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**PUB001 EGFR TKI Erlotinib in Patients with Advanced Squamous Cell Carcinoma of the Lung: A Retrospective Analysis from India** Devavrat Arya, Manish K. Singhal *Medical Oncology, Fortis International Oncology Centre, Noida, Uttar Pradesh/India*

**Background:** Erlotinib has proven efficacy in patients with advanced non-small cell lung cancer, especially adenocarcinoma which harbour activating EGFR mutations. In squamous cell carcinomas, it has been used in second line treatment and beyond, especially in patients with poor performance status. The aim of this study was to evaluate the efficacy of erlotinib in patients with advanced squamous cell carcinoma of lung (SCC). **Methods:** We retrospectively reviewed medical records and serial chest images of lung cancer patients with SCC histology and history of erlotinib treatment. The primary objective was to assess overall response rate (ORR) and disease control rate (DCR) and the secondary objective was to assess progression-free survival (PFS) and overall survival (OS). **Results:** A total of 20 patients were analyzed (18 men and 2 women, median age of 63 years).Seventeen patients were current or former smokers and three were non smokers. Ninety percent of patients had a poor performance status (Eastern Co-operative Oncology Group Performance Status 2 or 3). Three patients achieved partial response and 7 had stable disease. The ORR was 15 % and the DCR was 50%. The median PFS was 4.3 months (range, 1.0 – 8.0 months). Overall Survival (OS) data was not mature at the time of reporting. EGFR mutation status of three patients subjected to EGFR analysis were all negative. The PFS was longer in patients who were non smokers as compared to those who gave a history of current or former smoking (median PFS, 5.3 vs. 4.1 months). Five patients (25%) had PFS more than six months. **Conclusion:** A significant proportion of lung SCC patients derive a clinical benefit from erlotinib treatment. This needs further evaluation that includes testing for activating EGFR mutations in these patients particularly those who have longer progression free survivals.
**Keywords:** Erlotinib, Squamous Cell Carcinoma Lung, Disease Control Rate, Progression Free Survival

**PUB002 Accidental Intrathoracic Disseminated pM1a - Distinguished Lung Cancer with Favorable Prognosis** Wei Li, Wen-Zhao Zhong, Xue-Ning Yang, Ri-Qiang Liao, Qiang Nie, Song Dong, Xu-Chao Zhang, Yi-Long Wu *Guangdong Lung Cancer Institute, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou/China*

**Background:** In the 7thedition of lung cancer TNM stage, the prognosis of the pM1aⅣ is better than pⅢB. Subgroups of lung cancer patients who underwent incomplete resection (R1/R2) gain favorable prognosis. This study compares the prognosis between accidental local residue and intrathoracic disseminated pM1a after incomplete resection. **Methods:** Patient characteristics, histological and molecular profiles of lung cancer patients who receiving accidental incomplete resection were retrospectively collected. All patients were divided into local residual group and intrathoracic disseminated pM1a group. Progression-free survival (PFS) and overall survival(OS) were evaluated by Kaplan–Meier and Cox regression. **Results:** From 2008 to 2013, 1483 lung cancer patients received thoractomy in Guangdong Lung Cancer Institute. 58 patients receiving incomplete resection(R1/R2) were enrolled, including 38 patients of local residue(2.6%) and 20 patients of disseminated pM1a (1.3%). Compared to local residual group, disseminated pM1a group includes more female(P=0.002), more patients younger than 60 years old(P=0.01), more non-smokers(P=0.037), higher R2/R1 resection ratio(P=0.013), less patients with lymph nodes metastasis(P=0.013), higher stage Ⅳ/ⅢB ratio P<0.001), more adenocarcinomas( P<0.001), more adenocarcinomas with lepidic pattern(P<0.001), higher EGFR mutation rates(P<0.001), lower EGFR expression (P=0.022) . Median PFS of local residue and disseminated pM1a were 8.7 and 18.8 months(P=0.120), and median OS were 11.9 and 36.0 months(P=0.002), respectively. Cox regression analysis revealed that group (local residue vs. disseminated pM1a) was the only independent prognostic factor(P=0.005) for OS. **Conclusion:** Accidental intrathoracic disseminated pM1a is a distinguished lung cancer subtype with favorable prognosis comparing to patients of local residue. The prolong PFS and OS might contribute to the natural history of the distinguished subtype and the favorable response to EGFR-TKI.

**PUB003 Prognostic Analysis of High Selected En-Bloc Resected Chest Wall Involving Non-Small Cell Lung Cancers** Rui Mao, Chang Chen *Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

**Background:** Factors influencing long term survival of NSCLC invading chest wall have been under debates. Considering the advances in examinations and treatments during the past several decades, this study is an attempt to investigate the possible prognostic factors of this group of patients. **Methods:** We reviewed data of all patients with NSCLC invading chest wall, who underwent complete(R0) surgical treatment of en-bloc resection at our hospital from 1994 to 2014. Superior sulcus tumors, neoadjuvant therapy receivers and patients need vertebrectomy and reconstruction were excluded. All patients were classified according to the current TNM classification. **Results:** One hundred and four patients were included. Adjuvant therapy(chemoradiotherapy or chemotherapy) was administered according to the various advises of referring physicians, so no uniform protocol was employed. All tumors received en-bloc resection. Complete resection was achieved in all cases. There were 61 IIB tumors(T3N0) and 41 IIIA tumors (T3N1, 18 patients; T3N2, 22 patients; T4N1, 1 patients) and 2 IIIB(T4N2) tumors according to the current TNM classification. Lobectomy, bilobectomy, pneumonectomy, wedge/segmentctomy and sleeve lobectomy/plastic lobectomy were required in 80, 2, 9, 3 and 10 cases. Adjuvant therapy was administrated in 61 patients while 33 patients needn't. Depth of invasion limited to partial pleura or intercostal soft issue in 60 cases, infiltrated into rib in 44 patients. Of 66 CT available cases, tumor's location arrived at spine was found in 19 and away from in 47 cases. furthermore, distance to transverse process was more far than 5cm in 28 while closer in 19. There were 4(3.85%) perioperative mortalities caused by PE or respiratory failure. Overall 5 year survival was 41.6%. Local-regional recurrence occurred in 5 patients with 45 patients developing systemic recurrence. The adjuvant therapy (yes versus no,$p$=0.0005), depth of invasion(rib versus other, $p$<0.0001), tumor size(≤3 versus >3cm, $p$=0.017) and tumor's location(arrival versus away, $p$=0.034; near versus far, $p$=0.019)(fig. 1) were found as prognostic factors in univariate analysis. I have to mention that the near goup can surprisely better the suvival as opposite to what we have historically thought. Two independent factors affecting long term survival are adjuvant therapy ($p$=0.002) and depth of invasion($p$=0.028) according to multivariate analysis.

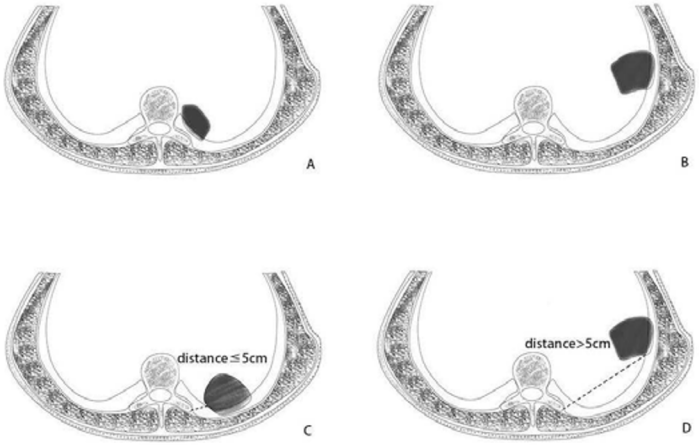
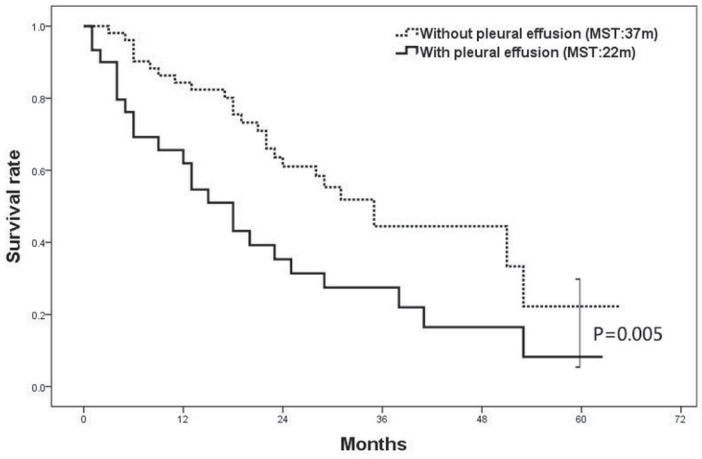


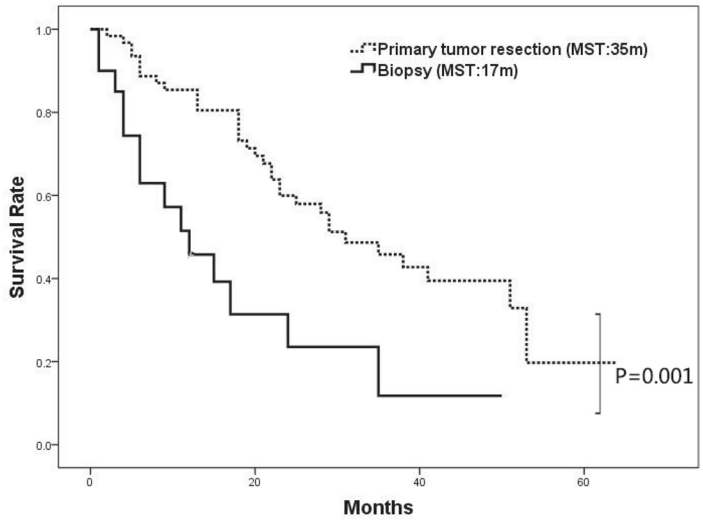

fig.1: A: arrival; B: away; C: near; D: far. **Conclusion:** Adjuvant therapy and depth of invasion are independent factors influencing prognosis of en-bloc resected chest wall involving non-small cell lung cancers, the role of tumor's location needs more investigations.
**Keywords:** complete resection, non-small cell lung cancer, en-bloc, prognostic factor

**PUB004 Primary Tumor Resection Showed Survival Benefits for Non-Small-Cell Lung Cancers with Unexpected Malignant Pleural Dissemination** Yijiu Ren, Yunlang She, Chenyang Dai, Gening Jiang, Ke Fei, Pengqing Ying, Chang Chen *Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai/China*

**Background:** Although non-small-cell lung cancer (NSCLC) with malignant pleural nodules is generally contraindicated for surgery, there is no consensus concerning on-site operative decisions for unexpectedly intra-operatively encountered malignant pleural disseminations. The rationale underlying the primary tumor removal and other aggressive interventions remains controversial. **Methods:** All surgical NSCLC cases of Shanghai Pulmonary Hospital between January 2005 and December 2013 were reviewed. Among them, 83 cases met the definition of "unexpected" malignant pleural nodules, despite routine preoperative evaluations for tumor metastasis. No pleural effusion was visualized in 52 cases during operations, and 31 had pleural effusion in minimal volume. Survivals were calculated with Kaplan–Meier method and risk factors were evaluated by the log-rank test. **Results:** The overall 3- and 5-year survival rates were 36.1% and 16.8%, respectively. The median survival time (MST) after surgery was significantly longer in the group without pleural effusion (37 months) compared to group with pleural effusion (22 months, p=0.005) (Fig 1). Patients with primary tumor resection had significantly better outcome compared to biopsy (MST: respectively, 35 vs. 17 months, 3-year survival 45.8% vs. 11.8%, p=0.001) (Fig 2). No baseline differences emerged in characteristics between biopsy (n=21) and primary tumor resection (n=62) groups including targeted therapy. Multivariate analysis showed that primary tumor resection (HR: 3.678, p=0.014), no pleural effusion (HR: 3.409, p=0.001), N0/1 status (HR: 5.937, p=0.002), and adenocarcinoma (HR: 5.481, p=0.002) were favorable prognostic factors in patients with malignant pleural nodules.




**Conclusion:** Patients with malignant pleural nodules but without pleural effusion had better survival compared to those with effusions. Primary tumor resection had survival benefits for patients with unexpected intra-operatively proven malignant pleural nodules.
**Keywords:** lung cancer, Surgery, Malignant pleural dissemination, Prognosis

**PUB005 Therapeutical Effect of Intrapleural Circular Hyperthermic Perfusion Chemotherapy on Malignant Pleural Effusion under VATS** Feng Xing[1], Hong Jiang[1], Shenglin Ma[2] [1]*Department of Thoracic Surgery, Hangzhou First People'S Hospital, Hangzhou, P. R. China, Hangzhou/China,* [2]*Department of Radiation Oncology, The First People' S Hospital of Hangzhou Medical Group, Hangzhou/China*

**Background:** Malignant pleural effusion (MPE) is defined as the identification of malignant cells in plural fluid or on pleural biopsy, which is often caused by primary pleural malignancy and tumors with pleural extension. It is a common complication of advanced malignant disease. According to the recently UICC revised staging system, the presence of MPE was upstaged from T4 to M1a with poor prognosis. The 30-day mortality is 29 to 50% and the median survival is 3 to 12 months. Given these considerations, the management of MPE is usually palliative, with promptly relieving of symptoms, reducing discomfort, and raising the patient's quality life. There is no standard treatment for patients with these malignancies. And the therapeutic outcomes remain to be unsatisfactory. Recent reports have demonstrated the effectiveness of hyperthermic pleural perfusion with cisplatin. But only few MPE patients had adopted the therapy in several institutions reports. The true long-time therapeutic effect, toxic side reactions, and the patient's remaining days were still to be greatly expected. The purpose of this study is to assess the feasibility, toxicity, and final results of intrapleural circular hyperthermic perfusion chemotherapy on MPE under VATS **Methods:** Between February 1999 and March 2012, eighty patients with symptomatic MPEs were performed on ICHPC under video-assisted thoracoscopic surgery (VATS). All had been proved to be as pleural spreads with malignant effusion due to primary or pleural malignancy. After breaking up the pleural adhensions under VATS, the 43℃ distilled water 3000ml containing cisplatin (200 mg/m$^2$) was circularly perfused into the pleural cavity for one hour through extracorporeal circulation unit. The improvement on patient's symptoms - the change for Karnofsky score(KPS)、the effect on MPEs, and the adverse reaction were observed after the treatment. The concentration change of carcino-embryonic antigen (CEA), cytokeratin-19 fragments(CYFRA21-1), neuron-specific enolase(NSE) were compared before and after the treatment. Meanwhile, the pathological and electron microscopic morphological change with pleural carcinomatoid tissue, as well as paraneoplastic normal tissue were observed after ICHPC. **Results:** The symptoms such as dyspnoea, shortness of breath disappeared. And MPEs were effectively controlled with total response rate of 100%. All patients KPS exceeded seventy. Moreover, the concentration of CEA CYFRA21-1 NSE dramatically descended with tolerably adverse effects. Mass necroses with pleural carcinomatoid were observed in post-treatment microscope. And chromatin condensation、apoptotic body occurrence and nuclear fragmentation in tumor cells were also found in post-treatment electron microscope. **Conclusion:** ICHPC has the evident therapeutical effect on MPE with less adverse reactions and invasiveness. And it is also suitable for the old and rigid patients with MPEs. We think it would be highly valued in controlling the MPEs
**Keywords:** Video-assisted thoracic surgery, intrapleural perfusion hyperthermic chemotherapy, lung cancer, malignant pleural effusion

**PUB006 The Efficacy and Safety of Higher-Dose Icotinib in Non-Small Cell Lung Cancer Patients after Progression with Normal Dose** Xiaoqing Liu[1], Weixia Wang[1], Chuanhao Tang[1], Xiaoyan Li[1], Jianjie Li[1], Wanfeng Guo[1], Haifeng Qin[1], Lili Qu[1], Hongjun Gao[1], Fenlai Tan[2], Lieming Ding[2] [1]*Department of Pulmonary Oncology, 307 Hospital of the Academy of Military Medical Sciences, Cancer Center, Beijing/China,* [2]*Betta Pharmaceuticals Co.Ltd., Hangzhou/China*

**Background:** Icotinib, an oral EGFR tyrosine kinase inhibitor, had shown antitumor activity and favourable toxicity in clinical trials. A phase III clinical study revealed icotinib was non-inferior to gefitinib in efficacy with favorable safety. Phase I trials established that icotinib anti-tumor efficacy increases with dose escalation. The objective of this study is to investigate the efficacy and safety of higher-dose icotinib in non-small cell lung cancer (NSCLC) patients after disease progression with normal-dose icotinib. **Methods:** Patients with NSCLC would be administered with higher-dose icotinib (250 mg three times per day) after disease progression with 125-mg icotinib, until second progression or intolerable toxicity. The primary endpoint was progression-free survival (PFS1) following progression at standard dose of icotinib (125 mg), secondary endpoints included objective response rate (ORR), disease control rate (DCR) and safety. The safety and efficacy of 375-mg icotinib will also be explored in those patients experiencing a second progression. This study is registered at ClinicalTrial.gov as NCT01465243. **Results:** A total of 32 NSCLC patients were enrolled, mostly stage IV (29/32), ECOG score 0-1 (32/32), adenocarcinoma (29/32) and non-smokers (21/32). The median PFS of 125-mg icotinib (PFS0) was 150.0 days (95% CI 111.0 - 267.0 days). All 32 patients experienced disease progression and thereafter were given 250-mg icotinib three times daily. All patients had progressed disease and were evaluable for efficacy. Median PFS in icotinib 250 mg tid extension period (PFS1) was 64.0 days (95% CI 50.0-103.0 days). Six patients were further given 375-mg icotinib after disease progression with 250-mg icotinib with a median PFS2 (PFS in 375-mg extension period) of 68.5 days (95% CI 30.0 ~ 117.0 days). In the extension period of 250mg and 375mg, the ORR was 15.6% (5/32) and 0% (0/0), DCR was 62.5% (20/32) and 66.7%(4/6), respectively. The PFS1 was significantly longer in patients with PFS0 > 3 months, compared to patients with PFS0 < 3 months (91.0 vs. 43.0 days, long-rank p = 0.0046). Thirty-two patients were included in safety analysis, the incidence of overall adverse reactions (ADR) was 56.3% (18/32). The most common ADRs were rash (34.4%), diarrhea (9.4%), and transaminase elevation (18.8%). Only one serious adverse event (SAE) was reported (grades 3 urine leukocytosis), which was unrelated to drug by investigator evaluation. No interstitial lung disease (ILD) or treatment-related deaths were reported. **Conclusion:** Higher-dose icotinib continuation was well tolerated with favorable efficacy in NSCLC patients after disease progression with normal dose, especially for patients with a median PFS more than 3 months in 125-mg period.
**Keywords:** higher dose, icotinib, non-small cell lung cancer, progression

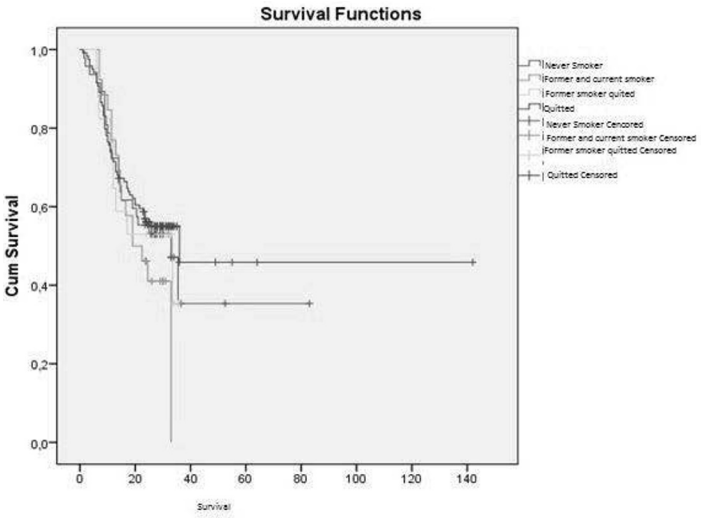
**PUB007 TTF-1 Expression Is Significantly Associated with Mutations in Exon 21 of the EGFR Gene in Chinese Patients with Lung Adenocarcinoma** Ying Li, Hongyu Liu, Qingchun Zhao, Yongwen Li, Jun Chen *Tianjin Medical University General Hospital, Tianjin/China*

**Background:** Non-small cell lung cancers (NSCLCs) make up 85% of lung cancers, with a 5-year survival rate of only 15%–17%. Adenocarcinoma of the lung is one of the main subtypes of NSCLC. With the identification of epidermal growth factor receptor (EGFR) gene mutations in NSCLCs and the development of the EGFR tyrosine kinase inhibitors (TKIs), such as gefitinib and erlotinib, the survival and quality of life of adenocarcinoma patients have improved greatly. Along with EGFR mutations, thyroid transcription factor-1 (TTF-1), a biomarker for lung adenocarcinoma, was reported to have a much higher rate of expression in the lung adenocarcinoma specimens of Asian, female, and nonsmoking lung cancer patients. The NEJ 002 clinical trial also found that the rate of EGFR mutations was significantly higher in lung adenocarcinoma specimens that were positive for TTF-1 expression than in specimens that were TTF-1 negative. Therefore, clarifying whether there is a relationship between EGFR mutations and TTF-1 positivity in lung adenocarcinomas and whether TTF-1 can be a biomarker of EGFR mutation status is essential, especially for some patients with advanced lung cancer with inadequate specimens for evaluating EGFR status. **Methods:** There were 200 lung adenocarcinoma patients who were enrolled in this study. Tumor specimens of these patients were investigated for TTF-1 expression using immunohistochemistry and mutations in *EGFR* were determined by a liquidchip platform for DNA analysis of slides with sections of formalin-fixed, paraffin-embedded specimens. **Results:** The rates of TTF-1 expression and *EGFR* mutations were 81.5% and 45.5%, respectively, in the lung adenocarcinoma specimens of recruited patients. Among female nonsmokers (n = 72), 93.1% of specimens were positive for TTF-1 expression, and 63.9% had *EGFR* mutations. Of 89 patients with *EGFR* mutations, 83 (50.9%) specimens were simultaneously positive for TTF-1 expression. Kaplan-Meier analysis of all patient specimens found that postoperative survival time was not significantly associated with

TTF-1 expression and the presence of *EGFR*mutations. However, patients with stage III-IV disease whose tumors were positive for TTF-1 expression and *EGFR* mutations had better postoperative survival than similar patients whose tumors were negative for TTF-1 expression and *EGFR*mutations. **Conclusion:** Our study showed a significant association between TTF-1 positivity and the presence of EGFR mutations (exon 21) in the lung adenocarcinomas of Chinese patients. In clinical practice, TTF-1 expression may be a marker for planning therapy for certain patients with lung adenocarcinomas, especially for selection of EGFR TKIs.

**PUB008 The Impact of Continued Cigarette Smoking on Prognosis in Lung Cancer Patients Receiving Chemotherapy** Serap Hastürk, Fatma I. Uzel, Sezin Altunbay *Pulmonary Medicine, Yedikule Chest Diseases and Thoracic Surgery Training Hospital, Istanbul/Turkey*

**Background:** Lung cancer is one of the leading causes of mortality worldwide. Cigarette smoking is the most important etiologic risk factor, but there are discordant and scarce data on the impact of continued smoking during and after chemotherapy on prognosis in lung cancer patients. The aim of our study was to investigate the effects of cigarette smoking during and after chemotherapy on prognosis in patients with lung cancer. **Methods:** We reviewed the medical records of lung cancer patients who received chemotherapy at our hospital between January 2012 and December 2012. **Results:** Of the 209 patients 26 (12.4%) were female, 183 (87,6%) were male with the mean age of 58±8,4 years. Histologic distribution was as follows: 56 ( 26,8%) adenocarcinoma, 85 (26,7%) squamous cell carcinoma, 19 (9,1%) small cell carcinoma, 49 (23,4%) unclassified non-small cell carcinoma. 22,5% of patients were never-smokers, 56,9% were former smokers, 8,1% were them who quitted smoking during treatment, 12,4%were current smokers. No relationship was detected between smoking during and after treatment and gender, comorbidities, stage of the disease, histology, performance status and former smoking habit. The survival time was not different in the same stage disease according to smoking status. The mean survival time in patients who were smoking during and after treatment was 19±4 months, who were nonsmokers was 33±6 months, who quitted smoking 33±14 months and who were long time quitters was 36 months (p=0,69). Although these differences did not prove to be statistically significant, patients who continued smoking had remarkable shorter survival times.




**Conclusion:** We did not detect any statistically significant prognostic influence of smoking during and after chemotherapy in lung cancer patients. As the survival time in patients who continued smoking was remarkably shorter than nonsmokers, we recommend to incourage patients to quit smoking. **Keywords:** lung cancer, smoking, Prognosis, chemotherapy

**PUB009 Effective Resolution of Lung Cancer Related Tracheal and/or Bronchial Obstruction with External Beam Radiotherapy** Erkan Topkan[1], Berna Akkus Yildirim[1], Yurday Ozdemir[1], Ozan C. Guler[1], Fatih Kose[2] [1]*Radiation Oncology, Baskent University Faculty of Medicine, Adana/Turkey,* [2]*Medical Oncology, Baskent University Faculty of Medicine, Adana/Turkey*

**Background:** We retrospectively evaluated the efficacy of external beam radiotherapy (EBRT) in relieving lung cancer related tracheal and/or bronchial obstruction and associated factors. **Methods:** Medical records of 72 patients with metastatic lung cancer and a mass obstructing the trachea and/or bronchi treated with EBRT were analyzed. Fifty-three (73.6%) and 19 (26.4%) patients had non-small cell lung- (NSCLC) and) small-cell lung cancer (SCLC), respectively. EBRT dose was 8 to 40 Gy (median; 30 Gy) administered in 1 to 13 fractions (median; 10 fractions). The primary end point was the rate of resolution of obstruction after EBRT which was assessed with the changes in between the radiographic findings and/or subjective symptoms between the pre- and post-EBRT evaluations. Overall survival and EBRT toxicity rates constituted the secondary end points. **Results:** The median follow-up duration was 5.6 months (range; 1.3-17.8). Treatment was relatively well tolerated with only 5 (6.9%) acute grade 3 toxicity( 2 pneumonitis and 1 esophagitis, and no late grades 3-5 toxicity After EBRT the airway obstruction was improved to some degree in 58 patient (80.6%) on chest X-ray. The median time for maximum obstruction resolution was 23 days (range; 3-86) from the commencement of EBRT. The rate of improvement in obstruction was significantly higher in SCLC (89.5%) than the NSCLC (77.3%) patients (p=0.02). Time to maximum resolution was also significantly shorter in SCLC than the NSCLC patients (5 vs. 28 days; p=0.02). The median survival was only 2.3 months (rang: 1.1-3.5) in non-responder patients which was significantly lower than the 8.9 months (rang: 4.2-13.6) achieved in responders (p=0.007). The largest diameter of obstructive lesion less than 5.3 cm (p=0.02) the biologically effective dose ($BED_{10}$) of ≥ 39 Gy (p=0.002) were factors associated with better resolution of the airway obstruction. On multivariate analysis only the SCLC histology and $BED_{10}$ ≥ 39 Gy retained their significant association with better response. **Conclusion:** EBRT is a relatively safe and effective treatment option in relieving tracheal and/or bronchial obstruction without severe toxicities in acute and chronic phase in metastatic NSCLC and SCLC patients. Higher EBRT doses ($BED_{10}$ ≥ 39 Gy) should be preferred inorder to achieve superior response rates. **Keywords:** Radiotherapy, Airway obstruction

**PUB010 Factors Associated with Brain Metastasis Development in Radically Treated Stage IIIB Non-Small Cell Lung Cancer Patients** Erkan Topkan, Berna Akkus Yildirim, Ozan C. Guler, Yurday Ozdemir *Radiation Oncology, Baskent University Faculty of Medicine, Adana/Turkey*

**Background:** We retrospectively investigated the factors associated with brain metastasis (BM) development following radical concurrent chemoradiotherapy (C-CRT) in stage IIIB non-small cell lung cancer (NSCLC) patients. **Methods:** Institutional records of 767stage IIIB NSCLC patients with available pretreatment brain MRI and treated between January 2007 and December 2012 were analyzed. FDG-PET-CT was the standard staging procedure either during diagnsis or as a re-staging method prior to thoracic radiotherapy. All patients received at least 1 cycle of platinum-based doublet chemotherapy during the course of 3D-conformal 60-66 Gy (2 Gy/fr) thoracic radiotherapy. Primary endpoints were the incidence of BM following C-CRT and associated risk factors. **Results:** Median follow-up was 24.7 months (range, 2-61 months). Two-year survival rate was 31%. One-year incidence of brain metastasis was 28.7%. In univariate analysis showed that patients younger than 60 years of age had more brain metastases than older patients (36% vs 15%, p= 0.01). Brain was more frequently thefirst site of metastases in younger patients than >60years (22% vs 9%, p> 0.05). Histology also significantly affected the development of brain metastasis (43.2% in adenocarcinoma, 16.4% in epidermoid carcinoma, p= 0.004). On multivariate analysis, only age was found to be significant prognostic factor (p= 0.01). **Conclusion:** Age and histology significantly effects development of brain metastasis in locally advanced NSCLC. Younger age was the only significant variable for brain metastasis. **Keywords:** Brain metastasis, Stage IIIB Non-Small Cell Lung Cancer

**PUB011 Comparison of Maintenance Therapy in EGFR Mutation Negative and EGFR Mutation Positive NSCLC Patients** Amit Joshi[1], Vanita Noronha[1], Abhishek Mahajan[2], Amit Janu[2], Anuradha Chougule[1], Nirmala Jambhekar[3], Rajeev Kumar[3], Kumar Prabhash[1] [1]*Medical Oncology, Tata Memorial Hospital, Mumbai/India,* [2]*Department of Radiodiagnosis, Tata Memorial Hospital, Mumbai/India,* [3]*Department of Pathology, Tata Memorial Hospital, Mumbai/India*

**Background:** Platin based doublet is standard of care in locally advanced and metastatic NSCLC. Maintenance pemetrexed and tyrosine kinase inhibitior both have shown to improve outcomes in patients with favourable response to induction therapy. **Methods:** Data of patients with locally advanced and metastatic non squamous NSCLC who received induction pemetrexed platin doublet were retrieved from prospectively maintained lung cancer database registered between June 2011 and March 2014.Patients who received maintenance pemetrexed and maintenance TKI being EGFR mutation negative and positive respectively were chosen for final analysis. Kaplan Meir survival analysis was used for Progression free survival and overall survival. Log rank test was used to evaluate and compare factors affecting outcome. **Results:** Median follow up is 16 months. Out of 268 patients who had favourable response to induction pemetrexed platin doublet, EGFR mutation result was available in 238 (89%) patients. Patients who were EGFRF mutation negative and received maintenance pemetrexed were 138, while those with EGFR mutation negative and received maintenance TKI were 80.Median PFS with maintenance TKI in EGFR mutation positive patients was significantly better than that of maintenance pemetrexed in EGFR mutation negative (11 months versus 8 months; p=0.01), while the overall survival was 19 months and 20 months respectively. Older age, females, non smoker, no baseline effusion and partial response to induction did better with maintenance TKI. **Conclusion:** Maintenance TKI in EGFR mutation positive non squamous NSCLC delays disease progression more than maintenance pemetrexed in EGFR mutation negative NSCLC. Both option fare favourably to improve outcomes after response to induction therapy. **Keywords:** Maintenance, Tyrosine kinase inhibitors, pemetrexed.

**PUB012 The National Lung Matrix Trial: Multi-Drug, Genetic Marker-Directed, Multi-Arm Phase II Trial in Non-Small Cell Lung Cancer** Gary Middleton[1], Sanjay Popat[2], Ian Walker[3], Clive Mulatero[4], James Spicer[5], Yvonne Summers[6], Timothy A. Yap[7], Laura R. Crack[8], Lucinda J. Billingham[9] [1]*School of Cancer Sciences, University of Birmingham, Birmingham/United Kingdom,* [2]*Royal Marsden Hospital, London/United Kingdom,* [3]*Strategic Partnerships, Cancer Research UK London/United Kingdom,* [4]*Leeds Teaching Hospitals NHS Trust, Leeds/United Kingdom,* [5]*Guy'S & St. Thomas' NHS Trust; King's College London, London/United Kingdom,* [6]*Department of Medical Oncology, The*

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**Background:** Management of NSCLC has been transformed by precision medicine. There are an increasing number of potentially actionable targets and a pressing need to efficiently test the activity of targeted therapies aimed at these actionable changes. The National Lung Matrix Trial (NLMT) is a large country level study investigating genetic biomarker/targeted therapy combinations. Each arm is non-randomised with the primary objective in most cases being objective response rate in order to screen for biomarker-drug combinations with high signals of activity. CR-UK's Stratified Medicine Programme 2 will undertake large volume national molecular pre-screening integrated with the NLMT, funded by CR-UK, in partnership with AstraZeneca/MedImmune and Pfizer. The trial opened to recruitment in March 2015. The multi-centre trial will be open at all UK Experimental Cancer Medicine Centres and will be carried out under a single clinical trial protocol and regulatory submission. Key translational analyses include ctDNA for emergence of resistance, and whole genome analysis, if content permits, for predictive biomarkers. This will be complemented by pre-treatment DNA/RNA analysis for biomarker discovery and post-treatment biopsies for resistance mechanisms. **Methods:** In the NLMT there are currently 8 targeted drugs and 23 different drug-biomarker combinations. The aim is to determine whether there is sufficient signal of activity in any drug-biomarker combination to warrant further investigation. We have chosen to use a Bayesian adaptive design that gives a more realistic approach to decision-making and flexibility to make conclusions without fixing the exact sample size. The screening platform for the NLMT is an adaptable 28-gene Nextera Next Generation Sequencing platform designed by Illumina. This covers the range of molecular abnormalities being targeted in the trial. The NLMT is an adaptive design allowing new biomarker-drug combinations to be tested via incorporation by substantial amendment. The pre-clinical data supporting each arm has been rigorously assessed and the implications incorporated into selection of biomarkers for each drug. In the FGFR arm we are only including mutations that have been specifically demonstrated to be transforming and tumourigenic. In the AKT inhibitor arm we are excluding patients with concomitant KRAS mutations as repression of 4E-BP1 is also driven by ERK activation. In the CDK4 inhibitor arm we are clinically testing the synthetic lethality concept in KRAS mutant adenocarcinoma of the lung; we are excluding all concomitant abnormalities which can activate AKT/MTOR signalling as this has been shown to inhibit KRAS driven oncogene induced senescence.

| **Molecular Cohorts** | AZD4547 | AZD2014 | Palbociclib | Crizotinib | Selumetinib + Docetaxel | AZD5363 | AZD9291 |
|---|---|---|---|---|---|---|---|
| FGFR2/3 mutation | x | | | | | | |
| TSC1/2 mutation | | x | | | | | |
| LKB1 mutation | | x | | | | | |
| Proficient Rb and p16 loss – SCC | | | x | | | | |
| CDK4 amplification | | | x | | | | |
| CCND1 amplification | | | x | | | | |
| KRAS mutation - ADC | | | x | | | | |
| Met amplification | | | | x | | | |
| ROS1 fusions | | | | x | | | |
| NF1 mutation – SCC | | | | | x | | |
| NF1 mutation – ADC | | | | | x | | |
| NRAS mutation – ADC | | | | | x | | |
| PIK3CA mutation - SCC | | | | | | x | |
| PIK3CA mutation - SCC | | | | | | x | |
| PIK3CA amplification - SCC | | | | | | x | |
| PI3K/AKT deregulation - ADC | | | | | | x | |
| PTEN mutation - SCC | | | | | | x | |
| PTEN loss - SCC | | | | | | x | |
| AKT1 mutation | | | | | | x | |
| EGFR+& T790M+ | | | | | | | x |

**Results:** Not applicable **Conclusion:** Not applicable **Keywords:** national clinical trial, precision medicine

**PUB013 Identification of Existing Targeted Drugs That Inhibit NTRK and ROS1 in Lung Cancer** Curtis Chong[1], Dalia Ercan[1], Marzia Capelletti[1], Magda Bahcall[1], Taebo Sim[1], Lynette Sholl[2], Mizuki Nishino-Habatu[3], Bruce E. Johnson[1], Nathanael Gray[1], Pasi A. Janne[1] [1]*Medical Oncology, Dana-Farber Cancer Institute, Boston/United States of America,* [2]*Department of Pathology, Brigham and Women'S Hospital, Boston/MA/United States of America,* [3]*Radiology, Brigham and Women'S Hospital, Bosston/MA/United States of America*

**Background:** Patients with oncogenic driver mutations in non-small cell lung cancer (NSCLC) who are treated with a targeted agent will eventually develop resistance. **Methods:** In an effort to identify inhibitors of NTRK1 and ROS1, which are inappropriately activated in some patients with NSCLC, we created and screened a library of existing targeted drugs against Ba/F3 cells transformed with these oncogenes. **Results:** This screen identified the FDA-approved drug cabozantinib (XL184) as a potent inhibitor of CD74-ROS1 ($IC_{50}$ = 9 nM), including the crizotinib-resistant mutants G2032R ($IC_{50}$ = 26 nM) and L2026M ($IC_{50}$ = 11 nM), with no inhibition of the parental BaF3 cells ($IC_{50}$ > 10 uM). AP26113, a dual ALK/EGFR inhibitor undergoing phase I/II clinical trials, also potently inhibited CD74-ROS1 ($IC_{50}$ = 30 nM), including the crizotinib-resistant mutants G2032R ($IC_{50}$ = 170 nM) and L2026M ($IC_{50}$ = 220 nM), with weak inhibition of the parental BaF3 cells ($IC_{50}$ > 1 uM). Both cabozantinib and AP26113 inhibited ROS1 autophosphorylation and downstream ERK activation in CD74-ROS transformed Ba/F3 cells and in the *SLC-ROS1*-rearranged NSCLC cell line HCC78. The FGFR3 inhibitor dovitinib, which is in phase III clinical trials for renal cell carcinoma, potently inhibited *NTRK1* transformed compared to parental Ba/F3 cells ($IC_{50}$ = 69 nM vs > 1 uM), and blocked NTRK1 autophosphorylation and ERK activation in transformed 3T3 cells. A patient with metastatic *ROS1*-rearranged NSCLC with progression on crizotinib was treated with cabozantinib and experienced a partial response. This patient had a novel *ROS1*-rearrangement with *RNPC*, which encodes RNA binding protein 40, a component of the U12-dependent (minor) spliceosome. **Conclusion:** While acquired resistance to targeted therapies is a major clinical problem, this study highlights other existing agents that may overcome resistance, and identifies several promising candidates for clinical trials. **Keywords:** Drug repurposing, cabozantinib, ros1

**PUB014 Survival Impact of Concomitant Medications in Advanced Lung Cancer** Mahender Yellu[1], Shuchi Gulati[2], Nabeela Siddiqi[1], Jane Pruemer[1], Changchun Xie[3], Nagla A. Karim[1] [1]*Internal Medicine, Universitty of Cincinnati, Cincinnati/OH/United States of America,* [2]*Internal Medicine, Universitty of Cincinnati, Cincinnati/United States of America,* [3]*Environmental Sciences, Universitty of Cincinnati, Cincinnati/OH/United States of America*

**Background:** Limited and conflicting data is available regarding the impact of non-chemotherapy drugs such as antidepressants, low molecular weight heparin (LMWH) and statins on overall survival (OS) in advanced stage lung cancer. We conducted a retrospective study to investigate the impact of individual and combined effect of these medications followed by a subgroup analysis for LMWH. **Methods:** Retrospective analysis of patients with advanced stage lung cancers including non-small cell lung cancers (NSCLC), small cell lung cancers (SCLC) and rare histopathologic types was conducted at the University of Cincinnati (UC) between January 2004 and June 2013. Patients with early stage lung cancer and those without a tissue diagnosis were excluded from the study. Antidepressants (comprising of duloxetine, trazodone, and mirtazapine) other than tricyclic antidepressants (TCAs) and selective serotonin receptor inhibitors (SSRIs) were grouped separately. Patients not on any of the above medications were used as control arm. Death was the end point. Kaplan-Meier method was used to calculate median OS with 95% confidence intervals (CI). Cox model was used to test the treatment effect adjusted for age and gender. Data was analyzed using SAS (Ver 9.4). **Results:** A total 200 patients were included in the study, 40 patients were on antidepressants, 28 on LMWH, and 42 on statins. Median age of the study population was 61 years and median OS was 539 days (CI 376-839). A trend towards protective effect (cox model) was noted in SSRIs (HR 0.836, P 0.590) and other antidepressants (HR 0.840, P 0.660), while inferior survival was noted in patients receiving TCAs (HR 1.943, P 0.163). Similarly statins have showed a trend towards protective effect (HR 0.840, P 0.513). Therapeutic LMWH used for patients with thrombosis had negative effect on OS (HR 1.335, P 0.339), but better OS was observed when used as prophylaxis (HR 1.202, P 0.751). None of these results achieved statistical significance.

| Drug | OS in study arm (days) | OS in control arm (days) | P value | Hazard ratio |
|---|---|---|---|---|
| **TCAs** | 307 | 560 | 0.163 | 1.943 |
| **SSRIs** | >463 | 539 | 0.590 | 0.836 |
| **Other antide-pressants** | 805 | 531 | 0.660 | 0.840 |
| **LMWH** | 460 | 539 | 0.339 | 1.335 |
| **Statins** | 648 | 539 | 0.513 | 0.840 |

**Conclusion:** Our study demonstrated a protective effect of SSRIs, other antidepressants and statins although statistical significance was not achieved. For unknown reasons TCAs and LMWH increased the risk of death. Since our sample size is small and also a retrospective analysis, a larger prospective study would help determine the impact of these medications on OS. **Keywords:** concomitant medications, lung cancer, antidepressants, low molecular weight heparin, statin

**PUB015 Clinical Investigation into the Initial Diagnosis and Treatment of 539 Patients with Ⅳ Stage Lung Cancer** Bin J. Li, Qian Shao *Department of Radiation, Shandong Cancer Hospital and Institute, Jinan/China*

**Background:** The aim of the present study was to analyse clinical data obtained from Ⅳ stage lung cancer patients, including the initial clinical symptoms upon diagnosis, duration of patient delay in presenting to a doctor, pathological classification, transferred organs, treatment strategy and prognosis. **Methods:** A retrospective analysis was conducted of the clinical features of 539 lung cancer patients(Ⅳ stage) who were initially diagnosed and treated at Shandong Cancer Hospital and Institute (Jinan, China) in 2009. the clinical features of 539 cases of patients, including male 351 cases (65.1%) , female 188 cases (34.9%).The maximum and minimum age were 88 and 19 years old, respectively. The average age was 58.51and the median age was 59, but the age less than 60 years old was 282 cases (52.3%).The main symptoms were cough, sputum, blood in phlegm, chest pain, chest tightness, holding breath, fever and extrapulmonary symptoms. The shortest duration of patient delay in presenting to a doctor was 3 days and the longest was 24 months, the average time was 2.36 months and the median time was 2.0 months. The pathological type and/or cytology: adenocarcinoma, squamous carcinoma, small cell carcinoma, large cell carcinoma, Adenosquamous carcinoma and other types were respectively 377 cases (69.9%), 95 cases (17.6%), 50 cases (9.3%), 9 cases (1.7%), 5 cases (0.9%) and 3 cases (0.6%). The metastases from one single organ and multiple organs were 393 cases (72.9%), 146 cases (27.1%), respectively. Single organ metastasis such as pleura, brain, bone, lung, liver, adrenal metastasis is respectively 112 cases (28.5%), 100 cases (25.4%), 78 cases (19.8%), 60 cases (15.3%), 29 cases (7.4%), 14 cases (3.6%). The Kaplan Meier method and multivariate Cox regression analysis were performed to analyse the influence of age, predominant symptoms, pathological classification, transferred organs, treatment strategy on patient's overall survival. **Results:** The 1, 2 and 3 year survival rates were 64.2% (346 cases), 19.7% (106 cases) and 1.5% (8 cases),respectively. The liver metastases were poor prognosis and the bone metastases were relatively well. The prognosis of single brain metastasis is relatively better than that of multiple brain metastases. The radiotherapy doses of brain metastases tumor were positively correlated with survival, and radiation dose more than 6000cGy was better than that of less than 6000cGy. Multi-factor analysis showed that the patient's age, different organs transferred, The number of transferred organs and treatment were independent risk factors on survival. **Conclusion:** The clinical symptoms of patients with Ⅳ stage lung cancer are diversiform and have no specificity. The duration of patient delay in presenting to a doctor and the prognosis is poor. The patient's age, different transferred organs, the number of organs transferred, and treatment affect patient's survival. **Keywords:** diagnosis, Therapy, Prognosis, Carcinoma, lung

**PUB016 Bevacizumab Combined Chemotherapy Significantly Improved PFS and ORR of Patients with Advanced Non-Small Cell Lung Cancer** Hua R. Guo, Yi X. Lu, Cheng C. Xiang *Oncology, The First Affiliated Hospital of Nanjing Medical University, Nanjing/China*

**Background:** This study aimed to explore whether bevacizumab concomitant with pemetrexed and platinum could offer benefits for patients with advanced NSCLC by observing their influence on the clinical antitumor efficacy, survival time and safety. **Methods:** Patients with stage IIIB/IV, recurrent, or metastatic histologically- or cytologically- confirmed non-squamous non-small cell lung cancer (ns-NSCLC), 25-76 years of old, performance status 0-2, were treated with platinum-based pemetrexed (500 mg/m2) and bevacizumab (7.5 mg/kg) on day 1 of a 21-day cycle until disease progression, unacceptable toxicity occured, or patients asked for treatment withdrawal. The primary end point of this study was the response rate (RR) and disease control rate (DCR). **Results:** Between October 2011 and November 2014, 33 patients were enrolled (72.7% male, 93.9% adenocarcinoma, median age was 56 years), out of whom thirty-two patients were included in the response analysis. Combination therapy was delivered for a median time of 4.35 cycles (95%CI=3.14-5.57cycles), overall response rate was 50% (95%CI=31.9%-68.1%) and disease control rate (CR+PR+SD) was 90.625% (95%CI=75.0%-98.0%). Median Progression-free survival (PFS) was 6.23 months (95 % CI 4.80–7.66 months). All patients were evaluable for toxicity analysis. Grade 3 or higher adverse events included leukopenia (3.03%), anemia (6.06%), bleeding (3.03%), infection (6.06%) and anorexia (3.03%). No patient experienced drug-related deaths. **Conclusion:** The addition of bevacizumab to chemotherapy of pemetrexed and platinum can significantly improve PFS and ORR in treatments of advanced NSCLC, with an acceptable risk of bleeding events, hypertension and proteinuria. However, whether bevacizumab plus pemetrexed and platinum can prolong OS need further validation. **Keywords:** NSCLC, bevacizumab, chemotherapy

**PUB017 A New Approach for Management of EGFR TKI's Skin Rash Toxicities** Alberto Fulvi[1], Maria C. Romano[2], Serena Ricciardi[1], Maria R. Migliorino[1] [1]*Department of Respiratory Disease, San Camillo-Forlanini High Specialization Hospitals, Rome/Italy,* [2]*Dermatological Unit, San Camillo-Forlanini High Specialization Hospitals, Rome/Italy*

**Background:** EGFR tyrosine kinase inhibitors (EGFR-TKIs) are commonly associated with a large number of skin adverse events. Strategies to manage those adverse effects are essential to increase patient's compliance, quality of life, and overall outcome of the treatment. Through a proper and early management, EGFR TKIs may provide a less

toxic treatment option for patients suffering from advanced NSCLC. **Methods:** Between January 2014 and March 2015, 42pts with common EGFR mutation (exon 19 and 21) were treated with TKI's, 35 with irreversible inhibitors and 7 with reversible. Skin's toxicity of each patient is carefully monitored every 15 days in our DH through periodic checks carried out by a multidisciplinary team, which includes a dermatologist, in order to prevent skin toxicity grade 3-4. The inflammation and the alteration of the corneum stratum was treated with water- free unguents, made from vegetable oil (containing no mineral oil (petroleum) or steroids) as well as antibiotic local cream. We use oral antibiotic and steroid only very occasionally. Skin's toxicity was evaluated according to the System of CTCAE 2014. We evaluated the skin's toxicity of our patients with a proactive approach from the beginning to the end of the TKI's treatment, as well its modification over the course of time. **Results:** Rash has appeared in all pts within 2 wks as of the beginning of the treatment. G3 skin toxicity was detected in 3% of the pts treated with irreversible TKI and in 1% of the other group. No pts had to stop the treatment for more than 3 days because of dermatological toxicity. **Conclusion:** Our observation has demonstrated that a proactive dermatological approach could reduce the percentage of treatment suspension and skin's toxicity grade. Strategies to improve the management of EGFR TKI related adverse events should improve clinical outcomes, compliance, and QoL in patients with advanced NSCLC. **Keywords:** Skin Toxicity TKIs

**PUB018 The Efficacy of Erlotinib as Molecularly Targeted Maintenance Therapy in Advanced (NSCLC) Case Reports in Western Iran** Mehrdad Payandeh, Masoud Sadeghi, Edris Sadeghi *KUMS, Kermanshah/Iran*

**Background:** In developing countries, majority of cancer patients have low income. Therefore, we could hardly do maintenance therapy about the number of patients with non-small-cell lung cancer and other cancers. Maintenance therapy for advanced non-small-cell lung cancer (NSCLC) refers to the use of an effective agent in the absence of disease progression following platinum-based combination chemotherapy to improve progression-free survival. In our Clinic, we identified three cancerous patients with metastasis for lung cancer. The Epidermal Growth Factor Receptor mutation on exon 19 started erlotinib therapy for several courses. After a short time, in all patients, lesions decreased and patients became stable. **Methods:** Case reports **Results:** of the study suggested that first of all, these case reports show that maintenance therapy with erlotinib according to molecular markers (TTF-1 and kind of EGFR mutation) can help survival rate in patients. Second, in this report illustrates erlotinib may to cross the blood-brain barrier. **Conclusion:** Our department of oncology is in Kermanshah province, which is one of western provinces in IRAN, and neighbor with Iraq country. In 2009, a study [8] showed that health care payments in western Iran, compared with other developing countries in Asia, are very high. Majority of peoples this province and surrounding provinces are rural and living in (IRAN-IRAQ) war zone. In 2012, Rostaei S et al. [9] reported that 43% of people in Kermanshah city are below the poverty line. Therefore, majority of cancer patients may have low income ($35 - $150 per month). In recent years, due to sanctions on Iran, and since majority of patient samples should be sent to Tehran (capital of Iran) for further evaluation, diagnosis, treatment and drug costs have had a huge increase. Despite financial limitations for majority of patients, because of appropriate clinical facilities in Kermanshah province compared to the neighboring provinces, the number of patients referred to our clinic is very high, and over a few past years we could do maintenance therapy for the number of wealthy cancer patients. In this way, so we could stable lung cancer for three patients (top case reports). **Keywords:** Brain blood barrier, EGFR mutation, Maintenance therapy, NSCLC, TTF-1

**PUB019 Randomized Study of Two Schedules of Oral Vinorelbine in Advanced NSCLCr Patients Unfit for Platinum-Based Chemotherapy** Filippo De Marinis[1], Renan Fougeray[2], Carole Levrault[2], Marcello Riggi[2] [1]*European Institute of Oncology, Milan/Italy,* [2]*Pierre Fabre Medicament, Boulogne Billancourt/France*

**Background:** Chemotherapy with a single agent is an appropriate therapeutic option suitable for a large number of patients with advanced NSCLC who are unfit for a platinum-based chemotherapy because of comorbidities, cardio-vascular problems, creatinine clearance decrease and age when it is correlated with functional impairment .Among available drugs, oral vinorelbine (NVB) at weekly doses is suitable for patients unfit for platinum-based chemotherapy. Oral metronomic NVB has been tested in phase I trials at 50 mg three times a week (Monday-Wednesday-Friday), highlighting the excellent safety of this scheme. On the basis of these grounds, patients with advanced NSCLC unfit for platinum-based chemotherapy are randomized to receive either metronomic or weekly oral NVB as first-line single agent treatment. **Methods:** Open label, prospective, multicentre, randomized Phase II study (1:1), with 83 randomised NSCLC patients per arm defined unfit for a platinum-based chemotherapy based on at least one or more of the following criteria: Previous adjuvant platinum-based chemotherapy for resected NSCLC; Creatinine Clearance < 60 ml/min; Heart Failure NYHA class II-III; Hearing Loss > Grade 2 ; Medical condition impairing platinum-based chemotherapy according to physician's opinion. Primary Objective is Progression Free Survival (PFS) without Grade 4 toxicity (G4PFS) in both arms. Arm A: metronomic schedules: Oral vinorelbine 50 mg three times weekly. Arm B: weekly schedules: Oral vinorelbine: 60 mg/m$^2$ weekly, for cycle 1, then 80 mg/ m$^2$ weekly. Both treatments are delivered until progression. The study accrual is planned to start on T3/2015 for a duration of 24 months**Results:** not applicable **Conclusion:** not applicable **Keywords:** Advanced NSCLC, Chemotherapy, Metronomic

**PUB020 Systemic and CNS Activity of Combined RET and mTOR Inhibition in RET Re-Arranged NSCLC** Vivek Subbiah[1], Michael Roxas[2], Siraj M. Ali[3], Zhenya Zhenya[2], John V. Heymach[2] [1]*Investigational Cancer Therapeutics, UT MD Anderson Cancer Center, Houston/United States of America,* [2]*MD Anderson Cancer Center, Houston/United States of America,* [3]*Foundation Medicine, Boston/MA/United States of America*

**Background:** In-frame fusion RET transcripts have been characterized in 1-2% of non-small cell lung cancers and are known oncogenic drivers. The RET tyrosine kinase inhibitor, vandetanib, suppresses fusion-induced, anchorage-independent growth activity. A retrospective evaluation of RET biomarker status and outcome to vandetanib monotherapy in four phase III randomized NSCLC trials failed to show any differential advantage in RET fusion patients. We hypothesized that combined RET and mTOR pathway inhibition may overcome the innate and/or acquired resistance to RET-targeted monotherapy.Moreover,*in vitro* studies with a co-administration of vandetanib and everolimus was shown to enhance the brain accumulation of vandetanib by modulating P-gp/Abcb1- and Bcrp1/Abcg2-mediated efflux. We designed a phase 1 trial combining vandetanib and everolimus. **Methods:** Fluorescence in situ hybridization (ISH) of paraffin-embedded tissue sections was performed using a clear-view FISH RET dual-color breakapart probe from Cymogen DX. Hybridization capture of 315 cancer-related genes plus introns from 28 genes often rearranged or altered in cancer was applied to >50 ng of DNA extracted from samples and sequenced to high, uniform coverage in a CLIA certified lab ( Foundation medicine, Boston, MA). Therapy was given in the context of a phase I clinical trial vandetanib (300 mg Q daily) and everolimus (10 mg Q daily) ClinicalTrials.gov Identifier (NCT01582191). **Results:** Among > 50 patients with NSCLC screened for RET rearrangement, a deletion of 5'-RET (red signal) was observed in four patients with NSCLC, indicating a RET gene rearrangement. Comprehensive genomic profiling confirmed RET fusions in 3 patients (*KIF5B-RET* n=2; CCD6-RET,N=1). Druggable co-occurring alterations included *AKT2* amplification in 1 patient and full homozygous loss of *CDKN2A/B* in 2 patients. Patients have been enrolled on the vandetanib/everolimus clinical trial and have tolerated therapy (G1 diarrhea, G1 mucositis). The patient with co-occurring *AKT2* amplification completed 2 cycles. Re-staging MRI brain showed a decrease in the intracranial disease burden and PET/CT showed systemic response. Re-staging 3 patients is pending. Biopsies at the time of progression are planned. **Conclusion:** The combination of vandetanib and temsirolimus demonstrated both cns and systemic activity in a patient with ret fusion NSCLC. Further evaluation of this regimen is ret fusion NSCLC is in progress **Keywords:** Everolimus, RET, mTOR, Vandetanib

**PUB021 Bone Metastasis in EGFR Mutant Non-Small Cell Lung Cancer** Shu-Mei Huang[1], Jin -Ji Yang[2], Yi-Sheng Huang[2], Hua-Jun Chen[2], Xiao-Yan Bai[2], Qing Zhou[2], Han-Yan Tu[2], Yi-Long Wu[2] [1]*Guangdong Lung Cancer Institute, Guangdong General Hospital ,Second Clinical Medical Committee, Southern Medical University, Guangzhou/China,* [2]*Guangdong Lung Cancer Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou/China*

**Background:** To elucidate factors affecting overall survival (OS) and skeletal related events (SREs) on EGFR mutant NSCLC patients with bone metastasis. **Methods:** Data of patients from Guangdong General Hospital who were diagnosed EGFR mutant advanced stage NSCLC between June 1st 2002 and May 31st 2012 were retrospectively collected. Patients were excluded who were confirmed secondary primary carcinoma within two years of the diagnosis of advanced stage NSCLC. Variables were collected including age at diagnosis, gender, performance status, smoking status, histology, EGFR mutation status, treatment strategy for entire patients and location, amount, property, SREs and zoledronic acid for patients with bone involvement. Patients were stratified by initial diagnosis into three cohorts: extraosseous metastasis, both bone and extraosseous metastasis, and only bone metastasis. Kaplan-Meier survival curve was conducted for survival and Log-rank analysis was conducted for cohort comparison. Univariate and multivariate analysis of survival were conducted by a backward Wald Cox-regression model. Risk factors of SREs were analyzed using a backward Wald logistic regression model. **Results:** Throughout disease courses, 55.9% (287 of 513 patients) were found bone involvement, of which 17.8% with extraosseous metastasis, 57.8% with both bone and extraosseous metastasis and 24.4% with only bone metastasis. 40.8% of bone lesions were osteoblastic (117 of 287 cases) Both bone and extraosseous metastasis at diagnosis was related to a significantly decreased survival (for the three cohorts, mOS (95% CI), 29.0m (24.5m,33.5m), 17.0m (14.8m,19.2m) , 24.0m (19.5m,28.5m), respectively; $p<0.001$ )) (Figure 1) In multivariate analysis using Cox-regression, male gender and both bone and extraosseous metastasis at diagnosis (HR for both bone and extraosseous at diagnosis 1.982[95%CI 1.381, 2.846];$p<0.001$) indicated a poorer prognosis of overall survival for patients with bone metastasis In multivariate analysis using logistic regression , bone symptoms at diagnosis, and osteolytic lesions (OR for osteolyticlesions 2.164 [95%CI 1.200, 3.903];$p=0.010$) indicated higher risks of SREs, and EGFR-TKIs treated as first line had a lower risk of SREs (OR for EGFR-TKIs treated as first line 0.579 [95%CI 0.322, 1.041]; $p=0.068$), administration of zoledronic acid (63 of 287 cases) was of no statistical significance in both univariate and multivariate analysis

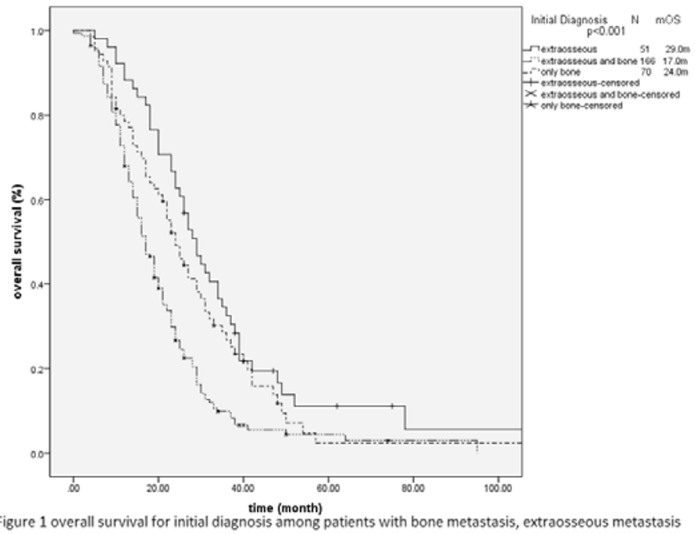
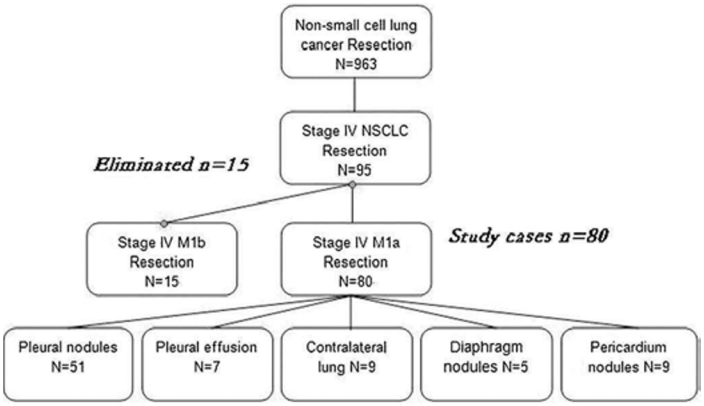



Figure 1 overall survival for initial diagnosis among patients with bone metastasis, extraosseous metastasis at diagnosis, both bone and extraosseous metastasis at diagnosis, and only bone metastasis at diagnosis.

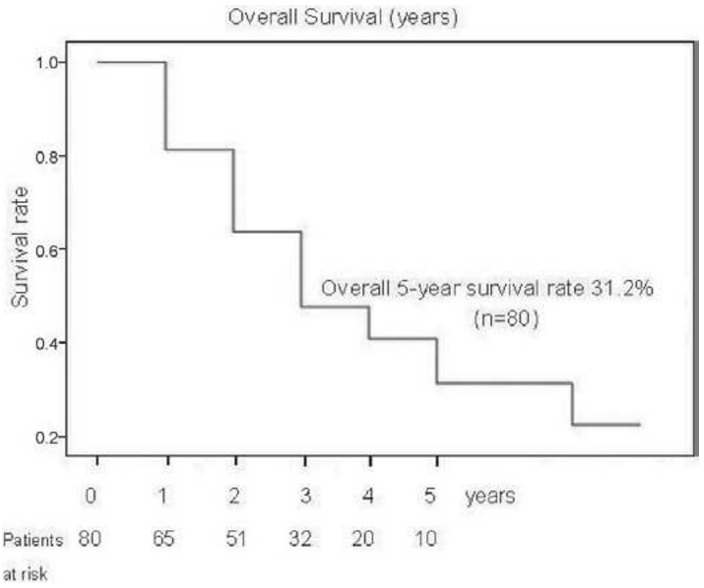
**Conclusion:** Both bone and extraosseous metastasis at diagnosis is a poor prognostic factor for overall survival. EGFR-TKIs treated as first line decreases the risk of SREs. **Keywords:** skeletal related events, non-small cell lung cancer, EGFR mutation, bone metastasis

**PUB022 Survival of M1a Non-Small Cell Lung Cancer Treated Surgically**
Tieqin Liu, Hongxu Liu *Thoracic Surgery, First Affiliated Hospital China Medical University, Shenyang/China*

**Background:** Stage IV non-small cell lung cancer (NSCLC) usually has a poor prognosis and surgical procedure is rarely success. This study aimed to retrospectively investigate the effectiveness of surgical treatments to these patients. **Methods:** The outcomes of 80 NSCLC M1a patients with a median age of 58 years (range 38 to 80 years) were analyzed retrospectively after surgery. Eight parameters were used for assessment including age, gender, smoking, current drinking, metastatic location, pathology type, resection condition status, and adjuvant treatment which may impact the survival time of patients.




**Results:** Eighty patients (49 males, 61%) with a median age of 58 (range, 38–80) were included. Metastatic sites included: pleural nodules with or without effusion metastasis (51, 63.8%), pleural effusion without nodules (7, 8.8%), contralateral lung (9, 11.3%), diaphragm nodules metastasis (5, 6.3%), and pericardium nodules metastasis (8, 10%). Histology was adenocarcinoma in 55, squamous-cell carcinoma in 16, large cell in 5 and other in 4 patients. Types of lung resection performed for primary tumors were complete resection in 43 and limited resection in 37 patients. Survival at 5 years for the overall population reached 31% (95% confidence interval, 19.4–43%). The median overall survival time was 34.3 months. Ten (12.5%) patients survived for more than 5 years. Smoking status and postoperative adjuvant treatment were independent prognostic factors (p =0.006 and 0.013). There was no impact on survival for the other six variables.




**Conclusion:** Surgical treatments for NSCLC M1a patients demonstrated better survival status than that described in the most of previously publications and might be adopted in well selected patients who were in good performance status. Nonsmoking histology may be regarded as a beneficial predictor to survival time in these patients. **Keywords:** Local metastasis, non-small cell lung cancer, Surgical resection

**PUB023 Survival of Patients with Non-Small Cell Lung Cancer and Its Relation with Clinical Trial Enrollment**
Carlos A. Carmona[1], Eleazar O. Macedo[2], Laura-Alejandra Ramírez-Tirado[3], Oscar Arrieta Rodriguez[4] [1]*Internal Medicine, Medica Sur Foundation and Clinic, Mexico/Mexico,* [2]*Unit of Thoracic Oncology, Department of Medical Oncology, Instituto Nacional de Cancerología México D, F., México Distrito Federal/ Mexico,* [3]*Laboratory of Experimental Oncology, National Cancer Institute, Mexico, Df/ Mexico,* [4]*Laboratory of Experimental Oncology and Thoracic Oncology Unit, National Institute of Cancer, Mexico City/Mexico*

**Background:** Lung cancer remains the leading cause of cancer-related death for both genders worldwide. Oncological up-to-date management has been made, traditionally, through the development of Randomized Clinical Trials (RCT). Therefore, treatment within clinical trials have also been seen as another promising therapeutic alternative for patients as it has been strengthened the scientific evidence on the limited antitumor efficacy of the traditional chemotherapeutic approaches. The clinical effect of patients due to the enrollment on clinical trials has been a subject poorly studied. However, the results with respect to clinical benefit associated with whether or not patients have been enrolled on a trial have been inconsistent. The aim of this study was to analyze the survival of patients with non-small cell lung cancer and its relation to clinical trial enrollment. **Methods:** Patients from the Thoracic Oncology Unit at Instituto Nacional de Cancerologia of Mexico were included in the study. Data was collected from medical records included demographic and clinical characteristics, participation in a clinical trial. Comorbidities, chemotherapy treatment, disease stage, histology, presence of brain metastasis, and survival details were collected from medical records and were updated over time. Multivariable survival analyses using Cox regression were conducted to determine the association between enrollment in a clinical trial and survival adjusting for age, comorbidities, presence of brain metastasis, stage IIIB versus IV, and cancer histology. **Results:** There were 1042 patients of which, 295 were on a clinical trial and 747 outside of it, there were no statistically differences when comparing age, gender, disease stage, ECOG-PS, wood smoke exposure and Kras status. There were statistically significant differences in adenocarcinoma histology ($p$= 0.001), Tobacco use ($p$= 0.004), EGFR mutation ($p$= 0.001) and the presence of brain metastases ($p$= <0.001). For the whole group, median OS at one-year survival were 22.1 months (18.6 - 25.7). The differences in median OS at one-year between the groups were significant (18mo (14.5–21.6mo) *vs.* 30.1mo (21.0-40.3mo)$p$=0.0001) in favor to on-trail patients. When multivariate analysis was conducted the patients enrolled in a trial showed HR of 2.22 [95% CI 1.38 - 3.58] $p$=≤0.0001. For the whole group, patients who received second line chemotherapy had better OS ($p$=≤0.0001). More patients in the trial group received second line chemotherapy ($p$=0.0004). The difference in the median OS between the groups continued to be significant even after patients who received second line chemotherapy were censored ($p$= 0.001). **Conclusion:** Patients with lung cancer who participate in clinical trials at our institution have improved survival compared with those who are treated with standard therapies. No other factors examined were associated with treatment completion or survival. Improved survival. Despite the significant difference in the presence of EGFR mutation that could explain differences in survival outcomes, being enrolled in a RCT has a significant improved survival after multivariate analysis. So patients with cancer should be encouraged to enroll in clinical trials on the basis that those enrolled has better outcomes. **Keywords:** Survival, NSCLC, enrollment, clinical, trial

**PUB024 Bone Metastases in Non-Small Cell Lung Cancer: A Retrospective Study** Puneet K. Bagri, Saurabh Samdariya, Puneet Pareek *Radiation Oncology, AIIMS, Jodhpur/India*

**Background:** Bone is one of the most common sites of metastasis in patients with advanced cancer. Bone metastases often cause skeletal-related events (SREs). Despite advances in the treatment of primary lung cancer, SREs still affect many patients. The aim of this retrospective study to investigate the clinical impact of SREs, and to compare differences in the therapeutic outcome between patients with and without bone metastases or SREs. **Methods:** 512 patients with histologically proved nonsmall cell lung cancer (NSCLC) who consulted the department of Oncology at Regional cancer institute between May 2009 and July 2011. We assessed their TNM stage, presence of bone metastases (on bone scan, CT/MRI, and plain X-ray films), and outcome parameters such as SREs, analgesic use, and survival. **Results:** A total of 164 patients (32.03%) were found to have skeletal metastases during their clinical course and 96 patients (58.54%) out of all 164 patients had SREs. Among 315 stage IV patients, a total of 147 (46.67%) had bone metastases, and 72 of these 147 patients (48.98%) had SREs. The most common SREs were the need for radiotherapy (48%). Patients with SREs tended to have worse survival, while no significant difference of survival was observed between patients with and without bone metastases. **Conclusion:** It seems to be important to prevent SREs during the treatment of NSCLC, so further studies evaluating bisphosphonates in combination with chemotherapy are warranted. **Keywords:** NSCLC, Bone metastasis, Skeletal-related events

**PUB025 Effect of the Newcastle Disease Virus with NP Regimen for Patients with NSCLC** Ying Hua[1], Xiujuan Tao[2] [1]*Shandong Cancer Hospital and Institute, Jinan/China,* [2]*Oncology, Liaoning Cancer Hospital, Shenyang/China*

**Background:** not applicable' **Methods:** A total of 140 patients with advanced NSCLC were enrolled in the study. The patients were randomized to experimental and control groups. Newcastal disease virus combined with NP regimen was given to the experimental group, and the NP regimen only was given to the control group .The chemotherapy was performed for four cycles every 28 days. The therapeutic efficacy was evaluated every 2 cycles.The following indications were observed : level of hemoglobin, white blood cell ,platelet, Tcell subpopulation ,as well as short-term sfficacy, adverse effects, and QOL. **Results:** The response rate in the experimental and control group were 50.68% and 41.10%, respectively. The CD4/CD8 ratio increased in the experimental group but decreased in the control group. **Conclusion:** The newcastle disease virus combined with the NP regimen showed a better therapeutic effect. **Keywords:** carboplatin, newcastle disease virus, NSCLC, drug therapy

**PUB026 The Value of Intraoperative Frozen Section of Lymph Nodes in the Surgery of Non-Small Cell Lung Cancer** Wei Li, Wen-Zhao Zhong, Xue-Ning Yang, Song Dong, Ri-Qiang Liao, Qiang Nie, Yi-Long Wu *Guangdong Lung Cancer Institute, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou/China*

**Background:** This paper discusses the value of intraoperative rapid pathology of the lymph nodes in non-small cell lung cancer(NSCLC) treatment. **Methods:** From 2010 to 2014, 2057 lung cancer patients received thoracotomies at the Guangdong Lung Cancer Institute (GLCI). Patients had their first station (station N1) draining lymph nodes screened according to the location of the tumor and/or suspected metastatic lymph nodes with the naked eyes for frozen pathology. Analysis of the preoperative radiological staging (cN), intraoperative frozen pathological stage (sN), postoperative pathological staging (pN), pseudo operation mode, actual operation mode, intraoperative lymphadenectomy or lymph node sampling was conducted. The corresponding rate of preoperative, intraoperative, and postoperative N staging and the effects of lymph node frozen pathology on the operation mode of non-small cell lung cancer were explored. **Results:** In 74 lung cancer patients with submitted frozen lymph nodes, the coincidence rate of preoperative imaging cN staging and intraoperative frozen pathological sN staging was 62.2% (46/74); the coincidence rate of preoperative imaging cN staging and postoperative paraffin pathological pN staging was 63.5% (47/74); the coincidence rate of intraoperative frozen pathological sN staging and postoperative paraffin pathological pN staging was 71.6% (53/74); and the positive rate of intraoperative lymph node rapid pathology was 18/74 (24.3%). According to the frozen lymph node results combined with pulmonary function in patients with other diseases, the operation process, intrathoracic adhesions and operation strategy were adjusted in 18 cases (five cases of sN positive, 13 cases of sN negative) during the operation. Among these patients, nine had a lung parenchyma resection, including five patients with an enlarged pulmonary parenchymal resection range (one case of left pneumonectomy, one case of right middle and lower lobectomy, and three cases of right upper and middle lobectomy) and four patients with a reduced lung parenchyma resection (one case of left upper lung lymph node sampling + R2 resection, one case of left pulmonary lobectomy, and two cases of pulmonary wedge resection). Nine patients had changed the scope of lymph node dissection (the scope of the lymph node dissection was narrowed in all cases). **Conclusion:** Pathological examination of frozen lymph nodes may change the range of pulmonary parenchyma resection and the degree of lymph node cleaning, Which needs further exploration.

**PUB027 Surgery vs SBRT for Early-Stage Non-Small Cell Lung Cancer: A Meta-Analysis** Melina Shoni[1], Michiel Ijsseldijk[2], Charles Siegert[3], Jan Seegers[2], Ton Van Engelenburg[2], Thomas Tsai[1], Richard Ten Broek[2], Abraham Lebenthal[1] [1]*Surgery, Brigham and Women'S Hospital, Boston/United States of America,* [2]*Surgery, Slingeland Hospital, Doetinchem/Netherlands,* [3]*Surgery, Brigham and Women'S Hospital, Boston/AL/United States of America*

**Background:** Lobar resection (LR) is considered the standard of care for patients diagnosed with early-stage (I and II) non-small cell lung cancer (NSCLC). Recent studies indicate that less invasive treatment options, such as sublobar resection (SR) (segmentectomy or wedge resection) and stereotactic body radiation therapy (SBRT) may have similar oncologic efficacy. Elderly and medically 'inoperable' patients pose a therapeutic challenge and may benefit from limited therapy. To overcome the high heterogeneity of studies published on this matter, we conducted a systematic review and meta-analysis to properly compare the oncologic and survival outcomes of LR, SR and SBRT in stage I-II NSCLC. **Methods:** A systematic search of published literature was conducted using the main databases [MEDLINE, PubMed, EMBASE, Web of Knowledge Search and Cochrane Central Register of Controlled Trials (CENTRAL)] to identify pertinent clinical trials and cohort studies published up to December 2014. Two independent researchers performed the screening and selection of the eligible studies, utilizing the early review organizing software (EROS). We only considered peer-reviewed articles studying cohorts with ≥ 20 patients, ≥ 85% biopsy-proven treated lesions, ≥ 24 months follow up time and reporting relevant survival data. Articles published prior to 2000, non-English, including neo-adjuvant therapies, as well as conference abstracts were excluded. The inverse variance method and the random effects method for meta-analysis were utilized to assess the pooled overall survival (OS) estimates of individual studies and their corresponding 95% confidence interval (CI). **Results:** A total of 5230 non-duplicate records were identified by the original search strategy. After screening by title and abstract, 720 potentially eligible records were identified. Only 141 articles finally met the inclusion criteria and underwent subsequent analysis. Pooled data for the surgical arm included 26373 patients with a median age of 65.5 years undergoing LR, and 6616 patients with a median age of 70.6 years undergoing SR. Pooled data for the SBRT arm included 2151 patients with a median age of 74.5 years and treated with a total radiation dose range of 36-72.5 Gy. The 3-year OS was: **79%** for LR (95% CI: 75%-84%), 79% for SR (95% CI: 61%-96%), and **63%** for SBRT (95% CI: 55%-71%). Statistical significance was seen only between LR and SBRT arms. The survival gap significantly widened for 5-year survival: LR **73%** (95% CI: 59%-86%), SR **64%** (95% CI: 45%-83%), SBRT **44%** (95% CI: 31%-57%). These differences were maintained when controlled for age. **Conclusion:** In early-stage NSCLC, our meta-analysis demonstrates an unequivocal survival superiority of LR over SBRT at 5 years. To date, the best pooled results of SBRT at 3 years are still inferior to LR at 5 years. Thus, SBRT should be only offered to patients who are medically unfit as a possible alternative to surgery.

**PUB028 How Does 4DCT Spare Normal Tissues in NSCLC Radiotherapy by Defining ITV?** Jian Zhu, Yong Yin *Radiation Oncology Physics, Shandong Cancer Hospital & Institute, Jinan/China*

**Background:** To investigate how does the four-dimensional CT (4DCT) technique spare normal tissues in non-small cell lung cancer (NSCLC) radiotherapy by defining individualized internal target volume (ITV). **Methods:** GTV and CTV were contoured on all 10 respiratory phases of 4DCT scans in 10 patients with peripheral NSCLC. Both 3D and 4D treatment plans were performed for each patient using PTV3D (derived from a single CTV plus conventional margins) and PTV4D (derived from ITV4D, which included all 10 CTVs plus setup margins). DVH and NTCP values were compared for lung, heart and spinal-cord between 3D and 4D treatment plans. **Results:** The average PTV volume of the 4D plans (127.56±70.79) was less than 3D plans (147.65±76.89). The 4D plans spared more surrounding normal tissues than 3D plans, especially lung. Compared with 3D plans, V5, V10, V20 and V30 of total lung decreased from 41.25%, 37.75%, 24.25%, 17.00% to 38.13%, 33.00%, 21.25%, 15.13% respectively. Without increasing the NTCP of lung significantly, the 4D plans allowed to increase the average prescription dose from 60Gy to 66.00±4.62Gy. **Conclusion:** The 4DCT based plans can reduce the target volumes, spare more normal tissues and allow dose escalation compared with 3D plans in NSCLC radiotherapy. **Keywords:** internal target volume, dosimetry, non-small cell lung cancer, 4DCT

**PUB029 Manage of Vascular Injury in VATs LOBECTOMY** Yun Li *Department of Thoracic Surgery, People's Hospital of Peking University, Beijing/China*

**Background:** Bleeding caused by vascular injury is one of the most critical intra-operative complications associated with minimally invasive surgery[1]. Thoracoscopic lobectomy is attracting more and more interest in the field of thoracic surgery in this representative minimally invasive procedure, this problem is more prominent[2-5]. The main procedure is completed by anatomic dissection of the blood vessels. The thoracic blood vessels have relatively thin and brittle walls compared to the blood vessels in other anatomic sites of human body. Therefore, vascular injury and subsequent intra-operative bleeding is a concern for every thoracic surgeon[6,7]. Intra-operative bleeding is difficult to handle and there have been no specialized reports regarding the management of intra-operative bleeding caused by vascular injury during thoracic lobectomy. We collected data from 1006 consecutive cases in our hospital over a period of approximately 6 years and analyzed various causes of vascular injury and corresponding treatment measures. **Methods:** From September 2009 to April 2013, 125 patients that the blood loss in VATs lobectomy were exceed 400ml (male=82,

female=43). The lobectomy consist of 42 right upper lobe, 9 right middle lobe, 19 right lower lobe, 40 left upper lobe and 15 left lower lobe. The procedure consist of 99 simple lobectomy, 4 lobectomy combine with partial chest wall resection, 16 compound lobectomy, 3 sleeve lobectomy with bronchoplasty and 3 pneumonectomy. The main procedure was completely video-assisted anatomical lobectomy with mediastinal lymphadenectomy. **Results:** Among 125 cases with > 400 ml of blood loss, there were 3 injury of pulmonary vein, 2 were repaired endoscopiclly and 1 case conversed to open thoracotomy to control bleeding and repair the vein. There were 13 injury of pulmonary artery, in 2 cases that the proximal trunk of ipsilateral pulmonary artery was blocked endoscopically and repaired artery endoscopiclly; in 11 case, conversed to open thoracotomy to control bleeding and repair the artery. There were 22 cases need blood transfusion in the operation or post-operation. All patients recovered well, 47 patients (36.0%) experienced a minor complication. **Conclusion:** injury of blood vessels was common and troublesome in completely thoracotomy lobectomy, and always lead to conversion to thoracotomy. The surgeon should deal with it based on the character of vessles, condition of injury and experience of the surgeon. **Keywords:** injury of blood vessls, VATs lobectomy, bleeding

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**PUB030 Sequence of Vessel Interruption in VATs Lobectomy for Early-Stage NSCLC** Yun Li *Department of Thoracic Surgery, People's Hospital of Peking University, Beijing/China*

**Background:** Surgical treatment is optimal for early lung cancer, but there are still 40-50% of patients who would suffer metastasis after the operation. How to improve the methods, reduce the incidence of metastasis, promote the surgical curative effect are the direction of thoracic surgeons. Besides, the effect of the cut order of blood vessels on the dissemination and accelerating metastasis is always the focus of discussion. Recently, most doctors suggest to cut vein first, and then artery, in the process of lung lobectomy. They think in this way dissemination will be reduced, which is matching the principles of surgery. However, there is no final conclusion yet. In contrast, those scholars who think should cut artery first, believe that it can reduce the bleeding. But some studies show that the two methods have the similar impact on cancer dissemination. The studies are all in a thoracotomy lobectomy, with relatively short follow-up time, fewer cases in the group, lack of hierarchical analysis, excessive interference factors in the control group, no strong enough markers.As a result, the conclusions remain to be further confirmed. This article is to study the curative effects of pulmonary arteriovenous cut order on stage Ⅰ～Ⅱ non-small cell lung cancer in the completely thoracoscopic lobectomy. **Methods:** From September 2006 to June 2013, 1337 patients underwent lobectomy in our hospital, including 334 cases of patients underwent completely thoracoscopic(VATs) lobectomy who were identified as stage Ⅰ～Ⅱ non-small cell lung cancer(NSCLC). They were divided into 3 groups according to the order of cutting the blood vessels, including vein cut first group (Group V) with 174 cases, artery cut first group (Group A) with 93 cases and Mixed group (Group M) with 67 cases,. The preoperative condition, operative factors and the prognosis of the three groups were reviewed. We compare with the survival and recurrent the patients. **Results:** All procedures were uneventful, with a median operative time of 181.7 min and a median blood loss of 128.0 mL. The three groups were similar in the age, main complication, cancer history, diameter, preoperative tumor markers and preoperative lung function, with fewer smokers and more lung Infestor in Group A. The average operative bleeding during operation was 105.1ml in Group A, which is more than Group V (148.3ml) and Group M (107.0ml). The three groups have the similar complication during and after the operation. The recurrent in three groups are all far distance metastasis. And there is no significant difference in disease free survival (DFS) and overall survival (OS). **Conclusion:** For the treatment of stage Ⅰ～Ⅱ non-small cell lung cancer in total thoracoscopy, to cut the pulmonary artery first could reduce the blood loss during VATs lobectomy, but it did not influence the surgical difficulty and postoperative complications. The sequence of blood vessels interruption has no influence in recurrence and prognosis. **Keywords:** Sequance of Pulmonary vessel Inerruption, VATs lobectomy, NSCLC

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**PUB031 Outcomes following Anatomical Resection for Lung Cancer in High Risk Patients** Henrietta Wilson, Tom Routledge, Karen Harrison-Phipps *Thoracic Surgery, Guy's Hospital, London/United Kingdom*

**Background:** Surgery remains the gold-standard for patients with resectable non-small cell lung cancer. Unfortunately, though improving, resection rates in the UK remain low (between 18 and 25%). Current guidance identifies patients with an estimated post-operative predicted (ppo) FEV1 or TLCO of less than 40% to fall within a high-risk cohort. Advances in surgical techniques and peri-operative care have however allowed surgeons to offer resection to selected patients within this group. The aim of this study was to determine the outcomes of anatomical resection in patients deemed high risk based on pulmonary function. **Methods:** A retrospective review of patients undergoing lobectomy or pneumonectomy between January 2013 and January 2015 was performed. Patients with a ppo FEV1 or TLCO of less than 40% were included. The main outcomes were post-operative complications (graded based on the Ottawa TM&M classification), admission to ITU, length of stay and 30 day in-hospital mortality. **Results:** Surgery was performed in 53 patients with a ppo TLCO or FEV1 less than 40% (median ppo TLCO 35%, median ppo FEV1 54%). Twelve patients had both ppo FEV1 and TLCO less than 40%. The median age was 70yr (range 39-86) with 57% (n=30) being female. Forty six patients underwent lobectomy with 52% performed thoracoscopically. Three patients underwent bilobectomy and four pneumonectomy. There was no operative mortality. Sixty four percent had no complications (n=34), twenty-six percent had one or more minor complication (n=14) and 9% had a major complication (n=5) as shown in table 1. Nine patients required admission to ITU with three being planned electively. Median length of stay was 7 days in the whole cohort and 5 days in the thoracoscopic group. One patient was discharged home on oxygen.

**Table 1: Summary of complications (Ottawa TM&M classification) and number of patients affected**

| | Grade I | Grade II | Grade IIIa/b | Grade Va/b |
|---|---|---|---|---|
| **Pulmonary Complications** | | | | |
| Pneumonia | | Antibiotic therapy only = 7 | | Requiring intubation = 1 |
| Atelectasis | | | | Requiring intubation = 1 |
| **Pleural Complications** | | | | |
| Prolonged airleak | | > 5 days but no further intervention = 3 | | |
| Empyema | | | Surgical intervention under GA = 1 | |
| **Cardiac Complications** | | | | |
| AF | Cardioversion with correction of electrolytes = 2 | Cardioversion following medication = 4 | | |
| Myocardial ischaemia | | | | Associated with single organ failure = 1 |
| **Renal Complications** | | | | |
| UTI | | Medical therapy only = 1 | | |
| Acute kidney injury | No intervention required = 1 | | | |
| **Gastrointestinal Complications** | | | | |
| Ischaemic bowel | | | | Life-threatening requiring urgent surgery = 1 |

**Conclusion:** Anatomical lung resection can be performed safely in selected high risk patients based on pulmonary function without significant increase in morbidity or mortality. The majority of patients had an uneventful post-operative period or developed only minor surgical complications. Length of stay as expected was slightly longer than the average for all comers although this was lower following thoracoscopic surgery. Given that complications following lung resection are multi-factorial, fitness for surgery should be thoroughly assessed in all patients with resectable disease within a multi-disciplinary setting. High operative risk by pulmonary function tests alone should not preclude surgical resection. This approach combined with further research into sub-lobar resection may allow improved resection rates for non-small cell lung cancer. **Keywords:** Thoracic Surgery, Pulmonary function tests, lung cancer

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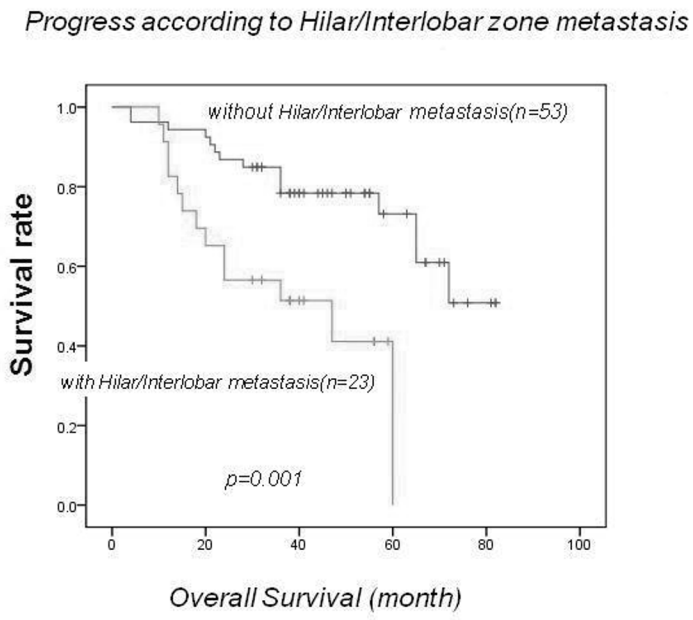
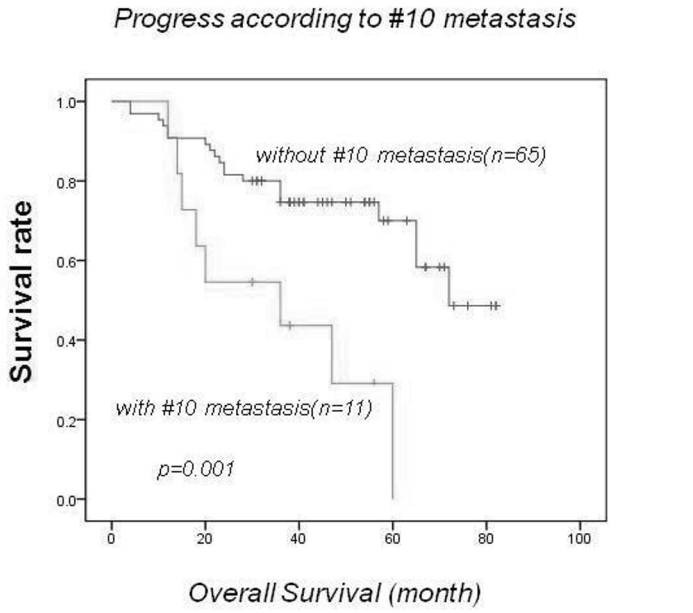
**PUB032 Prognostic Factors in Resected Pathological Right Middle Lobe Non-Small Cell Lung Cancer** Tieqin Liu[1], Hongxu Liu[2] [1]*Thoracic Surgery, First Affiliated Hospital China Medical University, Shenyang/China,* [2]*China Medical University, Shenyang/China*

**Background:** Patients (pts) with right middle lobe non-small cell lung cancer (NSCLC) were not well studied. This study analyzed the prognostic factors in resected pathological right middle lobe NSCLC. **Methods:** 76 pts with completely resected right middle lobe NSCLC were stratified on age, gender, smoking status, tumor diameter, metastatic status of lymph nodes and histologic subtype. The status of hilar /interlobar lymph nodes was assessed according to the seventh edition of the TNM classification for lung cancer. Overall survival (OS) as the primary endpoint was defined as the interval between surgery and death from the tumor or the most recent follow-up. Outcome was computed using Kaplan-Meier curves and correlation was assessed via Cox regression. **Results:** The median follow-up was 47 months. Overall, 28(36.8%) pts died during follow-up. The 1-, 3- and 5-year overall survival rates were 90.8%, 71.1% and 47%, respectively. No significant differences were noted in the age, gender and histologic subtype. There was a trend towards worse overall survival in those with larger tumor size (p=0.087). The lymph node metastases and active smoking inversely correlated with OS (50 vs. 34 month; p<0.001 and 41 vs. 38 month; p=0.029, respectively). There were 31 pts found to have hilar / interlobar zone lymph nodes metastases. This subgroup included 14 node 2 (N2) pts and 17 N1 pts. In N1 possive pts, the median overall survival was 40 months for the Hilar/ Interlobar zone positive cohort while 32 months for the negative cohort (P=0.123). In multivariate analyses, the presence of lymph node metastases (p<0.001) and smoking status (p=0.031) were revealed to be significant independent prognostic factors.




**Conclusion:** In a single institution cohort, we validate lymph nodal involvement and active smoking inversely correlated with OS in resected right middle lobe NSCLC. However, in N1 possive pts, the presence of Hilar/Interlobar lymph node metastases maybe protective predictor for survival. **Keywords:** Right middle lobe NSCLC; Lymph node metastasis; Hilar/interlobar zone metastases.

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**PUB033 Three-Incision versus Four-Incision Procedure of Video-Assisted Thoracoscopic Surgery Lobectomy for NSCLC: Ergonomic Comparison**

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**Background:** Presently, both three-incision and four-incision procedure are applied for video-assisted thoracoscopic surgery (VATS) lobectomy plus mediastinal lymph node dissection for non-small cell lung cancer. However, which procedure is superior remains uncertain. In this study, we aim to compare the two procedures from the aspect of ergonomic evaluation (operating efficiency, clinical outcomes and surgeons' working fatigue). **Methods:** From January 2014 to February 2015, a total of 129 patients with NSCLC who underwent VATS lobectomy plus mediastinal lymph node dissection were enrolled in this study. And 67 cases were performed in three-incision procedure (one surgeon and one thoracoscope holder), while 62 cases in four-incision procedure (one surgeon, one assistant and one thoracoscope holder). All operations were completed with the same type of operative devices by experienced surgeons. Clinical characteristics including patient demographics and operative outcomes were collected and compared between the two groups. Operating efficiency was compared by surgical time. The rating scale of musculoskeletal discomfort (score ranging from 0 (uninfluenced) to 100 (maximum fatigue, cease to rest)) was record preoperatively and postoperatively to evaluated the surgeons' working fatigue. **Results:** Two groups were comparable in patient demographics (age, gender, body mass index, ASA score, tumor location, histological type and clinical stage). There were 2 cases had conversion to thoracotomy (one in each group). In terms of operative features, four-incision group had a little shorter surgical time than three-incision (92±26 min versus 97±25 min, p=0.274), though no significant difference was confirmed. Besides, the clinical outcomes between two groups were similar, including blood loss (three-incision group vs four-incision group: 91±64ml vs 97±63ml, p=0.610), number of lymph nodes harvested (14.2±3.6 vs 14.0±3.6, p=0.722), postoperative hospital stay (6.7±2.5d vs 6.9±2.4d, p=0.545) and total complications (10.4% vs 11.3%, p=0.878). No 30-day mortality occurred in two groups. In terms of surgeons' fatigue evaluation, the increased score after surgery was much higher in three-incision group than four-incision group (left upper limb: 65.4±19.2 versus 42.4±14.2, p=0.000; right upper limb: 61.0±19.9 versus 55.3±13.4, p=0.018; shoulder-back: 39.1±12.5 versus 25.5±8.4, p=0.000).**Conclusion:** The study shows that both procedures are safely and effective for VATS lobectomy plus mediastinal lymph node dissection, though four-incision procedure could provide better ergonomic condition and less working fatigue for surgeons, compared with three-incision procedure. Therefore, surgeons could make their choice according to their own experience and habits. **Keywords:** Video-assisted thoracoscopic surgery, lobectomy, mediastinal lymph node dissection, Ergonomic Evaluation

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**PUB034 Weight Loss before Radical Chemoradiotherapy Is Associated with Poorer Survival Outcomes in Overweight Locally Advanced NSCLC Patients**

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**Background:** Presence of weight loss (WL) has been demonstrated to be associated with poor outcomes in locally advanced nonsmall-cell lung cancer (LA-NSCLC) patients. However, data regarding the impact of presentation with WL before radical C-CRT is scarce. Therefore, we aimed to investigate the impact of WL in radically treated overweight (body mass index>25 kg/m$^2$) LA-NSCLC patients. **Methods:** Medical records of 192 stage III NSCLC (squamous cell- or adenocarcinoma) patients with BMI>25 kg/m$^2$ those underwent platinu-based C-CRT between January 2007 and December 2014 were retrospectively analyzed. All patients received 60-66 Gy (2 Gy/fx; 5 days a week) three-dimensional conformal radiotherapy. Patients were dichotomized into 2 groups according to presence (WL+) and absence (WL-) of WL for comparative analysis. Primary end point was the overall survival difference between two groups. **Results:** Median age was 62 years (range: 36-74), 129 (67.2%) patients were male, 77% had stage IIIB disease, and 55.8% had squamous cell carcinoma.Median follow-up was 23.2 months (range: 4.7-83.2). Median and 5-year overall survival (OS) rates for overall study population were 23.6 months and 16.8%. Sixty-seven (34.9%) patients had WL before onset of C-CRT. (Patients with WL had significantly shorter median OS time (17.8 vs. 27.8 months; p< 0.001) and lower 5-year OS rates (3.8% vs. 21.3%; p< 0.001) than those patients without. This difference was significant across the stage (A vs. B), histology (squamous cell- vs. adenocarcinoma), and ECOG performance status (0-1 vs. 2). Multivariate analysis revealed that the presence of WL before C-CRT was independently associated with poorer survival in overweight LA-NSCLC (p<0.001). **Conclusion:** Presence of weight loss prior to C-CRT in overweight LA-NSCLC patients is associated with poorer survival outcomes indicating the importance of prevention of malnutrition and early use of nutritional support in such patients in an effort to preventor at least prolong the progress of anorexia-cahexia complex, and therefore, to prolong survival outcomes. **Keywords:** Overweight, Locally advanced NSCLC, Poorer Survival

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**PUB035 Phase III Study of Concurrent DDP with Pemtrexed or Vinorelbine and LACHRT Based on Normal Tissue for Unresectable Stage III NSCLC**

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**Background:** Concurrent chemoradiotherapy hasbeen the stadard management for unresectable stage III NSCLC. However, the outcome is not satisfactory yet. This phase III study was designed to evaluate cisplatin with pemtrexed or vinorelbine with concurrent late course accelerated hyperfractionated radiotherapy (LCAHRT) for the disease. **Methods:** Eligible patients were randomly assigned to two concurrent regimens: NP arm with cisplatin (DDP) at 25 mg/m$^2$ on days 1-3, 22-24 and vinorelbine at 25 mg/m$^2$ on days 1, 8 and 22, 29 with concurrent LCAHRT based on bilateral lungs V20 = 33%; DDP at 25 mg/m$^2$ on days 1-3, 22-24 and pemtrexed at 500 mg/m$^2$ on days 1 and 22 with the same radiotherapy protocol in PP arm. The primary endpoint was overall survival (OS) and secondary endpoints included progression-free survival (PFS) time and toxicities. **Results:** A total of 105 patients were enrolled in this study, and 100 ones analyzed for efficacy and safety. The median survival time (95% CI) was 27.0 (18.9-35.0) and 31.0 (13.8-48.1) months for NP and PP arm respectively. The PFS and 2-, 3-year survival rates were 12.0 months and 57.6%, 38.9% in NP arm, 19.0 months and 56.9%, 49.1% in PP arm. The median survival time (MST) of squamous cell carcinoma was 25.5 months, while non-squamous cell carcinoma was not reached in PP arm ($p$ = 0.163). The incidences of grade 3 to 4 neutropenia, hemotoblatin, and radiation pneumonitis were significantly higher in NP arm than those in PP arm regimen. **Conclusion:** Current study demonstrated that there was no

statistically significant difference in OS between the NP and PP regimens. However, the PP regimen resulted in significant reduction of toxicity and a trend in improvement of PFS in Chinese population with inoperable stage III NSCLC regardless of pathology. **Keywords:** chemotherapy, non-small cell lung cancer, Radiotherapy

**PUB036 Study on Predictive Factors of Anti-Angiogenesis Therapy Combined with Neoadjuvant Chemotherapy for Phase IIIA Non-Small Cell Lung Cancer**
Changli Wang *Department of Thoracic Oncology, Tianjin Medical University Cancer Institute & Hospital, Tianjin/China*

**Background:** To explore the therapeutic predictive factors of anti-angiogenesis therapy combined with neoadjuvant chemotherapy in the treatment of phase IIIA non-small cell lung cancer (NSCLC). **Methods:** Twenty-four patients with phase IIIA (N2) NSCLC were divided into trial group (n=16) and control group (n=8) according to the proportion of 2 : 1. Trial group was treated with NP+Endostar, while control group with NP chemotherapy alone. Administration method: Endostar (7.5 mg/m$^2$), intravenous dripping, d1∼14; vinorelbine (25 mg/m$^2$), intravenous dripping, d1 and d8; DDP (75mg/m$^2$), intravenous dripping, d1 ∼3, 28 days as one cycle. The efficacy was assessed after two cycles. Therapeutic evaluation indexes primarily include response rate (RR), clinical benefit rate (CBR) and tumor regression rate (TRR), and secondary indexes were disease-free survival (DFS) and overall survival (OS). **Results:** Compared with control group (40%, 60%, 9.1%), the overall RR of trial group increased by 10%, total CBR by 27.5% and TRR by 10%. After treatment, the blood flow (BF), permeability surfaces (PMS) and microvessel density (MVD) in serum vascular endothelial growth factor (VEGF) and CT perfusion indexes went down dramatically in trial group by comparison to treatment before ($P$<0.05). Significant differences were presented regarding VEGF and MVD before and after treatment ($P$<0.05). Endothelial progenitor cells (EPC), VEGF, BF, PMS and MVD in patients with clinical benefit (BF) in trial group changed dramatically before and after treatment, in which the changes of BF, PMS and MVD were the most significant ($P$<0.01). But compared with control group, the changes of EPC and MVD were more evident before and after treatment. The change rates of EPC, PMS and MVD in trial group were all correlated with tumor regression rate (TRR) positively ($P$=0.009; $P$=0.012; $P$=0.000), and those of EPC and PMS also had a positive correlation with MVD ($P$=0.049; $P$=0.022). **Conclusion:** Anti-angiogenesis therapy combined with neoadjuvant chemotherapy can improve the CBR of patients with phase IIIA NSCLC and reach the purposes of clinical down-staging and increased operation resection rate. Both PMS and EPC of CT perfusion imaging may be more effective and easier therapeutic predictive factors for combined therapy. **Keywords:** anti-angiogenesis; neoadjuvant chemotherapy; non-small cell lung cancer; Endostar, predictive factors

**PUB037 Age-Related Risk Assessment for Lung Cancer Surgery in Elderly Patients**
Nazar Lukavetskyy, Taras Fetsych *Oncology, Lviv Medical University, Lviv/Ukraine*

**Background:** The elderly population is heterogeneous, ranging from healthy seniors with no disability and few comorbidities to frail seniors who are disabled and have multiple comorbidities. This makes the assessment and management of this population challenging, especially when deciding on cancer treatment modalities. The purpose of the present study was to identify preoperative risk factors related to age of the patients focusing on comorbidities.The elderly population is heterogeneous, ranging from healthy seniors with no disability and few comorbidities to frail seniors who are disabled and have multiple comorbidities. This makes the assessment and management of this population challenging, especially when deciding on cancer treatment modalities. The purpose of the present study was to identify preoperative risk factors related to age of the patients focusing on comorbidities. **Methods:** Retrospective review of the clinical records of all patients operated on thoracic department in 2000-2003. A comparison was carried out between patients with lung cancer 70 years and older (38 patients), and younger lung cancer patients (44patients) who underwent curative open operation. The influence of comorbidity (cardiac, pulmonary, second primary cancer, anemia, diabetes mellitus etc) in postoperative complication were also analyzed. None of the patient received preoperative chemo and/or-radiotherapy. Type of surgery, histology type of tumors was compared in both groups. **Results:** No significant difference was observed in the comorbidities between elderly and young patients. The 30-day operative mortality rates were 6.25% in elderly population, postoperative morbidity was " 40.0% - significantly higer in elderly lung cancer population (p0.05). **Conclusion:** Elderly patients undergoing curative surgery for lung cancer have a higher risk of developing postoperative complications, but mortality rates is equal to younger population. Age or the presence of comorbidity should not be considered contraindications for lung resection. Additional functional evaluation is indicated in specific subgroup of elderly lung cancer patients. **Keywords:** risk assessment, Elderly patients, lung surgery

**PUB038 New Practical Database: Personalized Staging**
Seyda Ö. Kaya, Demet Yaldiz, Kenan C. Ceylan, Tevfik İ. Akçam, Özgür Öztürk *Thoracic Surgery, Dr.Suat Seren Thoracic Surgery and Chest Diseases Training Hospital, Izmir/Turkey*

**Background:** Hence the importance of regionel and national cancer database is growing, establishment of cancer survival datas and evaluation of results is extremely important for the treatment and follow-up. There isn't still a national cancer database system in our country. In the current database programs, all datas of the patients are needed to be entered manually into these programs and most of the datas are not numerical. Studies show that the clinicians are needed to seperate their 50-60% of average daily overtime to enter patient datas. Therefore, we performed a database software that is easy and reliable to use and more importantly needs no time for simultaneous data entry. **Methods:** The most important feature of the program is the automatically entrance of patients' demographic data, medical history, co-morbidity, operative notes, laboratory and the radiological findings into the database program. Moreover, the death time of the patient are also automatically added from the national population registration system so clinical follow-up calculations can securely be performed. When this program is also being used by other clinics; recurrence, metastasis and treatment modalities can easily be monitored in real time. **Results:** In this study, 1320 patients of non small cell pulmonary carcinoma who were operated in our clinic, between the years 2005-2014 are recorded and followed-up in this database program. Unresectabl cases, early mortalities, T0 tumors owing to neoadjuvant therapy and patients lacking data were excluded. Overall 1056 cases were included in the study. 22 datas such as demographics, comorbidities, tumor attributes, cell type, differentiation, the number of metastatic lenf nodes and stations as well as the TNM staging were included and evaluated statistically in the study. All analyses were performed with SPSS 22.0. In analyzing the datas, ROC (Receiver Operating Curve), the Kaplan-Meier (product limit method), Cox Regression, Spearman's rho and Fisher's Z transformation were used. Firstly, significant risk factors associated with mortality and survival were determined by Kaplan-Meier method. Then these factors are statistically evaluated with Cox regression test to estimate the probability of death. The hazard function was calculated for each patient using this method. New database system has been succesfully used in this study. It is found that the most important variables in determining the survey, in addition to the TNM staging were adjuvant chemotherapy and radiotherapy, tumor location and the presence of additional tumors. When the probability of death basing on these factors was correlated with the survey, a strong negative correlation (r = - 0.802) was observed (p<0.001). The probability of death explained 64.3% (r2) of the surveillance. A weak and significant negative correlation was determined between the staging and surveillance (r = -0130). According to this, the stage described 1.7% (r2) of the surveillance. When the probability of death-surveillance r value is compared with the stage-surveillance r value with the Fisher Z method, probability of death-surveillance r value was significantly higher than the stage-surveillance r value statistically (z = 14.874). **Conclusion:** According to our results, the current staging system is important in assessing the treatment modalities but it is found insufficient in estimating surveillance. The variables adjuvant chemotherapy and radiotherapy, tumor location and the presence of additional tumors when analised with the 'Survival function evaluate at the current case', it is found that these variables are more accurate than TNM staging in predicting the prognosis. In conclusion our study is a pilot study, and has learning algorithms that could easily be integrated in the structure. Finally we aimed to take a step for the "personalized staging" that all the prognostic factors are calculated individually. At present, while genome analysis has begun to show the way to personalized treatment, the importance of "personalized staging" is obvious. Available in the future we believe that software systems will be transformed into artificiel intelligency and current staging system will change to individually "personalized staging" that a lot of factors to be analised. **Keywords:** database, Personalized staging, lung cancer

**PUB039 Dividing Procedures of Right Upper Lobectomy as aB-VA Indicate Better Operative Outcomes for Patients with Lung Cancers**
Hao-Ran Zhai[1], Wen-Zhao Zhong[2], Xue-Ning Yang[2], Song Dong[2], Qiang Nie[2], Ri-Qiang Liao[2], Qing Zhou[2], Jin-Ji Yang[2], Yi-Long Wu[2] [1]*Guangdong Lung Cancer Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences; Southern Medical University., Guangzhou/China,* [2]*Guangdong Lung Cancer Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou/China*

**Background:** The most common location of primary lung cancers is right upper lobe(about 30.0%) and procedures of right upper lobectomy(RUL) vary frequently. Rare analyses of thoracoscopic RUL focus on clinical benefits from different procedures with a traditional order of dividing right upper pulmonary vein-artery branches-right upper bronchus(VA-B or AV-B) versus an innovational order of posterior ascending branch of the pulmonary artery-bronchus-pulmonary veins and artery branches(aB-VA). This study aimed to address advantages of operative outcomes and technical feasibility of RUL with a dividing order of aB-VA over VA-B/AV-B. **Methods:** A total of 198 consecutive patients with primary lung cancers undergoing RUL assisted by video-assisted thoracic surgery(VATS) at Guangdong General Hospital from January 2013 to December 2014, were analyzed retrospectively. Two grouping factors were included: procedures of aB-VA and VA-B/AV-B as P1 and P2, respectively; surgical team of Team 1 and Team 2 Surgery as T1 and T2, respectively. Since no P1 was conducted in T2, there were three groups in this study: one, 78 patients in P1T1; two, 56 patients in P2T1; three, 64 patients in P2T2. Operative outcomes and surgical complications were compared between groups. **Results:** Clinical characteristics of age, gender and TNM staging were well balanced among groups, except for smoking index, pathological types and the number of ports during surgeries. Most patients with adenocarcinoma(89.9%,70/78) and less patients with squamous cell carcinoma(5.1%, 4/78) were included in P1T1. The average operative time and estimated blood loss in three groups were 168±59 minutes *vs*. 211±61 minutes *vs*. 233±87 minutes(P<0.001) and 94±84 mL *vs*. 171±215 mL *vs*. 109±107 mL(P=0.001), respectively. The rates of conversion to open thoracotomy were 0% (0/78) *vs*. 23.2%(13/56) *vs*. 3.1%(2/64) (P=0.001), respectively. The number of staplers during surgeries was 5±2 *vs*. 6±2 *vs*. 8±2 (P<0.001), respectively, although total costs of staplers were not statistically significant (P=0.810) . Tube duration of patients in three groups were 3.4 ±2.7 days *vs*.3.7±2.9 days *vs*. 6.3±5.8 days (P<0.001), respectively. Surgical costs per patient in P1T1 were less than that in other groups (3.80±0.85 ten-thousand-yuan RMB *vs*. 3.90±0.97 ten-thousand-yuan RMB *vs*. 4.33±1.01 ten-thousand-yuan RMB, P<0.001). Even though, complication rate in P1T1 was lower than other groups without significance (15.4% *vs*. 25.0% *vs*. 28.1%, P=0.161); the same circumstances in length of hospital stay after surgery (P= 0.210). In the subgroup analysis, 46.2%(36/78) patients in P1T1 received RUL during which pulmonary veins and artery branches were divided using a same stapler, resulting in significant decrease of operative time(P<0.001)

 

and the number of staplers; but no statistical significances were observed on other operative outcomes. **Conclusion:** Procedures of RUL as posterior ascending branch of the pulmonary artery-bronchus-pulmonary veins and artery branches for patients with lung cancers could reveal more benefits of operative outcomes and is quite technically feasible. Shorter operative time and tube duration, and less estimated blood loss were observed. No significance existed when dividing pulmonary veins and artery branches separately or together, except for shorter operative time and less staplers. **Keywords:** Right upper lobectomy, Video-assisted thoracic surgery, Primary lung cancers

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**PUB040 Learning Curve of Uniportal Lobectomy for NSCLC. How Many Cases Are Needed to Reach Competence under Guidance?** Hongjun Chu, Rujian Lu
*Cardiothoracic Surgery, Nantong Third People'S Hospital, Nantong University, Nantong/China*

**Background:** Uniportal video assisted thoracoscopic lobectomy plus mediastinal lymph node dissection is an innovative technique shown to be less minimally invasive for the treatment of early non-small cell lung cancer (NSCLC), though it is quite technically difficulty. This study aimed to describe the learning curve for this minimally invasive surgery with guidance by experienced consultant surgeon. **Methods:** From January 2014 to March 2015, a total of 45 patients with early NSCLC underwent uniportal VATS lobectomy plus mediastinal lymph node dissection in our low-volume center. The procedures were guided by experienced consultant surgeons. The patients were divided into three groups. Group A included the first 15 cases. Group B comprised the middle 15 cases, and Group C included the final 15 cases. The demographic characteristics and the intra- and postoperative data were collected retrospectively and analyzed. **Results:** There was no significant difference found among the three groups in age, gender, body mass index, ASA score, tumor location, histological type and clinical stage. No postoperative death occurred. Three patients required conversion (1 cases in Group A converted to open surgery; 1 cases in Group A and 1 case in Group B convered to three-port VATS lobectomy). Compared with group A, a significant decrease in intrathoracic operative time (146±29min vs 215±41min; P=0.000), blood loss (138±73ml vs 214±105ml; P=0.006), but more retrieved nodes (12.0±2.9 vs 9.5±3.2; P =0.040) was observed in group B, while the postoperative hospital stay was similar (8.6±3.7days vs 9.3±4.1 days; P=0.276). AND compared with group B, the last 15 patients (group C) involved less intrathoracic operative time (131±23min vs 146±29 min; P=0.193), less blood loss (98±55ml vs 138±73ml; P=0.000), more retrieved nodes (14.4±3.2 vs 12.0±2.9, p=0.045) as well as a shorter postoperative hospital stay (6.5±2.5days vs 8.6±3.7days; P=0.033). A decline in the overall morbidity from group A to group C (46.7%, 33.3%, 13.3%, P=0.117) was also observed. **Conclusion:** This study suggests that at least 30 cases were needed to reach the plateau of uniportal VATS lobectomy plus mediastinal lymph node dissection for early NSCLC. The guidance of experiened consultant surgeons might be meaningful to reduce the learning curve. **Keywords:** learning curve, uniportal lobectomy, NSCLC

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**PUB041 CAP1 Is Associated with the Metastasis of Lung Cancer** Changhui Wang, Shuanshuan Xie *Department of Respiratory Medicine, Shanghai Tenth People Hospital, Tongji University, Shanghai 200072, Peoples R China, Shanghai/China*

**Background:** This study was designed to predict non-small cell lung cancer metastasis and explore mechanism of lung cancer cell proliferation, metastasis and migration in vitro and vivo. **Methods:** Firstly, Adenylate cyclase-associated protein 1, CAP1 were determined by real-time PCR and western blot analysis and IHC in 82 lung cancer specimens. Secondly, BM group (n =50) and non-BM group (n =70) were treated and followed up by 4 years. Thirdly, we characterized the expression of CAP1 in lung cell by using Western blot and RT-PCR analyses. In addition, Si-CAP1, empty vector, over-CAP1 in cultured A549,95-C,95-D by using MTT, wound Healing, Transwell invasive, Western blot, and IHC analyses and nude mouse. **Results:** We provided evidence that overexpression of CAP1 in lung cancer cells, particularly at BM [figure1] . In addition, these findings suggest that CAP1 promotes the lung cancer cell proliferation and migration in vitro as well as its growth and metastasis in vivo via LIMK/cofilin I [figure2].

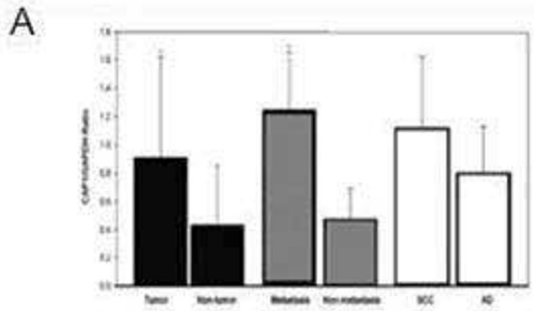



Figure 1. Relative cyclase-associated protein 1 (CAP1) mRNA levels (i.e., CAP1/GAPDH mRNA ratios) in non-neoplastic lung tissue and lung tumors of different stage and histological type. $P<0.05$, comparison made within the same type of bar.

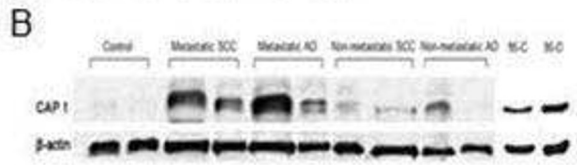



Figure 2. A representative western blot analysis showing cyclase-associated protein 1 (CAP1) and β-actin bands in indicated biopsy specimens (two representative samples from each of the patient groups) and cultured lung cancer cells.

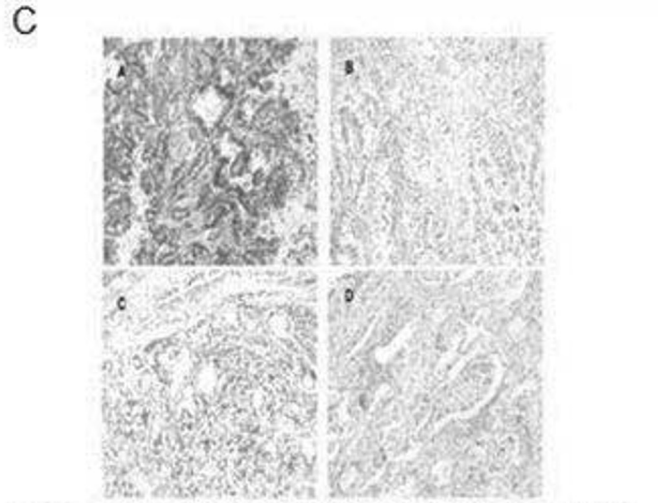



Figure 3. Representative sections of pathological lung cancer specimens after immunohistochemical staining. (A) Adenocarcinoma (AD) showing a high percentage of cyclase-associated protein 1 (CAP1)-positive cells; (B) AD showing a low percentage of CAP1-positive cells; (C) squamous cell carcinoma (SCC) showing a high percentage of CAP1-positive cells; (D) SCC showing a low percentage of CAP1-positive cells.

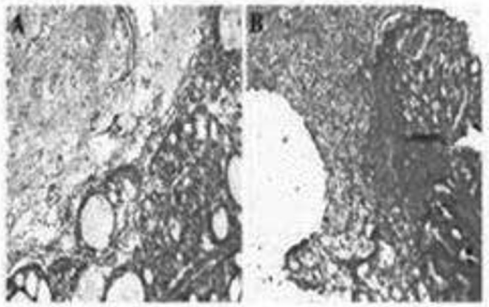
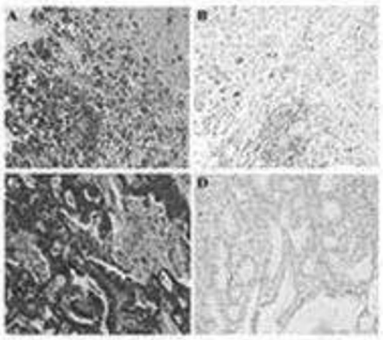



Figure 5. Hematoxylin and eosin (H&E) staining of histological tissues. H&E in brain metastasis of non-small cell lung cancer (NSCLC) patients. Brain biopsy specimens showing (A) squamous cell carcinoma (SCC) and (B) adenocarcinoma (AD) cancer nests.



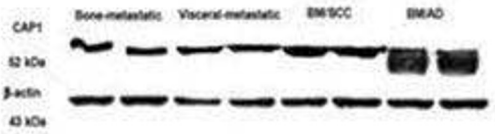
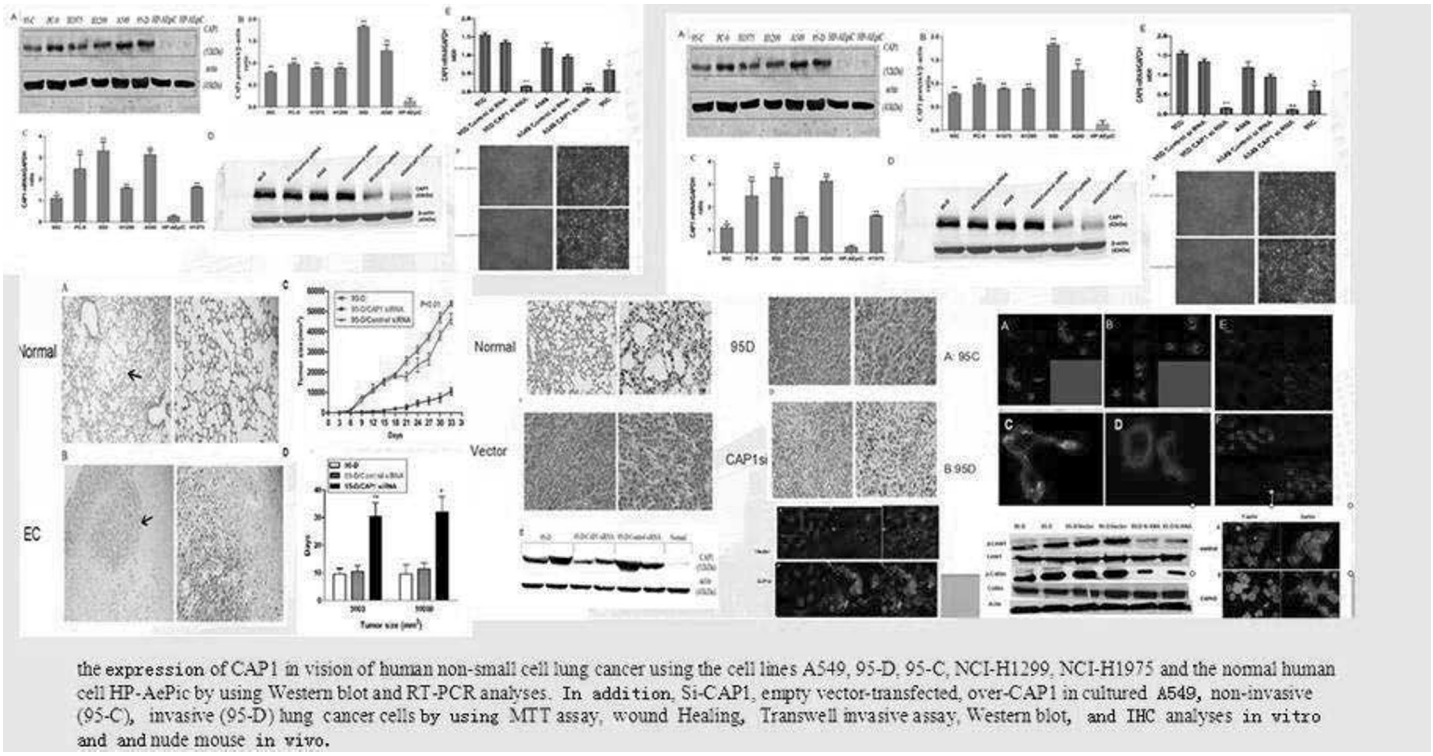




Figure 7. A representative western blot analysis showing cyclase-associated protein 1 (CAP1) and β-actin bands in indicated metastatic biopsy specimens (two representative samples from each of the patient groups). BM, brain metastasis; AD, adenocarcinoma; SCC, squamous cell carcinoma.

Table II. Correlation between immunoreactive CAP1 signals and brain metastasis.

| Biomarkers | Brain metastasis, n (%) | Non-brain metastasis, n (%) | P-value |
|---|---|---|---|
| CAP1 + | 31 (79.5) | 23 (32.9) | <0.01 |
| CAP1 - | 8 (20.5) | 47 (67.1) | |

CAP1, cyclase-associated protein 1.




the expression of CAP1 in vision of human non-small cell lung cancer using the cell lines A549, 95-D, 95-C, NCI-H1299, NCI-H1975 and the normal human cell HP-AePic by using Western blot and RT-PCR analyses. In addition, Si-CAP1, empty vector-transfected, over-CAP1 in cultured A549, non-invasive (95-C), invasive (95-D) lung cancer cells by using MTT assay, wound Healing, Transwell invasive assay, Western blot, and IHC analyses in vitro and and nude mouse in vivo.

**Conclusion:** CAP1 is associated with metastasis of NSCLC especially in BM patients and promotes the lung cancer cell proliferation and migration in vitro and vivo by limk1-cofilin. **Keywords:** lung cancer, metastasis, Adenylate cyclase-associated protein 1

**PUB042 Involvement of Protein Kinase CK2 in the Radioresistance of Lung Cancer Cells** Qianwen Li, Gang Wu, Rui Mng *Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan/China*

**Background:** As radiotherapy is the main treatment of advanced non-small cell lung cancer, resistance to radiotherapy becomes a key limitation for the treatment. To overcome this problem, we investigated the correlation between lung cancer radioresistance and Protein kinase CK2, a constitutively active serine/threonine kinase, which is widely overexpressed in human cancers. Protein kinase CK2 is involved in many cellular processes including proliferation, survival and viability, and also proved to be linked to DNA damage response through phosphorylation of and interaction with several key molecules. **Methods:** Clonogenic assays were performed to assess the effect of a CK2 inhibitor, Quinalizarin, on the radiosensitivity of A549 and H460 cells. The effect of the combination of Quinalizarin and X-ray irradiation on apoptosis and cell cycle of A549 and H460 cells was measured by Flow cytometry. Immunofluorescence assays were performed to detect the expressions of $\gamma$-H2AX and 53BP1, and the average fluorescent values were obtained. The protein expression of DNA-pk was measured by Western Blotting assays. **Results:** We found that A549 and H460 exposed to Quinalizarin have an increased radiosensitivity, decreased proliferation and impaired DNA repair. Down-regulation of CK2 results in significant increase of $\gamma$-H2AX foci and reduction of 53BP1 foci and DNA-PK protein expression in cells after ionizing radiation. In addition, we observed an extended G2/M arrest but not increased apoptosis after ionizing radiation in the absence of CK2. **Conclusion:** In conclusion, inhibition of protein kinase CK2 might be a promising way to increase the radiosensitivity of non-small lung cancer cells, and further experiments need to be conducted to elucidate its underlying mechanisms. **Keywords:** non-small cell lung cancer, Protein Kinase CK2, radiosensitivity, Quinalizarin

**PUB043 Using Multiplexed Assays of Oncologic Drivers to Select Targeted Drugs** Elizabeth Cathcart-Rake[1], Christopher Corless[2], Alan Sandler[1], Carol Beadling[1], Andrea Warrick[2], Beth Wilson[2], Andrea Burt[1], Grant Roesler[2], Ariel Lopez-Chavez[1] [1]*Knight Cancer Institute, Oregon Health and Science University, Portland/United States of America,* [2]*Knight Cancer Institute, Oregon Health and Science University, Portland/OR/United States of America*

**Background:** Multiplex genotyping from patients with metastatic adenocarcinomas of the lung is feasible, informs treatment decisions, and facilitates clinical trial enrollment. Identification of certain genomic alterations may also potentially impact survival. We describe a single institution experience with multiplex genotyping of patients with non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), and thymic malignancies. **Methods:** Patients with advanced NSCLC, SCLC including lung neuroendocrine tumors, and thymic malignancies were enrolled from Oregon Health and Science University. Biopsies of tumors were obtained and screened concurrently for over 200 genetic alterations using the Sequenom MassArray and / or Ion Torrent platforms. Mutation frequencies and overall survival data were calculated. Genetic mutation information was used for enrollment in the treatment arms of the CUSTOM trial. **Results:** From February 2011 to December 2012, 264 patients were enrolled and underwent molecular profiling. KRAS was the most frequently mutated gene in NSCLC with a frequency of 25.6%, followed by TP53 at 21.9%, and PTEN at 18.8%. EGFR mutations were detected in 17.4%, and BRAF in 2.4%. In SCLC, TP53 was the most commonly mutated gene at 21.4%, followed by NOTCH1 at 16.7, and PIK3CA at 6.7%. In thymic malignancies, no tested mutations were positive. Overall survival was defined by individual mutation; patients with EGFR mutations had the longest survival times of 1.83 years. Genetic mutation information was used to enroll patients into the CUSTOM clinical trial treatment arms. Twenty-five percent of patients with NSCLC had actionable mutations. Five patients were enrolled in the treatment arm of the CUSTOM trial. **Conclusion:** We report on a single institution's experience with multiplex genotyping for multiple histologic types of thoracic malignancies. Information regarding genomic aberrations was used to guide treatment with well-known genetic-based agents, like erlotinib, as well as enrollment into the CUSTOM clinical trial, where patients were assigned treatment based on specific mutations. Multiplex genotyping from patients with metastatic non-small cell lung cancer, small cell lung cancer, and thymic malignancies is feasible, informs treatment decisions, and facilitates clinical trial enrollment. **Keywords:** oncologic drivers, multiplexed assays, non-small cell lung cancer, small cell lung cancer

**PUB044 Comparison between 5-Aminolevulinic Acid Based Photodynamic Therapy on Human Lung Adenocarcinoma Cells Grown in Monolayers and Spheroids** Haydee Fukuda[1], Maria J. Teijo[2], Berenice A. Diez[2], Alcira M.D.C. Batlle[2] [1]*Biological Chemistry, Faculty of Sciences, University of Buenos Aires, Buenos Aires/ Argentina,* [2]*Conicet, Cipyp, Buenos Aires/Argentina*

**Background:** Photodynamic therapy (PDT) is a therapeutic modality for the treatment of obstructive or microinvasive lung cancer. After the administration of a photosensitising drug (PS) which selectively accumulates in the tumor cells, irradiation with an appropriate wavelength light triggers photochemical reactions inducing Reactive Oxygen Species (ROS) production with the consequent cellular damage, which ultimately lead to cell death. Porphyrins are the only PSs endogenously synthesized by means of incubation with the biological precursor, 5- aminolevulinic acid (ALA). **Methods:** ALA-PDT was performed on A 549 human lung adenocarcinoma cells, growing in monolayer or multicellular spheroids (MCSs), by incubation with 1mM ALA for 3h, followed by irradiation with two fluorescent lamps (Osram L36W/10) for different times, and within 1 h analyzed for PDT-induced events. MCSs were initiated by seeding $5.10^4$ cells/ml on 3% agar : RPMI (1:1) coated wells and harvested after 7 days with periodic fresh medium renewal (MCSs are three-dimensional compact cellular aggregates that mimic micro-tumors with no vascular irrigation, representing a suitable model for the study of PDT-induced cell death, since tumor vasculature has a controversial role in tumor eradication by PDT). Porphyrins were extracted from the cells with 5% HCl and quantified spectrofluorometrically. Effects of PDT treatment were analyzed by the MTT and the APH assay, and by acridine orange/ethidium bromide staining and AnnexinV-FITC/propidium iodide labelling, visualized under optical and confocal microscopy, and analyzed by flow cytometry. **Results:** Porphyrin synthesis was not significantly different between monolayers and MCSs, neither quantitatively (monolayers: 0,109±0,1 pg/cell; MCSs: 0,09±0,1 pg/cell) nor qualitatively, since PpIX fluorescence distribution was uniform along all sections of the spheroids analyzed

under confocal microscopy. However, in the monolayer a plateau in the porphyrin synthesis was attained at 0.5 mM ALA concentration, and in the MCSs, at 1 mM. With incubation times longer than 3 h, kinetics of porphyrin biosynthesis was faster in the monolayer. Survival curves after performing ALA-PDT showed that DL50 (irradiation time producing 50% of cell death) in MCSs was 2 min higher than in the monolayer, and according to these results, a higher percentage of viable cells when 20 min-irradiation PDT was performed, was observed in the MCSs (66,57±6,5%) compared to monolayers (3,5±0,2%). Moreover, caspase-3 expression and cytochrome c release were also lower in MCSs. **Conclusion:** With normal PpIX synthesis and distribution, the limiting factor on ALA-PDT efficacy in the 3D growing cells, could be the light penetration into the inner section of the MCSs, or the lower oxygen availability conditioning the generation of ROS.
**Keywords:** aminolevulinic acid, Lung adenocarcinoma cells, photodynamic therapy

**PUB045 Activating Mutant EGFR Upregulates HIF-1$\alpha$ to Promote a Hypoxic Phenotype Independent of Hypoxia in Non-Small Cell Lung Cancer**
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**Background:** Activating EGFR mutations L858R and del19 define a subset of lung adenocarcinomas that are addicted to EGFR signaling for growth and survival. Clinical and pre-clinical data have demonstrated that the activating EGFR mutations confer sensitivity to EGFR tyrosine kinase inhibitors, such as erlotinib and gefitinib, in non-small cell lung cancer (NSCLC). The mechanism by which the activating mutant EGFR renders the receptor more sensitive to the effects of the inhibitors has not been well defined. We investigated the impact of activating mutant EGFR on hypoxia-inducible factors (HIFs) and cellular response. **Methods: Protein expression was examined using either western blotting, ELISA, or IHC. mRNA expression was examined using real-time PCR or cDNA microarray. Transcription activity was measured using corresponding promoter-driven luciferase expression.** Functional analysis of genes was performed by gene set enrichment analysis. Xenograft study was performed in mice to examine the effects of VEGF inhibitor bevacizumab on lung cancer cells with either wild-type EGFR or activating mutant EGFR. **Results:** In NSCLC cells bearing EGFR-activating mutations, canonical hypoxic response was diminished and EGFR was a dominant regulator of HIF-1a and, to a lesser extent, HIF-2a via affecting their mRNA expression and protein stability. Microarray analysis of 53 NSCLC cell lines demonstrated elevated*HIF-1a* and *HIF-2a* mRNA and enrichment of HIF-regulated genes in cells with activating mutant EGFR, indicating that these mutants result in constitutive, ligand-independent upregulation of HIF- and hypoxia-regulated genes in normoxia, leading to a hypoxic phenotype. Inhibition of EGFR activity reduced the level of *VEGF*, a well-characterized HIF-responsive gene, in cells with activating mutant EGFR but not in cells with wild-type EGFR, and these effects were independent of oxygen level. Xenografts with activating mutant EGFR were more sensitive to VEGF inhibition than xenografts with wild-type EGFR. **Conclusion:** Together, our results suggest that cells expressing activating mutant EGFR uncouple HIF expression and hypoxia, providing an important mechanism through which cells can upregulate HIF and its target genes in the absence of hypoxia, thereby hijacking an important cellular response regulating invasiveness and tumor aggressiveness. Our results also suggest that patients with activating mutant EGFR will benefit from VEGF inhibition related therapy.
**Keywords:** VEGF, lung cancer, EGFR, HIF1A

**PUB046 Prognostic Stratification of Patients with Lung Cancers by EMT-Related 4-Gene Signature**
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**Background:** This study aimed to investigate the association between epithelial-to-mesenchymal transition (EMT) molecular events in morphologically normal tumor-adjacent tissues and the outcome of lung cancer patients. **Methods:** EMT was induced in an immortalized human bronchial epithelial cell line by TGF-$\beta$1. Gene expression of the EMT-induced cells and morphologically normal tumor-adjacent tissues derived from 60 patients with squamous cell carcinoma (SCC) in lung was profiled by microarray and real-time PCR. An independent cohort of 50 lung SCC patients was applied to validate the prognostic value of the candidate gene signature by real-time PCR. **Results:** A 4-gene signature that was related to EMT in vitro was activated in morphologically normal tumor-adjacent tissues from the 60 lung SCC patients, and associated with lymph nodes metastasis. Up-regulated expression of the 4-gene signature in tumor-adjacent tissues was also significantly associated with poor overall survival in the independent cohort of lung SCC (N=50, P=0.009). **Conclusion:** An EMT-related 4-gene signature expressed in tumor-adjacent morphologically normal tissues is associated with outcome in lung cancer patients.
**Keywords:** tumor-adjacent tissue, EMT, Gene signature, Prognosis

**PUB047 The Increased Serum Norepinephrine Is Associated with Poor Prognosis in Non-Small Cell Lung Cancer and Contributes to Cancer Cell Metastasis**
Wei Zhao, Bin Zhang, Xiaoyuan Wu *Central Laboratory, Nanjing Chest Hospital, Nanjing/China*

**Background:** Lung cancer is the most common cancer worldwide. Non-small cell lung cancer (NSCLC) accounts for 85% of lung cancer. Norepinephrine (NE) regulates tissue response to stimulation through binding to receptors, which locate on cell surface. Recently, NE was reported to promote ovarian cancer, melanoma, breast cancer, colon cancer and prostate cancer program. **Methods:** Serum NE was detected in 58 NSCLC patients and 70 healthy controls by Elisa kit. The associations between serum NE level with patient's prognosis and survival were analyzed by SPSS 17.0 statistical software. Add NE and/or NE $\beta$1 receptor blocker into NSCLC cell medium, MTT and transwell assays were employed to measure proliferation and metastasis changes, respectively. **Results:** Serum NE is significantly higher in NSCLC patients, compared to the healthy controls ($P < 0.003$). In addition, High level of serum NE was correlated with tumor size ($P = 0.012$) and N stage ($P = 0.026$). Kaplan-Meier analysis indicated that patients with higher serum dopamine had a poor overall survival ($P = 0.0311$). Additional NE promoted NCI-H322 proliferation and metastasis, whereas NE $\beta$1 receptor blocker reversed NE effect to NSCLC cell. **Conclusion:** Our data indicates that NE regulates NSCLC cell proliferation and metastasis through $\beta$1 receptor and blockage of NE might be a novel therapeutic strategy in NSCLC patients.
**Keywords:** non-small cell lung cancer, norepinehrine, proliferation, metastasis

**PUB048 Demographic Profile of Lung Cancer in India**
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**Background:** Lung cancer is a common problem worldwide and an important public health problem in India. There are over 1.8 million cases of lung cancer worldwide with 1.6 million deaths per year, a large proportion of which occurs in the developing world. Lung cancer is one of the commonest cancers in India, is a major public health problem and a leading cause of cancer related deaths. While there are direct links with smoking, there has been an increase in the non-smoking lung cancers worldwide. The clinico-pathological profile of lung cancer has also changed considerably over the last two decades. The epidemiology has changed from a predominant squamous histology to adenocarcinoma which is now the most common.Published literature as well as unpublished observations indicate that the features of lung cancer in India like prevalence, incidence, aetiopathogenesis and presentation vary markedly from the west. We performed a prospective study to evaluate the unique demographic features of lung cancer in India, with specific emphasis on smoking and histopathological trends. **Methods:** We performed a prospective study between Dec 2012 and Dec 2014 to study the demographic and clinic-pathological profile of lung cancer patients registered in the thoracic oncology services of India's largest tertiary referral cancer centre. Data was collected directly from patients' paper and electronic medical records. All patients of histologically proven lung cancer were included. Data of patients who did not consent was excluded. The study was initiated after approval from the Institutional Review Board of the Tata Memorial Hospital. Data was entered into Statistical Program for Social Sciences (SPSS version 18 for Windows) software and analysed as percentages and as descriptive data. **Results:** A total of 2085 patients were included in the database of which 44 patients were excluded for significant missing data. There were 1512 male (74.1%) and 529 women (25.9%) with a M:F ratio of 3:1. Over half (50.6%) patients were active or past smokers, while 45.3% patients had not been exposed to active or passive smoking. Beedi (local rolled tobacco) smoking was more common (29.7%) than cigarettes (15.1%) while 2.8% smoked both; exclusive chewed tobacco use was seen in 8.3% while combined use of chewed and smoked tobacco was seen in 3.1% patients. The proportion of women never-smokers with lung cancer was significantly higher (87%) compared to men (32%). More than two-thirds patients (67.7%) presented with metastatic disease.Amongst patients with a definitive cytohistological diagnosis, the prevalence of adenocarcinomas was highest (70.3%) followed by squamous (20.8%), small cell (5.8%) and NSCLC NOS (3.2%). **Conclusion:** The demographic profile of patients with lung cancer in India is unique with a much higher proportion of never smokers, especially in women. Most patients present with metastatic disease with significant epidemiological trends towards a predominant adenocarcinoma histology. Urgent studies are required to analyse these epidemiological trends especially in non-smoking women.
**Keywords:** never-smoker, lung cancer, demography, India

**PUB049 Downregulated the Non-Coding RNA AK126698 Promotes Cisplatin Resistence in Non-Small-Cell Lung Cancer by Targeting FZD8**
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**Background:** Cisplatin is one of the widely used chemotherapeutic drug for the treatment of patients with advanced lung cancer. However, chemoresistance to cisplatin is common in patients with lung cancer. In our previous study, we have demonstrated that lncRNA AK126698 regulated A549 cells cisplatin resistance partly through Wnt/$\beta$-catenin signaling. However, the precise molecular mechanism is not yet fully understood. **Methods:** LncRNA AK126698 expresion was detected in NSCLC cell lines A549, NCI-H520, A549/DDP and NCI-H520/DDP, and then the effects of AK126698 on the proliferation and chemosensitivity of cancer cells was investigated, using both gain- and loss-function studies. The correlation between AK126698 level and

 

chemoresistance was further investigated in clinical NSCLC specimens. **Results:** LncRNA AK126698 levels were dramatically downregulated in the cisplatin-resistent cell lines A549/DDP and NCI-H520/DDP compared with their respective parental cell lines. Overexpression of AK126698 also could increase the sensitivity of A549/DDP and NCI-H520/DDP cells to cisplatin in vitro. Furthermore, we showed that AK126698 inversely regulates FZD8 expression in NSCLC cell lines. The results also show that LncRNA AK126698 increasing chemosensivity was associated with inhibition of cell proliferation, induction of G0/G1 cell-cycle arrest and apoptosis enhancement through regulation of FZD8 expression along with decreased activity of Wnt pathway. Importantly AK126698 expression levels were significantly lower in NSCLC tissues with high levels of FZD8 and ERCC1, a marker for cisplatin-resistance. **Conclusion:** Our findings suggest that downregulation of LncRNA AK126698 contributes to the cisplatin resistence of NSCLC cells, at least in part, through the regulation of FZD8 expression.
**Keywords:** long non-coding RNA, NSCLC, FZD-8, cisplatin resistence

**PUB050 Clinical Significance of Reduced GPRC5A Expression in Surgically Resected Non-Small-Cell Lung Cancers**
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**Background:** GPRC5A (G protein-coupled receptor, family C, group 5, member A) was initially identified as a retinoid-inducible gene, while retinoid plays a pivotal role in regulation of many physiological and pathological processes, including cell growth and differentiation. GPRC5A has been characterized as a lung cancer suppressor gene, although clinical significance of GPRC5A in NSCLC remains to be determined. **Methods:** This study detected GPRC5A expression in NSCLC for association with clinical significance of NSCLC patients. GPRC5A messenger RNA (mRNA) and protein were assessed by using quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) and Western blot, respectively in 30 NSCLC and matched normal tissue samples. Immunohistochemistry was to detect GPRC5A expression in 110 NSCLC and 60 para-tumor tissues. **Results:** The data showed that levels of GPRC5A mRNA and protein in NSCLC tissues were significantly lower than those in corresponding noncancerous tissues (P<0.001). Loss of GPRC5A expression was associated with tumor histological type (P=0.008), poor tumor differentiation, lymph node metastasis, and tumor-node-metastasis (TNM) stage (P<0.001). Furthermore, Kaplan-Meier curve analysis revealed that patients with low GPRC5A expressed tumor had shorter survival than patients with GPRC5A expressed tumor (P=0.010), while the multivariate Cox analysis revealed that lost GPRC5A expression was an independent prognostic factor for NSCLC patients (P<0.001). **Conclusion:** The data from the current study demonstrated that detection of GPRC5A expression might serve as a valuable biomarker for prediction of NSCLC differentiation and survival of NSCLC patients.
**Keywords:** NSCLC, biomarker, GPRC5A

**PUB051 T-Type Calcium Channels and Non-Small Cell Lung Cancer**
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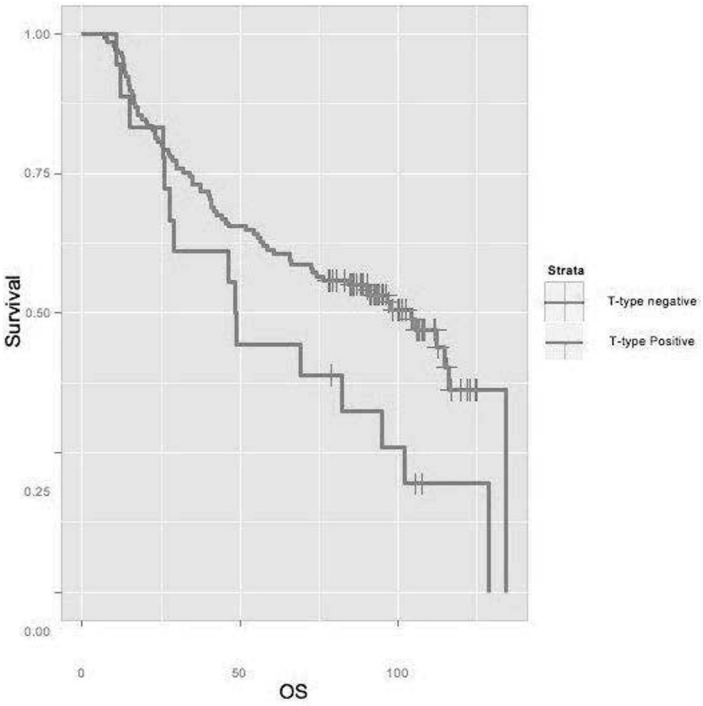
**Background:** Lung cancer is the leading cause of cancer deaths worldwide. Currently, tumor resection, radiation, and chemotherapy are the standard treatments for NSCLC. As with most cancers, targeted therapies are being researched and developed in an attempt to mitigate or avoid adverse side effects. T-type calcium channels, low-voltage gated transmembrane proteins, have recently been pathologically implicated in ovarian, breast and esophageal carcinomas. Our in vitro studies have indicated the presence of t-type calcium channels in NSCLC cell lines. Furthermore, IHC staining of 193 tumors from Albertan NSCLC patients have shown t-type calcium channel expression within the tumors and a significant correlation of this expression to poorer overall survival. Finally, specific t-type calcium channel inhibitors have already been approved for use with other diseases and show promise in depressing proliferation of various carcinoma cell lines. **Methods:** All Stage I-III NSCLC patients diagnosed between 2003 and 2006 at the Tom Baker Cancer Centre were included in the Glans-Look Lung Cancer Database. Demographic details and clinical variables were collected retrospectively, with overall survival continually being updated every 3-4 months. Tissue micorarrays were generated from formalin embedded tumors for the included Stage I-III NSCLC patients. 5µm thick slices were stained for pan-cytokeratin to identify tumor cells and for t-type calcium channels using anti-cav3.1 antibodies. Tumor samples were labeled positive or negative for t-type calcium channel expression and clinical and demographic data was statistically analyzed with relation to expression.




**Results:** Expression of t-type calcium channels is significantly correlated with poorer overall survival in the patients included in the Glans Look Lung Cancer Database with a p-value of 0.0339. **Conclusion:** T-type calcium channel expression was seen in 18 of 163 NSCLC tumor samples from patients included in the Glans Look Lung Cancer Database. In all these patients, expression was only found within the tumor and not in adjacent healthy tissue. Furthermore, overall survival was significantly worse in patients with t-type calcium channel expression. Previous research by other groups has shown depressed proliferation of ovarian, esophageal and breast carcinomas using t-type calcium channel blockers. These blockers may potentially provide a targeted treatment for NSCLC given that t-type calcium channels are expressed in the malignant tumors of patients and not in the healthy tissues. Further work must be done to determine the influence of t-type calcium channels in NSCLC tumors, specifically their affect on proliferation, which could lead to targeted therapy with minimal side effects.
**Keywords:** t-type calcium channels, Targeted therapy

**PUB052 JAK2 Participates in Lung Cancer Progression**
Yanjun Xu, Yun Fan *Chemotherapy, Zhejiang Cancer Hospital, Hangzhou/China*

**Background:** Lung cancer ranks as the first most common cancer and the first leading cause of cancer-related death in China and worldwide. Due to the difficulty in early diagnosis and the onset of cancer metastasis, the 5-year survival rate of lung cancer remains extremely low. JAK2 has emerged as pivotal participant in biological processes, often deregulated in a range of cancers, including lung cancer. Recently we found that JAK2 might play an important role in lung cancer pathogenesis as an oncogene. While our understanding of JAK2 in the onset and progression of lung cancer is still in its infancy, there is no doubt that understanding the activities of JAK2 will certainly secure strong biomarkers and improve treatment options for lung cancer patients. **Methods:** The expression of JAK2 protein level was assayed using the Western Blot assay. MTT assay, Scratch-wound healing assay, Transwell migration and invasion assay were conducted to study the proliferation, migration and invasion abilities of lung cancer cells independently. The RNAi and over expression plasmids were conducted. **Results:** JAK2 is up-regulated in lung cancer tissues when compared with their adjacent non-tumor tissues. Downregulation of JAK2 inhibits the proliferation, migration and invasion abilities of lung cancer cells. Moreover, over expression of JAK2 induced the proliferation, migration and invasion abilities of lung cancer cells. **Conclusion:** These findings demonstrate that JAK2, whose expression is up-regulated in lung cancer, may participate in lung cancer progression by regulating cancer cells proliferation, migration and invasion.
**Keywords:** JAK2, lung cancer

**PUB053 Primary Lung Cancer in Morocco: Results of a Retrospective Study**
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**Background:** Lung cancer is one of the most common cancers in the world, accounting for 13% of all cancers. It is the third most common cancer and the third most common cause of cancer death in both men and women in Northern Africa, with an estimated 14 506 new cases of lung cancer and 12 940 cancer deaths in 2012 (GLOBOCAN

2012). The aim of this study is to determine the epidemiological characteristics of primary lung cancer in Morocco. **Methods:** This is a descriptive retrospective study of all patients treated for primary lung cancer at Al Azhar Oncology Center in Rabat between 1994 and 2004. **Results:** During the period of study, 299 cases of primary lung cancer were diagnosed; 265 (88.6%) in men and 34 (11.4%) in women, giving a male-female ratio of 7.8 and representing 4.2% of all new cases of cancer reported during this period. The average age at diagnosis was 58.6±12.8 years (range 20-90 years). Lung cancer is strongly related to age with only 5.4% of cases diagnosed in persons younger than 40 years, 82.5% in those aged 40-74 years and 12.1% in those aged 75 years and over. Among all detected cases, 89 (29.8%) died from lung cancer during the study period, accounting for 7.5% of all cancer deaths. **Conclusion:** The most recent estimates of lung cancer incidence and mortality in the world reveal sharp differences between developed and developing countries possibly related to missed opportunities for early diagnosis and incomplete reporting of lung cancer in Africa. **Keywords:** lung cancer, epidemiology, Morocco

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**PUB054 Clinically Relevant Gene Sequencing in Lung Cancer**
Patricia L. Thompson, Terri Redmond, Christopher Parks, Rabih Bechara *Thoracic Oncology, Cancer Treatment Centers of America, Newnan/United States of America*

**Background:** Individualized cancer treatment is the ultimate goal of clinicians and their patients. We report the results of a commercially available next-generation sequencing assay in advanced lung cancer. **Methods:** We retrospectively analyzed all the reports of biopsies from advanced lung cancer which were sent for testing using a commercial next-generation sequencing platform from a network of five tertiary referral centers during the year 2013. **Results:** 258 unique reports belonging to 258 patients with a diagnosis of advanced lung cancer were analyzed. Of these, 182 (70.54%) formalin fixed paraffin embedded tissue were sent for genomic testing with 182 yielding reports. 177 reports had at least 1 genomic alteration, 3 had no alterations and 2 failed test results. There were a total of 23 genomic alterations detected, 21 in Adenocarcinoma, 14 in Squamous cell, 6 in Small cell , 2 in large cell and 2 in Adenosquamous. Overall median age of patients was 57 years (range 28-78) having received a median of two prior lines of chemotherapy. Non-Small cell lung cancer (NSCLC) was present in all cases except 11 (6.04%) which were small cell lung cancer. Of the NSCLC, the reports were subdivided into Adenocarcinoma 134 (73.62%), Squamous cell 21 (11.54%), Large cell 8 (4.40%), Adenosquamous 3 (1.65%) and Others (Lung Adenoid Cystic Carcinoma 2 (1.10%), Lung Sarcomatoid Carcinoma 2 (1.10%), Lung Typical Carcinoid 1 (0.55%)) KRAS was most commonly mutated in Adenocarcinoma 51/134 (38.06%), CDKN2A in Squamous Cell 8/21 (40%), RB1 in Small Cell 5/11 (45.45%), Tp53 in Large Cell 2/4 (50%) and Adenosquamous 3/3 (100%). Of 177 reports, about one third 56 (31.64%) had at least 1 FDA approved treatment for lung cancer, two thirds 132 (74.58%) had at least 1 FDA approved treatment from another tumor type. 143 (80.79%) reports had at least 1 "actionable result" (FDA approved treatment to patient's or another tumor type) and 168 reports (93.78%) had at least one clinical trial for a targeted genomic alteration (in clinicaltrials.gov) in addition to FDA approved treatments in patients patients' cancer or another malignancy. **Conclusion:** Molecular profile based therapy represents a milestone in the goal to develop personalized cancer therapies. We propose that future trials should address the molecular profile of each individual patient and treat each patient based on their molecular fingerprint. **Keywords:** gene sequencing lung cancer

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**PUB055 Clinicopathological Features of Resected Peripheral Squamous Cell Carcinoma of the Lung and Relation to Long Term Survival** Qianjun Zhou
*Shanghai Chest Hospital, Shanghai Jiaotong University School of Medicine, Shanghai/China*

**Background: Incidence of peripheral squamouscell carcinomas (p-SqCCs) of the lung has increased over decades, however, clinicopathological prognostic factors have not been well studied. Methods:** We evaluated clinicopathological features in 251 patientswith resected peripheral lung SqCCs (which located in or more peripheral to the fourth branching bronchus), measuring ≤70mm in size, and analyzed the relation to the overall survival (OS) and recurrence-free survival (RFS) according to the primary location. **Results:** Multivariate analysis in all stages of patientsshowed that high CEA and CK19 level, vascular invasion, nodal metastasis were significant unfavorable prognostic factors. Among T1 tumor patients (≤30mm in diameter), high serum CEA level, vascular invasion and nodal metastasis were also strongly correlated with poor prognosisindependently. Among T2 tumor patients (≤70mm in diameter), high serum CK19 level, vascular invasion,nodalmetastasis, N2 percentage were also strongly correlated with poor prognosis. **Conclusion:** High CEA and CK19 level, vascular invasion, nodal metastasis were significant unfavorable prognostic factors for completely resected p-SqCCs. **Keywords:** Peripheral squamous cell carcinoma, NSCLC,Vascular invasion, Prognostic factor

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**PUB056 Clinical Impact of Solid or Micropapillary Subtypes in Lung Adenocarcinoma** Naoki Yanagawa[1], Satoshi Shiono[2], Masami Abiko[2], Masato Katahira[2], Mitsumasa Osakabe[1], Shin-Ya Ogata[1], Toru Sato[2], Gen Tamura[1]
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**Background:** Lung adenocarcinoma (ADC) presents various histologic images. Predominant growth patterns according to new ADC classification proposed by the International Association for the Study of Lung Cancer, American Thoracic Society, and European Respiratory Society (IASLC/ATS/ERS) are correlated with patients' outcome. In particular, the patients with solid or micropapillary predominant growth pattern show a worse prognosis than other predominant growth patterns. However there are a few reports which have examined second and third dominant subtypes aside from predominant subtypes and the meaning is unclear. We aimed to investigate a clinical impact of these subtypes. **Methods:** We reclassified 531 ADCs according to the new ADC classification. The percentage of each histopathological subtype was determined in 5% increments. The relationship between these results and clinicopathological data including outcome was investigated statistically. **Results:** The histopathological assessment according to the IASLC/ATS/ERS classification presented that 8.1% (n = 43) of the cases were adenocarcinoma in situ (AIS) ; 8.7% (n = 46) were minimally invasive adenocarcinoma (MIA) ; 17.9% (n = 95) were lepidic predominant ; 20.0% (n = 106) were acinar predominant ; 29.6% (n = 157) were papillary predominant ; 10.4% (n = 55) were solid predominant ; 2.1% (n=11) were micropapillary (MP) predominant, and 3.4% (n=18) were invasive mucinous adenocarcinoma (IMA). In univariate analysis, the patients with solid predominant and MP predominant presented a worse disease-free survival (DFS)($p<0.01$) and overall survival ($p<0.01$) than the patients with other predominant subtypes. Next, we examined the second dominant and less than the third dominant subtypes of lepidic, acinar, papillary predominant aside from solid and MP predominant, AIS, MIA and IMA. Sixty-six patients had solid or MP predominant, 27 patients had solid or MP second dominant, 37 patients had less than third solid or MP dominant and 294 patients had neither solid nor MP subtypes. The patients with solid or MP predominant presented a worse DFS than those with neither solid nor MP subtypes (Hazards ratio (HR): 3.34, 95% Confidential interval (CI): 2.32-4.82, $p<0.001$). The patients with solid or MP second dominant also presented a worse DFS than those with neither solid nor MP subtypes (HR: 2.16, 95%CI:1.20-3.89, $p=0.01$). The patients with less than third solid or MP dominant also presented a worse DFS than those with neither solid nor MP subtypes (HR: 1.71, 95%CI:1.02-2.85, $p=0.041$). **Conclusion:** The patients with solid or MP subtypes had a worse prognosis even if their subtypes were not predominant. Therefore we need to take care of solid or MP subtypes at the time of diagnosis. **Keywords:** Adenocarcinoma, subtypes, Prognosis

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**PUB057 COX-2 Mediate Acquired Gefitinib Resistance in Non-Small Lung Cancer Cells via MAPK-Dependent Pathway** Qin F. Deng[1], Yin M. Zhao[2], Bo Su[2], Jian F. Xu[1], Cai C. Zhou[1] [1]*Department of Oncology, Shanghai Pulmonary Hospital, Tongji University, Shanghai/China,* [2]*Central Laboratory, Shanghai Pulmonary Hospital, Tongji University, Shanghai/China*

**Background:** Epidermal Growth Factor Receptor (EGFR) and Cyclooxygenase-2(COX-2) contribute to the development and progression in NSCLC. Overexpression of COX-2 could induce non-EGFR dependent activation of extracellular signal regulated kinase. Our previous studies had shown that simultaneous blockage of EGFR and COX-2 may restore acquired gefitinib-resistant cells' sensitivity to gefitinib. In this study, we explored the role of COX-2 and relevant signaling pathway in acquired gefitinib resistance in NSCLC. **Methods:** Gefitinib-resistant PC9/G cell lines was induced by exposure of PC9 cell lines to MNNG and gefitinib and maintained in the mediua containing 0.05 umol/L of gefitinib. A combination of EGFR tyrosine kinase inhibitor (TKI) gefitinib and a COX-2 inhibitor celecoxib were studied for theirs effects on the cell proliferation, cell cycle and apoptosis in two cell lines by MTT assay and flow cytometry analysis. Western Blot was used to detect expression of COX-2,NF-$\kappa$B,EGFR, phospho-EGFR, Akt and phospho-Akt, Erk, phosphor-Erk. **Results:** Resistant index of PC9/G cells to gefitinib was about 147- to 198-fold higher than PC9 cells, and it was accompanied by significant increase of COX-2 expression in PC9/G cells. Inhibition of COX-2 with celecoxib in PC9/G resulted in dramatic inhibition of proliferation and promotion of apoptosis in response to gefitinib. PC9/G cells' sensitivity to gefitinib is restored. Western blotting showed decreased expression of p-EGFR and COX-2 with both gefitinib and celecoxib treatments, but most pronouncedly in the combined group ($P<0.05$) in PC9/G cells. Furthermore, the combination as compared with effect of single agents showed strong reductions of NF-$\kappa$B,p-ERK and PGE2 of PC9/G cell line. **Conclusion:** These findings suggest that COX-2 may be involved in the resistance of NSCLC to EGFR TKI. COX-2 signaling by ERK pathway may be a mechanism of acquired gefitinib resistance and may serve as an alternative therapeutic target for NSCLC unresponsive to EGFR TKIs. **Keywords:** lung cancer;target therapy;drug resistance;COX-2

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**PUB058 CXC195 Induce Apoptosis and Endoplasmic Reticulum Stress in Human Non-Small Cell Lung Cancer Cells via IRE1$\alpha$-Dependent Pathway** Jiexia Zhang[1], Ying Liang[2], Yongbin Lin[3], Yuanbin Liu[1], Weiqiang Yin[1], You You[1] [1]*State Key Laboratory of Respiratory Disease, Department of Medicine, Guangzhou Institute of Respiratory Disease, Guangzhou/China,* [2]*Medical Oncology, Sun Yat-Sen University Cancer Center, Guangzhou/China,* [3]*Thoracic Surgery, Sun Yat-Sen University Cancer Center, Guangzhou/China*

**Background:** This study was to investigate the anti-cancer effect of CXC195 against human non-small cell lung cancer (NSCLC) A549 cells and the underlying mechanisms. **Methods:** The effect of CXC195 on cell viability was assessed in A549 cells at various concentrations and time points by measuring MTT production. Annexin V/PI straining was used to investigate whether apoptosis can be induced by CXC195. We examined the expressions of ER stress-associated proteins by RT-PCR. Cell lysates were immunoprecipitated with anti-IRE1$\alpha$ antibody. We transfected with IRE1$\alpha$ siRNA following treatment with CXC195. **Results:** First CXC195 inhibited the proliferation and induced cell cycle arrest and apoptosis of A549 cells. Second,Caspase3, 8, 9 and PARP-1 activation, and Bax/Bcl-2 ratio analyses demonstrated that the anti-cancer effect of CXC195 in A549 cells was mediated by promoting caspase- and mitochondria-dependent apoptosis. Furthermore, CXC195 induced ER stress in A549 cells as evidenced by elevated levels of GRP78, GRP94, CHOP, IRE1$\alpha$, TRAF2, p-ASK1

 

and p-JNK, and enhanced formation of an IRE1α-TRAF2-ASK1 complex. Knockdown of IRE1α by siRNA suppressed activation of IRE1α, TRAF2, p-ASK1 and p-JNK in CXC195 treated A549 cells. In addition, the effects of CXC195 on the formation of an IRE1α-TRAF2-ASK1 complex, caspase- and mitochondria-dependent apoptosis were also reversed by IRE1α siRNA in A549 cells. **Conclusion:** We showed that CXC195 induced apoptosis of A549 cells were through IRE1α-TRAF2-ASK1 complex-mediated ER stress, JNK activation, and mitochondrial dysfunction. These insights on this novel compound CXC195 may provide a novel anti-cancer candidate for the treatment of NSCLC. **Keywords:** apoptosis, IRE1α, non-small cell lung cancer, CXC195

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**PUB059 Macrophages Promote Tumor Transformation of Human Bronchial Epithelial Cells via NF-κB and STAT3 Signaling in a Bionic Airway Chip Culture**
Qi Wang, Encheng Li, Zhiyun Xu, Hui Zhao *Respiratory Medicine, The Second Affiliated Hospital, Dalian Medical University, Dalian/China*

**Background:** Numerous epidemiological studies have indicated that chronic inflammation may play a critical role in lung tumorigenesis. However, the key molecules and signaling pathways that are involved in inflammation-mediated lung tumorigenesis remain to be fully elucidated. The chronic inflammatory microenvironment containing inflammatory cells, cytokines, and chemokines can promote malignant transformation of bronchial epithelial cells. Among these inflammatory cells in the lung, macrophages are the most abundant and the key components that link inflammation and cancer. To date, most studies have focused mainly on the role of macrophages in tumor progression based on an established tumor model with or without metastasis, but macrophages are rarely involved in tumor initiation. **Methods:** The role of macrophages and their related molecular mechanisms in lung tumorigenesis were assessed using a BaP-induced tumor transformation model with a bionic airway chip *in vitro* and animal models. Cell morphology, proliferation, anchorage-independent growth, tumor formation in nude mice, and molecular signaling pathways were also analyzed. **Results:** The bionic airway chip culture data showed that macrophages promoted BaP-induced malignant transformation of human bronchial epithelial cells, which was mediated by nuclear factor (NF)-κB and STAT3 pathways to induce cell proliferation, colony formation in chip culture and tumorigenicity in nude mice. However, blockage of interleukin (IL)-6 or tumor necrosis factor (TNF)-α signaling or inhibition of NF-κB, STAT3, or cyclinD1 expression abrogated the effect of macrophages on malignant transformation of bronchial epithelial cells in the bionic airway chip culture. In vivo, macrophages promoted lung tumorigenesis of carcinogen-induced animal model. Similarly, blockage of NF-κB, STAT3, or cyclinD1 using siRNA transfection, decreased the carcinogen-induced tumorigenesis in rats. **Conclusion:** Macrophages were critical in promoting lung tumorigenesis and that the macrophage-initialed TNF-α/NF-κB/cyclinD1 and IL-6/STAT3/cyclinD1 pathways were primarily responsible for promoting lung tumorigenesis. **Keywords:** macrophages, NF-κB, STAT3, malignant transformation

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**PUB060 Clinical Characteristics of T790M in Pre and Post Treatment with EGFR TKIs**
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**Background:** *T790M* mutation was first discovered in patients who acquired resistance to gefitinib or erlotinib. It has then been shown to be a "second-site mutation" in approximately 50% of EGFR-mutant lung cancers that have developed acquired resistance to EGFR-TKI. However, in some patients, the *T790M* mutation was also detected as a primary event before drug exposure, at a frequency that is highly dependent on the technique used. **Methods:** 6554 DNA samples from lung cancer patients in Guangdong General Hospital during 2005-2014 was retrospectively collected for both EGFR sensitive mutation (exon 19 deletion and *L858R* mutation) and *T790M* mutation analysis, by either direct DNA sequencing or amplification refractory mutation system (ARMS). **Results:** Of 6046 patients whose tumor samples were collected before EGFR-TKI exposure, the frequency of *de novo T790M* mutation was as low as 0.5%. Gender (p=0.026) and smoking status (p=0.020) correlated significantly with *T790M* mutation frequency, whereas age, disease stage and histology type were not. The *T790M* mutation frequency was higher in female non-smoking patients compared with male smoking patients. Of 508 patients who had a post-TKI biopsy, the incidence of *T790M* mutation was 22.5%. And ARMS was shown to be more sensitive than direct DNA sequencing (27.8% vs 19.6%, p=0.034). In mutation-positive subgroup, the prevalence of concomitant*T790M* was 1.4% in TKI-naïve samples and 39.9% in TKI-treated samples. No difference between exon 19 deletions and L858R mutations existed in pre-TKI samples (1.1% vs 1.6%, p=0.438), whereas a higher frequency of *T790M* mutation was found in exon 19 deletions in post-TKI samples (40.1% vs 28.3%, p=0.034). **Conclusion:** Tumors with a preexisting *EGFR T790M* mutation are extremely rare when tested by the traditional techniques. The observed mutation frequency suggests that the majority of *T790M* mutation emerge during EGFR-TKI exposure and it might occur more frequently in exon 19 deletions. **Keywords:** T790M mutation, lung cancer, epidemiology, Epidermal growth factor receptor-tyrosine kinase inhibitors

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**PUB061 Bexarotene Inhibits the Viability of A549 Cells via slc10a2/PPARγ/PTEN/mTOR Signaling Pathway**
Xinghao Ai, Shun Lu *Shanghai Lung Tumor Center, Shanghai Chest Hospital, Shanghai/China*

**Background:** Thirty to forty percent of non-small cell lung cancer (NSCLC) patients developed higher hypertriglyceridemia in the process of treatment with bexarotene, and the high-grade hypertriglyceridemia patients had significantly longer survival. The bioinformatics studies discovered that the expression of slc10a2 was increased in high-grade hypertriglyceridemia patients, but the detailed mechanism still not clear. The purpose of this study is to explore the mechanism which slc10a2 may involve in this process. **Methods:** Bexarotene-mediated growth response and pathway activation were examined in human NSCLC A549 cell lines. The effect of Bexarotene combined with SLC10a2 over expression or down-regulation on cell proliferation was detected by cck-8 assay, the potential of cell invasion was employed by transwell invasion assay and the induction of apoptosis was tested using the AnnexinV-PI reagent assay. Apoptosis related gene and anti-oncogenes wre also conducted by Quantitative-PCR and PPARγ pathway associated genes was analyzed by using a western blot analysis. **Results:** We found that the proliferation and migration were inhibited and the apoptosis of A549 cells was accelerated by bexarotene. In addition, over expressed slc10a2 in A549 cells can further suppress the proliferation and migration, and promote apoptosis under the treatment of bexarotene. Moreover, the expression of caspase 7, PTEN, P21, P53, LKB1, TSC2 were increased and the expression of Bcl-2, cyclin D1, c-FLIP were declined in A549 cells and slc10a2 over expressed A549 cells with the treatment of bexarotene. The opposite results were obtained after slc10a2 gene was silenced in A549 cells treated with bexarotene. The further studies revealed the increased expression of slc10a2 activated the expression of PPARγ, then up-regulated PTEN expression and down-regulated mTOR expression. **Conclusion:** These results suggest that bexarotene inhibits the viability of lung cancer cells via slc10a2/PPARγ/PTEN/mTOR signaling pathway.

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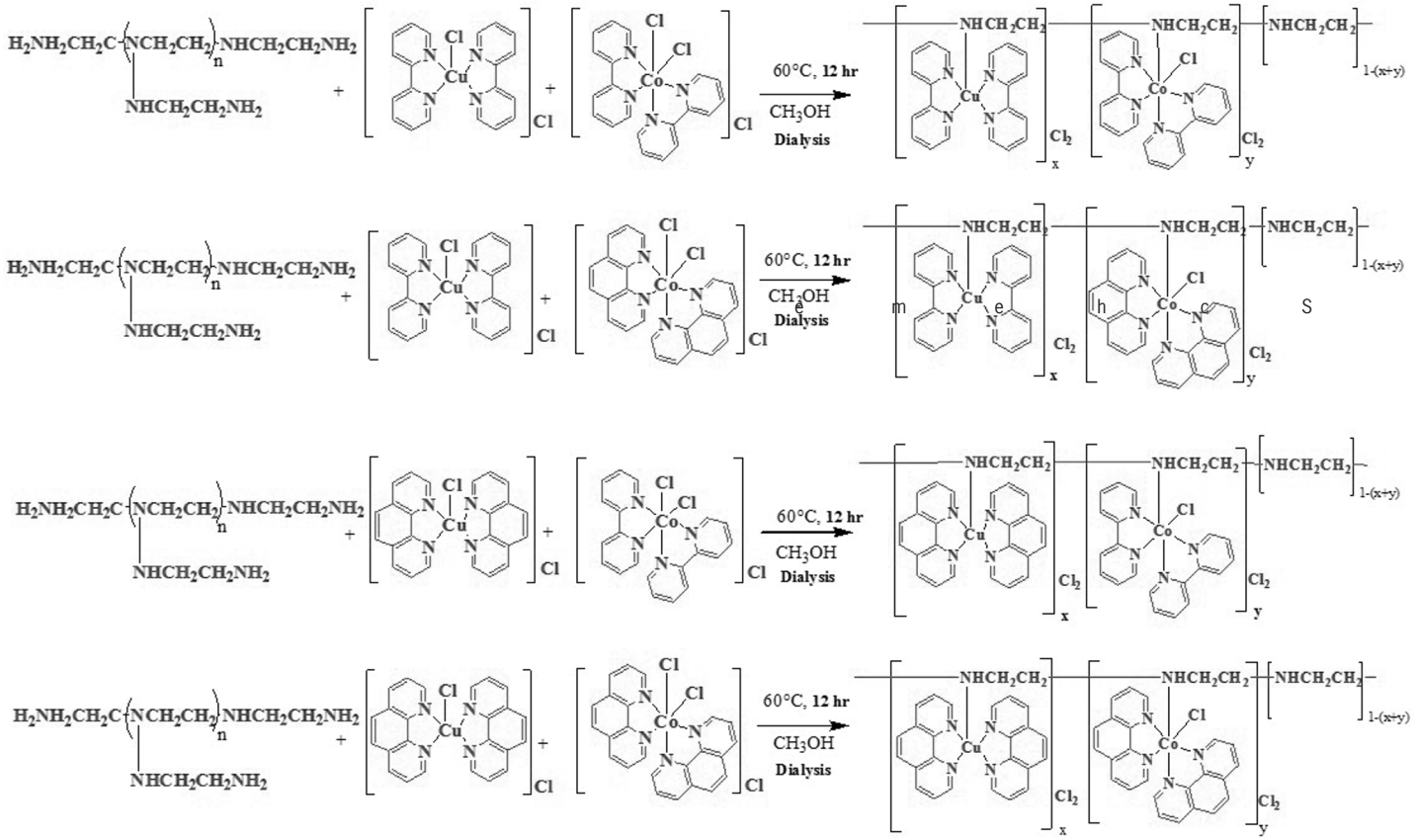
**PUB062 Triggered Cancer Therapeutics: Synthetic Polymer Metal Complex Conjugates**
Ilayaperumal Pradeep, Sankaralingam Arunachalam, Balagurusamy Balajothi *School of Chemistry, Bharathidasan University, Trichy/India*

**Background:** Recently Studies on the polymer-metal complexes have received increased interest in various branches of chemistry. At the same time, significant developments have also occurred in recent years in the field of biopolymers and biomaterials. Many reports are available on pharmacologically active polymers (polymer drugs) which by themselves may act as drugs or alternatively may act as carriers for normal pharmaceutical agents. Applications for polyetheleneimine (PEI) have emerged in biology and medicine. The branched form of PEI has yielded significantly greater success in terms of cell transfection and a possible alternative to viral and liposomal routes of gene delivery. Metal complexes are presently an object of great attention in the field of medicinal chemistry, especially many copper and cobalt have been reported as promising cytotoxic agents on the basis of invitro anti-proliferative assays and their mechanisms of action. Gene carriers fabricated by conjugation of branched polyethyleneimine (BPEI) 25 kDa, molecular weight of BPEI and consequently improved DNA binding, condensation and transfection efficiency. These investigations have resulted in the synthesis of many new polymer metal complexes. In this work a new class of water soluble polymer metal conjugates were prepared, characterized and anticancer properties were tested with A549 lung cancer cell lines. **Methods: MTT assay** To find out the synthesized PMCCs quality of being cytotoxic to A549 cells we performed dimethyl thiazolyltetrazolium bromide (MTT) assay. **Apoptosis study** The influence of PMCCs to induce apoptosis in lung cancer cells were confirmed using an acridine orange (AO) and ethidium bromide (EB) (1 mg/ml for both AO and EB in phosphate-buffered saline) staining method. **Materials** Branched polyethyleneimine (BPEI) 25 KDa, Calf thymus DNA (Sigma Aldrich), $CoCl_2$ anhydrous (Acros.), $CuCl_2$ $2H_2O$ (Merck) 2,2'–bipyridyl (SpectroChem), 1,10–phenanthroline (Spectrochem), NaCl (Loba chemie) and Buffer capsules (Merck) pH ~ 7.1 were used as received.




1. Schematic representation for PMCC **1-4** preparation. **Preparation of PMCC** Each PMCC with different amount of cobalt(III) and copper(II) chelates content in the polymer was synthesized by ligand substitution method in which labile chloride ligand in the $[Co(bpy/phen)_2Cl_2]Cl$ and $[Cu(bpy/phen)_2Cl]Cl$ was replaced by the amine group of the BPEI. **Results:** The IC50 of four PMCCs good compared to other clinical drugs and PMCC **4** is high when compared to other PMCC **1-3**.**Conclusion:** The *in vitro* cytotoxicity study demonstrates that the PMCC **1-4** have good anticancer activity against A159 lung cancer cell lines. So these PMCCs are alternative for better anti-cancer drugs and combined drug therapy. **Keywords:** Polymer metal complex conjugates

**PUB063 The Role of Vascular Endothelial Growth Factor in Pathogenesis of the Non-Small Cell Lung Cancer** Anna Shchayuk[1], Michael Shepetko[2], Elena Mikhalenko[1], Natalia Chebotaryova[1], Evelina Krupnova[1] [1]*Institute of Genetics and Cytology of the National Academy of Sciences of Belarus, Minsk/Belarus,* [2]*Belarusian State Medical University, Minsk/Belarus*

**Background:** Angiogenesis is an important process in pathogenesis of any malignancies, including non-small cell lung cancer (NSCLC). The vascular endothelial growth factor VEGF-A plays the central role in angiogenesis. The aim of the present study is to evaluate possible associations of functional VEGF -2578C>A, -634G>C, and +936C>T polymorphisms with the risk for occurrence and progression of NSCLC in patients living in the territory of the Republic of Belarus. These polymorphisms are located in key regulatory elements of gene VEGF: -2578C>A in promoter region, -634G>C in the 5 ' and + 936C> T in the 3'-UTR of the gene elements that influences the efficiency of protein translation and the expression of VEGF in tumor tissue. **Methods:** In all 202 patients with NSCLC were included in the study. The control group consisted of 336 individuals without an oncopathology who matched to the patients in age-, gender- and comorbidity. **Results:** Comparative analysis of genotype distribution of three gene VEGF polymorphisms with the tumor size has revealed no significant associations between the studied polymorphic allelic variants and regional and/or distant metastatic spreading. No association were found between polymorphic variants in the position -634G>C and survival the patients with NSCLC. In the carriers of -2578C C genotype, a greater degree of tumor spreading (T2-T4) occured significantly more often (p =0,002) than the smaller extent of primary tumor (T1), while small non-invasive cancer (T1) occurs more often in the carriers of –2578C A (p =0,021). The carriers of –2578CA genotype were significantly more often observed in the "follow-up" group. The carriers of heterozygous genotype +936CT gene VEGF were significantly more often (p=0,012) included in the observation group. **Conclusion:** The results of study demonstrate that VEGF –2578A/C and +936C/T polymorphisms are among the factors determining the individual peculiarities of NSCLC course in this population and can be used for clarifying the prognosis of the disease. **Keywords:** vascular endothelial growth factor (VEGF), polymorphism, non-small cell lung cancer

**PUB064 Analysis of the Immune Contexture in Tumor and Tumor-Adjacent Stroma in Resected NSCLC** Marta Usó[1], Eloisa Jantus-Lewintre[2], Rafael Sirera[3], Sandra Gallach[4], Silvia Calabuig-Fariñas[5], Ricardo Guijarro[6], Jerónimo Forteza[7], Carlos Camps[8] [1]*Molecular Oncology Laboratory/Department of Medicine, Fundación Investigación Hospital General Universitario/Uv, Valencia/Spain,* [2]*Molecular Oncology Laboratory/ Department of Biotechnology, Fundación Investigación Hospital General Universitario/Upv, Valencia/Spain,* [3]*Department of Biotechnology, Upv, Valencia/Spain,* [4]*Molecular Oncology, Fihguv, Valencia/Spain,* [5]*Molecular Oncology Laboratory/Department of Pathology, Fundación Investigación Hospital General Universitario/Uv, Valencia/Spain,* [6]*Department of Thoracic Surgery/Department of Surgery, Consorcio Hospital General Universitario/Uv, Valencia/Spain,* [7]*Instituto Valenciano de Patología, Valencia/Spain,* [8]*Department of Medicine/ Department of Medical Oncology, Uv/Consorcio Hospital General Universitario, Valencia/ Spain*

**Background:** The analysis of immunologic features of tumor microenvironment is leading to the development of new immunotherpies and the identification of biomarkers. Therefore, it would be interesting to better understand the key elements involved in shaping the immune microenvironment in solid tumors. In this study, we have investigated the immunologic markers, especially those related to immunoregulation in resected NSCLC. **Methods:** In this retrospective study, FFPE samples from 122 early-stage NSCLC patients of primary tumor tissue were used. Laser capture microdissection was carried out in order to separately obtain tumor and stroma areas. Thirty-eight genes relevant to tumor immune response and immunoregulation were assessed by relative gene expression analysis by RTqPCR using hydrolysis probes. Furthermore, the presence of CD4+, CD8+ and FOXP3+ lymphocytes was also assessed in 84 of these FFPE samples by immunohistochemistry. All statistical analysis were considered significant at p< 0.05. **Results:** Survival analysis carried out with cluster groups obtained from unsupervised hierarchical clustering analysis based on gene expression data showed that patients in stromal Cluster I had a worse PFS than in Cluster II (17.4 vs. 44.3 months, $p$ = 0.006). With regard to the tumoral clustering, patients in Cluster II had a worse OS than patients in Cluster I (34.4 vs. 70.4 months, $p$ = 0.005) as well as a shorter PFS (19.1 vs. 32.5 months, $p$ = 0.010). Those clusters associated with better survival presented higher levels of gene expression in general. Furthermore, the presence of CD8+ cells in the tumor compartment was significantly associated with better OS (73.9 vs 40.4 months, p=0.021) and PFS (56.8 vs 23 months, p=0.026). We also investigated whether there were significant differences in gene expression patterns according to CD4+, CD8+, and FOXP3+ cell infiltration. Interestingly, tumors with higher levels of CD8+ cell infiltration expressed significantly higher levels of genes related to immunosuppressive factors ($p$ = 0.008), chemokines and their receptors ($p$ = 0.017), MDSCs ($p$ = 0.008) and TAMs, and other APCs ($p$ = 0.006). Moreover, significant positive correlations were observed between higher levels of CD8+ cell infiltration and the expression of certain individual genes such as IDO1 ($p$ < 0.001), CCL5 ($p$ = 0.005), CD209 ($p$ = 0.031), CD86 ($p$ < 0.001), and IL23A ($p$ = 0.008), whereas IL8 expression was inversely correlated ($p$ = 0.015). **Conclusion:** Our results indicate the existence of two possible immune-scenarios in NSCLCs. One major subset presents a T cell-inflamed

phenotype consisting of infiltrating T cells, which reflects innate immune cell activation, and in which immunoregulation processes are activated in order to resist immune attack. In this case patients had better outcomes. The other major phenotype lacks this T-cell inflamed phenotype and resists immune attack through immune system exclusion or ignorance. These results provide new insight into the tumor immunity field in NSCLC, and could be useful in the future development of prognostic and therapeutic tools. **Keywords:** NSCLC, immune ckeckpoint, biomarker

**PUB065 Angiogenic Factors and Angiogenesis Inhibitors in Malignant Pleural Effusion Associated with Patient Survival in Lung Cancer** Yu Zhang, Wei Hu, Guo-Jun Lu *First Department of Respiratory Medicine, Nanjing Chest Hospital, Nanjing/China*

**Background:** Angiogenesis is important in malignant pleural effusion (MPE) formation and it is regulated by a number of pro- and anti-angiogenic cytokines.This study aimed to evaluate the prognostic value of angiogenic factors vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), and angiogenesis inhibitors endostatin, pigment epithelium-derived factor (PEDF), in lung cancer patients with MPE. **Methods:** Using enzyme-linked immunoadsorbent assay, the concentrations of VEGF, bFGF,endostatin and PEDF were measured in MPE from a total of 70 lung cancer patients with MPE. **Results:** There were statistically signifiant correlations between VEGF and endostatin levels (r=0.287, p=0.019),and VEGF and bFGF levels in MPE (r=0.33, p=0.012).The levels of VEGF and PEDF, bFGF and endostatin,PEDF and endostatin were not correlated.By univariate and multivariate analysis, pleural VEGF and endostatin levels were independent prognostic factors in lung cancer patients with MPE. **Conclusion:** There may be some homeostatic interrelationship between pro- and anti-angiogenic substances. Our results suggest that VEGF and endostatin may be potential prognostic parameters for lung cancer patients with MPE. We need more in-depth studies to explore whether measurement of these pro- and anti-angiogenic cytokines can guide treatment. **Keywords:** malignant pleural effusion, Prognosis, vascular endothelial growth factor, endostatin

**PUB066 Gene E: A New Suicide Gene Therapy for Non-Small Cell Lung Cancer** Ana R. Rama, Rosa Hernandez, Gloria Perazzoli, Jaime Oliver, Laura Cabeza, Cristina Jiménez-Luna, Maria Carmen Leiva, Julia Jiménez, Jose C. Prados *Institute of Biopathology and Regenerative Medicine (Ibimer), Granada/Spain*

**Background:** The potential use of combined gene therapy is under intensive study to improve the effectiveness of these cytotoxic agents and reduce their adverse effects. In this context, the association of the cytotoxic drugs with killer genes could enhance their antiproliferative effect. The gene E from *ΦX174* encodes for a membrane protein with a toxic domain which causes cell lysis. To improve the antitumoral effect of some classical citotoxic agents we investigated a combined suicide gene therapy on A-549 cells (lung cancer). **Methods:** The gene E was cloned into the plasmid pcDNA3.1 (pcDNA3.1-E) and the lung carcinoma cell line A-549 were grown in monolayer. Experiments were performed in two groups: - Gene E alone: A-549 transfected (pcDNA3.1-E). - Combined gene therapy: A-549 transfected and non-transfected cells were exposed to Paclitaxel (Pac), Carboplatin (Car) and Gemcitabine (Gem), all of them to 100, 50 and 1 μM concentration. We evaluated the effect of gene E and its combination with the cytotoxic drugs by several techniques. **Results:** Our results showed that the E expression in A-549 cells carried to ultrastructural changes, including dilated mitochondria. These findings were corroborated with a significant decrease in mitochondrial transmembrane potential ($p<0.05$). On the other hand, assays with combined therapy showed that effect of the drugs at all different concentration was enhanced by gene E expression. Pac induces the greater inhibition of the proliferation, showing at the average concentration and transfecting 3 times 85% of growth inhibition, just as the therapy only with Pac to the maximum concentration. Parental and cancer cells treated with combined therapy or with citotoxic or gene E separately were analysed by FACscan after anexin-PI staining. The results indicated the ability of gene E to stimulate apoptosis in A-549 treated with their respective drugs. **Conclusion:** In conclusion, gene E has a killer effect in A-549 lung cancer cells which enhances growth inhibition cell when used with citotoxic drugs. That suggests a possibility to reduce the dose of cytotoxic agents applied in the tumours. These results indicate that this combined therapy may be of potential therapeutic value in lung cancer **Keywords:** gene E, suicide gene therapy, lung cancer, chemotehrapy

**PUB067 Protection of Radiation-Induced Cytotoxicity and DNA Damage in Chinese Hamster Lung Fibroblast Cells by Dietary Compound Zingerone** Nageshwar Rao[1], Satish R. B[2] [1]*Microbiology, Mamata Medical College, Khammam/India,* [2]*Radiation Biology, Manipal Life Science Center, Manipal/India*

**Background:** Radiotherapy is commonly used to treat several neoplastic diseases. During irradiation of tumors the deleterious effects of radiation are also felt by the normal tissue surrounding the neoplastic lesions. This limits the dose of radiation to cancer; as a result the effective treatment of tumor may not be affected. Therefore, any agent with its radioprotective effect on normal tissue toxicity will be clinically useful. The present study will be of great importance, as we do not have an ideal radioprotective agent for its application in Radiotherapy. If Zingerone (ZO) renders radiation protection as that of the standard drug Amifostine (WR 2721), it may have its potential for clinical application. Besides, the anticlastogenic and free radical scavenging potential of the Zingerone may have varied applications not only for radiation protection but also in the areas of chemoprotection and against any other free radical mediated pathological conditions. The results of the proposed study may give one such a potential candidate drug which may be useful as radioprotector with further investigation. The radioprotective effect of Zingerone (ZO) a dietary compound was investigated for its ability to protect against radiation induced cytotoxicity and genotoxicity in Chinese hamster lung fibroblast (V79) cells growing in vitro. **Methods:** The radiation antagonistic potential of ZO was assessed by MTT, clonogenic, micronucleus and apoptotic assays. **Results:** Treatment of V79 cells with ZO (10 μg/ml) prior exposure to 10 Gy gamma radiation resulted elevation in the cell survival as evaluated by MTT assay. Similarly, there was a significant increase in the surviving fraction observed with 10 μg/ml of ZO treatment one hour prior to graded doses of gamma radiation. The genotoxic effect of radiation increased in a dose dependent manner indicated by increased in micronuclei frequency with increasing radiation dose. ZO (10 μg/ml) treatment significantly reduced the radiation induced micronuclei formation. Further, treatment with ZO (10 μg/ml) before irradiation significantly decreased the percentage of apoptotic cells (sub-G1 population) analyzed by flow cytometric method and DNA ladder assay. To understand the mechanism of action of ZO, separate experiments were conducted to evaluate the various free radical scavenging generated in vitro. ZO was found to inhibit the generation of free radicals in a dose dependent manner up to a dose of 100 g/ml for majority of the radicals and plateaued thereafter. **Conclusion:** Our study demonstrates the antagonistic effect of ZO against radiation-induced cytotoxicity and genotoxicity by elevating the antioxidant status and reducing the membrane lipid peroxidation and therefore ZO may have its application as a radioprotective agent. **Keywords:** lung fibroblast, radiation, DNA damage, cytotoxicity

**PUB068 EGFR Gene Mutation in Advanced Non-Small Cell Lung Cancer - A Case** Tahir Mehmood, Muhammad Irfan, Asma Rashid *Radiation Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore/Pakistan*

**Background:** Molecular targeted therapy based on TKIs, directed at the Epidural growth factor receptor (EGFR) is one of the recent option for the management of advanced Non-Small Cell Lung Cancer (NSCLCs). EGFR gene mutations, exon 19 deletions (LREA deletions) and exon 21 (L858R) are most common and good predictions of response to EGFR-TKI treatment. EGFR gene mutations are found in approximately 10% of Caucasian patients and up to 50% of Asian populations. Recent studies have endorsed these incidences in European and Asian populations. The frequency of EGFR mutation is higher in non-smokers and in women. To objective of this study was to determine the frequency of EGFR gene mutations in non–small-cell lung cancer patient presenting at our institute. **Methods:** Between September 2011 to September 2013, we sent EGFR mutation testing for 39 patients with proven histology of TTF-1 positive adenocarcinoma lung. EGFR gene mutations in exons 18, 19, 20 and 21 were carried out by National University Hospital Singapore and at Shaukat Khanum Memorial Cancer Hospital Lahore, Pakistan. **Results:** 72% of the patients were males and 28% were females. 49% were smokers, 41% were non-smokers and this information was missing in 10% of the patients. 18.5% of the patients were found to have EGFR gene mutation positive; 28.5% on exon 18, 28.5% on exon 19, 14.5% on exon 20 and 28.5% on exon 21. Among patients having EGFR gene mutation positive, 57% were smokers while 43% were non-smokers. **Conclusion:** The frequency of EGFR mutation in our institution was 18.5% and all these patients were male, with almost half of the patients being smokers. This trend is not in accordance with published literature and merits similar study with a larger number of patients to find out the real trend of EGFR gene mutation in our population. **Keywords:** EGFR, NSCLC

**PUB069 Exploration of ALK Fused Gene Expression in Non-Small Cell Lung Cancer Patients by Immunohistochemistry** Jie L. Cao *Pulmonary Medicine, Anhui Provincal Hospital, Hefei Anhui Province/China*

**Background:** With RT-PCR as a reference , our aim is to explore the accuracy of ALK fused gene expression by immunohistochemistry in NSCLC patients, and to establish an economical feasible method for the screening of ALK positive NSCLCs. We also investigate the clinical and pathological features of ALK-positive NSCLC patients. **Methods:** By using rabbit monoclonal D5F3 antibody, ALK IHC was performed on 234 NSCLC patients. ALK positive cases were confirmed by RT-PCR. **Results:** The positive incidence of ALK by IHC in 234 NSCLC specimens was 8.97% (21/234), the positive rate of ALK fused gene verificated by RT-PCR was 5.98% (14/234). There is significant difference with histological type, age, stage-related ($P<0.05$); but no significant difference with gender, smoking history, tumor differentiation. Of 21 cases of ALK-positive NSCLC patients,The consistency of IHC and RT-PCR increased with the increasing of IHC-positive level. The consistency of IHC and RT-PCR was 0 when IHC wan 1+ ,however, when IHC was 3 + or immunohistochemical score was > 120, the consistency rate was 100%. **Conclusion:** Although immunohistochemical expression of ALK fused gene may have a certain false positive, IHC 3+ or immunohistochemical score> 120 show very high value for ALK fused gene RT-PCR followed by ALK immunohistochemistry in lung cancer is a economical and feasible method for the valuation of ALK fused gene.

**PUB070 Acquired Genetic Changes Identified in Lung Adenocarcinoma with ALK Translocation** Sana Yokoi[1], Soutaro Kanematsu[2], Hitomi Kondo[2], Hideki Kimura[3], Toshihiko Iizasa[4] [1]*Cancer Genome Center, Chiba Cancer Center Research Institute, Chiba/Japan,* [2]*Genetic Diagnostics, Chiba Cancer Center, Chiba/Japan,* [3]*Respiratoly Surgery, Saiseikai Narashino Hospital, Narashino/Japan,* [4]*Thoracic Surgery, Chiba Cancer Cener, Chiba/Japan*

**Background:** *Anaplastic lymphoma kinase (ALK)* is the oncogenic kinase activated by chromosomal translocation in pulmonary adenocarcinoma. Although ALK inhibitor was effective, the recurrence was observed in the patient without ALK mutation. **Methods:** To explore the novel therapeutic targets of the ALK-positive lung cancer patients, we

analyzed genome wide copy number aberrations in 12 ALK-positive lung tumors by using array-comparative genomic hybridization. For the loci with copy number loss, the mRNA expression of the gene on the loci were analyed. Moreover the methylation status of the promoter region of the gene was evaluated by pyrosequencing. **Results:** The 111 loci showed copy number losses. The down-regulated gene was demonstrated in these loci with hyper methylation in tumor tissues compared with their non-tumorous counterparts. In pulmonary adenocarcinoma, the tumors with ALK showed lower expression than those without ALK. The patients with lower expression of the gene showed poor prognosis in lung adenocarcinoma. **Conclusion:** These results demonstrated that acquired genetic changes in ALK-positive cancer may relate to be a secondary pathway of ALK. **Keywords:** ALK, translocation, copy number, methylation

**PUB071 A Lung Cancer Bayesian Network Facilitated Identification of Key Regulators of Epithelial to Mesenchymal Transition (EMT)** Seungyeul Yoo[1], Li Wang[1], Sachiko Takikawa[1], Mark J. Schliekelman[2], Samir M. Hanash[3], Charles A. Powell[1], Jun Zhu[4] [1]*Icahn School of Medicine at Mount Sinai, New York/United States of America,* [2]*Fred Hutchinson Cancer Research Center, Seattle/AL/United States of America,* [3]*The University of Texas MD Anderson Cancer Center, Houston/TX/United States of America,* [4]*Icahn School of Medicine at Mount Sinai, New York/NY/United States of America*

**Background:** Epithelial to mesenchymal transition (EMT) is a key process associated with tumor progression and metastasis. The EMT process is complex and regulated at multiple levels. Multiple in vitro and in vivo omics signatures based on mRNA, microRNA, DNA methylation and proteomic profiles have been generated for portraiting EMT process in non-small cell lung cancers (NSCLCs). Currently, there is no drug targeting metastasis. We aim to identify key regulators of EMT for therapeutic development. However, given these diverse omics signatures it is still not clear which genes are key regulators of EMT. **Methods:** Network approaches have been commonly used to integrative analyze diverse omics signatures. There are multiple types of networks that can be used for network analysis. We selected two representative networks, a protein-protein interaction (PPI) network from Human Protein Reference Database (HPRD), which represents general non-context specific regulations, and a Bayesian molecular causal network constructed from large scale molecular profiling of NSCLCs, which represents context specific regulations. We compared the two networks in term of their abilities for bridging multiple lung cancer related molecular signatures in public databases. The lung cancer Bayesian network performed much better than the PPI network from the HPRD in both sensitivity and specificity. **Results:** Using the Bayesian network constructed from NSCLC profiling data for representing lung cancer network we applied network analysis to multiple omics signatures related to EMT that we generated. The EMT related subnetwork identified was significantly enriched for genes involved in cytoskeleton modeling. We further inferred *TPX2*, *BIRC5*, *EMP3*, and *PMSD9* as putative key regulators of the EMT subnetwork and experimentally validated their contribution to EMT by in vitro migration and invasion assays. **Conclusion:** Our network analysis of multi-omics EMT signatures identified multiple key regulators of EMT that can be targeted for against lung cancer metastasis and invasion. **Keywords:** Network analysis, Bayesian Network, EMT

**PUB072 Correlates of Tobacco Cessation Counseling across Health Professional Groups - Findings from India** Rajmohan Panda, Divya Persai *Public Health Foundation of India, New Delhi/India*

**Background:** Tobacco cessation counseling by health professionals is an effective approach to increase cessation rates among tobacco users. The present study aimed to compare cessation counseling practices across the four health professional groups including physicians, nurses-midwives, lab technicians and pharmacists. We also identify the correlates of tobacco cessation counseling associated with each group. **Methods:** The study was a cross-sectional study conducted among 1483 health professionals (Physicians-345; Nurses-midwives-800; lab technicians and pharmacists-338) working in primary health care in 12 districts of Andhra Pradesh and Gujarat in India from June to August 2013. The health facilities were chosen using systematic random sampling. We used multiple regression analysis to identify independent correlates of counseling score within each health professional group. **Results:** Findings indicate that three factors emerged consistently across most groups as positively associated with counseling, including the belief that counseling is the role of health professionals, knowledge of tobacco cessation techniques and training in tobacco cessation. Physicians who have sufficient knowledge on tobacco cessation techniques (OR-5.7; CI:1.6-20.1) and received training in tobacco cessation (OR-3.5;CI:1-11.8) were more likely to provide counseling services as compared to nurses and midwives (OR-2.2 CI-0.7-6.5).**Conclusion:** The correlates of cessation counseling differ across health professional groups. Interventions that address knowledge of health professionals on tobacco cessation techniques and training in tobacco cessation may result in improved cessation counseling practices among health professionals. An intensive intervention needs to be designed for nurses-midwives, lab technicians and pharmacists to enhance their counseling practices in tobacco cessation. **Keywords:** Tobacco cessation, Health Professionals, India

**PUB073 Perceptions of Carcinogenic Effects of Smokeless Tobacco Products among Out-Of-School Youths in Lagos, Nigeria** Olanrewaju O. Onigbogi[1], Omobola Ojo[2] [1]*Community Health, University of Lagos, Team/Nigeria,* [2]*Comm Health, Lagos Univ Teaching Hosp, Lagos/Nigeria*

**Background:** There have been speculations about introduction of smokeless tobacco products to the African markets in the near future. There are already indications that this marketing strategy may be adopted soon in Nigeria. This study was designed to elicit the perceptions of out-of-school youths about the carcinogenic effects of smokeless tobacco products. **Methods:** Participants were recruited among one hundred and thirty two youths in Ibadan who had been out of school for at least one year. All the participants were males. Ten focus group discussion sessions were then conducted for willing participants who said they had used or come into contact with a smokeless tobacco product before. The discussions were audio-taped, transcribed and coded using the NUDIST software. Inter-observer variability was 82%. **Results:** The responses could be classified under four major themes were identified: (1) Smokeless tobacco products are used by females or by males (2) Smokeless tobacco products are not necessarily safer (3) Smokeless tobacco products are less carcinogenic and (4) Smokeless tobacco can be used by "social smokers" and should be easy to quit. Comments include "Smokeless tobacco products will not cause cancer because it will not get into the lungs". **Conclusion:** Perceptions about the carcinogenic effects of these products and the purported ease of cessation of their users suggest a need to design and test true knowledge and attitude patterns among Nigerian tobacco users. There is also a need to further explore perception of smokeless tobacco products in the larger population. **Keywords:** smokeless, tobacco, carcinogenic

**PUB074 20-Years of Lung Cancer Incidence and Baseline Survival Rates in the Gambia, West Africa** Ebrima Bah[1], Maria P. Carrieri[2], Omar Sam[3], Swaminathan Rajaraman[4] [1]*Directorate of Public Health Research, Ministry of Health & Social Welfare, Serekunda/Gambia,* [2]*Ird, Université Aix Marseille, Marseille/France,* [3]*World Health Organisation, Bobodulaso/Burkina Faso,* [4]*Cancer Institute (Wia), Chennai/India*

**Background:** The monitoring of lung cancer occurrence provides fundamental information for tracking and stopping the tobacco epidemic globally, regionally and nationally. Information on lung cancer incidence and survival from the disease which is an important piece in such endeavors is very scarce in sub-Saharan Africa. This is mainly due to the fact that less than 10% of this vast continent is covered by population-based cancer registries (PBCR). PBCR can assist in monitoring the tobacco epidemic and the evaluation of interventions against it by providing information on lung cancer occurrence. There is no dispute among researchers that tobacco use, especially, via smoking, causes lung cancer. In The Gambia, legislature against tobacco use have been introduced a couple of years ago as part of the country's implementation of her ratification of the World Health Organization's (WHO) Framework Convention on Tobacco Control (FCTC). A PBCR was already established to study the incidence of all cancers including lung cancer since 1986. This made it possible for us to utilize the data collected over a period of 20-years via the PBCR to:

- assess for the first time, the evolution of the incidence rates and baseline information on survival rates of lung cancer diagnosis in The Gambia
- demonstrate the role of the PBCR in cancer control, specifically in monitoring the tobacco epidemic in sub-Saharan Africa.

**Methods:** Age-Standardized Incidence Rates (ASR (W)) of lung cancer diagnosed and registered in the population of The Gambia during the period 1990 - to - 2009 were estimated by gender. To enhance the analysis and interpretation of our findings, we divided the registration period into four 5-year intervals and estimated incidence rates for each interval. The (ASR) (W)) was standardized to the world standard population commonly used by PBCR to aid the comparison of incidence rates between populations. Using data collected from 1993 – to – 1997 and with patients followed-up to 31st December, 1999, baseline 5-year Relative Survival Rates were analyzed for males. In The Gambia cancer registration is more active than passive and patient follow-up to assist population-based survival analysis is predominantly active and based on home-visits by trained health workers. **Results:** Lung cancer is the third commonest cancer in males accounting for 5% (158 cases, ASR (W)) = 2.45 per 100, 000 person-years) of all male cancers. The 5-year relative survival in males was estimated to be 29%. The disease is uncommon among female Gambians. Over the 20-year period, only 29 cases of lung cancer were observed among female Gambians, which translates to ASR (W)) = 0.4 per 100,000 person-years. **Conclusion:** Further study of this population via regular analysis of the PBCR database and the conduct of epidemiological studies to adequately document the tobacco epidemic is necessary. Such information is fundamental to stopping the tobacco epidemic nationally and elsewhere in sub-Saharan Africa were such information is non-existent.The monitoring of lung cancer occurrence through PBCR is a key public health pre-requisite for rational planning and implementation of targeted interventions for health protection, health improvement and health promotion in Africa. **Keywords:** survival, Incidence, Gambia, Cancer

**PUB075 Plain Packaging of Tobacco Products: Dressing Down the Tobacco Industry** Karuvaki Mohanty *Legal, Hriday, New Delhi/India*

**Background:** Plain packaging of tobacco products results in reduction of brand imagery which would diminish the attractiveness of tobacco products, promote cessation-related behaviours among some smokers, and reduce initiation. However, the multinational tobacco companies have misinterpreted the relevant legal issues related to plain packaging and have exaggerated the restraints that the investment and international trade agreements can impose on the autonomy of the countries and the respective governments to ensure protection of public health.[1] The tobacco industry has a history of using international trade agreements to force open new markets in low and middle income countries, greatly increasing tobacco use and the consequent death/disease it causes. These companies argue that against tobacco control laws like mandatory plain packaging breach international laws. necessary that the key decision makers and the governments of nations are completely aware of the tobacco industry tactics and use flexibilities provided under WTO agreements to the advantage of public health policies for the greater

purpose of promoting and protecting public health.[2] Positive Measures of advocacy for plain packaging has also started in India taking clue from Australia which has adopted plain packaging. To bring plain packaging to India, a Bill, *Cigarettes and other Tobacco Products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Amendment Bill, 2014* has been introduced in the Parliament by Member of Parliament Mr Baijayant J Panda seeking amendment in the Cigarettes and Other Products Act, 2003. [1] Davison Mark, Liberman Jonathan, Andrew Mitchell, Responding to the tobacco industry's claims that plain packaging breaches international trade and investment law, [Internet] 2014 [cited 2014, Nov 19]. Available from: http://www.mccabecentre.org/blog-main-page/respondingtothetobaccoindustrysclaims.html [2]*Id*. **Methods:** A theoretical research approach has been undertaken including perusal of published research articles, academic journals, opinion of judiciary and other primary, secondary data regarding the relevance of plain packaging has been analysed. **Results:** The opposition against plain packaging by the tobacco industry shows the real image of the multinational companies and their intention to market harmful tobacco products through coloured, attractive packaging. The industry is only concerned about the marketing and sale of their products and is least concerned about the harm that such products cause to the consumers using them. The international treaties like WHO Framework Convention on Tobacco Control, Doha Declaration related to tobacco control, the **Punta del Este Declaration, the TRIPS agreement provide for the parties to take steps to protect public health and this justifies the incorporation of plain packaging as an anti-tobacco measure.** Right to free trade comes with certain reasonable restrictions which include taking measures to restrict marketing strategies of products harmful to health. Moreover, plain packaging only places restrictions on the display of the brand logo and brand name, colour combination and does not completely disallow the sale of such products. **Conclusion:** Packing cigarettes and other tobacco products in plain single dull drab colours will make the products unattractive and reduce acceptability amongst youth thereby bringing down the youth initiation of tobacco. **Keywords:** Unattractive tobacco products, Plain Packaging tobacco use public health

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**PUB076 Missed Opportunities for Brief Intervention in Tobacco Cessation in Primary Care in India** Rajmohan Panda, Divya Persai *Public Health Foundation of India, New Delhi/India*

**Background:** Tobacco use is ranked as the one of the major preventable risk factors for mortality and morbidity in India. Tobacco cessation can substantially reduce tobacco-related morbidity and mortality. Brief intervention has been recommended as a best practice for tobacco cessation. The present study aims to investigate the brief intervention practices of Health Service Providers (HSPs) in tobacco cessation and the factors influencing screening practices of HSPs for tobacco usage in patients attending health facilities providing primary care. **Methods:** The study was a cross-sectional study conducted among 1,549 patients aged more than 18 years visiting health facilities providing primary care in 12 districts of two high tobacco burden states i.e. Andhra Pradesh (AP) and Gujarat in 2012. The study was conducted in 200 health facilities providing primary care. The health facilities were chosen using systematic random sampling. The study participants were recruited through simple random sampling. **Results:** Only 136 (36%) of the patients reported to have been counseled. Less than one-third (447) of patients were screened for tobacco use during their visit to the health facility. 'Number of quit attempts in the past 12 months' was strongly associated with the outcome of being screened for tobacco use. Patients who had made '1 to 5 quit attempts' and '>5 quit attempts' were associated with an OR of 1.54 (95% CI: 1.16 to 2.05) and 1.99 (95% CI: 1.03 to 3.85) respectively of being screened for tobacco use than those who had never attempted to quit tobacco. **Conclusion:** Our results show that opportunities for screening and providing tobacco use cessation advice were largely missed by the health service providers. There is an urgent need to incorporate tobacco cessation interventions as part of standard practice in primary care. **Keywords:** Tobacco cessation, Primary care, India

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**PUB077 A Survey on Tobacco Use in Chennai City** Clement Joy Kingsly Francis[1], Delfin Lovelina Francis[2] [1]*Finance and Economy, Nestle India Private Limited, Gurgaon/India,* [2]*Public Health Dentistry, Tagore Dental College and Hospital, Chennai/India*

**Background:** India is the second largest consumer of tobacco products and third largest producer of tobacco in the world. Tobacco is a major, preventable cause of premature death and disease, currently leading to over five million deaths each year worldwide, which is expected to rise to over eight million deaths yearly by 2030. Vast majority of these deaths are projected to occur in developing countries. Nearly eight to nine lakh people die every year in India due to diseases related to tobacco use. Majority of the cardio vascular diseases, cancers and chronic lung diseases are directly attributed to tobacco consumption. Almost 40% of tuberculosis deaths in the country are associated with smoking. MMTR statistics revealed that 43% of all cancers among men and 17% of all cancers among women occurring in Chennai are related to tobacco use in some form. An efficient and systematic surveillance is essential for a comprehensive tobacco control effort to monitor the epidemic. Considering the burden of diseases caused by tobacco and the benefits we get by reversing the epidemic, effective interventions and evaluation strategies are need of the hour. Therefore, this study is aimed to evaluate tobacco usage in Chennai city covering both urban and rural population. **Methods:** The modified version of the GATS questionnaire developed by WHO was used for the survey. GATS is intended to assist countries to design, implement and evaluate tobacco control and prevention programme. The survey was conducted as follows 1) the selected households were visited to identify the adult family members in each household from the available adult respondents. 2) Each adult (15 years and above) was contacted over phone or in person to elicit the details of their tobacco use, exposure to second hand smoke, quit attempts, the impact of tobacco control and prevention initiatives, etc. Their response was recorded and the questionnaires were statistically analyzed. **Results:** Prevalence of consumption of tobacco products was very high (57%). Most of them started using tobacco products in age less than 18 years (70%) and associated factors for tobacco use are due to friends and their influence (78%). Awareness level was (48%) but still uses tobacco products because of its addiction (73%). In their opinion, increase in tax may reduce it consumption and the majority (70%) think that tobacco must be banned. 42% used tobacco as second hand exposure in job places and only 14% from all males enrolled, were smoking in public places. **Conclusion:** Outreach programmes from hospitals can educate the community about the dangers of tobacco and the signs of tobacco-related cancer. These programmes can attract tobacco users (smokers and smokeless) to its cessation. Anti-tobacco education must be imparted through schools, hospital outreach programmes, existing government health programmes such as maternal and child health programmes and routine home visits, using suitable materials **Keywords:** Tobacoo, smoking, prevalence, second hand smoke.

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**PUB078 Tobacco Use, Awareness and Cessation Among Malayali Tribes, Yelagiri Hills, Tamil Nadu, India** Delfin Lovelina Francis[1], Clement Joy Kingsly Francis[2] [1]*Public Health Dentistry, Tagore Dental College and Hospital, Chennai/India,* [2]*Finance and Economy, Nestle India Private Limited, Gurgaon/India*

**Background:** Health is a state of complete wellbeing free from any discomfort and pain. Despite remarkable world-wide progress in the field of diagnostic, curative and preventive medicine, still there are large populations of people living in isolation in natural and unpolluted surroundings far away from civilisation, maintaining their traditional values, customs, beliefs and myths. India has the second largest tribal population of the world next to the African countries. About half of the world's autochthonous people live in India, thus making India home to many tribes which have an interesting and varied history of origins, customs and social practices. The primitive tribal communities (comprising 635 tribal communities) have been identified by the Government of India on the basis of their pre agricultural level of technology, extremely low level of literacy and small, stagnant or diminishing population. The present study was conducted to assess the tobacco use, awarness and its effect on health among Malayali tribes, Yelagiri Hills, Tamil nadu, India. **Methods:** The inhabitants of the 14 villages of the Yelagiri hills, who have completed 18years and residing for more than 15years present on the day of examination and who were willing to participate in the study were included. Ethical clearance from the Institution Review Board, permission from the Village panchayat leader and informed consent from individual subjects were obtained. Participants were selected using cluster random sampling method. Data was collected from a cross-sectional survey, using a Survey Proforma, clinical examination and a pre-tested questionnaire which included Demographic data, tobacco habits. An intra-oral examination was carried out by a single examiner to assess the Oral Health Status using WHO Oral Health Surveys – Basic Methods Proforma (1997). The data recorded were transferred and tabulated. SPSS version15 was used for statistical analysis. The alpha error (Type I error) was assumed to be 0.05. 95% confidence limit was set for the above analysis. Chi-square test for quantitative and Mann-Whitney U test for qualitative data were used for compare the prevalence of oral diseases between males and females. **Results:** Results showed that among 660 study population, 381(57.7%) had no formal education. Among the study population 75%) had the habit of alcohol consumption. Of those who had the habit of smoking, 26% smoked beedi, 10.9% smoked cigarette, 65% chewed raw tobacco, 18% chewed Hans and 28% had a combination of smoking and smokeless tobacco usage. The reason for practicing these habits were as a measure to combat the cold, relieving stress and body pain after work, and the lack of awareness of the hazards of the materials used. Prevalence of oral mucosal lesions in the study population was due to tobacco usage and alcohol consumption and lack of awareness regarding the deleterious effects of the products used. **Conclusion:** From the results of this study it may be concluded that the Malayali tribes were characterized by a lack of awareness about oral health, deep rooted dental beliefs, high prevalence of tobacco use and limited access to health services. **Keywords:** Malayali tribes, Tobacco usage, oral health status, WHO oral health proforma, Beliefs.

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**PUB079 Will Any Future Increase in Cigarette Price Reduce Smoking in Saudi Arabia?** Sara I. Altraif, Omar Almohrej, Hani Tamim, Hana Fakhoury *King Saud Bin Abdulaziz University for Health Sciences, Riyadh/Saudi Arabia*

**Background:** In Saudi Arabia, no studies have been conducted on the correlation between any possible cigarette's price increase and its effects on cigarette consumption. **Methods:** A cross-sectional study was conducted in April and May 2013. The subjects included were 2057 Saudis of both genders aged 11-70 years. We developed an Arabic questionnaire with information on demographic and socioeconomic factors, smoking history, and personal opinion on the effect of price increase on cigarette consumption. The questionnaire was distributed in public places such as malls and posted on famous Saudi athlete media's twitter accounts. **Results:** Among the 2057 included responses, 802 (39%) were current smokers. The smokers' population constituted of 746 (92%) males, of which 546 (68%) had a monthly income equal or greater to 3,000 Saudi Riyal (800 US dollars), and 446 (55%) were aged between 21 and 30 years. Multivariate analyses of the risk factors for smoking showed that male gender and older age were associated with greater risk. Despite the current low prices of 10 Saudi Riyal (2.67 US dollars), 454 smokers (56%) thought that cigarette prices are expensive. When asked about the price of cigarettes that will lead to smoking cessation, 443 smokers (55%) expected that a price of 31 Saudi Riyal (8.27 US dollars) and more per pack would make them quit. **Conclusion:** Increasing the price of popular cigarettes pack from 10 Saudi Riyal (2.67 US dollars) to 31 Saudi Riyal (8.27 US dollars) is likely to lead to smoking cessation in approximately 39% of Saudi smokers. **Keywords:** price increase, cessation, cigarette, saudi arabia

**PUB080 Environmental Tobacco Smoke as a Risk Factor to Increasing Respiratory Childhood Infection and Pneumonia in South-West Region Nigeria**
Seye O. Omiyefa *Programs, Youth Action on Tobacco Control and Health, Ibadan/Nigeria*

**Background:** There is consistent evidence that children exposed to environmental tobacco smoke (ETS) have higher incidence of asthma, ear- and throat disease, worsening of asthma symptoms and lung symptoms as cough, wheezing and pneumonia. A child exposed to ETS has about 30% higher risk of absence from school due to illness. Evidence clearly implicates (ETS) as a cause of lung cancer, excess respiratory disease, and cardiovascular disease mortality in non-smokers. Few studies have looked at the interaction of tobacco use or ETS exposure with occupational and ambient air pollution (both indoor and outdoor) in contributing to chronic obstructive pulmonary disorders in developing countries, or the importance of ETS as a risk factor for the already high burden of childhood respiratory infections. **Methods:** A descriptive cross sectional study was carried out in 5 states (Ogun, Lagos, Akure, Oyo and Ekiti). A multistage cluster random sampling was employed to select 450 families in each state. Data was collected using structured questionnaires by trained interviewers. **Results:** About 2113 records were available for analysis. There were 1298(60.7%) males and 815(38.1%) females aged 10 and below. A Majority, 807(38.0%) live with both parents, 213(10.0%) live with mother alone while 265(12.5%) live with relatives. The prevalence of children exposed to ETS in the southwest region Nigeria was 73.2%, the study further revealed that 28.5% of children in this region with respiratory childhood infection are exposed to environmental tobacco smoke and 18.4% pneumonia cases are attributed to ETS. However, (122, 14.7%) parents or relatives don't see a problem with using tobacco products. It is also clearly stated that about 46.9% cases of respiratory childhood infection and pneumonia combined are caused by ETS in the south west region Nigeria. **Conclusion:** Since Environmental Tobacco Smoke has this much negative effects on children in the south west region Nigeria. Efforts should be tailored towards protecting children from ETS to reduce the rate of children exposed to ETS, thereby curbing or reducing respiratory childhood infection and pneumonia in Nigeria
**Keywords:** ETS, Tobacco Control, Pneumonia

**PUB081 Former Cigarette Smokers and the Risk of Lung Cancer Development**
Irina Pavlovska, Nikola Orovcanec, Biljana Taushanova, Beti Zafirova *Department of Epidemiology, Institute of Epidemiology and Biostatistics, Skopje/Macedonia*

**Background:** Cancer is a leading cause of death worldwide. There were 14,1 million new cancer cases, 8,2 million cancer deaths and 32,6 million people living with cancer (within 5 years of diagnosis) in 2012 worldwide. The leading kind of cancer in the world is the lung cancer (LC). This is the most frequent cancer localization in many countries. In the Republic of Macedonia LC is on the first place among the ten most common primary sites of cancer. The principal risk factor for LC is smoking, which is largely responsible for the development of the disease in men and women. Approximately 85% of LC can be directly attributed to smoking and secondhand smoke. The **aim** of this study was to determine the eventual causal associations between the habit of cigarette smoking and onset and distribution of lung cancer. **Methods:** This investigation was a case-control study. It comprised 185 patients with LC (investigated group-IG) and matched controls with no malignant diseases (control group-CG). In the study were included only interviewees with pathohistologically confirmed LC. By calculating the odds-ratios, the risk factors that play a role in the disease onset, have been estimated. Statistical significance of the examined variables as risk factors has been defined with confidence intervals (CI). **Results:** According to the investigation results, among patients were 67% of current smokers (CS), 23,8% of former smokers (FS), and 9,2% of never smokers (NS), compared to 40,5% of CS, 28,7% of FS and 30,8% of NS among controls. The risk of LC development in FS is almost three-times (OR=2,78; 95% CI, 1,42-5,46), significantly greater compared to the NS (p<0,01). Up to the age of 20 years, 81,8% of the diseased persons started smoking, while in the CG that percent is 56.6%. FS who started smoking up to 20 years of age have 3,45 times significantly higher risk to become ill (95% CI, 1,35-8,82), compared to those who started with this habit after the age of 20. The mean values of daily (IG-32,50±16,51; CG-26,62±15,04), and maximally (IG-43,18±19,20; CG-35,19±17,29), smoked cigarettes are higher in the diseased individuals. More than 40 cigarettes/day were smoked by 25% of the FS with LC. More than a half of the FS (56,5%), practiced this habit ranging from 31-45 years. FS who smoked >40 years had 5,35 times (95% CI, 2,11-13,57), significantly higher risk to become ill, compared to those which years of smoking is <40. Greatest percent of the FS stopped smoking 1-5 years ago (59,1%), while in the CG this percent is 15,1%. FS who stopped smoking 1-10 years ago had 3,56 times significantly greated risk to become ill (95% CI, 1,27-9,92), compared to those who abandoned this habit 11-20 years ago. **Conclusion:** Lung and other cancers caused by tobacco are often untreatable at the time of diagnosis. The key to reducing these cancers is to prevent initiation of smoking in young people, and to encourage smokers to quit. Quitting smoking substantially reduces cancer risk.
**Keywords:** lung cancer, cigarette smoking, former smokers

**PUB082 Study on Differences in Lung Cancer Between Male Smokers and Never-Smokers**
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**Background:** To investigate the effect of smoking on male patients with lung cancer. **Methods:** Clinical data of 1298 male patients with lung cancer who were diagnosed by histology or cytology were collected and retrospectively analyzed. Patients were divided into smoking group and non-smoking group. **Results:** 79.2% patients were never smokers and 20.8% were smokers. There were more squamous cell carcinoma patients and small cell carcinoma patients in smoking group than non-smoking group($P<0.01$), but less adenocarcinoma patients in smoking group than non-smoking group($P<0.05$). Patients with different pathological types in squamous cell carcinomas of the highest rates of smoking (84.6%), followed by small cell lung cancer (67.3%). More atients in smoking group suffered from cough ($P<0.05$) and hemoptysis ($P<0.01$). The asymptomatic patients in non-smoking group were more than those in smoking group ($P<0.01$). **Conclusion:** In male smoking patients with lung cancer, the proportion of squamous cell carcinoma is high, and the symptom of cough and hemoptysis is obvious. In male non-smoking patients with lung cancer, adenocarcinoma is common, and clinical manifestation is not obvious. Smoking is one of the important factors which lead to lung cancer.
**Keywords:** lung cancer, smoking

**PUB083 Role Models "A Tool for Effective Tobacco Control Campaign"**
Seye O. Omiyefa *Programs, Youth Action on Tobacco Control and Health, Ibadan/Nigeria*

**Background:** Each day, nearly 6,000 children under 18 years of age start smoking; of these, nearly 2,000 will become regular smokers. That is almost 800,000 annually. Approximately one half of continuing cigarette smokers will die prematurely from tobacco use; this is mostly after several years or more of excess disease and disability. **Methods:** Experience has showed that adolescent and youths all over the world especially Nigeria are attracted to media of any form. Role Models will be used through the help of the media and the entertainment industries to give a tobacco control sensitization talk for two minutes each on a video that will be televise. This video will also be uploaded on "Facebook", Twitter, Whatsapp and "YouTube" for a wider viewing of this campaign; these role models are mentors to many other youths in Africa. **Results:** These methods will creatively increase the awareness level of young people in Nigeria and Africa on the harmful effect of tobacco smoking and promote the campaign against tobacco smoking. The methods will also reduce the rate of youth smoking in Nigeria and Africa, as some of these role models are also models to many youths in other African countries. **Conclusion:** Evidence has showed that some of these role models are used as a campaign tool by the tobacco industry in Nigeria and other countries. It is therefore systemic and appropriate to use the same method to reduce the current upsurge in youth smoking and cancer related disease in Nigeria and Africa
**Keywords:** Role Model, Tobacco Control, Youth

**PUB084 Knowledge, Attitudes, and Smoking Behaviours Among Dental and Medical Students in Chennai, Tamil Nadu, India**
Delfin Lovelina Francis[1], Clement Joy Kingsly Francis[2] [1]*Public Health Dentistry, Tagore Dental College and Hospital, Chennai/India,* [2]*Finance and Economy, Nestle India Private Limited, Gurgaon/India*

**Background:** Tobacco use continues to be the leading cause of preventable disease and it is responsible for more than 5 million deaths each year worldwide. Despite this, there are still 650 million smokers in the world. The prevalence of smoking among adults accounts for approximately 25% deaths annually. Undoubtedly, there has been a gradual reduction in smoking prevalence in the last years in the western countries, but smoking remains the main cause of mortality and morbidity in the developing nations. Healthcare professionals have an important role to play both as advisers influencing smoking cessation and as role models. However, many of them continue to smoke. Several studies have demonstrated the efficacy of smoking cessation programs and the importance of physician's advice to their patients. The aims of the present study are as follows: (i) to evaluate smoking prevalence, knowledge and attitudes, and tobacco cessation training (ii) to examine the difference between smokers and nonsmokers; (iii) to estimate the extent of teaching about tobacco and smoking cessation techniques (iv) to recommend the integration of tobacco-related education in the curriculum. **Methods:** A structured questionnaire consisting of 14 questions related to tobacco/smoking habits, cessation training and role of health professionals in tobacco control were asked to the study population and their response was recorded. Random sampling method was used and data was collected from a cross-sectional survey. The survey was conducted between January and February 2015. Statistical analysis was done using SPSS version 17 and Logistic regression model was used to identify possible associations with tobacco smoking status. The level of significance was. **Results:** A total of 259 answered the questionnaire of which 29% declared to be smokers. About 53% of the males have smoked at least once in their life and the age of cigarette initiation was 16-17 years for 28% of the sample.76% considered health professionals as behavioural models for patients, and 96% affirmed that health professionals have a role in giving advice or information about smoking cessation. Although 87% heard about smoking related issues during undergraduate courses, only 17% received specific smoking cessation training during specialization. 93% of the sample agreed that health professionals should receive specific training on smoking cessation according to while 6% were of the opposite opinion. **Conclusion:** All healthcare professionals play an important role in the process of smoking cessation both as advisers and behavioural models for the general population. The present study highlights the importance of focusing attention on smoking cessation training, given the high prevalence of smokers among physicians specializing in medicine and dentistry, their key role both as advisers and behavioural models, and the limited tobacco training offered in the curriculum. In the field of public health, tobacco screening, and intervention is one of the most effective clinical preventive services. Planning and implementing smoking cessation training and cessation tailored to these young health professionals is therefore strongly recommended.
**Keywords:** Medical Students, smokers, non-smokers, tobacco cessation

**PUB085 A Cross-Sectional Study on Tobacco Consumption Pattern Among Auto Rickshaw Drivers in Chennai City, Tamil Nadu, India** Clement Joy Kingsly Francis[1], Delfin Lovelina Francis[2] [1]*Finance and Economy, Nestle India Private Limited, Gurgaon/India,* [2]*Public Health Dentistry, Tagore Dental College and Hospital, Chennai/India*

**Background:** Tobacco use is a major preventable cause of premature death and diseases, currently leading to five million deaths worldwide which are expected to raise over eight million deaths worldwide by 2030. About 29% of adults use tobacco on a daily basis and an additional 5% use it occasionally. The habit has very high opportunity cost as it reduces the capacity to seek better nutrition, medical care and education. In line with the WHO Framework Convention on Tobacco Control (FCTC), the Cigarettes and Other Tobacco Products Act (COTPA) is a powerful Indian national law on tobacco control. The prevalence of tobacco use among adults (15 years and above) is 35% and the prevalence of overall tobacco use is 48% among males. This study is contemplated with an aim to assess the prevalence of tobacco consumption and the associated factors involved in its consumption, as this group of the population is under constant pressure and account for the workforce of the country. So through this study we could be able to know * The reasons of consumption. * Amount of consumption *Awareness of ill effect of tobacco consumption * Out of Pocket expenditure. **Methods:** A Cross sectional descriptive study was conducted among Auto Rickshaw Drivers in Chennai City. Auto drivers who were working for more than two years and present on the day of examination and who were willing to participate in the study were included. Cluster random sampling technique was used. 400 samples were selected from 40 auto stands of various parts of Chennai City. Data was collected using a Survey Proforma which comprised of a Questionnaire which can assess the frequency of consumption, age of initiation, the amount of consumption, mental stress, economic factors, any past history of disease and most importantly the awareness towards oral cancer. The data recorded was transferred and analysed using SPSS version 20. Age, tobacco consumption pattern, reasons of consumption, amount of consumption, harmful effects of tobacco are the variables. Chi- square test was used to test the significance between groups. **Results:** Prevalence among auto rickshaw drivers for consumption of tobacco products was very high (87%). Auto rickshaw drivers were mostly used tobacco in the form of Gutkha (72%) and bidi (40%) in comparison to other products. It also shows that they use cheap tobacco products. Most of the auto rickshaw drivers start using tobacco products in age less than 18 years (80%) and associated factors for tobacco use are due to friends and their influence (78%). Awareness level among auto rickshaw driver was high (70%) but still uses tobacco products because of its addiction (66%). In the opinion of auto rickshaw drivers increase in tax may reduce it consumption and the majority of drivers (70%) think that tobacco must be banned. **Conclusion:** Prevalence of tobacco use was very high. Mostly they use tobacco products to reduce stress, to be awake or to remove nervousness but a large number of participants also use them without any reason. They are in definite need of tobacco cessation activities. **Keywords:** Tobacco, Awareness, Prevalence, Addiction.

**PUB086 Smoking Habits and Awareness about Anti-Smoking Acts among General Public in Gurgaon, Haryana, India** Clement Joy Kingsly Francis[1], Delfin Lovelina Francis[2] [1]*Finance and Economy, Nestle India Private Limited, Gurgaon/India,* [2]*Public Health Dentistry, Tagore Dental College and Hospital, Chennai/India*

**Background:** India is the world's third largest tobacco-growing country. The Indian scenario as far as tobacco consumption is concerned is far worse because of the prevalence of the tobacco chewing habit which covers a wide spectrum of socioeconomic and ethnic groups and is spread over urbanized area as well as remote village. Tobacco use is alarming in terms of its current and projected future impact on global mortality. Recent shift in global tobacco consumption to developing countries indicate that an estimated 930 million of the world's 1.1 billon in India alone. Despite the facts, that the harmful effects of tobacco chewing and smoking are widely known, many young people start smoking during adolescence, largely because they believe that smoking will boost their social acceptability and image. This study was contemplated with an aim to assess tobacco / smoking habits and awareness about anti-smoking act among general public in Gurgaon, Haryana, India. **Methods:** A structured questionnaire consisting of 14 questions related to tobacco/smoking habits and awareness about anti-smoking act were asked to general public and their response was recorded. Random sampling method was used and data was collected from a cross-sectional survey. Anti-tobacco counselling was given on the spot and followed. **Results:** The study population consisted of total 430 individuals , male 364 (84.65%) and females 66 (15.34%) . Then the questionnaires were asked and statistically analyzed. Around 286 (78.57%) from 364 male were indulged in some form of tobacco usage (smoker =32.86% , tobacco chewer = 16.78% , both =11.18 % , alcohol + tobacco user =21.67%). In the present study , most common cause of tobacco use was pleasure 40.5% , inducing factor were friends 53.1% followed by parents and siblings . 36.20% patients used tobacco as second hand exposure in job places. 54.8% were aware about the anti-smoking act in public places, so only 8.6% people from all males enrolled, were smoking in public places. **Conclusion:** Even though there exist Anti-smoking Law in the country, General public are unaware. Involvement of Healthcare proffessionals becomes mandatory to overcome this issue. **Keywords:** Tobacoo chewing , smoking , anti-smoking act , prevalence

**PUB087 A Study on Seven Years Hospital Based Cancer Incidence in Nepal (2003 -2009)** Kishore K. Pradhananga *Cancer Prevention, Control and Research, BPK Memorial Cancer Hospital, Chitwan/Nepal*

**Background:** The objective of the study gives overview to reliable information about Seven yrs cancer incidence in Nepal. It helps to make some prevention and control plan and policies to the clinicians, policies makers to give priorities for the cancer prevention and control activities. **Methods:** The total 34,940 cases were included in this study to know the burden of cancer patients in seven major government and non-government hospitals of Nepal where cancer diagnosed and treated from 2003-2009. This was descriptive type of study and all cases were collected from medical record section of seven collaborative institutions for data analysis. **Results:** In this study Female (53.3%) cases were diagnosed more than males (46.7%). Overall, the most common cancer sites in Males were lungs, stomach and leukemia but in Females Caner of cervix uteri , breast and lung . More cancer cases (67.7%) seen in Female but in Males found 52.5% in the broad age group 35 to 64 yrs. In young age leukemia and lymphoma were more common replaced by lung, oral and stomach cancer in middle age but in older lung, stomach and larynx cancer were found in males but in females breast cancer in young, cervix uteri cancer in middle and followed by lung cancer in older age. **Conclusion:** This type of study shows burden across a greater proportion of cancer from 7 major hospitals where cancer is diagnosed and treated, but the coverage may not represent the whole country. More than 50% cancer was diagnosed in BPKM national cancer hospital. Population based cancer registry program is not yet established so, it is difficult to reflect the burden of cancer in the country. **Keywords:** Incidence, Cancer Registry, Burden of cancer, Prevention and control policies

**PUB089 Mathematics Diagnosis Model to Differentiate Multiple Primary Lung Cancers from Intra-Pulmonary Metastases** Feng Li[1], Wen-Zhao Zhong[1], Fei-Yu Niu[1], Chao Liu[2], Zhi-Yong Chen[1], Ning Zhao[1], Jin -Ji Yang[1], Yi-Long Wu[1] [1]*Guangdong General Hospital, Guangdong Lung Cancer Institute, Guangdong Academy of Medical Sciences, Guangzhou/China,* [2]*Department of Pathology,Guangdong General Hospital, Guangdong Academy of Medical Sciences, Guangzhou/China*

**Background:** It is important to differentiate multiple primary lung cancers(MPLC) from intra-pulmonary metastases(IPM) for the patients with multiple lung nodules. Currently, there are several criteria to distinguish MPLC from IPM but with conflict results. **Methods:** Five criteria including Martini and Melamed guideline, American College of Chest Physicians (ACCP) guideline, radiological evaluation, comprehensive histological assessment (CHA) and genetic profiles (EGFR, KRAS and ALK gene detection) were applied to evaluate the origin of tumor cells in paired lung specimens respectively. Finally, the multi-disciplinary consultation are considered as golden standard of the diagnosis, 65 cases of five definite independent results were enrolled as training set, while 9 cases of one method without definite results were enrolled as validation set. Based on Bayes discriminant analysis, we developed mathematics diagnosis model ultimately. Kaplan-Meier analysis was used to analyze the prognosis by mathematical diagnosis model. **Results:** Totally, 74 consecutive patients with multiple lung nodules confirmed with adenocarcinoma were enrolled in the study from 2457 surgical resected lung cancer between January 2007 and July 2014. Among 74 cases with multiple lung nodules, 63 cases were identified as MPLC and 11 cases as IPM by Martini and Melamed guideline; 39 cases were identified as MPLC and 29 cases as IPM by ACCP guideline, while 6 cases cannot be classified; 39 cases were identified as MPLC and 35 cases as IPM by radiological evaluation; 53 cases were identified as MPLC and 21 cases as IPM by CHA; 45 cases were identified as MPLC and 26 cases as IPM by gene detection, while 3 cases cannot be identified because of triple negative results of gene detection, so the identification rate was 95.9% (71/74). The Bayes discriminant analysis method was applied to develop mathematics diagnosis model as following, Y=-83.11+34.998*G+ 13.932*C+4.553*R+1.874*A -0.339*M(Abbreviation, G: genetic profile; C: CHA; R: radiological evaluation; A:ACCP guideline; M: Martini and Melamed guideline). The value and significance of five criteria are as following,"1" is for MPLC and "2" is for IPM. When Y>0, the diagnosis is intended for IPM, when Y≤0, the diagnosis is intended for MPLC. The retrospective and prospective accuracy rate of the model in 65 cases and 9 cases was 96.9% and 88.9% respectively. Kaplan-Meier analysis was used to explore the prognosis by mathematical model, which show that the prognosis of MPLC patients are better than that of IPM patients(P = 0.006). **Conclusion:** The practical mathematical diagnosis model was developed to distinguish MPLC from IPM in the patients with multiple lung nodules of adenocarcinoma. The prognosis of MPLC patients are better than that of IPM patients. **Keywords:** multiple primary lung cancers, Prognosis, Mathematics diagnosis model, Intr-pulmonary metastases

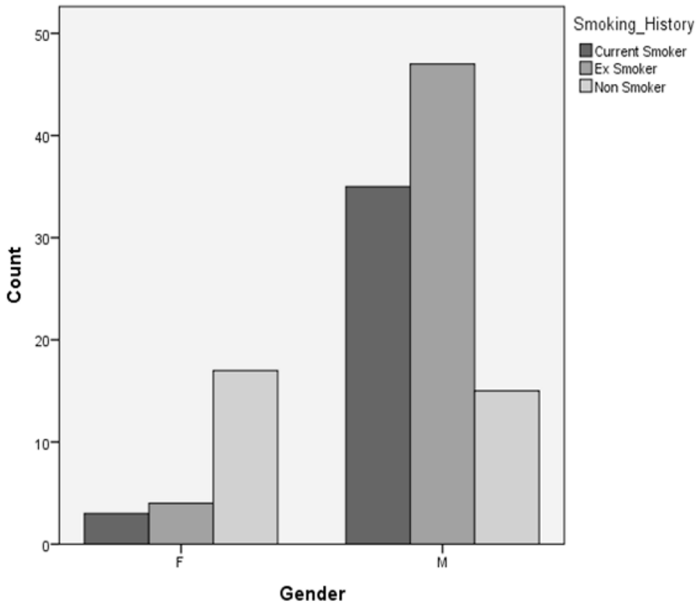
**PUB090 Lung Cancer in Niger: An Analysis of the National Cancer Registry Data** Salamatou Mamoudou Garba[1], Hinde Hami[2], Harouna Mahamadou Zaki[1], Abdelmajid Soulaymani[2], Abdelrhani Mokhtari[2], Hassan Nouhou[1], Ali Quyou[2] [1]*Laboratory of Pathological Anatomy and Cytology, Faculty of Health Sciences, Abdou Moumouni University, Niamey/Niger,* [2]*Laboratory of Genetics and Biometry, Faculty of Science, Ibn Tofail University, Kenitra/Morocco*

**Background:** Lung cancer is a major cause of morbidity and mortality worldwide, with an estimated 1.8 million new cases of lung cancer (13% of the total) and 1.6 million cancer deaths in 2012 (19.4% of the total) (GLOBOCAN 2012). The aim of this study is to estimate the incidence and determine the epidemiological characteristics of lung cancer in Niger. **Methods:** This is a descriptive retrospective study of lung cancer cases, reported between 1992 and 2009 to the Niger Cancer Registry. The sites of lung cancer include the following: trachea ($C_{33.9}$), main bronchus ($C_{34.0}$), upper lobe, lung ($C_{34.1}$), lung, not otherwise specified ($C_{34.9}$) and pleura, not otherwise specified ($C_{38.4}$). **Results:** During the period 1992-2009, there were 61 cases diagnosed with lung cancer in Niger, which was 0.87% of all new cases of cancer reported during the study period. More than 85% of the cases were men with a male-female ratio of 5.78. The incidence of lung cancer was 0.54 cases per 100 000 persons. The average age of the patients at diagnosis was 54.80±14.32 years (range 20-85 years). According to the available data, 77% of the patients came from the Niamey region. The commonest histological type was carcinoma (11.4%). We

registered 22 deaths, with a lethality rate of 36.06%. **Conclusion:** Despite the limitations of the available data, it is clear that there are several barriers to access to cancer control in developing countries. This includes prevention, early detection, diagnosis and treatment. **Keywords:** epidemiology, Niger, lung cancer

**PUB091 Epidemiological, Clinical and Radiological Profiles of Lung Cancer Patients in a Tertiary Care Hospital of Pakistan** Madiha Tawfik, Nadeem Rizvi *Jpmc, Karachi/Pakistan*

**Background:** Among the various cancers worldwide, lung cancer continues to be one of the leading causes of morbidity and mortality. According to WHO in 2012, 1.8million estimated new cases of lung cancer occurred globally with 58% belonging to less developed countries.We evaluated the common factors contributing to this fatal disease as it has been proven that 5 years and even 10 years survival rates close to 90% can be achieved by screening programs. **Methods:** A cross sectional study done in Pulmonology Department from December 2013 -2014. Total 125 lung cancer suspects, selected through consecutive sampling, were admitted through the Outpatient Department after counseling and written consent for invasive tests. Basic biodata, smoking history, biomass exposure, symptoms and signs related to lung cancer, laboratory and radiological findings deduced via workup were entered in questionnaire. After assessing patients, CT guided or bronchoscopic biopsies were done and tissue samples sent for histopathology. Clinical records of 121 cases, confirmed on histopathology as lung cancer, were compiled and evaluated. Frequency and percentage for qualitative variables including gender, smoking history,biomass exposure, signs and symptoms, Tuberculosis history, laboratory, radiological, bronchoscopic and histopathological findings were calculated. Mean ± standard deviation for quantitative variables including age and pack years were calculated. **Results:** In all, 67.8% cases belonged to 41 to 60years age group, mostly males, ex smokers with 57.3% having more than 30 packyears smoking history. Non smokers were 26.4 % and among females diagnosed of lung cancer 70.8% were nonsmokers as seen below:




There was history of biomass exposure in 46.3% cases and Tuberculosis in 28.9% cases. Most common symptom and sign was breathlessness and anemia respectively. Radiographically, 53.7% cases showed right lung involvement,predominantly upper lobe. Laboratory workup revealed anemia in 81%, thrombocytsois in 16.5%,hyponatremia in 25.6% and hypercalcemia in15.7% cases. CT guided biopsy was done in 68 cases and bronchoscopy in 53 cases. Among those who underwent bronchoscopy, right main bronchus and endobronchial involvement was mostly seen. Histopathology showed Squamous Cell Carcinoma in 48.8%, Adenocarcinoma in 28.1%, Small Cell Carcinoma in 20.7% and Large Cell Carcinoma in 2.5% cases. 54.2% females were diagnosed with Adenocarcinoma and 53.6% males with Squamous Cell Carcinoma.Those diagnosed with Adenocarcinoma were mostly non smokers (52.9%) while rest were predominantly smokers. **Conclusion:** Despite the advances made for lung cancer diagnosis, survival hasn't improved much. By evaluating common profiles,we may be able to screen suspects and help diagnose lung cancer earlier especially in those who are non smokers. **Keywords:** Pakistan, lung cancer, Common Profiles, Screening

**PUB092 Difficulty of Low Dose Computerized Tomography (LDCT) as a Lung Cancer Screening Tool in an Endemic Area of Tuberculosis** Natthaya Triphuridet, Sutida Singharuksa, Sirachat Vidhyarkorn, Naree Chuengkhlay, Supapun Luengingkasoot, Waraporn Krongthong *Medicine, Chulabhorn Hospital, Bangkok/Thailand*

**Background:** Pulmonary Tuberculosis (TB) and lung cancer are major health problems in developing countries. The radiographic findings of TB can mimic lung cancer even after a complete anti-TB treatment. Low-dose computerized tomography (LDCT) is a current standard technique for lung cancer screening, however, no clear evidence of benefits from lung cancer screening has been established in a high-risk population residing in an endemic area of TB. **Methods:** A prospective lung cancer screening using LDCT enrolled 635 former or current heavy smokers (≥30 pack-years) aged 50-70 years without a history of active TB within a recent year between July 2012 and January 2014 at Chulabhorn Hospital Cancer Centre in Thailand. **Results:** 635 subjects were enrolled. At baseline LDCT, 419 cases (66%) had lung nodule(s); half of them had 2-10 lung nodules, 41.7% had a single nodule, and 8.6% had lung nodules >10 nodules. Of these 419 cases, 63% had benign nodule(s) characteristic, 15.2% had nodule(s) with lesion suspected inflammation or infection, 15.5% had nodule(s) with diameter 5·0–9·9 mm, and 5.7% had nodule(s) with diameter ≥10·0 mm. Nine cases(1.4%) were proven to have lung cancer (56% stage I, 22% stage II/III, 22% stage IV) within 12 months. Of these 9 participants 8 had nodule(s) with diameter ≥10·0 mm and the other had mediastinal lymphadenopathy from baseline LDCT. Most of them (66%) had 2-10 lung nodules that all were non-stage 4 lung cancers, while only 33% had single nodule including 2 cases of stage 4 lung cancers. Three cases were diagnosed active pulmonary TB within 12 months (one culture positive TB, one caseous granulomatous inflammation and one chronic inflammation on tissue pathology) and all were responded to antituberculosis drugs. **Conclusion:** Despite a high burden of TB in Thailand, LDCT screening in heavy smokers could yield a high rate of primary lung cancer in this population at risk. However, high prevalence of lung nodules is one of the major problems in diagnosis and staging lung cancer in endemic area of Tuberculosis. **Keywords:** lung cancer screening, low-dose computerized tomography (LDCT), Pulmonary Tuberculosis (TB), Endemic Area

**PUB093 Relationships Between Circulating Tumor Cells and Platelets, D-Dimer and Fibrinogen in the Patients With Lung Cancer** Chunhua Liu, Ping Gong, Jie Yang *Department of Radiotherapy, People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi/China*

**Background:** To investigate the relationships between circulating tumor cells (CTCs) and platelets (PLT), D-dimer (D-D) and fibrinogen (FIB) in the patients with lung cancer. **Methods:** The clinicopathological files of 79 initially-treated patients with primary lung cancer were collected. The number of CTCs in peripheral blood and levels of D-D, PLT and FIB in plasma were respectively detected, and their relationships were analyzed. **Results:** The level of D-D was associated with the presence or absence of distant metastasis in patients with lung cancer ($P$=0.046), FIB with clinical staging ($P$=0.028) and presence or absence of distant metastasis ($P$=0.004) as well as PLT with the age ($P$=0.000), clinical staging ($P$=0.000) and presence or absence of distant metastasis ($P$=0.000). Among 79 patients with lung cancer, there were 45 ones with positive CTCs and 34 with negative CTCs. The levels of D-D, FIB and PLT in patients with positive CTCs were dramatically higher than those with negative CTCs ($P$<0.05). The positive detection rate of CTCs in the patients with distant metastasis was significantly higher than those without distant metastasis (83% vs. 42%, $P$=0.000), and the levels of D-D, FIB and PLT were all higher than those without distant metastasis ($P$<0.05). **Conclusion:** CTCs can predict the metastasis of lung cancer early, and blood hypercoagulable state is likely to promote the occurrence of distant metastasis of lung cancer. **Keywords:** lung cancer; circulating tumor cells; D-dimer; fibrinogen, platelets

**PUB094 Image Guided Biopsy of Thoracic Masses and Reduction of Risk of Pneumothorax: 25 Years Experience in a Remote Cancer Center** Binoy K. Choudhury *Department of Radiology and Imaging, Dr. B. Borooah Cancer Institute, Guwahati/India*

**Background:** The purpose of our study was to determine the role, accuracy and reliability of image guidance of thoracic biopsy and to know the efficacy of uses of different measures to reduce the risk of pneumothorax. **Methods:** Needle aspiration biopsies were performed in 1520 patients from February,1989 to December,2013 using Fluoroscopy, Ultrasound and Computed Tomography ( CT ) as Image guidance. Ultrasound guidance was used for peripheral lesions abutting the chest wall. Fluoroscopic and CT guidance were used for both peripheral and central lesions. After reviewing the patient, chest skiagram, CT Scan and coagulation profile, a plan is formulated to the safest approach to the thoracic lesions. A needle was guided to the thoracic lesion with an appropriate Image technique and material was aspirated with 20 cc plastic syringe and smeared on slides. Several measures were applied to reduce the risk of pneumothorax. Immediately after the technique, puncture site was put on dependant position ( Roll-over technique ) to reduce the risk of pneumothorax. Other measures taken to reduce the pneumothorax risk included selection of appropriate image guidance, accurate and delicate performance of needle manipulation, extra pleural approach, widening of extrapleural parasternal and paravertebral space by saline injection, pathway through non-aerated lung, minimized the pathway of normal aerated lung, avoiding fissure & bullae, limited number of pleural puncture, small bore needle, up & down movements of needle tip were very slowly & carefully done in a small lesion. Needle biopsy was not performed in bronchoscopically accessible hilar or central lesions. All patients underwent chest radiography to detect a pneumothorax. **Results:** There were 1201 male and 319 female in the range of 12 to 91 years. Fluoroscopy, US and CT as guidance were used in 170 ( 11.18%), 259 ( 17.04%) and 1091 ( 71.78%) cases respectively. The diameter of masses ranges from 1.2 cm to 12 cm. Procedure time was significantly less under US guidance. 152 cases ( 10%) needed repeat biopsy and most of these were Fluoroscopic or CT guidance. Results obtained in 1292 cases ( 85%). Malignant cases were 982 (76%). Complications included haemoptysis ( six ) and pneumothorax in 35 ( 2.3%). There was no pneumothorax in US guided biopsy. Pneumothorax occurred in 10 cases following fluoroscopic guidance and 25 cases in CT guided biopsy. Only three cases of pneumothorax required placement of a chest tube, rest were small and resolved spontaneously. Incidence of pneumothorax dropped significantly after we started meticulous planning using

several measures as mentioned above in the methods. **Conclusion:** Image guided Needle aspiration biopsy is a safe, swift, easy and reliable method in tissue diagnosis of thoracic lesions. Morbidity is very low and accuracy is very high. Most important and common complication of the procedure is pneumothorax. Risk of pneumothorax can be significantly reduced by meticulous planning using several measures. Roll-over technique plays an important role in reduction of incidence of pneumothorax. **Keywords:** Image-guided, FNAB, Thoracic masses, Pneumothorax

**PUB095 Thoracic Malignancies in Cameroon. Twenty Years Experience**

Nkegoum Blaise[1], Mboumtou Liliane[2] [1]*Pathology and Oncology, University Hospital Center, Yaoundé/Cameroon,* [2]*Pathology and Oncology, University Hospital Center, Yaounde/Cameroon*

**Background:** Cameroon Is an underdevelopped country of 20 millions inhabitants located in Central Africa. It Is a blank area on the world cancer map as cancer registration Is scarce or inexistent. The University Hospital Center hold the oldest Pathology department in the country With four full Time pathologists.Only 10 percent of malignant tumours are confirmed by histology as other cancer patients are managed by traditional healers and marabouts. **Methods:** We recorded all cases of thoracic malignancies microscopically confirmed from the registries of Yaounde University Hospital from 1995 to 2015 **Results:** 29 cases of thoracic malignancies were recorded for this 20 years period. 21 Non Small Cell Lung Cancers, 7 lymphomas, one thymoma and one Small Cell lung cancer were observed. 90 percent of our patients had Previous history of tobacco smoking. Two patients With lymphomas were Hiv positive. All patients in this series present with advanced stage disease. None undergone curative teatment. Only the lymphomas cases and the thymoma undergone immunohistochemestry for typing as Rituxumab Is offered at low priize for our cancer patients. No other targeted treatment Is available in the country for lung cancera and we do not target ALk in our institution. Unfortunatelly, 18 patients With suspected thoracic malignancies on xrays or Scan refused or were unable to pay for biopsie and the diagnosis was not available for this study. Three patients were HIV positive in this series and superior vena cava syndrome followed By death was observed in four other cases. **Conclusion:** Thoracic malignancies are common findings and are underdiagnosed in Cameroonian settings. Tobacco and HIV infection infections may be Ricks factors. Patients présent at late stage when no curative Treatment Cannot be offered. Lymphomas are not cured because no patient cannot buy new drugs. Most of our patients died With or without final diagnosis **Keywords:** Cameroon, New drugs, Thoracic malignancies, HIV and tobacco

**PUB096 A Role of Diffusion-Weighted MRI in Prediction of Mediastinal Lymph Node Metastasis in Patients with NSCLC: Comparison to PET Results**

Erkan Yilmaz[1], Uygar Teomete[2], Atila Akkoclu[3], Kemal C. Tertemiz[3], Ahmet Onen[4] [1]*Radiology, Sifa University, Izmir/Turkey,* [2]*Radiology, Miami University, Miami/FL/United States of America,* [3]*Respiratory Medicine, Dokuz Eylul University, Izmir/Turkey,* [4]*Thoracic Surgery, Dokuz Eylul University, Izmir/Turkey*

**Background:** To compare the diagnostic efficacies of diffusion-weighted magnetic resonance imaging (DWI) and fluorine 18 fluorodeoxyglucose (18F_FDG) positron emission tomography (PET) findings for the preoperative prediction of mediastinal nodal metastasis in patients with non–small cell lung cancer (NSCLC). **Methods:** The study included total 126 mediastinal lyph nodes of 57 patients (35 men and 22 women; mean age, 63.4 years) with NSCLC underwent both DWI (using a sigle-shot echo-planar sequence with diffusion factor of 0-600 s/mm$^2$ at 1.5 T) and PET examinations. A lymph node was considered as metastasis at DWI, when it showed apparent diffusion coefficent (ADC) value more than 0.95 s/mm$^2$, regardless of nodal size. In PET, a lymph node was regarded as positive for malignancy when it showed value of ≥3 in maximum standardized uptake value (SUV). Two observers evaluated prospectively and in consensus the mediastinal nodes by analyzing both DWI and PET images. Histopathologic results served as the reference standard. In terms of mediastinal lymf node metastasis, statistically significant differences between DWI and PET were determined with p<.05 obtained by using the McNemar test or as with a generalized estimating equation. **Results:** Mediastinal lymph nodes were positive for malignancy in 76 (60%) of 126 nodes and 25 (44%) of 57 patients. According to the diagnosis of malignant nodes, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of DWI were 81.5% (62 of 76 nodes), 82% (41 of 50), 87.3% (62 of 71), 74.5% (41 of 55) and 81.7% (103 of 126) respectively; whereas those of PET were 86.8% (66 of 76), 74% (37 of 50), 83.5% (66 of 79), 78.7% (37 of 47) and 83.3% (105 of 126). Specificity difference between two modalities was statistically significant (p<.05). There were 9 false-positive interpretations at DWI, compared with 13 false-positive on PET scans. There were 10 false-negative interpretations on PET scans, while 14 false-negative assessments were done at DWI. **Conclusion:** DWI allows reliable differentiation between benign and malign mediastinal lymph nodes in patients with NSCLC. Although DWI shows better sensitivity, it has a similar accuracy for prediction of mediastinal lymph node metastasis compared to PET. Therefore DWI may have a potent alternative imaging method for the preoperative diagnosis of mediastinal lymph node metastasis in patients with NSCLC. **Keywords:** diffusion-weighted imaging, lymph node, mediastinal, magnetic resonance imaging

**PUB097 Plasma Epitome Profiles Are Specific for Early Stage Lung Cancer**

Laszlo Takacs *Biosystems International Kft, Debrecen/Hungary*

**Background:** Lung cancer (LC) mortality worldwide is at about 84%, the five-year survival rate improved unfortunately only by 4-5% since 1975. At the same time, survival rates of other types of cancers have significantly improved over the same period. Considering the frequency of LC (≈ 250 000 new cases just in the US/yr) we are faced with the most significant cancer lethality: more people die each year of LC than breast, prostate and colon cancers together. Early diagnosis at asymptomatic stages is key to increase the success of surgical and combined the treatment regimes, in order to increase survival rate. **Methods:** To better address proteome variability we generated large non redundant natural epitome specific mAb libraries (QuantiPlasmaTM). For epitome profiling we developed an easy to use capture inhibition assay and applied to the sensitive Evidence InvestigatorTM biochip platform manufactured by Randox Ltd. **Results:** We show apparent epitome profile differences of plasma proteins from COPD patients compared to matched LC. In a four center clinical trial of 1,200 subjects, we confirm that combined biomarker panels detect symptomatic and operable LC with sufficient sensitivity (>80%) and specificity (>90%) for early diagnosis **Conclusion:** As diagnostics, epitomic biomarker panels may contribute to LC survival in the future. The Randox Evidence InvestigatorTM biochip technology with Biosystems' QuatiplasmaTM libraries is suitable for LC testing **Keywords:** NSCLC, Early Detection, copd, blood proteomics panel

**PUB098 The CRP Combined with LDH Was an Independent Prognostic Factor for Limited Stage SCLC**

Fang Wang[1], Jian Rong[2], Heping Li[3], Wenzhuo He[4], Huiwen Weng[3], Chang Jiang[4], Sheng Ye[3], Qiong Yang[5], Liangping Xia[4] [1]*Department of Medical Oncology, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou/China,* [2]*Department of Extracorporeal Circulation, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou/China,* [3]*Department of Oncology, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou/China,* [4]*Collaborative Innovation Center for Cancer Medicine, Sun Yat-Sen University Cancer Center, Guangzhou/China,* [5]*Department of Oncology, The Second Affiliated Hospital of Sun Yat-Sen University, Guangzhou/China*

**Background:** The prognostic value of inflammation related factors were rarely studied in patients with small cell lung cancer(SCLC), especially the limited-stage. The aim of this study is to screen the potential significant inflammatory factors in the subgroup patients. The prognostic value of inflammation related factors were rarely studied in patients with small cell lung cancer(SCLC), especially the limited-stage. The aim of this study is to screen the potential significant inflammatory factors in the subgroup patients. The prognostic value of inflammation related factors were rarely studied in patients with small cell lung cancer(SCLC), especially the limited-stage. The aim of this study is to screen the potential significant inflammatory factors in the subgroup patients. **Methods:** The data were collected retrospectively for 240 limited-stage small cell lung cancer patients who received the initial treatment in Sun Yat-sen University Cancer Center from October 1st, 2006 to July 1st, 2013. Pretreatment modified Glasgow Prognostic Score (mGPS), C-reactive protein, Lactate dehydrogenase, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio were chosen as inflammation related prognostic factors of overall survival. **Results:** Median age was 59 years old. 209 patients (87.08%) were male. 94 patients (39.17%) were characterized by elevated CRP combined with LDH (scored: 1-2). The CRP combined with LDH, mGPS, stage, prophylactic cranial irradiation, response to the initial treatment, respectively, were significant factors for OS in univariate analyses. Among them, the overall survival was independently associated with CRP combined with LDH (OR: 1.346, 95%CI: 1.007-1.346) $p$=0.045), prophylactic cranial irradiation (OR: 1.571, CI: (1.096-2.253), $p$=0.014) and response to the initial treatment (OR: 1.749, CI: (1.295-2.363), $p$<0.001).

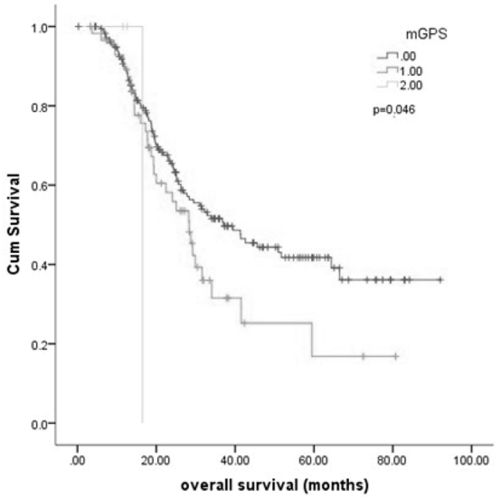



**Figure 1.** The relationship between the modified Glasgow prognostic score (score: 0, 1, 2 from top to bottom) and overall survival in patients with limited-stage small cell lung cancer ($p$ = 0.046).

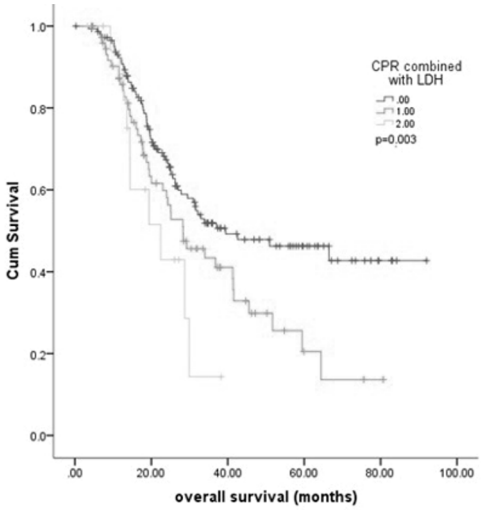



**Figure 2.** The relationship between the CPR combined with LDH (score: 0, 1, 2, from top to bottom) and overall survival in patients with limited-stage small cell lung cancer ($p$=0.003).

**Conclusion:** The CRP combined with LDH was demonstrated as the unique independent inflammation related prognostic factor of OS for limited-stage SCLC. **Keywords:** Limited-stage small cell lung cancer, C-reactive protein combined with Lactate dehydrogenase, modified-Glasgow prognostic score, Neutrophil-to-lymphocyte ratio

**PUB099 Intensity-Modulated Radiotherapy in Treatment of Small Cell Lung Cancer** Charu Singh, Shivani Gupta *Department of Radiation Oncology, Sms Medical College and Hospital, Jaipur/India*

**Background:** This study was done to analyze the feasibility of omitting clinical target volume (CTV) for limited small cell lung cancer treated with chemotherapy and intensity modulated radiotherapy. **Methods:** The study was done from June 2011 to January 2015. 80 patients of small call lung cancer with limited disease were selected, from which 40 patients were irradiated with target volume without CTV, and 40 patients were irradiated with CTV. Both arms were irradiated to post chemotherapy tumor extent and elective nodal irradiation was omitted. Dose prescription was 95% PTV56-63 Gy/28-35 F/5.6-7 weeks. **Results:** The arm without CTV had local relapse rate of 15% and arm with CTV had local relapse rate 17%. The distant metastases rates were 42.5% and 50% respectively. Grade 3-4 hematological toxicity and radiation esophagitis had no significant difference, but grade 3-4 radiation pneumonia was observed in only 7% in the arm without CTV, compared to 20% in the arm with CTV. The 1 year and 2- years' survival rates of the arm without CTV and the arm with CTV were 81.0%, 65% and 90%, 60% respectively. The distant metastases were significantly related to overall survival. **Conclusion:** Target delineation omitting CTV in patients of small cell lung cancer with limited disease receiving IMRT is feasible. **Keywords:** small cell lung cancer, intensity modulated radiotherapy, clinical target volume

**PUB100 Hypofractionated Prophylactic Cranial Irradiation – Analysis of Efficacy and Impact on Neuro-Intellectual Function** Subrata Saha[1], Aloke Ghosh Dastidar[2], Partha Das Gupta[3], Subrata Chattopadhyay[4], Amitabha Manna[5]
[1]*Radiotherapy, Apollo Gleneagles Cancer Hospital, Kolkata/India,* [2]*Radiotherapy, Ipgmer, Kolkata/India,* [3]*Radiotherapy, R G Kar Medical College, Kolkata/India,* [4]*North Bengal Medical College, Kolkata/India,* [5]*Radiotherapy, Calcutta Medical College, Kolkata/India*

**Background:** Prophylactic cranial irradiation plays a crucial role in prevention of brain metastasis from small cell lung cancer (SCLC) – be it limited stage **(LS)** or extensive one **(ES)** – who respond to initial therapy. To attain better quality-adjusted life expectancy and to avoid neurointellectual impairments (**NIP**), optimum dose and fractionation for PCI needs to be explored, **with due consideration to coexisting medical co-morbidities** that might enhance the adverse events. Contrary to conventional 30 Gy/10 fractions, short-course PCI is gaining popularity in recent time. Aim of this study is to find the safety and efficacy of PCI with 20 Gy/5 fractions and to analyze its impact on NIP with special focus on any possible influence of age and medical co-morbidities. **Methods:** This is an on-going single arm multicentric trial initiated in February 2011 where both LS- as well as ES-SCLC patients who responded to initial therapy and were not having any visceral metastasis are offered PCI for a dose of 20 Gy in 5 fractions with CT-based planning. All patients received Platinum + Etoposide for 6 cycles. LS-SCLC patients received, in addition, concomitant thoracic radiation after 2 cycles of chemotherapy. To minimize neuro-psychological impairment, at least 2 weeks gap is given before PCI and after completion of all chemotherapy. All relevant medical comorbidities (Diabetes, Hyperlipidimia, previous history of CVA including lacunar infarcts) are carefully recorded. Neuropsychological screening measure of immediate and delayed verbal memory by using Hopkins Verbal Learning Test - Revised (HVLT - R), assessment of cognitive function using Mini-Mental Status Examination (MMSE) are applied before initiation of PCI and on follow up at 3 monthly interval. **Results:** Result of first 42 patients receiving PCI (LS- SCLC = 28, ES-SCLC = 14) with minimum duration of follow up of 18 months is being presented. There was no significant baseline difference in neuropsychological screening using HVLT. Brain metastasis, in spite of PCI was in none. Median survival was 9 months for ES and 14.5 months for LS-SCLC. 2/14 ES-SCLC and 18/28 LS-SCLC lived one year. Corresponding data for 18 months is 0/14 and 5/28 respectively. MMSE deterioration was noted in 18/42 patients. Subset analysis of these 18 patients revealed 3/18 were in the age group of 55 - 65 years (N= 24) and remaining 15 were between 65 to 72 years (N = 18); P <0.0001. Interestingly all 3 of these below 65 years patients and 13/15 of above 65 years patients were having long-standing hyperlipidimia and nearly half of them were Diabetic also. HVLT decline in immediate recall **(16/42)** was in 14/18 patients having MMSE deterioration and 13 out of these 16 had delayed recall deterioration as well. Subset analysis of neurointellectual impairment (as evidenced by HVLT in 16 patients) revealed its presence among 14/20 patients having medical co- morbidities (Hyperlipidimia, Diabetes etc) and in only 2/ 22 without any (P <0.0001). **Conclusion:** 20Gy/ 5 fractions is an effective, safe, patient-compliant PCI protocol for well-selected patients aged below 65 years without medical comorbidities, specially those which have established role in causing cerebral microinfarcts. **Keywords:** Neurocognitive function, Hypofractionation, Small cell carcinoma, PCI

**PUB101 Multiple Spinal Intradural -Intramedullary Involvement by Metastatic Small Cell Carcinoma Lung - An Unusual Presentation** Anshu Gupta, Sachin Sinha *Pathology, Institute of Human Behavior and Allied Sciences, Delhi/India*

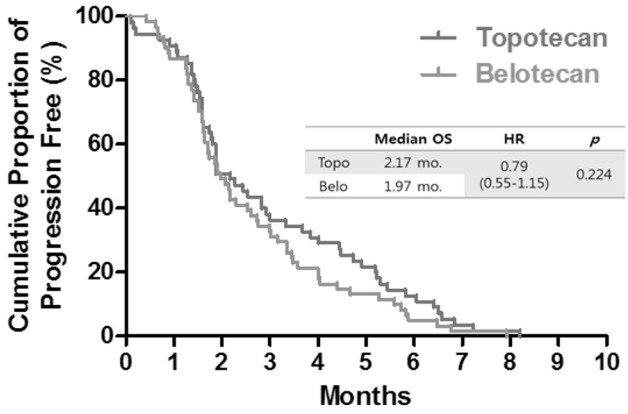
**Background:** Intramedullary metastases to the spinal cord is infrequent. Between 5-10% of cancer patients develop spinal meastasis during the course of their diseases. Intramedullary tumors are rare, comprising 3.5% of spinal metastasis. Most metastatic spinal lesions (70%) are found at the thoracic level, 20% in lumbar region and 10% in the cervical region. We report a rare biopsy proven case of intramedullary spinal metastatic carcinoma with neuroendocrine differentiation , involving spine at multiple noncontiguous levels, which appeared as irregular small nodules on MRI. The primary tumor was most likely from occult primary in lung.Biopsy from the spinal lesion established the diagnosis of metastatic carcinoma with neuroendocrine differentiation. We highlighted herein the clinical presentation, radiological findings particularly MRI and role of biopsy in the diagnosis and treatment of intramedullary spinal metastasis. **Methods:** Intra-operative biopsy from nodular lesion in dorsolumbar spine was performed and sent to pathology department for frozen section examination. A provisional diagnosis of malignant small round cell tumor was made on frozen section by cryostat. Based on the provisional diagnosis, further excision biopsy done to relieve compression symptoms and sent for microscopic examination. The biopsy specimen showed multiple grayish brown soft tissue pieces that together measured 2.8x2.5x0.5 cms grossly. Cut surface was gray white with few hemorrhagic areas. Paraffin sections were prepared from tissue sent and stained with routine Haematoxylin and Eosin(H&E) stain, special stains such as reticiulin & vimentin and immunohistochemical stains for cytokeratin, synaptophysin,S-100 and chromogranin. **Results:** On microscopic examination, biopsy showed a cellular tumor in which cells were arranged in sheets, well defined clusters, trabeculae, around blood vessels forming pseudo-rosettes and scattered diffusely in highly vascularised fibrocollagenous stroma. Tumor cells were small, monomorphic round to oval to elongated with moderate atypia, stippled chromatin and inconspicous nucleolus. Cytoplasm was scanty and barely visible. Nuclear moulding was seen in occasional cells. Some of the cells were slightly larger and showed moderate amount of eosinophilic cytoplasm. Mitosis was infrequent. Reticulin stain showed reticular fibers around group of cells . On immunohistochemistry, tumor cells showed diffuse positivity for cytokeratin, synaptophysin and chromogranin . S-100 was focally positive. Vimentin positivity is seen in fibro connective stroma. Findings were that of metastatic carcinoma with neuroendocrine differentiation. **Conclusion:** Keeping in view the pathological findings, occult small cell carcinoma lung was considered the first possibility despite no supportive clinical and radiological evidence as chest X-ray and CT lung were normal. Thus, a thorough work up is advised in patient with spinal metastasis to evaluate primary site. This help to delineate the nature and the extent of the systemic disease. No treatment has been proven to increase the life expectancy of patients with lung cancer and spinal metastasis. Pain relief and maintenance of quality of life must be balanced against the patient life expectancy, presence of co-morbidities, immunological, nutritional and functional status. **Keywords:** Spinal cord, metastasis, carcinoma, neuroendocrine

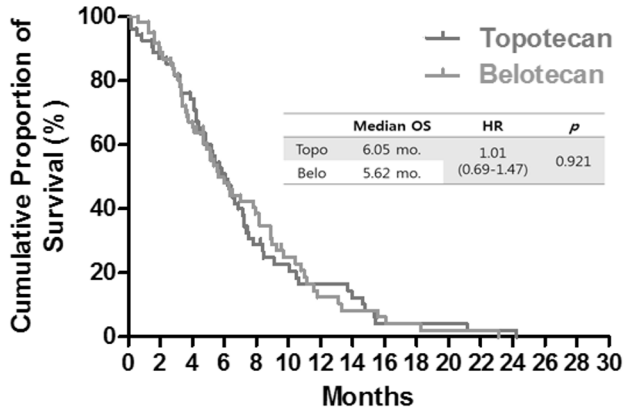
**PUB102 Randomized Phase II Study of Belotecan or Topotecan as Second-Line Chemotherapy after Platinum Based Chemotherapy for Small Cell Lung Cancer** Shinkyo Yoon[1], Dae Ho Lee[2], Chang-Min Choi[3], Jae Cheol Lee[4], Jung-Shin Lee[4], Sang We Kim[5] [1]*Oncology, Asan Medical Center, Seoul/Korea,* [2]*Department of Oncology, University of Ulsan College of Medicine, Asan Medical Center, Seoul/Korea,* [3]*Department of Pulmonary and Critical Care Medicine, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul/Korea,* [4]*Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul/Korea,* [5]*Asian Medical Center, Seoul/Korea*

**Background:** Topotecan has been accepted as second-line therapy for small cell lung cancer (SCLC), in addition, belotecan also reported with significant response rate. Based on these results, we designed prospective randomized phase II trial of belotecan as second-line treatment in patients with SCLC, who experienced disease progression within 6 months after first-line platinum containing chemotherapy or chemo-radiotherapy. **Methods:** We randomly assigned patients to belotecan 0.5 mg/m$^2$ (n=61) or topotecan 1.5 mg/m$^2$ (n=55) for 5 days every 21 days, stratified by response to

first-line chemotherapy. The primary end points was response rate (RR). The secondary end points were progression free survival (PFS), overall survival (OS) and safety profiles. **Results:** From August 2006 to December 2013, a total of 116 patients were enrolled. The median age was 64 years (range, 28-82), and ratio of males to females was 0.89. In total, 186 cycles of topotecan (median 2, range 1-9) and 180 cycles of belotecan (median 2, range 1-8) were administered. Median follow-up was 5.6 months. RR of belotecan and topotecan was 19.7% (12/61) and 18.2% (10/55), respectively (p=0.92). Median PFS and OS of belotecan and topotecan was 2.1 months (95% CI 1.43-2.72) versus 2.3 months (1.46-3.07) and 11.2 months (10.2-12.1) versus 12.1 months (10.1-14.0), respectively (p=0.167, 0.659) (Figure 1). Grade 3/4 hematologic adverse events in belotecan and topotecan were anemia (13.1% versus 14.5% (p=1.000)), thrombocytopenia (3.3% versus 7.3% (p=0.421)), neutropenia (21.3% versus 43.6% (p=0.016)).




**Conclusion:** Belotecan showed comparable efficacy with topotecan and more favorable toxicity profiles in neutropenia. **Keywords:** second-line chemotherapy, topotecan, belotecan, small cell lung cancer

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**PUB103 Prognosis of Initial Care Patterns of Small Cell Lung Cancer in Chinese Patients** Lan-Ying Gou, Yi-Long Wu, Jin -Ji Yang *Guangdong Lung Cancer Institute, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou/China*

**Background:** Small Cell Lung Cancer (SCLC) is a most fatal cancer, some patients refused to receive anticancer treatment after diagnosis. There is no any report about initial care patterns on prognosis of SCLC in China.

**Methods:** Patient characteristics and initial care patterns were investigated retrospectively from June 2004 to December 2012 using the database of electronic medical record of Guangdong General Hospital (GGH) in China. All of the patients were divided into anticancer treatment group, support care group and no-treatment group. Kaplan-meier analysis was used to estimate and compare the overall survival among groups. The reasons of no-treatment were analyzed. **Results:** From June 2004 to December 2012, a total of 474 patients with SCLC were included in this retrospective study. All of the patients were divided into three groups: 405 patients were in anticancer treatment group (group A); 12 patients were in support care Group (group B) and 57 patients didn't receive any treatment at their disease course (group C). The median overall survival (OS) of three groups was 15.27 months, 4.37 months and2.53 months, respectively ($P<0.001$). The reasons of the patients refused anticancer treatment were: afraid of toxicity and side effect of chemotherapy (31.9%), poor financial support (27.5%), elder age (23.2%), poor performance status (10.1%) and unknown (7.2%). **Conclusion:** The prognosis of the patients refused anticancer treatment was much worse than the patients received anticancer treatment even best support care. Afraid of treatment toxicity is the most reason to refusing anti-cancer treatment. **Keywords:** Small cell lung cancer(SCLC), initial care patterns, Prognosis, reasons

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**PUB105 Mesothelioma Rates in South Africa: Trends 1995-2008** Cornelius Nattey *Epidemiology & Surveillance, National Institute for Occupational Health, Johannesburg/South Africa*

**Background:** Mesothelioma is a rare neoplasm which is caused by asbestos exposure. South Africa has mined and refined all three types of asbestos since 19th century with the peak of production in1940-1980s. At present asbestos use and production is banned in South Africa. Trend 1995-2008 in mesothelioma rate was assessed to determine burden of asbestos related deaths due to mesothelioma by year and gender. **Methods:** Death certificates with underlying cause of death stated as C45 were selected for the study in 1995-2008. For each year of study, age and gender distribution was obtained from the national statistical releases. Mesothelioma rates, 95% confidence interval were calculated for each year and sex, and for age groups and sex .Poisson regression was used to test for trend. **Results:** In total 2497 cases were identified of deaths due to mesothelioma, 1919 in men and 578 in women in the study period. There was 3:1 male to female ratio. The trend was stable and constant over time for both men and women cases. Mortality rate in men was 8-16 per million and in women 2-5 per million respectively **Conclusion:** If mortality rate remains at current estimates we can expect 2 134 cases until 2020. These mortality rates are much lower than expected, given the historical production and use of, and high exposure to, asbestos in South Africa. Possible reasons for this are discussed, including the effect of HIV which has been instrumental in reducing the life expectancy of South Africans in the last two decades. Asbestos-exposed individuals may not live long enough to develop mesothelioma. Competing causes of death need to be taken into account when constructing models to predict mesothelioma mortality rates. **Keywords:** rates, Poisson, asbestos, Mesothelioma

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**PUB106 Long-Term Administration of Endostar Combined with Chemotherapy in Hemangioendothelioma of Bone Accompanying Pulmonary Metastasis** Ningrong Yang, Lin Wang, Chen Xue, Shukui Qin *The 81St Hospital of PLA, Nanjing/China*

**Background:** To explore the feasibility for long-term administration of rh-endostatin injection (YH-16,endostar) combined with chemotherapy in the treatment of hemangioendothelioma of bone accompanying pulmonary metastasis. **Methods:** One case of hemangioendothelioma of bone accompanying pulmonary metastasis, who received Endostar, 15 mg daily. Additionally, the patient was treated with TE regimen (paclitaxel 90mg d1, d8, d15, epirubicin 90mg d1, q4w) for 6 cycles and TP regimen (paclitaxel 90 mg on d1, d8, cisplatin 20 mg on d1 ~ d5, q3w) for 4 cycles. After all the chemotherapy, the Endostar was used as maintenance therapy (Endostar d1~14 q8w). Efficacy evaluation was conducted according to RECIST(1.0) criteria. **Results:** The patient got partial response(PR) after the application of endostar combined with taxane-based chemotherapy. Long-term using Endostar as monotherapy, the patient got long-term disease control and good quality of life for 3 years.. There was no drug related adverse event during the long-term therapy of Endostar, **Conclusion:** Endostar combined with chemotherapy can help achieve a convinced therapeutic effect for treatment of hemangioendothelioma of bone accompanying pulmonary metastasis. And use of endostar as maintenance treatment after patient got the optimal efficacy is feasible and profitable. This treatment method is worthy of further observed. **Keywords:** Hemangioendothelioma of bone; Endostar; Anti-angiogenesis; Maintenance therapy

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**PUB107 18F-FDG PET/CT Diagnosis of Bronchopulmonary Carcinoids versus Pulmonary Hamartomas** Oscar Grundberg *Department of Pulmonary Medicine, Karolinska Univeristy Hospital, Stockholm/Sweden*

**Background:** Radiological characterization of pulmonary tumors may be difficult and invasive. Needle biopsy may produce false negative results. $^{18}$F-FDG PET/CT is an established non-invasive procedure for lung tumor characterization and staging. **Methods:** In a retrospective analysis of 118 patients, with surgically resected pulmonary carcinoid tumors and hamartomas, 87 of those selected had also undergone $^{18}$F-FDG PET/CT preoperatively and constituted the study population. In order to better assess the tracer accumulation, especially in small lesions, the $^{18}$F-FDG uptake (SUV) in the tumors was corrected for partial volume effects (PVC) by applying recovery coefficients corresponding to the respective various specific tumor volumes, as extrapolated from those obtained from experiments in a NEMA phantom. **Results:** The $SUV_{max}$ was higher in the pulmonary carcinoids (mean 3.9) than in the hamartomas (mean 1.4) ($p \leq 0.00001$) and higher in the subgroup of peripheral carcinoids than in hamartomas ($p \leq 0.00001$). The $SUV_{max}$ was similar for the atypical and typical carcinoids, 5.0 and 3.8, respectively, because of the large variation in the data ($p = 0.11$). **Conclusion:** Using PET measurements of the $^{18}$F-FDG-uptake ($SUV_{max}$) in the tumors, corrected for partial volume effects, it was possible to differentiate the carcinoids from the hamartomas, but the clinically more aggressive atypical carcinoids could not be differentiated from the typical carcinoids. **Keywords:** Pulmonary carcinoid, harmartoma, 18F-FDG PET/CT, bronchial NET

**PUB108 Dietary Intake in Lung Cancer** Rosemary Poulose[1], Itisha Kulshreshtha[1], Anant Mohan[2] [1]*All India Institute of Medical Sciences, New Delhi/India,* [2]*Pulmonary Medicine, All India Institute of Medical Sciences, New Delhi/India*

**Background:** Lung cancer is associated with loss of appetite, weight loss and reduced dietary intake. This study aims to analyze the dietary intake in lung cancer patients and correlate it with body mass index (BMI), exercise capacity, and metabolism. **Methods:** This prospective observational study was carried out from 1 Feb 2011 to 31 Jan 2014. Patients with confirmed cytological/histological diagnosis of lung cancer were screened and staged according to the American Thoracic Society TNM classification. Subjects were recruited after obtaining informed consent. Dietary intake was calculated using twenty four hour dietary recall method, recommended calorie intake was estimated using the Harris Benedict equation and the Resting Energy Expenditure (REE) was calculated using the Katch-McArdle formula. Nutritional profile included assessment of body composition by bioelectric impedance method and anthropometric measurements of skin fold thicknesses. **Results:** A total of 148 subjects were studied (87% male). The mean (SD) age was 56.6(9.7) years, median pack years was 20 (range 0-120) and median duration of symptoms was 159 days (range 15-1080). The commonest symptoms were cough (80%), chest pain (68%), loss of weight (55%), hemoptysis (45%), fatigue (43%), shortness of breath (41%), and loss of appetite (31%). The mean (SD) energy intake was 1576.9(149.2) kcal/day which was significantly lower than the recommended calorie intake (p=0.04). The mean percentage deficit in energy intake was 13.9 and ranged from a deficit of 88.4% to an excess of 128.7%. Mean(SD) protein intake was 48.2(23.4) g/day, ranging from 4.8 to 88.9 g/day. The mean protein intake per kilogram of body weight was 0.9(0.1) g/kg/day, which was significantly lower than recommended (p<0.01). Dietary macronutrient composition did not differ from the general population.Six (4%) patients were hypometabolic, seventy three (49.3%) were having a normal metabolism, and sixty nine (46.6%) were hypermetabolic. Dietary intake did not differ significantly between underweight, normal weight or over weight patients, nor did it differ significantly between the normo- and hypermetabolic patients. There was no significant difference between patients with an adequate or higher calorie consumption and those with a deficient energy intake in the distance covered in the 6 minute walk test. **Conclusion:** Dietary intake of calories and protein were significantly lower than recommended, which may adversely affect the quality of life and survial of cancer patients.Hypermetabolism, although frequent, was not compensated by increased dietary intake indicating that in cancer, there may not be an up-regulation of dietary intake in response to increased energy expenditure.Measures to counteract hypermetabolism and improved dietary intake have been demonstrated to have a role in the survival, function and quality of life of cancer patients and should be further explored in interventional studies. **Keywords:** diet, hypermetaboilsm

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**PUB109 Evaluation of Hyponatraemia in Lung Cancer Patients: A U.K. Teaching Hospital Experience** Ankit Jain, Mariam Jafri, Salma Alam, Sophie Mascall, Rhian Thomas, James Kendrick, Joyce Thompson *Medical Oncology, Birmingham Heartlands Hospital, Birmingham/United Kingdom*

**Background:** Hyponatraemia, defined as a serum Na of <135mEq/L, is the commonest electrolyte abnormality in oncology practice. Among cancer patients, it occurs most frequently in small cell lung cancer(SCLC) and is due to inappropriate antidiuretic hormone secretion (SIADH), a paraneoplastic syndrome. The incidence of SIADH in SCLC is 11-15%. We describe the demographics, oncological management and response of hyponatraemia to oncological treatment modalities in hospitalised patients with lung cancer in a large inner-city teaching hospital. **Methods:** We retrospectively analysed the serum sodium levels in all lung cancer patients admitted to a teaching hospital in the West Midlands between 2007-2013. Data was collected on baseline demographics, histology, tumour stage and grade of hyponatraemia. Mild hyponatraemia was defined as a serum sodium between 130-135mEq/L, moderate between 125-129mEq/L, and severe as <124mEq/L. **Results:** 182 (108 male; 74 female) patients with lung cancer and documented hyponatraemia were hospitalised between 2007-2013. The median age of patients on admission was 69.2 years (range 33-92 years). 119(65%) had mild, 58(32%) moderate and 5(3%) severe hyponatraemia. 74(40%) were adenocarcinomas , 58(32%) squamous carcinomas, 43(24%) SCLC and 7(4%) had unspecified non small cell lung cancer. 89(49%) had metastatic disease at diagnosis. 18/43 (42%) small cell, 14/58 (33%) squamous , 23/74 (31%) adenocarcinoma patients had moderate to severe hyponatraemia. 132(74%) of this cohort had active oncological treatment: 93(51%) chemotherapy, 25(14%) radiotherapy, 17(9%) surgery whilst 47(26%) had best supportive care. 28(15%) had a biochemical response to their treatment, 11(39%) of these patients were adenocarcinomas, 10(36%) squamous carcinomas and 7(25%) SCLC. **Conclusion:** Hyponatraemia in lung cancer patients is widely distributed in various age groups and histological subtypes as shown from our data. Among those admitted with hyponatraemia, severe cases (<124mEq/L) were rare. Higher rates of SIADH are seen in SCLC than in any other malignancy and our data confirmed that, proportionately, more SCLC patients had moderate - severe hyponatremia than non small cell lung cancer patients. Hyponatraemia does respond to active oncological treatment including chemotherapy, radiotherapy and surgery. Although historically, hyponatraemia is considered as a poor prognostic marker and has been shown to be significantly associated with shorter survival duration, this should not preclude active oncological management. Asymptomatic patients with SIADH have been managed initially by fluid restriction but patient compliance is usually poor. Older medications such as demeclocycline, urea and lithium are limited by variable efficacy, poor palatability and/or toxicity, thus underscoring the need for new approaches. Tolvaptan, a new vasopressin receptor antagonist, can improve hyponatraemia due to SIADH and allow patients to receive appropriate treatments or palliate symptoms. Further studies are needed to evaluate the prognostic value of hyponatraemia and it's treatment in cancer patients. **Keywords:** Hyponatremia in lung cancer

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**PUB110 The Burden of Lung Cancer and the Various Factors Deciding the Treatment of Lung Cancer in the Developing World** Ramesh Kandel[1], Santosh Maharjan[2], Gyan Kayastha[1] [1]*Department of Medicine, Patan Academy of Health Sciences (PAHS), Kathmandu/Nepal,* [2]*Radiology, Institute of Medicine, Kathmandu/Nepal*

**Background:** With the global rise in the prevalence, lung cancer has become an unavoidable reality of old age, especially in the developing world with high prevalence of chronic smoking. As the treatment of lung cancer is dependent on functional status, a substantial number of patients get excluded, due to perceived loss of functionality and disability of old age. In this study, co-morbidity and functional status of older lung cancer patients was assessed and their impact on management was observed. **Methods:** In a cross-sectional study in a tertiary medical facility in Nepal, lung cancer patients aged 65 years or more, were recruited before the start of treatment. Comprehensive geriatric assessment, functional status and co-morbidities were evaluated as per various validated scales. The management of patients at the cancer centre was observed. **Results:** Two-third of 1450 patients (68.6%males) were between 65 and 80 years of age(mean:71.4 yrs). 80.4% of the patients were current smokers. The number of lung cancer patients abruptly declined after the age of 85. 58.3% were diagnosed in stage-4 and none in stage-1. The common co-morbidities were hypertension (30.8%), diabetes (15.2%) and Chronic obstructive pulmonary disease (14.9%). Vision problem with cataract was the commonest disability. 42.6%were depressed. 32.7% had cognitive impairment. 55.2% were independent in activities of daily living (ADL). 64.5% had their ECOG status score between 0-2 (thereby eligibility for treatment). However, 49.4% of older cancer patients did not receive any form of treatment including the palliative one. In multivariable analysis, age more than 70 year (P<0.001), ECOG status 2 or more (P<0.005) and low ADL score (P<0.004) were associated with ineligibility for treatment by the oncologists. **Conclusion:** Older patients with lung cancer were victims of ageism. These observations are congruent with the global cancer scenario. Greater effort is required for timely detection of lung cancer among older people along with improved criteria for selection for treatment. **Keywords:** ageism, lung cancer, functional status

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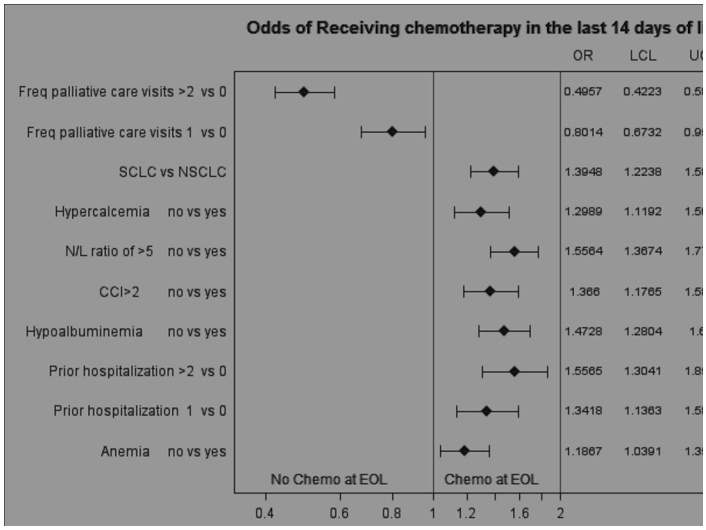
**PUB111 Chemotherapy at the End of Life (EOL) for Patients with Lung Cancer within the VA System** Rafael Santana-Davila[1], Michael J. Kelley[2], Christina D. Williams[3], Keith Eaton[1], Jeffrey C. Whittle[4] [1]*University of Washington, Seattle/United States of America,* [2]*Duke University, Durham/United States of America,* [3]*Duke University/Va Hospital, Durham/NC/United States of America,* [4]*Medical College of Wisconsin, Milwaukee/WI/United States of America*

**Background:** It is well established that chemotherapy given at the EOL is not associated with any survival advantage, prevents access to other services such as hospice and is considered a measure of low quality of care. While many studies have been done to determine the rate of chemotherapy at EOL, little is known about the patient/physician characteristics of those receiving/prescribing it. In this study we used a detailed database of patients treated with metastatic lung cancer within the Veterans Affairs (VA) health system to investigate the clinical characteristics of those who receive chemotherapy at the EOL. **Methods:** Using the VA Central Cancer Registry, patients with stage IV lung cancer diagnosed between 2001 and 2010 were identified. For analysis, patients were included if chemotherapy was initiated within 4 months of diagnosis. **Results:** In a database of 12,928 patients with metastatic lung cancer (68% NSCLC and 32% SCLC) that received chemotherapy within the VA, 2,067 (16%) patients received chemotherapy within 14 days of death. The majority (71.4%) of these patients was receiving first line therapy and had worse prognostic factors at the initiation of chemotherapy compared to patients that did not receive chemotherapy at EOL (Table 1). A multivariable logistic regression analysis identified several prognostic factors that were independently associated with receipt of chemotherapy at the EOL (Figure 1). The number of palliative care visits was associated with a reduction in the odds of having chemotherapy at the EOL.

Clinical characteristics of patients

| Variable at the start of treatment | Received Chemotherapy at EOL | No Chemotherapy at the EOL | P value |
|---|---|---|---|
| Age >65 | 49.2% | 46.2 | 0.0143 |
| Anemia (Hgb<12 g/dl) | 42.6% | 34% | <0.0001 |
| Hypoalbuminemia (serum albumin<3.5 g/dl) | 66.1% | 49.8% | <0.0001 |
| Neutrophil to Lymphocyte ratio >5 | 59.6% | 44.3% | <0.0001 |
| Chronic Kidney Disease (EGFR<60mg/dl) | 22.8% | 15.9% | <0.0001 |
| Hypercalcemia (corrected serum calcium>10) | 26% | 20% | <0.0001 |
| >1 Hospitalization in the year preceding treatment | 32.3% | 24.3% | <0.0001 |
| >10% Weight loss | 34.8% | 28.7 | <0.0001 |
| Comorbidity Index >2 | 20.1% | 15.9% | <0.0001 |




**Conclusion:** Our results demonstrate that within the VA the majority of patients that receive chemotherapy at EOL do so during first line treatment, these patients have worse prognostic factors at the initiation of treatment that could be used to identify them. Higher frequency of palliative care visits was associated with lower receipt of chemotherapy at the EOL.
**Keywords:** end of life, palliative care, chemotherapy

**PUB112 Trends in Lung Cancer Mortality in South Africa: 1995-2008**

Cornelius Nattey *Epidemiology & Surveillance, National Institute for Occupational Health, Johannesburg/South Africa*

**Background:** Cancers remains a major cause of morbidity and mortality in the world today. The global burden of cancer is expected to continue to increase with much of the burden being borne by developing countries. This study presents the trends in lung cancer (and all respiratory cancers) mortality for the South African national population, and by gender. **Methods:** Using the country's annual mortality and population estimate data from Statistics South Africa, we calculated lung cancer and all respiratory cancers age-adjusted mortality rates per 100 000 people for the period 1995-2008. The South African population structure for the year 2001 was used as the reference population. To determine trends in mortality, scatter plots were plotted and regression models were fitted to assess for linear trends in the age-adjusted cancer mortality rates for the period. This was done for the entire population and by gender. **Results:** Lung cancer caused 61 418 deaths and other respiratory cancers, 6 445 deaths, during the study period. Males accounted for 70.5% of lung cancer deaths and 71.7% of all respiratory cancer deaths. The majority of deaths (56%) were in the 50-69 year age group. While the age-adjusted lung cancer mortality rates for males decreased by 23.1%, the rates for females increased by 26.4%. Similar gender differences were observed for all respiratory cancers. **Conclusion:** The declining lung cancer mortality rate in men is welcome but the increasing rate in women is a public health concern and requires intervention
**Keywords:** lung cancer, mortality, rates, regression