell lung cancer (NSCLC), correlated with lymph node metastasis, shorterned survival time. ADAM9 has been known of being able to enhance the expression of epidermal growth factor receptor (EGFR) pathway, here, we investigate the expression of EGFR in surgically resected NSCLC, to elucidate the relationship between EGFR expression and lymph node metastasis, prognosis, and further evaluate the consistence of ADAM9 expression and EGFR expression, and their significance as novel biomarkers in molecular staging, predicting the prognosis for surgically resected NSCLC. **Methods:** One hundred and six cases of completely resected stage Ⅰ, Ⅱ and Ⅲ NSCLC with mediastinal N2 lymph nodes dissected were immunohistochemically analyzed for EGFR and ADAM9 protein expression. Survival analysis was conducted to assess the significance of EGFR and ADAM9 expression and the relationship with other clinicopathological characteristics. **Results:** Of the 106 NSCLC, 49 were stage Ⅰ, 16 stage Ⅱ and 41 stage Ⅲ; 60.4% was found with EGFR protein highly expressed (EGFR+), significantly higher when compared with normal control lung tissues (P=0.000). The EGFR+ rate in stage Ⅱ and Ⅲ NSCLC was 73.7%, significantly higher than 44.9% in stage Ⅰ (P=0.003). Stratified, EGFR+ rates in N1 and N2 cases was 72.0%, significantly higher than 50.0% in N0 NSCLC (P=0.021); the difference between EGFR+ rates in T factor groups was not statistically significant (P>0.05). The overall 5-year survival rate was 55.7% for this group of 106 completely resected NSCLC. The 5-year survival rate in EGFR low expression (EGFR-) group (42 cases) was 74.9%, however, the 5-year survival rate was sharply decreased to 43.2% in EGFR+ group (64 cases) (P=0.001). For ADAM9, the ADAM9+ rates in stage Ⅱ and Ⅲ NSCLC was significantly higher than in stage Ⅰ (P=0.013). Stratified, ADAM9+ rates in N1 and N2 cases was significantly higher than in N0 NSCLC (P=0.040). The difference between ADAM9+ rates in T factor groups was not statistically significant (P>0.05). The 5-year survival rate in ADAM9+ group was statistically lower than in ADAM9- group (P=0.040). EGFR expression was revealed correlated positively and significantly with ADAM9 expression in this group of surgically resected NSCLC (Pearson r=0.275, P=0.004). **Conclusion:** This report for the first time revealed the relationship of expression of EGFR and ADAM9 protein in human lung cancer tissues. EGFR and ADAM9 are highly expressed in human resected NSCLC, correlated with lymph node metastasis and pTNM stage; highly expressed EGFR and ADAM9 predicts worse prognosis, suggesting that EGFR and ADAM9 are useful molecular staging biomarkers, and prognostic biomarkers for NSCLC. EGFR and ADAM9 may also become useful predictive biomarkers helping decide if postoperative chemo-radiation therapy should be selected or not. (This study was partly supported by grants from the Education Department of Liaoning Province, China, No. 20060991; the Nature Science Foundation of Liaoning Province, China, No.20102285; and the Fund for Scientific Research of The First Hospital of China Medical University, No.FSFH1210).
Keywords: EGFR, molecular stage, Prognosis, ADAM9

POSTER SESSION/ BIOLOGY, PATHOLOGY, AND MOLECULAR TESTING
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P3.04-134 Cancer-Specific Production of N-Acetylaspartate via NAT8L Overexpression in Non-Small Cell Lung Cancer and its Potential as a Biomarker Tzu-Fang Lou[1], Deepa Sethuraman[2], Patrick Dospoy[3], Pallevi Srivastva[1], Hyun Seok Kim[4], Joongsoo Kim[5], Xiaotu Ma[6], Pei-Hsuan Chen[7], Kenneth E. Huffman[8], Robin E. Frink[8], Jill E. Larsen[9], Cheryl Lewis[10], Sang-Won Um[11], Duk-Hwan Kim[12], Jung-Mo Ahn[5], Ralph J. Deberardinis[7], Michael A. White[13], John D. Minna[8], Hyuntae Yoo[14]
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Background: Lung cancer is the leading cause of cancer death worldwide, leading to 1.6 million deaths every year. The majority of lung cancer cases are diagnosed in late stages, and early-stage detection and treatment are now known to reduce mortality rates, as recently reported for non-invasive screening with low-dose CT (LDCT) scan. Currently, LDCT screening is recommended only for the high-risk population of smokers over 55 years of age. This limitation is due to high false positive rates (96.4%) as well as risks of radiation exposure in LDCT. For better screening methods, recent studies have attempted to use diverse biological fluid samples from patients for finding new lung cancer biomarkers. Unlike diagnostic biomarkers that are required to have high sensitivity for clinical application, screening biomarkers must have high specificity (i.e. low false positive rates) in order to avoid a large number of people without lung cancer from undergoing invasive or costly procedures for confirmation. Among recent studies on new lung cancer biomarkers, only one small-scale study identified a panel of blood microRNAs with cancer-specificity higher than 99%. **Methods:** In order to expedite the discovery of candidates for cancer-specific metabolites in lung cancer, we exploited a unique system of a non-small cell lung cancer (NSCLC) cell line and a line of immortalized bronchial epithelial cells derived from the same patient, HCC4017 and HBEC30KT, for the initial discovery. After molecular characterization, we validated the selected candidate's cancer specificity in additional NSCLC cell lines and NSCLC tumors. The mechanistic basis of this cancer specificity was further investigated with NSCLC cell lines, and its clinical potential as a circulating biomarker of lung cancer was evaluated with selected blood samples from lung cancer patients. **Results:** Among several metabolites with significant cancer/normal differences, we identified a unique metabolic compound, N-acetylaspartate (NAA) in cancer cells ¾ undetectable in normal lung epithelium. NAA's cancer-specific detection was validated in additional cancer and control lung cells as well as selected NSCLC patient tumors and control tissues. NAA's cancer-specificity was further supported in our analysis of NAA synthetase (gene symbol: NAT8L) gene expression levels in The Cancer Genome Atlas: elevated NAT8L expression in approximately 40% of adenocarcinoma and squamous cell carcinoma cases (N=577), with minimal expression in all non-malignant lung tissues (N=74). We then showed that NAT8L is functionally involved in NAA production of NSCLC cells through siRNA-mediated suppression of NAT8L, which caused selective reduction of intracellular and secreted NAA. Our cell culture experiments also indicated that NAA biosynthesis in NSCLC cells depends on glutamine availability. For preliminary evaluation of NAA's clinical potential as a circulating biomarker, we developed a sensitive NAA blood assay and found that NAA blood levels were elevated in approximately 40% of NSCLC patients (N=13) in comparison with age-matched healthy controls (N=21) among individuals aged 55 years or younger. **Conclusion:** Taken together, these results indicate that NAA is produced specifically in NSCLC tumors through NAT8L overexpression and its extracellular secretion can be detected in blood.

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POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
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P3.05-001 The Role of Big Tobacco in the Creation of the Expanding Epidemic of Smoking-Related Adenocarcinoma of the Lung Gary Strauss[1], Alejandro Moreno-Koehler[2], Matthew Finkelman[3] [1]*Hematology/Oncology, Tufts Medical Center, Boston/MA/United States of America,* [2]*Tufts Medical Center, Boston/MA/United States of America,* [3]*Tufts University School of Dental Medicine, Boston/MA/United States of America*

Background: In 1950, when the relationship between cigarette smoking and lung cancer was definitively demonstrated, adenocarcinoma of the lung comprised approximately 5% of lung cancers and appeared to be unrelated to smoking. Subsequently, the incidence

of lung adenocarcinoma increased sharply, and became strongly related to smoking. Utilizing SEER data on 419,941 lung cancers diagnosed between 1973 and 2011, we demonstrate that adenocarcinoma now comprises 55% of all lung cancers in the US. Adenocarcinoma rose in conjunction cigarette design changes introduced by the Tobacco Industry beginning in the 1950s in response to mounting evidence that smoking caused other forms of lung cancer. The objective of this abstract is to address how actions of Big Tobacco were primarily responsible for the rise of adenocarcinoma of the lung. **Methods:** Because SEER contains no information about cigarette smoking, other sources were utilized to correlate changing histology to time trends in smoking prevalence, the changing cigarette, and Tobacco Industry actions. These include internal Tobacco Industry documents, historical documents describing Tobacco Industry actions, several Surgeon General Reports, NCI Monograph #13, and the verdict of Civil Action No. 99-2496: "United States versus Phillip Morris et al." **Results:** Mounting evidence from population-based epidemiological analyses, the 1953 mouse painting experiments, and extensive press reporting created a crisis for the Tobacco Industry, as smoking rates temporarily dropped in the early/mid 1950s. While the Tobacco Industry consistently denied the evidence, they introduced filters and low yield cigarettes, inferring that modifications in cigarette design were safer. Indeed, many public health professionals believed that there would be some benefit from these changes insofar as compensation by smokers would be incomplete. Moreover, numerous epidemiologic studies appeared to support that filtered and low yield cigarettes conferred a lower lung cancer risk. Indeed, the 1981 Surgeon General Report on "The Changing Cigarette" concluded that individuals unable to quit should switch to filtered and low tar cigarettes. It was not until the analysis of Brown & Williamson internal documents in 1994 and other previously secret Tobacco Industry documents after the Master Settlement Agreement in the 1998 that it became abundantly clear regarding the extent to which the Tobacco Industry had knowingly deceived both the public and federal government about the safety of cigarette design changes for decades. **Conclusion:** Big Tobacco intentionally and extensively deceived the public during the second half of the 20th century. Trends in the rising incidence of adenocarcinoma of the lung correlate with the wide-scale adoption by smokers of filtered and low-yield cigarettes. Actions of Big Tobacco were predominantly responsible for the current epidemic of smoking-related lung adenocarcinoma.

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P3.05-002 Heterogeneity of Metformin Response for Lung Cancer Chemoprevention Michael Asiedu[1], Matthew Barron[1], Marie Christine Aubry[2], Dennis Wigle[3] [1]*Thoracic Surgery, Mayo Clinic, Rochester/United States of America,* [2]*Mayo Clinic, Rochester/MN/United States of America,* [3]*Thoracic Surgery, Mayo Clinic, Rochester/MN/United States of America*

Background: Squamous cell carcinoma accounts for about 25-30% of all non-small cell lung cancers. Metformin is a drug commonly prescribed as first-line treatment for type-2 diabetes, with some evidence showing that the drug can also act directly on cancer cells. Recent observational studies and meta-analysis show that diabetic patients who are long term users of metformin have lower risk for breast cancer and that metformin use lowered cancer development in the liver and lung. The goal of this study was to determine metformin response in different cell lines and different cellular contexts, and to use that information to work towards the generation of a metformin "sensitivity index" that could be used guide individualized chemoprevention. **Methods:** We performed cell survival analysis to assess differences in the sensitivity of patient-derived fibroblast cells and squamous cancer cell lines exposed to metformin. We also evaluated metformin response of Nkx2.1 positive lung progenitor cells that were differentiated from induced pluripotent stem (iPS) cells to identify differences for cells in different cellular contexts. Gene expression profiling and DNA sequencing analyses were performed to identify genes, pathways and genomic alterations that mediate metformin response in order to generate a "sensitivity index" for predicting metformin response. **Results:** Cell survival analysis showed that different cell lines respond differently to metformin, and cells of identical genotypes in a variety of differentiated states or cellular contexts also show differential response to metformin. Gene expression profiling of metformin treated cells identified eight differentially expressed gene including ADH1B, TMEM161B, CPED1, SNAI2, FOXF1 and DLGAP1 that may mediate metformin response. Exome sequencing and analysis identified unique single nucleotide variants (SNV) in TRAF3IP3, DMBT1, RIT2, SERPINB2, PIK3R2 that were present in all non-responders but absent in all responders. SNVs and indels present in all responders but absent in all non-responders included those in GRK7, SMARCA5, CTSB, CHD4, PLCB2, ZADH2, RPLP2, CLASP2, NEDD4, DNAH17, CPXCR1, LDHD and CLTC. **Conclusion:** Differences in response to metformin treatment across a variety of cell lines and cellular contexts suggest heterogeneity that may be patient-specific. A list of differentially expressed genes and genetic mutations can be used as a metformin "sensitivity index" to stratify patients into metformin responders and non-responders and guide individualized chemoprevention. **Keywords:** metformin, sensitivity, squamous cell cancer

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P3.05-003 Beliefs, Attitudes and Treatment Access to Lung Cancer amongst Nigeria Rural Men Malcolm O. Tagbarha *Public Health, University of Abuja, Abuja/Nigeria*

Background: Evidences of lung cancer cases from scientific researches have being on the rise in the last few decades and tobacco which is a major risk factor causes about 90% of cancer diagnosed around the world. The need to reduce this scourge has become more important **Methods:** An interview guide was designed specifically for these studies in which 1500 rural men in Nigeria most of which were age 35 and over took part in. It contained questions about beliefs, orientation, knowledge, understanding and attitudes about Lung Cancer Diagnosis and incidences. In addition, questions assessing the variables of the Health Belief Model and health motivations also were included. The data were obtained during face-to-face interviews in the primary language of the participating people. The interviews were translated into English **Results:** Out of the 1500 men who participated, only 10% of the participants knew about lung cancer, 5% had undergone at least one Lung Cancer Diagnosis during their lives, and 85% were not aware of the disease. There was little or no access to treatment even at early detection in these rural areas thereby causing vulnerability to loss of life. Majority of these men (95%) said they knew little or nothing about lung cancer. While 10% of the men said detecting cancer early was important, only 5% reported that cancer could be cured. Age, education, or mother tongue showed no statistically significant relationship with the lung health practice scores. However, proficiency with the English language ($p = 0.009$) and number of years exposed to awareness and education ($p = 0.009$) had a significant relationship with the lung health practice scores. The significant explanatory factor for the variable lung health practices was a cue to action ($p = 0.009$) **Conclusion:** The level of awareness and treatment access to lung cancer amongst Nigeria's rural men is extremely low thereby making them not to engage in screening and/or detection practices. This alarming situation calls for urgent intervention of medical/health organizations to provide immediate lung cancer awareness, diagnosis and care so as to reduce incidences or threat at early detection. Tobacco which is known as a major cause of cancer (90%) is widely used by these rural men thereby making them so vulnerable. Awareness is suggested while providing smoking cessation for smokers who intend to quit **Keywords:** lung cancer, tobacco, Smoking Cessation, lung cancer diagnosis

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
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P3.05-004 Lung Cancer Perception and Treatment Access Among Rural Smokers in Northern Nigeria Emmanuel Odiase *Epidemiology, University of Ibadan, Abuja/Nigeria*

Background: Despite alarming evidences of the damages smoking causes to health which includes lung cancer. A large number of rural populaces in disadvantaged regions still have little or no knowledge about lung cancer which is a major disease caused by smoking. **Methods:** We organized a community tobacco awareness program in four states in northern Nigeria. An interview guide was designed mainly for this purpose in which 1200 rural/illiterate smokers, male and female, aged 45 and over who had smoked for at least 15 years took part in. The interview guide contained questions about year of smoking initiation, number of sticks smoked daily, number of years as smoker. It also contained questions about the knowledge of smoking damage and/or lung cancer perception. In addition, questions assessing the variables of the Health Belief Model and health motivations also were included. The data were obtained during face-to-face interviews in the primary language of the participating people. The interviews were translated into English. **Results:** All together, 15% of the participants agreed that smoking was dangerous to their health. Only 5% had heard about lung cancer and 4% had undergone at least one Lung Cancer Diagnosis during their lives. There was little or no access to treatment even at early detection in these rural areas thereby causing vulnerability to loss of life. 15% of these rural smokers said detecting cancer early was important, only 3% reported that cancer could be cured. Age, education, or mother tongue showed no statistically significant relationship with the lung health practice scores. However, proficiency with the English language ($p = 0.009$) and number of years exposed to awareness and education ($p = 0.009$) had a significant relationship with the lung health practice scores. The significant explanatory factor for the variable lung health practices was a cue to action ($p = 0.009$). **Conclusion:** The level of awareness, perception of lung cancer and treatment access among rural and illiterate smokers in northern Nigeria is unacceptably low thereby making them not to engage in screening and/or detection practices. This alarming situation calls for urgent intervention of not-for-profit advocacy groups, tobacco-related medical/health organizations to provide immediate lung cancer awareness, diagnosis and care so as to reduce incidences or threat at early detection. **Keywords:** lung cancer, nigeria, rural, tobacco

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
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P3.05-005 Trends in Lung Cancer Survival in Middle East and Africa, 1995-2009 Zoubida Zaidi[1], Mokhtar Hamdi Cherif[2] [1]*Epidemiology, University Hospital of Setif, Setif/Algeria,* [2]*University Hospital of Setif, Setif/Algeria*

Background: Lung cancer is the most common cancer in men and the third most common in women. Tobacco smoking, including second-hand smoke, is the predominant cause of lung cancer worldwide. Screening for lung cancer is under development. It is one of the most aggressive human cancers, with a 5-year overall survival of 10-15%. **Methods:** Individual lung tumour records were submitted by 11 population-based cancer registries, 03 in Arab countries in Middle East (Jordan, Saoudi Arabia and Qatar) and 08 in Africa (Algeria, Lybia, Tunisia, Mali, Mauritius, Nigeria, South Africa and Gambia) for 6535 adults (15-99 years) diagnosed during 1995-2009 and followed up to 31 December 2009 . Estimated five-year net survival, adjusted for background mortality by single year of age, sex, calendar year in each country . **Results:** Age standardised five year net survival was generaly low in the range 10-20% for most geographical areas both in the developed and developing world. Survival was very low less than 10% (only 02% in Lybia). **Conclusion:** Surveillance of cancer survival is seen as important by national and international agencies, cancer patient advocacy groups, departments of health and research agencies. Cancer survival research is being used to formulate cancer control strategies to prioritise cancer control measures and to evaluate both the effectiveness and cost-effectiveness of those strategies.

Keywords: Cancer Registry, tobacco, mortality, Cancer Survival

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.05-006 Tobacco Control and the Trend of Lung Cancer Histology in Taiwan, 1994-2011 Yung-Hung Luo[1], Chun-Ming Tsai[2], Yu-Chin Lee[2], Jacqueline Whang-Peng[3], Yuh-Min Chen[2] [1]*Chest Medicine Division of Medicine Department, Fenglin Branch/ Department of Chest Medicine, Taipei Veterans General Hospital, Taipei/Taiwan,* [2]*Department of Chest Medicine, Taipei Veterans General Hospital, Taipei/Taiwan,* [3]*Taipei Cancer Center, Taipei Medical University, Taipei/Taiwan*

Background: Tobacco control policies in Taiwan have resulted in substantial declines in smoking prevalence and cigarette consumption. The ingredients of cigarettes have changed under government regulations. The changing epidemiology of lung cancer has also been observed in recent years. In this study, the lung cancer incidence and trend of histological types after the initiation of tobacco control policies were evaluated. **Methods:** We examined the data from Taiwan Cancer Registry to evaluate lung cancer incidence rates and frequencies of different histological type. The information of tobacco control and smoking prevalence from Health Promotion Administration and Food and Drug Administration in Taiwan were analyzed to identify the relation between tobacco control and lung cancer trend. **Results:** In total, 135073 individuals were diagnosed with lung cancer from 1994 to 2011 in Taiwan. The age-standardized incidence rate (ASIR) of all lung cancer patients increased significantly (22.3 per 10^5 in 1994 to 34.04 in 2011), and the average annual percentage change (AAPC) was 2.6 [95% confidence interval (CI): 2-3.2, $p < 0.0001$]. The ASIR of female lung cancer patients (13.82 per 10^5 in 1994 to 24.79 in 2011, AAPC 3.6, 95% CI: 2.8-4.5, $p < 0.001$) rose more rapidly than that of male patients (30.11 per 10^5 in 1994 to 44.21 in 2011, AAPC 2.4, 95% CI: 1.8-3, $p < 0.0001$). Adult (≥18y/o) and male smoking prevalence decreased gradually (29.1% in 1994 to 19.1% in 2011, 54.8% to 33.5%, respectively) after the initiation of Tobacco Hazards Prevention Act in 1997. In addition, tobacco health welfare surcharge was gradually increased by the government, and adult smoking prevalence also decreased at the same time. However, female smoking prevalence remained relatively low level during the study period (3.3% in 1994 to 4.4% in 2011), so no obvious decline was observed. Therefore, decreased male smoking prevalence may contribute to the lower AAPC in male population than in females. The upper limit of tar and nicotine in each cigarette were gradually reduced under government regulations (tar: 15mg/cigarette in 2001 to 10 in 2009; nicotine: 1.5 mg/cigarette in 2001 to 1 in 2009), and there was a decline in average contents of tar and nicotine in each cigarette during study period. The increasing proportion of adenocarcinoma (45.5% in 1995 to 60.3% in 2011) and decreasing proportion of squamous cell carcinoma (SCC) (32.6% in 1995 to 19.1% in 2011) were observed during study period. The correlation coefficient (CC) between the content of tar per cigarette and proportion of SCC was 0.988 ($p < 0.001$). The CC between the content of nicotine per cigarette and proportion of adenocarcinoma was -0.942 ($p < 0.001$). The changes in the composition of cigarette may have influence on the trend of lung cancer histology. **Conclusion:** Tobacco control policies have led to reduction in adult smoking prevalence, but failed to decrease the overall lung cancer incidence. However, they may reduce the ascending rate of lung cancer incidence. The changing trend of lung cancer histology may be affected by the different composition of cigarettes. **Keywords:** lung cancer, Tobacco Control, cigarette

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P3.05-007 Lung Cancer and Multiple Causes of Death, Puerto Rico, 2010 Juan C. Orengo[1], Cecile Marques-Goyco[2], Felipe Arbelaez[2], Homero Monsanto[2], Vivian Green[3] [1]*Medical Department, Merck & Co, Carolina/Puerto Rico,* [2]*Medical Affairs, Merck & Co, Carolina/Puerto Rico,* [3]*Public Health, Ponce Health Sciences University, Ponce/Puerto Rico*

Background: In 2010, 615 people died from lung cancer in Puerto Rico, representing 11.8% of all deaths from cancer and 2.1% of all causes of death. Objectives: The objectives were to: a) determine the underlying cause of death; b) determine the prevalence of conditions reported; c) determine the place of death; and d) determine the marital status as a proxy of network support; all the previous objectives were analyzed by gender. **Methods:** The Mortality Multiple Cause-of-Death Public Use Record from the National Center for Health Statistics for Puerto Rico (2010) was analyzed. The variables analyzed were: sex, age, place of death (Hospital, Clinic or Medical Center – Inpatient; Hospital, Clinic or Medical Center - Outpatient or admitted to Emergency Room; Hospital, Clinic or Medical Center - Dead on Arrival; Decedent's home; Hospice facility; Nursing home/long term care; Other; Place of death unknown), marital status (divorced, married, never married, widowed, marital status unknown), underlying cause, number of condition and condition. Relative and absolute frequencies were calculated; and for the gender comparisons, T-test, Chi square and OR were used. **Results:** The underlying most frequent cause of death (610 deaths, 99.2%) was the malignant neoplasm of unspecified part of bronchus or lung (ICD-10 code C34.9), four deaths (0.6%) were attributed to primary metastatic malignant neoplasm involving the trachea (ICD-10 code C33) and another death (0.2%) was from malignant neoplasm of upper lobe, bronchus or lung. More than 68% of deaths presented 3 or less conditions (including the underlying condition). The most prevalent conditions were: diseases of the circulatory system (67.3%; women (68%) and men (67%)), diseases of respiratory system (48.4%; women (46.3%) and men (49.5%)), other malignant neoplasm (13.9%; women (17.4%) and men (12.1%)), diabetes (11.7%; women (12.9%) and men (11.1%)), and zoonotic and bacterial infections (10.2%). More men (67.3%; n=414) than women (32.7%; n=201) died from lung cancer. A great majority of the deaths were in individuals 65 years and older (86.4%; n= 530). The most frequent places of death were in the decedent's home (47%; n=289) and as an inpatient in a Hospital, Clinic or Medical Center (44.2%; n=272). No significant differences were found between place of death and gender. Regarding the marital status, 47% (n=289) were married (women (36.8%) men (52%); $p < 0.05$), 15.6% (n=96) were divorced, 14.3% (n=88) had never married, and 23% (n=141) were widowed (women (36.3%) men (16.4%); $p<0.05$). **Conclusion:** The majority patient who die from lung cancer have important comorbidities that need to be addressed during the disease, die at home or as inpatients, and are not married. Given these findings, a strong support network may be important for the patient who has lung cancer. **Keywords:** mortality, multiple causes, place of death, underlying cause

POSTER SESSION/ PREVENTION AND TOBACCO CONTROL
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P3.05-008 Lung Cancer, Burden of Disease, Puerto Rico 2000-2010 Juan C. Orengo[1], Felipe Arbelaez[2], Cecile Marques-Goyco[2], Homero Monsanto[2], Vivian Green[3] [1]*Medical Department, Merck & Co, Carolina/Puerto Rico,* [2]*Medical Affairs, Merck & Co, Carolina/Puerto Rico,* [3]*Public Health, Ponce Health Sciences University, Ponce/Puerto Rico*

Background: The Annual Percent Change (APC) of lung cancer mortality has decreased from 1987 until 2010 by 1.5% for men and 1.1% for women, representing 13.8% and 9.7% of all cancer deaths among men and women for the period 2006-2010, respectively (Puerto Rico Cancer Registry, last issue from 2011). Objectives: The objectives were to: a) estimate both Years of Potential Life Lost (YPLL) and Potentially Productive Years of Life Lost (PPYLL) for lung cancer in Puerto Rico (2000-2010) by gender; b) estimate the Average Years of Life Lost (AYLL) by gender; c) estimate the cost associated with YPLL by gender. **Methods:** Mortality data from the National Center for Health Statistics for Puerto Rico (2000 and 2010) was analyzed. An upper limit of 80 years was established for the YPLL, in accordance with WHO guidelines. The YPLL was divided by the total deaths in each year to calculate the Average Years of Life Lost (AYLL). The PPYLL was calculated by setting an interval from 16 to 65 years (Puerto Rico Labor Department). The method of willingness to pay, using three times the GDP per capita in 2010 (US$82,353) (Puerto Rico Planning Board), with a discount rate of 3% and an annual increase of 1%, was used to calculate the economic cost. **Results:** In 2010, the YPLL for lung cancer represented a total of 6,311 years, 11.2% of YPLL for all cancer types, while in 2010 it represented a total of 5,893 years, 10.6 % of YPLL for all cancer types. The YPLL for men in 2000 accounted for 4,301 years (71.5% of YPLL for lung cancer) whereas in 2010 it accounted for 3,843 years (65.2% of YPLL for lung cancer). For women in 2000, the YPLL accounted for 2,010 years (28.5% of YPLL for lung cancer) while in 2010 it accounted for 2,050 years (34.8% of YPLL for lung cancer). The YPLL for both genders decreased 6.6% in the period 2000-2010. The AYLL for men in 2000 and 2010 was 13.5 years and 12.4 years, respectively, and for women 14.4 years and 15.2 years, respectively. The PPYLL in 2000 was 1,085 years for men and 479 years for women, whereas in in 2010 it was 776 years for men and 589 years for women. The economic cost (willingness to pay) associated to YPLL for men was $287.6 million and $261.5 million for 2000 and 2010, respectively, and for women it was $134.5 million and $134.4 million for 2000 and 2010, respectively. **Conclusion:** The YPLL has remained stable for women and decreased for men from 2000 to 2010 and the PPYLL has decreased for men when compared to women. Lung cancer deaths occur in younger women than men. The financial burden associated with women has remained constant while for men it has decreased. These findings suggest that lung cancer continues to be a public health problem with substantial burden of disease among men and women in Puerto Rico. **Keywords:** burden of disease, mortality, Years of Potential Life Lost, willingness to pay

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P3.05-009 Tobacco Consumption in Cancer Patients from Colombia's Coffee Zone Paula Londno[1], Jaime A. Echeverri F[2], Jose W. Martinez[1], Felipe Parrado[1], Carolina Angel[1], Dahiana Gallego[1], German A. Moreno[1] [1]*Oncologos Del Occidente S.A., Pereira/ Colombia,* [2]*Pulmonary Medicine, Oncologos Del Occidente, Pereira/Colombia*

Background: The General Surgeon has been reporting the similarities of the addiction magnitude of nicotine, heroin and cocaine. The criteria for diagnosis of dependency to nicotine have been established by the DSM-IV which includes impulsivity for consumption, lack of control despite the negative effects of smoking, and a high motivation to consume above other activities that can be done instead. Other elements of diagnosis are signs of physical dependency and tolerance which demands an increase in consumption. The effects of nicotine have been related to the fact that inhalation of nicotine by a large body surface such as the lungs, which is dissolved at a high pH fluid, which is transported from the lungs to the heart and quickly reaches the brain. The high rate of absorption and large amount of nicotine is concentrated in the brain are the two causes that generate dependency. Smoking also affects the processes of tissue repair and states that the mortality among current smokers is 2 to 3 times as high as that among persons who never smoked. We evaluate cigarette smoking in cancer patients "Colombia's Coffee Zone" **Methods:** *Oncologos del Occidente* has clinics for the attention of cancer patients throughout "Colombia's Coffee Zone" conformed by Caldas, Quindio and Risaralda states. Inhabited by 4.8% of the national population and during 2004, 4340 cancer patients had their first medical appointment. We measured cigarette consumption with surveys and validated tests and the level of dependency to tobacco of these new patients through a systematic sampling **Results:** The prevalence of cigarette consumption through life was 44.6% ($IC_{95\%}$ 37.0-52.5) in 168 tested patients; former smokers consumed an average of 0.7 cigarette packs per year during 21.6 years. Current smokers consume an average of 0.67 cigarette packs per year during 42 years. The 61% of these patients wait until 30 minutes to consume their first cigarette of day, after they get up from bed. The 38% of the current smokers do not like to avoid the first cigarette of the day.

The 50% smokes even when they fill ill and stay in bed, meanwhile the 16.7% of the patients want to smoke "right now"; the 22.2% feel less depressed and tired when they smoke. **Conclusion:** There is a high frequency of consumption among these cancer patients who also present high levels of dependence; this is why they require support to quit smoking tobacco. The pharmacological effects of nicotine must be medically evaluated. We propose a clinic to support these patients in the cessation of tobacco consumption.
Keywords: Cigarette smoking; Knowledge; Behaviors; Cancer; Prevention

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P3.05-010 Incidence and Survival of Lung Cancer at Oncosalud: Dynamic Cohort Study Alfredo Aguilar[1], Claudio J. Flores[1], Luis Mas[1], Gustavo Sarria[2], Luis Pinillos[2], Carlos Vallejos[1] [1]*Oncosalud - Auna, Lima/Peru,* [2]*Radioncología - Auna, Lima/Peru*

Background: Lung cancer is the most common malignancy in many countries and regions; it represents the first cause of death in the world and the fourth cause of death in the Peruvian population. The incidence of lung cancer in a population affiliated with a prepaid system is important for the implementation of prevention programs. The arm of study was to determinate the incidence rate of lung cancer in a population of affiliates and the survival rate of patients treated in a private institution (ONCOSALUD - AUNA). **Methods:** In a study of dynamic cohort, the incidence of lung cancer was evaluated in a population of affiliates to ONCOSALUD - AUNA between 2008–2013 (n = 1'096,140). Overall survival (OS) was evaluated in patients treated in ONCOSALUD - AUNA between 2000-2005 (n = 241). The incidence rate was calculated based on new cases/persons-year of observation. The OS was calculated according to Kaplan-Meier method. **Results:** The median age was 33 years and 55.7% were women. A total of 2'611,438.3 persons-year of observation was produced and 394 affiliates were diagnosed with lung cancer. The median age at diagnosis was 70 years. The standardized incidence rate by age was 7.9 per 100,000 persons-year (6.5 and 10.0 in women and men per 100,000 persons-year, respectively) and 74 years cumulative risk was 1.0% (0.8 and 1.2% in women and men, respectively). For survival assessment, the median age was 69 years, 39.4% were women and 76.4% had advanced disease (CS III: 18.3% and CS IV: 58.1%). With a 10.6 years follow-up, the median survival was 7.5 months. The OS rate at 2, 5 and 10-years was 24.3%, 16.4% and 12.9%, not showing significant difference in relation to sex (p=0.687), age (<60 vs. > 60 years: p=0.116) and shows significant difference according clinical stage (CS I-II vs. III-IV: p <0.001). **Conclusion:** The incidence rate of lung cancer in our population is lower than reported by the IARC for the Peruvian population. The survival rate at 2, 5 and 10-years is similar to reported for other series.

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P3.05-011 Tumour Microenvironment: A Potential Role for Curcumin in Lung Cancer Chemoprevention Jagdish N. Mahale, Gintare Smagurauskaite, Karen Brown, Lynne Howells *Department of Cancer Studies, University of Leicester, Leicester/United Kingdom*

Background: Recent studies have shown that the tumour microenvironment plays a crucial role in regulating tumor progression and cell migration. This is of particular importance in diseases such as lung cancer, which exhibit dense stroma. Cell-cell interactions and the effect that drugs have upon them can be investigated via use of in vitro 3D organotypic co-culture models. Curcumin, a naturally occurring polyphenol, is reported to exhibit strong anti-inflammatory, antioxidant, anti-proliferative and chemopreventive activity. An organotypic co-culture model representative of a tertiary prevention model system was used to study lung cancer tumour-stroma interactions and to investigate anti-invasive properties of curcumin. Fibroblast-secreted HGF is reported to stimulate invasion and migration of tumour cells by activation of the cMet pathway. In this study we also determined the potential for curcumin to elicit chemopreventive efficacy via disruption of this pro-proliferative c-Met signalling axis. **Methods:** A549 lung adenocarcinoma cells and MRC5 normal human lung fibroblasts were used for the study. For air-interface organotypic co-culture, a gel matrix consisting of matrigel and rat tail collagen was embedded with MRC5 fibroblasts and a combination of A549 and MRC5 fibroblasts seeded on to the gel. The gel was then placed onto a metal grid in a 6-well plate. Curcumin-containing media was added to the well so that it just touched the bottom of the gel. After 12 days, gels were processed for formalin fixation and paraffin embedding (FFPE). The objectives were as follows: i) to evaluate invasiveness of A549 cells in the absence of fibroblasts; ii) to determine the effect of differing ratios of A549:fibroblasts on invasion; iii) to determine the effect of curcumin treatment on invasion of A549 cells. For HGF estimation, MRC5 fibroblasts were treated with a single dose of curcumin at concentrations ranging from 0 to 5μM. On day 6, media was collected and analysed for determination of HGF levels using ELISA. **Results:** The IC50 value of curcumin for A549 and MRC5 was found to be 4.7±0.8μM and 1.5±0.3μM respectively. In the absence of MRC5 fibroblasts in co-culture, A549 cells did not invade. Five different ratios of A549:MRC5 (1:5, 1:2, 1:1, 2:1 and 5:1) were used to determine effect on invasion. The 1:5 ratio showed maximum invasion whereas 5:1 showed minimal or no invasion. Organotypics (1:5 ratio) were treated with curcumin concentrations ranging from 0μM to 5μM. Curcumin treatment significantly inhibited invasion of A549 cells by 24.39±8.39% in organotypic co-cultures. HGF ELISA on curcumin treated MRC5 media revealed that curcumin significantly inhibited HGF secretion by 67.87±5.96% when adjusted for cell number, at concentration as low as 0.25μM. **Conclusion:** A549 cells require the presence of fibroblasts to invade in the organotypic co-culture model, and invasive index increases with increasing ratio of fibroblasts. Intervention with curcumin in contact with fibroblasts only, suggested that this is sufficient to inhibit invasion of A549. The potential mechanism for this may be via the ability of curcumin to inhibit paracrine signalling networks between the two cell types, which impinge on the cMet signalling axis.
Keywords: curcumin, chemoprevention, tumour microenvironment

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P3.05-012 Hookah Smoke Mediates Cancer-Associated Alterations in Normal Human Respiratory Epithelial Cells Yin Xiong[1], Sichuan Xi[1], Jigui Shan[2], Mary Zhang[1], Saïd Azoury[1], Julie A Hong[1], David S. Schrump[1] [1]*Tgib, Nci/Ccr/Nih, Bethesda/MD/ United States of America,* [2]*National Cancer Institute, Frederick, Frederick/MD/United States of America*

Background: Cigarette smoking is the leading cause of lung cancers worldwide, and numerous countries have initiated public health programs to curtail cigarette abuse. Although hookah tobacco is perceived to be a safe alternative to cigarettes, the effects of hookah smoke in human respiratory epithelial cells and lung cancer cells are currently unknown. The present study was undertaken to examine if hookah smoke mediates cancer-associated alterations in normal respiratory epithelia and lung cancer cells. **Methods:** Human small airway epithelial cells (SAEC), cdk4/hTERT-immortalized human bronchial epithelial cells (HBEC) and lung cancer cells (Calu-6 and A549) were cultured in normal media in the presence or absence of waterpipe condensates (WPC) or cigarette smoke condensates (CSC) under relevant exposure conditions. MTS, quantitative RT-PCR and western blot techniques were used to examine the effects of hookah smoke on cell proliferation, mRNA/ microRNA expression and the histone code relative to those induced by cigarette smoke. **Results:** Five day WPC exposures mediated variable effects in cultured respiratory epithelia and lung cancer cells. In SAEC and HBEC, WPC mediated dose-dependent growth inhibition. In Calu-6 cells, low dose WPC (0.1mg/ml and 0.5mg/ml) enhanced proliferation, whereas higher concentrations of WPC (1.0mg/ml and 2.0mg/ml) inhibited growth. High concentrations of WPC (2.0mg/ml) inhibited proliferation of A549 cells. Similar to CSC, WPC decreased H4K16Ac and H4K20Me3 levels in SAEC and HBEC. In addition, like CSC, WPC increased miR-31 and decreased miR-487b expression in SAEC, HBEC and lung cancer cells. Furthermore, WPC increased expression of *Cyp1b1* in SAEC cells, enhanced expression of *ABCG2, Lin28B, Myc, SALL4*, *CTCF, JARID2* and *Cyp1a1* in HBEC cells, up-regulated *ABCG2* and *Cyp1a1* in Calu-6 lung cancer cells, and induced dose-dependent up-regulation of *Cyp1a1* and *Cyp1b1* in A549 lung cancer cells. WPC exposure significantly decreased expression of *Dkk-1* in HBEC and Calu-6 cells. Cigarette smoke induced similar changes in these cells. **Conclusion:** These preliminary findings demonstrate that hookah smoke mediates cancer-associated alterations in human respiratory epithelial cells, and suggest that waterpipe tobacco is not a safe alternative to cigarettes.
Keywords: Normal Respiratory Epithelial Cells, Cancer-Associated Alterations, lung cancer, Hookah Smoke

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POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-001 Clinico-Pathological Profile of Lung Cancer at New AIIMS Hospital in Eastern India Prasanta R. Mohapatra[1], Sourin Bhuniya[1], Manoj K. Panigrahi[1], Susama Patra[2], Pritinanda Mishra[2], Saroj K. Das Majumdar[3], Gourahari Pradhan[1], Priyadarshini Behera[1], Anupam Dey[4] [1]*Pulmonary Medicine, All India Institute of Medical Sciences, Bhubaneswar/India,* [2]*Pathology, All India Institute of Medical Sciences, Bhubaneswar/ India,* [3]*Radiation Oncology, All India Institute of Medical Sciences, Bhubaneswar/ India,* [4]*General Medicine, All India Institute of Medical Sciences, Bhubaneswar/India*

Background: Lung cancer is one of the commonest cancers worldwide. The pathological profile varies among different geographical regions. In India squamous cell carcinoma or adenocarcinoma has been reported as the common histological type in all the series. Odisha is socioeconomically behind some states of India. There is no epidemiological published data on lung cancer from this part of the country. The aim of the study was to analyse the epidemiological, clinical and pathological profile of lung cancer patients at a newly established tertiary level Government hospital in Odisha. **Methods:** We analysed 87 lung cancer cases registered at our centre over a period of initial 18 months in the department of Pulmonary Medicine of this newly opened Government Institution. They were evaluated for their epidemiological, clinical and pathological profiles. The data were recorded in Excel spreadsheets and subjected to appropriate statistical analysis. **Results:**Average age was 57 years with a male: female ratio of 2.6:1. About 48% of patients were smokers. Non-small cell lung cancer (NSCLC) was the predominant pathological variant in about 92 % and small cell lung cancer (SCLC) in only 3% of the cases. Among the patients with NSCLC, adenocarcinoma was the commonest histological subtype after the pathology review. **Conclusion:** Adenocarcinoma now be the commonest histological subtype. Prevalence of lung cancer among non-smokers is also high in the eastern part of India. Most of the patients present at an advanced stage with poor outcome, probably due to lack of awareness and limited resources in this part of the country.
Keywords: epidemiology, India, lung cancer, Odisha

POSTER SESSION/ SCREENING AND EARLY DETECTION
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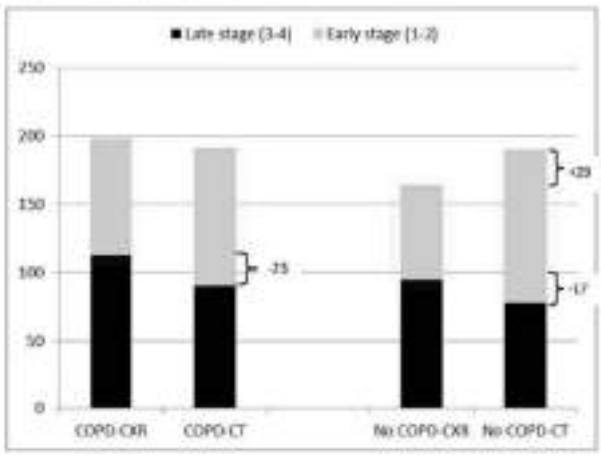
P3.06-002 Favourable Stage-Shift Limited to Screening Participants with COPD in a Biomarker Sub-Study of the National Lung Screening Trial (NLST) Robert Young[1], Caroline Chiles[2], Raewyn J. Hopkins[1], Fenghai Duan[3], Greg D. Gamble[1], Denise R. Aberle[4] [1]*University of Auckland, Auckland/New Zealand,* [2]*Wake Forest University Baptist Medical Center, Winston-Salem/AL/United States of America,* [3]*Department of Biostatistics and Center for Statistical Sciences, Brown University School of Public Health, Providence, Rhode Island, Providence/United States of America,* [4]*Department of Radiological Sciences, David Geffen School of Medicine at UCLA, Los Angeles/CA/United States of America*

Background: Based on a 20% reduction in lung cancer deaths in participants of the National Lung Screening Trial (NLST), CT screening for lung cancer is now widely recommended in the US. However concerns remain regarding the cost-benefits of screening due to overall low detection rates, over-diagnosis and high false-positive rates. Using the spirometric data available from the ACRIN-biomarker sub-study of the NLST (n=18,714), we examined the effect of Chronic Obstrucitve Pulmonary Disease (COPD) status on lung cancer detection in the NLST screening participants. Specifically we compared lung cancer incidence, histology and stage shift in those with and without COPD based on baseline pre-bronchodilator spirometry. **Methods:** Baseline spirometry results were available for 18,475 (99%) of the total cohort of 18,714, (6,436 with COPD and 12,039 with no COPD). Spirometry results were available for 758 (99%) of the 768 histology-confirmed lung cancer cases diagnosed over the 7 year follow-up period. After lung cancer cases were sub-grouped by spirometry-defined COPD (GOLD 1-4, n=401) and no baseline COPD (n=357) it was possible to compare the number of cancers, histology and stage according to screening arm. Differences in lung cancer incidence rates were compared by incident rate ratios, while prevalence, histology and stage shift, were compared by chi-square frequency tables. **Results:** In this NLST-ACRIN Biomarker sub-study, we found the demographic variables were comparable to those from the full NLST study. Regardless of screening interval, we found the lung cancer incidence was 2 fold greater in those with COPD compared to no COPD (P<0.0001). In those with COPD, we found a signficant reduction in adenocarcinomas and bronchioloalveolar carcinomas. After stratification by COPD status, when comparing CT versus CXR screening arms, we found no excess lung cancers and comparable lung cancer histology. However, a clinically significant stage shift favouring increased early stage (+17) and reduced late stage cancers (-23) was found (P=0.05). In contrast, in cancer cases with no COPD, we found an 18% excess of lung cancers in the CT arm (+29) which were of a BAC/AC histology. After correction for this overdiagnosis from these excess cancers, the stage shift no longer favoured early stage over late stage.

Figure 1. Stage shift according to screening arm (CXR vs CT) in the NLST-ACRIN substudy (N=18,714) after stratification by COPD status.



Conclusion: These data suggest that in those with COPD at baseline, CT screening (vs CXR) was associated with no excess cancers, no histology shift but a clinically significant stage shift favouring early over late stage cancers. In those with no COPD, CT was associated with excess cancers and a marginal stage shift. **Keywords:** National Lung Screening Trial, COPD, overdiagnosis, stage shift

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-003 Effectiveness of Lung Cancer Screening Comparing Computed Tomography (CT) to Chest X-Ray (CXR) to No Screening in PLCO and NLST Randomized Trials John Paul E. Flores[1], Alejandro Moreno-Koehler[2], Matthew Finkelman[3], Jaime Caro[4], Gary Strauss[1] [1]*Hematology/Oncology, Tufts Medical Center, Boston/MA/United States of America,* [2]*Tufts Medical Center, Boston/MA/United States of America,* [3]*Tufts University School of Dental Medicine, Boston/MA/United States of America,* [4]*Mcgill University, Montreal/QC/Canada*

Background: We sought to estimate the relative effectiveness of CT and CXR versus no screening in the context of a comparative cost-effectiveness analysis of lung cancer screening. CXR is considered ineffective because no randomized population trial (RPT) has shown a lung cancer mortality reduction. In the Mayo Lung Project, however, CXR screening produced a significant survival advantage which was not attributable to overdiagnosis or other screening biases (JCO 20:1973-83; 2002). The lung portion of the Prostate Lung Colon Ovary (PLCO) Cancer Screening Trial reported no lung cancer mortality reduction with CXR versus no screening, and it is considered to be a negative trial. The National Lung Screening Trial (NLST) was the first lung cancer screening RPT to report a mortality reduction comparing CT to CXR, but lacked an unscreened control. Survival from these trials has not been reported. **Methods:** To compare effectiveness of CXR and CT versus no screening, we calculated mortality, survival, and stage distribution in an intent-to screen analysis of PLCO and NLST data. Only lung cancers diagnosed within 7 years of randomization in PLCO were considered to match the median 6.7 years follow-up in NLST. Kaplan-Meier survival was compared by the log-rank test. Incidence, mortality, and stage distribution were compared with Fisher's exact test. All p-values are two-sided. **Results:** In PLCO, 154,897 participants were randomized to either four annual CXRs over 3 years or to no screening. Within 7 years of randomization, 1072 and 1022 lung cancers were diagnosed, respectively (RR=1.05; 95%CI 0.96-1.14; p=0.271). 5-year survival was 27% and 18% (p<0.001). Mortality analysis revealed 764 and 811 lung cancer deaths in CXR and control groups (RR=0.94; 95%CI 0.85-1.04, p=0.244). The CXR group had significantly more stage IA cancers (RR 1.70; 95%CI 1.33 – 2.16; p<0.001) and fewer advanced stage IIIB and IV cancers (RR=0.87; 95%CI 0.76 – 0.99; p=0.044). NLST randomized 53,452 participants to either three annual CTs or CXRs over 2 years. There were 1089 and 969 lung cancers in the CT and CXR groups respectively (RR=1.12; 95%CI 1.03-1.22; p=0.007). 5-year survival was 49% and 33% (p<0.001). Mortality comparisons revealed 449 and 528 lung cancer deaths in the CT and CXR groups (RR=0.850; 95%CI 0.751-0.964, p=0.012). There were significantly more stage IA cancers (RR 2.16; 95%CI 1.82 – 2.56; p<0.001) and fewer advanced stage IIIB and IV cancers in the CT versus CXR groups (RR=0.74; 95%CI 0.63 – 0.87; p<0.001). **Conclusion:** Based upon similar lung cancer incidence, improved survival, and a more favorable stage distribution (particularly a reduction in the number of advanced cancers) in PLCO, CXR screening is superior to no screening, and overdiagnosis does not account for this advantage. While CXR screening is superior to no screening, CT is more efficacious than CXR in NLST. As CT is more expensive, has a higher false positive rate, and is more likely to detect overdiagnosed cancers than CXR, CXR may still be cost-effective compared to CT. Accordingly, a cost-effectiveness analysis employing NLST and PLCO data is ongoing. **Keywords:** Screening, lung cancer

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-004 Update in the Surgical Outcomes in a Large Clinical Low-Dose Computed Tomographic Lung Cancer Screening Program Christina Williamson[1], Bryan Walker[2], Shawn Regis[3], Paul J. Hesketh[4], Andrea Mckee[3], Carla Lamb[5], Sebastian Flacke[6], Christoph Wald[7], Brady Mckee[8] [1]*Thoracic and Cardiovascular Surgery, Lahey Hospital and Medical Center, Burlington/MA/United States of America,* [2]*Tufts University Medical School, Boston/United States of America,* [3]*Radiation Oncology, Lahey Hospital and Medical Center, Burlington/MA/United States of America,* [4]*Medical Oncology, Lahey Hospital and Medical Center, Burlington/United States of America,* [5]*Pulmonary Medicine, Lahey Hospital and Medical Center, Burlington/United States of America,* [6]*Lahey Hospital and Medical Center, Burlington/MA/United States of America,* [7]*Diagnostic Radiology, Lahey Hospital and Medical Center, Burlington/MA/United States of America,* [8]*Diagnostic Radiology, Lahey Hospital and Medical Center, Burlington/United States of America*

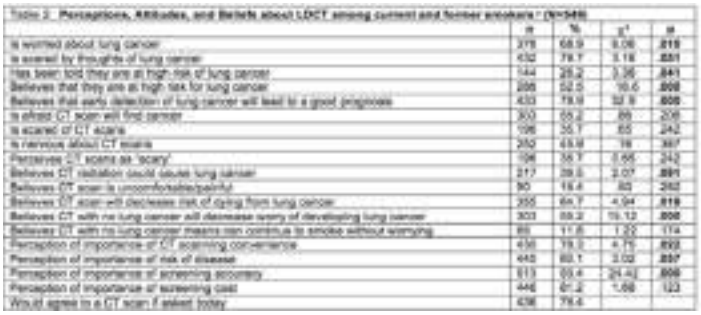
Background: Lung Cancer screening with low-dose computed tomography (LDCT) has been shown to reduce lung cancer mortality in high-risk individuals. Critics raise concern over the potential for unnecessary surgical procedures for benign disease as a result of screening. We have up-dated our surgical outsomes in a large clinical lung cancer screening program to assess the number of surgical procedures done for benign disease. **Methods:** We retrospectively reviewed our surgical outcomes of consecutive individuals who underwent LDCT lung cancer screening from January 2012 through March 2015 using a prospectively collected database. All patients met the National Comprehensive Cancer Network (NCCN) Lung Cancer Screening Guidelines high risk criteria. **Results:** There were 2,043 screened individuals during this interval with clinical follow-up at Lahey Hospital and Medical Center. Thirty-nine of the 2.043 (1.9%) had surgery. Twenty-eight (72%) had lung cancer, 25/28 (89%) had early stage and 3/28 (11%) had advanced stage lung cancers. Four (10%) had non-lung cancer malignancies. Seven of thirty-nine (18%) were found to have benign disease. There were no in hospital or 30 day mortalities in those who had surgery and only one (2.56%) major surgical complication. **Conclusion:** The incidence of surgical intervention for non-lung cancer diagnosis was low (0.56%) and is comparable to the rate reported in the National Lung Cancer Screening Tria; (0.62%). Surgical intervention for benign disease was rare (0.34%) in our experience. **Keywords:** lung cancer screening, surgical outcomes

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-005 Attitudes and Beliefs Toward Lung Cancer Screening Among Older Smokers Janine K. Cataldo *Physiological Nursing, University of California, San Francisco, San Francisco/CA/United States of America*

Background: Lung cancer (LC) is the leading cause of cancer in the U.S. with 85% caused by smoking. There is recent strong evidence that LC mortality is decreased by 20% with low-dose computed tomography (LDCT) screening for healthy individuals with an elevated risk for lung cancer. Previous studies have shown that those at higher risk (i.e., older smokers) are less interested in being screened despite awareness of risk. **Methods:** The aims for this study were, among older smokers: 1) Identify the demographics, smoking

history, knowledge, and attitude factors associated with willingness to have a CT scan and 2) Provide a predictive model of factors to explain willingness to have a CT scan. This was a cross-sectional national survey study with 549 older adult (≥ 45 years) current and former smokers (≤ 2 years quit). **Results:** There were no significant differences between current and former smokers on all variables. After controlling for age, gender, ethnicity, income and education, all perception and belief variables significantly associated with agreement to have a LDCT scan were included in a logistic regression analysis to develop a predictive model for agreement to have a LDCT scan.



	n	%	χ^2	p
Is worried about lung cancer	378	68.9	8.06	.018
Is worried by thoughts of lung cancer	432	78.7	5.18	.881
Has been told they are at high risk of lung cancer	144	26.2	3.36	.841
Believes that they are at high risk for lung cancer	286	52.5	10.6	.008
Believes that early detection of lung cancer will lead to a good prognosis	433	78.9	32.9	.000
Is afraid CT scan will find cancer	303	55.2	69	.206
Is scared of CT scans	196	35.7	65	.242
Is nervous about CT scans	202	36.8	19	.997
Perceives CT scans as "scary"	196	35.7	3.66	.242
Believes CT radiation could cause lung cancer	217	39.5	3.07	.891
Believes CT scan is uncomfortable/painful	90	16.4	82	.202
Believes CT scan will decrease risk of dying from lung cancer	355	64.7	4.94	.819
Believes CT with no lung cancer will decrease worry of developing lung cancer	303	55.2	10.12	.000
Believes CT with no lung cancer means non continue to smoke without worrying	85	11.6	1.22	.114
Perception of importance of CT scanning convenience	436	79.5	4.75	.893
Perception of importance of risk of disease	445	82.1	3.02	.897
Perception of importance of screening accuracy	513	93.4	24.42	.000
Perception of importance of screening cost	446	81.2	1.66	.123
Would agree to a CT scan if asked today	436	79.4		

Variables in the Equation

	Beliefs and Perceptions	B	S.E.	Wald	df	Sig.	OR	95% CI for OR Lower	95% CI for OR Upper
Step 1[a]	Believes that early detection of LC will result in a good prognosis	1.33	.26	27.89	1	.000	3.788	2.30	6.17
	Perceives accuracy of CT scan as important factor in the decision to have a CT scan	1.21	.42	8.20	1	.004	3.348	1.49	7.66
	Believes that they are at high risk for LC	0.72	.29	6.37	1	.012	2.073	1.18	3.65
	Believes a CT scan with a negative result would decrease worry about developing LC	0.64	.24	7.17	1	.007	1.898	1.19	3.03
	Constant	-1.18	.42	8.27	1	.004	0.303		

Conclusion: Older smokers are interested in LC screening and overall, their attitudes are positive. Eleven variables had a significant association with the decision to have a CT scan. In the final model, four beliefs were significant predictors of whether older smokers would agree to a scan. The strongest predictor was "believes that early detection of LC will result in a good prognosis," followed by perception of accuracy, belief that they are at high risk for LC, and belief it will decrease worry about LC. An effort needs to be made to improve smokers' knowledge of the potential benefits and risks when they are making decisions about participation in screening. **Keywords:** older smokers, Screening

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-006 Extent of Progression for Small Cancers in a Screening Program Even with Proper Follow-Up Ricardo S. Avila[1], Artit Jirapatnakul[2], David F. Yankelevitz[2]
[1]*Accumetra, Rexford/NY/United States of America,* [2]*Radiology, Icahn School of Medicine at Mount Sinai, New York/United States of America*

Background: Current guidelines for repeat CT imaging of small nodules detected during screening are a function of the size and consistency of the nodules and the round it was detected. They attempt to balance the frequency with which a change would genuinely occur (i.e. the frequency with which a nodule of a given size is a cancer) with the ability to actually measure the change should it have occurred. Recently the American College of Radiology has established a new set of guidelines for this purpose called LungRads. This study analyzes the change in nodule volumes and doubling times for small nodules if the LungRads guidelines are followed. **Methods:** The LungRads protocol focuses on providing categories for nodules based on their degree of suspiciousness and provides suggestions for follow-up. They also provide criteria so as to determine when growth is genuine —that is, the change in size is beyond what could have occurred solely as a result of measurement error. Genuine growth defined as increase in diameter of >1.5 mm. For purposes of estimating change in nodule volume and doubling times associated with them, we used the time intervals in LungRads for follow-up and derived the doubling times necessary for a nodule to reach the definitional growth threshold. We assumed a spherical model for the nodules and used a simple exponential growth rate. We focused on solid nodules where the range of growth rates is known to be large and they are most accurately measured. **Results:** For LungRads Category 2, where 6 month follow up CT is recommended, in order for a 4 mm nodule to grow sufficiently so as to pass the size threshold where change could be detected, it would need to have a doubling time faster than 129 days, anything slower would not achieve the necessary size change and it would only then be rescanned 6 months later at an annual repeat scan and it would then potentially reach a size of 8.0 mm. For category 4A, LungRads recommends repeat scanning in 3 months. According to the protocol, a 6 mm nodule would need a doubling time of 92 days for detection otherwise at one year it will reach a size of 15.1 mm. **Conclusion:** The change threshold for growth and time intervals between scans can have serious consequences downstream in terms of how large a tumor might become before it can reliably be diagnosed. The ability to better define the threshold for when change has occurred will always be beneficial as it will allow not only the very fast growing tumors to be diagnosed but those with more typical doubling times as well. The LungRads protocol keeps the smallest size category of tumors from growing beyond 15 mm when workup is initiated. **Keywords:** Lung-RADS, growth rate, CT

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-007 Discovery and Validation of Potential Glycoprotein Biomarkers in the Airway Fluid to Improve the Detection of Lung Cancer from Benign Lung Nodule Qing Kay K. Li[1], Edward Gabrielson[2], Frederic Askin[2], Daniel W. Chen[2], Hui Zhang[2] [1]*Pathology, The Johns Hopkins Medical Institutions, Baltimore/United States of America,* [2]*Pathology, Johns Hopkins Medical Institutions, Baltimore/United States of America*

Background: Recent clinical screening trials using highly sensitive low-dose computed tomography (LDCT) demonstrated an increased detection proportion of stage I lung cancers and improved overall survival of lung cancer patients as the result of early detection. However, lung cancer screening trials also showed high repeat screening rates and false-positive rates causing unnecessary second-line invasive procedures and surgery. New strategies are still needed to improve the specificity of lung cancer screening. The airway fluid, bronchoalveolar lavage (BAL), is commonly used for the evaluation of lung nodules and diagnosis of lung cancers. Proteins in the BAL fluid may serve as potential biomarkers for cancer detection. In this study, we examined the protein profile, particularly the signature of glycoprotein in normal and lung cancer patients. **Methods:** We collected BAL fluid after cellular components were harvested for cytological examination in the cytology laboratory. Protein profile and *N*-glycoproteins were analyzed using the solid-phase extraction of *N*-glycoprotein (SPEG) and liquid chromatography tandem mass spectrometry (LC-MS/MS). Sixteen BAL samples, including four cases each of benign lung disease, adenocarcinoma (ADC), squamous cell carcinoma (SqCC), and small cell carcinoma (SCLC), were analyzed. **Results:** A total of 1013 unique peptides from 457 glycoproteins were identified and quatified. Among them, 286 proteins were identified in BAL of ADC, 363 in squamous cell carcinoma (SqCC), 298 in SCLC and 330 in benign BALs. In addition to common proteins found in all groups, we identified 113 unique proteins that were differentially expresssed in benign disease, ADC, SqCC and SCLC, respectively. The levels of Napsin A, periostin, Galectin-3-binding protein (G3-BP) and myeloperoxidase (MPO) in cancer and benign BALs were further validated using independently collected BAL specimens by ELISA assays (**Table 1**).

Table1. Detection of Proteins in BAL from lung cancer and benign lung disease by ELISA assays.

Protein	Benign* (n=7)	ADC* (n=18)	SqCC* (n=9)	SCLC* (n=6)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P value
Napsin A	55±39	295±104	102±34	50±28	83.3	66.7	88.2	57.1	<0.05
Periostin	255±104	4002±218	3496±1765	1772±1119	73.68	71.43	87.5	50.0	<0.05
G3-BP	168±29	290±70	240±65	132±65	47.4	11.8%	69.2	23.1	>0.05
MPO	3227±2948	0.08±0.03	1.6±0.7	0.1±0.06	33.3	100	100	83.3	<0.05**

protein concentration was expressed as ng/mg total BAL protein. for benign lesions. **Conclusion:** Our study demonstrates that potential protein biomarkers in BAL fluid can be identified and quantified. They have the potential to improve the specificity of lung screening tests and to reduce unnecessary surgery in patients with benign lung nodules. **Keywords:** improve detection specificity, BAL fluid, protein biomarkers, lung cancer

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-008 Meta-Analysis Criteria Used to Rank Biomarkers for Validation Testing: What Works? Brad Rikke[1], Murry Wynes[1], Leslie Rozeboom[1], Anna E. Barón[2], Fred R. Hirsch[1] [1]*Division of Medical Oncology, University of Colorado Anschutz Medical Campus, Aurora/CO/United States of America,* [2]*Department of Biostatistics and Informatics, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora/CO/United States of America*

Background: Hundreds of biomarkers are being developed for the screening and early detection of lung cancer. The vast majority, however, even after extensive internal validation, will likely fail during external validation. For biomarkers to reach the clinic, therefore, it's imperative that external validation studies focus on the most promising candidates. Towards this end, various strategies have been proposed to rank order and prioritize biomarker candidates. These strategies range from simple, highly intuitive ideas to highly sophisticated statistical analyses. To our knowledge, however, none of these strategies has itself been validated externally, which is an important consideration given that each strategy involves making subjective decisions. Here we conducted an independent validation test to assess the performance of the "vote-counting strategy", a straightforward, commonly used strategy that ranks biomarkers on the basis of three highly intuitive criteria: the number of supporting studies in the literature, the combined sample size in the supporting studies, and the average fold change difference associated with the biomarker. **Methods:** We obtained vote-counting biomarker rankings from two recent meta-analyses that together surveyed over 180 miRNAs reported to distinguish lung tumor tissue from normal. We compared the rankings of 50 top candidates and 22 unranked miRNAs to our RT-qPCR results obtained from 45 tumor-normal pairs. We tested for a statistically significant Pearson correlation (r) between biomarker performance and the rankings according to each of the three ranking criteria. **Results:** We found that the number of supporting studies in the literature was indeed a statistically significant predictor of biomarker performance (r = 0.44, n = 50, p = .0006). Our results also suggested that markers supported by two studies in the literature had approximately a 50% chance of being confirmed, markers supported by 3 studies about a 67% chance, and markers supported by 6 studies about a 90% chance. Our unranked markers showed only a 5% chance of being confirmed. At the same time, we found that the combined sample size in the supporting studies was not a predictor of biomarker performance (r = 0.11, n = 50, p = 0.29). We also found that the mean fold change associated with each biomarker was not a predictor (r = 0.12, n = 47, p = 0.22) because large fold-change differences were also associated with large amounts of variability between studies. **Conclusion:** Considering that vote counting has obvious limitations (such as selection bias, not counting negative votes, and the variation in how different studies define significance) counting the number of supporting studies in the literature appears to work remarkably well for ranking biomarker candidates. On the other hand, using total sample size or mean fold change in the supporting studies to rank biomarker candidates appears to provide little, if any, added value. Our results also indicate a need for external validation testing of the current strategies being used to rank biomarkers across studies. **Keywords:** miRNA, microRNA, validation testing, biomarkers, meta-analysis, lung cancer

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-009 Evaluation of Bone Metastasis Using Serial Measurements of Serum NTx in Patients with Lung Cancer: A Prospective Study Takayuki Shiroyama[1], Motohiro Tamiya[1], Shinya Tokunaga[2], Hideaki Okada[2], Hidekazu Suzuki[1], Norio Okamoto[1], Naoko Morishita[1], Natsuko Miyamoto[2], Koichi Taira[2], Haruko Daga[2], Koji Takeda[2], Tomonori Hirashima[1] [1]*Department of Thoracic Malignancy, Osaka Prefectural Hospital Organization Osaka Prefectural Medical Center for Respiratory and Allergic Diseases, Habikino/Japan,* [2]*Clinical Oncology, Osaka City General Hospital, Osaka/Japan*

Background: The bone resorption biomarkers cross-linked N-telopeptide of type I collagen (NTx) have been shown to aid in the diagnosis of metastatic bone disease from lung cancer (MBDLC). Patients with MBDLC are often treated with zoledronic acid (ZA). ZA reduces the levels of NTx and also lowers the risk of skeletal adverse events in patients with MBDLC. **Methods:** Patients with MBDLC at initial diagnosis were included in this study. Serum NTx (sNTx) was measured once a month using the OSTEOMARKTM sNTx assay (Alere Medical). MBDLC was assessed by monthly physical examinations and bone scintigraphy every 3 months for 12 months. Progression of bone metastases during the follow-up period was defined as when the number of bone metastases as assessed by bone scintigraphy had increased from the previous follow-up measurement. The optimal cut-off value of sNTx levels indicative of progression of bone metastasis was evaluated by performing a receiver operating characteristic (ROC) curve analysis. In this ROC analysis, we evaluated the change rate of sNTx per month. The change rate per month was defined as "The change rate of sNTx between at the minimum levels of NTx and at the worsening bone metastasis / the number of month from the minimum levels of sNTx to the worsening bone metastasis" **Results:** Twenty patients were enrolled between June and December 2010. The sNTx concentration at baseline was 19.8 ± 5.8 nmol bone collagen equivalents (nM BCE)/L. In the 16 patients receiving ZA, the levels of sNTx showed a significant decrease after the first month of treatment (baseline vs. 1 month of treatment: 21.3 ± 5.5 vs. 13.6 ± 2.7 nM BCE/L; $p < 0.01$). During the follow-up period, 13 of the patients treated with ZA experienced worsening bone metastasis. There were statistically significant differences in the levels of sNTx at baseline (20.3 ± 4.8 nM BCE/L), at the lowest levels after the administration of ZA (11.8 ± 2.9 nM BCE/L vs. baseline; $p < 0.001$), and at the point of measurable disease progression (14.1 ± 4.6 nM BCE/L vs. baseline; $p < 0.05$). In the ROC analysis, the optimal change rate of sNTx per month was 4.0% (sensitivity: 53.8%, specificity: 100%, area under the curve = 0.564). **Conclusion:** The administration of ZA significantly decreased the levels of sNTx within one month of the initiation of therapy. However, the levels of sNTx was slightly elevated when the bone metastasis has been aggravated during ZA treatment. The serial measurements of sNTx might prove to be useful in selecting drug treatment and evaluating drug efficacy for bone metastasis. **Keywords:** bone metastasis, lung cancer, NTx, cross-linked N-telopeptide of type I collagen

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-010 The Performance of a Novel Amino Acid Multivariate Index for Detecting Lung Cancer: A Case Control Study in Korea Kye Yonng Lee[1], Hee Joung Kim[1], Seung Hun Jang[2], Jeong Seon Ryu[3], Jeong Eun Lee[4], Young Chul Kim[5], Min Ki Lee[6], Tae Won Jang[7], Shin Yup Lee[8], Hidehiro Nakamura[9], Natsumi Nishikata[9], Maiko Mori[9], Yasushi Noguchi[9], Hiroshi Miyano[9] [1]*Internal Medicine, Konkuk University Medical Center, Seoul/Korea,* [2]*Internal Medicine, Hallym University Sacred Heart Hospital, Anyang/Korea,* [3]*Internal Medicine, Inha University Hospital, Inchoen/Korea,* [4]*Internal Medicine, Choongnam National University Hospital and Cancer Research Institute, Deajon/Korea,* [5]*Internal Medicine, Chonnam National University Medical School, Hwasun Hospital, Hwasun/Korea,* [6]*Pusan National University Hospital, Pusan/Korea,* [7]*Kosin University Medical College, Pusan/Korea,* [8]*Kyungpook National University Hospital, Daegu/Korea,* [9]*Institute for Innovation, Ajinomoto Co. Inc., Kawasaki/Japan*

Background: Previous studies have shown that plasma free amino acid (PFAA) profiles are altered in cancer patients compared with healthy controls. A multivariate index based on PFAAs was generated from a Japanese dataset and has been previously demonstrated to be clinically valuable for discriminating patients in the early stages of lung cancer. However, it remains unclear whether similar PFAA profile changes occur in cancer patients from other populations. Therefore, this study aimed to validate the performance of this index in discriminating lung cancer patients from controls in the Korean population. **Methods:** Samples were collected from a total of 142 Korean subjects (72 lung cancer/70 controls) for this study. PFAAs were quantified by high-performance liquid chromatography-electrospray ionization-mass spectrometry, and the clinical performance characteristics of the amino acid multivariate index were evaluated across cancer stages and histological types. **Results:** The concentrations of several PFAAs were significantly decreased in the Korean lung cancer patients compared with the controls. Significant decreases in threonine, citrulline, histidine and tryptophan and increases in proline, isoleucine, phenylalanine and ornithine were observed, which are similar to the PFAA changes reported by a previous Japanese study. The area under the receiver-operator characteristic curve (AUC of the ROC) for the index was 0.80, and similar performances were demonstrated for the different histological types. **Conclusion:** These results suggest that the amino acid multivariate index previously developed from a Japanese dataset has the potential to aid in the early detection of lung cancers of different histological types in Korean patients. **Keywords:** plasma free amino acid, lung cancer, Early Detection

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-011 Unique Combination of 6 Circulating microRNAs for Early Detection of Lung Cancer Ann R. Halvorsen[1], Maria M. Bjaanæs[1], Are Holm[2], Nils Bolstad[3], Luis Rubio[4], Juan C. Peñalver[5], José Cervera[6], Julia C. Mojarrieta[7], Jose A. López-Guerrero[4], Odd Terje Brustugun[8], Åslaug Helland[9] [1]*Department of Cancer Genetics, Oslo University Hospital Radiumhospitalet, Oslo/Norway,* [2]*Department of Respiratory Medicine, Oslo University Hospital Rikshospitalet, Oslo/Norway,* [3]*Department of Medical Biochemistry, Oslo University Hospital Radiumhospitalet, Oslo/Norway,* [4]*Laboratory of Molecular Biology, Fundación Instituto Valenciano de Oncología, Valencia/Spain,* [5]*Department of Thoracic Surgery, Fundación Instituto Valenciano de Oncología, Valencia/Spain,* [6]*Department of Radiology, Fundación Instituto Valenciano de Oncología, Valencia/Spain,* [7]*Department of Pathology, Fundación Instituto Valenciano de Oncología, Valencia/Spain,* [8]*2Department of Oncology, Oslo University Hosital,The Norwegian Radium Hospital, Oslo/Norwa, Oslo/Norway,* [9]*Department of Oncology, The Norwegian Radium Hospital, Oslo/Norwa, Oslo/Norway*

Background: Worlwide, lung cancer is the primary cause of cancer death. Today 75% of patients are diagnosed in a locally advanced or metastatic inoperable stage, and a new tool for early detection of lung cancer is urgently needed in order to improve the outcome. Circulating microRNAs have emerged as stable, non-invasive and promising biomarkers for diagnosis, prognostication and prediction in cancer. The purpose of this study was to identify circulating microRNAs for detection of early stage lung cancer, capable of discriminating lung cancer patients from those with chronic obstructive pulmonary disease (COPD) and healthy normal individuals. **Methods:** We profiled the expression of 756 unique microRNAs in sera from 38 patients with NSCLC, 16 patients suffering from COPD and 16 healthy volunteers, to explore the potential of the microRNAs as diagnostic biomarkers. For validation of our results, we analyzed serum from an independent cohort of high-risk individuals enrolled in the IELCAP screening trial (n=161) using RT-qPCR **Results:** Focusing on microRNAs upregulated in sera from lung cancer patients, we identified a unique set of 6 microRNAs with significantly higher abundance compared with sera from COPD patients and healthy normals. Validation of the 6-miR signature demonstrated a sensitivity of 86% and specificity of 79.3% **Conclusion:** Considering their accessibility and stability, circulating microRNAs can be a diagnostic tool for clinicians in the future, and may lead to increased fraction of lung cancers diagnosed in an early curative stage. The 6-miR signature may be a basis for a screening study and can easily be implemented in the clinic to identify those who should be further examined for lung cancer **Keywords:** screening study, circulating microRNA, Early Detection, diagnostic biomarker

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-012 cfDNA in Lung Cancer Patients and People with High Risk of LC Exposed to Environmental Pollution Marta Adonis[1], Carolina Tamayo[2], Ulises Urzua[2], Marco Chahuan[3], Veronica Rosana Miranda[4], Monica Campos[3], Alcides Zambrano[5], Hugo Benitez[5], Pedro Marin[5], Lionel Gil[2] [1]*Cetecancer, ICBM, University of Chile, Santiago/Chile,* [2]*Cetecancer, University of Chile, Santiago/Chile,* [3]*Adult Pulmonary, Hospital San Borja Arriarán, Santiago/Chile,* [4]*Hospital Barros Lucos Trudeau, Santiago/Chile,* [5]*Hospital Regional de Antofagasta, Antofagasta/Chile*

Background: In Chile, Lung Cancer (LC) has the second high mortality rate/100,000 for cancer, after to stomach cancer. During 2012, in the country the LC incidence for male was 17.1 with a mortality of 17.0, while for female the incidence was a 10.2, with a mortality of 8.8. In the same period, the Antofagasta region (North of Chile) showed a rate mortality of 31.6 for both gender, with a rate of 44.2 and 17.4, for men and women, respectively. According to this point of view, early detection and screening are imperative in order to increase survive to 5 years. Non invasive biomarkers, as complementary tools, might contribute with the early diagnosis of LC. In this context, free-circulating DNA (fcDNA) levels have been described as a potential tool to detect in comparison with controls. **Methods:** Volunteers enrolled, were classified as LC free subjects (C), Pre Neoplastic Lesions (PNL) and Lung Cancer (LC), according to results of Quantitative Automatic Cytology (QAC) in sputum specimen, DR70 tumor marker, and Auto fluorescence Bronchoscopy (AFB). Free circulating DNA (fcDNA) was isolated from serum of the three groups of volunteers, quantified by qPCR and amplified. The amplified fcDNA was co-hybridized against genomic DNA from total blood, using microarray-HGC. **Results:** The LC patients showed significantly higher levels of fcDNA (average, 16,13 ng/mL) than volunteers cancer free (CF) ($p < 0.01$) (average 2,692 ng/mL) and with Pre neoplastic Lesions (PNL) ($p < 0.001$) (average 1,961 ng/mL). Additionally, four recurrent and significant deletions were detected in 2p, 7q, 11q and 17p of LC volunteers. Non significant alterations were detected in PNL. Genes located in segments with CNAs were related in immune response, xenobiotic metabolism and oxidative phosphorilation and associated to , cell proliferation, cell cycle regulation, apoptosis, differentiation and cellular adhesion and migration, all functions relevant to neoplastic progression. **Conclusion:** . In conclusion; fcDNA levels were significantly associated to LC but not to PNL related to LC, fcDNA concentration could be a non invasive and complementary tool to diagnosis of LC, molecular characteristic of fcDNA suggest that its might be used as biomarker associated to malignancy of LC, as a non invasive and complementary tool for the diagnosis of LC. Supported by INNOVA CORFO Chile: Grants 07CN13B48 and 11IDL2-10634. **Keywords:** Early Detection, GENOMIC MARKERS, fcDNA, lung cancer

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-013 VOC Breath Testing in Squamous Cell Carcinoma (SCC) of Lung and Larynx Shows Distinct Profiles Each of Which Relate to Tumour Burden David Fielding[1], Mark Davis[1], Michael Brown[1], Annette Dent[2], Graham Dickie[3], Julienne Agnew[4], Robert Hodge[4] [1]*Thoracic Medicine, Royal Brisbane and Womens Hospital, Brisbane/Australia,* [2]*Thoracic Medicine, The Prince Charles Hospital, Brisbane/QLD/Australia,* [3]*Radiation Oncology, Royal Brisbane and Womens Hospital, Brisbane/Australia,* [4]*Surgery, Royal Brisbane and Womens Hospital, Brisbane/Australia*

Background: Early studies of volatile organic compound (VOC) testing in lung cancer suggested similar profiles for all stages of lung cancer, raising the possibility that in-situ cancer might be detectable by VOC profiling. It was hypothesized that a metabolic predisposition to cancer was being detected in VOC profiles, rather than VOCs arising from tumour bulk. In situ SCC can be detected in lung as well as the larynx allowing VOC profiles to be compared to advanced cancer. Because many lung cancer patients can develop Larynx cancer (and vice versa) profiling to determine the possibility of VOC testing in post treatment surveillance could provide useful data. **Methods:** Prospective pilot study. Breath samples were collected using the E-Nose Cyranose ®per established protocols prior to biopsy. Data were reduced to principal components for canonical discriminant analysis to determine differences between groups. Accuracy (CVV) was calculated using leave one out cross validation. All cases and controls had autofluorescence or Narrow Band Imaging bronchoscopy or microlaryngoscopy as well as CT chest. Histological confirmation was obtained. Control patients had negative larynx and bronchus on scopes. All patients had a smoking history. **Results:** Patients were as follows:

	Bronchus	Larynx						
	N	Age	M/F	Current smokers	N	Age	M/F	Current smokers
In situ	8	67±9	6/2	0	10	61±10	9/1	4
Advanced	10	71±6	7/3	5	10	65±9	10/0	4
Control	10	63±9	7/3	2	10	62±10	9/1	4

Factor analysis p values for advanced cancer compared to control were 0.05 for larynx and 0.08, NS for bronchus. Values for in situ for both sites compared to control were NS, but were significant when compared to advanced cancer (0.04 and 0.009 respectively). Advanced cancer of larynx compared to bronchus showed $p=0.001$, CVV 80%. **Conclusion:** These results suggest that VOC signal as measured by eNose relates to tumour bulk as opposed to a systemic metabolic predisposition to cancer, (which might have allowed in situ cancer to be detected). Whilst the inability to detect in situ SCC was disappointing, the clear differences between VOC profiles for advanced cancer suggest the Squamous cell carcinoma has different metabolic profiles in the 2 sites, and further study may allow development of VOC breath testing for surveillance of bronchial SCC after larynx cancer. It suggests that whereas SCC arises in the aerodigestive tract "field" there are different inputs into the tumour development at each site. **Keywords:** Breath testing, In situ Carcinoma, volatile organic compounds, Squamous cell carcinoma

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-014 Onset of Silicosis among Sandstone Mine Workers in Rural Rajasthan, India Absar Ahmad *Public Health, International Institute for Population Sciences,Mumbai, Mumbai/India*

Background: There are about 3 million workers at high potential risk of silica exposure in India and around 17 lakh in mining industry.But unofficialy figure for Rajasthan alone, over 2.5 million that are engaged in unorganized mine sector. The problem of silicosis is much more severe in the unorganized sector of industries like slate pencil cutting, stone cutting, and agate industry.The flaw here is because most industries belonging to the unorganized sector do not fall under the purview of Factories Act and Mines Act. **Methods:** Present study used the data from published report of detection of Silicosis by National Institute for Miner's health an autonomous Institute under Ministry of Mines, Government of India. ARAVALI a NGO based in Jaipur arranged for medical investigations (through Dang Vikas Sansthan (DVS), Karauli based voluntary organization, one of the ARAVALI"s field host organization since 2008), of persons which had the history of work in stone mines. That included detailed work history, respiratory symptoms, history of treatment, chest radiography, sputum examination and pulmonary function test. The medical records evaluated by three specialists experienced in the evaluation of chest radiographs as per ILO classifications of radiographs for Pneumoconiosis, 2000. The report has published in three different time, first were in 2011 (101 miners), second 2014 (314 miners) and third 2014 (157 miners). These reports cover stone miner from two districts of Rajasthan, named Karauli (first two reports) and Dhaulpur (third report). Reports include around 18 villages from Dhaulpur and 38 villages from Karauli. Thirty-four X-ray qualities were poor, and nine has no history of mining were not clinically evaluated for Silicosis. So, total 529 mine worker were clinically assessed for silicosis as per ILO classification of radiographs by the Institute. Cox regression is used for exploring the relationship between the onsets of silicosis among mine workers. **Results:** *Bivariate analysis of the study shows that 58 % of the mine workers those diagnosed for silicosis were previously treated for TB. TB treatment, working duration in mines (16-30 years) and (30+ years) were found to be risk*

factors for Silicosis. The corresponding adjusted hazard ratios were 1.299(95 % C.I. 0.895, 1.886), 5.605(95% C.I. 3.485, 9.016) and 3.689(95% C.I. 2.73, 4.984). By age 40, maximum miners get silicosis found in life table analysis. **Conclusion:***Sandstone miners affected with silicosis but getting treatment of TB. After 15 years of work in mine, miners get affected with silicosis and by age 65 all miner get affected with silicosis if he continued to work.*
Keywords: Sandstone mine, Silicosis, Karauli, Mine worker

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-015 Is the Development of Primary Lung Adenocarcinoma Simply Due To 'Bad Luck'? Maria Elena Cufari[1], Chiara Proli[1], Manraj Phull[1], Anna Allan[2], Hilgardt Raubenheimer[1], May Al Sahaf[2], Nizar Asadi[2], Periklis Perikleous[1], Hemangi Chavan[2], Lynn Shedden[1], Zakiyah Niwaz[3], Giulia Luciano[2], Maria Leung[4], Andre Kubler[1], Andrew G. Nicholson[5], Patrizia Viola[6], Vladimir Anikin[2], Emma Beddow[2], Niall Mcgonigle[2], Michael Dusmet[1], Simon Jordan[1], George Ladas[1], Eric Lim[1] [1]*Department of Thoracic Surgery, Royal Brompton and Harefield NHS Trust, London/United Kingdom,* [2]*Thoracic Surgery, Royal Brompton and Harefield NHS Trust, London/United Kingdom,* [3]*Clinical Outcomes Analyst - Lung Division, Royal Brompton and Harefield NHS Trust, London/United Kingdom,* [4]*Thoracic Surgery, Royal Brompton Hospital, London/United Kingdom,* [5]*Department of Histopathology, Royal Brompton and Harefield NHS Trust, London/United Kingdom,*[6]*Histopathology, Royal Brompton Hospital, London/United Kingdom*

Background: Recently, Tomasetti and Vogelstein proposed that the variation in cancer risk among tissue is explained by the number of stem cell division, and this was widely interpreted as "bad luck" due to random mutations arising during DNA replication in normal non-cancerous stem cells. Smoking is widely considered as the main aetiological risk factor for the lung cancer and the aim of our study is to evaluate the hypothesis comparing the differences in proportions of the two main histological subtypes in smokers and never smokers in a patients with early stage primary lung cancer to determine the impact of smoking on the development of squamous and adenocarcinoma. **Methods:** Data were retrospectively analysed from a prospectively collated database at our institution over a 7 year period. Histological data were extracted and compared for the two main historical subtypes of squamous and adenocarcinoma (subtyped according to the new IASLC adenocarcinoma classification). Frequencies were compared using Fishers exact or Chi square tests as appropriate to the data. **Results:** A total of 2170 patients underwent surgical resection for lung cancer at our institution from March 2008 to November 2014 of which 436 (20%) patients were never smokers. The mean age (SD) was 66 (12) years and 48% were female. The relative proportion of patients with squamous carcinoma was significantly different between smokers 323 (27.0%) and never-smokers 16 (5.7%) with P <0.001 with a risk ratio of 4.70 (95% CI 2.9 to 7.6). However the relative proportions between patients with adenocarcinoma were similar between smokers 578 (48.3%) and never-smokers (54.4%) P=0.06 with a risk ratio of 0.89 (0.79 to 1.00). **Conclusion:** Our results suggest that smoking remains an important aetiological risk factor for the development of primary lung squamous cell carcinoma. For adenocarcinoma, the relative proportions between smokers and never-smokers were similar (in fact lower for smokers) supporting Tomasetti and Vogelstein hypothesis of random mutations arising during DNA replication in normal non-cancerous stem cells– or simply put as "bad luck".
Keywords: smoking history, adenocarcinoma, spontaneous mutations

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-016 Upstaging of Lung Cancer - Use of Endobronchial Ultrasound in the Prediction of T4 Disease J. F. Turner[1], Scott Parrish[2], Robert Browning[2] [1]*Department of Medicine, University of Tennessee Graduate School of Medicine, Knoxville/TN/United States of America,* [2]*Pulmonary, Walter Reed National Military Medical Center, Bethesda/MD/ United States of America*

Background: There has been an increased utilization of radial and convex probe endobronchial ultrasound with application in the nodal staging of the mediastinum for bronchogenic carcinoma. Prior work has demonstrated that vascular invasion (Vi) is associated with upstaging and a worsened prognosis in those patients with non-small cell carcinoma. Utilization of endobronchial ultrasound has been promulgated to improve the sensitivity of transbronchial needle aspiration (TBNA), but also to avoid vascular puncture. As such, imaging of the pulmonary vasculature is routinely performed and may allow insight and confirmation of CT imaging of vascular invasion. **Methods:** We present the case of a patient presenting with scant hemoptysis where the CT scan was interpreted as possible invasion of the right pulmonary artery (Fig 1). The literature was reviewed as to the effect of vascular invasion on upstaging patients with lung cancer and he underwent a diagnostic procedure. **Results:** Bronchoscopy and endobronchial ultrasound were performed to allow nodal TBNA to permit pathologic diagnosis and staging of the patient's identified lung mass. During the procedure, ultrasound of the pulmonary vasculature revealed extensive invasion and mass effect from the central tumor mass (Fig 2). Using these synergistic techniques, the patient was upstaged to T4 and was referred for consultation with medical and radiation oncology. Fig. 1:

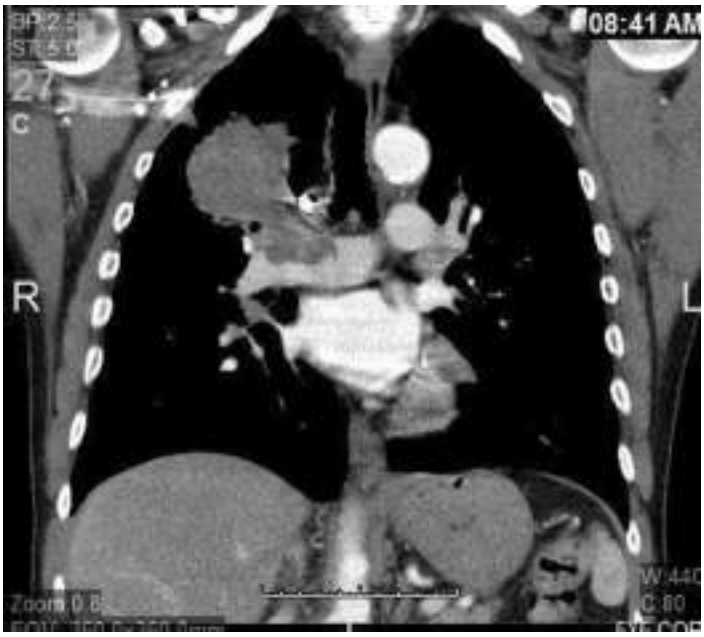
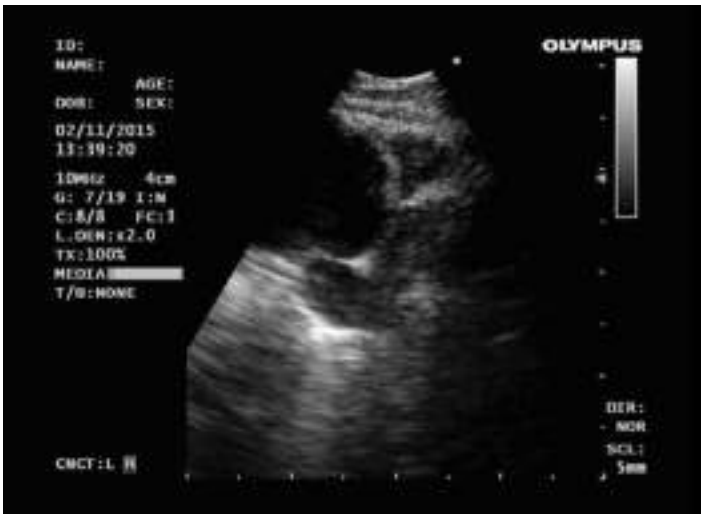


Fig. 2:



Conclusion: Vascular invasion has previously been demonstrated to result in upstaging and a poorer prognosis. Critical to the workup, then, is not only diagnostic pathology, but also rapid and accurate staging and a decision regarding appropriateness of surgical resection. We believe our case illustrates that with the synergistic use of convex or radial endobronchial ultrasound during initial bronchoscopy, vascular invasion may be accurately confirmed resulting in improved decisions in patient care.

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-017 The Search for Cancer: Procedures in High Risk Patients: Elevated Cardiac Risk in Patients Undergoing Bronchoscopy Dipaben Modi[1], Tina Dudney[2], J. F. Turner[2] [1]*Department of Medicine, University of Tennessee Graduate School of Medicine, Knoxville/United States of America,* [2]*Department of Medicine, University of Tennessee Graduate School of Medicine, Knoxville/TN/United States of America*

Background: There has been an increased utilization of tomographic imaging to aid in the acute evaluation of patients with chest complaints and in high-risk patients to screen for lung cancer with the recently reported National Lung Screening Trial (NLST). In particular, utilization of CT-angiograms in the emergency room may, increasingly, identify patients presenting with concurrent cardiac injury and imaging abnormalities concerning for lung cancer. **Methods:** We present the case of a 75 year old male with chest pain and a non-resolving pulmonary infiltrate concerning for lung cancer. Although the chest pain was felt to be secondary to the pulmonary abnormality, evaluation by the bronchoscopy and anesthesia services revealed severe hypertension and an elevated troponin. The procedure was cancelled and cardiology was consulted with cardiac evaluation, control of blood pressure, and subsequent bronchoscopy. **Results:** Although review of the literature revealed extensive study of preoperative risk stratification for surgery there was a paucity of studies regarding the performance of bronchoscopy in

the setting of hypertension and possible silent ischemia, particularly in patients with concurrent elevated troponin levels. We use this case to review the current literature and propose recommendations in the setting of cardiac ischemia with a rapid pathway for evaluation and treatment to allow needed bronchoscopic diagnostic procedures. **Conclusion:** Bronchoscopy in patients with hypertension or chest pain, particularly in the setting of elevated troponins, is poorly studied and may result in an increased risk of silent ischemia. Consideration for additional cardiac evaluation or peri-operative use of beta-blockers is warranted. Additionally, prospective studies to determine the incidence of silent ischemia in patients, such as presented, should be considered. **Keywords:** lung cancer, cardiac risk, bronchoscopy

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-018 Quick Radiological Course of Lung Cancer Mimicking Pulmonary Tuberculosis Nesrin Ocal[1], Deniz Dogan[1], Gurhan Taskin[2], Canturk Tasci[1], Hayati Bilgic[1] [1]*Chest Diseases, Gulhane Military Medical Faculty, Ankara/Turkey,* [2]*Intensive Care Unit, Gulhane Military Medical Faculty, Ankara/Turkey*

Background: Cavitary lung lesions are primarily due to pulmonary tuberculosis but they also can be associated with other etiologies such as lung malignancies, fungal infections. To exclude tuberculosis with ARB tests when these kind of lesions detected, is a generally accepted clinical approach. Rapid radiological progression in cavitary lesions are usually interpreted as tuberculosis while a slower progression is expected in malignancies. **Methods:** 'not applicable' **Results:** We presented this rare case because of a rapid radiological progression in a patient with lung cancer. Sixty-six year old male was admitted to our clinic with cough, weight loss, fever and fatigue. ARB test was planned and nonspecific antibiotherapy was started because of the cavitary lesions in left upper lobe on CT which was performed in another centre one week before admission to our clinic. ARB test was negative and control CT was planned. CT revealed prominent progression of the lesions. Although tuberculosis was the initial diagnosis because of this rapid progression diagnostic bronchoscopy was performed. Endobronchial lesion in the left upper lobe was detected and pathological examination revealed squamous cell lung cancer. **Conclusion:** Although cavitary lesions can be observed in lung cancer, such a rapid progression as observed in our case suggests infections, especially pulmonary tuberculosis rather than malignancies. We presented this case to be useful for the clinicians in cavitary lung lesion assessment process. **Keywords:** cavity, lung cancer, tuberculosis, mimicking

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-019 Lung Cancer Deaths in the NLST Attributed to Nonsolid Nodules Rowena Yip[1], Artit Jirapatnakul[1], Minxia Hu[2], Dongming Xu[1], Claudia I. Henschke[1], David F. Yankelevitz[1] [1]*Radiology, Icahn School of Medicine at Mount Sinai, New York/United States of America,* [2]*Department of Diagnostic Ultrasound, Beijing Tongren Hospital, Beijing/China*

Background: There has been increasing awareness of the more indolent course of cancers manifesting in nonsolid nodules, especially among those where the nodule is solitary or dominant. There have been reports of virtually 100% cure rates upon resection and most recently, the recommendation from the ACR in their Lung-RADS screening guidelines is for those nonsolid nodules less than 2 centimeters to be followed by annual screening without additional evaluation. In order to further evaluate the aggressiveness of these types of cancers in the screening setting, we determined how frequently they were the cause of death (COD) within the NLST. **Methods:** We searched the NLST database to identify all participants who had a diagnosis of lung cancer after a positive result on CT screening and whose death was attributed to lung cancer by the NLST endpoint verification process. Among them, 28 participants had at least one nonsolid nodule identified on CT in a screening round. Among these, all cases where the nonsolid nodule could not identified in the study year the cancer was first identified (cancyr) or in the location of the confirmed lung cancer were excluded. All images associated with the remaining 8 cases were downloaded from The Cancer Imaging Archive (TCIA) using the NLST Query Tool and reviewed by three radiologists (DY, DX, MH) to assess nodule consistency and location. **Results:** Among the 8 cases reviewed by the radiologists, only 5 cases had at least one nonsolid nodule. The remaining three cases had no CT evidence of a non-solid nodule (Table 1). Among the 5 cases with nonsolid nodules, 2 cases had another large solid nodule (average diameter of 54.5mm and 15 mm) in the same lobe which was the probable lung cancer that was the cause of death. In another case, the nodule was less than 5 mm in diameter and stable for 3 years, and in another the cause of death was small cell carcinoma which is not known to manifest as a nonsolid cancer. One case manifested on baseline scan with multiple nonsolid and part-solid nodules which all grew on successive annual scans.

Table 1. Lung cancer deaths with non-solid nodules in NLST database

Case	Any NS nodules	Size of largest NS	Multiple/ solitary	Stage/Cell-type	Comments
128534	Y	29 x 19	Solitary NS Solitary solid	IIIA/Squamous cell	Large solid nodule (57 x 52)
134088	Y	27 x 20	Multiple NS Multiple solid	IV/Small-cell	
212718	Y	26 x 26	Multiple NS Multiple PS	IV/BAC	Cancer reported in all lobes
116279	Y	5 x 4	Solitary NS	IV/Carcinoma NOS	NS nodule appears stable over 3 years
126576	Y		Multiple NS Solitary solid	IA/Adeno-mixed	Growing solid nodule, 15 mm
117025	N		Multiple solid	IV/Adeno NOS	
208792	N		Solitary solid	IIIA/Squamous cell	
218307	N		Solitary solid	IIIA/Squamous cell	

*ns-nonsolid; ps-part-solid **Conclusion:** It seems unlikely that within the NLST, there were cases of lung cancer specific death that were attributable to cancers manifesting as a solitary or dominant nonsolid nodule. This lends further support that lung cancers manifesting as nonsolid nodules have an indolent course. **Keywords:** non-solid, ground glass, mortality, CT

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-020 CT-Guided Percutaneous Fine Needle Biopsy for Small Lung Tumor (≤ 2cm) and Diffficult Pulmonary Lesions Jun Zhang, Xueshan Qiu *China Medical University Lung Cancer Center, The First Hospital of China Medical University, Shenyang/ China*

Background: lung cancer is increasing rapidly in China. There are more and more peripheral small lung cancer (≤2cm) was found. CT-guided percutaneous fine needle biopsy becomes first of choice for pathological diagnosis of peripheral small lung tumor (≤2cm) and some central pulmonary lesions which could not be pathologically diagnosed by fiberoptic bronchoscopy. We developed CT-guided percutaneous fine needle biopsy (CT-NB) for detecting early stage lung cancer (size ≤2cm peripheral small lung cancer) since 1992. We discuss typical cases here. **Methods:** Case1: Man, aged 52, right lower lobe 1.5cm ball tumor, no typical malignant sign; unwilling to undergo surgery due to years' coronary heart disease; CT-NB was performed and lung adenocarcinoma was diagnosed. Case2: Man, aged 63, right upper lobe 1.2cm ball tumor, with cardiopulmonary dysfunction; CT-NB was performed and found some inflammatory cells, but no malignant tumor cells found. Case3: Man, aged 40, heavy smoker, cough and blood-tinged sputum for one month, left lower lobe 3.5cm irregular mass, regional and subcarinal lymph node swollen, clinically progressed rapidly, suspected small-cell lung cancer (SCLC), T2N2M0; at least pneumonectomy was needed if want resected; CT-NB was performed and non-small cell lung cancer (NSCLC) was diagnosed, and SCLC was excluded. **Results:** For Case 1: right lower lobe resection and lymph node dissection was performed, postoperative diagnosis was adeno-squamous cell carcinoma, 1.5X1.3X1.3cm, lymph node negative, pT1N0M0 Stage I, early stage lung cancer. He was alive healthily more than five years postoperatively. For Case 2: considered as a benign disease; carefully follow-up for more than 5 years, no malignant sign. For Case 3: left pneumonectomy and lymph node dissection was performed; postoperative diagnosis was squamous cell carcinoma; pulmonary ligament lymph node positive, others negative, pT2N2M0 StageIIIA; radiation followed. He was alive healthily more than five years postoperatively. **Conclusion:** CT-NB is a very useful diagnostic method for peripheral small lung tumor (≤2cm) and some central pulmonary lesions with fiberoptic bronchoscopy failed. CT-NB could be used to confirm the diagnosis of lung cancer, to help make decision for surgical resection, to help cure more early stage lung cancer patients, to help improve the prognosis of lung cancer treatment. CT-NB could also be used to exclude lung cancer diagnosis, to avoid unnecessary surgery, especially for those aged, cardiopulmonary dysfunction, high risk patients. CT-NB could be used to confirm the pathological type of lung cancer before treatment applied, to help distinguish SCLC from NSCLC, to help select the best choice of treatment modality of chemotherapy and radiation according to patient's age, cardiopulmonary function status, pathological type, and gene types. **Keywords:** fine needle, small lung cancer, biopsy, CT guided

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-021 Lung Cancer Presented with Neurological Symptoms and Diagnosed after Brain Surgery Nesrin Ocal, Deniz Dogan, Seval I. Ozan, Canturk Tasci, Seyfettin Gumus, Ergun Ucar, Omer Deniz, Ergun Tozkoparan, Hayati Bilgic
Chest Diseases, Gulhane Military Medical Faculty, Ankara/Turkey

Background: Lung cancer is still one of the the most important and common mortality cause. Although, the presentation and course of the disease differ with the cell type, usually typical symptoms are seen. The most common symptoms include fatigue, weight loss, shortness of breath, and chest pain. These symptoms especially in smoking patients suggest lung cancer first. But in some cases paraneoplastic syndromes and symptoms of other systems caused by diffusing cancer come forward. Such findings are most common in small cell lung cancers (SCLC) among lung cancers. Because early metastasis and paraneoplastic syndromes SCLC can have very different clinical presentations. **Methods:** To emphasize this issue, we present a case of SCLC having only neurological signs. **Results:** 60 years old male patient with a history of 70 pack years smoking, admitted to neurology clinic with vertigo, headache, nausea, and changes in consciousness. Because of the tumoral lesion in the left cerebellum seen in brain computed tomography, he was referred to brain surgery. Although, a preoperative thorax tomography revealed a mass lesion in left lung, he was operated for palliation of neurological symptoms and pathological diagnosis. Intraoperative frozen sampling diagnosed as small cell lung cancer. Patient is still followed by our department and radiation oncology. **Conclusion:** We present this case as a reminder of lung malignancies can be met by different presentations.
Keywords: barin metastasis, lung cancer, neurological, Surgery

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-022 Huge Dilatation of the Azygos Vein (Aneurysms of the Azygos Vein). University Hospital 'Shefqet Ndroqi' Thorax Surgery Service Fadil Gradica[1], Lutfi Lisha[1], Dhimitraq Argjiri[2], Alma Cani[3], Fahri Kokici[3], Dorjan Bozaxhiu[4], Albert Leka[5], Silvana Bala[2], Loreta Karaulli[2], Flora L. Gradica[6] [1]*Thorax Surgery, University Hospital"Shefqet Ndroqi", Al/Albania,* [2]*Pnemology, University Hospital"Shefqet Ndroqi", Al/Albania,* [3]*Anestesiology Reanimacion, University Hospital"Shefqet Ndroqi", Al/Albania,* [4]*Visceral Surgery, University Hospital'Shefqet Ndroqi", Al/Albania,* [5]*Imagery, University Hospital"Shefqet Ndroqi", Al/Albania,* [6]*Farmacy, Farmacy "Gradica", Al/Albania*

Background: Huge dilatacion of the azygos vein (Aneurysms of the azygos vein) are rare and can sometimes mimic a paratracheal or posterior mediastinal mass. It is important to confirm the diagnosis with radiologic tools before performing invasive procedures, which carry the risk of hemorrhage. The usual diagnosis of a mediastinal mass by mediastinoscopy or percutaneous fine-needle aspiration or biopsy is very hazardous if there is a venous varix. Noninvasive thoracic CT scanning is a safe and better choice for diagnosis **Methods:** Here, we present a case in a 46-year-old symptomatic patient of an increasing azygos vein aneurysm that mimicked a growing paratracheal mass and posterior mediastinal mass. Review of images obtained using various modalities, including contrast CT scanner with out dynamic magnetic resonance image (MRI), revealed that the image findings were suggestive of azygos vein huge dilatation of the azigos vein (aneurysm). **Results:** Using this method, an exact diagnosis can be reached without resorting to invasive procedures or with mini-invassiv thorax surgery.The main causes of a dilated azygos vein include portal vein hypertension, obstruction of the superior vena cava, hypertension in the right-heart chamber, Budd-Chiari syndrome, hypervascular tumor draining into the azygos system, posttraumatic pseudoaneurysm, kinking of the aorta, and pregnancy. In some cases, no definitive cause is found. **Conclusion:** We report a case of azygos vein varix mimicking a mediastinal mass in a patient with flebotrombosis of right femoral vena.
Keywords: Azygos vein aneurysm, dynamic MRI, growing paratracheal or posterior mediastinal mass

POSTER SESSION/ SCREENING AND EARLY DETECTION
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.06-023 Optimizing Lung Cancer, Utility of Early Thoracoscopy vs Thoracocentesis Emmanuel Peña Gómez Portugal[1], Leticia S. Nieto[2], Francisco G. Ramirez[3], Salomon S. Ortiz[4], Ruben C. Mendez[4], Jorge O. Ortiz[5], Francina B. Morales[6], Enrique O. Lopez[7], Erick A. Neri[8] [1]*Thoracic Surgery, Pachuca General Hospital, Pachuca Hidalgo/Mexico,* [2]*Anestesia, La Raza Medical Center, Mexico/Mexico,* [3]*General Surgery, Pachuca General Hospital, Pachuca/Mexico,* [4]*Surgery, Pachuca General Hospital, Pachuca/Mexico,*[5]*Oncologuy, Pachuca General Hospital, Pachuca/Mexico,* [6]*Thoracic Surgery, National Institute of Nutricion, Mexico/Mexico,* [7]*Pulmonary Medicine, Escandon Medical Hospital, Mexico/Mexico,* [8]*Pathology, Pachuca General Hospital, Pachuca Hidalgo/Mexico*

Background: INTRODUCTION Prospective study from the work group in thoracic oncology in Hidalgo Mexico Lung cancer Still first cause of dead for cancer in wordlwide. Diagnosis, prevalence and therapeutic approach apperece directly with their clinic manifestation and deppends on economic an sociocultural patients behave. Being a non cover pathology by the State the patient has to pay all management and doctors visit. Eventhough hospital structure **Methods:** Retrospective study from january 2012 to december 2014 in Mexico including patients from public attendance and private all of them with autorized consecent We include 100 patients with massive pleural effusion, lung cancer risk factors like age more tan 50 years old, tabacco use with approximatly 30 annual package, Wood smoke 100 hr / year, work activity in mines, construction, masonry, or asbestos fibers at home or work. Sample include 54 male and 46 female. Diagnostic Thoracocentesis was done in all 100 patients with an amount of pleural effusion with range between 2.5 ml to 2500ml, aspect yellow to hematic an average of 248.6 ml. Only 8 patients (8%) Has oncologic diagnosis in pleural effusion; 40 patients (40%) with diagnosis in pleural tissue including 37 patients (37%) cáncer diagnosis and 3 patients (3%) tuberculousis. The rest 52 patients (52%) only mesothelial reaction in first thoracocentesis. From the 100 patients 60% do not return to confirm diagnosis or to reevaluate at 2 weeks with chest X ray and to explain first pathologic result arguing not having time, no money and no necesary if the first one was no cancer. **Results:** The present study shows how only in 8% can get in an oncologic diagnosis in pleural liquid in a thoracic reference hospital, on the other hand patients that had a complete protocol with a CT scan after thoracocentesis, and surgical intervention with thoracoscopy and pleural biopsy we can achieve an oncologic diagnosis in 29%, in patients with clinical features and risk factors for lung cancer. 29 patients that underwent single port thoracoscopy were previously rated for cardiovascular risk by a cardiologist, and for respiratory hazard by a pulmonologist. Surgical time varied from 1 to 2 hours, hospital stay was 2 to 5 days, those patients that persisted with high output from thoracic catheter tunneled were treated ambulatory and weekly consultation until chest tube withdrawal. **Conclusion:** Our study shows how a patient with a massive pleural effusion, with clinical data and risk factors for lung cancer, can get an oncological diagnosis by single port thoracoscopy as initial approach, with surgical staging, giving a quick resolution, and in selected cases offer a palliative treatment by a thoracic catheter tunneled and chemical pleurodesis, if indicated after making serial samples for histological study. Offering a resolutive treatment and a prompt diagnosis in a pathology that is increasing and with no satisfaying results in developing countries were a strict follow in many cases is no posible
Keywords: lung cancer, pleural effusion, thoracoscopy, thoracic tunneled catheter

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-024 Follow-Up Recommendation Compliance in a Clinical CT Lung Screening Program Sama Alshora[1], Brady Mckee[1], Shawn Regis[2], Christopher Bolus[3], Andrea Mckee[2], Robert French[1], Sebastian Flacke[1] [1]*Radiology, Lahey Hospital & Medical Center, Burlington/MA/United States of America,* [2]*Radiation Oncology, Lahey Hospital & Medical Center, Burlington/MA/United States of America,* [3]*Radiology, Beverly Hospital, Beverly/MA/United States of America*

Background: The efficacy and cost-effectiveness of CT lung screening will in part depend on patient compliance with CT lung screening exam recommendations. However, rates of patient compliance and the reasons for non-compliance have not been widely reported for clinical CT lung screening programs. **Methods:** We retrospectively assessed the rate of patient compliance with exam follow-up recommendations in our CT lung screening program. All patients evaluated fulfilled the NCCN high-risk criteria for lung cancer screening and underwent screening between 1/12/2012 and 6/12/2013. Screened patients referred from outside our institution were excluded due to limited followup. Patients with negative, benign, or probably benign results were recommended to have a repeat screening exam in 6-12 months. Patients with suspicious findings were recommended to undergo a pulmonary consultation. To be considered compliant, patients had to be no more than 90 days past due for their next recommended exam or clinical evaluation as of 9/12/2014. Patients who died, were diagnosed with cancer, exceeded the program age limit, or became otherwise ineligible for additional screening were considered adherent. Compliance rates were assessed across multiple factors including sex, age, smoking history, baseline exam result, and NCCN high-risk group status. **Results:** 901 high-risk patients from our institution underwent a baseline CT lung screening exam between 1/12/2012 and 6/12/2013. 772/901 (85.7%) were compliant as of 9/12/2014. 155/901 (17.2%) were non-compliant during the study interval of which 26 (16.8%) returned to screening compliance by 9/12/2014. The most common reasons for non-compliance were refusal to undergo the follow-up exam (66.7%), inability to contact the patient (20.9%), and patient inability to obtain a followup order from their physician (7.8%). 23/901 (2.6%) were discharged for reasons other than non-compliance. Subgroup analysis demonstrated a statistically significant increase in screening compliance among female patients ($p = 0.035$) and among those patients 65-73 years old ($p=0.040$). **Conclusion:** High rates of compliance with CT lung screening recommendations are achievable in clinical practice.
Keywords: compliance, CT lung screening, Follow-up recommendation

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-025 Electromagnetic Navigation Bronchoscopy in the Evaluation of Lung Lesions: The Carolinas Medical Center Experience Jaspal Singh[1], Shay Hatfield[2], Oshauna Morgan[1], John D. Doty[3] [1]*Charlotte Medical Clinic-Pulmonary Division, Carolinas Medical Center, Charlotte/NC/United States of America,* [2]*Medical Education, Carolinas Healthcare System, Charlotte/AL/United States of America,* [3]*Thoracic Oncology, Levine Cancer Institute, Charlotte/NC/United States of America*

Background: Electromagnetic Navigation Bronchoscopy (ENB) is a relatively new minimally invasive bronchoscopic procedure that can be used to diagnose lung cancer, allowing bronchoscopists to (1) navigate towards peripheral lung lesions unreachable by a traditional bronchoscope, and (2) to utilize tools that can potentially obtain tissue samples large enough to perform advanced diagnostic and molecular testing. Here we share the experience of ENB at a large community-based hospital, aiming to better understand the diagnostic ability of ENB as well as possibly identify success factors for the biopsy methodology. **Methods:** Between September, 2012 and June, 2014, ENB was utilized in 138 cases to diagnose pulmonary lesions. Retrospective chart review was performed to access patient personal demographic information and disease-specific information. True positive diagnostic procedures were defined as those with a pathologically confirmed cancer diagnosis. True negative procedures were defined as those in which the lesions were not cancerous and had either resolved on radiological follow-up or have

been stable over a period of 1 year. We assessed diagnostic yield percentages, lesion characteristics such as size and location, histological and staging characteristics of the tumor, outcomes of diagnostic tools, and size-tool correlation. **Results:** The ENB System carried an overall diagnostic yield of 75% with a sensitivity was 71.8% and specificity of 100%. 79% represented true positive results and 21% false negatives. Of the True Positives, 93% were non-small cell of which 73.6% were adenocarcinoma or had adenocarcinoma features. Of the latter, 82.1% of the adenocarcinomas diagnosed had enough tissue in the biopsy specimen for molecular testing. Of the negative results, 23% were later proven within 3-4 months of the initial biopsy and 77% after 3-4 months. The majority of cases attempted were stage I and II, with more success with lesions of larger tumor volume (greater than 500 mm^2). Of the four tools used for biopsy sampling: lavage, brush, fine needle aspiration (FNA) and forceps, the brush had the highest true value percentage at 82.6%, followed by forceps at 80.7%. Lesions located in the right lung produced a greater percentage of true diagnoses with the right middle lobe giving an 87.5% yield while having the lowest percentage of false diagnoses at 12.5%. Risks for the procedure was 3.6% with 4 patients having pneumothorax and 1 patient with hemorrhage requiring intervention **Conclusion:** ENB can be successfully used to diagnose lung cancer in a community setting with a minimally invasive approach, and do so with reasonable accuracy and minimal risk. Moreover, tissue yields from this procedure were sufficient in over 80% of adenocarcinoma cases for molecular testing. Success factors include greater lesion size and the deployment of multiple diagnostic tools to enhance diagnostic yield. Further study is needed to determine other success factors.
Keywords: nodules, bronchoscopy, navigation, Molecular

POSTER SESSION/ SCREENING AND EARLY DETECTION
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P3.06-026 Gene Expression Signature to Predict Early Development of Brain Metastasis in Lung Adenocarcinoma
Oscar Arrieta Rodriguez[1], Alette Ortega Gomez[2], Claudia Rangel[3], Camilo Molina Romero[1], Eleazar O. Macedo[1], Jorge Negueb[1], David Saavedra[1], Alfredo Hidalgo[4], Gabriela Mercado[4], Rogelio Hernandez Pando[5]
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Background: Advances in systemic treatment have substantially improved the overall survival of advanced lung adenocarcinoma patients, and risk of brain metastases(BM) is higher. The survival of patients with symptomatic BM is poor. The identification of NSCLC patients with a high risk of developing BM would enable pre-emptive intervention to improve the outcome. **Methods:** A total of 53 biopsies of primary lung tumor adenocarcinoma stage IV treatment-naïve were analyzed for gene expression profiling using Affymetrix HuGene 1.0 ST and were processed in R using Bioconductor libraries. All patients were evaluated with brain MRI at diagnosis with a 3-month follow-up for BM development. Patients were classified into two groups: early-BM(< 6 months) and late-BM(> 6 months). A second independent cohort of 55 patients was analyzed to validate the gene expression signature (ClinicalTrials.gov: NCT00862173). **Results:** Samples were classified as early-BM(17) and late-BM(6), the remainder 30 never developed BM. Significant changes in gene expression of about100 genes were found. Eleven highly significant genes (B-stat > 12) were associated with process of cell-migrationCNN3(down-reg.) and adhesionCDH10(up-reg); anti-apoptosisBAG1(up-reg); immunological evasionSSX2(up-reg) and RAET1E(up-reg); signaling pathways related to RAS gene RAB9A(up-reg) and RAPGEF5(down-reg); mRNA-tRNA translocationDUS2L(up-reg); methylation controlNOC2L(up-reg); and members of the EGFR family EPGN(up-reg) and IGFR, IGF2BP1(up-reg). **Conclusion:** We describe an 11-gene signature that may predict the risk of BM which has the potential to classify patients and evaluate screening strategies that would facilitate pre-emptive interventional trials such as prophylactic cranial irradiation.
Keywords: NSCLC, Expression Signature, brain metastases

POSTER SESSION/ SCREENING AND EARLY DETECTION
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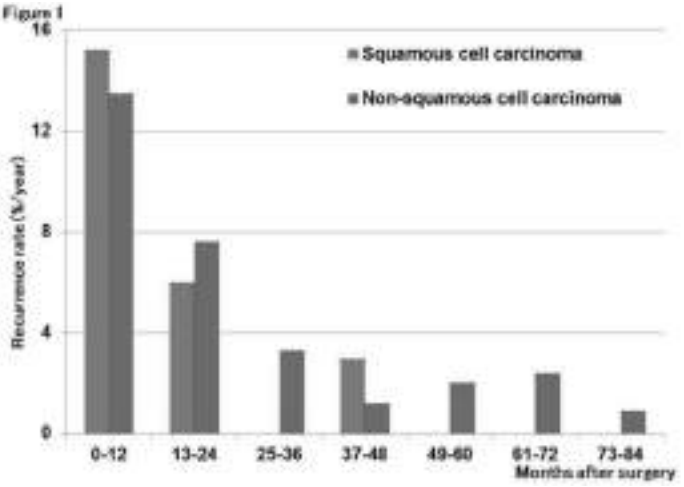
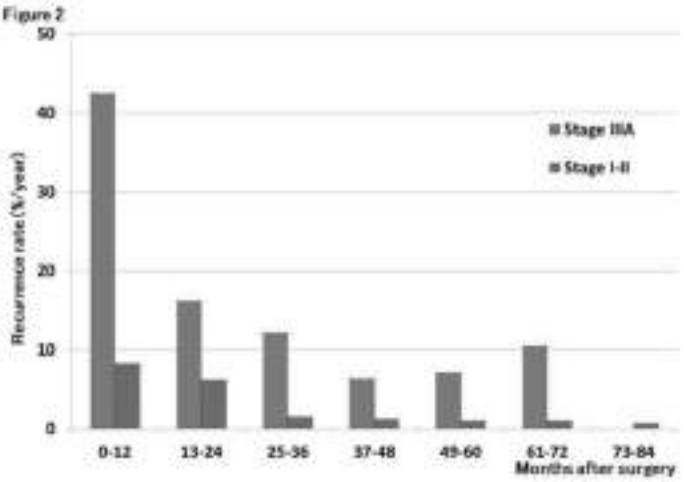
P3.06-027 Stage and Histology Specific Differences in Patterns of Recurrence in Early Stage and Locally Advanced Non-Small Cell Lung Cancer
Hideaki Kojima, Yoshiyuki Yasuura, Hiroyuki Kayata, Reiko Shimizu, Tomohiro Maniwa, Shoji Takahashi, Mitsuhiro Isaka, Yasuhisa Ohde *Division of Thoracic Surgery, Shizuoka Cancer Center, Shizuoka/Japan*

Background: Various guidelines have proposed continuous surveillance for non-small cell lung cancer (NSCLC) after curative therapy. Yet the optimal postoperative surveillance strategy remains unclear. **Methods:** Patients who underwent complete resection for stage I-IIIA NSCLC were analyzed. Complete resection was defined as lobectomy and lobe-specific systematic nodal resection or more. We compared patterns of recurrence in patients with histology and early stage vs locally advanced NSCLC. **Results:** From 2002 to 2010, 745 patients were identified. 106 of 625 patients (17%) with stage I-II NSCLC and 74 of 120 patients (62%) with stage IIIA NSCLC developed recurrences. Local recurrences were significantly frequent in stage IIIA patients (45 [61%] vs 29 [27%] for stage I-II patients), whereas distant recurrences were about the same frequency in stage I-II and IIIA patients (91 [86%] vs 64 [86%]). Approximately 90% of recurrences had occurred within 3 years after surgery and recurrence rate within first year was significantly higher in stage IIIA patients (51 [69%] vs 52 [49%] for stage I-II patients; p=0.008). Squamous cell carcinoma (SqCC) patients had tendency to relapse earlier than non-SqCC patients (Figure 1). In particular, all recurrences in stage IIIA-SqCC patients had occurred within first 2 years . Although the risk of recurrence in stage IIIA patients was highest in the first 2 years, it remained consequential up to 6 years after surgery (Figure 2).





Conclusion: Stage IIIA NSCLC patients had significantly higher risk of recurrence and this risk was continued to 6 years after surgery. SqCC patients had tended to recur earlier. Surveillance strategies may need to account for stage- and histology-specific differences.
Keywords: recurrence, non-small cell lung cancer

POSTER SESSION/ SCREENING AND EARLY DETECTION
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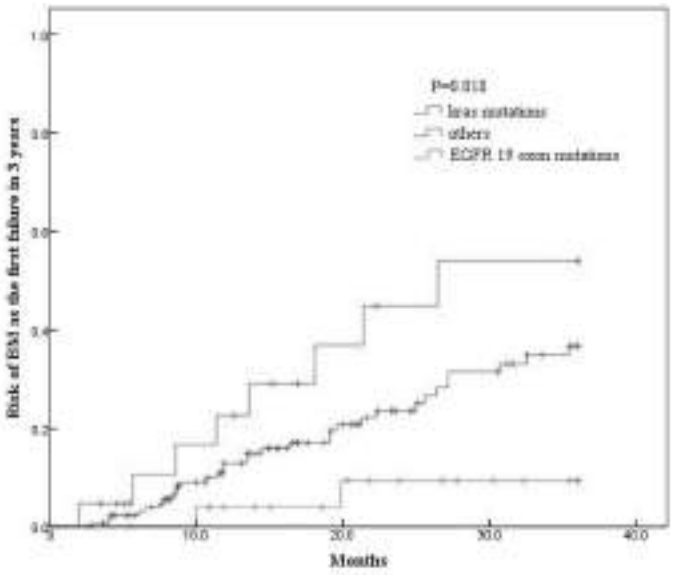
P3.06-028 Risk Factors of Brain Metastases in Completely Resected Stage IIIA(N2) Pulmonary Adenocarcinomas
Qin Zhang, Xiaolong Fu *Radiation Oncology, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai/China*

Background: Previous studies show that adenocarcinomas is the main high risk factor of brain metastases (BM) in NSCLC, and 90% of BM developes in 3 years. In patients with completely resected stage IIIA(N2) pulmonary adenocarcinomas, we aimed to identify the risk factors of BM as the first site of failure in 3 years on the basis of the new lung adenocarcinoma classification and molecular biology information. **Methods:** Patients with IIIA(N2) pulmonary adenocarcinomas, who had undergone radical surgery in our hospital from January 2005 to July 2012 were retrospectively reviewed. We observed the correlation among clinical factors, the new lung adenocarcinoma classification, lymph node status, microenvironmental factors, gene mutation status and BM to find out the risk factors of BM. DNA of EGFR and KRAS was extracted and purified from primary tumors embedded in paraffin blocks. KRAS and EGFR mutation analyses were performed by using DNA sequencing. Main outcome measure was BM as the first site of failure in 3 years.The cumulative incidence of BM as the first site of failure were determined using the Kaplan–Meier analyiss. The log-rank test was used for univariate analysis, and Cox regression was used for multivariate analysis. **Results:** 179 patients with completely resected stage IIIA(N2) pulmonary adenocarcinomas were included in this study. EGFR and KRAS mutations were found in tumors 41.3% and 11.7%, respectively. The most common EGFR mutations were deletions in exon 19 and the p.L858R point mutation in exon 21. The most common KRAS mutations were G-T or G-C point mutation in codon 12. Brain was the most common site of distant failure as the first failure, and 93.3% BM developed in 3 years after the complete resection. Multivariate analysis showed that the extra-capsular extension (ECE) , cN2 and KRAS mutations were significantly associated with the high risk of BM as the initial site of failure in 3 years, while EGFR 19 exon mutations were the low risk of BM. The risk of BM in patients with KRAS mutations were significantly higher than patients with EGFR 19 exon mutations or other EGFR mutaions (P=0.018).



Conclusion: In patients with completely resected stage IIIA(N2) pulmonary adenocarcinomas, ECE, cN2 and KRAS mutations were independent high risk factors for BM as the initial failure in 3 years. The EGFR 19 exon mutation may be a protective factor of BM. The new lung adenocarcinoma classification and tumor microenvironment were not statistically significant factors in our series. **Keywords:** EGFR, KRAS, pulmonary adenocarcinomas, brain metastases

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POSTER SESSION/ SMALL CELL LUNG CANCER
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P3.07-001 Anaplastic Lymphoma Kinase (ALK) Gene Rearrangement in Small-Cell Lung Cancer (SCLC): A Single Center Experience Birgitta I. Hiddinga[1], Karen Zwaenepoel[2], Christian Rolfo[3], Patrick Pauwels[2], Jan P. Van Meerbeeck[1] [1]*Thoracic Oncology, Antwerp University Hospital, Edegem - Antwerp/Belgium,* [2]*Pathology, Antwerp University Hospital, Edegem - Antwerp/Belgium,* [3]*Phase I Unit Medical Oncology, Antwerp University Hospital, Edegem - Antwerp/Belgium*

Background: In small-cell lung cancer little is known about harboring an ALK translocation [1, 2]. The aim of this study was to investigate the prevalence of ALK expression and rearrangement in patients with SCLC. **Methods:** In this retrospective series, archival tissue from 17 treatment naïve patients with SCLC and neuroendocrine tumors was analyzed to detect ALK expression by immunohistochemistry (IHC) in all samples. Cut-off value for positivity was similar as in non-small-cell lung cancer (NSCLC): focally strong staining of the tumor cells Fluorescent in-situ hybridization (FISH) with Vysis LSI ALK probe was performed in the IHC positive cases [3]. The ALK FISH positive cases were submitted for exome sequencing (NGS) (Illumina MiseQ). **Results:** Of the 17 patients 9 were male and 8 female. Of these 17 patients 12 had a SCLC, 3 a neuroendocrine tumor, and 2 a neuroendocrine carcinoma. Three specimens could not be analyzed. Six of 17 specimens were ALK IHC positive, of which one neuroendocrine tumor, one neuroendocrine carcinoma and 4 of the SCLC. **Conclusion:** The IHC expression of ALK suggests a possible role of ALK-TKI in the treatment of SCLC. Mature FISH and NGS data will be presented at the meeting. **Keywords:** small-cell lung carcinoma, neuroendocrine carcinoma, ALK IHC, ALK FISH

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P3.07-002 RBM5 Expression Correlates with Decreased Proliferation and Increased Cisplatin-Mediated Apoptosis Justin Roy[1], Sarah Hunt[1], Leslie Sutherland[2] [1]*Chemistry and Biochemistry, Laurentian University, Sudbury/ON/ Canada,* [2]*Advanced Medical Reseach Institute of Canada, Sudbury/ON/Canada*

Background: Lung cancer is the leading cause of cancer-related deaths in Canada, for both men and women. Small cell lung cancer (SCLC) is one subtype of lung cancer, and accounts for 15-20% of lung cancer incidence. SCLC is an aggressive cancer and commonly develops resistance to drugs used to treat it, including platinum-based agents such as cisplatin. RBM5 is a lung cancer tumour suppressor gene that is generally downregulated in lung cancer, and deleted in some. RBM5 is an RNA-binding protein that has the ability to regulate the cell cycle and modulate apoptosis. We hypothesize that reintroduction of RBM5 into an RBM5-null SCLC cell will result in decreased cell proliferation and increased apoptotic-like cell death in the presence of cisplatin. **Methods:** A SCLC cell line with an endogenous RBM5 homozygous deletion, and two previously established stable GLC20 sublines (T2 and C4) that express different levels of RBM5, were used for *in vitro* mechanistic studies. Proliferation changes were monitored using an MTT assay and a cell counting assay. Cisplatin-induced cell death was monitored by assessing cell viability (by nigrosin staining), PARP cleavage (by Western blot), chromatin condensation and phosphatidylserine flip (by fluorescence microscopy). **Results:** Decreased proliferation was observed in the high (C4) but not the low RBM5 (T2) expressing subline, compared to either the parental GLC20 cells or the empty vector control subline. Increased cisplatin-mediated cell death, observed as PARP cleavage, was observed in both T2 and C4, compared to either the parental GLC20 cells or the empty vector control subline. Fluorescence microscopy results will be presented. **Conclusion:** These results suggest that the loss of RBM5 expression in SCLC cells leads to increased proliferation and survival of SCLC cells. We hope to demonstrate the potential role of RBM5 as a predictive marker for cisplatin sensitivity in SCLC. **Keywords:** small cell lung cancer, RBM5, apoptosis, biomarker

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P3.07-003 A Phase Ib/II Trial of Doxorubicin with Ganetespib, a Novel Hsp90 Inhibitor, in Advanced Solid Tumors, with Dose Expansion in Small Cell Lung Cancer Deepa Subramaniam, Jillian Thompson, Jenna Kramer, Hongkun Wang, Giuseppe Giaccone *Medical Oncology, Georgetown University, Washington/United States of America*

Background: Relapsed/refractory small cell lung cancer (RR-SCLC) has a poor prognosis with median overall survival of only 2-3 months. Objective responses to single agent newer chemotherapy agents range from 14-29%. One of the key mechanisms for the development of acquired resistance of cancer cells to chemotherapy is the induction of a heat shock response. Over-expression of Hsp90 and its co-chaperones in tumor cells results in up-regulation of ATP-dependent transporters such as ABCG2 and RLIP76. Such transporters act as drug-efflux pumps for chemotherapeutic agents including doxorubicin, thus mediating drug resistance. Ganetespib, a next generation Hsp90 inhibitor devoid of liver and ocular toxicities that limit other agents in its class, is now in phase 3 evaluation in NSCLC. Targeting Hsp90, ganetespib affects multiple drug resistance pathways. We recently demonstrated in vitro and in vivo that the addition of ganetespib (G) to doxorubicin (D) can indeed overcome drug resistance (Lai et al., Oncogene 2014). The primary objective of this clinical study is to determine the maximum tolerated dose and the recommended Phase II dose (RP2D) of G + D in subjects with advanced solid tumors. The secondary objectives are to determine the dose limiting toxicities (DLTs) and to assess if there is preliminary evidence of activity for the combination of G + D in RR- SCLC by determining the objective response rate and response duration. We will also aim to establish conditionally reprogrammed cancer cell lines from tumor tissue in subjects with RR-SCLC to allow ex-vivo molecular characterization and drug sensitivity testing. **Methods:** The dose escalation phase will follow a standard 3+3 dose escalation scheme with 2 dose levels of G administered weekly on Days 1, 8 of a 21-day cycle, in combination with fixed dose D at 50 mg/m^2 on Day 1. After 4-6 cycles of the combination, continuation of single agent G is permitted in patients deriving clinical benefit. The RP2D determined at the end of the dose escalation phase will be used to conduct a dose expansion study in subjects with RR-SCLC. Key inclusion criteria are refractory solid tumors (in dose escalation phase) and RR-SCLC (in dose expansion phase), age >18 years, ECOG PS 0-1, adequate organ/marrow function. Key exclusion criteria include LVEF < 50%, lifetime cumulative doxorubicin dose >150 mg/m^2, untreated, symptomatic brain metastases, serious cardiac illness, QTc >470 msec, strong inhibitors or inducers of CYP 3A4 or 2C19. DLTs are defined as grade 4 hematologic toxicities or $\geq$ grade 3 non-hematologic toxicities including hypersensitivity reactions despite pre-medication and nausea, vomiting and diarrhea despite maximal medical therapy. Response assessment will be done using RECIST 1.1. **Results:** Clinical Trial Status: A total of 6 subjects have been enrolled thus far. With no DLTs observed in 5 subjects who have crossed the DLT evaluation period, the trial continues enrollment. **Conclusion:** Not applicable **Keywords:** small cell lung cancer, Hsp-90 inhibitor, ganetespib, chemoresistance

POSTER SESSION/ SMALL CELL LUNG CANCER
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.07-004 Clinical Impact of Post-Progression Survival for Overall Survival in Patients with Sensitive Relapse of Small Cell Lung Cancer Yosuke Miura[1], Hisao Imai[1], Reiko Yoshino[2], Sakae Fujimoto[1], Kyoichi Kaira[3], Noriaki Sunaga[4], Yoshio Tomizawa[2], Koichi Minato[1], Takeshi Hisada[5], Ryusei Saito[2], Masanobu Yamada[5] [1]*Department of Respiratory Medicine, Gunma Prefectural Cancer Center, Ota/ Japan,* [2]*Department of Respiratory Medicine, National Hospital Organization Nishigunma National Hospital, Shibukawa/Japan,* [3]*Oncology Clinical Development, Gunma University Graduate School of Medicine, Maebashi/Japan,* [4]*Oncology Center, Gunma University Hospital, Maebashi/Japan,* [5]*Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Maebashi/Japan*

Background: The effect of second-line chemotherapy on overall survival (OS) might be confounded by subsequent therapies in patients with sensitive relapse of small cell lung cancer (SCLC). But there is no research in this viewpoint. Therefore, we aimed to determine the relationships between progression-free survival (PFS), post-progression survival (PPS) and OS after second-line chemotherapy in this population. **Methods:** Between January 1999 and November 2013, seventy-seven patients with sensitive relapse of SCLC who had received second-line chemotherapy following first-line platinum doublet chemotherapy were analyzed. We retrospectively collected individual data at Gunma Prefectural Cancer Center and National Hospital Organization Nishigunma National Hospital from medical records, and evaluated patient characteristics, treatment data, tumor shrinkage, PFS, PPS and OS. **Results:** The median follow-up time was 13.1 months (range 2.3-80.8 months). The response rate, the disease control rate, median PFS and median OS were 58.4%, 93.5%, 5.1 months and 13.7 months, respectively. The relationships of PFS, PPS and tumor shrinkage with

OS were analyzed at the individual level. Spearman rank correlation analysis and linear regression analysis showed that PPS was strongly correlated with OS (r = 0.91, p < 0.01, R^2= 0.96), PFS was moderately correlated with OS (r = 0.58, p < 0.01, R^2 = 0.28), and tumor shrinkage was weakly correlated with OS (r = 0.34, p < 0.01, R^2 = 0.12). Using multivariate Cox proportional hazards model with a stepwise regression procedure to explore prognostic factors for PPS, the number of regimens after progression beyond second-line chemotherapy and performance status (PS) at the beginning of third-line treatment were both significantly associated with PPS (p < 0.01). **Conclusion:** PPS has more impact for OS than PFS in patients with sensitive relapse of SCLC. Moreover, this study suggests that subsequent treatment and PS after disease progression following second-line chemotherapy may be important factors that influence OS. **Keywords:** sensitive relapse, post-progression survival, retrospective analysis, small cell lung cancer

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P3.07-005 Maintenance Irinotecan Therapy in Extensive Disease Small Cell Lung Cancer: A Feasibility Study

Shoichiro Yamamoto[1], Shigeki Umemura[2], Yukio Hosomi[3], Atsushi Horiike[4], Noboru Yamamoto[5], Hiroyasu Kaneda[6], Takashi Seto[7], Shogo Nomura[8], Naoyuki Nogami[1], Koichi Goto[2], Tomohide Tamura[5], Yuichiro Ohe[5]
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Background: We performed a feasibility study of maintenance irinotecan therapy in patients with extensive disease small cell lung cancer (ED-SCLC) who responded to the induction irinotecan plus cisplatin (IP) therapy. **Methods:** The eligibility criteria included pts with ED-SCLC who responded to four cycles of induction IP therapy, ECOG performance status (PS) of 0 to 1, age of 20 to 70 years and adequate organ functions. Pts received irinotecan monotherapy at 60 mg/m2 on days 1, 8 and 15 of a 28-day cycles until disease progression. The primary endpoint was the proportion of treatment success (TS) at 6 months. Using a binomial design, a lower activity level (p0) of 0.25 and a target activity level (p1) of 0.50, the preplanned accrual of 28 patients was sufficient (alpha, 0.10 and power, 0.90). **Results:** Between August 2012 and August 2013, 22 pts were enrolled. However, accrual was discontinued because of the three grade 3 pneumonitis events (3 of 22 patients, 13.6%). Patient characteristics of the 22 eligible pts were as follows; the median age was 65 (54-70) years; 12 pts had a PS of 0, and 16 pts were male. The median number of cycles delivered was four (range, 1–31). Four of 22 (18.2%) patients achieved TS at 6 months. Median progression free survival and overall survival from the start of the maintenance irinotecan therapy were 3.2 months and 15.9 months, respectively. Grade ≥3 toxicities included neutropenia (4.5%), hyponatremia (4.5%), pneumonitis (13.6%) and cholangitis (4.5%). No treatment-related deaths occurred.

Table 1. Treatment delivery (N=22)

	No.	%
Median number of cycles delivered (range)	4 (1-31)	-
Treatment cycle		
Cycle 1	22	100.0
Cycle 2	19	86.4
Cycle 3	12	54.5
Cycle 4	12	54.5
Cycle 5	7	31.8
Cycle 6	5	22.7
Cycle ≥7	3	13.6

Conclusion: This trial was early terminated due to the unexpected toxicity, but maintenance irinotecan therapy was still active for a subset of ED-SCLC. **Keywords:** irinotecan, maintenance, pneumonitis, small cell lung cancer

POSTER SESSION/ SMALL CELL LUNG CANCER
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P3.07-006 Phase 2 Study of Aldoxorubicin versus Topotecan for Relapsed/Refractory Small Cell Lung Cancer

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Background: Aldoxorubicin is a novel prodrug that binds to albumin in the circulation. Doxorubicin is cleaved in low pH environments, allowing administration of 3.5-4-fold higher doses than standard doxorubicin and 10-fold greater cumulative doses. Patients with metastatic small cell lung cancer (SCLC) who have failed prior chemotherapies have a poor prognosis with response rates (ORR) of 5-20%, progression-free survival (PFS) of 2-4 months and overall survival of 6-10 months. Topotecan is the standard therapy for these patients. **Methods:** Open label study, 132 patients, (1:1 randomization) to receive either aldoxorubicin (230 mg/m^2, IV infusion, Day 1, every 3 weeks) or topotecan (either 1.5 mg/m^2/day IV, Days 1-5, every 3 weeks or 4 mg/m^2 IV infusion on Days 1, 8, and 15 every 28 days). Key inclusions: confirmed SCLC, relapsed or refractory to ≥ 1 prior chemo, ECOG 0-2, measurable tumor (RECIST 1.1). Key exclusions: >375 mg/m^2 prior doxorubicin, prior topotecan, active CNS mets, lab abnormalities (ANC <1500/mm^3, platelets <100,000/mm^3, Hgb <9 gm/dL, LFTs > 3 or 5x ULN), serious myocardial dysfunction, anion gap >16 meq/L or arterial blood pH < 7.30. Key stratifications: relapse < 90 days versus > 90 days; ECOG 0-1 versus 2. Primary endpoint: PFS (analysis after 110 events); assume PFS for topotecan = 3.5 months, aldoxorubicin = 6.5 months. Secondary endpoints: OS (analysis after 110 deaths; assumes OS for topotecan = 6 months, aldoxorubicin = 8 months), ORR, disease control rate, adverse events, tolerability, lab abnormalities. Study sites: Up to 40 sites in the US, Hungary, Spain, and Italy. **Results:** Not applicable. **Conclusion:** Not applicable. **Keywords:** SCLC, small cell lung cancer, Aldoxorubicin

POSTER SESSION/ SMALL CELL LUNG CANCER
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P3.07-007 Clinical Effect Observation of Compound Kushen Injection Combined with EP Regimen Chemotherapy for Small Cell Lung Cancer (SCLC)

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Background: To observe the clinical efficacy of Compound Kushen Injection combined with EP regimen chemotherapy for the treatment of small cell lung cancer SCLC). **Methods:** 98 cases of small cell lung cancer patients were chosen and randomly divided into experimental group and control group. 49 patients in experimental group were treatment with Compound Kushen Injection combined with EP regimen chemotherapy. 49 patients in control group received EP regimen chemotherapy alone. Both groups were repeated every 4 weeks and 3 cycles. All patients completed efficacy evaluation after treatment 3 cycles. **Results:** There was no significant difference in short-term effect between the two groups(P>0.05). The gastrointestinal reactions(represented as vomiting, anepithymia and diarrhea) and bone marrow depression(the toxicity on hemoglobin, leukocyte and platelet) in experimental group were alleviated compared with those in control group. There was significant difference between the two groups (P<0.05). The median survival time was 462d in experimental group while 268d in control group(P<0.05). KPS score after chemotherapy in all experiment groups was significantly higher than that in control group(P<0.05). **Conclusion:** Compound Kushen Injection combine with EP regimen chemotherapy shows precise therapeutic effect on SCLC, reducing adverse drug reactions, increasing median survival time and improving the life quality of patients. **Keywords:** Compound Kushen Injection, chemotherapy, SCLC, EP

POSTER SESSION/ SMALL CELL LUNG CANCER
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P3.07-008 Phase Ib/II Study of Pembrolizumab plus Chemotherapy in Advanced Cancer: Results of Lung Cancer Patients Receiving ≥ 1 Prior Line of Therapy

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Background: Pembrolizumab (pembro) is a selective anti-PD-1 antibody that blocks the interaction between programmed death-1 (PD-1) on T-cells and PD-L1 and PD-L2 on tumor cells. We report safety and clinical activity of pembro combined with chemotherapy in patients with advanced small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) progressing after ≥ 1 line of chemotherapy (NCT02331251). **Methods:** Patients were treated with pembro 2 mg/kg on day 1 every 21 days with either irinotecan on day 1 every 21 days or gemcitabine with or without vinorelbine on days 1 and 8 every 21 days until progression or toxicity. Eligibility included at least 1 measurable tumor lesion, Karnofsky Performance Status (KPS) of 70-100%, and adequate organ function. Tumors were assessed every 3 cycles using RECIST 1.1 and immune-related response criteria (irRC) and unconfirmed best overall response (BOR) was evaluated. **Results:** Eight lung cancer patients have been enrolled at the time of submission. Median age was 52.5 (range 33-74) and median KPS was 80%. Histology was adenocarcinoma (62.5%), including one with an EGFR T790M mutation and three SCLC (37.5%). One SCLC patient is on pembro plus gemcitabine 1,000 mg/m2, one NSCLC patient is on gemcitabine 1,000 mg/m2 and vinorelbine 25 mg/m2, and the remaining six patients were treated with irinotecan 250-300 mg/m2. Two NSCLC had prior exposure to nivolumab for ≥ 2 months. The maximum tolerated dose (MTD) was exceeded for irinotecan 300 mg/m2, and subsequently all patients receiving irinotecan are currently dosed at 250 mg/m2. Any grade drug-related treatment adverse events (AEs) occurred in 88% of patients; the most common (n>1) were skin rash, fatigue, diarrhea, anorexia, and extremity edema. No infusion-related reactions were observed. Dose limiting toxicities (DLTs) with pembro plus irinotecan were fatigue and nausea/vomiting. DLT with gemcitabine and vinorelbine was hypoxia. No grade 3 AEs were observed thus far with pembro plus gemcitabine. Five patients are currently evaluable for BOR. Two of two SCLC on pembro plus irinotecan have partial response as BOR and continue on study. One NSCLC patient on pembro plus gemcitabine and vinorelbine had stable disease, and two NSCLC patients had PD as BOR. **Conclusion:** In patients with previously treated SCLC and NSCLC, pembro plus chemotherapy appears to be safe to administer with a toxicity profile similar to the individual components of the regimen utilized. Establishment of the recommended phase 2 dose is ongoing for these treatment arms. Since the median follow-up is ~2

months, updated results including any new lung cancer patients enrolled, median progression-free survival (PFS), and overall survival will be presented at the WCLC. **Keywords:** Immunotherapy, chemotherapy, lung cancer, phase i

POSTER SESSION/ SMALL CELL LUNG CANCER
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.07-009 The Retrospective Analysis of Nab-Paclitaxel Regimens for Relapsed Small Cell Lung Cancer Patients Yujiro Naito[1], Akihiro Tamiya[1], Motohiro Tamiya[2], Kyoichi Okishio[3], Masaki Kanazu[1], Sayoko Tokura[1], Naoki Omachi[1], Nobuhiko Saijo[1], Yohei Kimura[1], Hidekazu Suzuki[2], Norio Okamoto[2], Naoko Morisita[2], Takayuki Shiroyama[2], Masanari Hamaguchi[2], Tomonori Hirashima[2], Shinji Atagi[3] [1]*Department of Internal Medicine, National Hospital Organization Kinki-Chuo Chest Medical Center, Osaka/Japan,* [2]*Department of Thoracic Malignancy, Osaka Prefectural Medical Center for Respiratory and Allergic Diseases, Osaka/Japan,*[3]*Department of Thoracic Oncology, National Hospital Organization Kinki-Chuo Chest Medical Center, Osaka/Japan*

Background: Although small cell lung cancer (SCLC) is initially chemo sensitive, most patients rapidly relapse. Prognosis of late line treatment for relapsed SCLC patients is generally poor. The efficacy of paclitaxel regimens for relapsed SCLC patients has been reported in some articles. But no specific study has been reported to our knowledge, about nab-paclitaxel administration for relapsed SCLC patients. **Methods:** By using the database of two hospitals, we underwent a retrospective analysis to evaluate the efficacy and safety of nab-paclitaxel regimens for relapsed SCLC patients. The data of patient characteristics, treatment efficacy and adverse events were collected from the medical records. **Results:** Fourteen patients (3 women and 11 men) with relapsed SCLC were administered weekly nab-paclitaxel or carboplatin plus nab-paclitaxel between February 2013 and July 2014 in our hospitals. The median age was 71 years old. Eight patients had comorbid pulmonary disease (5 had interstitial lung disease, 2 had chronic obstructive pulmonary disease, and 1 had both diseases). Five patients were administered nab-paclitaxel regimen as second line chemotherapy, five patients were as third line and four patients were as fourth or fifth line. Five patients achieved partial response, and four patients had stable disease. The response rate was 36%, and disease control rate was 64%. Most common toxicities were hematological adverse events such as neutrophil count and anemia. Severe neutropenia (Grade 3 or 4) appeared to some patients, but all patients were restored by treatment. The main non-hematologic adverse events were neurotoxicity and constipation, and these events were mild. **Conclusion:** The administration of nab-paclitaxel regimens to highly treated patients with relapsed SCLC demonstrated modest response rate and disease control rate. All adverse events were manageable, so that nab-paclitaxel regimens were well tolerated. Further clinical trial to evaluate the efficacy and safety of nab-paclitaxel regimens for relapsed SCLC patients is warranted. **Keywords:** nab-paclitaxel, small cell lung cancer

POSTER SESSION/ SMALL CELL LUNG CANCER
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P3.07-010 Phase II Trial of metronomic Temozolomide and Topotecan in patients with relapsed and/or refractory Small Cell Lung Cancer. Gouri Shankar Bhattacharyya[1], Purvish M. Parikh[2], Ghanashyam Biswas[3], Shailesh A. Bondarde[4], Hemant Malhotra[5], Amish Vora[6], K Govindbabu[7], Anantbhushan A.B. Ranade[8] [1]*Medical Oncology, Fortis Hospital, Kolkata/India,* [2]*Icon-Aro, Mumbai/India,* [3]*Sparsh Hospital and Critical Care, Bhubaneshwar/India,* [4]*Shatabdi Super Specialty Hospital, Nashik/India,* [5]*Medical Oncology, Sms Medical College Hospital, Jaipur/India,* [6]*Max Healthcare, Gurgaon/India,* [7]*Kidwai Memorial Institute of Oncology, Bangalore/India,* [8]*Deenanath Mangeshkar Hospital, Pune/India*

Background: The prognosis of recurrent or refractory small cell carcinoma of lung is poor with conventional therapies; one of the issues is the presence of brain metastasis. Topotecan is a topo-isomerase inhibitor with very good penetration to CNS system. The efficacy of topotecan in metronomic doses over a period of time is extremely well tolerated and effective. Topotecan is an approved drug for recurrent or refractory small cell carcinoma of lung. Temozolomide in metronomic dosing or in repeated small dosing can be an effective alternative to conventional dosing without the side-effects and has been shown to be effective in Neuro-endocrine tumors and Small Cell Carcinoma of Lung shows neuro-endocrine differentiation as well as the presence of unmethylated MGMT. **Methods:** This is a two arm Open Label Single Institute Phase II Study reviewed and approved by Institutional Review Board. Written Informed Consent was obtained from all patients. The study was conducted to find the safety and efficacy of this regime. All patients had recurrent small cell lung cancer that was sensitive or refractory to first line platinum therapy. Patients with brain mets were eligible. All patients had to have minimal functional reserves; had to be greater than the age of 18 years; Karnofsky scale > 60. Response evaluation by RECIST criteria Version 1.1 was used. Patients were treated with Topotecan 1mg per day along with Temozolomide 20mg in morning and in the evening, no food allowed 1hr before and 1hr after. The comparator arm was oral topotecan at standard dosage of 2.3mg/m^2 in Day 1 to Day 5. Patients were evaluated for toxicity every 3 weeks and for efficacy after every 12 weeks. There were 21 patients in each arm. Palliative medication and Best Supportive Care was offered to both the groups. **Results:** In the experimental arm vs comparator arm, response rate was as follows: · Complete response – 9.5% vs 0% · Partial response – 33.3% vs 23.8% · Stable disease in – 38.1% vs 28.6% Median Survival time was 38 weeks vs 25.9 weeks in the Intent to Treat population arm. (Log rank P=0.0104). Quality of Life had slower deterioration in patients with metronomic chemotherapy. Principal toxicities seen were mainly hematological toxicity in the standard arm 33% vs 4%; Grade IV thrombocytopenia in 7% vs 4%; Grade III/IV anemia in 25% vs 10%; Infection Grade III/IV in 16% vs 6%; Vomiting 6% vs 1%; Diarrhea 6% vs 0%; Dyspnea 9% vs 4%. Pain 6% vs 4%; Toxic death occurred in 6% in comparator arm. **Conclusion:** Metronomic Chemotherapy is associated with prolongation of survival and Quality of Life benefits in Relapsed Small Cell Lung Cancer. **Keywords:** Metronomic chemotherapy, Recurrent, SCLC

POSTER SESSION/ SMALL CELL LUNG CANCER
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P3.07-011 Profilattic Cranial Irradiation (PCI) Following Toracic CHT-RT for Small Cell Lung Cancer: Retrospective Analysis of 182 Consecutive Patients Alessio Bruni[1], Vieri Scotti[2], Gabriele Simontacchi[2], Katia Ferrari[3], Biancaluisa Lanfranchi[1], Laura Rubino[1], Daniele Scartoni[2], Ilaria Furfaro[2], Carla De Luca Cardillo[2], Filippo Bertoni[1] [1]*Radiotherapy Unit, -Aou Policlinico of Modena, Modena/Italy,* [2]*Oncology Department-Radiation Oncology Unit, Aou Careggi, Florence/Italy,* [3]*Pneumology Unit, Aou Careggi, Florence/Italy*

Background: The role of PCI in the management of Small Cell Lung Cancer (SCLC) pts is still debated. Several studies showed its effectiveness in terms of progression (PFS) and metastasis free survival (MFS), but advantages for overall survival (OS) are not always reported. The aim of our analysis is to retrospectively evaluate the current clinical impact of PCI in patients affected by SCLC. **Methods:** From April 1989 to May 2014 a total of 182 pts with SCLC underwent radical concomitant or sequential CHT-RT on thoracic disease +/- PCI in two different Italian Institutions. Thirty-eight pts were female, while 144 were male. Mean and median age were respectively 62.6 (range 38-86) and 63 years. Only 5 pts had "extended disease", while the other 177 had T1-T4 N0-N2 limited stage SCLC. Seven pts underwent surgery followed by adjuvant CHT-RT on mediastinal nodes while 8 pts didn't received any RT for primary disease; the remaining 167 pts received concomitant/sequential CHT-RT with radical intent. After receiving CHT or CHT-RT for thoracic disease, 66/182 pts received PCI, while 118/182 pts underwent regular clinical/radiological follow up. Most of patients were routinary followed in out-patient clinic every three months and they were also submitted to neurocognitive questionnaires. All PCIs were planned using opposite lateral fields with 2D technique or virtual off-line simulation; all pts received 25-30 Gy in 10 fractions within two weeks. Three- and 5-year OS,PFS and Brain mts free survival (BrMFS) were analyzed; univariate and multivariate analysis (using Kaplan Meier and Cox Regression tests) were performed due to identify patient, tumor and/or treatment related prognostic factors **Results:** : We retrospectively analyzed our cohort of patients using Kaplan Meier curves for survival and Cox regression tests for univariate and multivariate analysis. At a mean follow up of 32 months, no difference in terms of OS, PFS and brMFS was found comparing population referring to the 2 different centers. In the analyzed population 3- and 5-year OS were respectively 28.2 and 18.4%, while PFS were 22.4 and 18.9 respectively. Finally 3- and 5-year BrMFS were 56.3 and 50.2%. By multivariate analysis PCI and clinical response to primary thoracic treatment remain as independent variables being protective in terms of OS, PFS and BrMFS. Concomitant CHT-RT and RT on thoracic disease are positive factors just for PFS (respectively with $p<0.014$ and $p<0.025$). No G3 or G4 acute/late toxicities were found. **Conclusion:** PCI after primary thoracic CHT-RT with radical intent was confirmed as a "treatment-key" in the management of SCLC having also an optimal toxicity profile. Our data confirmed that PCI will be encouraged in all fit patients due to its potential benefit in terms of OS, PFS and BrMFS. Pts with Limited Stage SCLC having experienced a good response to primary CHT-RT treatment on thoracic disease seems to be the optimal candidate to PCI. **Keywords:** PCI, SCLC, concomitant CHT-RT, toxicity

POSTER SESSION/ SMALL CELL LUNG CANCER
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.07-012 Hiperfracctioned Radiochemotherapy in Small Cell Lung Cancer, a Monoinstutional Experience Begoña Taboada Valladares[1], Patricia Calvo Crespo[2], Antonio Gomez Caamaño[2], Martin Lazaro Quintela[3] [1]*Radiation Oncology, Clinic University Hospital of Santiago de Compostela, Santiago de Compostela/Spain,* [2]*Radiation Oncology, Clinical University Hospital of Santiago de Compostela, Santiago de Compostela/Spain,* [3]*Medical Oncology, University Hospital of Figo, Figo/Spain*

Background: To evaluate our experience in radical radiochemotherapy (RCT) twice daily in limited disease small cell lung cancer (SCLC) in term of effectiveness and toxicity. **Methods:** A retrospective review was performed to determine the local recurrence and survival rates for patients with SCLC localized disease undergoing RCT according Turrisi regimen between October 2004 and August 2014. All patients were treated with 3DRT, with a median dose of 45 Gy (150cGy twice daily), combined with chemotherapy based in cisplatinum-VP16. 73% received preventive cranial irradiation (ICP). 22% of patients underwent induction QT based in platinum-VP16. The primary objective was overall survival (OS); secondary objectives were progression free survival (PFS), local progression free survival (LPFS) and toxicity. OS was analized with Kaplan-Meier test. **Results:** 44 elegible patients were recruited (82% male, median age 62, with good performance status). The clinical stage was 89% E.III and 11% E.II. At a median follow-up of 18 months, the median OS was 21 months (95%CI: 16.3-25.4) and median PFS was 12.6 months (95%CI: 10.2-15). OS at 2 and 5 years were 38.6% and 24.8% respectively. LPFS was 14 months (95%CI: 10.5 -17.6) and systemic progression free survival was 14.2 (95%CI:10.1-18.2). During the RCT we reported anaemia (2%G3), neutropenia (7%G3, 16%G4), esophagitis (2%G3), dyspnea (2%G2), pneumonitis (7%G2). Induction QT did not improve the OS and PFS. **Conclusion:** In our experience radical radiochemotherapy twice daily is a feasible treatment option for small cell lung cancer, showing long-term survival with no inferiority results compared with the published and acceptable toxicities. **Keywords:** SCLC, toxicity, HIPERFRACTIONATED

POSTER SESSION/ SMALL CELL LUNG CANCER
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.07-013 A Retrospective Analysis of Adjuvant Chemotherapy in Patients with Completely Resected SCLC Yosuke Tamura, Yasuhito Fujisaka, Takahito Nakamura, Hiroyuki Tsuji, Ninso Matsunaga, Tetsufumi Kawaguchi, Masashi Imanishi, Syuhei Yoshida, Keiji Miyoshi, Soichiro Ikeda, Isao Goto, Toshiaki Hanafusa *Division of Internal Medicine（I）, Osaka Medical College Hospital, Takatsuki/Japan*

Background: Several clinical studies have demonstrated the efficacy and safety of the adjuvant chemotherapy for patients with small cell lung cancer (SCLC) , particularly in patients with stage Ⅰ disease. But it is unclear which chemotherapy regimen is the most efficacious for SCLC patients who underwent surgery, due to the rarity. The objective of this study was to analyze the efficacy and safety of adjuvant chemotherapy for patients with SCLC retrospectively. **Methods:** From January 2002 to September 2014, we retrospectively analyzed the clinical data of 23 patients with SCLC who received surgery in our institute. Seventeen patients received adjuvant chemotherapy. Six patients was observed with no chemotherapy after surgery, due to old age or poor condition（n=4）, patient refusal（n=1）, early post-operative relapse（n=1）. **Results:** The chemotherapy regimens were cisplatin and etoposide（PE）in 8 patients, and carboplatin and etoposide（CE） in 9 patients. Median time from surgery to starting chemothetapy was 1.5 months, and median follow-up time was 39.5 months. 12 pts （70%） received full cycles of chemotherapy. The recurrence was observed in 2 of 8 pts who received PE therapy and 2 of 9 patients who received CE therapy in April 2015. The median recurrence free survival (RFS) of patients who received adjuvant chemotherapy was not reached, and the RFS of patients with no chemotherapy was 7.62 months (Log-rank test P value 0.0007) . No treatment related death was observed. **Conclusion:** The adjuvant chemotherapy for patients with small cell lung cancer may be safe and efficatious. **Keywords:** SCLC surgery adjuvant-chemotherapy

POSTER SESSION/ SMALL CELL LUNG CANCER
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.07-014 Associations between Comorbidity, Treatment Toxicity and Overall Survival in Limited Disease Small-Cell Lung Cancer (LD-SCLC) Bjørn H. Grønberg[1], Stein H. Sundstrøm[2], Øystein Fløtten[3], Odd Terje Brustugun[4], Paal F. Brunsvig[5], Roy M. Bremnes[6], Stein Kaasa[1], Tarje O. Halvorsen[1] [1]*The European Palliative Care Research Centre and the Cancer Clinic, Norwegian University of Science and Technology and St. Olavs Hospital - Trondheim University Hospital, Trondheim/ Norway,* [2]*The Cancer Clinic, St. Olavs Hospital, Trondheim University Hospital, Trondheim/ Norway,* [3]*Department of Pulmonology, University of Bergen and Haukeland University Hospital, Bergen/Norway,* [4]*Dept of Oncology, University of Oslo and Oslo University Hospital, Radiumhospitalet, Oslo/Norway,* [5]*Dept of Oncology, Oslo University Hospital, Radiumhospitalet, Oslo/Norway,* [6]*Department of Oncology, Uit the Arctic University of Norway and University Hospital of North Norway, Tromsø/Norway*

Background: Concurrent chemotherapy and thoracic radiotherapy (TRT) is the recommended treatment of LD-SCLC. The treatment often causes severe toxicity. Many patients have comorbidity due to old age and smoking, and it is unclear whether these patients tolerate and benefit from the treatment as much as more fit patients. Studies have shown that comorbidity is a negative prognostic factor in many cancers (including lung cancer), but this has not been investigated in LD-SCLC patients receiving chemo-radiotherapy. We investigated whether comorbidity was a prognostic factor or associated with severe toxicity in a randomized trial comparing two schedules of TRT in LD-SCLC (n=157). **Methods:** Patients received four courses of cisplatin plus etoposide and were randomized to receive concurrent TRT of either 45 Gy/30 fractions (twice daily) or 42 Gy/15 fractions (once daily). Responders were offered prophylactic cranial irradiation of 30 Gy/15 fractions. The Charlson Comorbidity Index (CCI) was used to assess comorbidity from hospital medical records. The CCI rates common conditions associated with increased 1-year mortality with scores of 1, 2, 3 or 6 based on severity - and a total score ("CCI-score") is calculated. Toxicity was assessed using the CTCAE v3.0. We adjusted for treatment arm and established baseline prognostic factors in lung cancer (gender, stage of disease, appetite loss, weight-loss, age and performance status (PS) in the multivariate analyses. **Results:** 157 patients were analyzed (100%). Median age was 63 years, 52% were men, 16% had PS 2, 72% stage III, 30% weight-loss >5% last 3 months and 46% received twice-daily TRT. The most common grade 3-4 toxicities were pneumonitis (n=4; 3%); esophagitis (n=50; 32%) and neutropenic infections (n=64; 41%). 4 patients (3%) died from pneumonitis. 63 patients (40%) had CCI-score 0; 54 (34%) CCI-score 1; 23 (15%) CCI-score 2; 13 (8%) CCI-score 3; 3 (2%) CCI-score 4 and 1 patient had CCI-score 5 (1%). Most common comorbidities were chronic obstructive pulmonary disease (n=60, 38%), peptic ulcer disease (n=19, 12%), previous myocardial infarction (n=17, 11%) and diabetes (n=17, 11%). Median overall survival (OS) for the whole population was 22.7 months. There were no significant associations between CCI-score and median OS in univariate (CCI-score 0: 30.6 months; CCI-score 1: 15.1 months; CCI-score 2: 23.0 months; CCI-score 3: 23.0 months and CCI-score 4-5: 9.3 months, p=0.18) or multivariate analyses (HR: 0.97; 95% CI 0.79 – 1.18, p=0.74). Patients with comorbidity had a shorter survival than others in the univariate (CCI-score 0: 30.6 months, CCI-score ≥1: 18.8 months, p=0.047), but not in the multivariate analysis (HR: 1.27; 95% CI 0.82–1.98, p=0.29). Patients with comorbidity did not experience significantly more grade 3-4 pneumonitis (CCI-score 0: 3%, CCI-score ≥1: 2%, p=1.0), esophagitis (CCI-score 0: 38%, CCI-score ≥1: 28%, p=0.17), neutropenic infections (CCI-score 0: 41%, CCI-score ≥1: 40%, p=0.92) or deaths from pneumonitis (CCI-score 0: 2%, CCI-score ≥1: 3%, p=0.65). There were no other significant associations between CCI-scores and overall survival or toxicity. **Conclusion:** LD-SCLC patients with comorbidity had similar survival and toxicity as others, suggesting that they should be offered similar treatment as those without comorbidity. **Keywords:** Limited disease small-cell lung cancer, Comorbidity, survival, toxicity

POSTER SESSION/ SMALL CELL LUNG CANCER
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P3.07-015 Final Report of Phase I/II Study of Induction Carboplatin and Irinotecan Followed by TRT for Elderly Patients with LD-SCLC: TORG 0604 Terufumi Kato[1], Yuki Misumi[2], Hiroaki Okamoto[3], Katsuhiko Naoki[4], Yukio Hosomi[5], Noriyuki Masuda[6], Koichi Minato[7], Takuma Yokoyama[8], Kazuma Kishi[9], Masanori Nishikawa[10], Fumihiro Oshita[11], Nobuhiko Seki[12], Isao Goto[13], Koshiro Watanabe[14] [1]*Kanagawa Cardiovascular and Respiratory Center, Yokohama/Japan,* [2]*Department of Respiratory Medicine and Medical Oncology, Yokohama Municipal Citizens Hospital, Yokohama/Japan,* [3]*Department of Palliative Medicine, Yokohama Municipal Citizen'S Hospital, Yokohama-Shi/Japan,* [4]*Pulmonary Medicine, Keio University School of Medicine, Tokyo/ Japan,* [5]*Department of Thoracic Oncology and Respiratory Medicine, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo/Japan,* [6]*Dept. of Respiratory Medicine, Kitasato University School of Medicine, Kanagawa/Japan,* [7]*Department of Respiratory Medicine, Gunma Prefectural Cancer Center, Gunma/Japan,* [8]*Kyorin University Hospital, Mitaka/Japan,* [9]*Department of Respiratory Medicine, Respiratory Center,, Toranomon Hospital, Tokyo/Japan,* [10]*Department of Respiratory Medicine, Fujisawa City Hospital, Fujisawa/Japan,* [11]*Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama/Japan,* [12]*Dept. of Medical Oncology, Teikyo University School of Medicine, Tokyo/ Japan,* [13]*Division of Internal Medicine（I）, Osaka Medical College Hospital, Takatsuki/ Japan,* [14]*Thoracic Oncology Research Group, Yokohama/Japan*

Background: In elderly patients with LD-SCLC, the role of irinotecan has been unclear and the timing of TRT combined with chemo-therapy has not been fully evaluated. Furthermore, no standard treatment has been established for them. We report a phase I/ II trial of induction chemotherapy of carboplatin and irinotecan followed by sequential TRT in this population. **Methods:** Patients with untreated, measurable LD-SCLC >70 years with performance status (PS) 0 to 2 and adequate organ function were eligible. Treatment consisted of induction with carboplatin on day 1 and irinotecan on days 1 and 8 every 21 days for four cycles. TRT of 54Gy in 27 fractions was then administered sequentially. Carboplatin dose was escalated from AUC of 4 to 5 (Levels 1 and 2, respectively) with a fixed dose of irinotecan at 50 mg/m^2. The primary objective of the phase II portion was evaluation of efficacy. **Results:** A total of 41 patients were enrolled [median age 75 years, range 70-86 years; 31 male, 10 female; PS 0/1/2: 22/18/1]. At Level 1 (n=6), one patient experienced dose-limiting toxicity (DLT) as Grade 3 hypertension. At Level 2 (n=6), two patients experienced DLT as Grade 4 thrombocytopenia. Therefore, level 1 was chosen as the recommended dose. The phase II trial was then expanded by 35 patients in the level 1 based on the Simon minimax design. In all cohorts, the median chemotherapy cycle was 4 (1/2/3/4 courses administered as 4/2/2/33); median radiation dose was 54Gy (range 36-60). Toxicities were generally mild, as expected. Gr 3/4 leukopenia and thrombocytopenia were both observed in six (15%) patients. No Gr 3/4 diarrhea or esophagitis was noted. Although Gr 3 febrile neutropenia and Gr 3 pneumonitis were seen in two patients each, no treatment-related deaths occurred. There were five complete responses and 32 partial responses, for a response rate of 90%. With median follow-up of 80.4 months (n=41), median progression-free and overall survival times were 11.2 and 27.1 months, respectively. **Conclusion:** Induction chemotherapy with carboplatin plus irinotecan followed by sequential TRT was well tolerated and highly effective in elderly patients with LD-SCLC. Further confirmatory studies are warranted. **Keywords:** TORG, irinotecan, Limited Stage Small Cell Lung Cancer, thoracic radiotherapy

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P3.07-016 Survival of Patients with N3 Lymph Node Disease in a Cohort with Limited Disease Small-Cell Lung Cancer Receiving Concurrent Chemoradiotherapy Christine D. Valan[1], Tarje O. Halvorsen[1], Nina Levin[2], Roy M. Bremnes[3], Paal F. Brunsvig[4], Øystein Fløtten[5], Odd Terje Brustugun[6], Stein H. Sundstrøm[2], Bjørn H. Grønberg[1] [1]*The European Palliative Care Research Centre and the Cancer Clinic, Norwegian University of Science and Technology and St. Olavs Hospital - Trondheim University Hospital, Trondheim/Norway,* [2]*The Cancer Clinic, St. Olavs Hospital - Trondheim University Hospital, Trondheim/Norway,* [3]*Department of Oncology, University Hospital of North Norway and the Arctic University of Norway, Tromsoe/Norway,* [4]*Dept of Oncology, Oslo University Hospital - Radiumhospitalet, Oslo/Norway,* [5]*Department of Pulmonology, Haukeland University Hospital and University of Bergen, Bergen/ Norway,* [6]*Department of Oncology, Oslo University Hosital,The Norwegian Radium Hospital, Oslo/Norwa, Oslo/Norway*

Background: Treatment of small-cell lung cancer depends on the extent of disease. Concurrent chemotherapy and thoracic radiotherapy (TRT) is recommended if all lesions can be included in a radiotherapy field (limited disease – "LD"), while patients with more advanced disease (extensive disease – "ED") receive chemotherapy alone. LD is defined as confined to one hemithorax, but some have excluded patients with contralateral hilar and supraclavicular lymph node metastases (LNM). When the latest revision of TNM was published, it was recommended that N3-disease should be considered as LD with the possible exception of supraclavicular LNM – and that TNM-stage should be reported in clinical trials of LD SCLC to further explore this. We assessed extent of disease according to TNM v7 in patients from a randomized phase II trial comparing two schedules of TRT in LD SCLC (n=157) and investigated whether N3-disease was a negative prognostic factor; and whether there were survival-differences between the different N3-subcategories. **Methods:** Patients received four courses of cisplatin plus etoposide and were randomized to receive concurrent thoracic radiotherapy of either 45 Gy/30 fractions (twice-daily) or 42 Gy/15 fractions (once daily). Responders were offered prophylactic cranial irradiation of 30 Gy/15 fractions. Extent of disease was assessed from CT scans obtained three weeks before chemotherapy commenced. N3-disease was categorized according to contralateral supraclavicular, ipsilateral supraclavicular, contralateral hilar and contralateral mediastinal LNM. Weight loss was

defined as weight loss >5% the last 3 months prior to enrolment. **Results:** 150/157 patients were analysed (96%). Median age was 63 (40-85); 51% were men; 15% had PS 2 and 46% received twice-daily TRT. 1% had stage I disease; 14% stage II; and 84% stage III. Median overall survival (OS) for stage I: not reached, stage II: 41.1 months, and stage III: 20.9 months (p=0.022). 17% had N0-disease; 5% N1-disease; 30% N2-disease; and 47% had N3-disease. Among those with N3-involvement, 40 % had contralateral mediastinal LNM, 16% contralateral hilar LNM, and 17% supraclavicular LNM (13% ipsilateral and 7% contralateral supraclavicular LNM). 43% had LNM to more than one N3-station. Patients with N3-disease had inferior survival compared with N0-2 disease (18.0 vs. 33.7 months; p<0.001). All subcategories of N3 had inferior median OS compared with N0-2 disease (median 33.7 months): contralateral mediastinal LNM (18.0 months; p=0.022), contralateral hilar (19.8 months; p=0.021), supraclavicular LNM (15.1; p=0.003) [ipsilateral supraclavicular LNM (15.1 months; p=0.009) and contralateral supraclavicular LNM (13.8 months; p=0.007)]. There were no significant differences in median OS between the different N3-categories (p=0.84). Multivariate analyses adjusting for established prognostic factors in lung cancer (gender, age, PS, weight-loss and appetite loss) and treatment showed that N3-disease (HR 2.30; 95% CI=1.51-3.48; p<0.001), supraclavicular LNM (HR 1.67; 95% CI=1.01-2.77; p=0.046) and contralateral mediastinal LNM (HR 2.34; 95 % CI = 1.55-3.51; p<0.001) remained significant prognostic factors. **Conclusion:** Patients with N3-disease had inferior OS to those with N0-2 disease. All subcategories of N3 had inferior OS in the univariate analyses, while supraclavicular and contralateral mediastinal LNM remained significant in the multivariate analyses. Patients with supraclavicular LNM had similar OS as other N3 subcategories.
Keywords: Prognostic factors, N3 disease, TNM stage, small-cell lung cancer

POSTER SESSION/ SMALL CELL LUNG CANCER
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P3.07-017 The Prognostic Factors in the Elderly Patients with Small Cell Lung Cancer: A Retrospective Analysis from a Single Cancer Institute Hui Zhu, Sujing Liu, Hongbo Guo, Huihui Li, Yan Zhang, Li Kong, Jinming Yu *Shandong Cancer Hospital and Institute, Jinan,Shandong Province/China*

Background: We conducted a retrospective study to evaluate the prognostic factors of elderly patients with small cell lung cancer (SCLC). **Methods:** The records of elderly patients (≥65 years) with histologically-proven SCLC were reviewed. The patients' information including demographic, clinical and laboratory parameters, staging status on the VALG staging system, and treatment modalities were registered. Univariate and multivariate survival analysis was performed by the Kaplan-Meier method and Cox proportional hazards model, respectively. **Results:** Between January 2004 and December 2012, 247 elderly patients with SCLC were analyzed, 129 patients initially presented with limited stage and 118 with extensive disease. The median age of the patients was 70.7 (range 65–83). The median follow-up period for all patients was 22.0 months (range, 1.0–84.0 months) and 39.9 months for surviving patients (range, 4.7–84.0 months). The overall median survival time (MST) was 17.3 months, and the 2-y and 3-y OS rates were 36.3% and 22.7%, respectively. The MST, 2-y and 3-y OS rates were 22 months, 45.0% and 30.5% in patients with limited stage, versus 13.4months, 26.5% and 13.7% in patients having extensive diseases, respectively. The the median PFS, 2-year and 3-year PFS rates were 10.0 months, 23.5% and 18.3% for the whole group, respectively. The median PFS , the 2-year and 3-year PFS rates were 13.0 months, 31.6% and 25.7%, respectively in the LD-SCLC group; and those of the ED-SCLC group were 8.2 months, 13.3% and 7.6%, respectively. Multivariate analysis revealed that disease extent (HR=3.034; p<0.001) and the number of chemotherapy cycles (HR=0.486; p=0.003) were independent prognostic factors for the OS. **Conclusion:** Positive treatment was necessary to the elderly SCLC patients with good performance status. Fit elderly patients with SCLC could achieve a relatively prolonged survival.
Keywords: small cell lung cancer, Elderly patients, survival, prognosis factor

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P3.07-018 Outcomes in Small Cell Lung Cancer in India: A 15 Year Retrospective Analysis Navile A. Murali[1], T.G Sagar[2], Trivadi Ganesan[2], Krishna Rathinam[2], Rejiv Rajendranath[2], Prashanth Ganesan[2], R Swaminathan[2], Venkatraman Radhakrishnan[2] [1]*Medical Oncology, Cancer Institute (Wia), Chennai/India,* [2]*Medical Oncology, Cancer Institute(Wia), Chennai/India*

Background: Small Cell Lung Cancer has a aggressive clinical course and poor outcomes. Role of multi modality therapy and prophylactic cranial irradiation have been established in the last two decades. There is a paucity of studies on survival in SCLC in India and to our knowledge till date; only one study has been published from India. The current study is a retrospective review of outcomes in patients with SCLC in India **Methods:** All newly diagnosed small cell lung cancer cases from 2000 through 2014 who received treatment at Cancer Institute (WIA),Chennai were identified and clinical data from their hospital records, noted. The influence of various pretreatment factors on survival was investigated using Kaplan-Meier plots and Cox multivariate regression model. Only subjects who received intravenous chemotherapy were included in the analysis. **Results:** Forty seven subjects were included, 39 (83%) were males. Age distribution: Less than 50 years – 16 (34%), 50-59 years - 16 (34%),> 60 years – 15 (32%). Limited Stage: 21 (44.6%) and extensive stage: 26 (55.4%). Treatment outcomes in Limited stage disease (N=21): Sequential chemotherapy and radiation: N=11 (52.38%), median PFS was 8 months, 1 year OS was 72.9% (P<0.001) and 5 year OS was 0%. Concurrent chemotherapy and radiation: N=10 (47.62%), median PFS was 10 months, 1 year OS was 78.8% and 5 year OS was 26.3% (P<0.001). The improvement in overall survival when subjects received concurrent chemotherapy and radiation as compared to sequential chemotherapy and radiation was statistically significant (P<0.001). Treatment outcomes in Extensive stage disease (N=26); Chemotherapy alone: N=19 (73%),1 year PFS was 6.8% and 1 year OS was 9.1%, Sequential chemotherapy and radiation: N=7 (17%), 1 year PFS was 28.6% and 1 year OS was 53.6% (P=0.075). There were no survivors at 5 years in subjects with extensive stage disease irrespective of whether chemotherapy alone was used or sequential chemotherapy and radiation. In subjects with limited stage disease 9, (42.85%) received prophylactic cranial irradiation **Conclusion:** Subjects with limited stage disease who received concurrent chemo-radiation showed a better overall survival as compared to those who received sequential chemo-radiation. Subjects with extensive stage disease who underwent sequential chemo-radiation did not show any statistically significant improvement in overall survival as compared to those who received only chemotherapy. Concurrent chemo-radiation should be the preferred treatment approach in limited stage SCLC in spite of the significant increase in costs and side effect profile even in developing countries. Sequential chemo-radiation may not show any added advantage in extensive stage SCLC especially considering the added side effects as well as the burden on resources
Keywords: SCLC, survival, India, retrospective analysis

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POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P3.08-001 Hippo Pathway Dysregulation in Mesothelioma Cells Yoshitaka Sekido *Division of Molecular Oncology, Aichi Cancer Center Research Institute, Nagoya/Japan*

Background: Malignant mesothelioma (MM) is a highly aggressive tumor caused by asbestos exposure after a long latency. The *neurofibromatosis type 2* (*NF2*) tumor suppressor gene is mutated in around 50% of MM cases, and encodes Merlin that regulates the Hippo tumor-suppressive signaling pathway. We previously reported occasional genetic or epigenetic alteration in the *LATS2* and *AJUBA* genes in MMs, which encode components of the Hippo pathway. The *LATS2* inactivation was shown to lead to constitutive activation of YAP, a prooncogenic protein and transcriptional coactivator, which enhances multiple cell cycle regulation genes including *cyclin D1* (*CCDN1*). To further delineate the exact inactivation mechanism of this pathway and the roles of YAP in the development of MM, we established immortalized mesothelial cell lines and transduced YAP to determine whether or not YAP can confer the malignant phenotypes to these cells. **Methods:** Using retroviral transduction of HPV16 *E6/E7* and *hTERT* genes, immortalized human omental mesothelial cell lines (HOMCs) were established. Three sublines (HOMC-B1, A4, and D4) with different morphologies were cloned by limiting dilution from the pool of immortalized cells. Retrovirus expression vectors of wild-type YAP (YAPwt) and mutant YAP ($YAP^{S127}A$) were also synthesized. After retroviral infection of YAP expression vectors, transplantation of immortalized mesothelial cells was performed subcutaneously or intra-thoracically into nude mice. **Results:** We established immortalized mesothelial cell lines (HOMC) by transduction of HPV-E6/E7 and hTERT, and examined whether YAP activation induces malignant phenotypes in the cells. We found that transduction of both wild-type (YAPwt) and constitutively active-type ($YAP^{S127}A$) YAP, but not other cell cycle-promoting genes including CCDN1 and FOXM1, enhanced HOMC-cell proliferation *in vitro*. We also tested whether or not YAP-transduced HOMC cells showed enhanced tumorigenicity *in vivo* after inoculation into nude mice subcutaneously or intrathoracically. We found that YAPwt- and $YAP^{S172}A$- induced tumors which displayed more aggressive phenotypes. Meanwhile, we also transduced YAP vectors into normal mesothelial cells but they were shown to be unable to immortalize them. **Conclusion:** YAP activation is frequently observed in MM cells. Although enforced expression of YAPwt or $YAP^{S127}A$was insufficient to immortalize primary human mesothelial cells, the present study provides evidence for the crucial role of the disrupted Hippo pathway-activated YAP axis in the initiation of mesothelioma *in vivo*.
Keywords: tumorigenesis, NF2, Mesothelioma, YAP

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P3.08-002 Nanodiamonds-Conjugated Chemotherapeutic Agent Induces Cell Cycle Arrest and Apoptosis of Human Malignant Pleural Mesothelioma Cell Lines Bashir M. Mohamed[1], Gareth Clarke[2], Kieran Crosbie-Staunton[1], Steven G. Gray[1] [1]*Department of Clinical Medicine, Trinity College Dublin, and St James'S Hospital, Dublin/ Ireland,* [2]*Clinical Medicine Department, Trinity College Dublin and St James`S Hospital, Dublin/Ireland*

Background: The use of nanomaterials-based therapeutic systems is rapidly growing and covering a several biomedical applications such as detection, diagnosis and treatment. Recently, nanodiamonds (NDs) have been demonstrated to have great potential as a multimodal imaging/therapy platform. NDs enhance the ability of the drug to cross the cell membrane, increase intracellular drug delivery to the cancer cells, improve treatment efficacy, and decrease toxicity to normal cells or tissues. NDs are attractive for use in drug delivery because of their rich surface chemistry, advantageous size, and ability to act as transmembrane carriers. NDs have also been shown to enhance therapeutic efficacy of doxorubicin (DOX), particularly in treating murine liver and mammary tumor models, and lung metastasis of breast cancer. Yet, nothing similar has been done to translate ND-DOX systems to other cancers such as malignant pleural mesothelioma (MPM). In our study, we aimed to investigate the efficacy of ND-conjugated DOX on MPM cell lines. **Methods:** Bare, uncoated nanodiamonds were pegylated and functionalised with DOX. NDs/Dox were washed three times then re-suspended in water. Nanoparticle Tracking Analysis (NTA), FTIR and PL spectroscopy and TEM imaging were performed to

characterise the functionalisation. Human MPM cell lines such as REN and NCI-H2373 and human lung carcinoma cell line (NCI-H226) were used. LP-9 cell line, which resembles normal human mesothelial cells, was used as control. All cells were cultured and exposed to NDs, NDs/DOX or DOX alone. Cell cycle, cell viability, lysosomal mass/pH changes and mitochondrial membrane potential were examined using immunofluorescent staining techniques and data were collected and analysed with high content screening tools such as Cytell and IN Cell Investigator software. **Results:** Significant alterations of the examined biological markers were detected in human MPM cell lines such (REN and NCI-H2373) and human lung carcinoma cells (H226), while a slight changes were seen in the LP-9 cells. Interestingly, the MPM cells showed greater responses to NDs/DOX versus DOX alone. **Conclusion:** Our study demonstrates that NDs loaded with DOX exert significant inhibitory activities of human MPM cell lines and at concentrations that have minimal effects on normal pleura. Thus, ND-conjugated chemotherapy represents a promising, biocompatible strategy for enhancing chemotherapy efficacy and safety. **Keywords:** Nanodiamonds, malignant pleural mesothelioma, Doxorubicin

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P3.08-003 Incidence and Management of Malignant Pleural Mesothelioma Related Empyema Abdelrahman M. Abdelrahman[1], Rabab Gaffar[2], Hoda Baki[2], Ahmed Elbastaweesy[2], Fatma Aboulkasem[2] [1]*Surgery, National Cancer Institute, Cairo/Egypt,* [2]*National Cancer Institute, Cairo/Egypt*

Background: Empyema in relation to malignant pleural mesothelioma is a serious complication that may stop or delay the planned treatment. It may be secondary to surgery or non surgical , both are difficult to treat and are challenging to the thoracic surgeon as patients are usually too ill to tolerate therapy. **Methods:** We retrospectively reviewed the data of 443 patients with mesothelioma referred to the National Cancer Institute, Cairo between 2004 -2013. Extra pleural pnuemonectomy (EPP) was performed in 93 patients and radical pleurectomy / decortication in 12 . The remaining 338 patients received palliative chemotherapy or best supportive care. The frequency of empyema among those patients was 5.86% (26 cases). Full history and clinical examination was done for all patients, culture from the chest tube and or sputum culture was ordered for all, Computed tomography of the chest was done to evaluate empyema in all patients and bronchoscopy and biopsy to exclude stump recurrence was requested for patients with empyema secondary to EPP. **Results:** There were 23 males and 3 females , the right side was affected in 17 patients. Of the 338 patients with non operative therapy, 17(5%) developed empyema , 5 following repeated tapping of effusion ,8 with prolonged chest tube insertion and 4 after pleurodesis. Palliative pleurectomy was possible in 4 patients and was successful in 2. The remaining 13 patients were treated with second chest tube and repeated cavity irrigation with diluted bovidon iodine, 5 of them were improved within 2-3 weeks. Empyema secondary to EPP developed in 8 patients, 2 had early post operative empyema, one with stump dehiscence and one secondary to tube thoracostomy in the post pneumonectomy space. Surgery was successful in both. Of the remaining 6 patients, 5 had delayed bronchial stump fistula 1-3 years post pleuro pneumonectomy, All were re explored. Two patients were cured, the remaining 4 died from persistent sepsis. The last patient had infected mesh 3 years after surgery and was treated by re surgery and mesh removal. We had one patient with empyema following radical pleurectomy/ decortication due to residual space, wound depridement was done and the procedure was successful. **Conclusion:** Treatment of mesothelioma patients with empyema is challenging, every patient should be and evaluated and treated separately. In spite of high failure rate with surgery, it's considered the only treatment option, great effort by high volume thoracic surgeon should be offered to this group of patients. **Keywords:** mesothelioma, empyema, incidence , management

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P3.08-004 The Evaluation of Radiological Features for Pleural Mesothelioma Takumi Kishimoto *Asbestos Study Center, Okayama Rosai Hospital, Okayama/Japan*

Background: The differences of radiological features for pleural mesothelioma from other diseases such as lung cancer and sarcomas or pleuritis et al. is not evaluated and the also the difference of features among the histological manufestation is also not clear. **Methods:** Four hundred and twenty four cases of pleural mesothelioma who were clinically diagnosed, were evaluated. The chest CT which patients first visited to hospital were classified into 7 category such as 1)uni-mass formation, 2)pleural rind, 3) slight thickening of pleura, 4)thickening of mediastinal pleura, 5)pleural effusion without pleural changes, 6)multi-mass formation and 7)specific type. Furthermore, evidence of pleural effusion and the radiological patterns of the histological differences were evaluated. **Results:** The number of mesothelioma who were definitely diagnosed was 383 cases and 51 cases were not diagnosed mesothelioma but lung cancer, sarcoma or pleuritis or benign asbestos pleurisy et al. were diagnosed histologically. For mesothelioma cases, 230(60.1%) cases showed epithelioid histology, 62 cases(16.2%) biohasic type and 86 cases(22.5%) were sarcomatoid type and 5 cases(1.3%) were specific type and 89.6% showed pleural effusion. For the radiological patterns for 383 cases, pleural rind pattern occupied 42.2% and multi-mass formation 14.1%, pleural effusion without pleural changes 12.9% and uni-mass formation occupied 8.6%. As for the histological features, biphasic type showed only 2 cases(2.9%) uni-mass formation and 13.2% showed thickening of mediastinal pleura and sarcomatoid type only 4.4% showed pleural effusion without pleural changes. Other 51 cases who were not diagnosed mesothelioma such as lung cancer et al. showed 30.9% of uni-mass formation, pleural rind 21.8% and pleural effusion without pleural changes 18.2%. And 80.4% of them showed pleural effusion. **Conclusion:** Pleural mesothelioma shows various types of radiological manifestation and also other diseases such as lung cancer or sarcomas or benign pleuritis show similar patterns. Therefore, we try to make differential diagnosis when we suspect pleural mesothelioma by chest CT. **Keywords:** Pleural mesothelioma, Radiological features, Histological type, Pleural rind

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P3.08-005 Mesothelioma Diagnostic Panel Using Remote Digital Diagnostic System in Japan Kouki Inai[1], Takumi Kishimoto[2] [1]*Pathology, Pathological Diagnostic Center Inc., Hiroshima/Japan,* [2]*Asbestos Study Center, Okayama Rosai Hospital, Okayama/Japan*

Background: The pathological diagnosis as mesothelioma is difficult even if experienced pathologists do. Also the diagnosis of imaging including CT has no conclusive evidences as mesothelioma. Accordingly comprehensive diagnosis based on discussion by several pathologists and/or radiologists is necessary. However most of diagnostic specialists are too busy to have a meeting at designated date and venue. New remote diaignostic system will solve those problems and the accurate diagnosis as mesothelioma can be made. **Methods:** The remote pathological diagnosis consists of scanning of tissue slide by scanning equipment (NanoZoomer®), transmission of the digital data to cloud system (Google) by Internet. We have developed a new system named "LOOKREC" including pathological data and imaging data (chest X-P,CT and so on). The pathologists and radiologists as a member of special diagnostic group obtain a special account and access to the data on cloud by Internet. The diagnotic opinions made by individuals are entered into the discussion sheet and the organizer will decide a final diagnosis including whether mesothelioma or not, which type of mesothelioma, based on individual diagnostic opinions. **Results:** In Japan, the annual number of occurrence of mesothelioma is over 1200. The compensation or relief system for mesothelioma patients has been established ten years ago, and the accurate diagnosis is always required for adequate management of those systems. The number of mesothelioma showing diagnostic problems is about 10% of all mesothelioma cases. The cases with some difficulties of differentiation between early epithelioid mesothelioma vs reactive mesothelial hyperplasia, pleuritis, localized methelioma vs lung cancer will be presented and the points of differential diagnosis will be discussed. **Conclusion:** The new remote diagnostic system using Internet has been developed. It is expected that diagnostic accuracy will be improved when the observation of pathological findings as well as imaging and effective disccussion on the web will be done by pathologists and radiologists. **Keywords:** Mesothelioma, Accurate diagnosis, Remote digital pathology, Imaging diagnosis

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P3.08-006 NF2 Mutations in Malignant Pleural Mesothelioma Synchronous with Acoustic Neuroma: Disease-Causing Mutation or Chance Effect? Hitomi Kamiya[1], Takashi Nakano[1], Kozo Kuribayashi[1], Taiichiro Otsuki[1], Miki Honda[1], Eriko Masachika[1], Koji Mikami[1], Takayuki Terada[1], Yoshitaka Sekido[2], Seiki Hasegawa[3], Tohru Tsujimura[4] [1]*Division of Respiratory Medicine,Department of Internal Medicine, Hyogo College of Medcine, Nishinomiya, Hyogo/Japan,* [2]*Division of Molecular Oncology, Aichi Cancer Center Research Institute, Nagoya/Japan,* [3]*Department of Thoracic Surgery, Hyogo College of Medicine, Nishinomiya, Hyogo/Japan,* [4]*Department of Molecular Pathology, Hyogo College of Medcine, Nishinomiya, Hyogo/Japan*

Background: Patients with neurofibromatosis type 2 (NF2) are predisposed to schwannomas and meningiomas. Somatic *NF2* mutation has also been reported in patients with sporadic schwannomas and a variety of cancers. In particular, approximately 35–40% of patients with malignant pleural mesothelioma (MPM) carry inactivating mutations of *NF2*. In addition to *NF2*, BRCA1-associated protein-1 (*BAP-1*) has also been identified as a key genetic alteration in mesothelioma. Recently, a new familial cancer syndrome associated with germline mutations in *BAP1* was proposed, which includes MPM, ocular melanoma, and other cancers. However, *NF2* mutations do not usually cause mesothelioma synchronous with schwannoma. We here report two cases of MPM synchronous with vestibular schwannomas and analytical finding on *NF2* mutations **Methods: Case 1** was a 65-year-old man with epithelioid MPM. A unilateral acoustic neuroma was resected in 2010 because the patient experienced progressive hearing loss in the right ear since 2000. In April 2012, right pleural fluid was detected on chest X-ray and a thoracoscopical examination was performed. Epithelioid MPM was diagnosed pathologically. **Case 2** was a 72-year-old man with epithelioid MPM synchronous with unilateral acoustic neurinoma. The patient presented with DOE and hearing loss in the left ear that had progressed over the past month. Chest X-ray showed pleural effusion, and a biopsied specimen with thoracoscopy revealed epithelioid MPM. Brain MRI and CT showed a mass that was highly suspected to be acoustic neurinoma between the left cerebellopontine angle and the opening of the internal acoustic meatus. We performed whole-exome sequencing on DNA in tumor tissue and blood and immunohistochemical analysis of *NF2* gene encoding protein merlin. **Results:** Both patients were diagnosed with synchronous acoustic neurinoma and epithelioid MPM. *NF2* gene mutations were identified in both tumors of MPM and acoustic neurinoma in Case 1. And in Case 2, diagnosis of acoustic neurinoma was depended on typical findings of brain MRI/CT, for which surgical resection was not performed because of advanced stage of MPM. Tumor tissue of MPM in Case 2 showed positive result of *NF2* mutation. Both patients had a history of asbestos exposure. **Conclusion:** Although the role of *NF2* mutation as a possible disease-causing mutation in MPM and synchronous occurrence with schwannoma remain unclear, both cases showed the possible role of *NF2* mutation in asbestos-related neoplasm. We will show the pedigree of the patients' families. **Keywords:** Malignant pleural mesotelioma (MPM), NF2 mutation, BRCA1-associated protein-1 (BAP-1)

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P3.08-007 Fibulin-3: A Potential Prognostic Biomarker in Malignant Pleural Mesothelioma? Michaela B. Kirschner[1], Emily Pulford[2], Mir A. Hoda[3], Anita Rozsas[3], Kim Griggs[2], J James B. Edelman[4], Steven Kao[5], Rebecca Hyland[1], Yawen Dong[3], Viktoria Laszlo[3], Thomas Klikovits[3], Marko Jakopovic[6], Michael Vallely[4], Michael Grusch[7], Balazs Hegedus[3], Balazs Dome[3], Walter Klepetko[3], Nico Van Zandwijk[1], Sonja Klebe[2], Glen Reid[1] [1]*Asbestos Diseases Research Institute, Sydney/NSW/Australia,* [2]*Anatomical Pathology, Flinders University, Adelaide/SA/Australia,* [3]*Division of Thoracic Surgery, Medical University Vienna, Vienna/Austria,* [4]*Cardiothoracic Surgical Unit, Royal Prince Alfred Hospital, Sydney/ACT/Australia,* [5]*Medical Oncology, Chris O'Brien Lifehouse, Sydney/ Australia,* [6]*University Hospital Centre Zagreb, Zagreb/Croatia,* [7]*Institute of Cancer Research, Medical University Vienna, Vienna/Austria*

Background: Malignant pleural mesothelioma (MPM) is a highly aggressive asbestos-induced cancer arising from the mesothelium lining the thoracic cavities. The definitive diagnosis of MPM in most instances depends on the availability of a biopsy. A number of biomarkers have been proposed to assist in making the MPM diagnosis but none of them has yet reached the accuracy required for routine clinical use. Among the candidates is the secreted extracellular glycoprotein Fibulin-3 (FBLN3) (Pass et al, NEJM 2012; 367(15)). In this study, we have further investigated the potential of FBLN3 to serve as a biomarker for MPM. **Methods:** Cellular and secreted FBLN3 was measured (ELISA) in MPM and normal mesothelial cell lines, plasma of xenograft tumour-bearing mice, plasma from two independent series of MPM and non-MPM patients, and in malignant and non-malignant pleural effusions. The diagnostic and prognostic potential of FBLN3 was assessed by receiver operating characteristics curve analysis and the Kaplan-Meier method, respectively. **Results:** FBLN3 levels were significantly higher in MPM cells than in mesothelial cells, with a strong correlation between secreted and cellular levels. Human FBLN3 was also detectable in the plasma of tumour-bearing mice, suggesting that MPM cells were the origin of circulating FBLN3. Plasma FBLN3 levels found in MPM patients were lower than previously reported (Pass et al, NEJM 2012; 367(15)), but were comparable to those appearing in subsequent validation studies (Creaney et al, Thorax 2014; 69(10), Corradi et al, Anticancer Res 2013; 33(12)). Plasma FBLN3 was significantly elevated in MPM patients from a Sydney cohort, but far less in a Vienna cohort and the diagnostic accuracy of FBLN3 was insufficient in both cohorts [63%, (95%CI: 50.1-76.4) and 56% (95%CI: 41.5-71.0), respectively]. FBLN3 levels found in pleural effusions were comparable to those reported in previous studies, but the difference between cases and controls did not reach significance. In our series low levels of pleural effusion FBLN3 were again associated (p=0.002) with prolonged survival. In multivariate analysis taking histological subtype, age and gender into account FBLN3 remained significant with a hazard ratio of 9.92 (95%CI: 2.14–45.93). **Conclusion:** FBLN3 is overexpressed in MPM cell lines and may point to a potential oncogenic role for this protein. In contrast to the initial report linking FBLN3 to diagnosis in MPM, the levels of FBLN3 measured in plasma and pleural fluid of our series of MPM patients lacked diagnostic accuracy. However, the potential prognostic value of FBLN3 levels measured in pleural fluid was confirmed and in line with previous validation studies. These data underline the importance of validation studies for newly proposed biomarkers. **Keywords:** Mesothelioma, biomarker, Prognosis, Fibulin-3

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P3.08-008 Tip60 (KAT5) May Be a Candidate for Therapeutic Targeting in Malignant Pleural Mesothelioma Sian Cregan[1], Lauren Mcdonagh[2], Yun Gao[3], Martin P. Barr[1], Kenneth J. O'Byrne[4], Stephen P. Finn[5], Sinead Cuffe[6], Steven G. Gray[1] [1]*Thoracic Oncology Research Group, Trinity College Dublin/St. James'S Hospital, Dublin/Ireland,* [2]*Thoracic Oncology Research Group, Trinity College Dublin, Dublin/ Ireland,* [3]*Department of Oncology, Aerospace Central Clinical Medical College of Peking University, Beijing/China,* [4]*Cancer and Ageing Research Program, Princess Alexandra Hospital and Queensland University of Technology, Brisbane/Australia,* [5]*Department of Pathology, University of Dublin, Trinity College and St. James'S Hospital, Dublin/ Ireland,* [6]*Hope Department, St.James'S Hospital, Dublin/Ireland*

Background: Malignant pleural mesothelioma (MPM) is a rare aggressive cancer of the pleura. The most well established risk factor for this disease is exposure to asbestos. The current standard of care for patients suffering from MPM is a combination of cisplatin and pemetrexed (or alternatively cisplatin and raltitrexed). Most patients however, die within 24 months of diagnosis. New therapies are therefore urgently required for this disease. KAT5 (also known as Tip60) is the catalytic subunit of the NuA4 histone acetyltransferase complex which is involved in transcriptional activation of select genes. This complex may be required for the activation of transcriptional programs associated with oncogene and proto-oncogene mediated growth induction, tumor suppressor mediated growth arrest and replicative senescence, apoptosis, and DNA repair. KAT5 has also been linked with the development of cisplatin resistance. KAT5 may therefore be a significant element in MPM with respect to responses to cisplatin based therapy and could represent a novel candidate target for intervention. **Methods:** KAT5 has 4 variant mRNAs. Primers were designed to distinguish between all variants, and a panel of MPM cell lines was screened for KAT5 expression by RT-PCR. Levels of KAT5 were subsequently examined in a cohort of snap-frozen patient samples isolated at surgery comprising benign, epithelial, biphasic, and sarcomatoid histologies by RT-PCR. The effects of a small molecule inhibitor of KAT5 (MG-149) on cellular proliferation were examined. **Results:** Semi-quantitative densitometric analysis showed that the expression of KAT5 is dramatically increased in MPM for all mRNA variants. When separated according to histological subtype, significant differences were also observed between the various histologies. A small molecule inhibitor of KAT5 exists and treatment of cells with this small molecule inhibitor (MG-149) resulted in a significant inhibition of cellular proliferation ($p < 0.001$) in the NCI-H226 cell line. We continue to assess this compound by other methodologies to confirm its potential utility in the treatment of MPM. **Conclusion:** KAT5, a lysine acetyltransferase associated with cisplatin resistance in cancer is significantly altered in MPM. A small molecule inhibitor of this protein shows significant anti-proliferative effects in MPM cell lines. Targeting this protein may have important future implications for the management of MPM. **Keywords:** Tip60, Kat5, MG 149, lysine acetyltransferase

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P3.08-009 Diagnostic Efficacy of Electron Microscopy to Distinguish between Pleural Mesothelioma and Lung Adenocarcinoma in Pleural Effusion Cytology Oscar Arrieta Rodriguez[1], Hugo Domínguez-Malagón[2], Ana M. Cano-Valdez[2], Carlos E. González-Carrillo[2], Yelitza E. Campos-Salgado[1], Mariana Lopez-Mejia[1] [1]*Unidad Funcional de Oncología Torácica Y Laboratorio de Medicina Personalizada, National Cancer Institute, Mexico City/Mexico,* [2]*Pathology, National Cancer Institute, Mexico City/Mexico*

Background: Mesothelioma is a mesodermic tumor localized in the pleura in 70-90% of the presentations. In most cases the diagnosis is made by computed tomography-guided biopsy or thoracoscopy. Characteristically mesothelioma includes papillary structures which make it difficult to distinguish from adenocarcinoma on hematoxylin and eosin stain, making this entity its main differential diagnosis. Immunohistochemical studies in biopsy specimens aids in the obtaining of a precise diagnosis. Notwithstanding it is often difficult to distinguish between both entities, in which case, electron microscopy is the gold standard as it allows to observe the abundant long thin microvilli (characteristic of the mesothelium) in tumor cells. Sometimes patients have only pleural effusion cytology which makes the diagnosis more challenging. **Methods:** Twenty-five pleural effusion cytology samples were studied to evaluate electron microscopy and its efficacy for diagnosis, as well as by immunohistochemistry for the diagnosis of either lung adenocarcinoma or mesothelioma. **Results:** Five pleural effusion samples with the histological diagnosis of mesothelioma and twenty with the histological diagnosis of adenocarcinoma, all with confirmed biopsies by immunohistochemistry. Of the five pleural effusion samples with histological diagnosis of mesothelioma, cytology in electron microscopy showed morphological characteristics of mesothelioma (long thin microvilli, dense junctions, desmosomes and tonofilaments) in two samples (40%), and three were acellular (60%). Of the twenty pleural effusion samples with histologically confirmed diagnosis of adenocarcinoma (short microvilli, secretory vacuoles and intracytoplasmic lumens), eight were confirmed by electron microscopy (40%), eleven were acellular (55%), and one showed reactive mesothelium (5%). **Conclusion:** Pleural effusion cytology by electron microscopy showed that cells maintained their morphological features, either of mesothelioma or of lung adenocarcinoma, and can help in the diagnosis; however this is limited to the presence of cells in the pleural effusion **Keywords:** Mesothelioma, lung adenocarcinoma, electron microscopy

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P3.08-010 Pemetrexed and Cisplatin in Malignant Pleural Mesothelioma - Czech Experience Vitezslav Kolek[1], Libor Havel[2], Milos Pesek[3], Frantisek Salajka[4], Leona Koubkova[5], Jaromir Roubec[6], Jana Skrickova[7], Dimka Sixtova[8], Karel Hejduk[9], Zbynek Bortlicek[9] [1]*Respiratory Medicine, University Hospital, Olomouc/Czech Republic,* [2]*P Neumology and Thoracic Oncology, Municipal Hospital, Prague/Czech Republic,* [3]*Pulmonary Medicine, University Hospital, Plzen/Czech Republic,* [4]*University Hospital, Hradev Kralove/Czech Republic,* [5]*Pulmonary Medicine, University Hospital,, Praha/Czech Republic,* [6]*Pulmonary Medicine, University Hospital, Ostrava/Czech Republic,* [7]*Pulmonary Medicine, University Hospital, Brno/Czech Republic,*[8]*Pulmonary Medicine, Memorial Thomayer Hospital, Praha/Czech Republic,* [9]*Biostatistics, Iba Institute, Brno/Czech Republic*

Background: Malignant Pleural Mesotelioma (MPM) is a tumour with extremely unfavourable prognosis. Early diagnostic is rarely possible and chemotherapy has limited value in prolongation of survival. Pemetrexed with platinum is the standard 1st line chemotherapy. In the Czech Republic, the incidence of MPM is influenced mostly by former industry processing asbestos for roofs, other parts of buildings and isolation materials. Any work with asbetos is prohibited in the mean time. **Methods:** Treatment with pemetrexed and cisplatin was evaluated in a prospective study. Data of consecutive patients from 9 centers were prospectively collected from January 2008 till February 2015. Altogether 181 patients (47 women, 134 men) were evaluated. Mean age was 62 years, 71 pts were non smokers, 47 smokers, 61 ex smokers. Professional/ non-professional exposure was reported in 44/ 18 pts. Histology: 119 epithelial, 20 mixed, 12 sarcomatoid, not specified in 30 pts, TNM st.: I/II/III/IV in 19/32/48/78 pts, not assessed in 4 pts, PS: 0/1/2 in 39/130/12 pts. **Results:** Median of treatment was 18.5 weeks. Most frequent side effects (Gr 3, 4): leucopenia in 22, neutropenia in 15, anaemia in 15, trombocytopenia in 6, nausea/vomiting in 19, fatigue in 8 pts. Therapeutic response: CR in 5, PR in 47, SD 85, PD in 21 pts, overall disease control was 75.6 %. The median of overall survival (OS) was 19.8 months (16.2; 23.4), 1 year survival 67.9% (48.3; 71.5). Median of progression free survival (PFS) was 9.1 months (7.6; 10.7). Differences of survival were compared according to sex, smoking history, age, PS, TNM stage, treatment associated AE occurrence, type of exposure and histology. Significantly different results were achieved according to PS,TNM, exposure, AE and histology. **Conclusion:** Treatment of MPM with pemetrexed and cisplatinum in routine practice is effective and well tolerated. Prognosis is still poor and it is influenced by several clinical markers. Longer survival can be expected in PS 0, TNM I/II, unknown asbestos exposure, epitheloid histology and no treatment associated AE. Supported by national grant IGA MZ ČR NT/13569
Keywords: Mesothelioma, prognostic markers, survival

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P3.08-011 Avelumab (MSB0010718C), an Anti-PD-L1 Antibody, Evaluated in a Phase Ib Trial in Patients with Advanced Mesothelioma Anish Thomas[1], Raffit Hassan[1], Manish Patel[2], John Nemunaitis[3], Jaafar Bennouna[4], John Powderly[5], Matthew H. Taylor[6], Marcis Bajars[7], Anja Von Heydebreck[8], James L. Gulley[1] [1]*National Cancer Institute, National Institutes of Health, Bethesda/MD/United States of America,* [2]*Sarah Cannon Research Institute/Florida Cancer Specialists, Sarasota/FL/United States of America,* [3]*Mary Crowley Cancer Research Centers, Dallas/TX/United States of America,* [4]*Ico - Site René Gauducheau, Saint Herblain/France,* [5]*Carolina Biooncology Institute, Huntersville/NC/United States of America,* [6]*Oregon Health & Science University, Knight Cancer Institute, Portland/OR/United States of America,* [7]*Global Research and Early Development - Immunooncology, Emd Serono, Inc., Billerica/MA/United States of America,* [8]*R&D Global Biostatistics, Merck Kgaa, Darmstadt/Germany*

Background: The programmed death-1 receptor (PD-1) and its ligand (PD-L1) are key therapeutic targets in the reactivation of the immune response against multiple cancers. Avelumab* (MSB0010718C) is a fully human anti-PD-L1 IgG1 antibody currently being investigated in clinical trials. The phase Ib study (NCT01772004) is an open-label, parallel group expansion trial in patients with metastatic or locally advanced solid tumors that includes a cohort of patients with advanced, unresectable mesothelioma. **Methods:** This trial cohort is enrolling patients with histologically or cytologically confirmed unresectable mesothelioma (pleural or peritoneal) that has progressed after treatment with either a platinum-pemetrexed–containing regimen or a platinum-based regimen followed by pemetrexed (or vice versa). Eligible patients must have available tumor archival material or fresh biopsy, and an ECOG performance status of 0 or 1 at trial entry, and disease with at least 1 measurable lesion that has not been irradiated. Exclusion criteria include prior therapy with immune checkpoint drugs, a known history of autoimmune disease, or recent anticancer treatment (within the 28 days prior to study start). Up to 50 eligible patients will receive avelumab at 10 mg/kg as an infusion Q2W. Treatment will continue until disease progression, unacceptable toxicity, or any criterion for withdrawal occurs. Treatment may be continued despite progression according to RECIST 1.1 if the patient's clinical status is stable and, according to investigator opinion, there is no need to start salvage therapy. The primary objective of the trial is to assess the safety and tolerability of avelumab. Select secondary objectives include: assessment of best overall response (BOR) and progression-free survival (PFS) according to RECIST 1.1; assessment of immune-related BOR and immune-related PFS (using the modified Immune-Related Response Criteria); and assessment of overall survival. Association between tumor PD-L1 expression and efficacy will be evaluated. Changes in soluble factors and immune cell profiling will be characterized and immunomonitoring will occur at each visit. Tumor assessments will be performed every 6 weeks until progression. Tumor tissue from the most recent biopsy or surgical specimen will be collected prior to the initiation of trial treatment, and fresh biopsies may be optionally collected on day 43 and at the end-of-treatment visit. At each visit during the treatment phase, adverse events will be assessed and graded according to NCI-CTCAE v4.0. Enrollment in this study began in September 2014. *Proposed INN. **Results:** not applicable **Conclusion:** not applicable
Keywords: Mesothelioma, PD-L1, MSB0010718C, avelumab

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P3.08-012 Renal Safety of Sustained Pemetrexed/Platinum Treatment for Advanced Malignant Mesothelioma Meinolf Karthaus[1], K Tagizadeh[2] [1]*Hematology and Oncology, Klinikum Neuperlach, Munich/Germany,* [2]*Hematology and Oncology, Evkb, Bielefeld/Germany*

Background: Advanded malignant peritoneal mesothelioma (AbM) is a rare and aggressive neoplasm. The natural course of the disease is different from pleural mesothelioma. The optimal ctx duration for AbM remains undetermined. Ctx of AbM is commonly reported case by case. Efficacy of Pemetrexed (Pem)+cisplatinum (DDP) ctx has been demonstrated previously. A major obstacle to sustained Pem/DDP for AbM is renal safety beside neurotoxicity. At present, there are sparse data regarding renal safety in AbM pts receiving sustained ctx ≥6 cycles of Pem+platinum. **Methods:** We evaluated long-term renal safety of Pem (500 mg/m^2)+DDP (75 mg/m^2) in AbM prospectively. Ctx was given on d1 and repeated on d22 until disease progression or toxicity. Pts with impairment of renal function (Crea-Cl <60 ml/min) switched to carboplatin AUC5 (carbo). Pem ctx was stopped with a decline of Crea-Cl <45 ml/min. The trial was in accordance with the local ethics. Folic acid 400 µg po/d and vitamin B12 1000 µg i.m. qw 9 wks was administered to prevent severe AE. All pts received best supportive care with pre and post hydration as well as antiemetics including 5-HT3 antagonists and dexamethasone according to local standard of care. Study endpoints were long term renal safety in patients receiving sustained therapy of Pem + DDP followed by carbo and/or Pem-mono. **Results:** Between 2002 and 2014 staging revealed AbM in 19 pts. Initial ctx was Pem/DDP in 18 pts, except one who died prior to Tx. Ctx with Pem was given a mean of 12 cycles (range 1 to 37) with a mean of 259 d(range 21 to 1151). Mean dose of DDP was 678 mg(range 130 to 1335). Mean S-Crea(Crea-Cl) was 0,79 mg/dl(113 ml/min) prior and 0,95 mg/dl(97,4 ml/min) at the end of Pem/DDP. Pem/DDP was administered ≥6 cycles in 8 pts up to a max. of 10 cyles. DDP was stopped due to a decline in S-Crea in 6 out of 18 pts (33%). Renal tox was the reason for DDP cessation in all pts with >6 cycles, except 1. Five pts switched then to carbo due to renal tox with S-Crea(Crea-Cl) of 1,1 mg/dl(83 ml/min) prior and 1,2 mg/dl(79 ml/min) at the end of Pem/carbo. No renal toxicity was observed in those 4 pts with Pem-mono (max 10 cycles) subsequently after platinum ctx with S-Crea(Crea-Cl) prior 1,25 mg/dl(69 ml/min) and 1,14 mg/dl(72,5 ml/min) respectively. **Conclusion:** Sustained treatment for AbM is feasible but limited by renal tox of DDP, while subsequent Pem +/- carbo did not lead to additional deterioration of renal function, allowing sustained ctx for AbM.
Keywords: renal safety, pemetrexed and platinum, meosthelioma, sustained treatment

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P3.08-013 Twenty-Four Cases of Malignant Pleural Mesothelioma in Iwakuni, Japan Ryosuke Hirai[1], Shoichi Kuyama[2], Takahiro Umeno[2], Daisuke Nojima[2], Toshio Shiotani[3], Ryujiro Sugimoto[3], Kazuhiko Kataoka[3] [1]*NHO Iwakuni Medical Center, Iwakuni City/Japan,* [2]*Department of Respiratory Medicine, NHO Iwakuni Medical Center, Iwakuni/Japan,* [3]*Department of Thoracic Surgery, NHO Iwakuni Medical Center, Iwakuni/Japan*

Background: Asbestos had been stopped to use in Japan since the late 1970s. Asbestos exposure will increase the risk of mesothelioma and the interval between initial exposure and subsequent biological consequences is assumed more than 40 years. Iwakuni is part of the Seto Inland Sea industrial area and one of the oldest petrochemical industrial complexes in Japan is located. The incidence of mesotheliomas is expected to rise over the next decade. Treatment for mesothelioma includes surgery, chemotherapy, radiation therapy and their combination. Recently, cisplatin in conjunction with pemetrexed has shown advantageous results in reducing tumors, but pleural mesothelioma is still incurable fatal disease except specific case. In this study, we reviewed the clinical features of 26 patients with malignant pleural mesotelioma treated in our institute. **Methods:** Between January 2006 and December 2014, 26 patients were histologically diagnosed as malignant pleural mesotelioma. Retrospective review was performed and demographic, clinical, pathologic, treatment and survival data were collected. Overall survival were estimated by the Kaplan-Meier analysis. Surgery includes two patients treated by trimodality therapy (chemotherapy + extrapleural pneumonectomy + radiation therapy) and a patient treated by pleurectomy combined with hyperthermic therapy. Other four patients were treated by extrapleural pneumonectomy alone. **Results:** In the studied population,21 of 26 patients were male.the mean age of diagnosis was 72y. Each number of histological subtypes(epithelial,sarcomatoid and biphasic) were 15,6,and 5.The number of patients who treated with surgery were 8,with chemotherapy were 17 and best supportive care was 1. The median survival time of the 27 malignant pleural mesotelioma patients was 13.4 months. According to histological subtypes,the MTS of epithelial,sarcomatoid and biphasic were 21.4 months,6.5 months and 11.6 months The MTS of surgery and chemotherapy were 21.4 months and 13.2 months.One year survival rate were 85.7% and 47.6%. The MTS of the patients with and without pleural plaque were 13.4 months and 15.0 months. Female gender, epithelial subtypes, treatment of surgery and patients without pleural plaque showed relatively favorable outcome. **Conclusion:** Because of the appearance of effecive chemotherapies,such as Pemetrexed sodium hydrate,better survival has been observed in patients treated by chemotherapy. However, long-term survival was seen only in patients treated by surgery. Surgery allows us to accurately stage patients and provide data that may be useful in better patient stratification. Surgery should be selected for the operable patients with c-stage I-II and epithelial disease. We have to detect malignant pleural mesothelioma in early stage and treat in appropriate means.
Keywords: malignant pleural mesothelioma, Retrospective review

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P3.08-014 COMMAND: A Phase 2 Randomized, Double-Blind, Study of Defactinib (VS-6063) as Maintenance Therapy in Malignant Pleural Mesothelioma Hedy Lee Kindler[1], Dean A. Fennell[2], Paul Baas[3], Lee M. Krug[4], Marjorie G. Zauderer[5], Anna K. Nowak[6], Richard J. Gralla[7], Takashi Nakano[8], Marcelyne Joseney-Antoine[9], Anne Poli[9], Mitchell Keegan[10], Joanna Horobin[9] [1]*Section of Hematology/Oncology, University of Chicago, Chicago/IL/United States of America,* [2]*Mrc Toxicology Unit, University of Leicester & Leicester University Hospitals, Leicester/United Kingdom,* [3]*The Netherlands Cancer Institute-Antoni Van Leeuwenhoek Hospital, Amsterdam/Netherlands,* [4]*Medicine/Thoracic Oncology, Mskcc, New York/United States of America,* [5]*Medicine/Thoracic Oncology, Mskcc, New York/NY/United States of America,* [6]*School of Medicine and Pharmacology, University of Western Australia, Perth/WA/Australia,* [7]*Department of Medicine, Jacobi Medical Center - Albert Einstein College of Medicine, Bronx/NY/United States of America,* [8]*Department of Respiratory Medcine, Hyogo College of Medcine, Nishinomiya , Hyogo/Japan,* [9]*Verastem, Boston/MA/United States of America,* [10]*Verastem, Boston/United States of America*

Background: Malignant pleural mesothelioma (MPM) is an aggressive tumor in the pleural lining of the lung. Median OS with frontline chemotherapy of pemetrexed/cisplatin (pem/cis) is ~12 months. There is no established second line therapy. Pem/cis has been shown to enrich cancer stem cells (CSCs) in tumors. Focal adhesion kinase (FAK) inhibitors have been found to decrease CSCs in mesothelioma models. The use of a FAK inhibitor in a maintenance setting after frontline chemotherapy may therefore extend survival of MPM patients. Furthermore, approximately 40% of MPM tumors exhibit disruption of the NF2 tumor suppressor gene by mutation and/or deletion resulting in lack of expression of functional merlin protein. Mesothelioma cell lines that lack merlin are more sensitive to FAK inhibitors than those with wild type merlin. This Phase 2 study will determine if defactinib (VS-6063), an oral inhibitor of FAK, provides superior clinical benefit compared with placebo as maintenance treatment in patients with MPM following frontline pem/platinum therapy. **Methods:** COMMAND is a multinational, randomized, double-blind, placebo-controlled trial. Approximately 370 patients with PR or SD following ≥4 cycles of frontline pem/platinum therapy will be enrolled. Patients will receive defactinib 400 mg BID or matched placebo. Randomization will be stratified by merlin status, as determined by immunohistochemistry. Primary endpoints include OS and PFS. An adaptive enrichment design at the interim analysis (projected to occur in Q2 2015) may restrict patients to those with low merlin protein expression if greater benefit is observed among this subpopulation. Secondary endpoints include patient-reported outcomes, objective

response and safety and tolerability. The study is currently enrolling across 15 countries. Clinical trial: **NCT01870609**. **Results:** Not applicable **Conclusion:** Not applicable **Keywords:** Cancer Stem Cells, Mesothelioma

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P3.08-015 Naftopidil Is Effective in the Treatment of Malignant Pleural Mesothelioma Koji Mikami[1], Kozo Kuribayashi[1], Ryuji Ieki[1], Takayuki Terada[1], Taiichiro Otsuki[1], Hitomi Kamiya[1], Eriko Masachika[1], Akinobu Gotoh[2], Tomoyuki Nishizaki[3], Takashi Nakano[1] [1]*Division of Respiratory Medicine,Department of Internal Medicine, Hyogo College of Medcine, Nishinomiya, Hyogo/Japan,* [2]*Laboratory of Cell and Gene Therapy, Institute for Advanced Medical Science, Hyogo College of Medicine, Nishinomiya,Hyogo/Japan,* [3]*Department of Physiology, Hyogo College of Medcine, Nishinomiya, Hyogo/Japan*

Background: Naftopidil, an antagonist of the α1A/1D-adrenoceptor, was developed as a drug for the treatment of benign prostate hyperplasia and hypertension, and has recently been shown to exert antitumor activity in a variety of cancers. We previously discovered that naftopidil induces apoptosis of malignant pleural mesothelioma (MPM) cells in an α1-adrenoceptor-independent manner, as this was not reproducible using other α1-adrenoceptor-inhibitors such as prazosin. The present study was conducted to assess whether naftopidil is useful for the treatment of MPM. **Methods:** Cell viability of cultured NCI-H2052 human cells was evaluated using MTT. TUNEL staining was performed to detect *in situ* DNA fragmentation as a marker of apoptosis using an *in situ* apoptosis detection kit. Caspase activity was measured using a caspase fluorometric assay kit. NCI-H2052 cells were treated with naftopidil (100 μmol/L) and were subcutaneously inoculated into the right flank of BALB/c-nu/nu mice under pentobarbital-induced general anesthesia. Naftopidil was diluted with a physiological salt solution and injected intraperitoneally twice a week, starting 1 week after inoculation; the salt solution alone was used in control mice. The longer (L) and shorter (S) lengths of the induced tumors were measured using calipers, and tumor volume (V) was calculated according to the following equation: $V = (L \times S^2) \times 1/2$. **Results:** Naftopidil reduced NCI-H2052 cell viability in a concentration-dependent manner and significantly increased the number of TUNEL-positive NCI-H2052 cells compared to untreated cells. Naftopidil activated caspase-3 and -8, but not caspase-9. Naftopidil did not affect the expression of FasL protein in NCI-H2052 cells. Notably, however, it did significantly increase the concentrations of extracellular FasL protein in a bell-shaped, time-dependent manner. Intraperitoneal injection of naftopidil significantly inhibited NCI-H2052 xenograft tumor growth compared to tumors in control mice. All mice injected with naftopidil survived 8 weeks after the first injection, and the drug had no effect on their mean weight. **Conclusion:** The results of the present study suggest that naftopidil induces apoptosis of NCI-H2052 cells by stimulating the secretion of FasL, a ligand of the death receptor Fas. This in turn activates caspase-8 and the effector caspase-3, leading to the inhibition of NCI-H2052 xenograft tumor growth *in vivo*. This supports the concept that naftopidil could be developed as a therapeutic agent for the treatment of malignant pleural mesothelioma. **Keywords:** Cancer therapy, Naftopidil, FasL, malignant pleural mesothelioma

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P3.08-016 Role of Pro-Inflammatory Cells in Development of Mesothelioma Tatyana Chernova[1], Fiona Murphy[1], Xiao Ming Sun[1], Sara Galavotti[1], Stefano Grosso[1], David Dinsdale[1], Jonathan Bennett[2], Apostolos Nakas[2], Martin Bushell[1], Anne E. Willis[1], Marion Macfarlane[1] [1]*Toxicology Unit, Medical Research Council, Leicester/United Kingdom,* [2]*Glenfield Hospital, Uhl NHS Trust, Leicester/United Kingdom*

Background: Malignant mesothelioma is an aggressive tumour of the pleura or peritoneum and strongly related to asbestos exposure. Malignant pleural mesothelioma is the most common and occurs with a latency of up to 40 years. Long pathogenic fibres fail to clear through the lymph system and are retained in the pleura of the exposed individuals. During the long latency period, mesothelial cells remain exposed to paracrine signalling from inflammatory cells recruited to the fibre-retaining areas. However, the mechanism of malignant transformation is not well understood. Several studies have identified changes in defined signalling pathways in mesothelial and stromal cells, but the relationship between different cell types has not been explored. **Methods:** To examine the pro-oncogenic role(s) of different cell populations, the effect of primary fibroblasts from human mesotheliomas and fibre-activated macrophages on cellular signalling in normal untransformed mesothelial cells was monitored using imaging and immunoblotting techniques. **Results:** Paracrine signalling from activated fibroblasts or macrophages increased the levels of proliferation and motility in normal mesothelial cell cultures. Activation of pro-oncogenic signalling was demonstrated in the cultures subjected to 'cross-talk' with pro-inflammatory cells, including 'horizontal transfer' from activated fibroblasts. Normal mesothelial cells, co-cultured or treated with conditioned media from fibre-activated macrophages, also displayed signs of epithelial-to-mesenchymal transition. The levels of growth modulators and survival rates were also altered in these cells. **Conclusion:** Thus, non-mesothelial cells instigate pro-oncogenic alterations in cellular signalling in target mesothelial cells. Further integral examination of the aberrant signalling pathways, especially at early stages of neoplasia, will provide new insights into the mechanisms underlying malignant transformation of the mesothelium. **Keywords:** Mesothelioma, inflammation, oncogenesis, macrophage

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P3.08-017 Quality of Life Impact and Adverse Events after Pleurodesis in Patients with Recurrent Malignant Pleural Effusion Ricardo M. Terra, Priscila B. Costa, Pedro N. Araujo, Jose D. Andrade-Neto, Benoit J. Bibas, Paulo M. Pêgo-Fernandes *Thoracic Surgery, University of São Paulo, São Paulo/Brazil*

Background: Even though pleurodesis is the gold-standard procedure to manage recurrent malignant pleural effusion (RMPE), little is known of its impact on the quality of life (QOL), adverse events, and systemic inflammatory consequences. Our main objective was to evaluate the impact of pleurodesis on the QOL of patients with RMPE and the adverse events related to the procedure. The secondary objectives were to evaluate systemic consequences of pleurodesis and to identify predictors of QOL improvement after pleurodesis. **Methods:** Retrospective study including data from patients who underwent pleurodesis from 2005 to 2014 at our Institution. QOL was measured through WHOQoL-Bref instrument, pain visual analog scale, and British Medical Research Council dyspnea scale. Adverse events were systematically registered and classified according to the NCI–CTCAEV.4.0. Blood tests were collected before, 2, 5, and 10 days after the pleurodesis. To compare continuous variables we used paired-T test or Wilcoxon test. To find predictors we built linear regression models. We considered as significant tests which $p<0.05$. **Results:** 257 patients (77% female) with mean age of 69 years-old(± 13.01) were included. The most frequent primary malignancies were breast cancer (56%) and lung cancer (25%). The sclerosing agents used were talc (38%), silver nitrate (36%), and iodopovidone (25%). Clinical recurrence was observed in 8% of the patients and mean survival was 8 months. The physical domain of QOL as well as pain and dyspnea scores were the most abnormal results at baseline and were also the variables which improved the most 30 days after the procedure ($p<0.001$ for all 3 parameters). Female gender, low pleural fluid lymphocytes count, and the use of silver nitrate were associated with QOL improvement. Adverse events occurred in 43% of the patients, and in 16.3% we observed severe events (Grade 3 or higher). Hypoxia, renal failure, and pain were the most frequent. We observed significant variation in the following blood tests: C-Reactive Protein (rise), hemoglobin (decrease), platelets (rise), alkaline phosphatase (rise). **Conclusion:**Pleurodesis is associated with improvement of the QOL of patients with RMPE; nevertheless, it is also associated with high number of adverse events and systemic metabolic effects. **Keywords:** pleurodesis, quality of life, malignant pleural effusion

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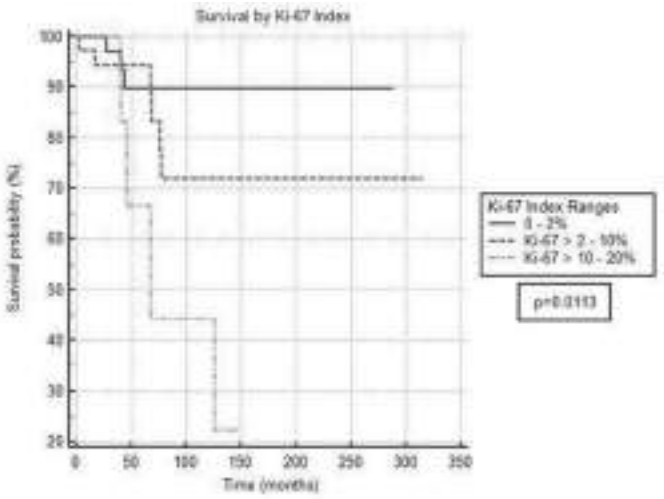
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.08-018 Clinical and Pathologic Characteristics of Bronchial Carcinoid Tumors: A Single Institution Review Robert A. Ramirez[1], David T. Beyer[1], Anne E. Diebold[1], Maria M. Chester[1], Yi-Zarn Wang[1], John P. Boudreaux[1], Eugene A. Woltering[2], Ann-Porter Uhlhorn[2], Pam Ryan[2], Richard J. Campeau[1], Lowell B. Anthony[3] [1]*Neuroendocrine Tumor Program, Ochsner Medical Center - Kenner, Kenner/LA/United States of America,* [2]*Neuroendocrine Tumor Program, Ochsner Medical Center - Kenner, Kenner/United States of America,* [3]*University of Kentucky Medical Center, Lexington/United States of America*

Background: Typical and atypical carcinoids represent about 2% of all lung tumors. Unlike most lung tumors, survival of patients with typical bronchial carcinoids is generally long but and is dependent on stage. We report the findings from the Ochsner/Louisiana State University (LSU) Neuroendocrine Tumor (NET) Program. **Methods:** A database with all patients who were seen at the Ochsner/LSU NET Program was queried for all bronchial NET patients. We included those who had confirmed pathological bronchial carcinoid and those who had at least one visit to our clinic. Typical and atypical bronchial carcinoids were defined by most recent WHO classification. Excluded were patients with large and small cell NETs, diffuse idiopathic pulmonary neuroendocrine cell hyperplasia, and inaccessible patient records. **Results:** One-hundred sixty-nine patients were included from January 1996 - March 2015. The mean age at diagnosis was 53 (range 12-92). There were 154 (91%) Caucasian, 10 (6%) African-American, and 5 (3%) other. Females represented 67% of all patients. 51% percent (86/169) were well differentiated, 12% (21/169) were moderately differentiated. Eighty-five percent and fifty-three percent were positive on PET and octreotide scanning, respectively. One-hundred fifty-five patients had adequate staging information. Overall survival and survival by stage and differentiation status is shown below. There was a statistically significant difference in survival by Ki-67 index.

Overall Survival			
N	Median	5-year	10-year
169	243 months	88%	74%
Survival by AJCC 7 Stage			
	N	5-year	10-year
I*	65	98%	91%
II*	23	95%	87%
III*	27	84%	66%
IV	40	73%	49%
Survival by Differentiation Status			
	Median	5-year	10-year
Well (n=86)	243	88%	81%
Moderate (n=21)	119	80%	42%
Survival by Typical/Atypical			
	Median	5-year	10-year
Typical (n=109)	243 months	89%	80%
Atypical (46)	126 months	84%	59%

A and B stages are grouped



Conclusion: Overall, patients with bronchial carcinoids experience high 5 and 10-year survival rates. As expected, there were significant survival differences between nodal status, differentiation status and typical versus atypical. Interestingly, there was a statistically significant difference in survival between low, low-intermediate and high-intermediate Ki-67 values. Our analysis showed that survival rates were much better for Ki-67 index value ranges from 0-2% versus >2-10% versus >10-20%. As with gastroenteropancreatic NETs, Ki-67 index could become a valuable prognostic indicator for bronchial carcinoids. **Keywords:** carcinoid, survival, neuroendocrine, Ki-67

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.08-019 Chemical Ablation Therapy of Recurrent Mediastinal Metastasis
Xinglu Xu *Department of Oncology, Pingyi Branch of Qilu Hospital; Shandong University, Pingyi, Shandong China;/China*

Background: To evaluate the treatment of post-radiotherapy recurrent mediastinal nodal metastasis. **Methods:** Post-radiotherapy thoracic cancer patients with mediastinal lymph node recurrence were enrolled in this study. Patients were randomized into the Radiation (+/- Chemotherapy) or the chemoablation group. Patients randomized to the chemoradiotherapy group received additional radiotherapy, second-line chemotherapy, or both. Patients randomized to the chemoablation group received CT-guided percutaneous chemical ablation. Clinical remission was assessed at one month by contrast CT. Reirradiation dose ranged from 2200-3600 cGy depending on dose limiting constraints in consideration of prior radiotherapy dose. The RECIST criteria were used in the evaluation of response to therapy. The median length of follow-up is six months. **Results:** Thirty-one patients were enrolled in the study. In the chemoradiation group, all patients underwent CT imaging at one month follow-up. Among these patients, 7 had progressive disease (PD), 5 had stable disease (SD), and 4 had partial response (PR). The six-month survival rate was 12.5%. In the chemoablation group at one-month follow-up, 12 patients had SD and 3 patients had PR and the six-month survival rate was 46.6%. **Conclusion:** Our results suggest that chemoablation therapy as salvage treatment after post-radiotherapy relapse is efficacious and safe. **Keywords:** mediastinal nodal metastasis, radiation therapy, chemical ablation

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P3.08-020 Clinicopathological Features of Primary Intra-Thoracic Follicular Dendritic Cell Sarcomas
Patrizia Viola[1], Katherine Vroobel[2], Simon Jordan[3], Andrew Wotherspoon[2], Andrew G. Nicholson[4] [1]*Histopathology, Royal Brompton Hospital, London/ United Kingdom,* [2]*Pathology, Royal Marsden Hospital, London/United Kingdom,* [3]*Department of Thoracic Surgery, Royal Brompton and Harefield NHS Trust, London/United Kingdom,*[4]*Pathology, Royal Brompton and Harefield NHS Foundation Trust and National Heart and Lung Institute, London/United Kingdom*

Background: Follicular dendritic cell sarcoma (FDCS) is defined in the WHO as a neoplastic proliferation of spindle/ovoid cells with morphological and immunohistochemical features of follicular dendritic cells. It is a rare tumour with no clear aetiology, often misdiagnosed and difficult to characterise. Occasionally it occurs in association with the hyaline-vascular type of Castleman disease which, in such cases, is considered its precursor lesion. Most cases are reported in lymph nodes, however several cases with extranodal presentation have been described. Despite the fact that metastasis are common in the lung, only 7 cases have been reported as primary pulmonary FDCS. Surgical excision with chemotherapy is the treatment of choice giving transient, partial response in some cases. We report our experience within the last 15 years of 6 cases of FDCS arising in the mediastinum and in the lung. **Methods:** The study included 7 patients referred to Royal Brompton Hospital between 2001 and 2014 with a diagnosis of FDCS. Criteria for inclusion were morphological and immunohistochemical: fascicles/ whorls of spindle to ovid cells with features resambling follicular dendritic cells and the expression of one or more specific markers (CD21, CD23 and CD35). We performed a broad immunohistochemical panel and we looked for the presence of Castleman's disease and the type of inflammatory infiltrate in the background. Clinical information were obtained from hospital records and clinicians. **Results:** After review, we identified 6 cases consistent with the diagnosis of FDCS, four males and two females between 25 and 61 years old. One case was excluded because of equivocal expression of specific markers. Three patients presented with a mediastinal mass and one having two recurrences within the study period. Two patients presented with a lung mass and one with a radiological pleurally based mass infiltrating the lung and chest wall. Clinical presentation was mainly with cough and chest pain due to the location of the tumour. Histologically all cases showed an atypical spindle cell proliferation with storiform pattern within a mixed inflammatory stroma. Mitotic rate was generally low except in case of recurrences. In three cases Castleman's features were present in the background. Five out 6 cases (83.3%) expressed CD21, CD35, p53 and cyclin D1, 3 cases (50%) expressed CD35, S100, lysozyme and bcl2 and 2 cases (33.3%) expressed KP1, PGM1, CD45, CD4, CD30 and bcl6. All were negative for keratins. Four cases (66.7%) were initially misdiagnosed as pleomorphic malignant tumour.Background showed a variably amount of B and T cells, with T cells expressing CD4 and PD1. Follow up data were available for 4 patients: one died after 5 years, 2 were alive with no recurrence after one year and one is alive after 8 years and two recurrences. **Conclusion:** FDCS is a rare tumour and should be considered in cases with a malingant spindle cells proliferation negative for the most common markers. Our series also showed Cyclin D1 expression in this tumour which has not previously been reported. This may raise the possibility for a new more effective therapeutic approach but further studies are needed. **Keywords:** Castleman disease, Cyclin D1, Follicular dendritic cell sarcoma

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.08-021 Bronchopulmonary Carcinoid: A Developing Nation Cancer Center's Perspective
Sunil Kumar[1], Ashish Jakhetiya[1], Palaniappan Ramanathan[2], Durgatosh Pandey[1], Svs Deo[1], Nootan Shukla[1] [1]*Surgical Oncology, All India Institute of Medical Sciences, New Delhi, New Delhi/India,* [2]*Surgical Oncology, All India Institute of Medical Sciences, New Delhi/India*

Background: Bronchopulmonary carcinoids are low grade malignant tumours and increased incidence has been noticed worldwide. Our aim was to study preoperative characteristics, surgical approaches and outcome in bronchopulmonary carcinoid patients treated at a institutional cancer center. **Methods:** Twenty patients with bronchopulmonary carcinoids were surgically treated at department of surgical oncology, IRCH, AIIMS between December 2006 and December 2014. Preoperative variables, postoperative outcome and histopathological features were analyzed retrospectively. All patients underwent a detailed clinical evaluation followed by CECT of chest and bronchoscopy with biopsy of the suspicious lesion. After preoperative optimization, all patients were treated with upfront surgery. Adjuvant chemotherapy was given in patients with lymph nodal metastasis. Patients were followed up at three monthly interval with Clinical examination, chest X ray and serum chromogranin in cases of suspected recurrence. Because of cost factors Dotanoc scans were done only in cases with radiological suspicion of recurrence. **Results:** Patient's median age was 40 years (range 18-62 years). All patients were symptomatic and median duration of symptoms before presentation was 18 months (range 6-72 months). Eight patients were treated with antitubercular drugs after presumptive diagnosis outside based on symptoms and Xrays. All the patients had lobar or main bronchial involvement which

was detected on bronchoscopy and biopsy. Ninteen patients underwent complete pulmonary resection with mediastinal nodal dissection and surgical approach included eight pneumonectomies, four bilobectomies, five lobectomies, two sleeve resections. After a median follow up of 15 months, all patients were alive with no local recurrence or distant metastasis. On Histopathology all the resections margins were free of tumor and lymph nodal involvement was found in one patient. **Conclusion:** Delayed presentation and misdiagnosis are major concern in our scenario because of high prevalence of tuberculosis and despite a small number of cases our study emphasises the need for early bronchoscopy in patients with persistent symptoms. Aggressive surgical resection with technical approach of lung preservation may provide optimal survival results
Keywords: bronchopulmonary carcinoid, surgery, developing nation

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-17:00

P3.08-022 Atypical Presentation of a Malignant Cardiac Tumor Ionela Erhan[1], Stefan Dumitrache-Rujinski[2], Dragos Zaharia[3], Adriana Iliesiu[4], Horatiu Moldovan[5], Miron Bogdan[6], Diana Leonte[1], Tuberiu Nanea[7] [1]*„Marius Nasta" Institute of Pulmonology, Bucharest, Romania, Bucharest/Romania,* [2]*„Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania, „Marius Nasta" Institute of Pulmonology, Bucharest, Romania, Bucharest/Romania,* [3]*Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania, „Marius Nasta" Institute of Pulmonology, Bucharest, Romania, Bucharest/Romania,* [4]*„Prof. Dr. Traian Burghele" Clinical Hospital of Urology, Department of Internal Medicine, Bucharest, Romania, „Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania, Bucharest/Romania,* [5]*„Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania„Prof. Cc Iliescu" Emergency Institute of Cardiovascular Diseases", Bucharest, Romania, Bucharest/Romania,* [6]*Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania „Marius Nasta" Institute of Pulmonology, Bucharest, Romania, Bucharest/Romania,* [7]*„Prof. Dr. Traian Burghele" Clinical Hospital of Urology, Department of Internal Medicine, Bucharest, Romania, „Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania, Bucharest/Romania*

Background: primary cardiac tumors are very rare pathological entities with an incidence (autopsy and surgical biopsies reports) ranging between 0,3% - 0,7 %. The main histopathological type of primary malignant cardiac tumors is represented by angiosarcoma, usually located within right atrium. The diagnosis may be delayed due to nonspecific symptomatology. Most cases are presenting with metastases to the lung in the moment of diagnosis and a median survival is less than one year (between 6 and 11 months). **Methods:** not applicable **Results: Case report**: we present the case of a non-smoker 19-year-old man, with right atrial angiosarcoma, with pericardial involvement and difuse limphohaematogenous pulmonary metastasis. The symptomatology consisted in: cough, difuse chest pain, progressive dyspnea, night swets, low grade fever and hemoptoic sputum. Chest X-ray revealed a diffuse micro nodular pattern, a resting pulseoxymetry with mild hypoxemia, no ECG abnormalities. No abnormalities on the clinical examination. The differential diagnosis included mainly: miliary tuberculosis (high incidence of tuberculosis in Romania) and Pneumocystosis. Bronchoalveolar lavage shows no fast acid bacilli, no Pneumocystis cysts, no neoplastic cells and HIV was negative. No inflammatory syndrome, normal WBC, no anemia and normal biochemistry. According to this data we decided to start antituberculous treatment and the patient was programed for thoracic CT scan. The clinical status rapidly deteriorated with worsening of dyspnea, respiratory failure and hypotension. Chest X-ray revealed enlargement of cardiac opacity and on ECG a micro voltage with an alternance in the QRS complex was identified. An echocardiography was performed in emergency and a massive mass of tissue occupying almost the entire right atrium with pericardial invasion and cardiac tamponed was identified. A median sternotomy with pericardial drainage , pericardial and tumor biopsy where performed. The patient died one week later with palliative care. The autopsy showed a right massive atrium tumor with myocardium, epicardium, and papillary muscle invasion, difuse lung nodular and micronodular metastases. The hystopatological / immunochemistry exam diagnosed a moderately differentiated angiosarcoma expressing CD 34, CD31. **Conclusions:** Tardive diagnoses of a massive right atrium angiosarcoma with bilateral pulmonary metastasis**. Particularity of the case:** rare cardiac malignant tumor revealed by respiratory symptoms dues to diffuse pulmonary micronodular metastases
Keywords: primary malignant cardiac tumor, angiosarcoma, lung metastases

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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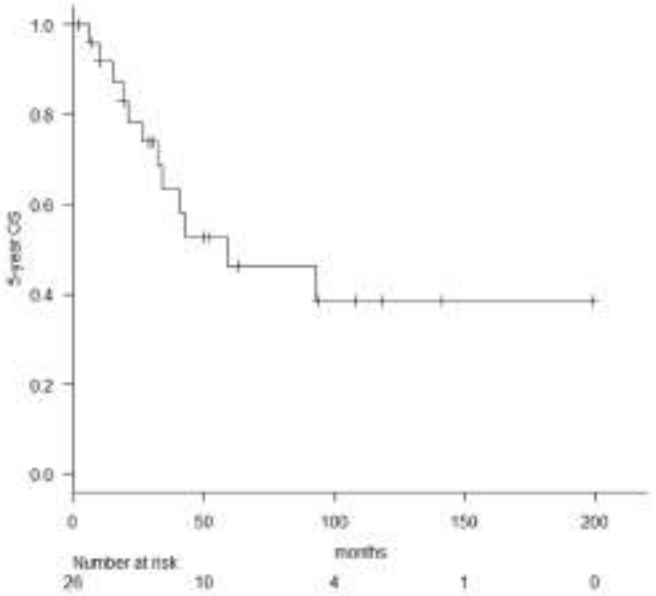
P3.08-023 Evaluation of Multiple Time Resection of Lung Metastases from Colorectal Cancer Kokichi Miyamoto, Masafumi Kataoka, Toshinori Ohara, Yoshihiro Akazai, Yasuki Nitta, Masanobu Maruyama, Hironobu Kawamoto *Okayama Saiseikai General Hospital, Okayama/Japan*

Background: Surgical resection of lung metastasis from colorectal cancer is beneficial for improving the prognosis of patients when no other metastatic lesions exist. However, the efficiency of multiple time resection of lung metastases has not yet been established. We investigated the characteristics and prognosis of multi-time lung resection cases in order to identify the appropriate indication for this procedure. **Methods:** Ninety-nine patients underwent resection of lung metastases from colorectal cancer between 1993 and 2013 at our institute. Among these patients, we investigated 26 cases who underwent lung resection more than twice. **Results:** With regard to the initial stage of disease, one case was stage I, 4 were stage II, 15 were stage III, and 6 were stage IV. Twenty-two patients underwent lung resection twice, and 4 patients underwent lung resection three times. The median follow-up time was 85 months (range, 36–215 months). Twelve cases died of colorectal cancer recurrence. Eight cases died due to metastases to multiple organs including the liver, lymph nodes, and lung. Two cases died of multiple lung metastases, one died of liver metastasis, and one died of mediastinal nodal metastasis. The overall survival curve from second lung resection is shown in the figure (Kaplan-Meier curve, log-rank test). The 5-year overall survival rate was 46.2%, and the 5-year disease-free survival rate was 44.1%. Three out of 4 cases who underwent lung resection three times died within a year after the operation.



Conclusion: A second lung resection seems to be feasible, while a third may not. Precise evaluation of metastatic lesions in other organs before operation and systemic therapy for preventing multiple metastases may be important.
Keywords: metastatic lung cancer, colorectal carcinoma, multiple time resection

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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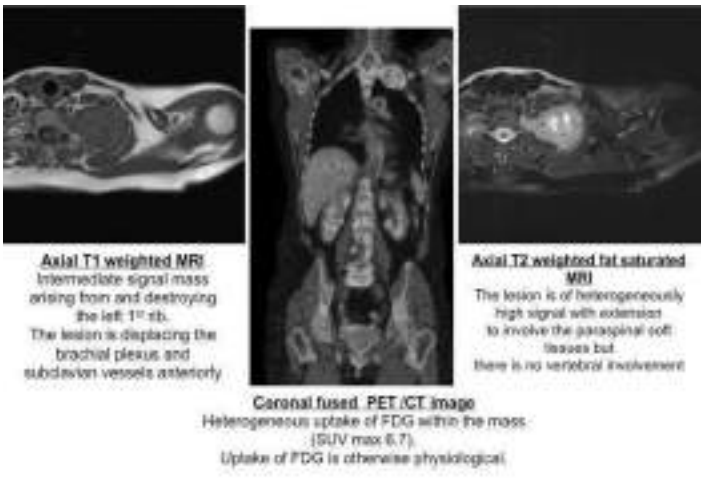
P3.08-024 A Rare Cause of Pancoast Syndrome Aleksander Mani[1], Lucy Cogswell[2], Kathleen Swalwell[1], Fiona Macleod[3], Nick Athanasou[4], Dionisios Stavroulias[1] [1]*Thoracic Surgery, John Radcliffe Hospital, Oxford/United Kingdom,* [2]*Plastic Surgery, John Radcliffe Hospital, Oxford/United Kingdom,* [3]*Radiology Department, John Radcliffe Hospital, Oxford/United Kingdom,* [4]*Histopathology Department, John Radcliffe Hospital, Oxford/United Kingdom*

Background: Alveolar soft part sarcoma (ASPS) is a rare tumour that was initially described by Christopherson et al. in 1952. It accounts for 0.5 - 1% of all soft tissue sarcomas. It most commonly presents in the 15 - 35 year age group with slightly higher incidence in females than males by a ratio of 3:2. **Methods:** We describe a case of a 55-year old woman who had a right mastectomy, adjuvant chemotherapy and radiotherapy 3 years prior to her presentation to our service with a left sided supraclavicular mass that was causing shoulder pain and left upper limb paraesthesia. The patient did not present Horner's syndrome. **Results:** Preoperative PET-CT showed a 5.8 x 4.5 x 5.5cm mass, moderately FDG avid (SUVmax 6.7), arising from the 1st rib. An MRI of the brachial plexus showed no vertebral body involvement, no vessel infiltration, but suspicion of left T1 nerve sheath involvement (Fig 1.). The patient underwent a CT-guided biopsy that classified the lesion as sarcoma. After being discussed at the local sarcoma MDT the patient underwent en-block complete resection of the tumour and of the posterior part of the first rib. Histology showed morphology typical of an ASPS which had arisen from the first rib and extended into the overlying soft tissues. There was nuclear expression of TFE3 and the (PAS+) tumour cells also unusually expressed CD68 and HMB45 as well as vimentin and NSE.



Conclusion: Cases of primary intraosseous ASPS are rare. To our knowledge this is the second description in the medical literature of an ASPS arising in a rib causing Pancoast syndrome. Chemotherapy and radiation have not proven beneficial in the treatment of ASPS, although new drug trials are ongoing. Even with en bloc surgical excision and adjuvant therapy, 5-year overall survival ranges from 20% for patients with metastatic disease to 88% for patients with local disease only at the time of presentation. **Keywords:** Pancoast syndrome, alveolar soft part sarcoma, Surgical resection

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P3.08-025 Clinical and Radiographic Manifestation of PPNHL in Chinese Patients: Differentiation of MALT Type and DLBCL Type Yinan Yao[1], Shan Lu[1], Yan Xu[2], Guangdie Yang[1], Junjun Chen[1], Hequan Li[1], Jianying Zhou[1] [1]*Respiratory Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou/China,* [2]*Intensive Care Unit, The Second Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou/China*

Background: Primary pulmonary non-Hodgkin's lymphoma (PPNHL) is a rare extranodal lymphoid neoplasm with few reports of Chinese patients. This study aims to analyze the demographic data, clinical features and radiographic presentation of Chinese PPNHL patients to obtain useful information for early diagnosis and differential diagnosis. **Methods:** A retrospective review of primary pulmonary non-Hodgkin's lymphoma diagnosed at our hospital from February 2007 to April 2014 was performed. **Results:** This study included 34 PPNHL patients, comprising of 25 cases of mucosa-associated lymphoid tissue (MALT) lymphoma and 9 cases of diffuse large B-cell lymphomas (DLBCL). Cough and expectoration were the most common symptoms, accounting for 57.9% of the patients with symptoms. Nodules, masses and consolidations were the most frequent radiologic abnormalities and right lung is often involved. Pericardial effusion and bronchial abnormalities were found only in DLBCL cases. CT-guided percutaneous transthoracic biopsy was performed in most of the patients (73.5%) for diagnosis. **Conclusion:** The clinical features of PPNHL lack specificity. Imaging findings indicated that DLBCL patients tend to have an elevated incidence of pericardial effusion and bronchial abnormalities than MALT types. These discoveries provide assistance for the early diagnosis and differential diagnosis of these subtypes. **Keywords:** PPNHL, MALT, DLBCL, differentiation

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

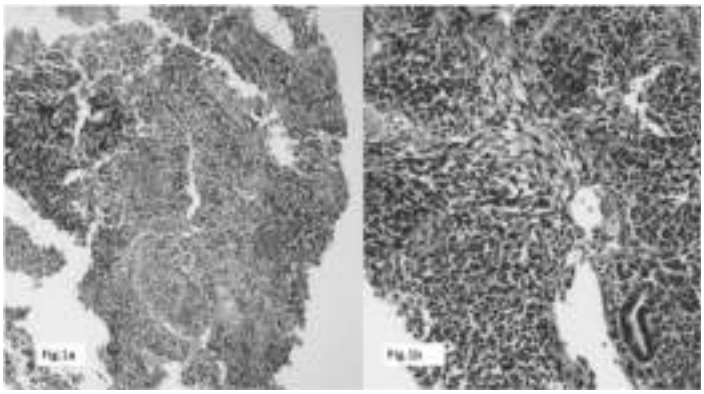
P3.08-026 Various Clinical Features in Lung Cancer, Dharmais National Cancer Hospital (NCH), Jakarta Fariha Ramadhaniah[1], Pradnya S. Rahayu[2], Evlina S. Sinuraya[2] [1]*Research and Development Department, Dharmais National Cancer Centre, Jakarta/Indonesia,* [2]*Research and Development, Dharmais National Cancer Centre, Jakarta/Indonesia*

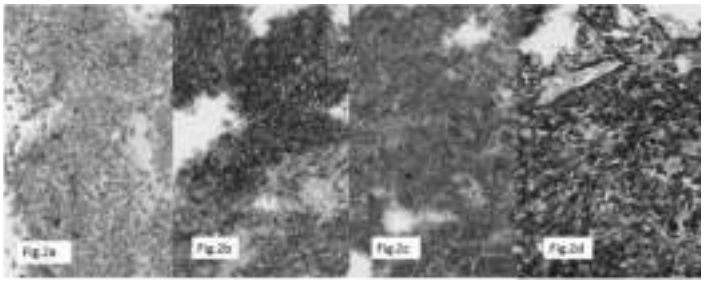
Background: Lungs are the respiratory system that resides in the bottom of the chest cavity adjacent to the heart and mediastinum. Based on Jakarta Population-Based Cancer Registry 2005-2007, the incidence of lung cancer is ranked first in men and fourth in women. The frequency of lung cancer in Dharmais 1993-2007 is 4.29 % ranks third of all cancer incidence. **Methods:** Cross-sectional study began in 1993-2007. Inclusion criteria are patients newly diagnosed of lung cancer microscopically, inside or outside Dharmais. Classification using the WHO-ICD-03. Determination of the sample with a precision formula with a total sample is 231. **Results:** Distribution by gender, 79.65% in males and 20.35% in women, higher in the age group above 59 years (52.72% male and 53.19% female). **Conclusion:** There are 14 variations of the main clinical features in men and 13 in women . The most common clinical picture of both men and women are cough, pain, and shortness of breath. **Keywords:** lung cancer, cancer registration, clinical features

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.08-027 Teratoid Wilms' Tumor of the Mediastinum in an Adult Konstantinos Syrigos[1], Ioannis Gkiozos[1], Dimitra Grapsa[1], Frosso Konstantinou[1], Penelope Korkolopoulou[1], Ioannis Ntanasis-Stathopoulos[2], Emmanouil Merikas[1], Maria Triantafyllou[1] [1]*University of Athens, Athens/Greece,* [2]*Oncology, University of Athens, Athens/Greece*

Background: Teratoid Wilms' tumor is an uncommon histologic variant of nephroblastoma, which is mainly characterized by a predominance of heterologous components within the tumor mass, and typically located in the kidney. Extrarenal forms of this neoplasm are extremely rare and have been previously described almost exclusively in pediatric patients. **Methods:** We herein describe the clinical, imaging, histological and immunohistochemical features of a mediastinal teratoid Wilms' tumor in a 63-year old female. Diagnosis was established following surgical resection and histopathological evaluation of the tumor specimen, along with documentation of complete absence of a primary renal lesion. **Results:** Microscopic examination of representative tumor sections showed the typical WT architecture consisting of blastemal, mesenchymal and epithelial components (fig.1). More than 50% of the tumor's volume was occupied by a variety of heterologous elements. Immunohistochemistry showed positive staining of the epithelial tumor cells for pankeratin (fig.2a), while the blastematous component stained positive for CD56 (fig.2b), CD99 (fig.2c) and WT1 (fig.2d). The patient received one preoperative course of carboplatin etoposide, as well as eight and four postoperative courses of carboplatin-etoposide and cyclophosphamide-doxorubicin, respectively. Disease progression was noted 15 months following administration of the first chemotherapy cycle, and the patient died 23 months after her initial presentation.



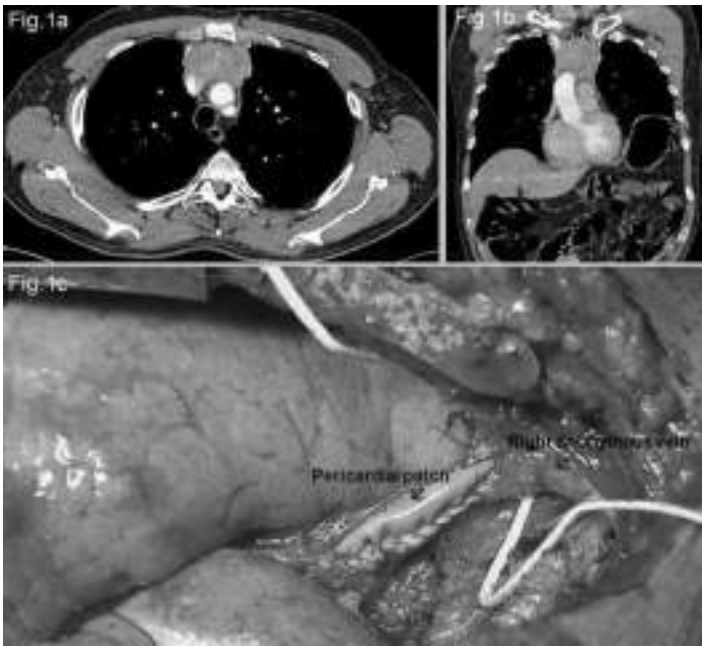


Conclusion: Identification of the typical triphasic WT histology along with a predominant heterologous differentiation –but without evidence of unequivocal heterotopic organogenesis- as well as documentation of complete absence of a primary renal neoplasm, are all required to establish the diagnosis of this extremely rare tumor. **Keywords:** mediastinum, teratoid, Wilms' tumor, extrarenal

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.08-028 Primary Large Cell Neuroendocrine Carcinoma of the Mediastinum Luigi Ventura[1], Letizia Gnetti[2], Luigi Rolli[1], Michela Solinas[1], Livia Ruffini[3], Paolo Carbognani[1], Enrico Maria Silini[2], Michele Rusca[1], Luca Ampollini[1] [1]*Thoracic Surgery, University Hospital of Parma, Parma/Italy,* [2]*Pathology, University of Parma, Parma/Italy,* [3]*Nuclear Medicine, University Hospital of Parma, Parma/Italy*

Background: to present a rare case of primary neuroendocrine carcinoma of the mediastinum treated by multimodal therapy. **Methods:** a 50-year-old man, non-smoker, with unremarkable past medical history, presented for asthenia, dyspnea and sub-sternal discomfort. A chest CT-scan showed a huge mass of 10,7x5,5x9,5cm in the anterosuperior mediastinum. The mass seems infiltrate both brachiocephalic veins, the superior vena cava, pericardium and both lungs (Fig.1a/b). PET-CT showed an intense hyperactivity of the mediastinal mass. CT-guided needle biopsy allows diagnosis of neuroendocrine carcinoma. After multisciplinary discussion, a multimodal approach was planned. The patient underwent 4 cycles of chemotherapy with cisplatin and gemcitabine. Since chest CT-scan showed a reduction of the tumor (7,4x5,6x9cm), a surgical resection was proposed.



Results: a median sternotomy was performed. On exploration, both lungs were marginally infiltrated. The pericardium was partially excised; the left anonymous vein was almost totally invaded by the tumor. The right anonymous vein was infiltrated at the confluence with the superior vena cava. After total caval clamping (clamping time: 27'), a partial section and reconstruction with bovine pericardium was performed (Fig.1c). The patient was discharged uneventfully on postoperative-day 9. The patient underwent 25 sessions of adjuvant radiotherapy. Currently, he's free of disease after 30 months. Macroscopically the mass measured 9x8x3cm, looks whitish with tense-elastic consistency. Microscopically it showed clusters of small uniform cells, sometimes with cuboidal morphology, with nuclear pleomorphism and small nucleoli, arranged in trabeculae, nests and lobules and immersed in a hyaline stroma with foci of necrosis (Fig.2a). Perineural and vascular invasion were present. Immunohistochemistry showed the tumor cells were positive for chromogranin (Fig.2c), synaptophysin (Fig.2d), cytokeratins and negative for TTF1, FAP, PSA. The proliferation index Ki-67 was 10% (Fig.2b). Considering the radiological, morphological and immunophenotypic characteristics, the diagnosis was consistent with primary neuroendocrine carcinoma of the mediastinum.

Conclusion: mid-term survival was achieved after aggressive multimodal therapy.
Keywords: Neuroendocrine tumor, Surgery, mediastinum

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.08-029 Benign Metastatizing Leiomyoma of the Uterus: 2 New Cases
Gunnar N. Hillerdal, Ocar Grundberg *Pulmonary Diseases, Karolinska Hospital, Stockholm/Sweden*

Background: Middle-aged and older women can present with dyspnoea and multiple well-demarcated rounded compact lesions of the lungs in different sizes, some very big. Investigation reveals no primary tumor but many years earlier an hysterectomi has been performed due to a big myoma, which was classified as benign. Biopsies of the lesions show the same picture. This is a very rare findings but we here present two cases seen recently by us. **Methods:** Two women with large probable metastases of the lungs were investigated. **Results:** Case 1: An exsmoking 74-year old woman was referred because of dyspnoea and pulmonary infiltrates. She had two lesions, one on each side approximately 2 cm in diameter. Laboratory tests normal .PET showed only minimal uptake. Needle puncture revealed leiomymatous cells with very low proliferation. Further questioning revealed that in 2008, an hysterectomy was performed because of a very large myoma, which was benign. Re-investigation of the myoma and of the biopsy from the lung lesion showed the same picture, and there were no signs of malignancy. Case 2: A neversmoking 68-year old woman was referred because of cough and pulmonary infiltrates. Multiple rounded lesions were seen on X-ray. Biopsy showed benign cells. In 1986 -29 years earlier - an hysterectomy had been performed because of pressure symptoms and a very large benign myoma was found. **Conclusion:** The diagnosis of "Benign metastasizing leiomyoma of the uterus" was established in the two cases. The name is an oxymoron; from the clinical view it must be regarded as a low-grade malignant leiomyosarcoma. Since its first description in 1939, around 100 case reports have been published. In rare cases, metastases in other organs than the lungs can also be found. Progression is usually extremely slow, no other organs are involved, and the main symptom is a slowly progressive dyspnoea, The prognosis in the short run (years) is very good, and specific treatment is lacking. If very big, surgical removal of lesions should be considered. We will just follow these patients since they have no symptoms.
Keywords: pulmonary metastases, leiomyoma

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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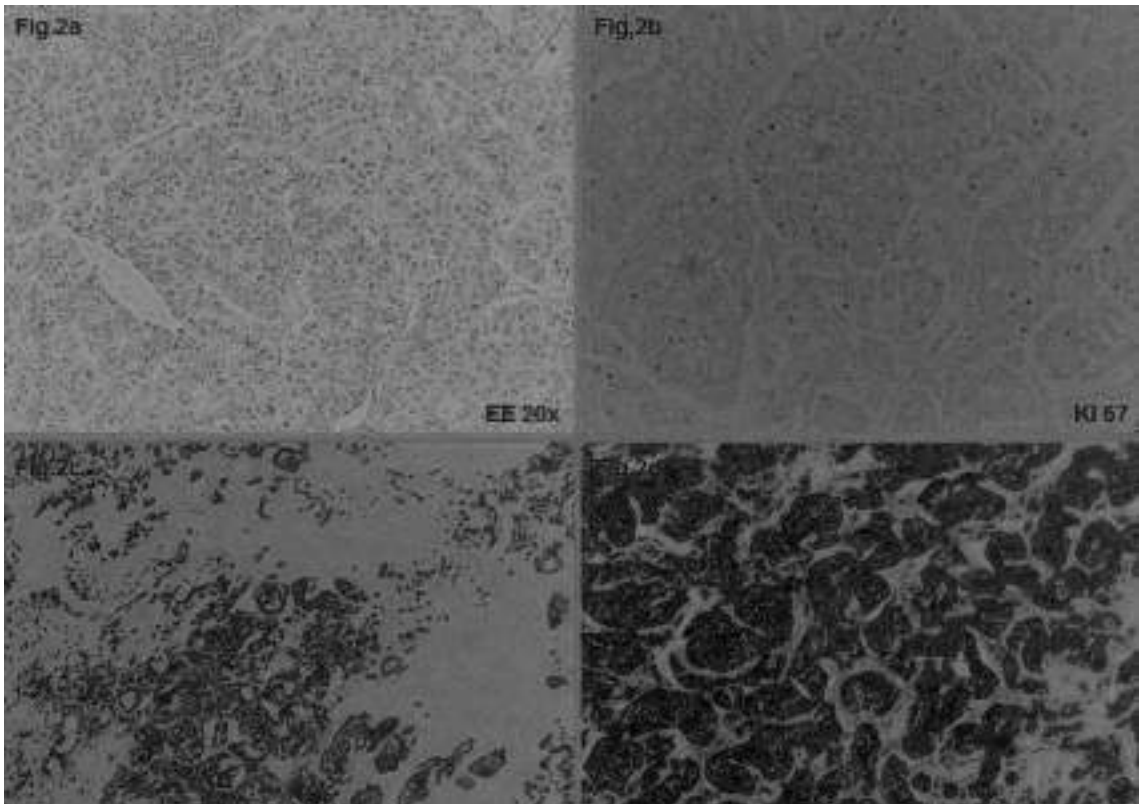
P3.08-030 Bronchoscopic Diagnosis of Esophageal Carcinoma Mimicking Lung Cancer
Deniz Dogan[1], Nesrin Ocal[1], Gurhan Taskin[2], Canturk Tasci[1], Ergun Tozkoparan[1], Hayati Bilgic[1] [1]*Chest Diseases, Gulhane Military Medical Faculty, Ankara/Turkey,* [2]*Intensive Care Unit, Gulhane Military Medical Faculty, Ankara/Turkey*

Background: Esophageal cancers are usually determined by examining the etiology of symptoms. Diagnosis in people without symptoms is rare and usually incidental. Although the most common symptom of esophageal cancer is dysphagia, in some cases clinical presentation can be different or misleading. Nevertheless, most esophageal



cancers do not cause symptoms until they have reached an advanced stage. Here, we present an esophageal cancer case which suggests pulmonary malignancy with the clinical presentation. **Methods:** 'not applicable' **Results:** 68-year-old male admitted our clinic with loss of appetite, weight loss and chest pain complaints. He had a smoking history of 30 packs/year. He was using LABA + ICS because of COPD. He told that his complaints had started 6 months before and gradually progressed. Because of the bilateraly suspicious hilar enlargement in chest X-ray, thorax CT examination was performed. In thorax CT, a conglomerate lesion, extending from subcarinal area to the posterior aspect of trachea, was observed. A clear distinction of lymphadenopathy/soft tissue could not be made. Diagnostic EBUS (endobronchial ultrasound) was performed to the patient under general anesthesia. During the process, a lesion protruded into the tracheal lumen with irregular surface was observed and biopsy was taken from this area. Also, EBUS guided biopsies were taken from the soft tissue lesions observed in thorax CT. In PET-CT of the patient, which was performed after this procedure, increased focal FDG uptake (SUWmax: 27.1) in the relevant field was observed without increased uptake elsewhere. Histopathological evaluations of these biopsies have been reported as esophageal squamous cell carcinoma. Subsequently, endoscopy was performed by gastroenterologists. In the course of [illegible] endoscopy process, an ulcerated lesion, 1.5 cm in diameter and obstructing approximately 1/3 of the lumen, was observed on esophageal Z line at 44th cm from the incisors. The results of the biopsies taken from this area were also reported as esophageal squamous cell carcinoma. Thereafter, the patient was referred to Medical Oncology Department for oncologic treatment and follow-up. **Conclusion:** We shared this case in terms of being an informative example for local metastasis of esophageal malignancies presented with pulmonary symptoms which must be considered in differential diagnosis of intrathoracic masses. **Keywords:** bronchoscopy, esophageal carcinoma, thoracic mass, mimicking

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P3.08-031 Endobronchial Spread of Malignant Melanoma to Lungs, a Case with Original Images Nesrin Ocal[1], Canturk Tasci[1], Gurhan Taskin[2], Deniz Dogan[1], Levent Yamanel[2] [1]*Chest Diseases, Gulhane Military Medical Faculty, Ankara/Turkey,* [2]*Intensive Care Unit, Gulhane Military Medical Faculty, Ankara/Turkey*

Background: Malignant melanoma, result of malignant transformation of melanocytes, metastasis mainly to regional lymph nodes, skeletal, and nervous systems. However, malignant melanoma can also metastasis to lung either. These metastases usually reach the lungs by tumor emboli to pulmonary arteries. Endobronchial spread of malignant melanoma to lungs diagnosed by bronchoscopy cases have limited number in literature. Here we share a malignant melanoma case spread endobronchially. **Methods:** 'not applicable' **Results:** 62 years old male patient known to have malignant melanoma, was accepted to intensive care unit with respiratory distress and was intubated. In first evalution of his HRCT, consolidation and pleural effusion, constitute with large part of left lung's atelectasis and less pleural effusion and partial atelectasis of neighbor parenchyma in right lung were seen. For both possible endobronchial metastasis causing airway obstruction and tumoral infiltration of parenchyma, bronchoscopy was performed through the endotracheal tube. Airway visualization revealed edema of the left main bronchus, concentrically significantly narrowed upper lobe, but segments were visible. Left lower lobe input was narrowed and segments were not visible. In entrance of left upper lobe there was an endobronchial lesion in brown- black color and slightly bulging form the mucosa like nevus. Transbronchial biopsy was taken from this nevus like formed lesion and left lung upper lobe apicoposterior. Both samples were reported as malignant melanoma by pathologist. **Conclusion:** We shared this case as an example of rare appearance of malignant melanoma with original images. We believe that this case report would be helpfull in terms of clinical practice. **Keywords:** metastasis, bronchoscopy, endobronchial, malignant melanoma

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P3.08-032 Maximizing Use of Robot-Arms in the Robot-Assisted Thoracic Surgery Naohiro Kajiwara, Yoshihisa Shimada, Sachio Maehara, Keishi Otani, Junichi Maeda, Koichi Yoshida, Yasufumi Kato, Masaru Hagiwara, Masatoshi Kakihana, Tatsuo Ohira, Norihiko Ikeda *Surgery, Tokyo Medical University, Tokyo/Japan*

Background: We have previously reported on the importance of appropriate robot-arm settings and replacement of instrument-ports in robot-assisted thoracic surgery. Because the thoracic cavity requires a large space to access all lesions in various areas of the thoracic cavity from the apex to the diaphragm and mediastinum and the chest wall. Moreover it can be difficult manipulate the da Vinci® Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA) using only arms No. 1 and No. 2 depending on the tumor location. In this report, we show how robot-arm No. 3 can be used with maximum effectiveness in the da Vinci®-assisted thoracic surgery. **Methods:** Robot-arm No. 3 of the da Vinci® Surgical System was usually positioned on the same side of arm No. 2, and sometimes it was used as an assistant arm to avoid conflict with other arms in our previous report. We describe new effective application of robot-arm No. 3 for the da Vinci S®-assisted thoracic surgery. A 62-year-old man had an anterior mediastinal tumor suspected to be non-invasive thymoma. Instead of arm No. 1, arm No. 3 was placed in the 6th intercostal in the mid-axillary line inserted from reverse the side, rotating it behind the body of the da Vinci® Surgical System. **Results:** Robotic surgery enables access to tumors located throughout in the thoracic cavity. The time required for the da Vinci S ®-setting was 12 minutes and the console-time (the da Vinci S ®working time) was 75 minutes. Thymectomy was performed successfully, and the amount of bleeding was 68 ml, and there were no complications. The pathological findings were thymoma, Masaoka stage II. **Conclusion:** Arm No. 3 has wider range of motion than other arms because it has one more additional joint. That is the reason why arm No. 3 enables good operability and ability to reach remote lesions, such as in the apex, diaphragm, or costophrenic angle. Moreover, between the space of the camera-arm and arm No. 3 make enough working space than using arm No. 1 to avoid conflict between arms. This use of the da Vinci S ® arms should be helpful in robotic procedures for thoracic surgeons in manipulating the da Vinci S ® instrument arms. Our recent experience has taught us that arm No. 3 is extremely useful when used as the main arm instead of arm No. 1. This idea should facilitate the da Vinci S®-assisted thoracic surgery procedures as a new effective application of robot-arm No. 3. **Keywords:** Thymoma, da Vinci® Surgical System, Robot arm, Robotic surgery

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P3.08-033 Expression of Excision Repair Cross-Complementation Group 1 and Class III β-Tubulin in Thymic Carcinoma Katsuhiro Okuda, Ayumi Suzuki, Tsutomu Tatematsu, Hiroshi Haneda, Satoru Moriyama, Motoki Yano, Risa Oda, Ryoichi Nakanishi *Dept. Oncology, Immunology and Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya/Japan*

Background: Thymic carcinoma is a rare mediastinum malignant tumor based on thymic epithelial cells. The complete surgical resection is considered as a best treatment for thymic carcinoma. However, except completely resected cases, the effective therapy has not been established for the advanced or relapsed thymic carcinoma. The expression of excision repair cross-complementation group 1 (ERCC1) and class Ⅲ β-tubulin (TUBB3) protein are respectively expected as an indicator for the anticancer activity of the platinum-based and taxane-based chemotherapy. **Methods:** We examined the expression of ERCC1 and TUBB3 protein in 40 thymic carcinoma patients who underwent either the surgical resection or the core-needle biopsy. We also evaluated the expression of ERCC1 and TUBB3 protein in 50 patients who underwent the curative resection for the non-small cell lung cancer (NSCLC). We investigated whether the expression of ERCC1 and TUBB3 protein were associated with some overall survival and clinic-pathological factors of thymic carcinoma patients. **Results:** The expression of ERCC1 and TUBB3 protein were positive in eight cases (20%) in thymic carcinoma patients. ERCC1 was expressed in twenty-one cases (42%), while TUBB3 was in twenty-seven cases (54%) in the fifty NSCLC patients. In all thymic carcinoma cases, the 3 year-survival was 67.3%. Only complete resection was associated with the better prognosis (p=0.0341). Other clinico-pathological factors including the expression of ERCC1 and TUBB3 protein showed no effect on the overall survival. **Conclusion:** High expression of ERCC1 and TUBB3 might be associated with resistance to the platinum-based and taxane-based chemotherapy. Our results suggest a possibility of better antitumor effects of the platinum-based and taxane-based chemotherapy on the thymic carcinoma patients. **Keywords:** ERCC1, TUBB3, chemotherapy, Thymic carcinoma

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.08-034 Chemotherapy and Radiotherapy in the Treatment of Malignant Thymomas after Subtotal Resection - Escalation of Toxicity Jan Stejskal[1], Martina Kubecová[2], Dana Dvořáková[3], Vít Ulrych[1], Jaroslav Vaňásek[1] [1]*Radiation Oncology, Regional Hospital Pardubice, Pardubice/Czech Republic,* [2]*Radiation Oncology, Charles University Hospital, Prague/Czech Republic,* [3]*Medical Oncology, Hospital Náchod, Náchod/ Czech Republic*

Background: Malignant thymomas are rare tumours. The optimal therapy after subtotal resection is still controversial. Patients with locally advanced stages and postoperative residual tumours have a high risk of tumor recurrence. Adjuvant therapy using chemotherapy and/or radiotherapy brings contradictory results and this treatment can be limited by escalation of toxicity. **Methods:** Between 1994 and 2012 we assessed and retrospectively analysed a total of 36 patients. All patients underwent subtotal resection to various extent. Sixteen patients (44%) were treated with the standard adjuvant radiotherapy (RT) only (group A). In group B, twenty patients (56%) were treated with the sequence of chemotherapy (CT) and conformal radiotherapy (3D-CRT). The CT regimens consisted of doxorubicin + cisplatin + cyclophosphamide ± vincristine). The planned doses of 3D-CRT ranged from 50 to 60 Gy. Both of them, acute toxicities (acute eosophagitis-AE, radiation pneumonitis-RP) and late toxicities (lung fibrosis-LF, heart failure-HF), were classified according to CTC v 3.0. The manifestations of RP were softened by oxygenotherapy, antibiotics, corticoids and pentoxifylline (PTX). Pentoxifylline (400 mg) was administered orally tid in patients with severe manifestation of RP grade 3/4. **Results:** The median age at the time of diagnosis was 56 (range, 38 – 75 years). By Masaoka staging system, 8 patients were stage II (24%) and 28 stage III (76%). The number of applied CT regimens ranged from 4 to 8 cycles. The median 3D-CRT dose was 55.8 Gy (range, 43.2 – 66.6 Gy). Thirty-eight percent of all patients (14/36) had myastenia gravis. AE of grade 1/2 was observed in 1 (6%) and 2 (10%) patients and grade 3/4 in 2 (13%) and 3 (15%) patients in groups A vs B. RP of grade 1/2 was observed in 5 (31%) and 10 (50%) patients in groups A and B, respectively. RP of grade 3/4 was observed in 2 (13%) and 9 (45%) patients in groups A vs B. Median time to recover RP grade 3/4 was 4.7 months in patients without PTX vs 2.6 months in patients using PTX. Radiographic changes of partial LF was observed in 3 (19%) and 8 (40%) patients in groups A and B, respectively. HF was diagnosed only in one of twenty patients (5%) in group B. In this patient degenerative and fibrosis changes of the heart were observed, which resulted in non-congenital aortic valvular stenosis 31 months after 3D-CRT and CT. The patient is still alive with OOS 77 months since the time of the diagnosis. A better local control of the disease was observed in group B where the median time to tumor progression was 49 months in comparison with 21 months in group A (p=0.0001). Five-year survival rates were 43.7% (7/16) and 85% (17/20) in group A vs group B, respectively (p=0.0001). **Conclusion:** Intensive

postoperative treatment leads to an improvement of the local control of this disease. The escalated acute toxicity, especially radiation pneumonitis, was not too serious and could be reduced with the benefit by application of pentoxifylline. Manifestation of late toxicities, predominantly lung fibrosis and heart failure, was acceptable. **Keywords:** Radiotherapy, Thymoma, toxicity, chemotherapy

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P3.08-035 Impact of Histological Subtypes on Clinical Outcome of Thymoma
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Background: Thymoma is a rare tumor with heterogeneous clinical outcome. We aim to assess if there is an arbitrary cutoff point of clinical significance to the histological subtypes of Thymoma **Methods:** this is a retrospective study including all eligible patients with Thymoma presenting to National cancer institute, Cairo University during the period from 2008 to 2015. Patients were divided in to two groups according to histological subtypes, first group: included patients with histological subtypes (AB+B1+B2) whereas second group included patients with histological subtypes (B3+C+ Thymic carcinoma). Endpoints were to compare the two groups with regard to clinical response to chemotherapy, progression free survival (PFS) and overall survival (OS) with concordance to standard clinicopathological factors. **Results:** 26 patients were included in the study with 69% in the first group (mean age = 45.44 years± 14.1 SD) versus 21% in the second group (mean age=41.63 ± 12.53 SD).Regarding clinical response to chemotherapy, 11.1% in the first group showed progressive disease as compared to 37.5% in the second group (p=0.51). Median PFS for all thymoma patients was 43.1 months (median ±SD = 43.1± 20.8). there was a trend towards better PFS in the first group where 2 years PFS in the first group was 68.4% versus 43.8 in the second group, p value= 0.09. Median OS for all thymoma patients was 76.7 months, (median ± SD = 76.7±29.8). 2 years OS was 72.6% in the first group versus 43.8 in the second group. (P- Value=0.24). **Conclusion:** although numerically better there was no statistically significant difference between the first and second groups with regard to clinical outcome. Collaborative studies including larger sample size are warranted. **Keywords:** Clinical outcome, Histological subtypes, Thymoma

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
WEDNESDAY, SEPTEMBER 9, 2015 - 09:30-16:30

P3.08-036 Stepwise Surgical Approach for Advanced Stage Thymoma Using Minimally Invasive Techniques
Jos Maessen[1], Marlies Keijzers[1], Monique Hochstenbag[2], Annemarie Dingemans[2], M Abdulhamid[3], Marc Debaets[1] [1]*Cardiothoracic Surgery, Maastricht University Medical Centre, Maastricht/Netherlands,* [2]*Pulmonolgy, Maastricht University Medical Centre, Maastricht/Netherlands,* [3]*Pathology, Maastricht University Medical Centre, Maastricht/Netherlands*

Background: Complete surgical resection is the best prognostic factor for thymomas. In advanced stage thymomas a complete surgical resection may require mutilating approaches, may not be performed because of anticipated technical difficulties or may just be considered not achievable. **Methods:** Retrospective analysis of patient files from April 2004 till March 2015 showed 239 patients who underwent a thymectomy in Maastricht University Medical Center. 15 patients (6.3%) underwent thymoma resection for Masaoka-Koga advanced stage III or IV. In all cases minimally invasive techniques were employed in patients-tailored stepwise treatment approaches. **Results:** A 66 years old male presented with a mediastinal mass with suspected invasion of the brachiocephalic vein and the ascending aorta (figure 1). Biopsy showed thymoma type B2/B3. Resection through sternotomy in a referral hospital was abrogated as invasion of the sternum was found. After the attempted resection the patient received chemotherapy (cisplatin-etoposid) however, the thymoma did not respond. In a multidisciplinary setting we decided on a bilateral robotic-assisted dissection and if successful, subsequent sternotomy for final removal of the giant mass. Minimally invasive dissection was started from the right side. With the help of the 10x magnification of the robot camera, the thymoma was freed from the sternum, the phrenic nerve and the major vessels. Macroscopic invasion of the pericardium and the brachiocephalic vein necessitated resection of the pericardium (12 x 4 cm) and the vein (3 cm). Complete inspection using the 30 degree robotic camera of both the right and left thoracic cavity revealed the absence of pleural metastasis, and no invasion of the phrenic nerve or the lung in the left thoracic cavity. An additional left-sided approach was therefore cancelled and sternotomy was performed to remove the specimen. Lymph nodes from the positions 4,5,6,7,10,11 as well as from the subclavicular area, were harvested. Pathological examination showed a thymic carcinoma/thymoma type B3, Masaoka-Koga stage III, and confirmed a R0 resection. All lymphnodes were negative for metastasis. Postoperatively, the patient was temporarily treated with an elastic sleeve because of oedema of the left arm. As of the histology of the tumor, the patient received postoperative radiotherapy. **Conclusion:** Complete surgical resection in advanced stage thymomas is be possible using a stepwise surgical approach including minimally invasive techniques. **Keywords:** Advanced stage, robotic, Thymoma

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P3.08-037 Management of Thymic Neoplasm: Egyptian NCI Experience
Hala A. Shokralla[1], Ahmed E. Fathalla[1], Ismail A. Mourad[2] [1]*Medical Oncology, National Cancer Institute, Garden City Cairo/Egypt,* [2]*Surgical Oncology, National Cancer Institute, Garden City Cairo/Egypt*

Background: Thymic tumors are rare entity with little information regarding outcomes after therapy with curative intent. We undertook a prospective analysis of all patients who underwent resection of thymic tumors at NCI hospitals. The optimal treatment includes surgical resection, chemotherapy, and radiotherapy.It is relatively uncommon(10%) but are highly aggressive. **Methods:** From 2008 to 2014, 13 patients (8 men, 5 women) underwent surgical resection of thymic tumor at a mean age of 47 years. Patient demographics, extent of surgical resection, and outcomes were compiled. Demographic variables, use of chemotherapy or radiotherapy, perioperative variables, recurrence rates, and long-term survival were analyzed retrospectively. The Masaoka stage and tumor diameter were recorded along with other variables that potentially influenced survival such tumor grade, site &number of metastatic disease. **Results:** The distribution of Masaoka stages at presentation was I in 6 (47%), II in 3 (23%), III in 1 (7%), and IV in 3 (23%). Neoadjuvant chemotherapy was administered to 3 patients (23%) whose tumors were deemed to be more locally invasive, two of them received neoadjuvant concomittant chemo-radiotherapy. Of the 13 patients in the surgical cohort, 8 (61.5%) were men. Mean age was 47 years (range: 21 to 58 years). No patient demonstrated an associated immunologic disorder such as myasthenia gravis. In all patients pathologic confirmation of thymic tumor was by CT giuded fine needle aspiration/biopsy as part of the diagnostic workup. Preoperatively, 3 of 13 patients (23%) received chemotherapy and 2 (15.5%) received radiotherapy. The decision to administer chemotherapy or radiotherapy preoperatively was individualized in each patient and based on the extent of tumor invasion. Complete tumor resection with pathologically confirmed negative resection margins (R0) was achieved in 12 patients (92.3%). The other 1 patient had microscopic residual disease (R1). Masaoka stage was I in 6 (47%), II in 3 (23%), III in 1(7%), and IV in 3 (23%). The most common approach to surgical resection was sternotomy, used in 11 patients (84.5%). Mean tumor size was 9.5 cm (range: 4.5 to 16 cm) for the 13 patients. Pulmonary wedge resection was done for only 2 cases,pleural resection 5 cases& lobectomy in only 1. No perioperative deaths occurred nor patients required tracheostomy for postoperative respiratory failure. The two patients who had unilateral phrenic nerve resection as part of their operation none of these patients underwent a diaphragmatic plication early in the postoperative course to improve respiratory insufficiency. Four patients received adjuvant chemotherapy or radiotherapy or both. Of those whose tumors were completely resected, 1 patient experienced a local recurrence. SurvivalMean length of survival in the entire group was 22.7 months (range: 14 to 36 months). At the last follow-up, 8 patients (61.5%) were alive without disease, 1 (7.5%) was alive with disease, and 4(31%) had died. **Conclusion:** Thymic tumor are amenable to surgical therapy, With increased use of computed tomography imaging, patients with early-stage disease are being identified more frequently, complete surgical resection appears to have favorable cure rates in these patients. Patients with locally advanced disease can experience long-term survival with a multimodality approach. **Keywords:** thymic -tumor-egypt-NCI

POSTER SESSION/ THYMOMA, MESOTHELIOMA AND OTHER THORACIC MALIGNANCIES
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P3.08-038 Targetable Cancer-Associated Antigens for Immunotherapy in Malignant Pleural Mesothelioma (MPM) - Mesothelin, CA125 and WT-1
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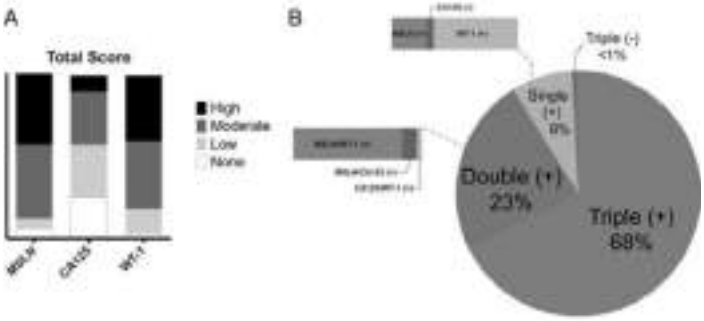
Background: Mesothelin (MSLN), CA125 (also know as mucin-16, MUC16) and WT-1 are cancer-associated antigens currently under investigation as targets for tumor-specific immunotherapy, based on published observations that antigen-specific immune responses to these antigens prolong survival. In solid malignancies, we (*Clin Cancer Res* 2012, 2013) and others have published the role of MSLN in promoting tumor aggressiveness. Additionally, MSLN has been demonstrated to interact with CA125 in promoting invasion and metastasis, resulting in poor clinical outcomes. In this study, we investigated the individual and correlative expressions of MSLN, CA125 and WT-1 in both epithelioid and non-epithelioid MPMs. **Methods:** All available H&E-stained slides from patients who were diagnosed with MPM (1989-2010) were reviewed; tumors were classified according to the WHO classification. We constructed tissue microarrays (6 tumor cores/tumor) from 273 patients (epithelioid=224; non-epithelioid, including biphasic and sarcomatoid =49). MSLN, CA125, and WT-1 immunohistochemistry were performed, and total scores for each antigen were determined by assessing the combined intensity and distribution of the antigen expression. **Results:** Epithelioid MPMs demonstrated positive MSLN expression in 92% of patient samples (73% high-moderate expression), CA125 expression in 72% (19% high-moderate), and WT-1 in 94% (63% high-moderate) (Fig.1A). Triple positive antigen expression was recognized in 68% of patients; co-expression of two antigens was demonstrated in 23% of epithelioid MPMs (Fig.1B). In non-epithelioid MPMs, MSLN, CA125, and WT-1 were positive in 57% (16% high-moderate), 33% (2% high-moderate), and 98% (43% high-moderate) of patient tumors, respectively. Triple and double antigen co-expression were demonstrated in 29% and 33% of non-epithelioid MPMs, respectively. Only 1% of epithelioid and 2% of non-epithelioid MPMs

demonstrated absence of expression of all three antigens: MSLN, CA125, and WT-1.



Conclusion: Our observation from a large cohort of MPM patients inclusive of all histological subtypes demonstrating greater than 98% positive expression of at least one of the three cancer-associated antigens in epithelioid and non-epithelioid MPMs, with strong antigen expression and high frequency of double and triple antigen expression, provides rationale to develop targeted therapies to these cancer-associated antigens for the treatment of MPM patients We are initiaiting a phase I clinical trial (NCT02414269) of mesothelin-targeted T-cell therapy for MPM patients at our center. **Keywords:** Mesothelin, CA125, WT-1, Mesothelioma, Antigen Expression, Immunotherapy

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POSTER SESSION/ PALLIATIVE AND SUPPORTIVE CARE
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P3.11-001 Hypertension Associated with Venous Thromboembolism in Patients with Lung Cancer Yuhui Zhang, Yuanhua Yang, Lirong Liang, Webhui Chen, Zhenguo Zhai, Lijuan Guo, Chen Wang *Beijing Chao-Yang Hospital, Capital Medical University, Beijing/China*

Background: Patients with lung cancer are at increased risk of venous thromboembolism (VTE). Patient-related factors may help estimate an individual's risk for VTE. Cardiovascular disease (CVD) risk factors increase the risk of arterial embolism, but it is less clear whether these factors increase the risk of VTE associated with lung cancer.We evaluated associations between major CVD risk factors and the occurrence of VTE in lung cancer patients using data from the Lung Cancer and Thrombosis Study conducted by the China VTE Study Group. **Methods:** A total of 632 hospitalized patients with newly diagnosed lung cancer were screened for VTE, and their major CVD risk factors were assessed at the baseline examination. Additionally, VTE diagnoses within the three months prior to recruitment were reviewed. **Results:** Eighty-six of the 632 (13.6%) experienced a VTE event, and 7.8%, 3.3%, and 16.6% of the patients also experienced diabetes, dyslipidemia and hypertension, respectively. Hypertension was more frequent in patients with VTE than in those without VTE (24.4% vs. 15.4%, *P*=0.04). Multivariate logistic regression analysis, including age, sex, smoking, body mass index, diabetes, dyslipidemia, hypertension and white blood cell count, found that hypertension (odds ratio [OR] 1.8; 95% CI 1.0-3.3; *P*=0.041) and leukocytosis (OR 2.7; 95% CI 1.5-4.8; *P*=0.001) were significantly associated with VTE in different tumor histology models and that hypertension (OR 1.9; 95% CI 1.1-3.4; *P*=0.029) and leukocytosis (OR 2.7; 95% CI 1.5-4.7; *P*=0.001) were also significantly associated with VTE in different tumor stage models. Leukocytosis was linearly associated with hypertension and VTE (Pfor trend = 0.006), and the ORs for VTE increased with leukocytosis (all *P* for trend < 0.05). **Conclusion:** Hypertension was associated with the risk of VTE in patients with newly diagnosed lung cancer, which may be mediated by the presence of inflammation. **Keywords:** lung cancer, venous thromboembolism, risk factors

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P3.11-002 Survival and Predictors of Mortality in Patients Submitted to Endoscopic Treatment of Malignant Airway Obstruction Benoit J. Bibas, Oswaldo G. Junior, Ricardo M. Terra, Helio Minamoto, Paulo F.G. Cardoso, Mauro F. Tamagno, Paulo M. Pêgo-Fernandes *Thoracic Surgery, University of São Paulo, São Paulo/Brazil*

Background: Neoplastic obstruction of the airways occurs in about 30% of lung neoplasms, and is often associated woth end-stage, or advanced disease. Nonetheless, endoscopic treatment of the obstruction may improve quality of life and survival in selected patients. The primary objective is to evaluate the median survival and the predictors of mortality in patients undergoing endoscopic treatment of neoplastic airway obstruction. The secondary objective is to evaluate the morbidity of the procedure. **Methods:** Retrospective study, from January 2010 to December 2014. All data was collected until February 2015. We included patients with neoplastic obstruction of the trachea and bronchi, that underwent endoscopic treatment. Procedures were performed in the operating room under general anesthesia, through rigid bronchoscopy or suspension laryngoscopy. Age, sex, neoadjuant chemo-radiotherapy, adjuvant chemo-radiotherapy, ECOG status, ASA status, urgent procedures, need for mechanical ventilation, reintervention procedures, site of obstruction, type of stent and tumor histology were considered predictors for mortality. The median survival was analyzed by Kaplan-Meier curve. Prognostic factors of mortality were analyzed by Cox regression. **Results:** We included 42 patients (25M / 17F) with a mean age of 54 ± 11 years, that underwent 68 endoscopic procedures. The most common histologic types were lung cancer (n = 15; 36%), esophagus (n = 11; 26%) and cystic adenoid carcinoma (n = 8; 19%). Twenty-five stents were placed. The silicone Y stent was the most common (n=14;56%). Eleven percent of patients required a tracheostomy. Complications occurred in 37.5% of cases; pneumonia (n = 10; 15%) and stent obstruction (n = 6; 9%) were the most frequent. The median survival was 221 days. The 30-day mortality was 14%, and overall mortality 40%. The predictors of mortality by Cox regression were re-intervention procedures (HR 5.9; p <0.001; 95% CI 2:25 to 15:45), mechanical ventilation before the procedure (HR 7:38; p = 0.015; 95% CI: 1.46- 37) and tumor hystology (HR: .23; p <0.001; 95% CI: .11 - .47). Individuals with esophageal cancer had a significant lower median survival, when compared with lung cancer and cystic adenoid carcinoma (94 vs 166 vs 346 days; p=0.002). **Conclusion:** The morbidity and mortality of patients submitted to endoscopic treatment of neoplastic airway obstruction is not negligible. Reintervention procedures, mechanical ventilation prior to treatment and tumor histology were significant predictors of mortality. **Keywords:** survival, mortality, Airway obstruction, Cancer

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P3.11-003 Contribution of the Comprehensive Geriatric Assessment on Management of the Cancer Theraphy in Elderly Patients Melike Sanem Erdas Umut, Ülkü Yılmaz, Derya Özaydın Kızılgöz, Tuba Inal Cengiz, Irem Şerifoğlu, Yurdanur Erdoğan *Ankara Ataturk Chest Disease and Surgery Education Training Hospital, Ankara/Turkey*

Background: Lung cancer is getting more common and important especially in 6th-7th decade. Several recently published studies showed that eveluating the elderly patients with only Eastern Cooperative Oncology Group (ECOG) to manage the treatment is not eough. It is needed to consider this elderly group of patients precisely. In our study we aim to search the the clinical value of the comprehensive geriatric assessment of the elderly patients as a a parameter that can be used to guide the treatment decision. **Methods:** In our study 65 years old and over newly diagnosed 74 lung cancer patients in our hospital from April 2013 to April 2014 were included. In order to evaluate the comprehensive geriatric assessment, we applied the activities of daily living (ADL's), instrumental activities of daily living (IADLs), mini-mental test, mini-nutritional test, Yesavage depression scale and Charlson comorbidity index . Receiving treatment and the survival were assessed with 6 other tests and ECOG in single and multi variable analysis. **Results:** Men were 94.6 % of all patients. In this group 6.8% in small cell carsinoma, 90.5% in non-small cell carsinoma, 2.7 % in malignant epithelial tumour were diagnosed. According to ADL's 86.5 % was independent and 13.5 % was semi-dependent as well as to IADLs 60.8 % was independent, 20.3 % semi-dependent and 18.9 % was dependent. %12.2 of the patients had malnutrition, %56.7 had malnutrition risk. The data provided that 54 % of all patients had severe dementia and 17.6 % has mild dementia. According to Yesavade depression scale 13.5% of patients were developed depression. Charlson comorbidity index provided the data that 2 % of patients had very high risk probability, 5% high risk, 42.5 % moderate, 25% low risk probability. It is found significant the relationship between the receiving treatment and results of ADL's, IADLs, mini-mental test, Yesavage depression scale, and ECOG as well as ADL's, IADLs, mini-mental test, Yesavage depression scale, ECOG and mini-nutritional test and the survival in single variable analysis (p<0,05). In order to consider which test will have more prominent role to receive the treatment ,multivariable analysis was performed and only IADLs was found significant as a determining factor for receiving or not receiving treatment (p=0,003). Yesavage depression scale was found more efficient to find out the factors affecting the survival in multivariable comparison analysis (p=0,011). **Conclusion:** The study published by Maione and collegues evaluating the relationship between functional status, comorbidity, life quality and the survival in 566 advanced stage non-small cell cancer patients showed that patients with beter IADLs (p= 0.04) have better survival as similarly obtained from our study. Buccheri and his group reported the data from 133 heterogeneous bronchogenic cancer patients developed depression,have a worse survival comparing with the patients having no depression. The results of our study indicates that assessing with ECOG is not enough for considering the treatment,but how CGA is important to consider it as well. Improving the life quality and the survival of the advanced stage elderly patients with cancer, future research requires a more wide population **Keywords:** lung cancer, comprehensive geriatric assessment, management of treatment in olds

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P3.11-004 Promising Effect of Olanzapine on Chemotherapy-Induced Nausea and Vomiting Uncontrolled with Conventional Antiemetic Therapy Masafumi Sata[1], Akimasa Sekine[1], Terufumi Kato[1], Ayako Takigami[2], Masashi Bando[2], Yukihiko Sugiyama[2] [1]*Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Center, Yokohama City/Japan,* [2]*Respiratory Medicine, Jichi Medical University Hospital, Simotsuke City/Japan*

Background: Chemotherapy-induced nausea and vomiting (CINV) is still a major adverse effect especially for patients treated with highly emetogenic chemotherapy (HEC). In clinical practice, 5-HT3 receptor antagonist, NK-1 receptor antagonist, and corticosteroids are widely used to alleviate emetic episodes during chemotherapy. With those drugs, acute-nausea and vomiting is successfully manageable. However, late-onset nausea and vomiting is sometimes difficult to be controlled and therefore, the promising

drugs is needed. Olanzapine is an antipsychotic agent which is approved for schizophrenia and bipolar disorder in Japan. Recently, the combination therapy with olanzapine and the conventional anti-emetic drugs has been reported highly effective to prevent late-onset CIMV after HEC. However, it remains unclear whether olanzapine is really effective for patients who develop acute- or late-onset CIMV after HEC. **Methods:** All consecutive patients, who were treated with HEC and olanzapine at Jichi Medical University Hospital from January 2014 to December 2014, were included. "Antimetic Response" was defined as the absence of nausea and vomitting, no use of breakthrough antiemetic medications, or increased dietary intake (≧50%). The details of clinical information were reviewed from the medical records . **Results:** Among 18 patients treated with HEC and olanzapine as antimetic medication, 11 were males and 7 were females, with a median age of 60.5 years (42-74 years). Primary tumors were non-small cell lung cancer in 11 cases, small cell lung cancer in 5, malignant mesothelioma in one case, and embryonal carcinoma in one case. Olanzapine was used for preventing CINV in 8 patients with the previous experience of late-onset CINV and in 2 patients without, for treating late-onset CINV in 6 patients and acute onset CINV in 2 patients. "Antiemetic response" has been observed in 15 patients (83.3%). Among 8 patients previously experiencing late-onset CINV, "Antimetic response" was obtained in 7 patients(87.5%). **Conclusion:** Our results strongly suggest the olanzapine provides an additional effect on CINV uncontrolled with conventional antiemetic therapy, regardless of whether CINV is acute or chronic. **Keywords:** olanzapine, highly emetogenc chemotherapy, chemotherapy-induced nausea andvomiting

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P3.11-005 Symptom Distress, Anxiety and Depression in Patients with NSCLC Undergoing Adjuvant Chemotherapy after VATS Lobectomy Hao Wang[1], Xiaoxia Jiang[2] [1]*Thoracic Surgery, Shanghai Zhongshan Hospital, China/China,* [2]*Thoracic Surgery, Shanghai Punan Hospital, Shanghai/China*

Background: The aim of this study was to investigate the symptom distress, anxiety and depression in patients with NSCLC undergoing adjuvant chemotherapy after VATS lobectomy. **Methods:** A total of 62 patients undergoing adjuvant chemotherapy from January 2013 to December 2014 after VATS lobectomy were enrolled. The M.D. Anderson Symptom Inventory (MDASI) and the Hospital Anxiety and Depression Scale (HADS) were used to assess the patients, symptom distress, anxiety and depression condition. **Results:** The patients averagely scored 3.02 points in symptom items, and 2.58 points in interference items, with the scores being positively correlated with anxiety and depression respectively (P<0.01 for both). The patients mainly reported symptoms of alopecia, lack of appetite, dyspnea, etc. **Conclusion:** Symptom distress is commonly seen in patients with NSCLC undergoing adjuvant chemotherapy after VATS lobectomy. And symptom distress, anxiety and depression react upon each another. Therefore physicians should pay more attention to these patients, mental state and guide them to rationally release their emotions. **Keywords:** VATs lobectomy, adjuvant chemotherapy, symptom distress

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P3.11-006 An Analysis of Factors Associated with in Hospital Mortality in Lung Cancer Chemotherapy Patients with Neutropenia Julia Cupp[1], Eva Culakova[2], Marek Poniewierski[3], David Dale[4], Gary Lyman[2], Jeffrey Crawford[1] [1]*Medicine, Duke University Medical Center, Durham/NC/United States of America,* [2]*Fred Hutchinson Cancer Research Center, Seattle/WA/United States of America,* [3]*Fred Hutchinson Cancer Research Center, Seattle/United States of America,*[4]*University of Washington, Seattle/WA/United States of America*

Background: Febrile neutropenia is considered a severe complication of cancer chemotherapy, and one for which lung cancer is frequently associated with higher mortality rates than other solid tumors. The focus of this analysis was to identify risk factors most associated with in-hospital mortality and to describe their impact on mortality in patients with lung cancer. **Methods:** Hospitalization data from the University Health Consortium database inclusive of the years 2004-2012 from 239 US medical centers were analyzed. The study population included all adult patients with solid tumors who had neutropenia. Cancer type, presence of neutropenia, comorbidities, and further subgroups were based on ICD-9-CM codes. The primary study outcome was in-hospital mortality in lung cancer patients vs. other solid tumors. Further analysis concentrated on comparisons of the two groups with respect to number and type of comorbidities, occurrence of sepsis, pneumonia, or any infection, and ICU stay and influence of these factors on mortality. Differences between the groups were compared using chi-square test. **Results:** The analysis was based on 61,086 adult patients, including 11,111 lung cancer patients and 49,975 patients with other solid tumors. Overall 4290 (7.0%) patients died. Lung cancer was the tumor type associated with highest mortality (11.2%, compared with other solid tumors, 6.1%; p <0.0001) Lung cancer patients were older: 50% of lung cancer patients were over age 65, compared to 31.6% of patients with other solid tumors (p<0.0001). Lung cancer patients were more likely to have multiple (≥2) comorbidities than patients with other solid tumors (57.3% vs. 37.3% p<0.0001). The risk of mortality was directly related to the number of comorbidities (ranging from mortality risk of 0.9% for patients with 0 comorbidities to 35.2% for patients with 5 or more). The comorbidity-mortality relationship was observed in lung cancer patients as well as patients with other solid tumors, and the association persisted after adjusting for multiple covariates, including age. Even independent of number of comorbidities and age, lung cancer patients had higher mortality (Odds Ratio (OR)=1.38, 95%CI: 1.28-1.48). Four risk factors for mortality in addition to number of comorbidities were identified: pneumonia, sepsis, *any documented infection,* and *ICU stay*. Pneumonia occurred more commonly in the lung cancer patients (26.4% vs. 10.3%; p<0.0001). Comorbid pulmonary disease was strongly associated with development of pneumonia (OR=4.52, 95%CI: 4.30-4.74) and occurred more often in the lung cancer patients (52.1% vs. 24.0%; p<0.0001). With or without pulmonary disease as a comorbidity, lung cancer patients were more likely to have pneumonia than other solid tumor types (with – 36.0% vs. 22.8%, p<0.0001) (without – 16.1% vs. 6.4%, p<0.0001). **Conclusion:** Lung cancer patients presenting with febrile neutropenia are older, have more comorbidities, have a higher incidence of comorbid pulmonary disease, and are more likely to have pneumonia. These factors may help explain their higher mortality. In order to reduce the mortality of chemotherapy in lung cancer patients, careful pretreatment assessment and optimal supportive care during therapy are critical. **Keywords:** Infection, Comorbidity, mortality, Neutropenia

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P3.11-007 How Fit Are Lung Cancer Patients? An Observational Study of Co-Morbidities and Physiology Matthew Evison, Stuart Britton, Haider Al-Najjar, Philip Crosbie, Richard Booton *Manchester Thoracic Oncology Centre, University Hospital of South Manchester, Manchester/United Kingdom*

Background: Co-morbidity is a key factor in determining prognosis and defining treatment in lung cancer. In the face of an ageing population and increasing prevalence of chronic medical conditions, lung cancer physicians will need to develop robust systems and services to ensure appropriate optimisation of co-morbidities during the diagnosis and staging pathway. The aim of this study was to provide a detailed description of co-morbidities and physiology in a UK lung cancer population. **Methods:** Prospective data was collected on all newly diagnosed lung cancer patients at the University Hospital South Manchester from November 2014 and February 2015. UHSM is a regional lung cancer centre and diagnoses over 200 lung cancers per year. Co-morbidities were assessed using the Charlson co-morbidity index. Performance status, MRC Dyspnoea Scale, BMI and physiological parameters for the cardiorespiratory and renal systems were also measured. **Results:** 73 patients were diagnosed with lung cancer in the study period. Mean age was 70 years and 35 (48%) were male. 37 (51%) had radiological evidence of emphysema on staging CT of the thorax. Co-morbidities and physiological parameters for the patient cohort are presented in tables 1 & 2.

Table 1: Charlson Co-morbidity Index

	n = 73 n (%)
0	9 (12%)
1-2	26 (37%)
3-4	16 (22%)
5-6	12 (16%)
≥7	10 (14%)
Chronic pulmonary disease	27 (37%)
Myocardial Infarction	14 (19%)
Cerebrovascular disease	13 (18%)
Diabetes without end-organ damage	10 (14%)
Congestive cardiac failure	7 (10%)
Peripheral vascular disease	7 (10%)
Moderate-severe CKD	5 (7%)
Dementia	3 (4%)
Diabetes with end-organ damage	3 (4%)
Connective tissue disease	3 (4%)
Chronic liver disease	2 (3%)
Lymphoma	1 (1%)

Table 2: Fitness and physiological parameters

PS 0-1	45 (62%)
PS 2-4	28 (38%)
MRC Dyspnoea Scale 1-2	38 (52%)
MRC Dyspnoea Scale 3-5	35 (48%)
BMI <20	17 (23%)
BMI 20-30	34 (47%)
BMI >30	22 (30%)
FEV1 % predicted, mean	77.1 ±26.7
FEV1:FVC	62.1 ±14.6
DLCO % predicted, mean	72.0 ±21.2
Shuttle walk distance, metres, mean	366 ±154
Lowest O2 sats during shuttle, %, mean	92 ±4.1
Peak VO2 % predicted, mean	71.7 ±17.8
Estimated glomerular filtration rate	75.4 ±18.9
Revised cardiac index ≥3	9 (12%)

Conclusion: Chronic respiratory disease and disability is a major component of co-morbidity and physiological impairment in lung cancer patients. Cardiovascular disease and abnormalities in BMI are also highly prevalent. These results inform the need for rapid and reliable access to prehabilitation and dietetic services, robust cardiorespiratory physiological testing and specialist cardiovascular teams for all lung cancer physicians. **Keywords:** lung cancer, Co-morbidities

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P3.11-008 An Assessment of the Frequency of Palliative Procedures in Thoracic Surgery Gabriel Arevalo, Richard Freeman *Thoracic Surgery, St Vincent Hospital, Indianapolis/United States of America*

Background: Palliative care is a medical specialty focused on improving the quality of life of patients and their families with life threatening illness by preventing or relieving suffering. An assessment of a thoracic surgery service was performed to identify the scope and frequency of care that was considered palliative and any implications the findings might have on the current thoracic surgery residency curriculum. **Methods:** A retrospective review of a prospectively collected database of general thoracic surgery procedures performed over a five year period at a single institution was performed. Procedures considered palliative were reviewed for demographics, diagnoses, palliative prognosis score, treatment, morbidity, operative mortality and survival. Excluded were referrals from thoracic surgery to other specialties for palliative procedures. **Results:** During the study period, 3842 procedures were performed of which 884 (23%) were palliative. Indications included pleural and/or pericardial effusion, dysphagia, hemoptysis, tracheobronchial obstruction, bronchopleural fistula and tracheoesophageal fistula. The majority was related to a malignancy. Only 127 patients (14%) had a palliative care assessment prior to thoracic surgery consultation. Mean survival following thoracic surgery intervention was 110 days for patients with malignancy. **Conclusion:** This investigation found that thoracic surgeons commonly care for patients when the intention is palliation. The majority of these patients have an associated malignancy, a poor performance status and a significantly decreased survival compared to the general population. Thoracic surgeons should be familiar with the concepts of palliative care and consideration should be given to expanding exposure to the principles of palliative care in the cardiothoracic residency training curriculum. **Keywords:** palliative thoracic surgery,

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P3.11-009 Lung Cancer in Nepal: Five Years Review from a Tertiary Cancer Center of Nepal Rashmey Pun[1], Madan K. Piya[2], Sandhya Chapagain[2] [1]*Clinical Oncolgy, National Hospital and Cancer Research Center, Kathmandu/Nepal,* [2]*Clinical Oncology, National Hospital and Cancer Research Center, Kathmandu/Nepal*

Background: Lung cancer is the leading cause of cancer related morbidity and mortality in both the sexes in Nepal. It accounts for 15.4 % of total cancer as per hospital based Cancer Registry in Nepal. The purpose of this study was to review the patient characteristics and sociocultural factors and their influences in lung cancer cases presenting to the National Hospital and Cancer Research Center of Nepal. **Methods:** A retrospective cross-sectional study was done for the lung cancer cases from January 2009 to May 2014. 72 cases were identified by searching through inpatient records at the National Cancer Hospital but only 43 cases were selected for the analysis purpose due to lack of complete data in other remaining cases. Mean age, gender, ethnicity, locality, smoking habits, histological cell types and staging of the lung cancer patients at the initial presentation time were evaluated. Data were analyzed using SPSS statistical software. **Results:** The highest incidence of lung cancer is seen between 61-80 years of age (62.7%). There was no significant difference between the number of cases among male (51.16%) and female (48.83%). Majority of cases were from central part of the country near capital city (76.7%) whereas eastern and the entire western regions contributed to 7.1% and 16.2% cases respectively which clearly shows the lack of easy accessibility among patient for treatment at tertiary cancer center. People from Newar (39.5%) and Chettri (30.2%) ethnic origin were among the group with highest incidence of lung cancer in our study. 79.06% were smoker than compared to 20.93% who were non-smokers. 76.47% of patient started smoking at age between 10-20 years. 85.29% of the patients consumed local brand cigarettes which has either poor filter or no filter at all. 88.37% of the patients were diagnosed with Non Squamous lung Cancer (NSCLC) and 11.62% were diagnosed with Small Cell lung Cancer(SCLC). In NSCLC majority had squamous cell carcinoma (68.42%) and adenocarcinoma (31.57%). 86.84% of the patients were diagnosed with advanced stage III/IV lung cancer at the time of presentation to the hospital which shows significant delay in getting early diagnosis and treatment in majority of patient with the lung cancer. **Conclusion:** Because of the negligence for the simple cough patient tend to come to see the doctors late. The other reason for late presentation (stage III and IV) being the terrain and lack of diagnostic facilities in many parts of the country. Other important aspect of late presentation is treating the lung lesions as Pulmonary TB by the general physicians because of TB being one of the most common pulmonary diseases in the country. Such a study in larger scale would be beneficial for the implementation of awareness campaign, early detection, and treatment of the disease at the possible early stage. **Keywords:** Lung cancer,, awareness, sociocultural factors, Staging

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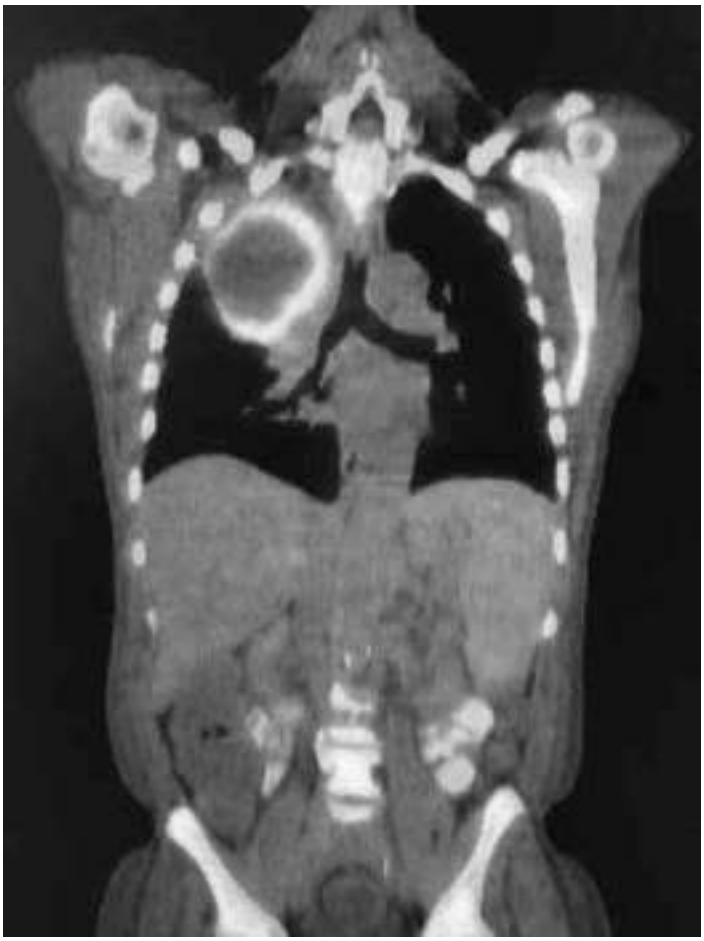
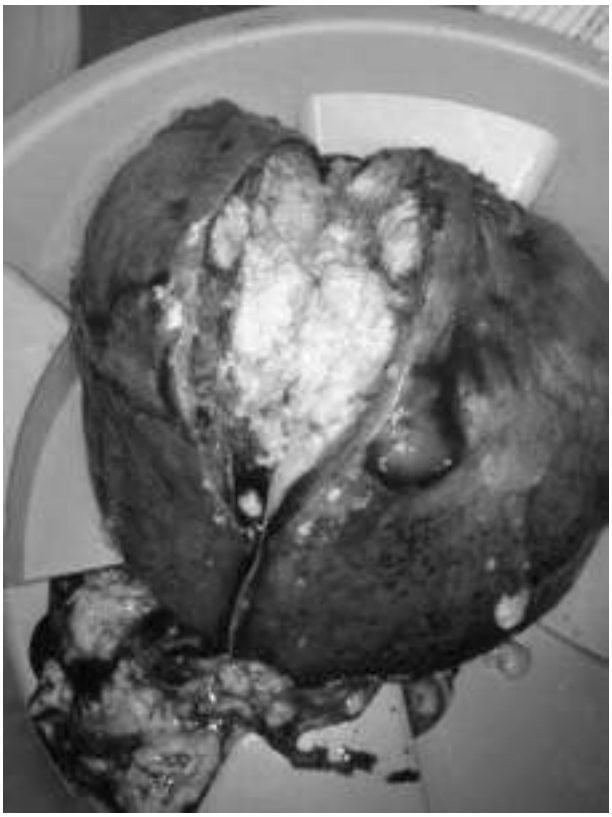
P3.11-010 Palliative Surgical Resection for Infection Superimposed on Malignancy Erica Blustein[1], Konstantinos Arnaoutakis[2], Matthew Steliga[3] [1]*Thoracic Surgery, University of Arkansas, Little Rock/AR/United States of America,* [2]*Winthrop P. Rockefeller Cancer Institute, University of Arkansas for Medical Sciences, Little Rock/United States of America,* [3]*Winthrop P. Rockefeller Cancer Institute, University of Arkansas for Medical Sciences, Little Rock/AR/United States of America*

Background: Typically, resection of non-small cell lung cancer (NSCLC) is done solely for curative intent. Rarely, a patient may benefit from aggressive palliative resection when non-oncologic conditions pose a greater threat to health and quality of life. A 59 year old man with cT3N1M1 NSCLC suffered from fevers, and relentless cough productive of copious foul sputum secondary to tumor necrosis and abscess (Fig. 1). Infectious symptoms worsened despite intravenous antibiotics. Clinical staging also suggested adrenal metastasis.



Methods: Cytology of pleural fluid was positive and right upper lobectomy revealed pT3N1 poorly differentiated squamous cell carcinoma. The specimen opened ex vivo was consistent with necrosis and abscess (Fig. 2).



Results: The patient tolerated resection very well, and was home without complication in 8 days. Infectious symptoms promptly cleared. He underwent six cycles of carboplatin and paclitaxel, without significant toxicity. CT and bone scan revealed no evidence of disease 18 months post-resection. **Conclusion:** In some NSCLC patients whose greatest threat to health and quality of life is related to complications such as lung abscess, focusing on clearing the infection rather than strictly adhering to oncologic curative intent criteria may improve quality of life, alleviate symptoms and improve survival. In this particular case, the patient had a relentless cough of putrid sputum and fevers. He was not a candidate for curative resection due to adrenal metastasis and positive pleural cytology. A palliative resection could be justified, as his symptoms were severe, potentially able to be resolved with surgery, and no other treatment options were available. Following resection, the infection cleared, and symptoms resolved. He then tolerated chemotherapy with a favorable response and over 18 month survival. **Keywords:** Surgery, Palliative, quality of life

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P3.11-011 Mesenchymal Thoracic Neoplasma Presenting as a Thromboembolism

Ana Laura Ortega Granados, Nuria Cárdenas Quesada, Natalia Luque Caro, Tamara Díaz Redondo, Capilla De La Torre Cabrera, Yéssica Plata Fernández, Francisco José García Verdejo, Irene González Cebrián, Pedro Sánchez Rovira *Medical Oncology, Complejo Hospitalario de Jaén, Jaen/Spain*

Background: In the screening of the possible etiology of pulmonary embolism rule out the presence of an occult neoplasia. Tumors more often associated with thrombotic phenomena are lung, pancreas and colon. The pulmonary artery sarcoma is a rare entity and its clinical diagnosis is complex. **Methods:** We report a case of a non-smoker 71 years old woman. In 1999 suffers first episode of thrombophlebitis. Since then presents several episodes of DVT in the lower limbs so it was anticoagulated with acenocumarol. In October 2014 she was admitted due to costalgia and fever and suspected diagnosis of pneumonia. She told a 3 months history of asthenia and progressive edema of the lower limbs. It is performed thoracic CT, with a massive pulmonary thromboembolism. The doppler sonography of lower limb show a chronic thrombosis. After clinical stabilization she was put under rivaroxaban. At 15th admission day, she starts with dyspnea with chest discomfort, and respiratory failure was found. In an urgent CT was shown a progression of the known embolism. Being a massive thrombosis refractory to treatment and progressive elevation of pulmonary pressure, surgeon was consulted, and is was performed a thromboendarterectomy and a pulmonary artery homograft replacement. In the pathology report, is reported a intermediate-grade sarcoma, suggestive of intramural primary origin and intimal type intimal grade. In January 2015 CT shows progression of local disease, and is discussed in the tumor board, considering unresectability of disesase, and it is proposed to start palliative chemotherapy **Results:** The pulmonary artery sarcoma is a rare disease, since its first description in 1923, there have been documented 200 cases. It can be classified according to their location relative to the vessel wall, or by histologic subtype. Usually located in the main pulmonary artery, diagnosis and complications arise from its intraluminal extension. Up to 50% of cases have pulmonary and mediastinal metastases at diagnosis and distant metastases in 16-19% It is an entity with very similar clinical and radiological features a thromboembolism, a fact that probably contribute to underdiagnosis. The symptoms are dyspnea (72-100%), chest pain (35-45%) and hemoptysis (15-24%), weight loss (21%), asthenia (10%) and fever (8%). The prognosis is poor, with survival reported between 6 months and 2 years (median 17 months) The treatment of choice is surgical approach, by pulmonary endarterectomy, lobectomy or pneumonectomy, with or without reconstruction of the pulmonary artery. In most cases R0 resection is not achieved. The role of radiotherapy (RT) and chemotherapy (CT) is not yet well defined. Regarding chemotherapy schedules, it have been used traditionally active drugs for the treatment of sarcomas **Conclusion:** The pulmonary artery sarcoma is a rare disease that should be suspected in patients with progressive or refractory pulmonary thromboembolism. **Keywords:** sarcoma, thromboembolism, pulmonary artery

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P3.11-012 Improving Clinical Trial Awareness in NSCLC: Pilot Testing a Novel Healthcare IT Platform for Incorporating Education at the Point of Care

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Background: Cancer clinical trial (CCT) participation is critical to improving the care of patients with Non-Small Cell Lung Cancer (NSCLC), yet low participation in CCTs persists. Little is known about the specific barriers to CCT participation among patients with NSCLC. The On Q Care Planning System (CPS) is an electronic tablet based platform adapted to address potential barriers to CCT participation through algorithm-driven identification of and education about patient specific CCTs at the point of care. The primary objectives of this study were to 1) characterize knowledge, attitudes and beliefs about CCTs among patients with NSCLC and their providers and 2) evaluate the impact of the CPS on CCT participation. **Methods:** We performed a multi-site pilot implementation project of CPS as a clinical decision support and patient education tool. Patients were eligible if they had recurrent/metastatic NSCLC. The CPS contained clinical trial eligibility criteria for many CCTs in NSCLC open at the primary research site, as well as selected CCTs from surrounding cancer centers. Study aims were evaluated using

patient and provider self-report surveys. Knowledge, attitudes and beliefs about CCTs for both patient's and provider's was captured through self-assessment surveys, using a combination of true/false questions and 1-5 Likert scale measures where 5 indicated highest level of agreement. Effect of CPS on CCT enrollment was measured by rate of enrollment in CCTs following the intervention, compared to historical rates of NSCLC CCT participation at our institution. **Results:** From April 2015 through July 2015, 9 providers (medical oncologists and nurse practitioners) and 79 patients with recurrent/metastatic NSCLC have been enrolled from 2 participating cancer centers. While providers reported being aware of open CCTs (mean score (m)=4.6), they felt that lack of adequate information about CCTs (m=3.0) and having time to review eligibility (m=2.6) were key barriers to CCT enrollment. Patients agreed that there were both the personal (m=3.7) and societal (m=4.1) benefits of CCTs. Similar to providers, key barriers to CCT participation for patients centered around lack of knowledge (concern about not knowing what drug they would receive (m=3.5) and that CCT agents would be too toxic (m=3.2)). Of the patients enrolled, 22 were at a point of new treatment or change in treatment and thus evaluable for rate of CCT referral and enrollment. In this subgroup, 21 (95.5%) received care plans with CCT recommendations. Following the study intervention visit, 8 (36.4%) of evaluable patients enrolled in a clinical trial. This compares favorably both with historical rates at our institution, where 13.8% of treatment eligible patients with lung cancer have been enrolled in CCTs, and with national averages which are less than 5%. **Conclusion:** CCT enrollment is critical to advancing the treatment of NSCLC, yet CCT enrollment in NSCLC remains low. For both providers and patients, the lack of readily accessible information about clinical trial eligibility and protocol details is a major barrier to CCT enrollment. The CPS is specifically designed to address these barriers. Indeed, in this pilot study, we showed a promising rate of CCT accrual with the use of the CPS. These findings should be validated in larger, randomized studies.

Keywords: clinical trial enrollment, Technology, Attitudes and Beliefs, Patient Education