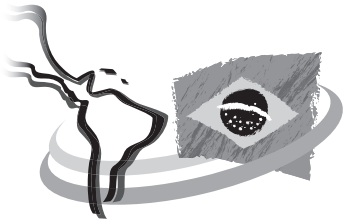

5th Latin American Conference on Lung Cancer

JULY 25–27, 2012 | RIO DE JANEIRO, BRAZIL

LALCA 2012 ABSTRACTS

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ORAL SESSION
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ORAL SESSION - July 26, 2012 08:00 – 09:15

O.01: THE FIRST INVESTIGATOR-INITIATED MULTICENTER RANDOMIZED PHASE III TRIAL IN BRAZIL: SINGLE AGENT PEMETREXED (P) VS. CARBOPLATIN AND PEMETREXED (CP) IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) AND PERFORMANCE STATUS (PS) OF 2

Carlos Gil M. Ferreira, C. Barrios, Jr Pereira, R. Ribeiro, C. Beato, Y. Neron, A. Murad, F. Franke, Lh De Lima Araujo, Cs Baldotto, Fm Alencar, P. Trovatti, M. Precivale, Ia Small, M. Zukin, R. Lilenbaum
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Background: Despite strong participation in international industry-sponsored trials, most Latin American countries have no established mechanism to conduct investigator-initiated multicenter clinical trials in cancer. We report the first such trial in Brazil.

Methods: A collaboration of 8 selected research sites was organized under the auspices of INCA (Brazilian National Cancer Institute), which served as the coordinating center. One site in the US was also included. Partial support from the pharmaceutical company, Eli Lilly, and funds from INCA and Fundação do Câncer were used to oversee the conduct of the trial and monitor the sites. Patients with advanced NSCLC, PS 2, and no prior chemotherapy were randomized to P alone (500 mg/m2) or CP (AUC 5 + same P) administered every 3 weeks for 4 cycles. The primary endpoint was overall survival (OS). The statistical analysis was independently performed and supported by INCA.

Results and Conclusion: Results: The protocol was developed between 2005 and 2006 and approved by the Brazilian regulatory agencies in 2007. A total of 217 patients were enrolled from April 2008 to July 2011. Twelve patients were ineligible and excluded. Enrollment was uneven among the sites, with about 60% of patients enrolled at INCA. There was significant improvement in survival for patients treated with the combination compared to single agent (median OS 9.1 months vs. 5.6 months (HR=0.57, 95% CI 0.41; 0.79, p=0.001). Conclusions: Combination chemotherapy significantly improves survival and represents a new standard in patients with advanced NSCLC and PS 2. This trial demonstrates the feasibility of an independent mechanism to conduct cancer trials in Latin America and represents a paradigm shift for clinical research in the region. This experience was the basis for the Brazilian Network for Cancer Clinical Research, launched in 2010 by INCA and the Ministry of Health.

Disclosure: No significant relationships.

ORAL SESSION - July 26, 2012 08:00 – 09:15

O.02: LUX-LUNG 3: A RANDOMIZED, OPEN-LABEL, PHASE III STUDY OF AFATINIB VS. PEMETREXED AND CISPLATIN AS FIRST-LINE TREATMENT FOR PATIENTS WITH ADVANCED ADENOCARCINOMA OF THE LUNG HARBORING EGFR ACTIVATING MUTATIONS

Ken O'Byrne[1], Martin Schuler[2], Nobuyuki Yamamoto[3], Vera Hirsh[4], Tony Mok[5], Dan Massey[6], Victoria Zazulina[7], Mehdi Shahidi[7], Lecia Sequist[8], James Yang[9]
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Background: Afatinib is a novel, selective, orally bioavailable, ErbB Family Blocker, irreversibly blocking EGFR (ErbB1), HER2 (ErbB2) and HER4 (ErbB4). In a Phase II, single-arm study (LUX-Lung 2), progression-free survival (PFS) was 13.7 months and the response rate was 66% in afatinib-treated, lung adenocarcinoma patients with EGFR exon 19 deletion and L858R mutations. In this study, the efficacy and safety of afatinib compared with pemetrexed and cisplatin as first-line treatment in patients with advanced adenocarcinoma of the lung harboring an EGFR activating mutation was investigated. This is the first study comparing EGFR mutation directed therapy to pemetrexed and cisplatin.

Methods: This was an open-label, randomized, global, Phase III trial with an accrual target of 330 patients, enrolling chemotherapy-naïve adult patients with pathologically confirmed Stage IIIB/IV lung adenocarcinoma and EGFR activating mutations (detected by central analysis; therascreen EGFR RGQ PCR Kit), and an ECOG performance status of 0 or 1. Patients were randomized (2:1) to receive daily, continuous, oral afatinib 40 mg, until progression or unacceptable adverse events, or intravenous pemetrexed 500 mg/m2 and cisplatin 75 mg/m^2 on Day 1 of each 21-day cycle for up to 6 cycles. Patients were prospectively stratified according to EGFR mutation (L858R vs. EGFR exon 19 deletion vs. other) and ethnicity (Asian vs. other). The primary endpoint was PFS, evaluated by RECIST 1.1 (independent review and investigator assessment). Response was assessed every 6 weeks until Week 48, then every 12 weeks. A stratified log-rank test will be used to compare the PFS of afatinib and chemotherapy. Secondary endpoints include objective response rate, disease control rate, overall survival and safety.

Results and Conclusion: The trial has completed accrual and analysis of the primary endpoint (PFS) is expected during the first quarter of 2012.

Disclosure: Ken O'Byrne: Compensated consultant for Boehringer Ingelheim, Lilly Oncology, compensated honoraria for Boehringer Ingelheim, Lilly Oncology, Research Funding as an investigator for this study, LUX-Lung 3 1200.32 study. Other remuneration for myself Ke

ORAL SESSION - July 26, 2012 08:00 – 09:15

O.03: NON INVASIVE NSCLC DIAGNOSIS: MULTIPLE MARKER DETECTION IN PERIPHERAL BLOOD

Paola Ulivi[1], Laura Mercatali[1], Gian Luca Casoni[2], Emanuela Scarpi[3], Lauro Bucchi[4], Rosella Silvestrini[1], Stefano Sanna[2], Marco Monteverde[2], Wainer Zoli[1], Venerino Poletti[2], Dino Amadori[5]
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Background: Non-invasive early detection of lung cancer

would help to reduce the number of patients diagnosed with advanced disease, which is associated with a grim prognosis. The availability of a non-invasive test, performed on peripheral blood, capable of discriminating between subjects with or without lung cancer, in theory could have two potential uses: 1) could be used as a preliminary screening method to select individuals at high risk of NSCLC, warranting further investigation with spiral CT; 2) it might help to discriminate between non-neoplastic disease and malignancies in subjects with suspect nodules detected by CT scans, thereby eliminating the need for serial CTs or invasive biopsy. We analyzed the diagnostic accuracy of a panel of peripheral blood markers in detecting non small cell lung cancer (NSCLC).

Methods: 100 healthy donors and 100 patients with NSCLC were enrolled onto this study. Free circulating DNA was determined in serum and mRNA expression of peptidylarginine deiminase type 4 (PAD4/PADI4), pro-platelet basic protein (PPBP) and haptoglobin was evaluated in peripheral blood using a Real-Time PCR-based method. The most efficient cut off values to discriminate between healthy donors and cancer patients were identified using receiver operating characteristic (ROC) curve analysis. All P values were based on two-sided testing and statistical analyses were carried out using SAS Statistical software version 9.1 (SAS Institute)

Results and Conclusion: Free circulating DNA, PADI4, PPBP and haptoglobin levels were all significantly higher in NSCLC patients than in healthy donors (P<0.0001, P<0.0001, P=0.0002 and P=0.0001, respectively). The fitted logistic regression model demonstrated a significant direct association between marker expression and lung cancer risk. The odds ratios of individual markers were 6.93 (95% CI 4.15-11.58; P<0.0001) for free DNA, 6.99 (95% CI 3.75-13.03; P<0.0001) for PADI4, 2.85 (95% CI 1.71-4.75; P<0.0001) for PPBP and 1.16 (95% CI 1.01-1.33; P=0.031) for haptoglobin. Combined analysis revealed that free DNA in combination with PPBP and PADI4 gave an area under the ROC curve of 0.932, 95% CI = 0.896-0.967, with sensitivity and specificity over 90%. Free circulating DNA analysis combined with PPBP and PADI4 expression determinations would appear to accurately discriminate between healthy donors and NSCLC patients. This non-invasive multi marker approach warrants further studies to assess its potential role in the diagnostic or screening workup of patients with suspected lung cancer.

Disclosure: No significant relationships.

ORAL SESSION - July 26, 2012 08:00 – 09:15

O.04: ROLE OF STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) IN STAGE I NSCLC

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Background: SABR has a definite role in the treatment of inoperable patients with NSCLC and it might become an alternative for surgery in operable patients. Based on our experience with stereotactic ablative radiotherapy (SABR) for early NSCLC in >900 treated patients, the prognostic factors will be discussed.

Methods: Between 2003 and 2009, 676 Stage I NSCLC patients were treated at VU University medical center. Patients treated for double or recurrent tumors were excluded from this analysis. Evaluations before and regularly after SABR included CT-scans and QoL evaluation. There were 378 T1N0 (56%) and 298 T2N0 (44%) tumors. The mean age was 74 years (range 41-91). All except four patients underwent ^{18}FDG-PET staging; 496 (73%) of patients were medically inoperable and 180 (27%) refused surgery or had a preference for SBRT. Pathological confirmation of malignancy was obtained in 245 patients (36%). All others had new and/or growing FDG-PET-positive lesions and CT-characteristics of malignancy. In the Dutch population, the risk of malignancy is more than 90% in these patients. The following risk-adapted SABR schemes were used: 3x20 Gy (n=246; 36%) for T1 tumors, 5x12 Gy (n=288; 43%) for T1 tumors adjacent to the thoracic wall/mediastinum or T2 tumors, and 8x7.5 Gy (n=142; 21%) for lesions adjacent to the pericardium, hilus or brachial plexus. After the introduction of volumetric modulated arc therapy (RapidArc,) which uses a more modern treatment planning algorithm, for SABR, doses were modified to 3x18 Gy, 5x11 and 8x7.5 Gy, respectively.

Results and Conclusion: Median survival was 37 months. 5-year survival was 27%. Local failure was seen in 29 patients), with an actuarial local failure-free survival rate of 91% at 3 years. The actuarial regional-free survival rate at 3 years was 91% and the actuarial distant failure free survival rate at 3 years was 83 %. Acute and late toxicity was limited with few patients experiencing grade 3 or higher toxicity. Chest wall pain was seen in 4% of patients, and rib fractures and pneumonitis each in 2%. There was no significant difference in tumor control and survival between patients with and without pathologically proven disease. In a subgroup analysis of 177 potentially operable patients treated with SABR, we found a 2-years survival of 88% and a median survival of 62 months. These results support ongoing randomized trials comparing surgery and SABR in these patients. In the absence of clinical trials, we recently published the results of a population based study, demonstrating that the introduction of SABR resulted in a 16% absolute increase in the use of radiotherapy in elderly patients in the Netherlands that this resulted in improved survival.

Disclosure: Speaker honorarium Varian medical systems

ORAL SESSION - July 26, 2012 08:00 – 09:15

O.05: MOLECULAR EVENTS IN LUNG SQUAMOUS CELL CARCINOMAS ASSOCIATED WITH ARSENIC EXPOSURE

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Background: Naturally occurring arsenic contaminated water is a global threat, currently affecting ~100 million people. If arsenic-related health effects occur at levels below the currently considered safe threshold (10µg/L), this number rises to several hundred million worldwide. Both genetic and epigenetic changes drive arsenic-induced carcinogenesis and lung cancer (LC) is one of the main consequences of this process. Interestingly, lung squamous cell carcinomas (SqCC) occur at higher rates than other subtypes following exposure, even in never smokers. Here, we have analyzed a panel of lung tumors from a population with chronic arsenic exposure (including a rare set of lung SqCC from never smokers) to identify whole

genome arsenic associated copy-number alterations (CNAs), copy-number variations (CNVs) and DNA methylation changes. Also, we have studied changes bronchial epithelial cell lines exposed to different arsenic metabolites, in order to elucidate key genomic and epigenomic changes.

Methods: Arsenic-exposed lung SqCC cases were investigated by whole-genome tiling path comparative genomic hybridization for CNAs. Additionally, non-exposed cases were also analyzed as controls. In addition, blood samples from arsenic-exposed individuals from Northern Chile (with no cancer diagnosed) were examined to identify naturally occurring germline CNVs. DNA methylation analyses for independent arsenic-exposed cases from never smokers were also performed. Human bronchial epithelial cell lines exposed to different arsenic compounds (non-methylated and methylated species) were used in order to evaluate functional genetic and epigenetic changes.

Results and Conclusion: We identified arsenic related changes occurring in lung SqCC, both at genetic and epigenetic level. The most recurrent events were represented by DNA losses at chromosomes 1q21.1, 7p22.3, 9q12, and 19q13.31. Intriguingly, we observed a single arsenic-associated DNA gain at 19q13.33, which encompasses genes related to key functions for oncogenic transformation, such as DNA repair. Additionally, distinctive DNA methylation patterns were associated to arsenic related lung SqCC, indicating these changes can have an impact on carcinogenic mechanisms for this subgroup of lung tumors.

Our study provides insights into the molecular pathways involved in arsenic-promoted malignant transformation in lungs. Findings specifically associated to lung SqCC cases among never smokers contribute to understand key events distinguishing this rare subgroup of lung cancer. Elucidation of mechanisms underlying the initiation and promotion of arsenic-driven lung carcinogenesis will be paramount for the design more effective and rationale-based strategies for prevention, monitoring and/or treatment of different types of cancer caused by this metalloid.

Disclosure: No significant relationships.

MINI ORAL SESSION
FRIDAY, JULY 27 08:00 – 09:15

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.01: ASSOCIATION OF CYP1A1, NAT2, GSTT1 GENE POLYMORPHISM WITH LUNG CANCER PATIENTS IN NORTHERN INDIA POPULATION

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Background: Lung cancer poses a major threat to human survival and health; both the incidence and death rate of lung cancer are in the first place among cancers worldwide. The rapid development of medical technology greatly improved health care quality, however, the recent situation in the diagnosis and treatment of lung cancer is far beyond what we have expected. Other previous studies have shown that lung cancer is affected comprehensively by smoking, environment pollution, individual genetic factors and so on. Xenobiotic metabolic enzyme genes, whose genetic polymorphism are considered to be predisposition factors to lung cancer. Thus, in our study, we look association of GSTT1, GSTM1, CYP1A1, and NAT2 gene polymorphism with the northern India lung cancer patients.

Methods: This is case control study; we were included 218 histological confirmed lung cancer patients and 238 control subjects. The lung cancer patients were recruited from Dept of Pulmonary Medicine, C.S.M.Medical University, (Erstwhile King Geroge's Medical College), INDIA. We applied the PCR & RFLP to explore the genetic polymorphism of the CYP1A1, NAT2 gene, and GSTT1 genetic polymorphism. The logistic regression analysis was carried out to estimate the association between genetic polymorphisms of these gene and lung cancer risk which was manifested by Odds Ratio (OR) and 95% confidential interval (95%CI)

Results and Conclusion: Results: The frequency of homozygous GSTT1 null was found to be significantly higher in Lung cancer patients as compared with healthy controls (OR=1.95; 95%CI=1.18-3.21; P=0.009), but there were no significant differences in the distribution of genotypes polymorphisms of GSTT1 and CYP1A1 msp1 between lung cancer patients and healthy controls. GSTT1 null genotype were significant associated with the smoker lung cancer patients, with odds ratio [OR] = 1.76; 95% confidence interval [CI] = 1.17-2.66; p= 0.007.But NAT2 fast acetylator genotype frequency of slow or fast acetylator genotypes was not significant in lung cancer patients alone (OR = 1.18, 95% CI: 0.69 - 2.03, p value = 0.583).in non-smoker (OR = 1.06, 95% CI: 0.43 - 2.64, p value = 0.899) and smoker (OR = 1.32, 95% CI: 0.59 - 2.93, p value = 0.494) when compared with controls.

Conclusion: Our study suggested null polymorphisms of the GSTT1 is associated with of the northern Indian lung cancer patients, but other polymorphism demonstrate that the CYP1A1 and NAT2 fast or slow acetylators genotype did not associated with the risk of developing lung cancer in North Indian population when compared with controls.

Disclosure: No significant relationships.

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.02: CLINICAL AND PATHOLOGICAL CHARACTERISTICS, OUTCOME AND MUTATIONAL PROFILES REGARDING NON-SMALL CELL LUNG CANCER RELATED TO WOOD-SMOKE EXPOSURE

Oscar Arrieta[1], Alma Delia Campos-Parra[2], Carlos Zuloaga[1], Alejandro Avilés[1], Roberto Sánchez-Reyes[1], María Eugenia Vázquez Manríquez[3], Emilia Covián-Molina[1], Luis Martínez-Barrera[3], Abelardo Meneses[4], Andrés Cardona[5], José R Borbolla-Escoboza[6]
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Background: Although smoking is the major risk factor for non-small cell lung cancer (NSCLC), other factors are also associated with lung carcinogenesis such as wood-smoke exposure (WSE). This article has been aimed at suggesting that lung cancer related to cigarette-smoking and WSE-related lung cancer has different clinical and genetic characteristics.

Methods: A cohort of 914 lung cancer patients was prospectively studied; they had been treated at Mexico's National Cancer Institute between 2007 and 2010. WSE and cigarette-smoking association with clinical characteristics, mutation profile, response to chemotherapy and EGFR-TKIs was analyzed, as well as overall survival (OS) rate. The trial was registered with ClinicalTrials.gov: NCT01023828.

Results and Conclusion: Results – 95.1% of the lung cancer patients studied were classified as coming within the NSCLC histology subtype; 58% of the patients smoked cigarettes, 35% had a background of WSE (exposure to both cigarette smoke and wood smoke was documented in 12.1% of all patients) and 19.4% patients had no smoke exposure background. WSE was associated with NSCLC and adenocarcinoma histology and was more frequently associated with EGFR- mutations than cigarette-smoking (50.0% cf 19.4%), whereas KRAS mutations were less common in WSE patients (6.7%) than in smokers (21%). WSE patients had a higher EGFR-TKI response rate (RR) (39.7%) than smokers (18.8%). The NSCLC patient WSE group's OS was longer (22.7 months) than that for smokers (13.8 months). Conclusion – NSCLC patients who smoked tobacco/cigarettes differed from those having a background of WSE regarding tumor histology, mutation profile, RR and OS, indicating that different carcinogenic mechanisms were induced by these two types of smoke exposure.

Disclosure: No significant relationships.

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.03: PHASE II TRIAL OF THE AKT INHIBITOR MK-2206 PLUS ERLOTINIB (ERL) IN PATIENTS (PTS) WITH ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) WHO HAVE PROGRESSED

AFTER PRIOR BENEFIT (RESPONSE OR STABLE DISEASE) FROM ERL: INTERIM RESULTS FROM PHII-108 (NCI 8698), A CALIFORNIA CANCER CONSORTIUM TRIAL

Primo Lara[1], Jeffrey Longmate[2], Philip C. Mack[3], Karen Kelly[3], Tianhong Li[3], Mariana Koczywas[2], Karen Reckamp[2], David Gandara[3]
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Background: Although EGFR tyrosine kinase inhibitors such as ERL are active in NSCLC, notably in tumors with EGFR activating mutations, resistance is universal and uniformly fatal. New agents that modulate ERL resistance are thus needed. Preclinical modeling in NSCLC lines demonstrated that in ERL-sensitive cells, stimulation with HGF (the ligand for cMET) reverses cytotoxic & cytostatic effects of ERL. Inhibitors targeting AKT also mitigated HGF-mediated resistance, partially restoring ERL activity. Elevated HGF plasma levels were seen in pts who progressed on ERL, suggesting that HGF contributes to ERL resistance in WT-EGFR tumors. MK-2206 is a novel, highly selective allosteric inhibitor of AKT. We developed a phase II trial of MK-2206 plus ERL in pts with advanced NSCLC who have progressed after previous benefit from ERL, stratified by EGFR mutation status. Here we present interim results of this ongoing trial.

Methods: Eligible pts must have progressive disease (PD) following prior response (or stable disease, SD) to ERL for at least 12 weeks prior to PD. Treatment: ERL 150 mg QD + MK-2206 45 mg po QOD. Cycle length is 28 days. Pts are stratified into 2 groups: (1) presence of an EGFR activating mutation; and (2) EGFR wild-type. Primary endpoints: Response rate >30% (stratum 1) and disease control rate at 12 weeks (stratum 2). Accrual was by a 2-stage design. In stratum 1, if at least 2 of the first 21 pts have a response, the study accrues to a final sample size of 41. In stratum 2, if 2 or more have disease control at 12 weeks, the study continues to 41 pts.

Results and Conclusion: As of 3/27/12, 42 pts have been accrued. Pt characteristics: median age (range) – 63 years (44-86); Sex – 11M/31F; KPS 90-100% - 28 pts; Presence of activating EGFR mutation: 24 (57%); Median number of cycles - 3 (range, 0-14). In stratum 1, four of 24 pts (17%) had a partial response, 7 (29%) had SD, 8 (33%) had PD, while 5 (21%) are not yet assessable. The first stage of accrual continues in stratum 2. Of 16 pts in this stratum, none had PR, four (25%) had SD, 7 (44%) had PD, and 5 not yet assessable. Treatment thus far has been tolerable with no grade 4 toxicities. Most common grade 3 toxicities are fatigue, decreased lymphocytes, and rash. Only one on-study death was seen; this was due to PD. Conclusions: To date, MK2206 plus ERL is feasible and active in ERL pre-treated NSCLC, with responses seen in the EGFR mutated stratum. Accrual is continuing in both strata. Updated results will be presented.

Disclosure: No significant relationships.

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.04: IRINOTECAN COMPARED TO ETOPOSIDE IN COMBINATION WITH PLATINUM ANALOG IN EXTENSIVE DISEASE SMALL CELL LUNG CANCER: SYSTEMATIC REVIEW AND META-ANALYSIS WITH GEOGRAPHIC ORIGIN SUB-ANALYSIS

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Background: Superiority of irinotecan regimens over etoposide - both combined with platinum analogs - in extensive disease small cell lung cancer (ED-SCLC) has been extensively debated, with contradictory results in randomized trials worldwide. Ethnic and pharmacogenomical issues were hypothesized as major causes of these divergent findings. A systematic review was sought to elucidate this confounding scenario.

Methods: Randomized controlled trials comparing first-line irinotecan-platinum doublets (IP) versus etoposide-platinum doublets (EP) in ED-SCLC patients were searched in MEDLINE, EMBASE, and CENTRAL databases, ESMO, ASCO, and IASLC meeting proceedings. Meta-analyses were performed using random-effects model. Subgroup analyses were undertaken comparing the geographical area of study and interaction test were used to compare subgroups. The outcomes of interest were overall survival (OS), Survival at one year (S1), survival at two years (S2), progression-free survival (PFS), and response rate (RR).

Results and Conclusion: Seven studies (1967 patients) were included. OS, S1, and S2 meta-analysis demonstrated superiority of IP over EP (OS HR = 0.88; 95% CI 0.80-0.95; P=0.002; I^2=0%; table 1). PFS meta-analysis was not feasible due to impending heterogeneity (I^2=86%), not related to geographical origin; RR was similar between IP and EP groups, absolute rates: IP 52%, EP 50%, P-value=0.31). The analyses according to geographical area demonstrated that patients around the world experienced similar benefit from IP, excepting for S2, where Asian and European patients derived larger benefits of IP (table 2). Meta-analysis Patients HR 95% CI P-value OS analysis 1967 0.87 [0.80 - 0.95] 0.002 1-year survival 1967 0.74 [0.60 – 0.91] 0.004 2-year survival 1967 0.80 [0.66 - 0.98] 0.049 Geographic analysis Patients HR 95% CI P-value Interaction test OS Western trials 1813 0.89 [0.81 – 0.98] 0.02 Reference OS Japanese trial 154 0.80 [0.66 – 0.98] 0.03 NS 2-year survival – America 933 1.05 [0.65 – 1.69] 0.91 0.009 2-year survival – Europe 792 0.41 [0.24 – 0.69] 0.003 Reference 2-year survival – Asia 154 0.23 [0.07 – 0.72] 0.01 0.36 Conclusions: This meta-analysis demonstrates that IP improved OS for both Western and Eastern patients. The survival at 2 years may vary according geographical origin of patients. The present findings corroborate the role of ethnic background in cancer therapy and demand further confirmation in a pharmacogenomic context.

OS Meta-analysis	Patients	HR 95% CI	P-value
OS analysis	1967	0.87 [0.80 - 0.95]	0.002
1-year survival	1967	0.74 [0.60 – 0.91]	0.004
2-year survival	1967	0.80 [0.66 - 0.98]	0.049

Geographic analysis	Patients	HR 95% CI	P-value	Interaction test
OS Western trials	1813	0.89 [0.81 – 0.98]	0.02	Reference
OS Japanese trial	154	0.80 [0.66 – 0.98]	0.03	NS
2-year survival – Europe	792	0.41 [0.24 – 0.69]	0.003	Reference
2-year survival – America	933	1.05 [0.65 – 1.69]	0.91	0.009
2-year survival – Asia	154	0.23 [0.07 – 0.72]	0.01	0.36

Disclosure: No significant relationships.

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.05: SENSITIVITY OF EGFR EXON 20 INSERTION MUTATIONS TO EGFR INHIBITORS IS DETERMINED BY THEIR LOCATION WITHIN THE TYROSINE KINASE DOMAIN OF EGFR

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Background: Epidermal growth factor receptor (EGFR) mutations define an important subgroup of non-small-cell lung cancer (NSCLC). Most patients whose tumors harbor exon 19 deletions or L858R EGFR have responses to reversible ATP-mimetic EGFR tyrosine kinase inhibitors (TKIs), gefitinib and erlotinib. Exon 20 insertion mutations comprise ~5% of EGFR mutations, mostly occur at the N-lobe of EGFR after its C-helix and nearly all NSCLCs with EGFR exon 20 insertion mutations display lack of responses to EGFR TKIs.

Methods: We have compiled genotype-clinical outcomes of EGFR exon 20 insertion mutations NSCLCs to EGFR TKIs, generated a comprehensive panel of exon 20 EGFR mutation constructs using site-directed mutagenesis for in vitro analysis, compared NSCLC cell lines with EGFR mutations to a novel malignant pleural effusion-derived cell line (BID007), and defined the pattern of response to EGFR TKIs of different exon 20 insertion mutations.

Results and Conclusion: The disease control rate of gefitinib or erlotinib was significantly higher in EGFR exon 20 insertion mutations located within the C-helix when compared to mutations following the C-helix (p=0.0017) and two patients with EGFR A763_Y764insFQEA (located within the C-helix of EGFR) mutated NSCLC had partial responses to erlotinib. Most other exon 20 insertion mutation-positive NSCLCs did not respond (p=0.0119). Seven representative exon 20 insertion mutations and more common EGFR mutations were studied (including EGFR-delL747_P753insS, delL747_P753insS+T790M, A763_Y764insFQEA, Y764_765insHH, M766_A767insAI, A767_V769dupASV, D770_N771insNPG, D770_N771insSVD, H773_V774insH, L858R and L858R+T790M). All, but A763_Y764insFQEA and the known EGFR TKI-sensitive delL747_P753insS and L858R, were resistant to micromolar concentrations of erlotinib. Ba/F3 cells with EGFR-A763_Y764insFQEA underwent apoptosis upon exposure to nanomolar concentrations of erlotinib. Cell line BID007 with EGFR-A763_Y764insFQEA was inhibited by siRNAs against EGFR and had phosphorylated EGFR, ERK and AKT inhibited by nanomolar concentrations of erlotinib whist undergoing apoptosis. The enzymatic kinetic behavior of A763_Y764insFQEA, A767_V769dupASV and D770_N771insNPG is being studied and will be compared to wild-type EGFR. Structural models of representative EGFR exon 20 insertion mutations are being generated. Conclusion: Most EGFR exon 20 insertion mutations are resistant to EGFR TKIs and enzymatic and crystal structure of representative mutations are ongoing to determine their mechanism of resistance to gefitinib/erlotinib. However, EGFR-A763_Y764insFQEA is an EGFR TKI-sensitive mutation and can be inhibited by clinically-achievable doses of gefitinib/erlotinib. These findings have clinical implications for the 10,000 cases of EGFR exon 20 insertion mutated NSCLC diagnosed yearly plus point towards the need to define the molecular mechanisms that underlie differential responses to EGFR TKIs and the need for development of novel EGFR inhibitors specific for the more prevalent exon 20 insertion mutations.

Disclosure: Pfizer (consultant 2011, compensated) Roche (consultant 2010, compensated) AstraZeneca (consultant 2011, compensated)

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.06: EFFICACY AND SAFETY OF CRIZOTINIB IN ADVANCED ALK-POSITIVE NON-SMALL CELL LUNG CANCER (NSCLC) RESULTS FROM A PHASE II GLOBAL TRIAL

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Background: In NSCLC approximately 3–5% of patients harbor an ALK gene rearrangement. The EML4-ALK fusion gene is a known oncogenic driver in a subset of NSCLC patients. Crizotinib is a first-in-class, oral, ATP-competitive, small-molecule ALK inhibitor with anti-MET activity.

Methods: An ongoing global, multicenter, open-label, single-arm, phase II study (PROFILE 1005) is evaluating the safety and efficacy of crizotinib (250 mg BID in 3-week cycles) in patients with advanced ALK-positive NSCLC who progressed after ≥1 chemotherapy for recurrent/advanced/metastatic disease. Tumor response was evaluated every 6 weeks (RECIST 1.1). Efficacy assessments included response rate, duration of response, disease control rate, and progression-free survival (PFS). Patient-reported outcomes and global quality of life (QOL) using the EORTC QLQ-C30 and LC-13 at baseline, day 1 each cycle and at end of treatment were assessed.

Results and Conclusion: 439 patients were evaluable for safety and 255 patients for tumor response (as of June 2011). Median age was 53 years. The majority of patients were female (53%), never smokers (65%), and had adenocarcinoma (92%), ECOG PS 0–1 (83%) and ≥2 prior chemotherapy regimens (85%). Of evaluable patients, median treatment duration was 25 weeks (77% of patients still ongoing). ORR was 53% (95% CI: 47–60), disease control rate was 85% (95% CI: 80–89) at 12 weeks, median duration of response was 43 weeks (96% CI 36–50) and median PFS was 8.5 months (95% CI: 6.2–9.9). Common treatment-related AEs included visual effects (50%), nausea (46%), vomiting (39%), and diarrhea (35%), mostly grade 1–2. Treatment-related SAEs were reported in 29 patients (6.6%) and included dyspnea and pneumonitis (4 patients each; 0.9%), and febrile neutropenia and renal cyst (2 patients each; 0.5%). Statistically significant ($p<0.05$) and clinically meaningful (≥ 10 points) improvement from baseline was noted for patient-reported overall pain, pain in chest, cough, dyspnea, insomnia, fatigue and global QOL. Crizotinib demonstrated a 53%

response rate, durable PFS, a favorable tolerability profile and improvement in patient-reported symptoms. These findings are consistent with earlier reports and results provide strong support for crizotinib as a standard of care for advanced ALK-positive NSCLC.

Disclosure: CG Ferreira, Y Shi, P-C Yang, and TM De Pas have no conflicts of interest to disclose. C Barrios has received honoraria and research funding from Pfizer Inc. AT Shaw has had a consultancy or advisory role for which compensation was received for Ariad, Chu

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.07: STAGING IMPLICATIONS OF INTRAOPERATIVE ULTRASOUND GUIDED MEDIASTINAL LYMPADENECTOMY IN NSCLC SURGERY

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Thoracic Surgery Dept., University Surgical Hospital, Split/CROATIA

Background: The extend of lymph node involvement in patients with non-small cell lung cancer (NSCLC) is the cornerstone of staging and influences both multimodality treatment and final outcome. We studied safety, accuracy and characteristics of intraoperative ultrasound (US) guided systematic mediastinal nodal dissection in patients with resected NSCLC.

Methods: Prospective randomized trial of intraoperative surgical staging after radical surgery for NSCLC was carried out. Intraoperative hand held ultrasound probe was used in systematic mediastinal nodal dissection in 124 patients after radical surgery for NSCLC and compared with 120 patients who underwent lung resections and standard systematic mediastinal nodal dissection. Mapping of the lymph nodes by their number and station followed by histopathologic evaluation was performed. Patients data were statistically analyzed.

Results and Conclusion: The surgical procedure used depended on the extent of the disease, as well as the cardiopulmonary reserve of the patients and was comparable in both groups of patients. Operating time was prolonged for 12 (6 – 20) minutes in patients with US guided mediastinal nodal dissection, but number and stations of evaluated lymph nodes was significantly higher (p>0.001) at the same group of patients. Skip nodal metastases were found in 24% of patients without N1 nodal involvement. We upstaged 22 (10%) patients using US guided mediastinal lymphadenectomy. Median follow-up was 38 (range, 10 - 52) months. Standard staging system seemed to be improved in US guided mediastinal lymphadenectomy patients. Complications rate showed no difference between analyzed groups of patients. Conclusion: Higher number and location of analyzed mediastinal nodal stations in patients with resected NSCLC using hand held ultrasound probe suggested to be of great oncology significance. Procedure showed absolute safety and high accuracy. Our results indicated that intraoperative US may have important staging implication. Further clinical studies should be carried out in order to improve intraoperative staging in NSCLC patients.

Disclosure: No significant relationships.

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.08: ANALYSIS OF PPGALNAC-T13 ENZYME AND ITS RELATIONSHIP WITH CLINIC, HISTOLOGIC AND BIOMARKERS PROFILE IN PATIENTS WITH NON-SMALL-CELL LUNG CANCER (NSCLC).

Diego Touya[1], Carmen Behrens[2], Luisa Solis[2], Ping Yuan[2], Rafael Alonso[3], Mario Varangot[1], Eduardo Osinaga[4], Ignacio Wistuba[2], Nora Berois[4]

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Background: O-gylcosylation alterations occur in most carcinomas, resulting in the expression of molecules which may constitute useful targets for diagnostic and therapy. ppGalNAc-T13 enzyme catalyzes a key step in the initiation of O-glycosylation. It is overexpressed in metastatic neuroblastoma, and has been correlated with the prognosis of patients with this tumor. In resected lung cancer specimens there is no information about ppGalNAc-T13 expression.

Aim: To study the frequency of expression of the ppGalNAc-T13 enzyme in a large set of surgically resected NSCLC tumor tissues, and its association with clinical, pathological and molecular characteristics including patients's recurrence-free survival (RFS) and overall survival (OS).

Methods: We used tumor tissue microarrays containing 443 NSCLCs, including 249 adenocarcinomas (ADCA) and 122 squamous cell carcinomas (SCC). We performed immunohistochemistry using a monoclonal antibody specific against ppGalNAc-T13. The cytoplasmic expression of the enzyme was quantified using a four-value intensity score (0, 1+, 2+, and 3+) and the percentage (0-100%) of the extent of reactivity in each tissue core. The final score was then obtained by multiplying the intensity and reactivity extension values (range, 0-300). The patients were divided into 2 groups: with (n=72, WNA) and without neoadjuvant (n=371, WONA) chemotherapy.

Results and Conclusion: Results: We found frequent ppGalNAc-T13 expression in NSCLC, without significant differences between WNA and WONA (p=0,20) groups. ADCAs expressed higher levels of the enzyme than SCCs in both groups (WNA, p=0.02; and, WONA, p<0.0001). In the ADCA patients, with or without neoadyuvant, ppGalNAc-T13 expression is different according histology pattern (WNA: p = 0.002 and WONA: p = 0.044) showed higher value with the presence of solid histology pattern and lower in lepidic histology pattern. Using Spearman Correlation test, ppGalNAc-T13 correlated significantly with EpCAM (p<0.001) and TTF-1 (p<0.01) expression, In ADCAs, we found no correlation between ppGalNAc-T13 expression and EGFR and KRAS mutation status and the presence of EML4-ALK fusion gene. Interestingly, in the ADCA-WNA subset, high ppGalNAc-T13 expression level was associated with worse OS (p<0.01 , HR=5.2), not significative in RFS (p= 0.15, HR=1.8). In contrast, we did not find any association between ppGalNAc-T13 expression and outcome in the ADCA-WONA subset of patients. Conclusions: ppGalNAc-T13 is frequently expressed in NSCLC and associates with worse prognosis in patients with ADCA who received neoadjuvant chemotherapy. Our data suggest that ppGalNAc-T13 is a novel marker associated to chemoresistance in NSCLC.

Disclosure: No significant relationships.

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.09: CONTEXT-DEPENDENT CONSEQUENCES OF AKT INHIBITION IN NSCLC CELL LINES

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Background: MK2206 is a selective, allosteric inhibitor of AKT, a key signal transduction intermediary. AKT is active in NSCLC, as indicated by elevated phosphorylation in tumor cells and is considered a critical component of signal transduction mediated by receptor tyrosine kinases (RTKs) such as EGFR and MET. However, mutations in factors immediately upstream of AKT, such PTEN and PI3K, are not a common pathology in NSCLC. Preclinical and early clinical investigations are underway to define optimal treatment strategies, identify target subpopulations, and elucidate biomarkers predictive of MK2206 activity. We evaluated the signal transduction, cytotoxic and cytostatic effects of AKT inhibition via MK2206 with or without the EGFR inhibitor erlotinib in a panel of 10 NSCLC with different oncogenic abnormalities in the presence or absence of HGF-induced Met activation.

Methods: Cell growth, cell cycling and apoptotic effects were evaluated by the MTT assay, PARP cleavage and flow cytometry. Changes in phosphorylation of signal transduction mediators and RTKs were evaluated by multiplex kinase arrays and Western analysis. Drug interactions were tested for synergy using Median Effect Analysis. Met activation was stimulated through exogenous addition of HGF (25ng/ul).

Results and Conclusion: In all cell lines tested, single-agent MK2206 ablated pAKT (T308 and S473) and showed additive-to-synergistic interactions between erlotinib and MK2206. Addition of the MET ligand HGF prevented erlotinib-induced cytotoxic and cytostatic effects in erlotinib-sensitive lines, coinciding with induction of both pERK1/2 and pAKT. MK2206, which ablated pAKT regardless of HGF treatment, could restore cytostatic activity to erlotinib. Of note, single-agent MK2206 resulted in compensatory upregulation in Erk1/2 and, in the presence of HGF, marked upregulation of pMET; however, these effects were mitigated by erlotinib. Conclusion: AKT inhibition by MK2206 resulted in significant compensatory effects, including upregulation of MET and ERK activity, when used as a single agent. However, the combination of erlotinib plus MK2206 showed additive-to-synergistic activity in all NSCLC cell lines tested, regardless of EGFR or KRAS status. Exogenous addition of HGF prevented erlotinib activity, and induced both pERK1/2 and pAKT. MK2206 could override this pAKT induction, restoring cytostatic activity of erlotinib. A California Cancer Consortium clinical trial (NCI 8698) is underway to test MK2206 plus erlotinib in patients who previously benefited from erlotinib.

Disclosure: No significant relationships.

MINI ORAL SESSION - July 27, 2012 08:00 – 09:15

MO.10: EVALUATION OF ALK IN NON-SMALL CELL LUNG CANCER USING FISH AND RT-PCR

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Background: Translocations involving the kinase domain of the anaplastic lymphoma kinase (ALK) gene have been identified in a number of different malignancies including non-small cell lung cancer (NSCLC). Although ALK has been demonstrated to fuse with a number of different genes, the echinoderm microtubule-associated protein-like 4 (EML4) gene is commonly associated with ALK in NSCLC. Crizotinib was recently approved for the treatment of ALK positive NSCLC patients as determined by the presence of an ALK gene rearrangement based on a companion diagnostic FISH assay. The frequency of ALK related NSCLC reported in the literature varies widely ranging from approximately 2 -12%. Part of this variability is likely due to the testing method. We sought to compare FISH with an RT-PCR reaction capable of detecting the 10 most common EML4-ALK variants.

Methods: 1133 formalin fixed paraffin embedded lung samples were assessed using the Vysis LSI ALK break apart rearrangement FISH probe and a variant specific RT-PCR which is capable of detecting the 10 most common EML4-ALK variants. For FISH, 50 tumor cells were enumerated for the presence of a break apart signal which was considered as present when at least one set of orange and green signals were 2 or more signal diameters apart or when a single orange signal without a corresponding green signal was observed in more than 15% of tumor cells. The RT-PCR reaction uses one-step chemistry and is capable of detecting each of the 10 fusion transcripts at a sensitivity of approximately 1%.

Results and Conclusion: Of the 1133 cases, 28 (2.47%) samples had a detectable break apart by the FISH assay. Nineteen of these samples were confirmed as a form of EML4-ALK by the RT-PCR while the other 9 did not generate a signal from any of the 10 EML4-ALK variant specific reactions. The 19 samples that were confirmed by RT-PCR consisted of 9 variant one, 4 variant two, 4 variant three and 2 variant five. The samples that were not confirmed by the RT-PCR suggest the possibility of an ALK translocation partner other than EML4. In addition to alternative ALK rearrangements, the FISH test identified 26 (2.3%) samples as having ALK gene amplification. FISH detected a break apart signal in 2.47% of samples, consistent with the reported literature. Attempting to detect the specific EML4-ALK variant by RT-PCR failed to identify 9 (32%) of the 28 ALK positive tumors identified by FISH suggesting that this method should not be used as the sole means of identifying patients who may benefit from Crizotinib therapy.

Disclosure: No significant relationships.

POSTER SESSION 1 · THURSDAY, JULY 26

POSTER DISPLAY TIME: 09:00 – 17:00

AUTHOR STAND BY TIME: 11:00 – 11:30 AND 16:00 – 16:30 (COFFEE BREAKS)

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Prevention, Early Detection, Epidemiology and Tobacco Control

P1.01: A MATHEMATICAL MODEL FOR PREDICTING MALIGNANCY OF SOLITARY PULMONARY NODULES

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Background: Detecting and diagnosing SPNs are critical since early identification of malignant nodules is crucial to the chance for successful treatment. SPNs, however, are usually small, located deep in the pulmonary parenchyma, and often yield atypical imaging findings. While researchers are seeking advanced image technique, more and more clinicians stressed that in addition to the radiographic and image characteristics. Confronting such massive data, clinical experience and judgment may not be reproducible or reliable, while a quantitative model might have its advantages in accuracy, reproducibility, uninfluenced by personal judgment, and outcome exchange ability. Researches began to suggest that a clinical prediction equation has the potential to facilitate clinical decision making.

To improve the accuracy of the model, a systematic and comprehensive clinical and imaging data with specific diagnosis is needed.. In this paper, we aimed to develop a prediction model for patients with SPN based on a comprehensive data collection and thorough analysis.

Methods: Records from 371 patients (197 male, 174 female) with SPN between Jan 2000 and Sep 2009 were reviewed (Group A). Clinical data were collected to estimate the independent predictors of malignancy of SPN with multivariate logistic regression analysis. And a clinical prediction model was subsequently developed. Between Oct 2009 and May 2011, data from additional 145 patients with SPN were used to validate this new clinical prediction model (Group B). The same dada were also estimated using two previously published models in order to compare with our new model.

Results and Conclusion: Results: Median patient age was 57.1 years in group A. 54% of the nodules were malignant and 46% were benign. Logistic regression analysis identified six clinical characteristics (age, diameter, border, calcification, spiculation, and family history of tumor) as independent predictors of malignancy in patients with SPN. The area under the ROC curve for our model (0.874 ± 0.028) was higher than those generated using another two reported models. In our model, sensitivity = 94.5%, specificity = 70.0% positive predictive value = 87.8%, negative predictive value = 84.8%). Conclusions: Age, diameter, border, calcification, spiculation, and family history of tumor were independent predictors of malignancy in patients with SPN. Our prediction model was sufficient to estimate malignancy in patients with SPN and proved to be more accurate than the two existing models.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Prevention, Early Detection, Epidemiology and Tobacco Control

P1.02: MOLECULAR MECHANISM OF CIGARETTE SMOKE INDUCED UNREGULATED PROLIFERATION OF HUMAN LUNG CELLS AND ITS PREVENTION.

Neekkan Dey, Shinjini Ganguly, Dhrubajyoti Chattopadhyay, Indu B. Chatterjee
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Background: Lung cancer is the leading cause of cancer-deaths throughout the World. Cigarette smoking is the strongest risk factor for developing lung cancer. Hyper-proliferation of cells occurs in response to cigarette smoke (CS) exposure. Unregulated cell proliferation together with suppressed apoptosis is a contributory factor for lung-carcinogenesis. However, the carcinogenic mechanism of cigarette smoking is not well understood. This is particularly because cigarette smoke is a complex mixture of about 4000 compounds and identifying the risk factor in CS is essential for achieving this goal.

Methods: Cytotoxicity was evaluated by the MTT assay. Cell cycle analysis was performed by propidium iodide (PI) staining followed by flow-cytometry. Apoptosis was assessed by AnnexinV- PI staining followed by flow-cytometry. Reactive Oxygen Species (ROS) production was detected by 2', 7'-dichlorodihydrofluorescein diacetate (H2DCFDA) fluorescence using confocal laser scanning microscope. Cell proliferation was assessed using "In Situ Cell Proliferation Kit, FLUOS" (Roche Applied Science, Germany). DNA double strand break was detected using "OxiSelect DNA Double Strand Break (DSB) Staining Kit" (CELL BIOLABS, INC.).

Results and Conclusion: We have identified p-benzoquinone (p-BQ) as a major risk factor that is produced from p-benzosemiquinone, which is present in high concentration (100-200 µg/cigarette) in CS. Using MTT assay, flow-cytometric analysis after AnnexinV-PI staining, cell cycle analysis and BrdU-incorporation assay we have observed that p-BQ has a biphasic-nature. Low concentration of p-BQ mimics CS-induced proliferation of cultured lung cells (A549). The proliferation is not restricted to A549 cells; it also occurs in other cell lines. However, under the experimental conditions the benzo[a] pyrene and nitrosamines (e.g. NNK and NNN) do not induce proliferation. In contrast, higher concentrations of CS/p-BQ result in cell death caused by oxidative stress and apoptosis. The oxidative stress has been evidenced by the formation of ROS and apoptosis by the AnnexinV-PI assay, phosphorylation of p53 and activation (cleavage) of caspase 3. No such oxidative stress or apoptosis was observed with low concentration of CS/p-BQ. Coimmunoprecipitation and immunoblot experiments indicate that p-BQ-induced proliferation is mediated via aberrant phosphorylation of EGFR that lacks c-Cbl mediated ubiquitination and degradation. This results in prolonged EGFR signaling leading to persistent activation of Ras (potent oncoprotein that play a major role in lung cancer), the downstream survival and proliferative signaling molecules Akt and ERK1/2, as well as the transcription factors c-Myc and c-Fos. In addition, p-BQ causes hyper-acetylation of histones, thereby enhancing transcription of proliferation-inducing genes.

Whereas, repeated p-BQ exposure generate high levels of DNA double strand breaks and induce cultured lung cells to evade the cell cycle checkpoints, that may cause mutation of different proto-oncogenes and tumor suppressor genes which ultimately lead to cancer. Both anti-p-BQ antibody and vitamin C (a strong reductant of p-BQ) prevent CS/p-BQ-induced activation of EGFR and proliferation of lung cells. Despite major advances in the treatment and management of lung cancer, most patients eventually die. Consequently, newer approaches such as chemoprevention(s) are necessary in the battle against lung cancer. We consider that prevention of CS-induced proliferation of lung cells by vitamin C and/or anti-p-BQ antibody may provide a novel intervention for preventing initiation of CS-induced lung cancer.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Prevention, Early Detection, Epidemiology and Tobacco Control

P1.03: REFERRAL OF LUNG CANCER PATIENTS TO SPECIALIZED CLINICAL ONCOLOGY CARE: INSTITUTO DO CANCER DO ESTADO DE SAO PAULO 2010-2011.

Rafael Caires-Lima, Tiago K. Takahashi, Milena P. Mak, Felipe S.R. Roitberg, Carlos H.A. Teixeira, Cristiane S. Mesquita, Andrea M. Marini, Renata E. Martins, Tereza Y. Takagaki, Pedro N. Araújo, Olavo Feher, Paulo M. Hoff, Gilberto De Castro Junior
Clinical Oncology, Instituto Do Cancer Do Estado De Sao Paulo, São Paulo/BRAZIL

Background: Lung cancer is the leading cause of death from malignancy in Western countries. To achieve better outcomes and improve quality of care, it is essential to know both patients and disease characteristics. Here we aim to describe epidemiological and tumor characteristics and their impact on survival outcomes, of patients admitted at Instituto do Câncer de Estado de São Paulo (ICESP) between January 2010 and July 2011.

Methods: It is a retrospective, descriptive, and uninstitutional study, of patients diagnosed histologically with lung cancer, consecutively admitted at ICESP between January 2010 and July 2011. Overall survival was the main endpoint. Frequencies were compared using chi-square test. Survival was estimated using the Kaplan-Meier methods, and the curves were compared by the log-rank test. This study was approved by the local IRB.

Results and Conclusion: 232 patients (pts) were included in this analysis: median age 65y (24-91), 57% male, 56% ECOG 0 - 1, and 83% previous or current smokers. Non small cell lung cancer (NSCLC) was the most common histologic type (213 pts, 92%). Small cell lung cancer (SCLC) was diagnosed in 18 pts (7.6%) and only one (0.4%) was a case of a carcinoid tumor. Regarding NSCLC histologic subtypes, adenocarcinoma was the most common (130 pts, 61%), followed by squamous cell carcinoma (63 pts, 30%) and large cell carcinoma (5 pts, 2%). In 17 pts (7%), it was not possible to determine the subtype, even with immunohistochemistry. In terms of staging, 155 pts (71%) with NSCLC presented metastatic disease (stage IV) at diagnosis, 27 pts (12%) were staged as IIIB, 15 pts (10%) IIIA, 8 pts (3.5%) II and 8 pts (3.5%) I. Among patients with SCLC, six (33%) had localized disease (LD) and 12 (67%) had extensive disease (ED). Analyzing only stage IV NSCLC pts, 123 (79%) were treated with first line chemotherapy, 56 (36%) with second line and 13 (8%) with third line systemic therapies; ECOG 0 - 2 NSCLC pts were more likely to be exposed to second-line therapies (46% vs 36%; p = 0.0002). In a median follow-up of 9.5 mo, median overall survival (mOS) was 9 mo for all pts in this analysis. Regarding NSCLC, in patients with stage I and II mOS was not reached (100% and 68% in 2 years for stage I and II, respectively). In patients with stage IIIA, IIIB and IV, the median OS was 15.2, 11.4 and 7 mo, respectively (p-trend = 0.0002). According to ECOG-PS, mOS was 11.3, 6.3, 4.1, and 2.2 mo for NSCLC pts with ECOG 1, 2, 3 and 4, respectively (p-trend < 0.0001). For SCLC pts, mOS was 12.9 mo among those with LD versus 4.9 mo in ED (HR 3.1; 95% CI 1.1 - 8.6; p = 0.02). Lung cancer survival rate remains poor. As expected, clinical stage and performance status were important prognostic factors. Primary prevention strategies (quitting smoking) and early diagnosis (screening) may be useful in this scenario.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Prevention, Early Detection, Epidemiology and Tobacco Control

P1.04: SPUTUM HYALURONAN ANALYSIS AS A NEW STRATEGY FOR THE SCREENING AND DIAGNOSIS OF LUNG CANCER

Maristela P. Rangel[1], Vanessa K. De Sá[1], João Roberto M. Martins[2], Edwin Roger P. Cuentas[1], Tereza Takagaki[1], Adhemar L. Filho[3], Rui Reis[3], Helena Nader[2], Vera L. Capelozzi[1]

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Background: Hyaluronic Acid (HA) concentration is elevated in several cancers, but there is no data regarding its concentration in the sputum of lung cancer patients.In this study, we examined the HA concentrations in the tissue and in the sputum of lung cancer patients and its impact on the screening and diagnosis of the disease.

Methods: HA was examined in 45 paired tissues samples and sputum samples were collected from 90 lung cancer patients. Twenty five COPD patients were selected to compose a high risk group and 15 healthy volunteers were analysed as controls. All the patients and controls underwent a sputum induction. Sputum samples were incubated with urea 7M and tissue samples were dehydrated with acetone prior to analysis. Afterwards both were incubated with a proteolytic enzyme. The levels of HA were measured by a noncompetitive ELISA-like fluorometric assay.

Results and Conclusion: A significant different concentration pattern of HA in the tissues was found between tumoral and non-tumoral samples (p<0.001). Equally significant was the difference found in the sputum among lung cancer, COPD and healthy individuals (p<0.001 Fig1A). When comparing the groups separately, a difference was found between sputum HA from LC vs.healthy volunteers (p<0.001) and LC vs.COPD patients (p=0.002). ROC curve between LC and healthy volunteers furnished an area of 0.821. Assuming a cut off value of 31,44ng/mg, the specificity was 100% and the sensitivity was 51% (Fig1B). ROC curve to distinguish COPD patients from LC patients showed an area of 0.698 and the cut off value of 48.3ng/mg presented 100% of specificity and 33% of sensitivity

(Fig1C). The results presented suggest a promising role of HA in the sputum as a novel screening and diagnostic marker for differentiating normal from LC patients.

Disclosure: No significant relationships.

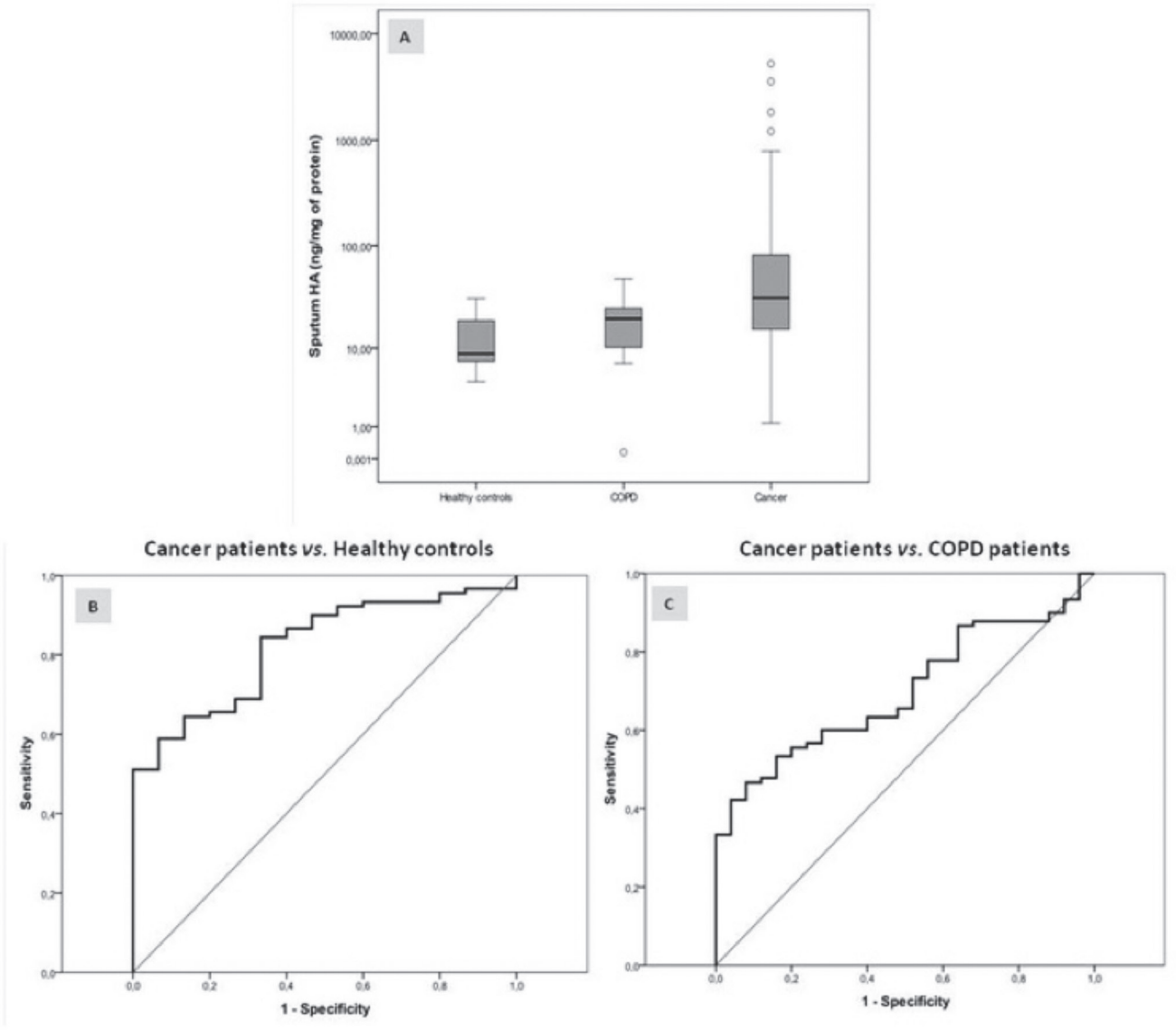

Figure 1: A - Patients with lung cancer had a significantly higher hyaluronan levels in sputum than that in the COPD and healthy controls (Log10 scale; p<0.001) **B/C** - ROC curves for sputum levels of hyaluronan. **B-** The cut off level of hyaluronan that result in the highest diagnostic accuracy was >31.44ng/mg. The cut-off point of hyaluronan discriminated between healthy controls and lung cancer patients, with 100% specificity and 51% sensitivity. The diagnostic accuracy was 82%. **C-** The cut-off point of hyaluronan that discriminated COPD and lung cancer patients, with 100% specificity and 33% sensitivity was >48.3ng/mg. The diagnostic accuracy was 69%.

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Prevention, Early Detection, Epidemiology and Tobacco Control

P1.05: PEQUI FRUIT (CARYOCAR BRASILIENSE CAMB) PULP OIL, A NATURAL SOURCE OF ANTIOXIDANTS, REDUCE THE OXIDATIVE STRESS STATUS AND DNA DAMAGE IN EXPERIMENTAL LUNG CANCER.

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Background: It is well known that the endogenous antioxidant enzyme defense as well as an adequate ingestion of exogenous sources of antioxidants prevents the oxidative damage caused by reactive species (ROS),including DNA damage, and can reduce the risk of cancer, atherosclerosis and other degenerative diseases. The pulp of Caryocar brasiliense Camb, most known as pequi, is a Brazilian fruit that has high levels of antioxidants properties, such as vitamin C, carotenoids, phenolic compounds like flavonoids, saponins and tannins, and essential oils. The aim of this study was to estimate and to evaluate the antioxidant enzyme activities of catalase (CAT) and superoxide dismutase (SOD), as well as the ratio between then, and the antioxidant activity of the pequi oil, measuring lipid peroxidation and DNA damage in experimental model of lung cancer induced by urethane.

Methods: The study was performed in 18 male BALB/c mice: 14 animals received by gavage 0,5µL/mg/day of pequi oil (PI0601631-6) (Control+CBCoil = 4) during 75 days. After 15 days of the beginning of the gavage, 10 of these mices received two doses of 1,5g/kg intraperitoneal of urethane (Urethane+CBC oil=10). The other 4 animals were only submitted to two doses of 1,5g/kg intraperitoneal of urethane (Urethane group=4). After 75 days, the three groups were sacrificed. The antioxidant activity of pequi oil was evaluated in the lung tissues by the biochemical TBARS (Thiobarbituric acid-reactive substances), CAT and SOD test. The DNA damage was estimated by the comet test method.

Results and Conclusion: The lung parenchyma from the Urethane groups without oil and with oil showed neoplasic formations induced by the chemical carcinogenesis in contrast with Control + CBC oil group. The results of the TBARS test showed a significant decreased of the lipid peroxidation in the Urethane + CBC oil, similar as values of the Control+CBC oil, when compared with Urethane group. The CAT and SOD test, as well as the ratio between then, didn't show a significant difference. The image analysis of the comet assay showed a statistical significant decreased of the DNA damage cells in the Urethane + CBC oil group when compared with urethane group (p=0.001). The decreased DNA damage was very similar that we obtained in the Control + CBC oil group. We conclude that the different natural antioxidant components found in the pequi oil are efficient to diminish the oxidative stress status and the DNA damage in chemical carcinogenesis induced by urethane experimental lung cancer, suggesting that this type of strategies may have a greater impact in lung cancer treatment. Financial Support: FAPESP, CNPq

Disclosure: No significant relationships.

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P1.07: TOXICITY PROFILE OF FIRST LINE TREATMENT WITH PEMETREXED, IN PATIENTS WITH NSCLC (NON-SQUAMOUS HISTOLOGY) AT A PRIVATE ONCOLOGY INSTITUTION IN SALVADOR, BAHIA, BRAZIL.

Maria Cecília Mathias, Oddone F.M. Braghiroli, Gildete S. Lessa, Clarissa Mathias, Eldsamira Mascarenhas
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Background: Lung cancer is a disease with high morbidity and mortality and the progress of chemotherapy has been a reality, also, the search for a personalized therapy has been the treatment goal. There are many chemotherapy regimens and the change in treatment according to tumor histology is a recent practice. Studies show that personalized treatments have clinical benefits with tolerable toxicity.

Methods: We performed a retrospective study evaluating the toxicity profile of patients with non small cell lung cancer (NSCLC) in our institution treated with pemetrexed and compared the obtained data with other already validated studies.

Results and Conclusion: As stated in Table 1, a tolerable toxicity profile was found, with few grade 3 and 4 events and with grade 1 and 2 fatigue as a very common finding.

	Grade							
	1		2		3		4	
Fatigue	15	33,33%	7	15,56%	1	2,22%	-	-
Increase of Hepatic Enzimes	1	2,22%	1	2,22%	2	4,44%	-	-
Nausea	10	22,22%	5	11,11%	2	4,44%	-	-
Vomiting	3	6,67%	2	4,44%	-	-	-	-
Mucositis	2	4,44%	1	2,22%	1	2,22%	1	2,22%
Neuropathy	1	2,22%	-	-	-	-	-	-
Lower Limb Edema	-	-	3	6,67%	1	2,22%	-	-
Alergic Reaction	-	-	-	-	1	2,22%	-	-
Prurience	2	4,44%	-	-	-	-	-	-
Diarrhea	1	2,22%	2	4,44%	1	2,22%	1	2,22%
Dehydration	-	-	-	-	1	2,22%	-	-
Rash	1	2,22%	-	-	1	2,22%	-	-
Neutropenia	-	-	-	-	1	2,22%	-	-
Thrombocytopenia	4	8,89%	-	-	-	-	-	-
Anemia	-	-	11	24,44%	3	6,67%	-	-

Conclusion: Lung cancer treatment has made great progress and each day longer survival rates are achieved with an improved quality of life. The toxicity profile in patients treated with pemetrexed combined with cisplatin or carboplatin was acceptable and very close to results already published in other important studies.

Disclosure: No significant relationships.

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P1.08: BIOLOGICAL BIOMARKERS FOR SCREENING OF PRE NEOPLASTIC LESIONS ASSOCIATED TO LUNG CANCER IN A RISK CHILEAN POPULATION

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Background: The high incidence of lung cancer (LC) has been associated with smoking habit, genetic diversity and environmental pollution, especially in those cities highly exposed to environmental carcinogens.

Methods: This is a report of an ongoing prospective bimodality cancer survillance trial for high risk LC voluntaries. Enrolment was based in a LC survey applied to 508 chilean voluntaries and 364 of them were included in this study, being classified as high risks subjects, exposed naturally to environmental pollution in Antofagasta and Metropolitan regions. Antofagasta region has the higher LC mortality rate in the country and inhabitants were exposed for 12 years to arsenic in drinking water concentrations as high as 870ug/L. Two biomarkers, Quantitative Automatic Cytology (QAC) and DR70 (Onko Sure), were used as tools in the detection of LC preneoplasic an neoplasic lessions. The study has also included Autofluorescent Bronchoscopy (AFB) as an additional technique.

Results and Conclusion: Results: AFB identifies PNL (metaplasia and dysplasia) better than the WLB. Fifty % of the samples, classify as suspicious by AFB, were confirmed as metaplasia or dysplasia by histopathology. The parallel combination of DR70 and AQC, showed a significant increased of sensitivity to 90.9% (95%IC: 69.4 -100) for LC and PNL with Predictive Positive Value (PPV) for LC and PNL of 13.2% and 20.4%, respectively and Negative Predictive Value (NPV) for LC and PNL of 99.5% and 99.6%, respectively. The prevalence for LC and PNL in this population was 3.74% (95% IC: 1.4 – 6.08). Conclusions: The combined tests can be used as complementary tools to identify individuals harbouring LC or PNL. This is the first study in Latin America to complement image techniques with cellular and molecular biomarkers, to detect LC and PNL. These results provide scientific and clinical information for Chilean health authorities to include early detection of LC in the AUGE government programme, that provide additional health services for patients. Supported by INNOVA-CORFO, Chile.

Disclosure: No significant relationships.

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P1.09: NANOCYTOMIC BIOMARKERS FROM THE BUCCAL MUCOSA FOR LUNG CANCER RISK STRATIFICATION: OPTIMIZATION AND DIAGNOSTIC SYNERGISM WITH MICRORNA EXPRESSION

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Background: The "field of injury" concept posits that the buccal mucosa should be a surrogate marker for lung cancer risk by recapitulating the tissue responsive to cigarette smoke carcinogens (Future Oncol. 2011). Our novel optics technology, partial wave spectroscopic microscopy (PWS or nanocytology), provides heretofore unattainable insights into cellular structure at the nanoscale (PNAS 2008). PWS represents a powerful modality for detecting the micro-architectural consequences of the genetic/epigenetic alterations in field carcinogenesis (Cancer Res 2009). We recently demonstrated that PWS analysis of the histologically normal cheek cells discriminated smokers with versus without lung cancer (Cancer Res 2010). However, buccal cells heterogeneity (stratified squamous epithelium ranging from small basal cells to larger more differentiated superficial cells) was not assessed in this initial proof of concept publication. To optimize clinical performance, we now took two approaches: standardize the buccal cell type by size and add microRNA biomarkers.

Methods: In this case-control study, we defined cases as having histologically confirmed but untreated and controls were smokers without evidence of lung cancer. Brushings from buccal epithelium was placed on a glass slide and ethanol fixed. PWS analysis was performed as previously described and the parameter disorder strength (Ld) was assessed (PNAS 2008, Gastro 2011). We dichotomized cell size at 60 μm ("small" versus" large" cells). MicroRNA analysis was using taqman real time PCR analysis.

Results and Conclusion: For this optimization study, our cohort was expanded to 175 patients with no statistical differences in age, gender or smoking history between cases and controls. Despite being microscopically identical, buccal PWS parameter Ld was markedly elevated lung cancer patients . "Large" cell analysis was superior to previous unselected analysis or focusing on "small" cells (see table). For microRNA analysis, we used our initial microarray analysis to select a single miR (miR15a) in order to mitigate concerns regarding overfitting and showed perfect discriminative ability. We demonstrate the ability of buccal PWS to serve as a minimally-intrusive modality for lung cancer risk stratification. The clinical performance is improved by targeting the more differentiated cells. Moreover, addition of a single microRNA showed outstanding diagnostics. While requiring larger dataset validation, this underscores the promise of buccal analysis with PWS (±microRNA) pre-screen. We envision that buccal PWS with a high negative predictive value threshold would allow many neoplasia-free smokers to forego the expensive low dose CT (LDCT). Furthermore, by enriching the disease prevalence in the LDCT population, this will dramatically

decrease the false positives and mitigate concerns over the harms associated with lung cancer population screening.

	Unselected cells (initial cohort)	Cells <60μm new cohort	Cells≥60 μm new cohort	Cells≥60 μm +miR15a
Sensitivity	78%	56%	89%	100%
Specificity	78%	75%	95%	100%
Area under ROC curve	0.85	0.82	0.94	1.00

Disclosure: Drs. Roy and Backman are co-founders/share holders of American BioOptics LLC and co-founders of Nanocytomics LCC.

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P1.10: SURGICAL PREVENTION OF DEVELOPMENT OF BRONCHOPLEURAL FISTULA AFTER PNEUMONECTOMY IN PATIENTS WITH LUNG CANCER

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Background: It is known that bronchial stump fistula (BSF) and related to it pleural empyema are general causes of efficacy decrease of surgical treatment of pulmonary cancer, purulent destructive pulmonary diseases and other surgical pathologies of thoracic organs. Development of BSF after pneumonectomy (PE) was always related to bronchial suture failure and unfavorable conditions of its healing. Nowadays in oncology a necessity of stratification of patients with local distributed and disseminated cancer forms of any localization is scientifically proved. It allows to determine heterogenicity of patients' group in relation to the nearest and remote prognosis as well as to work out and to implement optimal volumes of surgical treatment into practice.

Methods: Stratification data of risk factors of bronchial stump failure (BSF) development in 575 patients, who underwent primary pneumonectomy in this article were presented. Control group (CG) consisted of 477 patients, 390 patients of them had different tumors of the lungs and 87 patients had purulent diseases of the lungs. The main group (MG) consisted from 98 patients, 72 patients of them had pulmonary tumors and 26 patients had purulent pulmonary diseases. They underwent the worked out treatment tactics based on determination of risk groups development of bronchial failure after pneumonectomy. In the right sided PE minimum risk only into group of 6,7% patients were included (13), into group of mean risk - 70,3% (137) and into group of maximum risk - 23,1% (45) patients. In CG BSF developed in 52 (10,9%) patients, at the same time an incidence of this complication in patients of oncologic profile was 10,5% (41 patients), and in patients with purulent pulmonary diseases – 12,6% (11 patients). In MG BDF was observed in 3 (3,1%) patients, at the same time an incidence of this complication in patients of oncologic profile was 2,8% (2 patients), and with purulent pulmonary diseases – 3,8% (1 patient). To evaluate adequate a retrospective distribution of patients in risk groups in CG and prospective one in MG were performed. 271 patients were included in group of minimum risk that accounted for 47,1%, 220 patients were included in group of mean risk, which accounted for 38,3% and in group of maximum risk - 84 patients that accounted for 14,6%. Formation of risk groups depending on localization of disease showed that in the planning of left sided PE minimum risk was determined in 258 (67,9%) patients, mean risk - in 83 (21,8%) and maximum risk - in 39 (10,3%) patients.

Results and Conclusion: In accordance with factor estimation of risk degree of development of BSF worked out an accomplishment of PE was conjugated with minimal risk in 47,1% (271) patients, mean risk - in 38,3% (220) and maximal risk – in only 14,6% (84), at the same time depending upon a side of operation a 3-fold real increase of risk after PE to the right was registered. Thus, minimal risk of development of this complication reached 67,9% to the left and only 6,7% to the right, mean risk was 21,8% and 70,3% respectively, whereas maximal degree of risk was revealed in only 10,3% to the left and in 23,1% to the right. An incidence of BSF after PE in patients of CG accounted for minimal risk 1,3%, at an average – 16,0%, and maximal – 32,3%, in its turn, an implementation of factor estimation of risk degree of development of BSF after PE in MG allowed to reduce an incidence of this complication until 0,0%, 2,6% and 9,1% respectively. Conclusions. 1. Peculiarities of a tactics of surgical intervention in PE must be determined strong in accordance with risk degree of development of BSF and, depending on the latter, include various in their efficacy of hermetization as well as work volume of accomplishment methods of suturing bronchus stump and consolidation of suture line. 2. The right-sided PE in patients in a group of mean risk as well as PE to the left in patients with maximum risk cause a necessity to suture bronchus stump by manual method as the most hermetic as well as consolidation of suture line with pericardial flap. 3. Sternotomic approach is necessary for patients in a group of maximum risk for an adequate accomplishment of surgical intervention, and consolidation by a proposed method with omentum flap after suturing stump by manual method 5. Independence from risk degree of development of BSF after accomplishment of PE an incidence of lethality can reach 11,0% – at mean risk and 22,6% – at minimum risk, at the same time an introduction of tactics of surgical intervention based on the worked out factor estimation of risk degree of development of BSF after PE permitted to decrease an incidence of lethality from 7,1% (34 of 477 patients in control group) up to 3,1% (3 of 98 patients in main group).

Disclosure: No significant relationships.

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P1.11: EPIDEMIOLOGICAL AND TREATMENT OUTCOMES IN PATIENTS WITH METASTATIC LUNG CANCER AT AN ONCOLOGIC INSTITUTION IN SOUTHERN BRAZIL: UPDATED SURVIVAL ANALYSIS

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Background: In Brazil lung cancer is the third most common malignancy with 27,630 new cases estimated for the year

2010, divided in 17,800 men and 9,830 women. There is an increasing incidence especially in females, which is attributed to increased smoking habit in this gender. It is important to document the follow-up survival data in this southern Brazilian population. Our epidemiological profile of patients with non-small cell lung cancer (NSCLC) in advanced stage has been previously presented. We report here updated overall survival and progression-free survival data and confront the results of treatment with the data in the literature.

Methods: This retrospective study included 125 patients referred to the Clinical Oncology Service of our hospital with NSCLC in stage IIIB with pleural effusion and IV, from 2005 to 2010. For this updated survival analysis, the data cutoff was January 2012. The Kaplan-Meier method was used for survival analysis.

Results and Conclusion: There were 103 deaths in 125 patients enrolled. Of 125 patients studied, 52.8% were male, median age was 58 years, performance status (PS) was equal or less than 1 in 61.3% and subtype adenocarcinoma seen in 59.2% of cases. Among the 104 patients assessable for response, partial remission rate was 31.7% and stable disease 16.3%. Patients were treated with carboplatin-paclitaxel in first line in 88.6% and docetaxel in second line in 47.1%. Median survival was 8.3 months (95% CI 6.3 to 10.3 months) and PS continues to be important with a significant statistical difference in median survival between patients with PS equal or less than 1 versus those equal or greater than 2 ($p = 0.0116$). Progression-free survival was 5.0 months (95% CI 4.0 to 6.0 months). Prolonged follow-up of patients continues to show a survival difference between patients with with PS 0 or 1 versus those equal or greater than 2. Overall survival is still similar to that found in the world literature, as does the progression-free survival. This study shows the epidemiological profile and the treatment outcome of patients with lung cancer in a Southern Brazilian population

Disclosure: No significant relationships.

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P1.12: LUNG CANCER, CLINICAL PRESENTATION AT THE MEDICAL ONCOLOGY DEPARTMENT, CLINICS HOSPITAL, ASUNCION NATIONAL UNIVERSITY MEDICAL SCHOOL (ANUMS)

Vicente A. Villalba[1], Romy M. Gomez[2], Ita Yoffe[2]
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Background: Lung cancer is one of the most frequent in adults and is one of the main causes of cancer death in the world. In our country is one of the principal causes of cancer death, and generally the diagnosis is made when the patient is in an advanced stage. Objectives: To establish the clinical and pathologic figures of lung cancer patients seen in the Medical Oncology Department of the Clinics Hospital ANUMS

Methods: We made a retrospective descriptive study using the clinical charts of patients who attended in our service since January 2001 to December 2011.

Results and Conclusion: From January 2001 to December 2011, 85 patients with the diagnosis of lung cancer were received for treatment. They were 16 females and 69 males with ages between 16 to 87 years old, average of 59.Sixty five(76%)were active smokers,one a former smoker,4 passive smokers,8 were no smokers and in 7 we found no data of smoking habit in the charts. Adenocarcinoma represented 40% of cases,followed by undifferentiated large cell carcinomas and only 12% of squamous cell carcinomas. Small cell lung cancer was the diagnosis in 14% of the patients. In 7% the diagnosis was NSCLC without other specification, 6% were carcinoid tumors. The majority of small cell lung cancer had an extensive disease 71%. The TNM presentation stage of patients with NSCLC was ECII in five, ECIIIA in 10, ECIIIB in 26 and ECIV in 25. One patient came with a relapsed tumor and four patients were lost of follow up before the staging work up was completed. ECOG:8 ECOG 0;35 ECOG 1;19 ECOG 2;13 ECOG3;3 ECOG4 and in seven in the chart was no data of ECOG. Seventy percent of patients received chemotherapy,with platin containing regimens: 44% cisplatin and etoposide, 27% carboplatin plus paclitaxel,13%carboplatin and etoposide,10%gemcitabine and etoposide and in 6% other combinations. Eight patients underwent surgery and 17 radiation therapy. Twenty six patients died between 1 to 32 month after the admission in the Department with a median survival of 8,5 month.Tree are alive and asymptomatic with 28, 36 and 63 month of follow up, ten patients are in palliative treatment and 42 patients were lost of follow up, twelve of them with progressive disease and two asymptomatic with 12 and 13 month of disease free survival.

Disclosure: No significant relationships.

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P1.13: PREVALENCE OF SMOKING AMONG MEDICAL PROFESSIONALS OF A PUBLIC HOSPITAL

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Background: Smoking is considered a serious public health problem and a major avoidable risk factorfor major causes of morbidity and mortality today, such as cancer, cardiovascular andpulmonary diseases. According to estimates by the World Health Organization (WHO), six million deaths are a result of that harm. Despite such information, smoking persists among physicians when it should be a model group of anti-smoking campaign, as recommended by WHO. It is shown, thus the importance of research to assess theprevalence of smoking among physicians. The objetctive of this study is to determine the prevalence of smokers in a sample of physicians from a public hospital in the city of João Pessoa in the state of Paraíba, characterizing the smoking profile of this sample and the possible relationship with respiratory symptoms such as cough and / or dyspnea, as well as the relationship with secondhand smoke in domestic living.

Methods: It was used a questionnaire designed specifically for our objectives in a observational cross-sectional descriptive study. It was applied to all doctors of the hospital in the form of interviews in the hospital. It was performed through an active search and voluntary participation. It was asked about smoking, how long being skoming, the number of cigarettes

per day, having symptoms of cough and / or dyspnea, in case of being a former smoker (those with one or more years of total abstinence) how long and usage of medications for stopping. All interviewed ones were asked about secondhand smoke in home environment.

Results and Conclusion: There is a total sample of 447 practicing physicians in the hospital among the contracted, volunteers, residents and professors. In inferred results, 5.08% are smokers, 9.32% are former smokers and 18.64% being passive smokers. Thus, 66.96% of the sample behaves as nonsmokers. Among the 33.04 exposed to tobacco effects, 10.75% reported cough and/or dyspnea. The universe of non-smokers in this sample was greater than the others, however passive smokers constitutes a concern group similar found in the general population influencing the habit and exposing individuals to the harmful effects of smoking without offering them the right to choice. Similar groups have been found in the general population. Medical professionals in various age groups have shown a positive awareness about the harms of smoking.

Disclosure: No significant relationships.

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P1.14: EPIDERMAL GROWTH FACTOR RECEPTOR MUTATION IN NON SMALL CELL LUNG CANCER: VENEZUELAN EXPERIENCE

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Background: Lung cancer is the most common cause of cancer related death worldwide. The current treatment strategy includes the identification of somatic mutations of EGFR. In Venezuela, frequency and type of EGFR mutation in patients with NSCLC are unknown. Given its importance in treatment decisions, it was decided to conduct this study in order to know the characteristics of our population regarding the status and type EGFR mutation.

Methods: Since November 2010 until March 2012, we collected samples from 395 patients with NSCLC diagnosis in the country, and were evaluated to determine the EGFR mutation. We calculated 95% confidence intervals based on the binomial distribution.

Results and Conclusion: Among 395 patients, 80 had inadequate sample,19 missing data and 296 patients for analysis. We obtained a mutation rate of EGFR of 11.5%, being more frequent in males (56%) under 65 years (66%), former smokers (59%) with adenocarcinoma histology (97%). Regarding the type of EGFR mutation, the exon 21 mutation was detected in 59% of positive cases, and deletion of exon 19 in 38%. Conclusions: EGFR mutation is present in the Venezuelan population and shows a particular regional demographic behavior.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.17: OUTCOMES OF CISPLATIN PLUS PEMETREXED AS FIRST-LINE THERAPY FOR ADENOCARCINOMA OF THE LUNG - HOW AN ONCOLOGICAL CENTRE IN TAYSIDE, SCOTLAND COMPARES WITH THE LITERATURE

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Background: Evidence supports the use of cisplatin plus pemetrexed as first-line chemotherapy for advanced adenocarcinoma and large cell carcinoma of the lung. We review the outcomes of patients with such histologically-confirmed disease, treated with this regimen, in NHS Tayside, between June 2008 and April 2011.

Methods: Patients were identified from our departmental databases and patient demographics, smoking status, disease stage, toxicities, response to treatment and survival were collected,

Results and Conclusion: 16 patients were identified. 12 (75%) patients were male. 13 (81.3%) were 65 years or younger. 93.8% were current or ex-smokers. 87.5% had disease stage lV. 75% had a performance status (PS) of 1 with 25% having a PS of 0. Seven patients received only 1 cycle, due to rapidly progressive disease (5), toxicities (1) or a dislike of overnight stay (1). 6 patients received 4 cycles, one patient 3 cycles and 2 patients 6 cycles. 6 patients had a partial response, 2 stable disease and 6 disease progression, measured on CT. Grade 3 or 4 toxicities were recorded in 2 (13%) of patients (1 neutropenic sepsis and 1 fatigue). Median survival at the time of data collection was 284 days (range 11-578) with 5 patients still being alive. These local data, of a very small sample size, show a very similar median survival compared with published data (10.1 vs. 10.3 months). Our incidence of grade 3 or 4 toxicities is also higher than published literature (7% vs. 1% febrile neutropenia). Cisplatin plus pemetrexed is therefore not without toxicity and in our population challenges to administration exist.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.18: METASTATIC NON SMALL CELL LUNG CANCER (NSCLC) WITH MORE THAN 3 YEARS SURVIVAL

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Background: Metastatic NSCLC has a poor prognosis with a median survival around 12 months in treated patients. The published evidence suggests that females have a better survival than men and that EGFR mutated adenocarcinoma histology has a significant better prognosis. In this study we describe the

characteristics of a subpopulation of long survivors (>3 years) in patients with metastatic NSCLC.

Methods: A population of 313 patients with metastatic NSCLC were treated with at least 2 cycles of first line platinum based chemotherapy in our Thoracic Oncology Unit from April 2004 to April 2009. Metastatic disease was staged according to the 7th edition IASLC staging system. An analysis of the characteristics of the subpopulation of patients that had an overall survival over 3 years was performed.

Results and Conclusion: Results: Sixteen patients (5,1%) of the study population had an overall survival longer than 3 years. The characteristics of this group of long survivors were: 94% female, 6% men, 87,5% adenocarcinoma histology, 31% carriers of EGFR mutation. The location of metastatic disease at presentation was: 50% pleural/lung, 25% central nervous system, 12,5% bone and 12,5% lymphatic nodes. 87% of the patients received second line chemotherapy and 62% received third line chemotherapy.

Conclusion: This study suggests a clinical, pathologic and molecular profile of long survivors among metastatic NSCLC patients. Awareness of this profile may be of help in selecting adequate treatment for these patients.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.19: BEVACIZUMAB CONTAINING CHEMOTHERAPY AS THIRD TO FIFTH LINE OF SYSTEMIC TREATMENT FOR SELECTED PATIENT WITH ADVANCED LUNG ADENOCARCINOMA

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Background: Non-small cell lung cancer (NSCLC) are the most common and lethal malignancies of developed countries. Conventional chemotherapy has a limited impact only on the course of the disease and great expectations have been deposed in target therapies. Bevacizumab is a monoclonal antibody against vascular endothelial growth factor A, that inhibits neoangiogenesis and increases the effect of cytotoxic compounds in NSCLC. In Spain, Bevacizumab associated to platin-based chemotherapy is approved for first line treatment of unresectable or advanced non-squamous NSCLC. We report our experience applying Bevacizumab plus platin-based chemotherapy as third to fifth line systemic therapy for selected patients with lung adenocarcinoma.

Methods: Five patients with wild type epidermal growth factor receptor lung adenocarcinomas were treated in third (20%), fourth (60%) or fifth (20%) line of therapy. Four of them were women and one was a man. One patient received 4 cycles of Bevacizumab 7.5 mg/kg plus Carboplatin AUC 5 every 21 days. Two patients received Bevacizumab 7.5 mg/kg plus Carboplatin AUC 5 plus Paclitaxel 175 mg/m2 every 21 days for 2 and 5 cycles, respectively. And other two patients were treated with 2 cycles of Bevacizumab plus Carboplatin plus Paclitaxel, followed by 4 cycles of Bevacizumab plus Carboplatin, followed by triweekly Bevacizumab. One of them still maintains treatment with single agent Bevacizumab.

Results and Conclusion: Disease stabilization was observed in 60% of cases and partial response in 40%. Mean progression free survival was 5.04 months (range 1.4 to 9.8), and mean overall survival was 10.5 months (range 2.03 to 21.83). Three patients presented no relevant toxicity, grade-2 infection was observed in one patient, and grade-3 deep venous thrombosis was observed in another one. CONCLUSION: Bevacizumab in combination with carboplatin-based chemotherapy is active and secure for selected advanced patients with lung adenocarcinoma treated beyond the second line of therapy, and it could be applied in previously heavily treated patients.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.20: ERLOTINIB IS HIGHLY ACTIVE IN SELECTED PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC) HARBORING WILD TYPE EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR)

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Background: Gefitinib and Erlotinib are the only two Tyrosine Kinase Inhibitors of the epidermal growth factor receptor (TKI-EGFR) approved for the treatment of advanced NSCLC. The iPass Trial revealed that Gefitinib is only active for NSCLC harboring sensitizing mutation EGFR. Selected (female, Asian, non-smoker) patients with unknown or wild type EGFR (wtEGFR) does not significantly respond to Gefitinib. In the same way, Erlotinib has been reported to be especially active in NSCLC harboring sensitizing mutation EGFR. So, some physicians consider the administration of ITK-EGFR to mutation patients only. We report our experience applying Erlotinib as second, third or fourth line of therapy to selected stage IV wtEGFR NSCLC.

Methods: We retrospectively review 24 consecutive stage IV NSCLC patients treated with single agent Erlotinib between July, 2006 and September, 2011. None of them harbored mutation EGFR (18 patients were wtEGFR, tumor samples were non-valid in another 4, and they were not analyzed in 2). Selection criteria to receive Erlotinib includes female gender, and/or to be current or non-smoker, and/or non-squamous NSCLC histology, and/or to be younger than 60 years old.

Results and Conclusion: Patients' age ranged since 31 to 77 years old (mean 56.7 years old). Sixteen patients were women, and 8 were men. Non-smoker represented 62.5% of cases, 12.5% of patients smoked less than 5 cigarettes per day, and 25% were current smokers. NSCLC histology was adenocarcinoma in 70.8% of cases, squamous cell carcinoma in 17.7%, non-specified NSCLC in 8.4%, and large cell carcinoma in 4.1%. Single agent Erlotinib was administered as second line therapy in 45.8% of patients, third line in 41.7%, and fourth line in 12.5%. Estimated mean progression free survival was 5.6 months (29.16% progressed in the first 3 months of treatment, 33.33% progressed between the third and sixth month of

treatment, and 37.5% maintained treatment for more than six months). Mean overall survival was 10 months. Grade III asthenia, skin rash, and diarrhea appeared in 8.4% of patients only. CONCLUSION: Single agent Erlotinib could be a highly active and tolerable treatment for clinically selected NSCLC regardless the absence of sensitizing mutation EGFR.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.21: SALVAGE RADIOTHERAPY FOR SOLITARY FOCUS OF DISEASE PROGRESSION COULD ALLOW MAINTAINING THE EFFICACY OF ERLOTINIB IN ADVANCED NON-SMALL CELL LUNG CANCER

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Background: Incidence and lethality of non-small cell lung cancer (NSCLC) is high and conventional chemotherapy obtains limited benefits in the treatment of advanced cases. Accordingly, the introduction of gefitinib and erlotinib, two tyrosine kinase inhibitors of the epidermal growth factor receptor (TKI-EGFR), for the palliation of advanced NSCLC gave rise to great expectations. Sensitizing mutations of the EGFR select 16.6% of NSCLC who clearly benefit of TKI-EGFR. However, detection and reversal of acquired resistances to these TKI-EGFR, as well as consolidation with other therapeutic strategies, are warranted in order to prolong progression free survival and efficacy of erlotinib and gefitinib in NSCLC.

Methods: We report the experience of the NYU Cancer Institute and Langone Medical Center of New York (USA) and the University Hospital Arnau de Vilanova of Lleida (Spain) applying salvage radiation over solitary focus of disease progression in 5 patients with metastatic NSCLC to bypass the eventual acquired resistance to erlotinib or gefitinib.

Results and Conclusion: Table 1 shows characteristics of our patients and results. Progression was further avoided in all the cases with no apparent additional toxicity. TKI-EGFR administration was maintained, and progression free survival was increased 41 to 146%, suggesting prolongation of therapeutic benefit from these agents. CONCLUSION: Salvage radiation over solitary focus of disease progression is feasible and should be considered in selected NSCLC patients treated with TKI-EGFR.

Case	Race	Gender	Age Years	Mutation EGFR	Metastatic involvement	ITK-EGFR	PFS Days	Salvage Radiation	Benefit Days (%)
1	A	M	43	L858R	Lung, brain, bone, mediastinum	E	202	Bone 37.5 Gy	295 (146%)
2	C	F	78	E746-A750	Lung, brain, hilium	E	249	Lung 63 Gy	180 (78%)
3	C	F	69	ND	Lung	G	1440	Lung 50 Gy	1290 (89%)
4	C	F	73	ND	Lung	E	600	Lung 40 Gy	600 (100%)
5	C	M	61	p.6719R	Lung, bone	E	570	Bone 20 Gy	234 (41%)

Table 1. Metastatic NSCLC treated with TKI-EGFR that received salvage radiotherapy for solitary focus of progression, while TKI-EGFR was maintained. A Asian; C Caucasian; E erlotinib; F Female; G gefitinib; M Male; ND Non-determined; PFS Progression free survival.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.22: HERALD: A PHASE 1B/2 TRIAL OF HER3 INHIBITOR U3-1287 IN COMBINATION WITH ERLOTINIB IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)

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Background: Second- or third-line treatment with an EGFR tyrosine kinase inhibitor (TKI) is widely accepted as a standard option in advanced NSCLC; disease stabilization is expected in up to 45% of patients. However, all cases eventually develop therapeutic resistance. HER3 is a key dimerization partner of EGFR family members, and signaling through its dimers may play a role in EGFR TKI resistance. Thus, simultaneous inhibition of HER3/EGFR may be beneficial. U3-1287 is a fully human anti-HER3 monoclonal antibody with synergistic anticancer activity in combination with anti-EGFR inhibitors in preclinical models. The phase 1b/2 HERALD trial is investigating U3-1287 in combination with erlotinib in advanced NSCLC patients after failure of ≥1 prior chemotherapy. Interim results are reported as of February 16, 2012.

Methods: Eligible patients had EGFR treatment-naïve stage IIIB/IV NSCLC that progressed on ≥1 prior chemotherapy. In the open-label, dose de-escalating, phase 1b portion, patients received erlotinib 150 mg/day orally and U3-1287 18 mg/kg intravenously Q3W; as no DLTs were reported, dose was not de-escalated, and this regimen is the recommended phase 2 dose. The phase 2 portion of the study is a randomized, placebo-controlled, double-blind study assessing the efficacy and safety of U3-1287 combined with erlotinib relative to erlotinib alone. It is a 3-arm study of 150 mg/day erlotinib with U3-1287 low-dose (18 mg/kg loading dose followed by 9 mg/kg Q3W; based on PK simulation, this dose will produce trough blood levels ≥10-fold greater than those associated with maximal efficacy in mice), high-dose (18 mg/kg Q3W; to test if higher concentrations lead to more homogenous large tumor penetration), or placebo. Study end points include adverse event (AE) incidence, pharmacokinetics, human antihuman antibody (HAHA) formation, tumor response, and progression-free survival.

Results and Conclusion: The phase 1b portion of the trial enrolled seven patients (four male; median age [range], 68 years [48–78]). AEs grade ≥3 occurred in two patients; none were related to U3-1287. Three patients had four serious AEs: grade 3 pain (unrelated to study treatment), grade 3 dehydration (erlotinib-related), and grade 1 decreased appetite (erlotinib- and U3-1287-related) and grade 1 pyrexia (unrelated) in one patient. The only U3-1287–related AE reported in ≥2 patients was decreased appetite (2 patients). All patients tested negative for HAHA formation. No response was recorded; stable disease was noted in four patients (83, 87, 90, and 117 days). In the phase 2 portion, 109 patients (62 male; median age [range], 64 years [35–83]) have received study treatment as of February 16. Seventy-eight patients (72%) experienced an AE

during treatment; of these, 27 (35%) experienced AEs with a worst grade ≥3. Seven deaths were reported, all unrelated to study treatment. Most frequent AEs reported were diarrhea (42.2%), rash (40.4%), nausea (20.2%), decreased appetite (13.8%), vomiting (12.8%), and fatigue (10.1%). Twenty-eight patients (26%) experienced a serious AE; the most common were dyspnea (3 patients), diarrhea (3), respiratory failure (2), abdominal pain (2), vomiting (2), pain (2), and general physical health deterioration (2). Treatment remains blinded. Results to date indicate that toxicity associated with U3-1287 in combination with erlotinib is manageable.

Disclosure: CC and RB: stockholders and full-time employees of Daiichi Sankyo Pharmaceutical Development. RB: stockholder in Johnson & Johnson corporation. MD: served in advisor board committees, received speaker fees from Hoffmann LaRoche. JVP, TS, CS: none.

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Advanced NSCLC

P1.23: PHASE 1 SAFETY AND PHARMACOKINETIC (PK) STUDY OF VELIPARIB IN COMBINATION WITH WHOLE BRAIN RADIATION THERAPY (WBRT) IN PATIENTS (PTS) WITH BRAIN METASTASES

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Background: Veliparib is an oral PARP-1 and -2 inhibitor that enhances the antitumor activity of DNA damaging agents including radiation therapy in vivo (e.g colon carcinoma and NSCLC). In pre-clinical models, veliparib crosses the blood-brain barrier. This ongoing phase 1 dose-escalation study evaluates the safety, PK, and provides preliminary antitumor activity of veliparib in combination with WBRT in pts with brain metastases (NCT00649207).

Methods: Pts with brain metastases (including leptomeningeal) from primary non-CNS metastatic solid tumors (except germ cell cancer), adequate organ function, and RPA Class 2 and Karnovsky performance status ≥70 were treated with WBRT (37.5 Gy in 15 fractions or 30 Gy in 10 fractions) QD and veliparib BID with daily WBRT, in escalating doses of 10, 20, 30, 50, 100, 150, and 200 mg; the final WBRT fraction was followed by 1 extra day of veliparib. Safety, PK, and tumor response by RECIST were assessed.

Results and Conclusion: To date, 61 pts (M/F, 22/39; median age 57 y) have been treated. Baseline KPS was 70, 80, 90, and 100 in 8.2, 31.1, 39.3 and 21.3% pts, respectively; primary tumor types were breast (n=20), NSCLC (n=22), melanoma (n=9), colorectal (n=2), and others (n=8); 73.8% pts had multiple lesions, and 18.0% had prior brain stereotactic radiosurgery. Grade 3/4 treatment-emergent adverse events (TEAEs; ≥5%) were fatigue (6.6%) and other TEAEs (≥20%) were fatigue (57.4%), headache (42.6%), nausea (39.3%), alopecia (26.2%), vomiting (23%), radiation skin injury (21.3%), and decreased appetite (22%). PK of veliparib was approximately dose-proportional, with oral clearance of 21.6 ± 14.2 L/h (mean ± SD, n = 45), minimal drug accumulation at day 15, and no significant effect of food on bioavailability. Best tumor response was calculated using 41 pts who had measureable lesion(s) at baseline, had at least one post baseline tumor assessment, and had no leptomeningeal involvement (including intra and extra-cranial metastases). Best tumor response rate (CR or PR) and median survival time were 42.9% and 10 months (m) for NSCLC, and 52.9% and 12.5 m for breast cancer (excluding pts with leptomeningeal involvement [including intra and extra-cranial metastases]). Addition of veliparib up to 200 mg BID was well tolerated with concurrent standard WBRT. Dose escalation is ongoing. The PK of veliparib was dose proportional with no food effect. These encouraging safety and preliminary efficacy data suggest that veliparib requires further evaluation as a radiosensitizer with WBRT, in patients with NSCLC and brain metastases in a randomized trial.

Disclosure: Disclosures for M. Mehta: Employment: Pharmacyclics Honoraria: Merck, Grace, MDM,Prime Onc, Strategic, Edge, WebMD Consultant: Bayers, Elekta, Novartis, Quark, Tomotherapy, Vertex, BMS,USOnc Stock: Pharmacyclics, Colby, Accuray, Procertus, Stemina Disclo

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Advanced NSCLC

P1.24: LARGE CELL CARCINOMA [LCC] (CLASSICAL, LCC WITH NEUROENDOCRINE MORPHOLOGY [LCCNM], AND LARGE CELL NEUROENDOCRINE CARCINOMA [LCNEC]) AND SMALL CELL CARCINOMA [SCC] OF THE LUNG: SHOULD THEY BE TREATED EQUALLY IN ADVANCED STAGES?

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Background: Lung cancers have many subtypes, such as LCC, which may be divided in classical, LCCNM, and LCNEC. On the other hand, neuroendocrine lung tumors may be classified as typical and atypical carcinoids, LCNEC and SCC. They are different pathological lung cancer subtypes, but with some similarities. LCNEC is rare and also has a poor prognosis. The best diagnostic approach and systemic treatment in advanced stages for each of them remain to be defined.

Methods: In order to review and discuss different treatment approaches for LCC of the lung, we present a series of patients, describing clinical and treatment data, in addition to response rates and survival outcomes. Patients were followed and treated in: Centro Internacional de Pesquisa e Ensino (CIPE)/Hospital A. C. Camargo, Clínica D. Erlich, in Sao Paulo-SP, or Instituto de Oncologia de Jundiaí-SP; Brazil.

Results and Conclusion: The series of lung LCC is presented below, with clinical, treatment and outcome aspects.
Case #1 – Male, 63y, LCNEC, pT3N1M0. Surgery (S),

Chemotherapy (CT): etoposide+cisplatin x1 - bradicardia grade (G) 3, irinotecan+carboplatin x 3; Radiotherapy (RT): adjuvant. Survival 7+ months (m). Case #2 – Male, 55y, LCCNM, pT2aN0M1 (peri-hepatic lymph nodes). S, CT: pemetrexed+cisplatin x 6, pemetrexed maintenance x 15 – asthenia G2; susteined complete response (CR). Survival 18+ m. Case #3 – Male, 71y, LCNEC, cT4N2M1 (bone). CT: etoposide+cisplatin x 2: PD; pemetrexed+carboplatin+bev acizumab x 6 – myelotoxicity G4; partial response (PR), not sustained. Survival 9m. In conclusion, lung LCCs appear to be different, either in pathological or in clinical aspects. The best treatment approaches remain to be better studied and definied. Nonetheless, we believe that LCCNM should be treat as non-small cell lung cancer, and LCNEC (highly responsive to platinum-based CT) should be treated as SCC of the lung.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.25: INFLUENCE OF PALLIATIVE RADIOTHERAPY ON PROGNOSIS AND QUALITY OF LIFE FOR PATIENTS WITH STAGE IV NON-SMALL CELL LUNG CANCER

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Background: A retrospective analysis of palliative radiotherapy for stage IV non-small cell lung cancer prognosis and quality of life impact.

Methods: Clinical data of 318 advanced patients of non-small cell lung cancer who received palliative radiation was collected from January,2000 to December, 2009,and the patients cannot endure or receive chemotherapy for all kinds of reasons.Survival analysis was performed by the K-M method, comparison among groups was performed by log-rank test and multivariate analysis was carried out with the Cox proportional hazard model.

Results and Conclusion: 318 patients 1, 2-year survival rates, median survival time were 25.2%, 7.4%, 7 months. The response rate defined as palliation of stage IV NSCLC symptoms after palliative radiotherapy was 72.4% for cough, 80.6% for thoracic pain, 88.1% for haemoptysis, 60.8% for dyspnoea, 19.2% for hoarseness, Metastatic bone pain and brain metastases have different signs and symptoms ease or even disappear: 76.8% for bone metastases, 75.7% for brain metastases. Univariate analysis showed: KPS , histological type, brain metastases, multi-organ metastasis, primary tumor radiation dose correlated with prognosis, multivariate analysis showed: KPS , multiple organ metastasis were independently associated with OS. Conclusions Palliative radiotherapy in the treatment of stage IV NSCLC played relieve symptoms, improve quality of life and prolong survival role. KPS , multiple organ metastasis were independent prognostic factors.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.26: RACOTUMOMAB ADMINISTRATION IN PATIENTS WITH ADVANCED NON-SMALL-CELL LUNG CANCER (NSCLC) IN PROGRESSION AFTER FIRST LINE THERAPY

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Background: Racotumomab is therapeutic vaccine that induces an immune response against NeuGc-containing gangliosides, sulfatides and other antigens expressed in several human tumors but not in normal tissues. Previous trials have demonstrated low toxicity, high immunogenicity and survival benefit in advanced NSCLC when Racotumomab was administered in patients with objective response (partial or complete response or stable disease) to first line therapy.

Methods: An open, non- randomized, population- based study was performed in patients with recurrent and advanced stages (IIIB/ IV) of NSCLC after completion of first-line onco-specific treatment (surgery, chemotherapy and/or radiotherapy) as per the NCCN Oncology Therapeutic Guidelines who were vaccinated with Racotumomab. At inclusion patients presented progressive disease (PD) according to Recist. 89 patients were in stage IIIB, 71 were in stage IV (88.8%) and 20 patients (11.1%) presented with recurrent disease. For most patients prior chemotherapy was 4 to 6 cycles of cisplatin/vinblastin. Vaccination consisted of an induction period of 5 intradermic doses of 1mg of Racotumomab/ aluminum hydroxide (1 every 14 days), followed by a maintenance period of 1 dose every 28 days. Vaccination continued until patient refusal or worsening of ECOG status.

Results and Conclusion: 180 patients were included in an intent to treat (ITT) survival analysis (Kaplan Meier estimate), after at least 10 months of follow-up. Median survival was 8.06 months. Long-term OS rate (%) at 24 months was: 21%. Per protocol population (PPP) survival analysis included only the 124 patients (68.8%) who received ≥ 5 doses of vaccine. Median survival was 12 months. Long –term OS rate (%) at 24 months was 30%. Survival data of the 180 Racotumomab treated patients was compared with a control group of 85 consecutive patients treated at the same institution by the same investigators, who did not receive second line therapy after disease progression. Median survival in the control group was 6.26 months (log rank test p= 0.011). Long term OS rate (%) at 24 months was only 7%. The most common adverse events were mild and moderate local reactions at the injection site (pain, erythema, induration) and flu-like symptoms, none unexpected.

Our population based study with Racotumomab shows similar results to those previously reported in NSCLC clinical trials. Treatment was safe and showed a survival advantage in advanced NSCLC patients when Racotumomab was used as a second line therapy after disease progression.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.27: THE EFFECT OF WARFARIN ON SURVIVAL IN PATIENTS WITH LUNG CANCER

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Background: To assess the effects on survival of the low dose warfarin in patients with lung cancer.

Methods: In this single center, randomized study, patients with lung cancer were randomly assigned to warfarin or to control (no warfarin) in addition to their standard anticancer treatment. Warfarin was given orally starting on day 1 of chemotherapy at a dose of 5 mg/d to achieve a target interrnational normalized ratio (INR) of 1.5-2.5 for six months.

Results and Conclusion: A total of 44 patients were allocated to warfarin group, and 47 were allocated to the control group. The overall median survival was statistically higher on the warfarin group (358 days, 95% CI 226-489 days), as compared with the control group (236 days, 95% CI 187-284 days) (p=0.03). There was no statistically significant difference in the response rates (complete+partial) between two groups (56.8 percent in warfarin group vs. 36.1 percent in the control group, p=0.09). No significant difference between the warfarin group and the control group was detected in the rate of bleeding (15.9 percent and 6.3 percent, respectively, p=0.18). Warfarin may be effective in improving survival without increasing the risk of bleeding in patients with lung cancer.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.28: QUALITY OF LIFE IN ADVANCED NSCLC IN OLDER PEOPLE TREATED WITH CHEMOTHERAPY

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Background: To study the most common toxicities resulting from treatment in elderly patients with cancer. To compare the level and types of toxicities. Evaluate its correlation with comorbidities present. To analyze survival and quality of life.

Methods: 148 lung cancer pts were included. Pts selection was conducted using General Geriatric Assessment. PS (Performance status), ADL (Activity of Daily Living) and IADL (Instrumental of Daily Living) was studied before and after treatment. Pts underwent type and number of chemotherapy cycles. Pts were divided in older and younger than 70. All pts had adequate cardiac, hepatic, renal and bone marrow functions. Comorbidities studied were: hypertension, diabetes, COLD, arrhythmia, coronary disease and digestive disease. Toxicities were studied following the WHO criteria and correlated according to age, ADL, IADL, PS, WL, comorbidities, and the use of more than 3 drugs (Polypharmacy), in addition to the treatment. QoL was assessed through the evolution of ADL, IADL and PS. Statistical Methods: Pearson´s Chi-Square, Kaplan Meier´s Survival tests.

Results and Conclusion: The most frequent toxicity level was bone marrow function. 47.3% received second-line therapy and only 61.4% received > 4 cycles. There were No relationship was found between toxicities and age, irrespective of type and level. Toxicity level was found to be higher in the patients who used more than 3 other medications p=0.006. No Statistically significant association was found between comorbidities and toxicity levels. There was improvement in Qol through ADL, PS, and IADL evolution after treatment p= 0.001. Conclusions: The toxicities is not more severe in older than 70 yrs. Age is not a contraindication to lung cancer treatment. Pts selection is very important to optimize the outcome. Pts in good general condition and with controlled comorbidities may receive Chemotherapy, if this treatment modality results in improvement of their QoL. IADL and nutritional status are an important issue to consider.

Disclosure: No significant relationships.

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Advanced NSCLC

P1.30: RADIOLOGICAL FINDING OF PULMONARY EMBOLISMS (PE) BY MULTIDETECTOR COMPUTED TOMOGRAPHY (MDCT): RETROSPECTIVE MONOCENTRIC STUDY IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER

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Background: Thrombotic risk in cancer patients is increased of 2-7 fold and cancer-associated venous thromboembolism (VTE) is one of the leading cause of death for these patients. Incidence of VTE is equal to 1 event per 110-120 patients with cancer and most of pulmonary embolisms (PE) occur during the first year after diagnosis. Cancer patients with VTE have a 2.2-fold increase in mortality and lung cancer, considered worldwide the leading cause of cancer-related death, is the second tumor type with the highest incidence of VTE. Sistemic treatments represent the therapy of choice for advanced non-small cell lung cancer (NSCLC) patients, which account nearly 85% of all lung cancer cases. Considering that chemotherapy is associated with a 6 times increased risk of VTE and that biological agents, especially antiangiogenetic agents, determine an additional risk, the aim of the present study is to evaluate, after radiological retrospective imaging evaluation, the real incidence of PE in selected cohorts of patients with advanced NSCLC and the impact of PE on survival.

Methods: This retrospective monocentric study enrolled 141 patients with advanced NSCLC, diagnosed between June 2007 and June 2008, and between January 2010 and December 2010 (Table 1). Most of patients of both groups received at least a platinum-based chemotherapy; patients treated during their clinical history with biological agents were respectively 74.1% and 43.3%, with antiangiogenetic agents 39.5% and 21.7%, while 46.9% and 20.0% of patients was involved in double-blind clinical trials with biological drugs compared to placebo. Two different radiologists retrospectively reviewed 460 thoracic contrast-enhanced MDCT studies, looking for PE and reaching a

consensus for each one.

Table 1

	Group	
	2007 – 2008 N (%)	2010 N (%)
Patients	81	60
Median age *(range)*	63,0 *(35-78)*	62,9 *(36-78)*
Sex		
Men	62 (76,5%)	47 (78,3%)
Women	19 (23,5%)	13 (21,7%)
ECOG PS		
0	62 (76,5%)	53 (88,3%)
1	19 (23,5%)	7 (11,7%)
Stage		
IIIB	20 (24,7%)	13 (21,7%)
IV	61 (75,3%)	47 (78,3%)
Histology		
Adenocarcinoma	37 (45,7%)	38 (63,3%)
Squamous Carcinoma	20 (24,7%)	8 (13,3%)
Large Cell Carcinoma	3 (3,7%)	1 (1,7%)
Poorly Differentiated Carcinoma	5 (6,2%)	7 (11,7%)
NSCLC	16 (19,7%)	6 (10,0%)
Comorbidities predisposing to VTE	34 (42,0%)	42 (70%)
CVA	7 (8,6%)	5 (8,3%)
Antiaggregant/anticoagulant therapy	10 (12,3%)	11 (18,3%)

ECOG PS: Eastern Cooperative Oncology Group Performance Status; VTE: venous thromboembolism; CVA: central venous access

Results and Conclusion: Prevalence of PE corresponded to 13.6% in the 2007-2008 cohort and to 15.0% in the other one. Survival analisis, conducted according to Kaplan Meier method, didn't show any statistically significant differences in terms of OS and TTP in the 2007-2008 cohort. In the 2010 cohort, Kaplan Meier curves showed a statistically significant difference in terms of TTP in favor of patients who never developed PE, p-value=0.003. Similar results were observed at the subgroup analysis, performed considering as stratification factors the use of biological agents, p-value=0.007, and of antiangiogenic drugs, p-value=0.010. The higher incidence of PE in the 2010 cohort, despite a lower exposure to biological and antiangiogenic agents, could result from a greater thrombogenic action of these drugs, but also a higher prevalence of comorbidities predisposing to VTE. In this cohort, descriptive analysis was confirmed by survival data. This underlines the necessity of further evaluations to clarify the role of these drugs as predisposing factors for PE.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.32: ELECTROCARDIOGRAM QTC PROLONGATION IN PATIENTS WITH LUNG CANCER UNDER CHEMOTHERAPY TREATMENT

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Background: Electrocardiogram QTc interval prolongation associated with cancer chemotherapy is a frequent event. The objective of this study was explored the frequency of QTc prolongation episodes previous and post-chemotherapy cycle in patients with lung cancer, comparing these findings with those obtained from patients treated from other malignant neoplasms.

Methods: We included patients consecutively admitted to chemotherapy cycles at one oncology specialized service at a general hospital. An electrocardiogram was performed at baseline, and pre- and after- each chemotherapy infusion. QT interval between Q wave onset and end of the T wave on the electrocardiogram was quantify in milliseconds and corrected (QTc) according to Bazzet formula. A delta of at least 20 msec from the baseline QTc measurement and/or a QTc duration over 440 msec in men or 460 msec in women were considered as QTc prolongations for the research purposes.

Results and Conclusion: A total of 198 cycles were studied, involving a total of 60 patients (50% female; age: 63.1+12.5 yr; 24 of them with lung cancer at stages IIIb-IV). Mean of all pre-cycle QTc lengths: 430.1+27.1msec; Mean of all post-cycles QTc length: 437.7+40.6 msec. Mean first pre-cycle QTc length: 426.7+28.2 msec; mean first post-cycle QTc length: 444.3+64.9 msec (p=0.056). Post first cycle mean QTc length was 15.7 msec longer in patients with pulmonary cancer when compared with patients with other neoplasms (being slightly longer for non lung cancer patients at pre-cycle). Patients with non-pulmonary cancer entered into a 29.8% of their cycles with a QTc prolongation (generally considered as slight); for patients with pulmonary cancer, this proportion reached 37% of the cycles. Postcycle QTc prolongation was registered in 37.5% of cycles in non-lung cancer patients and in 42.6% of cycles with pulmonary cancer. Almost 26% of patients with lung cancer presented prolonged pre and post cycle QTc lengths. Precycle prolongations were strong predictors of postcycle increments in QTc lengths. In conclusion, QTc prolongation is a frequent event in lung cancer (both pre and post-chemotherapy administration)

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.33: ADVANCED SARCOMATOID CARCINOMA OF THE LUNG: A CASE REPORT AND LITERATURE REVIEW

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Background: Sarcomatoid carcinoma (SC) of the lung is a rare and aggressive malignancy, composed of both epithelial and mesenchimal-derived cells. It accounts for about 0.1% to 0.4% of all lung carcinomas and five different subtypes are described (WHO 2004). As to specific systemic treatment, there is little information available in the literature. Here we present the results of a literature review and also describe the outcomes of a patient with metastatic SC of the lung treated in our Hospital.

Methods: A literature search was conducted using the key words "sarcomatoid carcinoma" and "lung" in PUBMED database, in English, Spanish and Portuguese, limiting to studies in humans and adults. A total of 22 articles were retrieved and 16 were the focus of this review. Those six articles not analyzed were excluded either due to the absence of clinical data or because they contained only diagnostic pathological

features.

Results and Conclusion: Case report: A 67-year-old male with a history of heavy smoking and alcohol intake sought medical help after 2 months of fever, dry cough and weight loss. A 6.3-cm cavitated mass in the left superior lobe with extensive contact with the descending aorta was seen in CT scan, with metastasis in the left adrenal gland. SC was diagnosed, staged as T4 N2 M1. Patient was treated with pemetrexed-cisplatin, and died of progressive disease after two cycles. Results: 352 cases were reviewed, and both adeno- and squamous cell were described as epithelial components. Most patients (pts) were current or ex-smokers (212 out of 240 pts with available data, 88%), with predominance of males (280 pts, 80%) and median age 61.5 y. Overall, most pts presented with locally advanced or metastatic disease at diagnosis, with large and cavitated tumors. In rare cases of pts submitted to surgery with curative intent, adjuvant cisplatin-based chemotherapy did not seem to have impact on overall survival. No patient presented major tumor responses with classic platinum-containing regimens. Conclusions: SC is a rare entity, frequently associated with poor response to platinum-containing doublets. There is a clear need of a better understanding of this disease. Global, multicenter clinical trials should be designed in order to develop specific strategies to overcome difficulties in the management of this challenging rare entity.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.34: RETROSPECTIVE ANALYSIS OF NON-SMALL CELL LUNG CANCER PATIENTS WITH BRAIN METASTASIS TREATED IN A BRAZILIAN CENTER

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Background: The presence of brain metastasis (BM) is an important prognostic factor in non-small cell lung cancer (NSCLC) patients, frequently limiting therapeutic options. With emerging new therapies for this disease, a better understanding of this high-risk population becomes increasingly important. This study aimed to evaluate clinical characteristics and outcomes of NSCLC patients harboring BM, treated in a private oncology center in Brazil (Clínicas Oncológicas Integradas - COI).

Methods: A retrospective review of NSCLC patients medical records was performed between 1999 and 2010, and all patients with a confirmed diagnosis of BM were selected for analysis.

Results and Conclusion: Results: A total of 446 patients with NSCLC were included, and 73 patients had BM (16,4%) at diagnosis or follow-up. Most of them had non-squamous histology (68%) and were male (65.8%). Approximately 54.8% of patients were smokers or former smokers. Median age of the entire population was 65 years. (CI95% 27-92). Most patients who developed BM were younger than 65 years-old (69.9%) Only 9 patients (12.3%) were submitted to BM ressection, and 74% received palliative brain radiotherapy. Median overall survival was 13.8 months (m) (CI95% 13.6-22.7) for patients with BM, compared to 19.8m (CI95% 15.5-24.2) for non BM patients (p<0,0001). Median survival after the diagnosis of BM was only 7.3 m (CI 95% 3.0-11.6). Age < 65 y (OR=2.2; p<0,0001) and non-squanous histology (OR=1.25; p=0,047) were independent risk factors for BM development.

Conclusion: Our results are similar to previous published data, corroborating that this specific population is younger and carries a dismal prognosis.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.35: PANEL OF SERUM BIOMARKERS MAY PREDICT BENEFIT FROM BEVACIZUMAB (BEV) IN ADVANCED NSCLC PATIENTS

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Background: BEV has produced modest benefits in patients (PTS) with advanced NSCLC. Identification of positive predictors for BEV would have important implications for individual PTS and health care costs.

Methods: We performed a prospective exploratory analysis to identify serum biomarkers as predictors of improved outcomes with BEV. Pre treatment sera were collected from 93 pts prior to initiation of first line treatment for advanced NSCLC. Treatment drugs, including BEV, were prescribed according to treating physician's discretion. Seventy two serum biomarkers, relevant to angiogenesis and tumor progression, were recorded using Luminex immunobead platform. Serum levels were correlated with progression free survival (PFS) and overall survival (OS) and compared between patient treated with or without BEV containing regimens, BEV + and BEV- groups respectively. Log-rank and interaction p value tests were used to identify markers associated with longer PFS and OS in the BEV+ group but not in BEV- group.

Results and Conclusion: Characteristics for each group were: BEV+ (n=43, median age 65 y/o, 72% smokers, 60% females, 100% non-squamous). BEV- (n=50, median age 64 y/o, 84% smokers, 50% female, 70 % non-squamous). The BEV+ group had longer PFS (5.8 vs. 3.0 mos, log-rank p= 0.039) and OS (13.1 vs. 8.5 mos, log-rank p =0.11) when compared to the BEV- group. High serum levels of these markers resulted in a differential decreased hazard in the BEV+ group: PDGF-AB/BB (interaction p <0.01 for PFS, p=0.04 for OS), FGF (interaction p=0.15 for PFS, p<0.04 for OS), tenascin-c (interaction p=0.18 for PFS, p=0.04 for OS), RANTES (interaction p=0.04 for PFS, p=0.6 for OS), epiregulin (interaction p=0.31 for PFS, p=0.04 for OS) and anti-HGF (interaction p=0.18 for PFS, p=0.03 for OS). In the BEV+ group higher levels of PDGF-AB/BB were associated with a better outcome (log-rank p=0.05 and p=0.01 for PFS and OS respectively). We did not find significant correlations between serum levels of VEGF, anti-VEGF or VEGFR and benefit from BEV. This exploratory analysis suggests that these biomarkers may have predictive value for BEV in NSCLC PTS and

should be considered for further studies.

Disclosure: Dr. Philip Bonomi - Advisory role/Research funding - Genentech Dr. Mary Jo Fidler - Honoraria - Lilly and Genentech and expert testimony - Genentech

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.36: THE INNOVATIVE METHOD USING CIRCULATING TUMOR CELLS FOR PREDICTION OF THE EFFECT OF THE INDUCTION THERAPY TO LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER

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Background: While there is not an established standard therapy for locally advanced non-small cell lung cancer (NSCLC). Favorable prognosis has been reported in NSCLC patients who underwent induction chemoradiotherapy followed by surgery and subsequently achieved pathological complete response (CR). However, pathological therapeutic response is not sufficiently predictable before surgery at present, even with diagnostic imaging modalities, such as 18F-FDG PET/CT or re-mediastinoscopy. We confirmed that circulating tumor cells (CTCs) are more frequently detected in pulmonary venous blood than in peripheral blood in patients with NSCLC. Since CR refers to a condition in which no pathologically viable tumor cells remain, we assumed that CTCs are undetectable in patients who achieved CR in pulmonary venous blood. In order to assess whether CTCs are predictive of pathological response after induction chemoradiotherapy. We measured the number of CTCs in peripheral blood (p-CTCs) and in pulmonary venous blood (v-CTCs) and examined the relationship with histological response.

Methods: All patients were treated our institution from December 2010 to January 2012. The 9 patients who underwent induction chemoradiotherapy followed by surgery (I group), and the 6 patients who underwent surgery alone (S group). At the surgery, peripheral blood and pulmonary venous blood from the involved lobe were collected (7.5 mL each) for CTCs counting. CTCs were isolated using the CellSearch System (Veridex LLC). The result of two or more CTCs was judged positive. Correlation between the results of CTC count and pathological response was analyzed.

Results and Conclusion: All the patients of I group were clinical stage 3A. Pathological therapeutic response was CR in 4 patients and partial response (PR) in 5 patients. Two patients were each at clinical 1A and 1B and 1 patient was each at 2A and 2B in S group. All patients in I and S groups were negative for p-CTCs. Five patients in I group were positive for v-CTCs (mean: 57.8 cells). All these 5 patients showed PR. The remaining 4 patients who achieved CR were negative for v-CTCs. There was a significant difference in the numbers of v-CTCs between cases with PR and those with CR (p=0.012, Mann-Whitney's U test). All 6 patients in S group were positive for v-CTCs (mean: 207.5 cells), and the difference from I group was significant (p=0.038). CONCLUSION: All cases with CR were negative for v-CTCs (not more than 1 cell), and a significant difference was observed, though the sample size was limited. In addition, all patients who did not receive induction therapy were positive for v-CTCs regardless of disease stage. Status of v-CTCs seems to accurately reflect CR, and pathological response may be predictable through measurement of v-CTCs. While sampling of pulmonary venous blood is not easy at present, a new means of sampling other than surgery, should it become available, will enable preoperative check of CR after induction therapy. It may be able to verify for the efficacy of surgery after induction chemoradiotherapy in the treatment of locally advanced NSCLC.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.39: TARGET THERAPIES AS A WAY TO ACHIEVE COMPLETE RESPONSE IN SQUAMOUS CELL LUNG CANCER

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Background: The development of new strategies for the treatment of squamous cell lung cancer did not occur in the same speed when compared to other histologies. The use of platinum-containing doublets resulted in better outcomes. One strategy to improve response rate is the addition of targeted drugs to the cytotoxic chemoterapy. The FLEX chemoterapy regimen was associated with improved survival in NSCLC, including squamous cell lung cancer.

Methods: To describe the case of a patient who benefited of the addition of Cetuximab to chemotherapy, obtaining a pathological complete response that was kept.

Results and Conclusion: A 69-years old female patient was diagnosed with a tongue squamous cell carcinoma, cT2N2M0, in 2001 and treated with chemotherapy and radiotherapy. In 2007, a squamous cell NSCLC was diagnosed in the right upper lung lobe and staged as cT2N2M0. She was treated with neoadjuvant chemotherapy based on Cisplatin and Gencitabine followed by surgery, with complete pathological response (ypT0N0M0). Four years later, she developed a mediastinal linfonodal relapse in multiple echelon, diagnosed by positron emission tomography (PET-CT). A percutaneus CT-guided biopsy was displaying a squamous cell carcinoma. Radiotherapy was contraindicated due to the total cumulative dose in the low cervical region. She started treatment with Carboplatin AUC x 5 D1, Vinorelbine 25mg/m² D1 and D8, Cetuximab 400mg/m², (starting dose) and then 250mg/m² weekly, in 21-days cycles. She developed neutropenia and thrombocytopenia resulting in delays after the first cycle. It was opted to use filgrastim from D9 to D13 after the second cycle and to reduce Vinorelbine dose to 20mg/m² from fourth cycle on. After the third cycle, a PETCT showed no evidence of disease. The patient completed a total of six cycles and started the maintenance phase with Cetuximab 250mg/m² weekly. A PETCT was realized two months after the sixth cycle and the complete metabolic response was maintained. Future researches are necessary on squamous cell NSCLC to enable an treatment individualized fashion , based on the use of biomarkers that can allow the use of targeted

therapy, as also to permit an personalized medicine with predictive and prognostic factors and eventual improvement in response rate and survival.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.40: RESTROSPECTIVE COMPARATIVE STUDY OF CARBOPLATIN/PEMETREXED/BEVACIZUMAB AND PEMETREXED/CARBOPLATIN AS FIRST LINE TREATMENT IN PATIENTS WITH ADVANCED NSCLC

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Background: Studies E4599, AVAIL and SAIL showed that adding bevacizumab to the doublet platinum-based chemotherapy as first-line NSCLC patients with adenocarcinoma lineage increased the response rate, progression-free survival and overall survival. The Pemetrexed is an antimetabolite whose use in first line NSCLC was confirmed from the study published by Giorgio Scagliotti in 2008 and which demonstrated an increase in overall survival of patients with pulmonary adenocarcinoma treated with Pemetrexed / cisplatin vs gemcitabine / cisplatin as first-line chemotherapy (12.6 vs 10.9 months). The combination of pemetrexed / carboplatin / bevacizumab based on previous findings it is possible and has been tested in phase II studies (Patel, ASCO 2008) which showed an increase in progression-free survival to 14.1 months / 7.8m months patients using the combination of pemetrexed / carboplatin / bevacizumab vs pemetrexed / carboplatin, in patients with lung adenocarcinoma. AVAPERL study shows a significant increase in progression-free survival to 10.2 months in patients receiving pemetrexed / carboplatin / bevacizumab vs Pemetrexed / carboplatin / placebo.

Methods: In the medical oncology department of the Central Military Hospital of Mexico retrospective evaluation was conducted on the records of patients who were treated for NSCLC adenocarcinomas between 2008 and 2011, for those who use the combination of Pemetrexed / Carboplatin / Bevacizumab and Pemetrexed/carboplatin. The primary objectives of this study are an analysis of descriptive statistics on the following variables: progression-free interval, response rate , number of cycles received, toxicity, race, diagnosis and smoking history.

Results and Conclusion: Data were obtained from a review of thirty patients with lung adenocarcinoma stage IIIb and IV treated between the years 2008-2011 with the schemes of Pemetrexed / Carboplatin / Bevacizumab and Pemetrexed / carboplatin with the following results:

In this case series shows that adding bevacizumab to first-line treatment with chemotherapy in NSCLC based on Pemetrexed / carboplatin / bevacizumab in non selected patients results in PFS(8.5m vs 8.9m) with respect to the first-line chemotherapy based on Pemetrexed / carboplatin. In patients with smoker history the PFS was (10.2m Vs 8.1m) in favor of the combination with Pemetrexed/carboplatin/bevacizumab respect Pemetrexed/carboplatin. In Non smokers patients the PFS was (9.5mVs 8.1m) in favor of pemetrexed/carboplatin respect Pemetrexed/carboplatin/bevacizumab. In terms of response the Smoker group had a superior response with the combination of Pemetrexed/carboplatin/bevacizumab (PR+SD=66.6% Vs 33.4%)respect Pemetrexed/carboplatin - In turn, the hematologic and non-haematological toxicity was higher in the PCB arm vs. PC. There were no grade IV adverse events in this series of cases as well as bleeding events or deaths related to treatment. CONCLUSIONS: This retrospective study presents data suggesting that the benefit of adding bevacizumab to the combination of pemetrexed / carboplatin should be individualized, taking into account factors such as smoking history of patients. Add bevacizumab showed the greatest efficacy in the subgroup of patients with lung adenocarcinoma and smoking history regarding subgroup of nonsmoking patients

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.41: LOW DOSE ERLOTINIB AS FIRST LINE TREATMENT IN METASTATIC LUNG ADENOCARCINOMA WITH EGFR MUTATION

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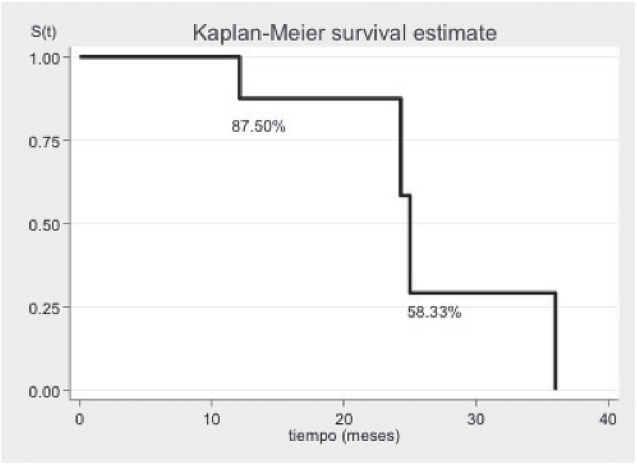
Background: Patients with metastatic adenocarcinoma with EGFR mutation must receive first line treatment with tirosine kinase inhibitors. Standard dose of erlotinib in this indication is 150 mg/day. Our clinical experience shows that tolerability of this dose is poor in chilean patients, putting compliance at risk. Evidence from a small trial performed in EGFR mutated cell lines and seven patients suggests that erlotinib doses as low as 25mg/day can have significant efficacy.

Methods: A subgroup of 12 patients with metastatic EGFR mutated adenocarcinoma were treated with erlotinib 75 mg/ day. Erlotinib tolerability and overall survival of this group of patients is described.

Results and Conclusion: Results: 10/12 subjects had exon 19 EGFR mutation and the rest exon 21 mutation. The survival curve of these patients is attached. Regarding tolerability, 3/12 patients experienced grade 1 cutaneous rash, 2/12 patients experienced grade 1 diarrhea. No other adverse events were described. Compliance with treatment was 100%.

Conclusion: Considering the limitation of being a retrospective study performed in a small number of patients, we consider erlotinib 75 mg/day may be a therapeutic alternative for patients that cannot be treated with the standard 150 mg/day dose either due to unacceptable toxicity or unavailability due to cost.



Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.42: MANAGEMENT OF PATIENTS WITH ADVANCED NON SMALL CELL LUNG CANCER PRESENTING TO A DEDICATED RAPID ACCESS LUNG CANCER CLINIC

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Background: A dedicated Rapid Access Lung Cancer clinic was initiated in 2008 in Beaumont Hospital Dublin with the purpose of expediting diagnosis and treatment in patients suspected of having lung malignancies. Suspected patients are assessed and managed within 2 weeks of referral by general practitioners, radiologists or other hospital based clinicians. Approximately, over one third of patients presenting to the clinic have a diagnosis of lung cancer, with non small cell cancer lung cancer (NSCLC) making up the highest proportion[1]. Currently, the standard treatment for advanced NSCLC (Stage IIIB/IV) is chemotherapy or palliative symptomatic care where aggressive interventions are not possible[2]. The first 500 patients presenting to the clinic were assessed with the aim of assessing the management of patients with advanced NSCLC.

Methods: Data of the first 500 patients presenting to the Rapid Access Lung Cancer Clinic was collected retrospectively. A database was established based on collation of information from patient records, electronic storage systems, intranetwork hospital databases, pathological reports and from clinical notes of the Lung Cancer Multi Disciplinary Team. The parameters analysed include patient demographics, disease profile and treatment modalities. The data was analyzed using standard descriptive statistics with SPSS.

Results and Conclusion: Of the five hundred patients that presented to the Rapid Access Lung Cancer Clinic, 201 (40.2%) had malignant disease and were referred for discussion at the Lung Cancer Multidisciplinary Meeting. Of those with malignant disease, 172 (85.6%) patients were diagnosed with primary lung malignancies. 145 (84.3%) patients were diagnosed with NSCLC with the remaining 27 (15.7%) being diagnosed with small cell lung cancer (SCLC). Out of those with NSCLC, 60 patients were diagnosed with advanced disease (34.9%). Of patients diagnosed with advanced NSCLC, about half (46.7%) of the patients received active treatment (chemotherapy). Of the patients managed at our centre, 18 (85.7%) had one line of treatment while 3 (14.3%) had two lines. Double agent chemotherapy were administered in 75% of the cases while single agent was used in 25%. The other half (53.3%) of the cohort did not received chemotherapy due to various reasons mainly relating to low performance status (71.9%), patient's preference (15.6%) and more rapid deterioration (12.5%). Most of the patients with advanced NSCLC (80%) evaluated had inpatients assessment by the palliative care service. This study suggests that approximately half of the patients diagnosed with advanced NSCLC received active therapy with chemotherapy. These findings pose significant implications for the management of advanced NSCLC and warrant further consideration of the expansion of palliative care services.

[1]Dunican E, Uzbeck M, Clince J, Toner S, Royston D, Logan MP, et al. 'Outcomes of patients presenting to a dedicated rapid access lung cancer clinic.', Ir Med J. 2011 Oct; 104(9), pp. 265-8. [2]Armstrong J, Breathnach O, Carney D, Eakin R, Grogan L, McDonnell T, et al. 'Guidelines For Clinical Management of Lung Cancer.'. Ireland: Ir Med J; 2004 Feb [cited 2012 Mar 24]. Available from http://www.imj.ie/Archive/Lung_Cancer_Guidelines.pdf

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Advanced NSCLC

P1.43: DELAY IN CHEMOTHERAPY TREATMENT AND ITS RELATIONSHIP WITH SURVIVAL IN PATIENTS WITH ADVANCED NSCLC

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Background: The impact of delayed chemotherapy in overall survival of patients with advanced NSCLC is uncertain. Several recently published trials proposed poorer PS as the main cause of worse outcomes in those who initiate chemotherapy earlier. Our goal is to assess whether the delay affects the results, and to test the former hypothesis in our population.

Methods: We prospectively evaluated 150 patients diagnosed with advanced stage NSCLC. They were included in three different groups according to the time between diagnosis and first infusion of chemotherapy. In group 1 it spent less than a month. In the second group, one to two months and in group three, it took more than two months. Chemotherapy regimens were platinum based doublets. The OS was evaluated by Kaplan-Meier curves and compared by the log rank test

Group 1 Group 2 Group 3 p
Age 69 67 67 NS
Sex Male / Fem 75% 25% 84% 16% 79% 21% NS
Tobacco YES / NO 80% 20% 81% 19% 90% 10% NS
Hemoptysis YES / NO 25% 75% 21% 79% 30% 70% NS
PS 0-1 vs. 2 82% 18% 69% 31% 88% 12% NS

Results and Conclusion: The three groups are well balanced with respect to known prognostic factors. In the first group, patients had a median survival of 8.24 months (n = 96). Group 2, 9.40 months (n = 32) and those in group 3 lived on average

14.95 months (n = 33). The test of interaction between the three groups did not reach statistical significance (p = 0.13). When comparing group 1 vs. group 3, the difference was statistically significant (p = 0.049) In our population, those patients who began chemotherapy treatment earlier had lower overall survival. This compares to recent international published trials. However, their hypothesis is discarded, as no differences were found in the three groups regarding performance status. This deserves further research, to find a cientific-founded explanation

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Pathology

P1.44: CLINICOPATHOLOGICAL INCIDENCE, SIGNIFICANCE, AND SURVIVAL OUTCOMES OF EML4-ALK TRANSLOCATION IN LUNG CANCER

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Background: Tumor budding is morphologically defined as infiltration by small clusters of cancer cells. The term tumor budding has been applied to single cells or small clusters of up to four cells within the stromal tissue at the invasive margin of tumor. Furthermore, the study (Yamaguchi Y., et al.) identified that tumor budding as a distinct morphologic feature that has biologic and prognostic significance; moreover, the presence was identified as a significant predictor of an unfavorable outcome. Recent studies also recognize the role of microenvironment in cancer, and tumor microenvironment is evaluated in our study. It was reported (Dacic S.et al, 2010) that the intensity of tumor-infiltrating lymphocytes is a predictor of EGFR mutations. It was shown that only stromal CD4+ tumor-infiltrating lymphocytes are associated with a favorable prognosis in non-small cell lung carcinomas (Wakabayashi O., et al. 2003). This is further supported by evidence (Hiraoka et al. 2006) that only concurrent infiltration by CD8+ and CD4+ T lymphocytes in the tumor epithelial cells is a good prognostic indicator. However, the infiltration of tumor inflammatory cells in ALK positive and ALK negative lung cancer cases have never been evaluated.

Methods: Methodology We are investigating the relationship between tumor budding and clinicopathologic parameters of non-small cell carcinomas of the lung and the prognostic significance of tumor budding and lymphocyte and macrophages infiltration by reviewing the cases of ALK positive and ALK negative retrospective patients with non-small cell carcinomas of the lung. To semiquantify budding, a field in which budding intensity is maximal is selected on the slide, and the number of budding in that field is quantified. The most representative tumor areas are selected and marked on the H&E stained slide for construction of microarrays. Survival outcomes is correlated with the T cell lymphocyte status. The evaluation of CD4, CD 8, CD31, CD68 immune markers is evaluated by immunohistochemistry. The grade of the immune cell infiltrate, i.e. low vs. high is evaluated. Foci of tumor budding are evaluated and intensity of lymphocytic response at the tumor invasive front is assessed. Analysis of the data and survival outcomes is correlated with ALK mutational status.

Results and Conclusion: Knowledge of the type of tumor-infiltrating inflammatory cells may open a new avenue for possible immunotherapeutic interventions that may potentially enhance a clinically desirable response to targeted therapies and outcome for lung cancer patients. This investigation of tumor budding and the incidence of ALK mutations in non-small cell carcinomas could help to individualize treatment options for patients with lung cancer.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Pathology

P1.45: SCLEROSING HEMANGIOMA OF LUNG: A CASE REPORT

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Background: Sclerosing Hemangioma of the lung is a infrequent bening neoplasm. Usually presents as solitary pulmonary nodule well defined, homogeneus, affecting more frequently female, with complex histology may suggest a number of malignancies.

Methods: Methods: We report a case: female patient 60 years old with a family history of Colonic cancer. In an incidental chest X-ray exam, a right basal solitary nodular lesion was detected (may 2010). CT scan, bronchoscopy and bone scintigraphy were performed.

Results and Conclusion: CTscan showed an irregular nodular lesion consistent with primary lesion . No mediastinal nodes were detected. Negative total body bone scan; normal spirometry. Bronchoscopy: no evidence of endoluminal lesions til 4th order bronchiole; no evidence of tuberculosis. Bronchial brushing reported atypical cells of undefined morphology.

In November 2010, surgical intervention was decided (right lateral thoracotomy). Intraoperative biopsy showed: atypical cells consistent with Adenocarcinoma. It was decided to perform right lower lobectomy with lymph node sampling. The final histopathological diagnosis was: Sclerosing hemangioma of the lung (with routine techniques and inmunohistochemistry). After 16 monthsfollow-up period the patient condition is satisfactory. Conclusion: Being a tumor of very low frecuency, ussually presented as a basal, homogeneus solitary lesion, ussualy detected in an incidental manner, sometimes presenting respiratory symptoms (eg: hemoptysis), suggesting malignant neoplastic disease, we discuss this case as an infrecuent differential diagnosis within the field of lung tumoral disease as an Adenocarcinoma (Bronchioloalveolar carcinoma).

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Pathology

P1.46: DIAGNOSIS OF PLEURAL DISEASES USING INMUNOHISTOCHEMISTRY (IH) ON CELULAR BLOCK (CB) IN ALCOHOL-PRESERVED MALIGNANT PLEURAL EFFUSION: A DESCRIPTIVE STUDY

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Background: The celular block (CB) is a less invasive technique than surgical pleural biopsy (SPB) for the malignant pleural efussion diagnosis. The immunohistochemistry (IH) could improve the diagnostic performance of CB and reduce futile diagnostic surgery. Several studies refer that alcohol-preserved samples are not useful to perform IH.However with new antybodies and the improvement of antigen retrieval we can perform diagnostic IH markers in alcohol preserves samples with a good diagnostic result.

Methods: All patients with pleural effusion evaluated by pleurocentesis with CB and SPB between 2009 and 2011 at the Instituto Nacional del Tórax (INT) where included in this study. Histologic and cytologic diagnostic was made to every SPB and CB by two different pathologist. IH to CB and SPB samples was performed with antibodies MOC-31, Calretinin and D-240. The pathologist who performed IH for CB was blind to final SPB diagnosis.

Results and Conclusion: 38 patients were included in this study. Six mesotheliomas, 22 adenocarcinomas, 1 adenocarcinoma with reactive mesothelial hyperplasia, and 2 signet ring adenocarcinomas, 4 carcinomas NOS, 3 epithelioid malignant tumors unable to diferenciate between mesothelioma and adenocarcinoma. Mesotheliomas expressed calretinin in 5 of 6 cases (83%) of SPB and 4 of 6 (63%) of CB. MOC-31 was negative in 5 of six (83%) of the cases of PB and 6 of 6 (100%) in CB. D-240 was observed in 5 of 6 (83%) of the cases of SPB and 4 of 6 (66%) of CB. In adenocarcinomas, Calretinin was negative in all 22 cases (100%) of SPB and CB. MOC-31 was positive in 19 of 22 (86%) in SPB and 17 of 22 (77%) in CB. D-240 was negative in 100% of the cases of SPB and CB. Conclusion: The use of IH in CB samples is a possible and a promising diagnostic tool. There is acceptable agreement between IH results of CB and SPB. The IH in CB samples can improve the diagnostic performance in patiens with malignant pleural effusion.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Pathology

P1.47: EGFR ACTIVATING MUTATIONS IN NSCLC: IMPORTANCE OF ROUTINE TESTING

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Background: EGFR activating mutations in NSCLC confer better prognosis and are also predictive of response to both chemotherapy and EGFR-tyrosine kinase inhibitors. Therefore, EGFR genotyping in NSCLC patients (pts) is very helpful in treatment decision. Here we report the first 25 pts whose tumors samples were tested for EGFR activating mutations in our Institution.

Methods: It is an observational study on all consecutively tested NSCLC samples from pts treated at ICESP. Briefly, all samples were formalin-fixed and paraffin-embedded. Tumor areas were selected and macrodissected, followed by whole DNA extraction and amplification by PCR. DNA sequencing (exons 18, 19, 20 and 21) was performed by Sanger´s methodology. Frequencies were compared by Fisher´s exact test.

Results and Conclusion: Results: 25 tumor samples were tested from Aug/2011 up to now: 20 pts were caucasian, 13 were male, 14 ex-smoker, 10 never smoker; 15 pts ECOG-PS 0-1 and 5 PS 2. Regarding histologic subtype, 22 were classified as adenocarcinoma and 2 SCC. Staging: 3 IIIA, 2 IIIB and 20 IV. Activating mutations were detected in 6 pts (24%): 4 in exon 19 (del 19), 1 in exon 21 (L858R) and in 1 pt two mutations were found (T790M and L858R). The frequency of these activating mutations was not related to gender (p=0.378), race (p=0.540) or smoking habits (p=0.350). In a short follow-up of 6 mo., no deaths occurred in pts whose samples were positive for activating mutations. Conclusions: In this very selected population, the frequency of EGFR activating mutations was 24%, with no correlation with gender, race or smoking habits. This reinforces the importance of testing EGFR activating mutations in all pts with lung adenocarcinoma.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Pathology

P1.48: FREQUENCY OF ALK TRANSLOCATIONS IN 8221 NON-SMALL CELL LUNG CANCER SAMPLES

Kenneth J. Bloom, Paul Choppa
Pathology, Clarient, A Ge Healthcare Company, Aliso Viejo/UNITED STATES OF AMERICA

Background: The anaplastic lymphoma kinase (ALK) gene codes for a transmembrane receptor tyrosine kinase (RTK) in the insulin receptor superfamily. It has been identified as the fusion partner in a number of different malignancies and has long been suspected as a driver oncogene in these conditions. Although a number of studies have been conducted, the frequency of EML4-ALK in NSCLC ranges from 2-7% likely due to variability of patient selection and testing platforms. Crizotinib was recently approved for the treatment of ALK positive NSCLC patients as determined by the presence of an ALK gene rearrangement based on a companion diagnostic FISH assay. We assessed a large series of patients to determine the positivity rate of this assay in a US based population.

Methods: 8221 consecutive formalin fixed paraffin embedded non-small cell lung cancer samples sent to our laboratory for determination of ALK rearrangement status were assessed using the Abbott LSI ALK break apart rearrangement FISH probe. Fifty tumor cells were enumerated for the presence of a break apart

signal which was considered as present when at least one set of orange and green signals were 2 or more signal diameters apart or when a single orange signal without a corresponding green signal was observed in more than 15% of the tumor cells.

Results and Conclusion: Of the 8221 samples tested, 201 (2.44%) samples demonstrated an ALK rearrangement and 8020 had no detectable alteration. The Abbott LSI ALK break apart FISH probe has excellent performance characteristics with a failure/suboptimal hybridization rate of approximately 1.5% in our hands. Although the ALK break apart probe does not specifically identify EML4 as the ALK fusion partner, the frequency of ALK rearrangements was 2.44% in our series of NSCLC patients. This number agrees with the expected rates based on previous studies and helps define the positivity rate in a US based population.

Disclosure: No significant relationships.

POSTER SESSION 1 - July 26, 2012 09:00 – 17:00

Pathology

P1.49: EGFR MUTATION RATES IN 21757 CONSECUTIVE NON-SMALL CELL LUNG CANCER SAMPLES

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Background: Non-small cell lung cancer (NSCLC) is the leading cause of cancer-related deaths worldwide. Two-thirds of patients present with advanced disease and have an average survival of less than 1 year with standard chemotherapy. Studies have demonstrated that exon 19 or L858R substitution in the EGFR gene are the most powerful predictive biomarkers in patients treated with erlotinib or gefitinib. This has led to the recommendation that EGFR mutational status be evaluated prior to initiating chemotherapy. We sought to determine the frequency and distribution of EGFR mutations in our laboratory over the past several years.

Methods: From June 2009 to October 2011 we have evaluated the mutational status of EGFR in 18246 formalin fixed paraffin embedded non-small cell lung cancer samples using an allele specific PCR procedure that is capable of detecting 29 of the most prevalent mutations in exons 18-21 of EGFR, (QIAGEN EGFR PCR kit). The assay uses a real-time PCR platform and is capable of detecting mutations at a sensitivity of 1-5% in a background of non-mutated alleles.

Results and Conclusion: Mutations were identified in 2877 (13.2%) of NSCLC samples tested. Of the 2877 samples with a detectable mutation 1479 (51.4%) harbored exon 19 deletions, 978 (34%) were L858R, 99 (3.4%) were mutations in codon 719, 95 (3.3%) were insertions in exon 20, 95(3.3%) were L861Q, 30 (1.04%) were S768I, 25 (0.87%) were T790M, 22 (0.76%) were L858R + T790M, 22 (0.76%) were S768I + G719X, 8 (0.28%) were L858R + S768I, 7 (0.24%) were T790M + G719X, 7 (0.24%) were L861Q + G719X, 4 (0.14%) were del exon 19 + T790M, 3 (0.1%) were del exon 19 + L858R, 2 (0.07%) were T790M + L861Q and 1 (0.03%) was L861Q + S768I Analysis of over 21000 consecutive non-small lung cancer specimens sent to our laboratory for evaluation of EGFR mutation status demonstrated that 13.2% harbored an EGFR mutation as detected by our allele specific PCR procedure. Approximately half, (51.4%) harbored an exon 19 deletion and about one third (34%) demonstrated the L858R substitution, while 2.6% revealed multiple mutations in the EGFR gene. This represents the largest analysis of EGFR mutational status in a US based population to date.

Disclosure: No significant relationships.

POSTER SESSION 2 • FRIDAY, JULY 27

POSTER DISPLAY TIME: 09:00 – 17:00

AUTHOR STAND BY TIME: 11:00 – 11:30 AND 16:00 – 16:30 (COFFEE BREAKS)

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.01: COMPARISON OF CLINICAL OUTCOMES FOR PATIENTS WITH CLINICAL N0 AND PATHOLOGIC N2 NON-SMALL CELL LUNG CANCER AFTER THORACOSCOPIC LOBECTOMY AND OPEN LOBECTOMY: A RETROSPECTIVE ANALYSIS OF 76 PATIENTS

Yun Li, Jun Wang
Department Of Thoracic Surgery, People's Hospital Of Peking University, Beijing/CHINA

Background: Video-assisted thoracoscopic surgery for lobectomy has been gradually accepted as a viable alternative for the treatment of non-small cell lung cancer since it was first introduced in 1995. It has been touted to provide intra-operative safety and superior outcomes as compared with open thoracotomy for patients with early-stage NSCLC . Due to the limitation of preoperative clinical examinations, about 10-20% NSCLC patients who were diagnosed with clinical N0 were confirmed as having pathologic N2 (cN0-pN2) during or after operation. It remains unclear whether intra-operative lymph node sampling reveals pN2 during VATS lobectomy. Is it necessary to convert from VATS to thoracotomy? Here we try to compare clinical outcomes between thoracoscopic lobectomy and open thoracotomy for the treatment of patients with cN0-pN2 non-small cell lung cancer (NSCLC).

Methods: Medical records of 182 cN0 patients (including 29 pN2) underwent VATS lobectomy between September 2006 and December 2009, and 204 cN0 patients (including 47 pN2) who underwent open thoracotomy between July 2000 and December 2009 were reviewed retrospectively. Pre- and intra-operative status and post-operative survival and recurrence of the patients between the two groups were compared.

Results and Conclusion: Results: There was no difference in age, sex, and preoperative pulmonary function, complications and clinical staging between two groups. The operation time and blood loss of VATS group was significantly lower than those of the open thoracotomy group. The number of dissected mediastinal lymph node (LN) stations was 3.3±1.1 in VATS group vs 3.3±1.3 in open thoracotomy group, and the total number of dissected mediastinal LN was 12.7±8.9 in VATS group vs 10.5±7.2 in open group. The 1- and 3-year disease-free-survival rate was 82.6% in VATS group vs 72.0% in open group, and 49.3% in VATS group vs 51.3% in open thoracotomy group (p=0.996), respectively. The 1- and 3-year survival rate was 84.9% in VATS group vs 71.2% in open group, and 64.0% vs 42.7% in thoracotomy group (p=0.121), respectively. Conclusions: This study has demonstrated that VATS lobectomy is comparable with open thoracotomy in both safety and curability for the treatment of cN0-pN2 NSLCL, without necessity of conversion to open surgery.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.02: EXPERIENCE OF COMPLETELY VIDEO-ASSISTED THORACOSCOPIC SLEEVE LOBECTOMY

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Background: Sleeve bronchial reconstruction was once seen as the relative contraindications of VATs procedure. With the technique of thoracoscopic lobectomy and accumulation of large number of cases, surgeons begin the attempt of bronchial reconstruction endoscopiclly. In 2002, Luigi Santambrogio reported the world's first completely thoracoscopic sleeve lobectomy, but because of this procedure required extremely high ttechnology and operation skills, so it developed slowly and were not popular.Here we summarize 8 cases of non-small cell lung cancer (NSCLC) that has accepted completely video-assisted thoracoscopic sleeve lobectomy in People's Hospital of Peking University in china, to explore the safety, effectiveness indications and experience of this procedure.

Methods: Between Sep 2011 and Mar 2012, Medical records of 8 cases of non-small cell lung cancer that has accepted complete thoracoscopic sleeve lobectomy were reviewed (7 male, 1 female). Median patient age was 62.4 years. And median maximal diameter of solid tumors was 2.3 cm. This group consisted of 5 cases of Right upper lobe sleeve lobectomy , 2 case of left lower lobe sleeve lobectomy and 1 case of left upper lobe sleeve lobectomy. The operation procedure was completely VATs anatomic sleeve lobectomy combined with systematic lymph node resection (at least 3 groups of lymph nodes in the mediastinum area). All procedure were underwent under general anesthesia with double-lumen endotracheal intubation. The patient was placed Lateral decubitus position. Three incision were made at 7th intercostal space on the median axillary line, 4th intercostal space anterior axillary line and 7th intercostal space subscapularis line. Bronchial were anastomosed combine with simple continuous suture anastomosis of membranous part of bronchus and simple interrupted suture anastomosis of cartilaginous part of bronchus, and then covered by surrounding tissue with blood supply.

Results and Conclusion: [Results] All procedures were carried out smoothly without serious complication. The median operative time was 240min median, the median bronchial anastomosis time was 45min, the median blood loss was 200ml, and median number of resected lymph nodes was 19.8. There were no conversion to open thoracotomy. Post operative show Pathology squamous cell carcinoma in 7 cases and adenocarcinoma in 1 case. pTNM staging show 1 case of T1aN0M0, 4 cases of T1bN0M0, 2 case of T1bN1M0 and 1 case of T1bN2M0. There was 1 case of slight post operative complication. The median postoperative chest tube drainage duration was 7.0 d, and median postoperative hospital stay was 9.0 d. All patients were well during the followed up for 2-7 months. [Conclusion] Completely thoracoscopic sleeve lobectomy was a safe and effective surgical procedure for patients with non-small cell lung cancer; the operative incision placed at 4th intercostal space anterior on the axillary line was convenient for anastomosis; anastomosis combine with simple continuous suture anastomosis of membranous part of bronchus and simple interrupted suture anastomosis of

cartilaginous part of bronchus was a fast and secure mode; keeping azygos vein does not affect the anastomosis.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.03: SYSTEMATIC LYMPH NODES DISSECTION IN TOTAL VIDEO-ASSISTED THORACIC LOBECTOMY USING VESSEL SEALING SYSTEM

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Background: We had reported that the Ligasure-V (LSV), electrothermal bipolar vessel sealer, was safe and useful in sealing of pulmonary artery and systematic lymph nodes dissection (Interact Cardiovasc Thorac Surg. 2010:229-33). A novel instrument, Ligasure-Blunt Tip (LSBT) was introduced for lung cancer surgery, we compared Ligasure-V with Ligasure-Blunt tip to avoid complications and to shorten the time required for the dissection of the superior mediastinal lymph nodes.

Methods: Forty-one patients with lung cancer were assessed and studied. All patients were performed totally thoracoscopic major lung resection and right superior mediastinal lymph nodes dissection using bipolar vessel sealers, LSV(n=24) or LSBT(n=17). No patient needed conversion to open surgery. Retrospectively, we examined all recorded operation DVD and the operation time of right superior mediastinal lymph nodes dissection and other parameters likes of postoperative complications.

Results and Conclusion: The lymph nodes dissection time was significantly shorter in the LSBT group than in the LSV group (unpaired t-test:P = 0.037, 1191 +/- 196 vs 1318 +/- 244 sec. F-study: p=0.148). Postoperative complications and median number of lymph nodes removed (17.5 vs 17 open) were similar in the 2 groups. No other parameters showed any significant differences between the two groups. Ligasure-Blunt Tip was safe and useful in lung cancer surgery. Ligasure-Blunt Tip is superior to Ligasure-V in terms of systematic lymph nodes dissection

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.04: PROTEIN SIGNATURE FOR NON-SMALL CELL LUNG CANCER PROGNOSIS

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Background: Lung cancer is the leading cause of cancer deaths worldwide. Despite recent advancement in diagnostic testing, surgical techniques and the development of therapeutic agents, the overall 5-year survival remains low for advanced lung cancer. Current histopathological classification and TNM staging have limited accuracy in predicting survival and stratifying patients for appropriate treatment. Our hypothesis is that the dysregulated regulatory proteins can add additional value for more accurate classification and prognostication of non-small lung cancer (NSCLC) since these proteins are critical in controlling cancer cell behaviors such as proliferation, invasion and metastasis.

Methods: The expression of 108 proteins and phosphoproteins in 30 paired NSCLC samples were assessed using Protein Pathway Array (PPA). The differentially expressed proteins were further confirmed using a tissue microarray (TMA) containing 94 NSCLC samples and were correlated with clinical data and survival. We recently developed a powerful Protein Pathway Array (PPA) analysis that allows to identify the important, but low abundance proteins and phosphoproteins in NSCLC. The proteins included in the PPA analysis are those important in carcinogenesis including cell cycle regulation and proliferation, adhesion, migration, invasion, metastasis and angiogenesis.

Results and Conclusion: Twelve of 108 proteins (p-CREB(Ser133), p-ERK1/2(Thr202/Tyr204), Cyclin B1, p-PDK1(Ser241), CDK4, CDK2, HSP90, CDC2p34, β-catenin, EGFR, XIAP and PCNA) were selected to build the predictor to classify normal and tumor samples with 97% accuracy. Five proteins (CDC2p34, HSP90, XIAP, CDK4 and CREB) were confirmed to be differentially expressed between NSCLC (n=94) and benign lung tumor (n=19). Furthermore, over-expression of CDK4 and HSP90 in tumors correlated with a favorable overall survival in all NSCLC patients and the over-expression of p-CREB(Ser133) and CREB in NSCLC correlated with a favorable survival in smokers and those with squamous cell carcinoma, respectively. Finally, four proteins (CDK4, HSP90, p-CREB and CREB) were used to calculate the risk score of each individual patient with NSCLC to predict survival. Our data demonstrated a broad disturbance of regulatory proteins in NSCLC and some of these could be selected as clinically useful biomarkers for diagnosis, classification and prognosis.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.05: GENOMICS MUTATIONS' BASED ARTIFICIAL NEURAL NETWORK AND FIELD PROGRAMMABLE GATE ARRAY FRAMEWORK FOR LUNG CANCER DIAGNOSIS

Emmanuel Adetiba[1], F A Ibikunle[2], E F Adebiyi[3]
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Background: Advances in Information and Communications Technology (ICT) supporting cancer research have accelerated the discoveries of new approaches for its diagnosis, prognosis and treatment. Sophisticated DNA sequencing has been used to study the whole genome sequence of different cancer tissues. The sequence information provides a detailed catalogue of the somatic mutations in the cancerous tissues. This provides a

good molecular and genetic understanding of cancer biology especially lung cancer.

In this work we utilized the genomes of Non-Small Cell Lung Cancer(NSCL) using Epidermal Growth Factor Receptor(EGFR) gene as a biomarker to produce training and testing datasets for an Artificial Neural Network(ANN) ensemble aimed at NSCL diagnosis electronically. Novel algorithms were developed and implemented in software for the pre-processing and features extraction stages while the ANN stage of the electronic diagnostic system was prototyped in hardware using Field Programmable Gate Array(FPGA) digital technology.

Methods: Some significant genes that have been identified in lung cancer formation and progression include FGFR1,BRCA1, INSR, EGFR, K-RAS and etc. In this study, Epidermal Growth Factor Receptor(EGFR) gene and the different mutations in this gene are used as biomakers for early detection of Non-Small Cell Lung Cancer(NSCLC). We extracted records of NSCLC patients that suffered significant mutations in the TK domain of EGFR genes from public genomics databases. Seven different types of mutations were detected in the sample data which includes; microdeletion,missense, microindel, microinsertion, duplication, nonsense and missense(TBM). Among these, the two most common are the microdeletion and missense mutations and they represent between 85-87% of all EGFR TK domain mutations. We extracted deletions and missense mutation features from our sample data to build numeric mutation profiles for the patients. Our electronic diagnostic platform which was developed with Artificial Neural Network(ANN) is therefore based on the numeric patients' mutation profiles. The phases for the system development are;

i.) data acquisition ii.) pre-processing iii.) features extraction iv.) ANN design, training, testing and validation. iv.) hardware prototyping with FPGA v.) performance evaluation

Results and Conclusion: We carried out five different experiments to train the ANN with hidden layer neuron ranging from 10 to 50 neurons.The best performance of 2.5169e-007 mean square error(mse) at 23 epochs was obtained when 50 hidden neurons were used to train the ANN at the fifth experiment. This confirms the validity of the hypothesis we formulated that the more the number of neurons in the hidden layer, the better the performance of the network. The confusion matrices showed various types of errors that occured for the trained network. 97.7% cases were correctly classified and 2.3% cases were misclassified. These results show a very good recognition of the NSCLC by our electronics based diagnostic platform.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.06: ROBOTIC STEREOTACTIC RADIOTHERAPY FOR EARLY STAGE LUNG CANCER: CLINICAL & DOSIMETRIC EVALUATIONS

Jean-Emmanuel Bibault, Bernard Prevost, Xavier Mirabel, Thomas Larcornerie, Eric Lartigau
Academic Radiation Therapy Department, Oscar Lambret Comprehensive Cancer Center, Lille/FRANCE

Background: Stereotactic radiation therapy is a new field of treatment for early stage lung cancer occurring in medically inoperable patients. The CyberKnife system allows for real-time tumor tracking under free breathing conditions. It could reduce toxicity while maintaining the same efficacy. We report our initial experience with 51 patients treated with the fiducial-less Xsight Lung Tracking System® and with a follow-up of at least 3 months, out of 241 patients treated with SBRT for lung cancer in our department. Potential dosimetric differences between the Ray-Tracing and the Monte-Carlo algorithms will also be presented.

Methods: Patients were accrued after evaluation by thoracic surgeons and oncologists. Selection criteria were: single T1 or T2 pulmonary tumor, tumor size between 15 and 60 mm, N0 and M0. Initial staging included CT-Scan with contrast agent and FDG-PET. Treatment were prescribed with Ray-Tracing (type A algorithm) and also calculated with Monte-Carlo (type B algorithm) to evaluate potential dosimetric differences. Response was evaluated with the modified RECIST criteria every 3 months and toxicity with the CTCAE v4.0 grading scale.

Results and Conclusion: 43 men (84%) and 8 women (16%) were treated for 25 T1 (49%) and 21 T2 (41%) lung cancer. 5 pts (10%) were treated for a relapse after prior surgery (4%) or radiation therapy (6%). Median follow-up was 15 months (5-30). Median age was 69 (50-85). All pts were smokers. Median tumor size was 24 mm (15-70). Median delivered dose was 60 Gy (36-60 Gy) in 3 fractions. Local control rate was 86%, including 16 complete responses, 16 partial responses & 12 stable diseases. 7 progressions were observed. 1 pt relapsed with mediastinal lymph nodes and 6 pts with distant metastases and subsequently received chemotherapy. Disease-specific survival rate was 98% at 15 months. 7 grade 1 (14%) & two grade 2 (4%) radiation pneumonitis were found on CT-Scan at 3 months and disappeared on later controls. Dosimetric differences between the Ray-Tracing and the Monte-Carlo algorithms will be presented during the congress. Conclusion Local control rate was high for these patients, while toxicity remained low. This method could represent a completely non-invasive curative treatment for inoperable patients.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.08: PHASE II TRIAL: CONCURRENT CHEMOTHERAPY AND RADIOTHERAPY WITH NITROGLYCERIN IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS

Dolores De La Mata, Mónika Blake-Cerda, Jesús Zamora, Omar Pena, Diana Flores-Estrada, Jenny Turcott, Oscar Arrieta
Radiation Oncology, Instituto Nacional De Cancerologia De Mexico, Mexico City/MEXICO

Background: The treatment of choice for locally advanced non small cell lung cancer (NSCLC) is concurrent chemoradiation (CRT). However, efforts to improve treatment results include targeted therapy and the use of radiosensitizers. Nitroglycerin (NTG), a nitric oxide (NO) donor agent, reduces expression of Hypoxia-Induced Factor, which is associated to both chemo and radio resistance.

Methods: This is phase II trial in patients with locally advanced NSCLC treated with chemotherapy (CT) based on Cisplatin and

Vinorelbin with NTG concurrent with radiation therapy. A 25 mg NTG patch was administered to the patients during the first 5 days of each induction treatment cycle and during chemo-radiotherapy. Blood samples of VEGF were taken before any treatment and after two cycles of CT. The protocol is registered with ClinicalTrials.gov, number NCT00886405.

Results and Conclusion: 35 patients were enrolled in this trial. Median Follow up was 16.6 months (SD ±13.6). Mean age was of 59.9 years (±10.8), 68.6% of the patients were smokers. ECOG status was 0 in 22.9%, 1 in 65.7% and 2 in 11.5%, respectively. Histopathology was adenocarcinoma in 68.6%, epidermoid in 17.1% and undifferentiated in 14.3%. Stage distribution was: IIIA- 57.6% and IIIB 42.5%. All patients completed CRT treatment and four underwent surgical treatment. Toxicity profile related to NTG was Grade I and II headache in 17.1%. Grade III and IV toxicities were esophagitis (17.1%), neutropenia (62.9%), and nausea (5.7%). Sixty Four per cent of patients achieved partial response after CT and 75.8% after CRT. PFS was 11.8 months (95%, IC 7.8-15.6) and OS was 42.9 months (95%IC 31.3-52.1). After two cycles of CT, plasma VEGF levels were significantly lower (median 132 vs. 53). No differences on PFS and OS were found between patients with a reduction ≥ 93 pg/ml (median of differences between VEGFR before and after chemotherapy). Conclusions: The addition of NTG to induction CT, and concurrent CRT on locally advanced NSCLC patients seems to increase the response rate, PFS and OS with an acceptable toxicity profile. A prospective trial is warranted to confirm these findings.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.09: LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER(NSCLC) IN THE ELDERLY: THE INCA EXPERIENCE

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Background: Combined chemoradiation (CRT) is the standard terapy in unresectable, locally advanced NSCLC. Nevertheless, the best approach in the eldery population is still poorly defined, since this subgroup was underrepresented in most clinical trials.

Methods: We retrospectively reviewed the medical charts of pacients with diagnosed stage III (6º AJCC), unresectable, NSCLC, treated at the Brasilian Nacional Cancer Institute (INCA) between 2003 and 2005. Patients with malignant pleural effusion were excluded (former "wet IIIB"). The primary outcome was overall survival(OS), measure from diagnosis until death. Prognostic factors were analyzed using log-rank and stepwise cox model. Palliative therapy (PT) included best supportive care, radiation terapy (RT;<40Gy), and palliative chemoterapy. Among patients treated with radical RT,OS was measured from date of treatment beginning until death (OST).

Results and Conclusion: One hundred fifteen patients were included. Median age was 71 years (range 65-83), 76% were male, 51% had squamous cell carcinoma, and 82% stage IIIB. Seventy percent of patients had more than 5% weight loss documented at the diagnosis, and most had performance status (PS) 0-1 (44%), while PS 2 and 3 were documented in 29% and 26%, respectively. Ninety percent were current/former-smokers, and Charlson index was 0 in 66% and 1-2 in 34%. Thirty-six percent received PT, 32% exclusive RT (>40 Gy), and 32% CRT (concomitant or sequential). Post-radiation surgery was not performed in our cohort. The median OS was 9.9 ms (95% CI, 7.2-12.6). Survival was significantly longer among patients with PS 0-1 (p<0.0001) and no weight loss (p=0.026), while histology (p=0.15), tumor stage (p=0.51), Charlson index (p=0.37), and age (p=0.54) were not prognostic factors. Patients treated with exclusive RT and CRT had better survival (median OS, 14.3 ms [95% CI, 11.7-16.9] and 17.0 ms [95% CI, 14.1-19.9], respectively) than patients receiving palliative therapy (median 4.1 ms [95% CI, 3.5-4.8]; p<0.0001). In the multivariate analysis, RT (HR 0.25 [95% CI, 0.15-0.42]; p<0.0001) and CRT (HR 0.16 [95% CI, 0.09-0.27]; p<0.0001) were independently associated with better survival in comparison to PT. Among patients receiving radical RT, the addition of chemotherapy was associated with longer OST (median 14.1 ms [95% CI, 10.7-17.4] vs 10.7 ms [95% CI, 8.7-12.6]; p=0.025). Elderly patients with locally advanced NSCLC derived significant survival benefit from radical RT and CRT, suggesting that age should not be a contraindication for these aggressive therapeutic strategies. In this setting, the highest survival was demonstrated in patients receiving a combination of CRT, either sequentially or concomitantly. Further prospective studies are encouraged to evaluate the best sequence and agents to be combined to RT in the elderly.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.10: SURGICAL MORTALITY IN RESECTIVE SURGERY OF LUNGCARCINOMAS AT A REFERAL PUBLIC HEALTH SYSTEM HOSPITAL

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Background: Surgical mortality (SM) is define as the death that occur during the first 30 days after surgery , even when the patient were out of hospital , or when it happened during the convalescence at hospital stay (no time limits).Our goa lis to analize the incidence of surgical mortality in patients operated with curative resective intention from a lung carcinoma in a referal public health system hospital.

Methods: During the period 1/1/1997 to 31/12/2011 109 patients were operated consecutively from a lung carcinoma with resective curative intention. 64,2% were men (n=70). Mean age 57.15 years (95% CI 55,35-58,99). Histology types : adenocarcinomas (n=67), Squamus (n=28), carcinoids (n=10), por dif. carcinomas (n=2), SCLC (n=2). Stages: Ela 8, Elb 35, Ella 4, Ellb 20, Ellla 29, Elllb 7,E lV 4 and 2 localized (SCLC). Procedures: bilobectomies 7, lobectomies 66, neumonectomies 18, sublobar resections 6, biopsies 12.

Results and Conclusion: The SM Rate was 7,2% (n=8), 7

were men, ASA lll, heavy smokers at the time of surgery and 6 of them had cardiovascular diseases (arterial hypertension, electrical disorders). Four of them died because of sepsis, one by intraoperative bleeding, one by posoperative bleeding and multiorgan failure, one by respiratory distress and the last because of heart failure after extracorporeal circulation. According the stage : Elb 1, Ellb 4, Ella 3. No one of them received induction therapy. Surgical procedure: lobectomies 5, neumonectomies 2, unresectable 1. Our Surgical Mortality Rate is higher than the published in the literature. We consider that this depends on several factors. The population of the Public Health System Hospitals use to have less resources tan the rest of the people (socioeconomics) and because of that they dont have periodical health controls, arriving in advanced stages of diseases (oncological, cardiovascular etc.). Many of the medical units in our hospital are assisted by residents that act not always under a staff supervision. The same surgical team (three of the authors) in its extrahospitalry activity has a surgical mortality rate in accordance with the international literaure.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.11: COMPLIANCE, TOXICITY AND SUCCESSFULL GOALS IN ADJUVANT SETTING.RESULTS FROM PUBLIC REFERAL HOSPITAL

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Background: Cisplatin based chemotherapy is the treatment of choice in the adjuvant setting of non small cell cancer (NSCLC) stages II-IIIA. Compliance, toxicity and follow up are issues of paramount importance. Series from Latinamerica were infrecuent. Objective: We report our experience with consecutive patients with NSCLC diagnosis and adjuvant treatment. Toxicity, compliance and follow up were the end points.

Methods: We report our experience with consecutive patients with NSCLC diagnosis and adjuvant treatment. Toxicity, compliance and follow up were the end points. The medical records of consecutive patients with NSCLC adjuvant treatment were reviewed.

Results and Conclusion: Records of twenty patients nine were reviewed (45%) were male and eleven (55%) female. Stage IB one patient (5%), one patient was stage IIA (5%), 9(45%) were IIB and 8 (40%) patients stage IIIA . Pathology was adenocarcinoma 15 patients (pts) (75%) and squamous cell carcinoma in five cases(25%).Perfomance Status at start of treatment were 0 in six pts, 1 twelve pts and 2 in two. All patients had accessibility (with or without insurance). The median days to start chemotherapy since surgery was 41 days (r.19-98).Regimes indicated were Cisplatin-Vinorelbine (70%), Cisplatin-VP-16 (20%), Carboplatin-Paclitaxel (10%).The median number of cycles were 4 (3-6). The Cisplatin-Vinorelbine regimen was completed in 75% of pts and related with more adverse events,others combo were completed with mild toxicity in 100% of cases. No Grade 5 toxicity were recorded. Toxicity was seen in 13 pts (65%), the toxicity more frequent was asthenia (7pts),neurotoxicity (5pts),pain at administration site (5pts) all with vinorelbine, febril neutropenia in 4 pts, trombocytopenia and neutropenia in 4 pts and anemia 3 pts. The pattern of recurrence were locoregional 3 pts (15%) and distant 8 pts (40%). Recurrence was in lung 3, bone 3, brain 2, liver 2, multiple sites 4 pts.No second tumors were reported and two lung cancers with different histology were recorded at follow up in 2pts. (10%). Conclusions: Adjuvant treatment of NSCLC were feasible, with high compliance and mild toxicity in a public hospital. The multidisciplinary approach in the follow up and surveillance of adverse events is the target.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.12: PULMONARY RESECTIONS IN A TERITIARY CARE CENTRE- A PROSPECTIVE OBSERVATIONAL STUDY OF OUTCOME

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Background: In order to assess short term outcomes and predictive factors for complications following pulmonary resections.

Methods: All patients who underwent pulmonary resections either for malignant or benign causes were included in the study prospectively from January 2011 to December 2011 in a single unit in a teritiary care cancer hospital, short term outcomes and predictive factors were analysed.

Results and Conclusion: Results: Twenty patients underwent pulmonary resections for malignant conditions and 8 patients for benign conditions. The characteristics and the procedures performed were given in (Table 1). Three patients underwent lobectomy with chest wall excision and was reconstructed with mesh and bone cement in two patients and only mesh in one patient (Fig.1). Of 8 patients who underwent wedge resection; 7 for benign causes and one for metastatic gestational trophoblastic neoplasia. One patient with pulmonary tuberculosis and bronchiectasis underwent lobectomy. Six patients developed postoperative complications and were described in Table 2. Two patients had minimal air leak which settled on conservative management. One patient had prolonged ICU stay for more than one week because of pneumonia. Of the two patients who had undergone mesh and bone cement reconstruction one got infected for which mesh was removed on 35th postoperative day, thoracoplasty was done and later the wound was sutured secondarily. Predictive factors were analyzed for all patients and were analysed. Pulmonary complications occurred in patients with DLCO <60 % in 2 patients one had pneumonia and the other patient was on prolonged mechanical ventilation for 48 hrs and ICU care for 9 days. Four of the patients who developed complication had ECOG performance status of 3 and other two had ECOG performance status of two. Conclusion: DLCO is an independent predictor for postoperative complication apart from performance status, pulmonary function tests, smoking, diabetes mellitus and age.

Table 1: Characteristics of Patients:

Characteristics	Number of patients (Total N = 28)
Age	
Mean	54.71 years
Range	8-72 years
Sex (M: F)	1.5 (18/12)
Clinical presentation	
Cough	18(64.2%)
Chest Pain	14(50%)
Breathlessness	4(14.2%)
Fever	1(3.5%)
Haemoptysis	5(17.8%)
Indications for Pulmonary resection	
Malignant	20
. Squamous cell carcinoma	11
. Adenocarcinoma	7
. Adenosquamous carcinoma	1
.Small cell carcinoma	1
. Metastases (Gestational Trophoblastic Neoplasia)	1
Benign	
. Hamartoma	8
. Tuberculosis	4
. Inflammatory fibromyoblastic tumor	2
. Neurofibroma	1
	1
Surgeries performed	
Lobectomy	9
Pneumonectomy	3
Bilobectomy	5
Wedge excision	8(Hamartomas(4), Tuberculosis(1), Inflammatory fibroblastic tumor(1), Neurofibroma(1), Metastectomy(1)
Lobectomy + Chest wall reconstruction	3
Comorbidities	
Smoking	16(57.1%)
Chronic Obstructive Pulmonary disease	14(50%)
Diabetes Mellitus	5(17%)
Hypertension	4(14.2%)
Congestive heart failure	1(3%)(Ejection Fraction-50%)
Pulmonary Function Tests (28)	
FEV 1	1.61(Range 0.6- 2.36)
FVC	2.23(Range 1.5-3.43)
FEV1/ FVC(%)	82.6(Range 58-111)
DLCO(<60)	2
Stage in Malignancy (N=19)	
Stage IIA	5
Stage IIB	13
Stage IIIA	1

Disclosure: No significant relationships.

Table 2: Postoperative complications and predicitive factors following Pulmonary resections

Complications	Number of patients (N=28)	Age	comorbidities	FEV1/FVC (%)	DLCO	ECOG performance status
Wound infection(superficial)	1(3.5%)	72	DM, COPD	64	> 60%	2
Mesh Infection (Deep)	1(3.5%)	70	COPD	70	>60%	3
Air leak	2(7%)	60, 54	COPD	61, 76	>60%	3,2
Pneumonia	1(3.5%)	68	DM, COPD	58	<60%	3
Prolonged ICU stay (1 week)	1(3.5%)	64	DM, COPD	60	< 60%	3

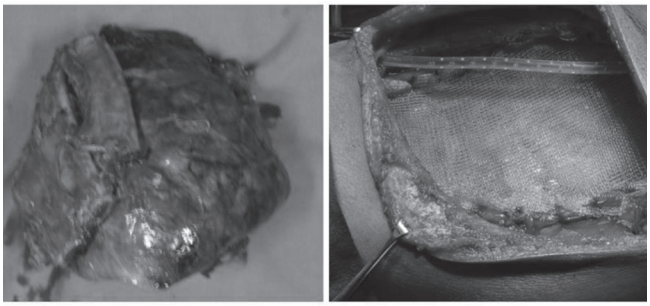

Fig. 1(a) Fig. 1(b)

Fig. 1(a) – Resected specimen of lobectomy with 4 ribs
Fig. 1(b)- Chest wall reconstruction with Prolene mesh

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Early Stage NSCLC (Stage I – III)

P2.13: TAXANE CHEMORADIATION FOR STAGE III NON-SMALL CELL LUNG CANCER: NEW STUDY DESIGN BASED ON PRE-CLINICAL AND CLINICAL OUTCOMES OF TWO PROSPECTIVE STUDIES

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Background: Aggressive chemoradiotherapy (CRT) is the current treatment standard for stage III non-small cell lung cancer (NSCLC), but the outcome remains poor due to both high rates of local disease failure and high rates of distant metastasis. Large phase III studies of combined CRT have yielded an average local failure rate at 50% and an average distant failure rate at 80%. The interim analysis of the ongoing RTOG randomized phase III clinical trial (RTOG 0617) comparing high dose (74Gy) vs. standard dose (60Gy) radiation and concurrent chemotherapy with the intent to improve local cancer control failed to demonstrate the benefit of high dose chest radiation (RT). Thus the local disease control issue remains unresolved, and there remains no major breakthrough in the efficacy of treating distant metastasis.

Methods: At our institution, two prospective phase I/II clinical trials have been sequentially conducted using taxane-based CRT for stage III NSCLC. Both studies were designed using pre-clinical information of paclitaxel, docetaxel and radiation treatments to lung cancer cell lines. URCC1597 applied low dose paclitaxel 15 -20mg/m2 three times per week (M,W,F), and daily delayed RT given at least 4 hrs after paclitaxel infusion to 64.5 Gy in 1.8 Gy daily fractions. URCC1500 applied one-cycle induction chemotherapy with docetaxel (75mg/m2) & cisplatin (75mg/m2), and rhG-CSF (150 mg/m2 days 2-10), followed by twice-weekly docetaxel at 12 mg/m2 (M,Th) and daily delayed RT to 64.5 Gy in 1.8 Gy daily fractions.

Results and Conclusion: Preclinical data from lung cancer cell lines showed that both paclitaxel and docetaxel had radiosensitizing effects, which was more pronounced with delayed radiation schedule after drug treatments. Docetaxel had much higher cytotoxic effects than paclitaxel when lung cancer cells were treated with drug alone. Pulsed low-dose paclitaxel CRT (URCC1597) for stage III NSCLC, yielded a 100% response rate, a 93% in-field tumor control, 75% chest disease control, and a median survival of 12 months. URCC 1500 yielded a response rate of 69%, a 55% in-filed tumor control, 25% chest disease control, and a median survival of 32 months. Hematologic and non-hematologic toxicities were very low in URCC1597, while high rates of grade 3 esophagitis was observed and led to dose reduction of the sensitizing docetaxel in URCC 1500. Based on outcomes of pre-clinical and two clinical studies of taxane-based CRT trials, we conclude that the ideal and logical study design that will maximally target distant metastasis and local chest disease of stage III NSCL is one cycle induction docetaxel (75mg/m2)/cisplatin (75mg/m2) ± G-CSF followed by pulsed low dose paclitaxel (20mg/m2) chemoradiotherapy to 65 Gy in 1.8 Gy daily fractions.

Disclosure: No significant relationships.

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Early Stage NSCLC (Stage I – III)

P2.15: IMPACT OF SMOKING ON POSTOPERATIVE COMPLICATIONS OF SURGICAL RESECTION FOR LUNG CANCER

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Background: Smoking is not only the most important risk factor identified for the development of lung cancer, but also for the genesis of many other diseases that cause a large increase in morbidity and mortality, such as COPD and atherosclerotic disease. It has been suggested that smoking per se increases the risk after surgery, possibly by increasing the overall inflammatory process. Objective: To analyze the influence of smoking on postoperative complications in patients with Non Small Cell Lung Cancer (NSCLC) undergoing a surgical procedure with diagnosis or curative intent.

Methods: Retrospectively collected data were analysed, at a single center, on 593 patients undergoing lung resection for NSCLC between January 1986 and November 2011. Smokers were those who had smoked at least 100 cigarettes in their life.

Results and Conclusion: Results: 593 patients were included (60.9 ± 10 year-old), reliable information about smoking was available in 564, 86.5% (487 patients) were smokers.

Smokers were, more often men (74.6 vs. 35.5%, p = 0.000), symptomatic (41.9 vs. 24.3%, p = 0.005) and had lower prevalence of previous malignancies (8.9 vs. 18.6%, p = 0.029) compared with non-smokers.

The frequency of presentation as SPN, right side, or the central location were not different, but smokers had significantly higher frequency of clinical N2 (10.8 vs. 2.7%, p = 0.029), prevalence of tumors larger than 3 cm (61.7 vs 44.6%, p = 0.009), and prevalence of squamous cell carcinomas (20.9% vs 6.6%, p = 0.003). Resection was complete in a similar percentage (86.8 vs. 91.8%, p = 0.231). The rate of postoperative complications (23.5 vs 21.9%, p = 0.758) or operative mortality (5.5 vs 5.3%, p = 0.920) were not different. However, when the period of the last 10 years was analysed, we observed a lower complication rate (15.6 vs. 29.4%, p = 0.001) and operative mortality (3.3 vs 7.4%, p = 0.025) compared with patients undergoing lung resection before 2002. In the whole population (smokers and non-smokers) logistic regression identified age over 75 years (OR 0.41 [95% CI, 0.20 to 0.81], p = 0.011), and surgery performed before 2002 (OR 2.14 [95% CI, 1.35 to 3.37], p = 0.001) as factors independently associated with postoperative complications: Smoking was not an independent predictor (OR 1.09 [95% CI, 0.55 to 2.15], p = 0.800).

Conclusions: A history of smoking was not a risk factor for complications and operative mortality in our series. We believe that improvement in perioperative management during the last decade has been responsible of counterbalancing the potential adverse impact of smoking.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Early Stage NSCLC (Stage I – III)

P2.16: PNEUMONECTOMY IN LUNG CANCER: ANALYSIS OF PREDICTIVE FACTORS OF POSTOPERATIVE MORBIDITY AND MORTALITY

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Background: Complete surgical resection in patients with lung cancer non-small cell (NSCLC) remains the only potentially curative option. The surgical discussion on pneumonectomy has focused on the high postoperative morbidity and mortality rate and its possible impact on long-term survival. Objective: To analyse predictive factors of postoperative complications and mortality after pneumonectomy.

Methods: Retrospectively collected data was analysed, at a single center, on 570 patients undergoing lung resection for NSCLC with curative intent between January 1986 and March 2011.

Results and Conclusion: Results: There were 66 pneumonectomies. Most were men (74.2%) and less than 70 years (97%). Smokers were 89.4%. The prevalence of previous malignancy was 4.7%, the frequency of presentation as SPN was 16.9%, right upper lobe location in 26.6%, 29.7% lower and 54.7% in middle lobe, and with involvement of bronchus 7.9%.The clinical stages were IA 16.7%, IB 43.9%, and IIB 39.4%.During surgery, the prevalence of tumors larger than 3 cm was 85.7%, N2 disease 34.4%, pleural invasion 15.6% and regional involvement 51.6%.The prevalence of adenocarcinoma was 47%. Pneumonectomy was considered curative in 71.9% with a postoperative complication rate of 43.1% and 20.6% operative mortality.In 50.8% of patiemts, the pneumonectomy was performed on the right side, with an operative mortality of 24.2% (vs. 16.7% on the left side, p = 0.542).The median survival of stage I patients was not different compared to other surgical procedure (51.03 vs. 142.27, Kaplan-Meier log rank p = 0.912).We performed a multivariate analysis of postoperative morbidity and mortality: complete resection (OR 0.18, 95% CI 0.04 to 0.75, p = 0.019) and curative resection (OR 0.15, 95% CI 0.04 to 0.58, p = 0.005) were protective factors; and age over 70 years old (OR 7.5, 95% CI 1.09 - 51.51, p = 0.04) and the presence of postoperative complications (OR 11.68, 95% CI 2.31 - 59.03, p = 0.002) were predictors of mortality.

Conclusions: Pneumonectomy has high postoperative morbidity and mortality. The age over 70 years old and the presence of postoperative complications were predictor factors of mortality. In our center, we found no significant difference in median survival, neither operative mortality in right pneumonectomy.

Disclosure: No significant relationships.

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Early Stage NSCLC (Stage I – III)

P2.17: DOES AGE INCREASE POSTOPERATIVE MORBIDITY AND MORTALITY IN PULMONARY RESECTION IN LUNG CANCER?

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Background: The diagnosis of non small Cell Lung Cancer (NSCLC) in elderly patients is increasing due to longer life expectancy. Although the surgery offers the best chance of cure in early stage; in the elderly, this is done with extreme caution because of the existance of high incidence of morbidity and mortality. Objective: to analyze the clinical characteristics, postoperative morbidity and mortality in patients over 75 years old diagnosed with NSCLC undergoing a surgical procedure with curative intent.

Methods: Retrospectively collected data was analysed, at a single center, on 593 patients undergoing lung resection for NSCLC with curative intent between January 1986 and November 2011. They were divided into 2 groups: under 75 (u75) and over 75 (o75).

Results and Conclusion: Results: The o75 were 47 (8%), with mean age 78.2 ± 3.2 (vs. 59.49 ± 9.04), there was no differences in sex between groups (men 61.7 vs 68.8%, p = 0.315). The o75 had a higher prevalence of previous malignancies (20 vs. 9.4%, p = 0.068) and lower proportion of smokers (including ex-smokers) (72.3 vs. 82.4%, p = 0.038). The frequency of presentation as SPN (34 vs. 38.9%, p = 0.537), right side (55.3 vs. 58.8%, p = 0.646), central location (25 vs. 26.3%, p = 1.000), asymptomatic (59.5 vs. 69%, p = 0.253) or clinical suspicion of N2 (4.3 vs. 10.4%, p = 0.299) were not different. The rate of postoperative complications

(35.7% vs. 21.7% p = 0.053) or operative mortality (6.4 vs. 4.8% p = 0.498) were not different; however, in 075 less pneumonectomies were performed (4.3 vs. 16.1%, p = 0.032) and had more days in hospital intensive care (3.13 ± 8.20 vs. 1.43 ± 3.12, p = 0.003). The prevalence of tumors larger than 3 cm. (71.4 vs. 58.1%, p = 0.103), the finding of N2 disease (18.6 vs. 20.8%, p = 0.846), pleural invasion (5.5 vs. 19%, p = 0.335) or regional involvement during surgery (42.5 vs. 31.3%, p = 0.159) were not different.

Both groups had the same proportion of adenocarcinomas (68.1 vs. 61.1 p = 0.434).

Surgery was considered curative in a similar percentage (89.1 vs. 86.9%, p = 0.820). The median survival was not different between both groups (37.9 vs. 70 months Kaplan-Meier log rank p = 0.064). When logistic regression was performed to find risk factors independently associated with postoperative complications, the age over 75 persists in the multivariate analysis (OR 2.00 [95% CI 1.03 to 3.91], P = 0.041); however, this does not occur when analyzing postoperative mortality (OR 1.23 [95% CI 0.35 to 4.27], P = 0.739). Conclusions: Our data shows that elderly patients do not have an increased morbidity and mortality after pulmonary resection, therefore should not be denied lung resection based on chronological age.

Disclosure: No significant relationships.

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Early Stage NSCLC (Stage I – III)

P2.18: IMPROVING OPERATIVE STANDARDS FOR LUNG CANCER BY AUDIT. WHY SOME PATIENTS DON'T GET THE BEST DEAL?

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Background: To audit anatomical resection and lymph node excision in patients undergoing lung cancer surgery according to the gold standards defined by the European Society of Thoracic Surgeons working group.

Methods: This is an analysis of all patients with primary lung cancer operated on by a single surgeon between July 2009 and December 2011. The patients are divided into 2 Groups: Initial Audit (100 patients, July 2009-October 2010) and Re-Audit (102 patients, November 2010-December 2011) that completed our Cycle.

Rates of anatomical resection and lymph node excision were measured from data obtained from histo-pathology reports and a surgical database. Uni- and multi-variate analyses were performed to identify reasons associated with diversion from set standards.

Results and Conclusion: RESULTS: 202 patients [120 male and 82 female, median age 70 (range 34-90) years] underwent surgery. Median PpoFEv1 was 58.2% (range 16 to 129). Median European Society Objective score (ESOS) was 5.4 (range 0.1 to 37.4) for Mortality and 24.3 (range 5.2 to 51.7) for Complications. A total of 29 (14.4%) procedures were completed by VATS approach. Anatomical resections were performed in 92% cases (88% in the initial group and 94% after the initial Audit). At least 1, 2 and 3 N2 lymph node stations were obtained in 88%, 69% and 51% respectively.

On Multivariate Regression Analyses History of another malignancy (p=0.01), VATS approach (p=0.001) and high ESOS score (p=0.02) were associated with more use of non-anatomical resections. Initial Audit group (p= 0.001) and VATS approach (p<0.001) were related to less complete mediastinal exploration on Logistic Regression.

CONCLUSION: Completing the Audit Cycle has helped to improve operative standards for lung cancer. Failure to perform extensive lymph node excision was unrelated to impaired spirometry, high ESOS score or advanced age. Our Audit demonstrates the need for attention to mediastinal lymph node dissection; specially during VATS lobectomies and might reflect the effects of a learning curve.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

SCLC, Mesothelioma, Thymoma

P2.19: PRIMARY PLEUOPULMONARY SYNOVIAL SARCOMA: A RETROSPECTIVE CLINICO-PATHOLOGIC STUDY OF 21 CASES FROM A SINGLE INSTITUTION

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Background: Primary pleuropulmonary synovial sarcoma (PPSS) is a rare neoplasm well described in literature over the last years. It represents from 7 to 10% of soft tissue sarcoma, being the most common areas of occurrence the thigh, knee, shoulder, foot and upper extremities, while in rare cases it could be diagnosed in the chest wall, mediastinum, lung parenchyma, pleura or heart. The discovery of the pathognomonic t(x;18) chromosomal translocation has enabled the diagnosis of an increasing number of these tumors.

Methods: This is a retrospective study of 21 consecutive patients (pts) with a diagnosis of primary PPSS treated or followed at the Institut Gustave Roussy (France) from 1998 to 2010. The main objective of this study is to identify the different ways of diagnosis, management and treatment for rare a disease, for which there is not a standard of care.

Results and Conclusion: Male/female ratio was 11/10, the median age 46 (range 16-72) with a median PS of 0 (1-2). Most commons symptoms were dyspnea, asthenia and cough, while in 4 cases the diagnosis was accidental. Tumors were localized in 12 cases in the lung, 6 were pleural, 2 mediastinal and in one case carinal. Six patients had synchronous metastases at diagnosis. Sixteen surgical interventions were performed: 11 lobectomies, 3 pneumonectomies, 1 atypical resection and 1 tracheal resection. A R0 resection has been achieved in 69% of the cases, while in the remaining there was evidence of a micro- or macroscopic residual (25% surgeries R1 and 6.25% R2). Neoplasms with monophasic component were the most prevalent (16/20, 80%) compared to those biphasic (4/20, 20%), and in 83% of cases (15/18) the tumors were grade 3 according to FNCLCC grading scale. Most of the neoplasm were

positive for the t(x,18) translocation (76.9%), and in 4 patients the fusion protein was searched (3 were positive for the SYT/SSX2 fusion and only one for the SYT/SSX1). Seven patients received a doxorubicin-containing chemotherapy (CT) regimen in adjuvant setting and only four underwent radiotherapy. R0 patients had a better disease free (22.7 vs 11.7 months) and overall survival (37.3 vs 23.2 months) comparing with R1-R2 patients. Thirteen cases of relapse were observed with a median time of 15,7 months (range 4,7- 59,7 months), 8 cases at thoracic level. Sixteen patients received a palliative chemotherapy. Seventeen (81%) died within 1 to 73 months (mean, 25 months), and 15 patients died within 5 years (71,4%). With a minimum follow-up With a minimum follow-up of 10 months, at the time of analysis three pts (14,3%) were alive with no evidence of disease and one was alive with evidence of disease. PPSS is a rare subset of intrathoracic sarcoma, and its clinical features suggest a more aggressive behavior than the synovialsarcoma of other counterparts, possibly related to the difficulty in obtaining adequate surgical margins. Adjuvant and neoadjuvant therapies need to be discussed in multidisciplinary committee and are indicated in these unfavorable diseases.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

SCLC, Mesothelioma, Thymoma

P2.20: MALIGNANT PLEURAL MESOTHELIOMA AND ERCC1 EXPRESSION

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Background: Advanced Malignant Pleural Mesothelioma (MPM) is a poor prognosis disease for which better treatment options and prognostic factors are urgently needed. Our study was to investigate the potential role of ERCC1 protein status as a prognostic factor in untreated patients with advanced MPM.

Methods: The study population consisted of 62 inoperable patients with advanced MPM enrolled betwen January 2003 and August 2010. None of the patients received chemotherapy due to non coverage by chilean public health system. All the patients received best supportive care. ERCC1 expression as a prognostic factor was evaluated by immunohistochemistry (IHC) on the formalin-fixed paraffin-embedded diagnostic biopsies.The tumor samples were separated according to this cutoff point into ERCC1-negative (H-score <= median) and ERCC1- positive (H-score> median) cases.

Results and Conclusion: Results: The 62 patients had tumor tisssue available for IHC.There were 71% ERCC1 negative, and 29% ERCC1 positive.There was no correlation between ERCC1 status and survival. Conclusion: Even if the literature suggests that ERCC1 can be a predictive factor of response to platinum-based chemotherapy, our retrospective study did not show ERRC1 expression to be an independent prognostic factor in untreated patients with advanced MPM.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

SCLC, Mesothelioma, Thymoma

P2.22: THORACIC E MEDIASTINAL PARAGANGLIOMA - A CASE REPORT

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Background: Paragangliomas are tumors that arise from the autonomic nervous system-associated paraganglia. These tumors can be hereditary cases and they are classified based on location and functioning character (catecholamine and serotonin secretors) and non-functioning character. Paraganglioma rarely occurs in the spinal canal and the extradural thoracic location is even less common. The treatment of choice is surgery when there is no metastasis. We report a case of a 36 year old woman with a thoracic paraganglioma. The patient first symptoms occurred in February 2010, when she presented shoulder and neck pain. At this time she was diagnosed as having stress. After that, she developed cough and posterior thoracic pain. Simultaneously, she presented progressive dysphagia and vomiting. In July 2011 she looked for medical assistance. The chest x-ray showed an increase of cardiac and mediastinal areas. At this time the patient become with dyspnea and to become dysphonic. Transthoracic echocardiogram performed in August 2011 demonstrated a low ejection fraction (57%) and a mass near pulmonary artery measuring 5.8x4.3cm with compression of pulmonary artery. CT done in August 2011 has shown 3 heterogeneous masses with low density: one localized in anterior compartment of mediastinum sized 7.5x 4.0 cm, the other close to right pulmonary artery (3.0X2.5cm), and the third in left paravertebral region (6,1X3,4cm). All others thoracic structures seemed to be normal. First biopsy was performed in August 2011. The anatomy pathologic diagnosis was paraganglioma. A second biopsy showed the same diagnosis and the immunohistochemistry analisys has shown neuroendocrine low grade carcinoma. At this time it was indicated surgery treatment. The surgery occurred in December 2011, when all but the lesion in contact with right pulmonary artery were submitted to excision. The postoperative evolution was favorable and the patient was dismissed from hospital within 7 days. The postoperative computed tomography control showed persistent mass at right pulmonary artery. Now there is a discussion about the next approach: radiotherapy or new attempt to surgical resection of the remain lesion?

Methods: The study is a case report description study.

Results and Conclusion: In present case, we has shown a partial succesfull treatment of a thoracic paraganglioma by surgical treatment.

Disclosure: No significant relationships.

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P2.24: VATS PLEURECTOMY/DECORTICATION FOR PALLIATION OF MALIGNANT PLEURAL MESOTHELIOMA

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Background: Surgery plays a role in the symptomatic management of Malignant Pleural Mesothelioma (MPM). We offer VATS debulking surgery to relieve symptoms in patients unsuitable for radical surgery. We present an operative video of the procedure. We aimed to assess the perioperative course and survival results of patients undergoing VATS Pleurectomy Decortication in the palliative management of MPM.

Methods: Over a 3-year period (2009-2011) 14 patients with MPM [13 male and one female, median age of 75 years (range 66-84) underwent VATS Pleurecomy Decortication with palliative intent under a single specialist surgeon. Indications for surgery were: Cytoreductive surgery as part of a randomised trial (n=3), elective debulking of trapped-lung síndrome (n=5) and Urgent inpatient surgery for malignant empiema, bleeding or dyspnea due to trapped-lung (n=6).

Median FEV1 was 52 (range 47 to 60) % predicted and patients had undergone a median of 2 (range 1-3) pleural invasive interventions prior to VATS debulking. The cell type was epitheloid and biphasic in 5 cases each and sarcomatoid in 4 cases.

Results and Conclusion: RESULTS:There was one perioperative death(7%) after bronchopneumonia following decortication fr a malignant empiema. The procedure was converted into a limited thoracotomy in 4 cases (3 out of the 6 Urgent cases and 1 out of the 8 Elective cases). The median hospital stay and duration of intercostal drainage were 8 (range 3 to 26) and 6 (range 2-51) days respectively. At a median follow-up of 16 months the median surcival was 9 months.

CONCLUSION: VATS pleurectomy/decortication is a valid surgical alternative in patients with Malignant Pleural Mesothelioma that are not candidates for radical surgey with aceptable complications. Inpatient salvage surgery carries poorer prognosis.

Disclosure: No significant relationships.

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SCLC, Mesothelioma, Thymoma

P2.25: USE OF BIOLOGICAL IMPLANTS FOR TISSUE RECONSTRUCTION AFTER THORACIC SURGERY FOR MALIGNACY

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Background: Synthetic materials have traditionally been used for tissue reconstruction in Thoracic Surgery. New biomaterials have been tested in other areas of surgery with good results. The aim of our study is to evaluate their use in extended thoracic surgery.

Methods: We reviewed all patients who underwent Thoracic Surgery requiring tissue reconstruction with bioprosthetic materials from August 2009 to January 2012. A total of 51 consecutive patients [46 male and 5 female, median age 65 (range 39-89) years] were included (42 elective admission and 9 with a contaminated/infected environment). Operations involved radical pleurectomy/decortication for Mesothelioma (n=39) and extended operations for thoracic malignancies (n=12)

Results and Conclusion: Results: A total of 94 patches were used (median of 2 per patient, range 1-3). Median hospital stay was 12 (range 5-149) days. Three patients died during postoperative period (5.8%): pulmonary embolism 5 days after intrapericardial pneumonectomy with chest wall reconstruction, fatal pneumonia 26 days after radical pleurectomy/ decortication for mesothelioma, and bronchopleural fistula 11 days after pneumonectomy with diaphragm and atrium excision for lung cancer after initial chemoradiotherapy. Six additional patients (10%) suffered majors complications: 3 required a reoperation (bleeding, tension pneumothorax, and release of a tight patch) and 2 patients suffered empyema treated conservatively. No other surgical exploration or removal of patches has been required for infection. Age, type of operation, number of patches, contaminated environment prior to surgery and emergency surgery did not increase postoperative dead, infection or complication rates. Conclusions: Our experience with the use of bioprosthetic patches for tissue reconstruction in Thoracic Surgery is proving satisfactory in extended/ complex procedures. The infection rates are low even when a proportion of procedures were performed under contaminated environments. Biological prosthesis should be part of the surgical options in Thoracic Surgery.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

SCLC, Mesothelioma, Thymoma

P2.26: PRESERVING THE LUNG DURING RADICAL SURGERY FOR MESOTHELIOMA: QUALITY OF LIFE, SPIROMETRY AND LUNG VOLUME MEASUREMENTS

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Background: To explore the changes in spirometry, lung volume measurements and quality of life after Radical Pleurectomy Decortication (RPD) for Malignant Pleural Mesothelioma (MPM)

Methods: Analysis of the changes in FEV1, Quality of Life (QoL)Questionnaires EORTC C30 and LC13, and volume measurements using CT scan software in the first 10 consecutives patients [8 male and 2 female, median age 62 (range 51 to 73 years] undergoing Radical Pleurectomy/ Decortication under a single surgeon from August 2009-March 2010.

Results and Conclusion: Results: There were no perioperative

deaths and no admissions to Intensive Care. The median hospital stay was 12 (range 10 to 20) days. All patients responded to QoL questionnaires pre and postoperatively at 3 month intervals. At median follow-up of 13 months (range 11 to 17) months, 7 patients remain alive. Ct scan were performed within 3 months from surgery and 9 of 10 patients underwent spirometry 3 months after surgery. At a median follow-up of 22 (range 14 to 25) months, the median survival is 20 (range 4 to 22) months. The FEV1 was reduced after surgery 17% (range 42% loss to 22% gain), but was not significant (p=0.5), and the lung volume changes ranged form loss of 57% to gain of 35% , but a the median change was only 1% (p=0.9).

QoL scores at 3, 6,9 and 12 months postoperatively showed no significant changes from preoperative responses. Conclusion: Preserving the lung parenchyma during Radical Surgery for MPM allows preservation of respiratory reserve and lung volumes. Some patients (the ones with a trapped-lung preoperatively) even improve their measurements. Patients reported preservation of QoL scores from 3 to 12 months.

Disclosure: No significant relationships.

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SCLC, Mesothelioma, Thymoma

P2.27: FINAL RESULTS OF THE PHASE I COMPONENT OF A PHASE I/IIA STUDY OF CHEMOTHERAPY WITH BENDAMUSTINE AND IRINOTECAN (BI) FOLLOWED BY ETOPOSIDE/CARBOPLATIN (EC) IN UNTREATED PATIENTS (PTS) WITH EXTENSIVE SMALL CELL LUNG CANCER (E-SCLC)

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Background: First-line therapy (EC) for E-SCLC produces a progression-free (PFS) and overall survival (OS) of 4 and 9 months, respectively. We evaluated safety and efficacy of a novel combination of BI followed by EC. Bendamustine and Irinotecan have single-agent activity in E-SCLC with tolerable toxicity.

Methods: This is a phase I/IIa study in untreated pts with E-SCLC, ECOG 0-2 and adequate organ function. Three dose levels (DL) of B (80, 100, and 120 mg/m2 - D1, 2) and I (150 mg/m2 - D1) every 3 weeks [Regimen A] for 3 cycles, followed by 3 cycles of E (100 mg/m2 - D1-3), and C (AUC 6, D1) [Regimen B] was evaluated in the phase I portion of the study. Regimen A dose limiting toxicity (DLT) and maximum tolerable dose (MTD) were evaluated in cycle 1 in 3-6 pts per dose level. Toxicity (CTCAE) was evaluated with CBC (weekly) and chemistry (every 3 weeks) and response (RECIST) by imaging at the end of Regimen A and B.

Results and Conclusion: 15 pts in 3 cohorts (cohort 1 (n=3); 2 (n=6); and 3 (n=6)) were enrolled in this phase I study. Baseline characteristics: median age 65 years, male 69%, increased LDH 54%, low albumin 31%, 1 pt with brain metastases. Regimen A, cycle 1 DLTs: Grade 3 diarrhea (cohort 2) and Grade 3 diarrhea/nausea/vomiting (cohort 3). Dose reduction was required in 2 and 3 pts in regimen A and B, respectively. Objective responses were observed in all three cohorts. Response rate on regimen A ~ 71% (CR-0; PR-10; 1-early for evaluation). Best overall response rate (regimen A/B) ~ 71% (CR-1; PR-9; 1-early for evaluation. Time to progression: median ~ 7 months [95% CI (2.0; 7.00)]. OS: median ~ 10 months [95% CI (5.0; 11.0)]. To date we have enrolled 8:15 pts needed in the phase II portion of the trial. Efficacy is too early to report. AE's to date: Grade 3's: nausea (cycle 1), neutropenia (cycle 1), weakness (cycle 2), fatigue (cycle 20), hyponatremia (cycle 1), dehydration (cycle 1), diarrhea (cycle 1) and dyspnea (cycle 1). Grade 4's: hyperuricemia, leukopenia (cycle 1). BI seems to be active and well tolerated in E-SCLC. DLTs were: diarrhea (n=11 [73%]; Grade 3 3:11)(cohort 2) and nausea, vomiting, diarrhea (cohort 3) of regimen A. Overall grades 3/4 myelosuppression were not significant in regimen A. Other adverse events in regimen A included nausea/vomiting, fatigue, and hypokalemia. Objective responses were observed in all 3 cohorts; best RDIs for regimen A and B were seen in cohort 2. For the phase 2 component of the study our recommended dose of Bendamustine is 100mg/m2 (d1, 2) plus Irinotecan 150mg/m2 (d-1).

Disclosure: No significant relationships.

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Biology and Pathogenesis

P2.28: GENDER DIFFERENCES OF ESTROGEN RECEPTOR BETA EXPRESSION IN NON-SMALL CELL LUNG CANCER

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Background: Important role of estrogens in occurrence and progression of non-small cell lung cancer (NSCLC) is recently shown. Estrogen receptor beta (ER beta) in the NSCLC tissue is a good prognostic marker and antiestrogen therapy target. We have supposed the level of ER beta expression in the tumor cells could be one of the reasons of gender differences in NSCLC progress. To check the supposition ER beta were quantitatively evaluated in NSCLC tissue – in the group of patients and separately in female and male. It was performed using immunofluorescence methodology developed by us.

Methods: NSCLC surgical specimens of 22 women and 79 men were analyzed by flow cytometry. Single-cell suspensions were incubated with primary antibodies (anti-ER beta 14C8 and isotype IgG2a, Abcam) overnight and with secondary FITC-conjugated antibody (F2772, Sigma) for 1.5 h. Mean cell fluorescence and number of stained cells were analyzed with WinMDI software and Kolmogorov-Smirnov statistical approach. ER beta expression intensity was estimated as ratio of the specific fluorescence to the isotypic one. MCF-7 cell culture was used as a reference for the control of antibody activity. Three indexes of ER beta expression level were used for the comparison: high – ER beta revealed more than in 50% of the cells; moderate – in 30-49%; low – less than in 30%. Two indexes of ER beta expression intensity were used: high – specific cell fluorescence is higher 2.0 times and more than

isotypic control; low – less than 2.0 times higher.

Results and Conclusion: In all investigated patients ER beta was revealed in about 80% of cases. Low ER beta level was shown in 42%, high – in 30% and moderate – in 28% of patients. Low expression intensity – was revealed in 46%, high – in 54% of cases. In women as compared to men median of ER beta level was in about 1.4 fold higher (46±19.2% and 34±16.8% respectively, p=0.01); but there was no significant difference in expression intensity (2.3±1.0 and 2.8±1.6, p=0.12). High ER beta level was revealed more frequently (p<0.05) in women (50% of patients) than in men (24% of patients). Low ER beta level was revealed more frequently in men than in women – in 19% and 63% of patients (p<0.05). Moderate ER beta level in women was the same as in men – in 32% and 27% of cases (p>0.05). High ER beta expression intensity was revealed in 68% of women and 49% of men (p<0.05), and low – in 32% of women and 51% of men (p<0.05). NSCLC is characterized by high and moderate level of ER beta in about half of cases. Higher ER beta level in women than in men could be one of the reasons in gender differences of NSCLC disease progress. We believe that at least half of the NSCLC patients (more often – women) with tumor ER beta expression could benefit from adjuvant antiestrogen therapy similarly to breast cancer patients. ER beta has to be obligate marker among the other proteins studying in NSCLC patients. Supported by RFBR (N10-04-00551-a,N12-04-00028-a).

Disclosure: No significant relationships.

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Biology and Pathogenesis

P2.29: REACTIVE OXYGEN SPECIES AS MAIN FACTORS CONDITIONING CELL DEATH IN RESPONSE TO ALA-BASED PHOTODYNAMIC THERAPY IN HUMAN LUNG ADENOCARCINOMA SPHEROIDS

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Background: Photodynamic therapy (PDT) is an approved anticancer treatment modality that eradicates tumor cells by the photochemical generation of reactive oxygen species (ROS) following absorption of visible light by a photosensitizer, which is selectively taken up by malignant cells. 5-Aminolevulinic acid (ALA) is the biological precursor of Protoporphyrin IX, the only endogenous photosensitizer. Multicellular spheroids (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. Previously, we found that cells cultured in MCSs appear to be more resistant to photodamage than cells cultured in monolayers, as the light dose yielding 50% cell death after PDT (LD50) determined by the MTT assay and the APH assay, was lower in cells growing in monolayers (7 min) than in spheroids (10 min). The aim of this study was to detect the limiting factors conditioning PDT efficacy in MCSs.

Methods: ALA -PDT was performed in A549 human lung adenocarcinoma cells growing as monolayers or as MCSs. These were initiated by seeding 5x104 cells/ml on 3% agar:RPMI (1:1) coated wells and harvested after 7 days with periodic fresh medium renewal. Cells were incubated with 1 mM ALA for 3 h followed by irradiation with a bank of two fluorescent lamps (Osram L36W/10, 0,4 J/cm2) for different times and within 1 h analyzed for PDT-induced events.

Results and Conclusion: Porphyrin synthesis was not significantly different between monolayers and MCS, 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. With normal PpIX synthesis and distribution, the limiting factor on PDT efficacy could be light penetration into the inner section of the MCSs. To this end, spheroids were trypsinized and cells counted for apoptosis by acridine orange/ethidium bromide staining and AnnexinV-FITC/propidium iodide labelling. Results showed a higher percentage of viable cells when 20 min-irradiation PDT was performed on spheroids (66,57±6,5%) compared to monolayers (3,5±0,2%). Moreover, caspase-3 expression and cytochrome c release were also lower in MCSs. To visualize cell photodamage in intact spheroids, histological sections were stained for general morphology with hematoxylin/eosin, PAS staining for mucopolysaccharides, and Ki67 immunostaining as proliferation marker. Results showed that not only can light pass through the structure of the spheroid, but also that PDT can disrupt cellular morphology, secretory differentiation (which is consistent with the adenocarcinoma histology of the cell line) and cell proliferation. Another limiting factor on PDT efficacy could be a defective ROS production in MCSs, therefore, singlet oxygen (the main effector of PDT-induced cell damage) and superoxide anion generation were assessed by flow cytometry. It was found that both ROS production were significantly lower in MCSs (1O2: 5,5±2,7%; O2-: 4,8±0,3%) compared to monolayers (1O2: 83,5±1,9%; O2-: 70,6±8,1%) after 20 min PDT. These results indicate that oxygen availability and not porphyrin synthesis or light accessibility might be the conditioning factor for the differential response of MCSs to ALA-based PDT.

Disclosure: No significant relationships.

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Biology and Pathogenesis

P2.30: TUMOR SUPPRESSOR FUS1 PROVIDES A MOLECULAR LINK BETWEEN INFLAMMATORY RESPONSE AND MITOCHONDRIAL HOMEOSTASIS

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Background: Fus1, a tumor suppressor on chromosome 3p21.3, is down-regulated, mutated, or lost in the majority of inflammatory thoracic malignancies. Although its biological function remains unknown, mitochondrial localization suggests involvement of Fus1 in mitochondrial activities. Our earlier studies revealed the importance of Fus1 for immune system regulation and inflammation.

Methods: In this work, we investigated how Fus1 modulates inflammatory response and mitochondrial function on a mouse

model of asbestos-induced peritoneal inflammation.

Results and Conclusion: We found that peritoneal infiltrate in Fus1-/- mice even without asbestos contained an ~8-times higher proportion of granulocytes than Fus1+/+ mice pointing at ongoing chronic inflammation. Asbestos treatment results in a decrease of Fus1 expression in WT peritoneal immune cells suggesting that asbestos exposure may compromise the Fus1-mediated inflammatory response. Indeed, disbalanced response in asbestos-treated Fus1-/- mice was apparent by the decreased immune organ weight and total protein concentration in peritoneal lavage alongside with the increased proportion of peritoneal macrophages. Fus1-/- mice showed augmented asbestos-induced activation of key inflammatory, anti-oxidant, and genotoxic stress response proteins ERK1/2, NFkB, SOD2, γH2AX, etc. Moreover, Fus1-/- mice showed altered dynamics of pro- and anti-inflammatory cytokine expression, such as Ifn-γ, Tnf-α, Il-1a, Il-1b, and Il-10. "Late" response cytokine Ccl5 was under-expressed in Fus1-/- immune cells at both basal and asbestos-activated states. Noteworthy, we observed a substantial asbestos-related difference in the size of CD3+CD4-CD8- DN T cell subset that was expanded 4-fold in Fus1-/- mice. Finally, we demonstrated profound Fus1-dependent basal and asbestos-induced changes in major mitochondrial parameters (ROS production, mitochondrial potential, and UCP2 expression) in Fus1-/- immune cells and in Fus1-depleted cancer cells, thus confirming our hypothesis that Fus1 may establish its immune and tumor suppressive activities via regulation of mitochondrial homeostasis.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Biology and Pathogenesis

P2.31: THE EFFECT OF GENDER ON RADIATION-INDUCED ACUTE LUNG INJURY IN A RAT MODEL

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Background: There are very few studies investigating of sex-specific differences in acute and late toxicity after radiotherapy in the literature. Our aim was to evaluate the effect of gender-related difference on acute lung injury induced by radiation (RT) in male and female Wistar rats.

Methods: Forty Wistar rats (Twenty male and twenty female) were divided into following groups: (1) control male - sham RT; (2) RT-male; (3) control female - sham RT; (4) RT-female. Radiation was delivered on a Linac unit using a single fraction of 10 Gy through an anterior portal covering the right lung in entirety. The rats underwent euthanasia at 6 weeks following radiation. The lungs were dissected and histopathological evaluation was performed.

Results and Conclusion: The development of RT-induced changes was statistically higher in the RT-male and RT-female groups as compared to the control groups (RT-induced pneumonitis: RT-male and control male, p=0.004, RT-female and control female, p=0.01; Vasculitis: RT-male and control male, p=0.009, RT-female and control female, p=0.08). No significant difference between RT-male group and RT-female group was detected in the development of RT-induced pneumonitis (60% vs. 50%, respectively, p=0.66) and vasculitis (80% vs. 70%, respectively, p=0.61).The data suggest that there are no gender-related differences in radiation-induced acute effects in the lung tissues of male and female rats. However, we believe that additional work is needed to better identify the influence of sex on RT-induced normal tissue injury.

Disclosure: No significant relationships.

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Biology and Pathogenesis

P2.32: EGFR AND K-RAS MUTATIONS IN FIXED AND FRESH SPECIMENS FROM TRANSESOPHAGEAL ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION (EUS-FNA) IN NSCLC PATIENTS

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Background: In Non Small Cell Lung Cancer (NSCLC) patients, somatic EGFR and k-ras mutations predict therapeutic effectiveness and resistance, respectively, to EGFR tyrosine kinase inhibitors (TKIs). Transesophageal ultrasound-guided fine needle aspiration (EUS-FNA) is a validated technique for diagnosis and staging of NSCLC. In the present study we compare the feasibility and reliability of EGFR and K-ras gene mutation analysis in fixed and fresh mediastinal lymph nodes and extra-lymphonodal samples obtained by EUS-FNA in patients suspicious for NSCLC.

Methods: Thirty-six patients were selected for the EUS-FNA procedure. A rapid on-site cytological examination (ROSE) was performed to assess the suitability of the sample. When a sample was identified as metastatic at ROSE examination, fresh material was collected in hypertonic solution (9%) and sent for molecular analysis. When possible, a sample obtained from metastatic nodes was processed as a histology core (cell block). Fixed and stained cytological smears, which had undergone selection of the tumor cells, were also sent for molecular analysis. For each patient, DNA was extracted from both fresh samples and fixed cytological smears. Exons 18, 19, 20 and 21 of EGFR and exon 2 of K-ras were amplified by PCR and mutation status was determined by direct sequencing and pyrosequencing analyses.

Results and Conclusion: All cases were eligible for analysis. NSCLC was diagnosed in 32 patients (25 adenocarcinomas and 7 squamous cell carcinomas) and 4 patients were free of malignancy. Of the 25 patients with adenocarcinoma, EGFR mutations were detected in 2 (8%) fresh tumor samples and in 3 (12%) fixed cytological smears. K-ras mutations were detected in 8 (32%) fresh samples, and in 9 (36%) fixed cytological smears. In conclusion we have demonstrated that EUS/FNA samples are suitable to define tumor EGFR and K-ras mutation profiles aimed at a personalized treatment, and that the accurate selection and cleaning of tumoral cells is mandatory for an accurate analysis. To this purpose, fixed and stained samples are more reliable than fresh materials.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Biology and Pathogenesis

P2.33: POTENTIAL LOSS OF P53/P21 FUNCTION IN A MURINE LUNG ADENOCARCINOMA CELL LINE PREVENTS TGFB1-INDUCED DORMANCY DESPITE P38A/B ACTIVATION AND DEC2 AND P27 INDUCTION

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Background: Disseminated tumor cells can reside in target organs in a state of dormancy for prolonged periods before developing into overt lesions. Studies using the HEp3 model of head and neck squamous cell carcinoma (HNSCC) showed that a low ERK:p38 signaling ratio predicts for cellular dormancy. Further, p38 activation induces the expression of p53 and the tumor/metastasis suppressor BHLHB3/DEC2. Also, p53 and DEC2 are positively regulated by transforming growth factor beta (TGFβ). Preliminary data studying the murine lung adenocarcinoma cell line LP07 suggested that TGFβ1 can only delay primary tumor growth with no effect on spontaneous metastasis development. This motivated us to test whether the effects of TGFβ1 signaling in this model might be short-circuited to prevent the activation of a tumor cell dormancy program as that described in HNSCC.

Methods: TGFβ1 (4ng/ml), an inhibitor of TGFβ-receptor kinase activity (TβR inhibitor, 2μM) or a MEK1 inhibitor (10μM) were used for LP07 cell treatment. In overexpression experiments, constructs containing DEC2, a constitutive active mutant of p38 (p38CA), or p53 were employed. Cell proliferation was assessed in vitro by manual cell counting and cell cycle distribution analysis; and in vivo by evaluating tumor growth. DEC2 mRNA expression was assessed by qPCR. Expression of downstream effectors of TGFβ1 and cell cycle regulatory proteins were assessed by western blot.

Results and Conclusion: TGFβ1 mediated arrest in G0/G1 phase of the cell cycle in LP07 cells, which was consistent with p27 upregulation. Concomitantly, TGFβ1 activated Smad2/3 and inhibited proliferation, all these events blocked by a TβR inhibitor. Consistent with these data, LP07 cells exhibited a high ERK:p38 ratio that was lowered by TGFβ1, primarily due to a strong p38 activation. Accordingly, we observed in vivo growth inhibition of TGFβ1-pretreated cells upon subcutaneous implantation in syngeneic BALB/c mice. However, sustained in vivo growth arrest was not observed. We also found an increased level of DEC2 mRNA in TGFβ1-treated cells. LP07 cells overexpressing DEC2 or p38CA had increased p27 expression, suggesting that the p38->DEC2 pathway can be re-activated. Upon treatment of the cells with a MEK1 inhibitor, p27 was also upregulated and phospho-histone-H3 was downregulated. p53 and p21 were refractory to modulation by these treatments, even following overexpression of p53. This suggests that p53 function might be disrupted and/or that p21 may be epigenetically silenced in this cell line. In conclusion, we have found that the LP07 cell line displays an ERK/p38 ratio and downstream signaling that predict for an efficient escape from dormancy. While the p38->DEC2-p27 pathway could be restored by establishing a low ERK/p38 signaling ratio, absence of functional p53 and p21 induction most likely explains why TGFβ1 only attenuates tumor growth. If p53 and p21 (also a target of DEC2) are silenced by DNA promoter methylation it is possible that restoration of p21 promoter sensitivity to DEC2 using 5-Aza-C may allow for reprogramming LP07 cells into a prolonged dormant state.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Biology and Pathogenesis

P2.34: ALTERED MRNAS EXPRESSION OF GENES INVOLVED IN CELLULAR IRON HOMEOSTASIS IN LUNG NON SMALL CELLS CARCINOMA

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Background: Iron is an essential element for cell proliferation and cell metabolism. The high proliferative rates in malignant cells are characterized by an increased requirement for iron. Recent study shows the association between tumors and altered cellular iron homeostasis. The transferrin receptor type 1 (TFRC), expressed on the cytoplasmatic membrane of human cells, is thought to play a crucial role in the control of cell growth mediated by iron. Abnormal expression of TFRC was identify in several tumors types, as carcinomas, sarcomas and some lymphomas and leukaemias. Furthermore, a correlation between lower intracellular iron content, due to decreased iron intake or high iron export, and patients favorable prognosis was recently identified in breast cancer. The purpose of the present study was to investigate the expression of some genes involved in cellular iron homeostasis in lung non small cells carcinoma (NSCLC) library. TFRC gene, that codifies for a protein involved in tranferrin dependent iron import, SLC40A1 gene, that codifies for the only known iron exporter, and FTL, that produces the main intracellular iron storage protein were analyzed. Moreover, the correlation between these genes expression and clinico-pathological factors were performed.

Methods: A real-time PCR analysis on matched cancer and corresponding normal tissues from 78 surgically resected patients has been performed. Expression levels of SLC40A1, TFRC, FTL and ESD as reference gene, were evaluated via SYBR technology with ABI PRISM 7900HT Sequence Detection System using specific primers.

Results and Conclusion: TFRC & SLC40A1 genes modulation were significantly dysregulated in lung tumors respect to matched normal tissues. In particular, TFRC was up- ($p=0.01$, mean $\log2(FC)=1.07$) while SLC40A1 was down-modulated ($p=0.001$, mean $\log2(FC)=-1.1$). Moreover, TFRC up-modulation was significantly associated with moderately and poorly differentiated lung cancers ($p=0.01$), squamous carcinomas ($p<<0.01$) and in active smokers/early formers ($p=0.03$). No correlations with patients survival rate were identified. FTL was expressed at high levels respect of the other mRNAs evaluated in both tumors and normal lung tissues, its down-modulation in tumor samples was associated to squamous tumor subtype ($p=0.02$). Down modulation of FTL under $\log2(FC)$ -1 was

associated with poor patients prognosis (p=0.01) and it resulted to be an independent prognostic factor for patients overall survival (HR=2.5; 95% CI, 1.20 to 5.3, p=0.01). These results indicate that transcription alteration of genes involved in cellular iron homeostasis occurs in lung cancers and that it could contribute to the carcinogenesis and de-differentiation of lung cancers. Furthermore, the discrepancies identified for the expression of some genes between the lung tumors subtypes could reflect differences in cellular iron intake and could be useful to better define the molecular differences between lung cancer subtypes and/or to develop future patients personalized therapy.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Biology and Pathogenesis

P2.35: ROS1 FUSION GENES: POTENTIAL DRUG TARGETS IN NON-SMALL CELL LUNG CANCER

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Background: Genomic rearrangements that fuse kinase domain-containing 3' regions of tyrosine kinase genes with 5' regions of unrelated genes are well characterized in cancer. The resulting fusion proteins often drive proliferation and invasion of tumor cells and thus represent attractive targets for therapeutic intervention. One such kinase that has been demonstrated to be involved in various genomic rearrangement events in non-small cell lung cancer (NSCLC), glioblastoma, and cholangiocarcinoma is the ROS1 receptor tyrosine kinase. To date, seven different 5' fusion partners for ROS1 have been identified.

Methods: In this study, we examined the frequency of ROS1 gene rearrangement in a panel of 428 patient-derived NSCLC tumor samples using a break-apart FISH assay.

Results and Conclusion: We found that approximately 1.2% of samples were positive. In positive samples, the expression of the fusion gene and the identity of the fusion partner were examined. HCC78 is a NSCLC cell line that has been demonstrated by us and others to express the SLC34A2-ROS1 gene fusion. In order to assess the cellular consequences of ROS1 inhibition, we treated HCC78 cells with two distinct small molecule kinase inhibitors that have activity against ROS1 (crizotinib and TAE684). We found that both drugs inhibited proliferation of HCC78 cells, down-regulated signaling pathways known to control cellular growth and survival, and disrupted normal cell-cycle progression. Finally, we report clinical data from a NSCLC patient with a ROS1 gene rearrangement who demonstrated tumor shrinkage when treated with crizotinib. This patient's tumor expressed the recently identified SDC4-ROS1 fusion. In conclusion, genomic rearrangements involving the ROS1 receptor tyrosine kinase are present in a subset of NSCLC patients and drugs that target ROS1 may be an effective treatment strategy for these patients.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Biology and Pathogenesis

P2.36: INTRAOPERATIVE BRONCHOSCOPIC COIL-MARKING, USING VIRTUAL BRONCHOSCOPIC NAVIGATION WITH ENDBRONCHIAL ULTRASOUND TO FACILITATE SMALL PERIPHERAL PULMONARY NODULE RESECTION

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Background: In thoracoscopic surgery, the identification of a lesion during the operation is important. It had been reported that the lesions that have diameters of <10 mm and that are >5 mm from the pleura were very difficult to thoracoscopically detected. To facilitate marking and to reduce its complications, we performed thin bronchoscopic coil-marking using virtual bronchoscopic navigation (VBN) with endbronchial ultrasound before fluoroscopy-assisted thoracoscopic surgery for small pulmonary peripheral lesions. We then evaluated the feasibility, safety, and efficacy of this technique.

Methods: Enrolled all subjects were consecutive patients with small pulmonary peripheral lesions (<15 mm) showing a CT scan-confirmed ground-glass opacity pattern who were referred to Kameda Medical Center for thoracoscopic surgery between June 2011 and March 2012. VB images to the planned marking sites near each lesion were produced from helical CT scan data. Based on these images, a thin bronchoscope was advanced to the target bronchus as far as possible in this pathway. Radial EBUS (R-EBUS) probe was then advanced to the target lesion under radiologic fluoroscopy guidance. After visualization of the lesion by R-EBUS, the probe was removed leaving the guide sheath in place, and platinum vascular coil was pushed to the target by guidewire and indwelling under fluoroscopy-assisted.

Results and Conclusion: Our study included 4 patients (4 females) with 4 lesions, mean age 69 years. The mean lesion size was 11.8mm in diameter. Pathologic studies revealed primary lung cancer in all lesions (papillary adenocarcinoma; 1, bronchioloalveolar adenocarcinoma; 3), the bronchial branching patterns seen in VB images were highly consistent with those confirmed using the bronchoscope. Therefore, thin or ultrathin bronchoscope could be guided to a median of the fifth generation bronchi (range, fourth to sixth generation bronchi) toward the planned marking sites. Marking was achieved without causing complications in any of the patients. The median shortest distance between the coil-marker and the lesion was 3mm (within 5 mm in 4 lesions). In patients undergoing thoracoscopic surgery, all coil-marked sites were identified by intraoperative radiographic fluoroscopy, and all lesions were resected. This method can be readily performed without complications and is a useful marking method before fluoroscopy-assisted thoracoscopic surgery for small pulmonary peripheral lesions showing a CT scan-confirmed ground-glass opacity pattern.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Biology and Pathogenesis

P2.37: STENTING OF UPPER AIRWAYS IN PATIENTS WITH PRIMARY AND RECURRENT LUNG CANCER

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Background: To evaluate the effectiveness of upper airway stenting in patients with primary and recurrent lung cancer.

Methods: From May 2007 to March 2012 31 patients (15 males, mean age 67±10.6 years) with primary (27) and recurrent (4) lung cancer (NSCLC – in 25, small cell – in 4, other - in 2) had 33 episodes of upper airway stenting (Ultraflex, Boston Scientific) under GA with fluoroscopic control as part of oncological treatment. There were 18 unilateral (right – in 8, left – in 10), 7 – tracheal, 2 - tracheobronchial and 6 – bilateral procedures. Covered stents were used 5 times only. Seven patients had a concomitant procedure (chest drain insertion – in 2, cryotherapy – in 2, empyema drainage – in 1, pleural biopsy – in 1 and oesophageal stent insertion – in 1) under the same GA. On 11 occasions the procedure was elective, on 19 urgent and 3 times it was an emergency.

Results and Conclusion: There was no intra-operative mortality. Two (6.4%) patients died in hospital prior to discharge, 19 discharged home and 12 were transferred to another hospital. Four patients required stent replacement or insertion of an additional stent during the follow up period. Tumour debulking with cryotherapy was required in 5 patients after stenting. Hospital stay ranged from 1 to 17 (mean – 4.2, median – 2) days. Hospital stay in patients with concomitant procedure ranged from 1 to 17 (mean – 7.8, median – 5) days. Total survival ranged from 2 to 590 (median – 55) days, in primary cancer subgroup – from 2 to 332 (median – 57) and in the recurrent subgroup – from 19 to 590 (median – 48) days. In urgent and emergency groups survival ranged from 2 to 332 (median 54) and in the elective group – from 8 to 590 (median – 97) days. Survival in patients with concomitant procedure ranged from 14 to 453 (median – 55) and without concomitant procedure from 2 to 590 (median – 55) days. All patients reported significant improvement of distressing symptoms. Upper airway stenting is a rapid and effective technique of palliation in patients with tracheobronchial stenosis caused by primary and recurrent lung cancer. Survival is better in patients with elective endobronchial stent insertion. Concomitant procedure does not adversely influence survival. Stent occlusion may be controlled by repeat stenting or endobronchial cryotherapy.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.38: 18[F] FDG- PET/CT FUSIONS IMAGING IS SUPERIOR, CRYSTAL CLEAR AND PREDICTS SURVIVAL OF LUNG CANCER PATIENTS

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Background: Lung cancer is the leading cause of cancer-related deaths in men and women worldwide. It is the most common malignancy and has the highest cancer related death rate. Non-small cell lung carcinoma (NSCLC) accounts for 80% of cases and small cell lung cancer (SCLC) accounts for the remaining 20%.Approximately 75% of SCLC cases presents with disseminated disease. Lung cancers most commonly metastasize to the lymph nodes, bone, brain, adrenal glands, and liver. Positron Emission Tomography and Computer Tomography with 18(F)-labeled Fluoro-deoxyglucose (18F-FDG PET/CT) plays a clear role in lung cancer management. PET/CT is increasingly used in the diagnosis, staging and monitoring response to treatment. Evaluation of response to treatment include the clinical response for example; symptom reduction, improved quality of life, disease-free survival, progression-free survival, and overall survival, and imaging response with PET/CT.

Methods: During the study period, 20 cases of lung cancer, 16 (80%) male and 4 (20%) female with age ranges from 26 to 71 years, were included and evaluated by PET/ CT. All the cases were diagnosed radiological and histopathologically,prior to this study. A standard dose of 10 mCi [370MBq] IV 18(F) FDG was injected to patients and after one hour, patients were taken for CT and PET examination. The SUVMax: > 2.5 is considered metabolically active.All the investigation(PET/CT) were reviewed in detail.

Results and Conclusion: The findings of PET / CT were reviewed and compared with other imaging (CT / MRI) and medical records, etc. During the interpretation of the PET/CT images, the findings were a focus / foci of markedly increased FDG uptakes in lung and metastasis in lymph nodes, brain, bones and adrenal glands. Of 20 cases, 15 (75%) were positive for primary cancer and metastasis in other organs, 5 (25%) were found normal in PET/CT. The organs involved in distant metastasis (n=15) in order of frequency were lymph nodes 6 (40%), bone 3(20%), adrenal glands 3 (20%), pleural effusion 1 (6.66%), liver 1 (6.66%), and lung metastasis in 1 (6.66%). 13 of 15 of our patient had multiple organ involvements. PET/CT is superior, crystal clear and useful imaging method which predicts survival of lung cancer patients. It is useful for detecting lung cancers and distant metastases and contributes to a more accurate staging.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.39: THE SYMPTOM MANAGEMENT MODEL(SMS) TOOL FOR PREDICTION AND ASSESSMENT OF CERTAIN SYMPTOMS THAT AFFECT QUALITY OF LIFE OF PATIENTS WITH SMALL AND NON SMALL CELL LUNG CANCER CANDIDATES FOR RADIOCHEMOTHERAPY

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Background: The communication of the diagnosis of cancer

has a devastating impact on QL of the patient worsens in stages during treatment,stage of disease and the prospect of life and this is evident in patients with lung cancer.Therefore,predict and understand these factors.is fundamental to the team in order to implement care interventions and targeted support.

Methods: The Symptom Management Model(SMM)was applied as the conceptual framework of the study, from December 2007 - March 2011 after information and written informed consent,acceded to the study 40 patients(34 men, 6 women) mean age 64,2 years(±SD 6.42),median 64 years)with small and non small cell lung cancer(histologically confirmed and clinically staged)candidates for radiochemotherapy under the DH.To pts were delivered to the following evaluation questions:4DSQ,FACIT,VAPS,HAM-D,BSDS and IBCSG-QL.All questionnaires were completed and delivered.The data were analyzed with statistical methods using Stepwise Regression Statistic(SRS).

Results and Conclusion: The predictive power was 82% of the variance(p<.01) indicating that the SMM is a useful guide for explaining and predicting quality of life of patients with lung cancer and for the clinical stage,are subjected to radiochemotherapy. The findings revealed that the mean scores of QL(X=66.43)was at the moderate level; significantly predictors were depression (p<.01), sleep disturbance (p<.01), fatigue(p<.01) and stage of disease (p<.01). Conclusion: pain,fatigue,and depression are complex affective,sensory,and cognitive phenomena and all of these symptoms, as well as sleep disturbances, are also in this type of patients known with lung cancer undergoing radiochemotherapy. Our results indicate that the questionnaires is a useful guide to explain and predict depression, sleep disturbance,fatigue and disease stage,parameters that would significantly QL

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.40: INCIDENCE OF PAIN IN CA. LUNG PATIENTS REFERRED TO PALLIATIVE CARE

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Background: Lung cancer being the major cancer in Men in the world, in developing country like India Ca. Lung constitutes 7.1%(Men) and 2%(Women). Still majority of our patients present to hospital in an advanced stage. More than 80%will be having pain in this stage and they need only palliative care as there is no role for curative treatment.

Methods: METHOD: 446 patients were screened who were referred to palliative care department over a period of 3 months from all the departments. Total 38 patients with diagnosis of Ca. lung were referred from Surgical and Medical oncology.

Results and Conclusion: Results: 90% of patients had pain at the time of reporting to palliative care centre. Conclusion: Routine referral to Palliative care centre from the day of diagnosis solve many problems in ca Lung patients. Early referral will improve patients comfort from pain.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.41: THE EFFICACY OF CT GUIDED PERCUTANEOUS CRYOABLATION IN LUNG CANCER

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Background: Lung cancer has been the commonest cause of cancer death, with a very poor survival rate. By the time of diagnosis, most cases are at an advanced stage. In recent years, little progress has been in improving the quality of life of patients with advanced lung cancer. This has added to the importance of alleviating the symptoms and improving quality of life for patients with advanced stage, inoperable patients. While the possiblity of surgery has been limited, the other palliative measures must be considered.

Methods: From Jan 2002 to Apr 2006, 816 patients(568 male and 248 female) at an median age of 64±1.2 years old(range from 12 to 95 years old) with primary or metastatic lung cancer were treated with cryoablation, including 685 patients with primary lung cancer with 46 patients in stage I, 137 in stage II, 296 in stage III and 206 in stage IV (small cell lung cancer n=51, non small cell lung cancer n=634, squamous carcinoma n=310, adenocarcinoma n=265, undifferentiated carcinoma n=40, alveolar cell carcinoma n=19) and 131 patients with metastatic lung cancer(breast n=45, colon n=42, prostate n=11, bone n=8, sarcoma n=2).. A total of 1139 cryoablations were done for 1014 lesions, which with mean diameter of 6.3±0.4 cm (ranged from 1.0 to 25.0cm). Cryocare Surgical System (CRYO-20 type) and cryo-probes with 1.7 mm or 2.0 mm in diameter were used in the present study. According to the size, shape and location of the lesion, 2-8 cryo-probes were inserted as following: 1-2 cryo-probes for the tumor smaller than 2 cm in diameter, 2-4 cryo-probes for tumor with 2-4 cm in diameter, and 5-8 cryo-probes for tumor up to 5 cm or more. Freeze-thaw cycle was set as 15 min of freezing at -140±10°C with argon and 5 min of thawing at 15±5°C with helium. Three freeze-thaw cycles were performed during each cryoablation. Recheck CT or PET/CT and reappraise Karnofsky Performance Status (KPS) every 1-3 monthes, and followed up every 3 months.

Results and Conclusion: There were 1006 lesions (68.3%) decreased in size, and with mean size reducing from 4.7±0.3 cm to 3.5±0.4 cm in diameter, (CR+PR+SD) 91.2%. Tumor activity of all lesions decreased or deactivated. Paitents showed obvious improvement after treatment, with Karnofsky Performance Status (KPS) rising form 77.8±9.3 to 85.92±7.8 (t=4.368, P=0.000). Among 202 patients with peripheral lung cancer and chest wall invasion who complained chest pain pre-cryoablation, 40 patients (19.8%) showed complete pain relief after cryoablation and 124 patients (61.4%) showed partially pain relief, respectively. The overall survival rates were 70.2%% for 1-year and 54.1% for 2-year. The 1-year survival rate were 100.0%, 93.5%, 84.1%, 57.6% and 49.0%, and 2-year survival rate were 100.00%, 81.36%, 71.27%, 48.19% and 38.48% for patients in stage I, stage II, stage III and stage IV of primary lung cancer and metastatic lung cancer, respectively. CT guided cryoablation showed some efficacy in controlling the progress of lung cancer and may contribute to pain relief and prolong

survival for lung cancer patients. KEYWORDS: Cryoablation, lung cancer, CT-guided, efficacy

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.42: ENOBOSARM IMPROVES PHYSICAL FUNCTION IN CANCER PATIENTS WITH < OR ≥ 5% WEIGHT LOSS IN A PHASE IIB TRIAL

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Background: Although cachexia has been defined as >5% weight loss, limited data exists on the prevention and treatment of muscle wasting prior to a patient becoming cachectic. Cancer induced muscle wasting can begin early in the course of a patient's malignancy resulting in decline in physical function and other detrimental clinical consequences including less tolerability to chemotherapy, worse outcomes, and shorter survival - underscoring the importance of diagnosing and treating this condition at an early stage.

Methods: We conducted a randomized, double blind, placebo controlled, multi-center study to evaluate the effect of enobosarm on physical function and muscle wasting in cancer patients. Subjects (n=159) were randomized to oral enobosarm or placebo for 16 weeks. Subjects were males >45y and postmenopausal females, with ≥2% weight loss in the 6 months prior to randomization and diagnosed with NSCLC, colorectal cancer, non-Hodgkin's lymphoma, chronic lymphocytic leukemia or breast cancer. We report on changes in physical function based on weight loss of < or ≥5% in the 6 months prior to randomization.

Results and Conclusion: Results: 103 subjects (MITT) had physical function assessed by stair climb at baseline and week 16 with 24% losing <5% weight in the previous 6 months. Distribution of weight loss was similar across genders, however subjects with <5% weight loss were more likely to be ECOG=0 (<5% loss: 46.2%; ≥5% loss: 35.8%). Subjects with ≥5% weight loss had worse physical function at baseline compared to those with <5% loss (P=0.048). A significant improvement in physical function was observed in subjects that received enobosarm regardless of baseline weight loss (<5% loss, P=0.041, ≥5% loss, P<0.001) while subjects that received placebo failed to improve. Conclusions: Enobosarm was generally well tolerated and showed a statistically significant improvement in physical function in cancer subjects regardless of baseline weight loss. These data provide evidence that enobosarm may play an important role in the management of cancer patients by not only treating, but also preventing further decline in physical function and muscle wasting before a patient becomes cachectic.

Disclosure: I am an employee of GTx, Inc.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.43: IN A PHASE IIB TRIAL IN CANCER PATIENTS WITH MUSCLE WASTING, ENOBOSARM IMPROVES PHYSICAL FUNCTION IN BOTH HYPOGONADAL AND EUGONADAL SUBJECTS

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Background: Hypogonadism has been associated with weight loss and poor outcomes in cancer patients. Up to 50% of males with advanced cancer are hypogonadal at presentation or during the course of treatment. Wasting in cancer patients has also been associated with a decline in physical function and performance status and has major public health significance. We conducted a Phase IIb, randomized, double blind, placebo controlled, multi-center study to evaluate the effect of enobosarm on muscle wasting and physical function in cancer patients.

Methods: Patients (n=159) were randomized to oral enobosarm (1 or 3 mg) or placebo daily for 16 wks. Patients were males >45 y and postmenopausal females, had ≥2% weight loss in the 6 mths prior to randomization, BMI <35 and either NSCLC, colorectal cancer, non-Hodgkin's lymphoma, chronic lymphocytic leukemia or breast cancer. We report on the incidence and impact of hypogonadism (T<300 ng/dL) in this population.

Results and Conclusion: Baseline testosterone levels were available for 93 of 103 men. 60% of male patients were hypogonadal at randomization. Distribution of hypogonadism was similar across cancers; however hypogonadal men were less likely to complete the study. Baseline T levels were positively correlated with weight loss (r=0.32, P=0.002,) with hypogonadal men demonstrating greater weight loss in the previous six months (median, -9.5%). Baseline physical function as measured by stair climb power was higher among eugonadal males compared to hypogonadal males (84.5 watts vs 70.6 watts; P=0.016). Enobosarm significantly improved physical function in this population regardless of baseline gonadal status (hypogonadal: 18.7%, P=0.0061; eugonadal: 13.2%, P=0.0032). The magnitude of improvement was greater in hypogonadal men. Conclusions Hypogonadism is common in male cancer patients and is correlated with weight loss and diminished physical function. In this randomized, placebo controlled trial, enobosarm improved physical function in both hypogonadal and eugonadal men despite poorer baseline physical function in hypogonadal patients. These data provide evidence that enobosarm may play an important role in the management of cancer related muscle wasting.

Disclosure: I am an employee of GTx, Inc.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.44: ASSESSMENT OF PAIN AND PULMONARY FUNCTION IN PATIENTS UNDERGOING THORACOTOMY BROAD AND MINIMALLY INVASIVE THORACOTOMY

Juliana D. Leandro[1], Rogério Traballi[2], Camila Guerra[2], Tiaki Maki[2], Adilson Antunes[2]
[1]Fisioterapia, Unip, Sao Paulo/BRAZIL, [2]Unip/BRAZIL

Background: In the diagnosis of lung tumors in common practice to total or partial resection of the lung tissue via thoracotomy in consist that large opening in the chest cavity for diagnostic or therapeutic purposes. However it is know that such a procedure because of the surgical procedure adopted, will cause acute pain and chronic long-term interfere significantly in their lung volumes and capacities. In order to prevent acute pain and respiratory change caused by thoracic interventions, new approaches are being practiced as thoracotomies minimally invasive. The advent of video-assisted surgery in the last two decades, the practice allowed access to the lower thoracic cavity resections and favored by many economic thoracotomies. This has reduced the incidence of postoperative pain and complications of lung function. AIM: the aim of this study was to compare pulmonary function and postoperative pain in patients undergoing thoracotomy broad and minimally invasive thoracotomy.

Methods: This study was conducted in a public hospital of São Paulo under the approval of the Ethics Committee in Research of Universidade Paulista- UNIP. Inclusion criteria were patients of both gender 45-65 years undergoing extensive thoracotomy and minimally invasive with a diagnosis of carcinoma of the lung base. For postoperative evaluation was used visual analogue scale (VAS) for pain and pulmonary function testing by spirometry on postoperative day 15.

Results and Conclusion: 15 days after the surgical procedures the patient underwent a minimally invasive thoracotomy were level of pain related to 2 and pulmonary functions test with 14% reduction in forced vital capacity (FVC), 18% of forced expiratory volume in first second (FEV1) and 12% reduction in peak flow expiratory (PFE). Patients who underwent thoracotomy had ample level of pain equivalent to 6 with 32% reduction in FVC, 36%FEV1 and 28% en PFE. Both figures by visual analogue scale as well as the reduction shown by spirometry were statistically significant when compared between groups. CONCLUSION: Patients undergoing minimally invasive thoracotomies intensidde less pain in the postoperative period showed fewer change regarding their lung volumes and capacities.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.45: ASSESSMENT OF QUALITY OF LIFE IN PATIENTS WITH LUNGCANCER TREATED WITH CISPLATINUM-BASED CHEMOTERAPY: A PROSPECTIVE COHORT STUDY

Burcu Ozdemir[1], Osman N. Hatipoglu[2]
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Background: To assess the quality of life (QoL) over the chemotherapy cycles, patients' survival, and a relationship between QoL and survival in patients with lung cancer given cisplatinum-based therapy.

Methods: A total of 166 cases of lung cancer planned to get received cisplatinum-based regimen were enrolled into this prospective and cohort clinical study between March, 2004 and September, 2006. Patients completed the Lung Cancer Symptom Scale (LCSS) at baseline and before each cycle. Adverse effects due to chemotherapy were scored according to the NCI CTC (National Cancer Institute Common Toxicity Criteria) after each cycle. Overall survival and days of hospital stay of all patients were recorded.

Results and Conclusion: The mean baseline LCSS scores were 29.03 ± 19.72 in patients with non-small cell lung cancer (NSCLC, n=125) and 30.73 ± 22.66 in patients with small-cell lung cancer (SCLC, n=41) (p=0.80). In patients with NSCLC, no significant difference in the LCSS score between before and after each chemotherapy cycles was detected (p>0.05 for each cycles). In patients with SCLC, according to the assessment before 3rd cycle, the LCSS score improvement was detected significantly (p<0.05). The mean overall survival time was 316 ± 25 days in patients with NSCLC and 415 ± 59 days in patients with SCLC. There was an association between the mean LCSS score and overall survival in patients with SCLC (p=0.00, r: 0.55) but this was not the case for patients with NSCLC (P=0.09, r: 0.12). The mean days of hospital stay was 43 days (13.5 % of overall survival) for patients with NSCLC and 47 days (11.3 % of overall survival) for patients with SCLC. The adverse events were observed in 6 (3.6%) patients. The most common side effects of chemotherapy were alopecia (96.7%), weakness (73.2%), nausea-vomiting (65.4%), and constipation (41.8%). The cisplatinum-based chemotherapy improve quality of life for patients with SCLC. However, for patients with NSCLC, chemotherapy may not have a positive effect on quality of life and larger studies are needed to assess the influence of chemotherapy on quality of life in this patients group.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.46: PATIENTS WITH LUNG CANCER PRESENTING WITH ACUTE ARTERIAL OCCLUSION

Turan Ege, Serhat Huseyin, Volkan Yuksel, Sahin Iscan, Ozcan Gur, Selami Gurkan, Suat Canbaz, Enver Duran
Cardiovascular Surgery, Trakya University Faculty Of Medicine, Edirne/TURKEY

Background: Although the close association between venous thromboembolism and malignancy established by research, there are only limited number of studies addressing the relationship between arterial embolism and malignancy. Furthermore, in the literature, very rare case of lung cancer presenting with acute arterial embolism have been reported. Here, we present our series of lung cancer presenting with acute arterial occlusion during the period of 13 years at our institution.

Methods: The patients who were operated for acute arterial occlusion between 1999 and 2012 were evaluated retrospectively. Doppler ultrasonography was performed in all patients presented with the symptoms of acute arterial occlusion, after the initial physical examination. Emergent surgery was performed as indicated. The patients who were diagnosed to have cancer at the time of the operation or during the follow up were identified.

Results and Conclusion: In 883 patients who were operated for acute arterial occlusion, 33 patients (3.7%) were identified to have a malign neoplasm. Of these patients, 20 (69.6%) had a history of malignancy. For 13 patients (39.4%), acute arterial occlusion was the presenting sign of their malignant disease. Of these 13 patients, 5 had an arterial embolism occurring before the discovery of the lung primary. In these 5 patients, 4 of them had non-small cell lung cancer and 1 of them had small-cell lung cancer. Their age was varying from 60 to 84. All details of these 5 patients will be presented and discussed.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.47: PHYSIOTHERAPY IN THE POSTOPERATIVE OF LUNG CANCER

Juliana D. Leandro, Tiaki Maki, Camila Guerra, Adilson Antunes, Rogério Traballi
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Background: Lung cancer is a malign expansion and transformation of the lung tissue. It is the most lethal type of cancer in the whole world, responsible for 1,2 million deaths every year. Smoking habits are the main cause of the disease. The treatment depends specially on the type, "stage" and estadio (dispersion grade) of the cancer. Surgery, chemotherapy and radiotherapy are the most common treatments available. Usually after a lung surgery, patients are referred to physiotherapy practice in order to enhance the lung perfusion and ventilation ratio, conventionally with respiratory exercise support. OBJETIVE: To analyze the physiologic changes caused by respiratory exercise in patients submitted to segmentectomy for lung tumor

Methods: 10 lung cancer patients with average age of 40 years old were submitted to the protocol. PROCEDURE: Heart rate, respiratory rate and blood pressure were analyzed in all patients, before and after the application of the protocol. The protocol is based on the application of 5 sets of 10 repetitions of the following exercises: maximum inhalation held for six seconds, fractioned inhalation and exhalation. The results were statistically analyzed through test-t students.

Results and Conclusion: The respiratory rate after the protocol decreased in 18,8% (from 19,6 ± 1,2 to 15,9 ± 1,5 rpm) ($p < 0,05$), the heart rate had a non significative increase of 6,9% after the protocol (from 81,8 ± 5,0 to 87,5 ± 5,3 bpm) ($p>0,05$), the systolic blood pressure had a non significative increase of 1,15% (from 130,5 ± 8,7 to 132 ± 9,8 mmHg) ($p> 0,05$) and the diastolic blood pressure had a non significative decrease of 3,2% (from 76,5 ± 2,7 to 74 ± 2,6 mmHg) ($p> 0.05$). Conclusion The respiratory exercise when applied under a standard don't present a significant interference on the vitals readings of a lung resected patient, however can be responsible for the adequation of the respiratory rate of those patients.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.48: SMOKING EFFECTS ON TOLERANCE TO PHYSICAL EXERCISE

Juliana D. Leandro, Rogério Traballi
Fisioterapia, Unip, Sao Paulo/BRAZIL

Background: Smoking is now worldwide considered a public health problem, which is responsible for the increased prevalence of lung cancer, chronic obstructive pulmonary diseases and coronary artery disease. Smoking is even more harmful when associated with a sedentary lifestyle, which is seen as a primary factor for cardiovascular disease. The six-minute walk test is being used as an alternative to evaluate the physical capacity of patients with heart or lung disease. The test measures the distance a patient can walk on their own in a corridor for six minutes. Along with the test, the Borg scale was used, therefore the subjective perception of intensity of effort by the patient could be measured in numerical values (degree of fatigue), contributing greatly to the interpretation of results. OBJECTIVE: Investigate the effects on tolerance to physical exercise in sedentary young women.

Methods: The evaluation of 40 sedentary women was divided into two groups: Control group (20 non-smokers) and Smoking group (20 smokers). Firstly, data was collected on respiratory rate, heart rate and blood pressure. In sequence, they took the six-minute walk test. Immediately after the test, the level of effort on the Borg scale was verified and the women were assessed again, according to the parameters mentioned above. The distance covered in the walking test was also measured. The data were analyzed using the "Student's t test"

Results and Conclusion: In the control group of nonsmokers, there was no statistically significant difference between the results of the pre-test and the test. Taking into consideration the distance traveled by these patients (628m), the difference was statistically greater than the distance traveled by the smoking group (536m). The smokers showed statistically significant difference for heart rate and respiratory rate in relation to its preliminary assessment. As for the Borg scale, this group had an average value of five, higher than the control group, whose average value was three. Conclusion After the six-minute walk, there was a marked increase in respiratory rate, heart rate and feeling of tiredness in the smoking group. Also, the distance traveled by the smoking group was statistically lower than the distance traveled by the control group.

Disclosure: No significant relationships.

POSTER SESSION 2 - July 27, 2012 09:00 – 17:00

Supportive Care and Others

P2.49: HOW TO DISTINGUISH AN ACTIVE AIR LEAK FROM A PLEURAL SPACE EFFECT BY MEANS OF A DIGITAL CHEST DRAIN SYSTEM

Rita D.F. Marasco[1], Cosimo Lequaglie[2]
[1]Thoracic Surgery, I.R.C.C.S. - C.R.O.B. Basilicata Regional Cancer Institute, Rionero In Vulture/ITALY, [2]Thoracic Surgery, I.R.C.C.S. - C.R.O.B., Rionero In Vulture/ITALY

Background: In this prospective study we aimed to recognize a pleural space effect, distinguishing it from an active air leak, by means of a digital chest drain system providing a continuous air flow and pleural pressures check.

Methods: Since March 2010 to October 2011, we employed 144 digital drains for 125 patients undergone 138 thoracic surgical procedures.

Results and Conclusion: We observed: 18 active air leaks (12.5%), among which 4 prolonged (2.8%), all characterized by high differential pleural pressure, especially due to an increased mean expiratory pressure (>1 cmH2O) (p <0.0001), and significantly related to upper lobe resections (p: 0.00017), a chest tube removal time later than the fifth post-operative day (p <0.0001), an increasing pneumothorax after a one day provocative clamping (p <0.0001); three late air leaks (2.1%), all long lasting (p <0.0001), predicted by pressure curves divergency before the air flow appearance. Moreover, we reported 25 pleural space effects (17.4%), equally characterized by a high differential pleural pressure, but mainly due to a lower mean inspiratory pressure (<20 cmH2O) (p <0.0001), and especially related to surgical pleurodesis procedures (p: 0.0003) and wide lung resections (p: 0.0002); none of these patients had an increasing pneumothorax after provocative clamping. Conclusions: A digital chest drain system ensuring a continuous air flow and pleural pressures measurement could clearly identify a pleural space effect, avoiding the frequent misinterpretation with an active air leak and allowing to safely remove a chest tube at the right time.

Disclosure: No significant relationships.

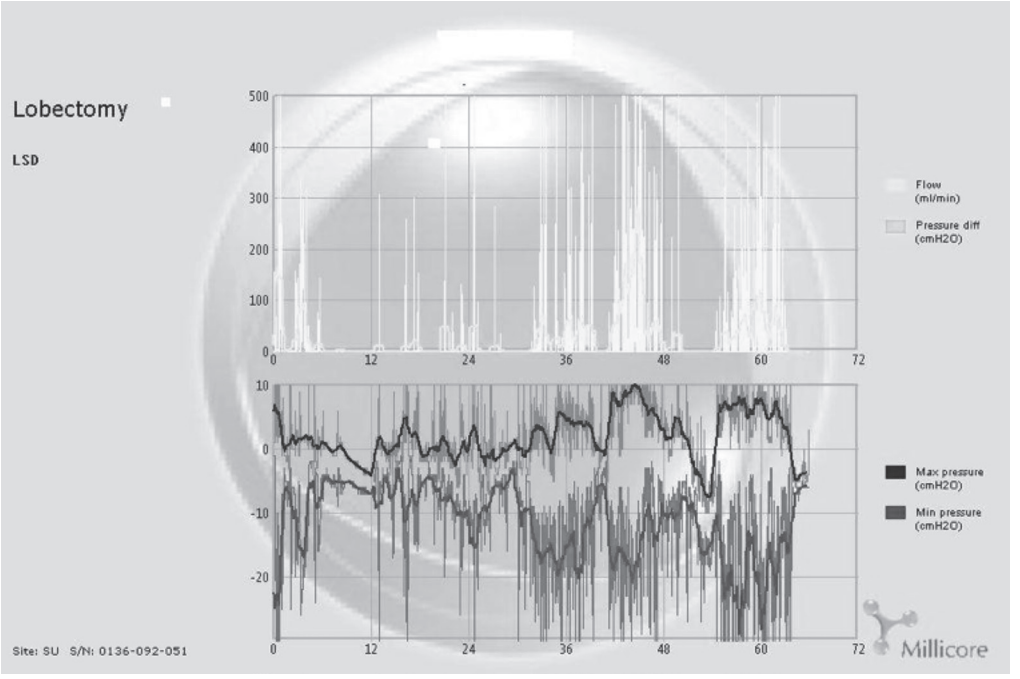

Fig.1: *Active air leak. The upper plot (yellow curve), showing air flows, clearly demonstrates an air leak; the lower plot, separately showing the expiratory pressure ("**pe**", blue curve) and the inspiratory pressure ("**pi**", azure curve), demonstrates an increasing pleural pressures span.*

P2.49:

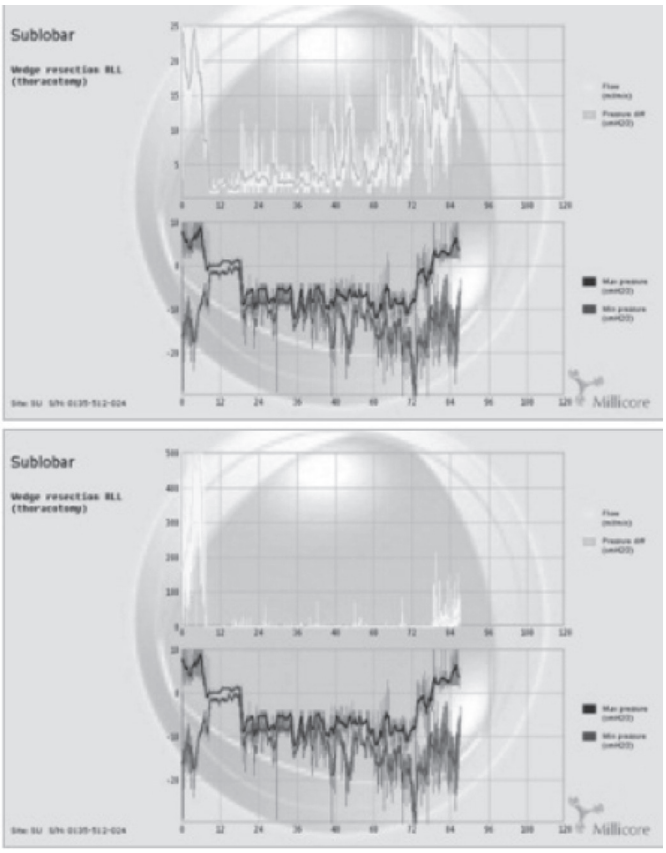

Fig.2: *Late air leak: a progressive pressure curves divergency anticipates the air leak appearance.In the lower plots we can observe an initial interspace between "**pe**" (blue curve) and "**pi**" (azure curve), then a pressure plateau, and finally a progressive curve divergency since the 2nd post-operative hour. a: the greenish-blue line illustrates the progressive increase of differential pressure (**Δ**p=pe-pi) approximately from the 2nd p.o. day.b: the yellow line shows air flows, revealing an air leakage reappearance, anticipated by the differential pressure increasing.*

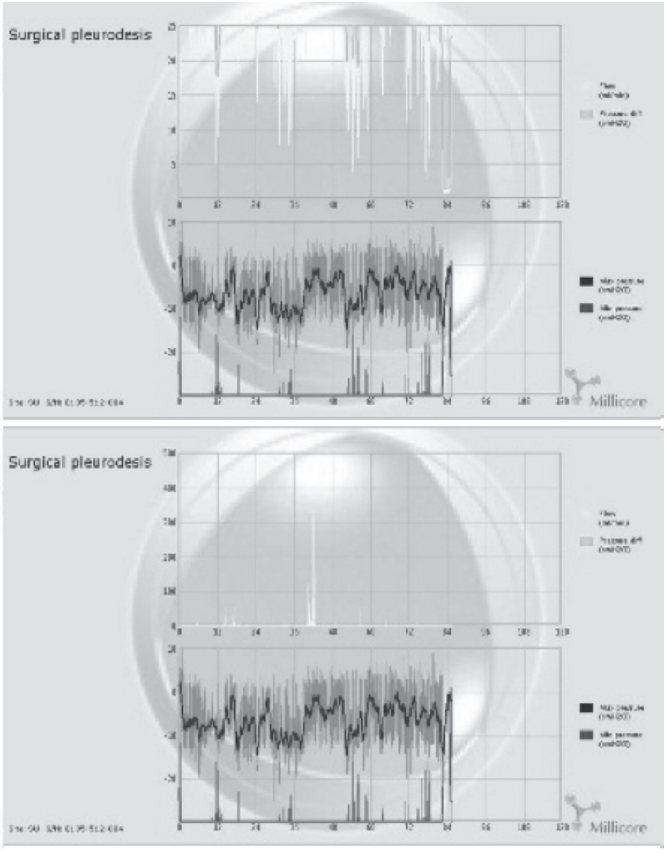

Fig.3: *a-b Pleural space effect: high differential pleural pressure without a significant air flow. In both illustrations, referring to a surgical pleurodesis, the lower plots separately show the expiratory ("**pe**", blue curve) and inspiratory pressures ("**pi**", azure curve), with a wide interspace. In "**a**", the upper plot (greenish-blue line) summarizes a high differential pleural pressure (**Δp=pe-pi**). In "**b**", the upper plot (yellow line) describes a sporadic, minimal air flow.*

AUTHOR INDEX

For presentation numbers in bold:
Author = Presenting Author

Meeting Announcements

April 18–21, 2012
3rd European Lung Cancer Conference
Location: Geneva, Switzerland
E-mail: pia.hirsch@ucdenver.edu

July 25–27, 2012
5th Latin American Conference on Lung Cancer
Location: Rio de Janeiro, Brazil
Contact: www.laics2012.org

September 6–8, 2012
Chicago Multidisciplinary Symposium in Thoracic Oncology
Location: Chicago, IL
Contact: www.thoracicsymposium.org

November 26–28, 2012
5th Asia Pacific Lung Cancer Conference
Location: Fukuoka, Japan
Chair: Dr. Yoichi Nakanishi
E-mail: nsaijo@med.kindai.ac.jp

IASLC

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

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