

alive. Median serum CRP values were 23.5 (0.2-122.6) mg/l and 3.72 (0.1-82.8) mg/l respectively ( $p=0.029$ ). No correlation between CRP and pathologic stage of disease was found. Pretreatment Cyfra 21-1 exceeded 3.3 ng/ml in 6/9 pts who died and 7/30 pts who were alive. Median Cyfra 21-1 concentrations were 5.29 (2.5-14.5) ng/ml and 1.92 (0.7-6.2) respectively ( $p=0.0003$ ). This difference was also significant if only stage I and II pts were taken into analysis.

**Conclusion:** Cyfra 21-1 and CRP are prognostic indicators in NSCLC patients treated by surgery and their influence on survival is probably partly independent from pathologic stage of disease.

P2-103

BSTB: Prognostic Factors Posters, Tue, Sept 4

### Cytological Status of Pre- and Post-Operative Pleural Lavage and Lymph Node Recurrence in Patients with Early Stage Non-Small Cell Lung Cancer

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**Background:** Intraoperative pleural lavage cytology (PLC) in patients with early stage of non-small cell lung cancer (NSCLCs) has been considered as possible aids to assess prognosis of lung cancers and was reported to be useful in detecting sub-clinical pleural dissemination, local and systemic recurrence. Many studies revealed that only pre-operative PLC is necessary. We conduct a prospective study to explore any possible association of pre- and post-operative PCL and lymph node recurrence and the potential usefulness of post-operative PCL.

**Methods:** From December 2004 to December 2006, PLC was performed before and after any manipulation or resection of the lung in 24 consecutive patients, who had no macroscopic pleural effusion, dissemination, or diffuse adhesion, and who subsequently underwent curative resection for NSCLCs. The operations were performed by only one surgeon and the results of PLC with reference to clinicopathologic characteristics were evaluated and reported by only one pathologist. Tumor recurrence (local and systemic) was analyzed.

PLC consisted of cytological analysis of 50 mL of saline irrigated over the lung surface immediately after thoracotomy and after complete curative resection with radical mediastinal lymph node dissection.

**Results:** Nine (38%) of 24 patients had positive cytological findings. Positive cytological findings were observed more frequently in patients with adenocarcinoma, pleural involvement of the tumor and male gender.

Five (55%) of 9 patients had positive cytology in pre-operative PLC, 3 (33%) in post-operative and 1 (11%) in both pre- and post-operative PLC. Exact McNemar significance probability test showed no association between pre- and post-operative cytological status ( $p=0.727$ ).

The risk of lymph nodes recurrence after 3 month of curative surgery in patients with negative and positive pre-operative PLC was 5.6% and 33.33% respectively (risk ratio = 6, 95%CI = 2 to 8,  $p=0.143$ ). In patients with both negative pre- and post-operative cytology, negative pre-operative but positive post-operative, positive pre-operative but negative post-operative, and positive both pre-and post-operative were 6.7%, 0%, 20.0% and 100% respectively ( $p=0.123$ ).

**Conclusions:** No relationship between cytological status of pleural lavage fluid pre-operatively and post-operatively was detected. The study showed that if malignant cells were found in pre-operative PLC, the risk of lymph node recurrence in 3 months increased by 6 times,

and maximum risk occurred when the malignant cells was found in both pre- and post-operative PLC. However, the increased risk was not statistically significant because of the lack of statistical power due to small study size. If sample size were increased it may reveal that PLC may also be required at the time of curative resection for non-small cell lung cancer in order to estimate the risk of lymph node recurrence.

P2-104

BSTB: Prognostic Factors Posters, Tue, Sept 4

### Role of ERCC1, XRCC3, Aurora A and TGFBR1 single nucleotide polymorphisms (SNP) and CHFR and 14-3-3 sigma methylation in a customized cisplatin (cis) trial based on ERCC1 mRNA levels in stage IV non-small-cell lung cancer (NSCLC) patients (p)

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**Background:** The primary aim of this trial was response. In both the control arm and in the genotypic arm with low tumor ERCC1 mRNA levels, p received docetaxel(doc)/cis; in the genotypic arm with high tumor ERCC1 mRNA levels, p received doc/gemcitabine. Response was significantly higher in the genotypic arms. We examined 324 p for genetic markers that could influence response, including ERCC1 118 C/T, ERCC1 C8092A, XRCC3 241 (Thr to Met), Aurora A 91 T>A, Aurora A 169G>A, a SNP within intron 7 of the TGFBR1 gene (Int7G24A), and an in-frame germline deletion (TGFBR1\*6A). Methylation of 14-3-3 sigma and CHFR were also analyzed.

**Methods:** DNA from peripheral lymphocytes was used for genotyping (Taqman assay) and methylation-specific PCR was used for 14-3-3 sigma and CHFR in pretreatment serum DNA.

**Results:** There were no differences in clinical characteristics among the different SNP types, except that p with Aurora A 91 AA had higher tumor ERCC1 mRNA levels ( $P=0.005$ ). No relationship was found between ERCC1 SNPs and tumor ERCC1 mRNA levels. A strong correlation was found between the Int7G24A and XRCC3 241 SNPs ( $P=0.03$ ). The Int7G24A GA type had a higher odds ratio (OR) of response (OR 2.32) than the AA type (OR 3.15) ( $P=0.02$ ). XRCC3 241 MetMet had a lower probability of response (OR 0.23) ( $P=0.04$ ). No other differences in response were observed according to any of the other SNPs or methylation. In the multivariate model, the best response was observed in p with performance status (PS) 0, low ERCC1 levels, and XRCC3 241 SNP (Table).

**Conclusions:** Further research is warranted to define the role of the T-GBFR1 Int7G24A gene in customized treatments.

	N	OR (95% CI)	P
<b>ARM</b>			
Control	126	0.57 (0.34-0.93)	0.02
Low ERCC1	114	1 ref	
High ERCC1	84	0.80 (0.46-1.39)	0.54
<b>PS</b>			
0	124	1 ref	
1	200	0.55 (0.35-0.85)	0.004
<b>XRCC3</b>			
ThrThr	138	0.82 (0.51-1.32)	0.42
ThrMet	155	1 ref	
MetMet	31	0.30 (0.12-0.72)	0.007

P2-105

BSTB: Prognostic Factors Posters, Tue, Sept 4

### Plasma LDH Levels as a Prognostic Factor for Evaluating Stages and Types of Local Advanced and Metastatic NSCLC

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Plasma lactate dehydrogenase (LDH) is a biochemical parameter supposed to get elevated in lung cancer, especially in advanced tumors. LDH is an important enzyme which catalyses lactate formation from pyruvate in anaerobic metabolism. It is called to be a non-specific indicator of dying tumor cells by reflecting their rapid turnover. In our study, we aimed to show that plasma LDH levels are found to be high in lung cancer and LDH can reflect the stage and prognosis of tumor.

We detected 40 patients with new diagnosis of non small cell lung cancer. We chose a control group of 40 patients with chronic obstructive pulmonary disease (COPD). In lung cancer group, we chose the patients without history of COPD; also COPD patients elected for control group didn't have diagnosis of lung cancer. The history of smoking wasn't thought to affect the results of our study as it was an intersection of both groups. Gender and age were found to be statistically similar for each group. We accepted the normal plasma level of LDH between 240-480 U / l.

The mean level of LDH was 606,5 U / l in lung cancer group when it was found as 387,3 U / l in control group which was statistically significant (p=0,002). In control group, we found 7 patients having a high value of LDH (15 %); it seemed to be high in 20 patients of lung cancer group (%50).

Afterwards, NSCLC group was examined if LDH levels differed according to stage and tumoral type. By using TNM staging, 26 of 40 patients were found to be in stage IV, 7 in stage IIIb and 7 in stage IIIa. Plasma level of LDH was high in 14 of 26 stage IV patients, 3 in 7 stage IIIb and 3 in 7 stage IIIa. We examined mean LDH levels according to stages of tumors: 453.8 in stage IIIa, 508.3 in stage IIIb, and 684.2 in stage IV, which shows that LDH is high in advanced NSCLC. However, LDH levels weren't found statistically significant according to stages. We think that the heterogen distribution of tumor stages can be the reason of it.

There were 15 squamous cell, 15 adenocarcinoma and 10 uncertain histopathological type of NSCLC in lung cancer group. LDH was high in 6 of 15 squamous cell, in 8 of 15 adenocarcinoma and in 6 of other 10 NSCLC. The mean LDH level was 504.1 in squamous cell, 642.5 in adenocarcinoma and 673 in other NSCLC; we can see that LDH levels are higher in adenocarcinoma. This data achieved according to tumor types wasn't found statistically significant; the limited number of the universe can explain this result.

The results of our study supports that plasma LDH levels are higher in patients with lung cancer. Although LDH levels were found to be high in advanced NSCLC and in adenocarcinoma, but statistically not significant, more advanced studies with a high number and homogen distribution of patients should have done to confirm these results.

P2-106

BSTB: Prognostic Factors Posters, Tue, Sept 4

### Gender differences in non-small cell lung cancer (NSCLC) patients (p): A retrospective study based in Spanish Lung Cancer Group (SLCG) trials.

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**Background:** There are some data supporting differences by sex in lung cancer. So we undertook a retrospective analysis of clinico-pathologic and genetic features in women (W) with advanced NSCLC participating in first-line chemotherapy (CT) SLCG trials.

**Methods:** Data on age, histology, PS, CT schedule, XRCC3 (DNA repair capacity gene) single nucleotide polymorphisms (SNPs) assessment in DNA from peripheral blood lymphocytes, CT outcomes, survival and disease free-survival were obtained.

**Results:** 1125 p included in 4 SLCG trials from 2001 to 2005 treated with CT based on CDDP/GEM, CDDP/DOC or DOC/GEM were analysed. 167 p (14.9%) were W. W were significantly younger than men (M) (median, 57 yrs vs 61 yrs, P<0.0001). Adenocarcinoma subtype was more predominant in W than in men (76% vs 47%, P<0.0001). There were not significant differences by sex considering PS (0/1)(P<0.85), stage (IIIB/IV)(P<0.18) or overall response rate (P<0.45). Median time to progression (TTP) was 6.8 months (m) vs 5.3 m (P<0.009) in favour of W. Median overall survival (OS) was 11.4 m for W vs 9.1 m for M (P<0.001). No differences were found in the subgroup of patients receiving DOC/GEM probably due to the small number of patients. XRCC3 SNPs were distributed similarly between sexes. SNPs genotype of both XRCC3 241Met/Met and Thr/Met correlates with better survival in W vs M (P<0.05 and P<0.008). In a multivariate analysis, sex was an independent predictive marker for both OS (HR 1.5, 95% CI 1.2-1.9, P<0.0001) and TTP (HR 1.4, 95% CI 1.1-1.7, P<0.001), others independent variables found were PS, age, type of CT, but not XRCC3 241 genotype.

**Conclusions:** In this retrospective analysis of four SLCG trials, women with NSCLC were found to have better prognosis than men. Results