416. Prognosis of lung cancer

P4164

Expression of macrophage migration inhibitory factor (MIF) in the serum and lung tissues in patients with non-small cell lung cancer (NSCLC)

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Objective: To study the expression of MIF in the serum and lung tissues of patients with NSCLC.
Methods: Eighty-eight patients of the 1st affiliated hospital of Sun Yat-sen university with diagnosis confirmed by pathology were recruited from 2011.10 to 2012.3, including 66 patients with NSCLC (group A) and 22 patients with benign lung lesions (group B). ELISA was done to compare serum MIF level in these two groups and in 30 healthy individuals. Immunohistochemistry(IHC) was done to compare the expression of MIF between group A and B. The correlationship between serum MIF level and high expression rate in lung tissues was analyzed.
Results: The serum MIF level in group A was significantly higher than healthy control(14.79 *Vs* 10.69ng/mL, *P*=0.001), but not significantly higher than group B (14.79 *Vs* 13.68 ng/mL, *P*=0.580). Among group A, the serum MIF level in patients with advanced stage (stage III and IV) was significantly higher than those with early stage (stage I and II) (17.53 *Vs* 10.45ng/mL, *P*=0.004). The MIF high expression rate in the lung tissues of group A was markedly higher than group B (30.3% *Vs* 4.5%, *P*=0.014). Among group A, there was significantly higher MIF expression rate in patients with advanced stage compared with those with early stage (42.1% *Vs* 14.3%, *P*=0.015). The serum MIF level had a positive correlation with MIF expression rate in the lung tissues in patients of group A ($P<0.05$).
Conclusions: The serum MIF level had a positive correlation with MIF expression rate in lung cancer tissues. Both of them were helpful for evaluation of the NSCLC clinical stage and histological grade. MIF is a good histological biomarker of NSCLC.

P4165

Clinical implication of stem cell markers in N2 positive non-small cell lung cancer

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Introduction: Non-small cell lung cancer (NSCLC) is one of the most commonly diagnosed malignancies and the leading cause of death worldwide. Caner stem cells (CSC) are proposed to be responsible for metastasis and chemoresistance.
Material and method: 72 patients were diagnosed with N2 positive NSCLC. They underwent surgical resection from 2006 to 2007 in Asan Medical Center, Seoul, Korea. Immunohistochemical staining for CD133, CD44, CD24, CXCR4, Nanog, Oct4, ABCG2, E-cadherin, vimentin, and Ki-67 was performed.
Result: Most frequently expressed CSC marker in primary tumor specimens of NSCLC was CXCR4 (92.2%), followed by CD44 (29.2%), CD24 (12.5%), and ABCG2 (9.7%). However, other markers such as CD133, Nanog, and Oct4 were not expressed. E-cadherin was expressed in 86.1% of primary tumor specimens, while vimentin was expressed in 20.8%. Cell proliferative marker, Ki-67, was expressed in 16.7% of primary tumor tissues. As for specimens of lymph nodes, most frequently expressed marker was CXCR4 (93.1%), followed by CD44 (15.2%), ABCG2 (12.5%), and CD24 (10%). In 85.1% of lymph node specimens, E-cadherin was positive. Vimentin was positive in 17.9%. Among the patients showing CD44 positivity in primary tumor specimens, 70% were negative for CD44 expression in lymph nodes. Survival analysis revealed that CD44 expression is a favorable prognostic factor for overall survival (p=0.024). Multivariate analysis using Cox-regression showed that NSCLC patients with CD44 positivity have trend towards increased overall survival.
Conclusion: Various CSC markers are expressed in patients with NSCLC. Immunoreactivity for CD44 is a positive prognostic factor for survival in N2 positive NSCLC.

P4166

Association of XPD and CDA polymorphisms with clinical outcome in non-small cell lung cancer in a Chinese population

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XPD plays a key role in the repair of DNA and platinum resistance lesions. Cytidine deaminase genes decide the velocity of catalyze gemcitabine. This study aims at investigating the relationship between the XPD, CDA genotypes and the outcome in NSCLC patients. We used RFLP to evaluate genetic polymorphism of the XPD Asp312Asn, XPD Lys751Gln, CDA Lys27Gln and CDA Ala70Thr in 93 NSCLC patients treated with cisplatin-gemcitabine regimen. 44% of patients carrying the XPD 312Asp/Asp had progression of disease, whereas 55.56% with heterozygous XPD 312Asp/Asn had progression of disease as well. There were no significant correlation between XPD Asp312Asn and clinical benefit (P=0.502). 53.95% of patients with wild-type had clinical benefit (PR and SD), 52.94% of patients carrying XPD 751Lys/Gln responded to therapy. There was no difference between different genotype (P=0.517). But the difference of OS between XPD 312Asp/Asp and XPD 312Asp/Asn was very significant (20.0 months vs 12.4 months, P=0.04). TTP had no difference between the patients with wide-type genotype (10.7 months) and those carrying XPD 751Lys/Gln (7.0 months); However, the OS of patients with wide-type genotype (20.5 months) was longer than that (11.5 months) of patients carrying XPD 751Lys/Gln. No significant differences in TTP or OS were observed in patients carrying different genotype of CDA Lys27Gln. This investigation provides suggestive evidence of a favorable effect about the XPD 312Asp/Asp and XPD 751Lys/Lys genotype on survival in platinum-treated NSCLC. But CDA 27 polymorphism does not affect the efficacy of gemcitabine.

P4167

The metallopeptidase neprilysin is a hypoxia-induced prognostic factor in lung adenocarcinoma

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Identification of hypoxia-induced pathways might lead to novel therapeutic targets in solid cancers. A comparative expression profiling study was performed in hypoxic and normoxic *ex vivo* cultured lung cancer fragments with preserved tumor stroma and 3D-structure. A considerable overlap was found between hypoxia-regulated genes from the *ex vivo* lung cancer model and published hypoxia-signatures. The stem cell marker neprilysin (membrane metallo-endopeptidase, MME, CD10), which was consistently up-regulated by hypoxia in the histological subtypes in our study, has not been reported so far to be hypoxia-induced in cancer. Neprilysin has been shown to be expressed by stroma cells, e.g. cancer-associated fibroblasts. Immunohistochemistry for neprilysin in fresh NSCLC specimens and normoxic or hypoxic fragments revealed a localization in both, stroma cells and neoplastic tumor cells. To assess a possible role of neprilysin in lung cancer progression we analyzed the association of neprilysin expression and overall survival in NSCLC patients from public microarray datasets. High expression of neprilysin was significantly associated with poor overall survival in 182 adenocarcinoma patients in a multivariate meta-analysis (P=0.000012) and in adenocarcinoma patients from two individual datasets. As a conclusion, neprilysin is a hypoxia-induced, independent adverse prognostic factor in surgically treated lung adenocarcinoma patients. The results of this study suggest an important role of stroma-derived hypoxia-induced factors for lung cancer progression.

P4168

Prognostic value of ERCC1 expression in advanced non-small cell lung cancer (NSCLC)

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Background: The immunohistochemical (IHC) detection of the "excision repair cross-complementation group 1" (ERCC1) protein in resected NSCLC is prognostically relevant. Pts with ERCC1-neg. tumors appear to benefit from adjuvant cisplatin-based chemotherapy (Ctx), whereas pts with ERCC1-pos. tumors do not.
Aim: We compared survival of pts with non-operated NSCLC III/IV according to ERCC1.
Methods: We analyzed 398 pts (m=248, f=150) newly diagnosed with NSCLC stage III/IV between 10/2009 and 12/2010. Prospectively, ERCC1 expression determined by IHC was measured and indicated as H-score. Pts where no IHC and/or no H-score could be performed were excluded.
Results: 271/398 cases (68%) were suitable for IHC. 175/271 (65%) of tumors were ERCC1 pos., 96/271 (35%) ERCC1 neg. 177/271 (65%) received platin. Survival times in days were (mean ± SEM): platin+/ERCC1- 404±25 (n=67); platin+/ERCC1+ 346±23 (n=110); platin-/ERCC1- 144±23 (n=29); platin-/ERCC1+ 268±33 (n=65). In Cox hazard regression analysis, the factors platinum (p<0.001) and ERCC1 (p=0.01) were not independent (p=0.001, interaction term).

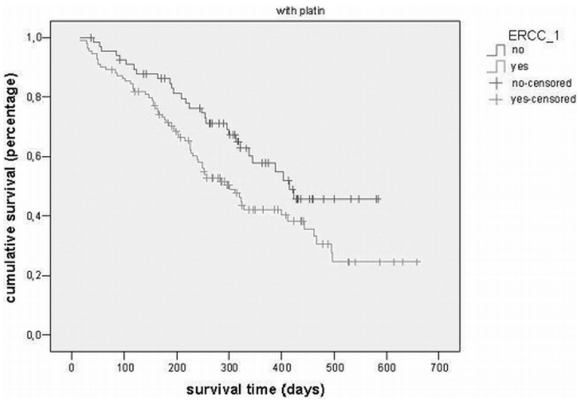

Figure 1. Kaplan-Meier survival analysis.

Conclusions: Pts with palliative platin-based Ctx for advanced NSCLC had significantly longer OS when the tumor showed no significant ERCC1 expression. In pts who did not have platin-based Ctx, the absence of ERCC1 expression was prognostically unfavorable. This study confirms observations from adjuvant therapy also for palliative Ctx.

P4169

EGFR exon in lung cancer: Survival predictors?

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EGFR mutations are associated with sensitivity to tyrosine kinase inhibitors (TKI) in patients with NSCLC.Studies point to different outcome to TKI treatment according to exon mutation.
Aim: Understand how different EGFR mutations predict TKI response and affect survival.
Methods: Records review of NSCLC patients with EGFR study (2006-2011). Epidemiological, clinical and outcome information was analyzed using SPSS19.0 (p<0.05).
Results: Of 409 patients studied 53 were EGFR-positive. After exclusion of 1 drug-resistant patient (exon 20) and patients who did not use TKI or had TKI as 1st therapeutic, 22 patients were considered - 50% male, 67.5±9.8y, 59.1% non-smokers.
Progression-free survival (PFS) was better in exon 19 mutations (p=0.04). Survival after TKI (STKI) was better in 18 and 19 mutated patients (no statistical difference - p=0.06).

Table 1

	18	19	20	21
% patients	13.6	40.9	9.1	36.4
STKI (m)	25.0 (3.9–46.1)	25.4 (18.2–33.3)	10.3 (4.0–16.5)	11.6 (5.7–17.4)
PFS (m)	22.1 (0–18.8)	8.0 (12.8–31.8)	7.1 (5.1–9.1)	8.6 (4.8–12.3)

In non-surgical stages (72.8%), exon 19 mutated patients had better global survival (GS), STKI and PFS than others (p>0.05).

Table 2. Stages IIIB/IV

	18	19	20	21
GS (m)	23.8 (0–64.8)	50.5 (17.8–83.2)	34.2 (8.6–60.0)	21.4 (7.7–35.0)
STKI (m)	14.1, CI 0–39.6	19.8, CI 12.1–27.5	10.3, CI 4.0–16.5	11.3 (4.6–16.1)
PFS (m)	10.1 (0–27.4)	11.8 (0.9–22.6)	7.1 (5.1–9.1)	8.1 (5.6–12.8)

Associating patients with exons 18 and 20 (described as less predictive of therapeutic outcome) GS29.1, STKI12.2 and PFS8.6 months, all higher than values found for exon21(p>0.05).
Conclusions: Exon 19 mutation confered better prognosis to patients treated with TKI. Exons 18 and 20 (22,7%) were not associated with worse prognosis than exon 21. Although this is a small group we believe that is worth to maintain analysis of the 4 exon mutation.

P4170

Prognostic value of fluorine-18 fluorodeoxyglucose (18-FDG) positron emission tomography imaging in patients with non-small cell lung carcinoma

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To determine whether the amount of 18-FDG maximum standardized uptake (SUVmax) value on the PET/CT imaging at the time of presentation has prognostic significance in patients with non–small-cell lung cancer (NSCLC).

Patients and methods: A retrospective review identified 142 patients with NSCLC who underwent 18-FDG PET/CT study at the time of diagnosis. Extensive clinical data, including tumor histologic cell type, stage at presentation, treatment, and SUVmax values in the primary tumor were recorded and survival was examined.

Results: Total 142 patients were included the study. 32 patients of them have stage I and II. The median SUVmax of early stage patients is determined 13.5. Early stage patient population was subdivided into two groups according to the median value for survival. The median survival of the 17 patients with the primary tumor having an SUVmax $\leq$ 13.0 was 32.5 months whereas the median survival of the 15 patients with the primary tumor having an SUVmax $>$ 13.0 was 19.0 months. There was no stastistical differences between two groups (p=0.463). The 110 patients were on advanced stage (stage III and 4). Using the median SUVmax of 12.5, the patient population was subdivided in two groups. The median survival of the 54 patients with the primary tumor having an SUVmax $\leq$ 12.5 was 12.0 months whereas the median survival of the 56 patients with the primary tumor having an SUVmax $>$ 12.5 was 11.0 months. There was no stastistical differences between two groups (p=0.236).

Conclusion: 18-FDG SUVmax uptake of the primary lesions in patients with a new diagnosis of NSCLC does not have a significant relationship with survival.

P4171

EpCAM-positive circulating cells in lung cancer patients

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Lung cancer is a very aggressive neoplasm characterized by high metastatic potential which is the main cause of therapeutic failures. The exact cell of origin of metastasis is not known, however several markers for them have been proposed. Recently, the epithelial cell adhesion molecule (EpCAM) has been identified as an additional molecule to enrich for circulating tumor cells (CTCs).

The aim of this study was to detect CTCs by flow cytometry applying anti-EpCAM antibody and to investigate its clinical significance.

Forty-one patients diagnosed with lung cancer were enrolled into this study. Patients did not receive anticancer treatment prior to the study. The cells bearing EpCAM were detected in tumor tissue, lung tissue and peripheral blood by flow cytometry with anti-EpCAM FITC antibody, analyzed in FACSCantoII, BD flow cytometer.

EpCAM+ cells were detected in the tumor tissue with higher proportion than in adjacent lung parenchyma and with higher proportion in adenocarcinoma (AC) than in squamous cell (SCC) type. The median proportion of circulating EpCAM+ cells was 0.0026% (260 per mL). No difference was found between SCLC and NSCLC. The fraction of EpCAM+ cells was higher in the patients with AD than SCC (0.0130 vs 0.0027%), was significantly lower in the blood of patients with advanced disease (IIIB,IV) when compared with lower stages (I-IIIA) (0.0018 vs 0.0067%, 230 vs 504 cells per mL) and was significantly lower in patients with metastases compared to those without metastases (0.0015% vs 0.0046%, p=0.012). Our study confirmed the presence of a rare subpopulation of the CTCs of the EpCAM+ phenotype in lung cancer patients with significant differences related to histological type and stage of the disease.

P4172

Independent prognostic und predictive value of blood vessel invasion (BVI) in curatively (R0) resected stage II and IIIA non-small cell lung (NSCLC) cancer patients

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Objective: A single center study was conducted to identify the prognostic and predictive value of blood vessel invasion (BVI) in surgically R0 resected stage II and IIIA non-small cell lung cancer patients.

Methods: A total of N=105 consecutive patients who had undergone complete (R0) resection for stage II/IIIA primary non-small cell lung cancer (NSCLC) between 01/2008 and 12/2010 at the Lung Cancer Center Nuremberg were evaluated. All pathological specimens were examined for evidence of BVI.

Results: The baseline clinical data showed no significant differences between patients with adjuvant chemotherapy (aCTx; cisplatin/vinorelbine; N=46) and without aCTx (N=59) beside of age (aCTx treated patients were younger p=0.03). Demographic data were as follows: age <65 years 53%; male 64%; ECOG 0/1/2 (47%/35%/3%); stage IIA/IIB/IIIA (13%/31%/55%); histology AC/SCC/other (53%/37%/10%); BVI 29%; pneumonectomy/lobectomy (19%/81%).

ECOG-PS 0 and no BVI were positive prognostic factors for both recurrence free survival (RFS) and overall survival (OS) in the group without aCTx and remained independent *prognostic* factors in the multivariate analysis (p<0.001; p=0.002). Additionally, ECOG-PS 0 and no BVI were independent *predictive* factors for RFS and OS in the aCTx treated group.

Conclusion: BVI is an independent prognostic and predictive factor in R0 resected stage II/IIIA NSCLC patients. This subset of patients may have a greater benefit from aCTx and may need to be followed-up more closely.

P4173

Impacts of multi and specific co-morbidities on the survival of non-surgical non-small cell lung cancer

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Background: The prognosis of patients with non surgical non-small cell lung carcinoma (NSCLC) is poor and the presence of co-morbidity may shorten the survival. This study aimed to determine the impacts of multi and specific co-morbidities on the survival of non-surgical NSCLC patients.

Methods: We prospective followed up 603 Chinese patients with newly diagnosed primary NSCLC who were consecutively recruited from a largest oncology center in Hong Kong during 2003-2006 and ineligible for surgery through 31 December, 2008. Multiple Cox's proportional hazard model was performed to evaluate the impacts of co-morbidity on survival.

Results: The median survival for all patients was 9.30 months (range: 0.17 – 70.6), and the cumulative 2-year survival rate was generally poor (<12%); 56.7% of patients presented any co-morbidity at the time of diagnosis and 14.3% of them had 3 co-morbidities. Multiple Cox's proportional hazard model showed that only the patients with the major co-morbidity group of 'endocrine, nutritional and metabolic disease and immunity disorder (240 - 279) (HR=1.33, 95% CI: 1.00 – 1.79) was significantly associated with shorter survival, while the effects were generally weak and borderline for most major groups or specific types of co-morbidities.

Conclusion: This study reveals that 'endocrine, nutritional and metabolic disease and immunity disorder' was the significant risk factor to shorten the survival for non-surgical NSCLC which raises special attention for better supportive or palliative care for lung cancer patients with this type of co-morbidity.

P4174

High mRNA expressions of KLF2 improve post operative prognosis of pulmonary adenocarcinoma correlation with chemokine receptor CCR7 and genetical mutations of p53

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Purpose: Chemokines and chemokine receptors not only have the powerful ability in cancer metastasis and tumorigenesis, but also act as anti-tumorgenic ability. Lung Krueppel-like factor (LKLF, KLF2) is a member of the family of the Krueppel-like factors (KLFs). KLF2 was initially described as a lung-specific transcription factor. KLF2 is reported to regulate some malignant cells. We examined and evaluated the effect of KLF2 on pulmonary adenocarcinoma and the relationship of their mRNA expression with CCR7, EGFR and p53 genetical mutations in pulmonary adenocarcinoma.

Patients and methods: 120 patients of stage I to IV with pulmonary adenocarcinoma were included in this retrospective analysis. The expression of CCR7 and KLF2 mRNA expression in surgically resected pulmonary adenocarcinoma specimens were examined and evaluated the relation to prognosis, the effect of EGFR and p53 genetical mutations.

Results: High mRNA expression of KLF2 in lung cancer patients indicated significantly good prognosis than the groups of low expressions (p= 0.0066, HR= 2.008, 95% CI of ratio 1.215 to 3.319). The expression of KLF2 mRNA had relationships with CCR7, CCL21 and CCL19 mRNA expression in pulmonary adenocarcinoma. Moreover the mRNA expression of KLF2 in pulmonary adenocarcinoma specimens was influenced by the mutation of p53 mutation in lung cancer specimens.

Conclusion: We propose KLF2 as clinical good prognostic factors and that KLF2 has strong relation with CCR7, the ligands and p53 genetical mutation mRNA expression in pulmonary adenocarcinoma.

P4175

Prognostic impact of nestin expression in resected large cell neuroendocrine carcinoma of the lung

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Large cell neuroendocrine carcinoma (LCNEC) of the lung is categorized as a high-grade neuroendocrine carcinoma with an aggressive clinical behavior. Nestin is a class VI intermediate filament protein expressed in stem/progenitor cells during central nervous system development. Recently, we reported that nestin expression is a prognostic indicator of a poorer survival probability in patients with resected NSCLC. In the present study, we aimed to determine its prognostic significance concerning survival in patients with resected LCNEC.
Nestin expression in tumor cells was immunohistochemically studied in 30 patients with resected LCNEC, and its associations with clinicopathologic parameters were evaluated. Kaplan-Meier survival analysis and Cox proportional hazards models were used to estimate the effect of nestin expression on survival.
Nestin expression was observed in 8 of the 30 (26.7%) LCNECs. Clinicopathologically, no significant association between nestin expression and age, gender, smoking habits, p-TNM stage, tumor size, or nodal status was observed. On survival analysis, nestin expression was significantly associated with a poorer prognosis in patients with LCNEC (P = 0.016). Multivariable analysis confirmed that nestin expression increased the hazard of death after adjusting for other clinicopathologic factors (HR= 3.53; 95% CI, 1.21-10.3).
The present study suggests that nestin expression is a prognostic indicator of a poorer survival probability in patients with resected LCNEC, although its prognostic significance still requires confirmation with larger patient populations.
This study was approved by Kitasato university human ethics comittee.

P4176

The impact of neuroendocrine differentiation in the prognosis of non-small cell lung cancer

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Introduction: Large cell carcinomas with neuroendocrine differentiation (LCNEC) consist a district subcategory and represent 2-3% of lung cancers.Retrospective studies have shown prognosis similar to this of patients with SCLC and worse prognosis after surgical resection in comparison to surgical resection in NSCLC.There are data showing that perioperative chemotherapy,especially platinum based combinations, improves survival.
Aim: Examine the overall survival (OS) between patients with LCNEC and NSCLC with neuroendocrine differentiation and the progression free survival (PFS) according to the stage and the therapy applied.
Method: Data of patients with LCNEC and NSCLC with neuroendocrine differentiation were collected from June 2005 to December 2010.
Results: Data from 26 patients were collected,21 men, median age 62 years old. 15 had LCNEC and 11 NSCLC with neuroendocrine differentiation,16 at stage I-III and 10 at stage IV. The majority were confronted with multimodality therapy (surgery, radiotherapy, chemotherapy).The median OS was 15 months for LCNEC and 15.5 months for NSCLC with neuroendocrine differentiation (95% CI).There was found no difference in OS between LCNEC and NSCLC with neuroendocrine differentiation for stages I-III (p=0.814) and IV (p=0.563) respectively.The median OS for all patients was 3.5 months and the median PFS 2.5 months (95% CI).Totally,12 patients received systematically sandostatin-LAR and 14 didn't receive without difference found in OS (p=0.140).
Conclusions: Randomised trials are needed in order to be proved which therapeutic intervention is the most proper and which chemotherapeutic combination is the best for lung cancer with neuroendocrine differentiation.

P4177

Long-term outcomes and prognostic factors for neuroendocrine G1 and G2 lung tumors

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Background: Bronchial neuroendocrine G1 and G2 tumors show a favorable outcome. However, survival depends on several prognostic factors such as histological sub-type, nodal involvement and other predictors.
Objectives: The presented study aimed to evaluate the long-term outcomes,survival rates and prognostic factors after resection of G1 and G2 neuroendocrine lung tumors according to the 7th edition of the TNM staging system.
Patients and methods: We conducted a retrospective review of 246 consecutive patients who underwent surgical treatment for G1 and G2 neuroendocrine tumors of the lung between 1998-2010.
Results: 246 patients (61% women) with G1 and G2 neuroendocrine lung tumor underwent thoracotomy. G1 tumors were found in 205 (83%) patients, while 41 (17%) had G2 disease. Follow-up was 65.9±40.3 months. In the total study cohort we analysed 5- and 10-year survival: G1 bronchopulmonary tumor (survival 96% and 94%) was significantly different (p<0.001) from G2 bronchopulmonary tumor (survival 87% and 46%), stage I (survival 94% and 85%) was significantly different (p=0.02) from stage >I (survival 86% and 59%), nodal involvement (survival 83% and 57%) was significantly different (p=0.02) in comparison to patients without nodal involvement (survival 94% and 84%), distant metastases (survival 80% and 27%) was significantly different (p=0.001) compared to patients without distant metastases (survival 94% and 84%), occurrence of symptoms before operation (survival 96% and 84%) was significantly different from patients presenting no symptoms before operation (survival 86% and 67%).
Conclusion: Prognosis was influenced by histological subtype, stage of disease, occurrence of symptoms before operation, lymph node involvement and distant metastases.

P4178

The increase of circulating B7-H4-expressing CD68$^+$ macrophage correlated with clinical stage of lung carcinomas

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Purpose: To investigate the B7-H4-expressing TAM in a series of 56 cases of lung carcinoma.
Methods: Tissue samples were obtained from patients with lung cancer, who underwent lobectomy surgery. B7-H4-expressing TAM was observed by confocal microscopy. B7-H4-expressing macrophage (CD68$^+$ cells) in peripheral blood was compared among patients with lung cancer, patients with tuberculosis and healthy donors by two-color flow cytometry. Correlation of B7-H4-expressing CD68$^+$ macrophage with histological types, tumor size and lymph node metastasis was analyzed.
Results: Lung cancer are infiltrated with Tumor-associated macrophages (CD68$^+$ cells) that expressed B7-H4.The circulating B7-H4-expressing CD68$^+$ cell were higher in the lung cancer group than in the tuberculosis group. The number of B7-H4-expressing CD68$^+$ cells was significantly correlated with the lymph node metastasis, and the tumor size. The proportion of B7-H4 positive CD68$^+$ cells among CD68$^+$ cells was also greater in late stage lung cancer than in serous early stage lung cancer. The intensity of B7-H4 staining was significantly correlated with lymph node metastasis, and the tumor size. Expression of B7-H4 was significantly higher in CD68$^+$ cells from the late stage lung cancer (stage III-IV, n=36) as compared with the CD68$^+$ cells from early stage lung cancer (stage I-II, n=20).
Conclusion: It is suggested that lung carcinomas increase B7-H4-expressing macrophages, which might favor tumor progression.

P4179

Prognostic value of SUVmax in patients with lung cancer who underwent surgical treatment

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Introduction: The metabolic activity of a tumor can be measured by the Standardized Uptake Value (SUV) of F-2-deoxy-2-fluoro-D-glucose (FDG), which may provide prognostic information.
Objective: To analyse the prognostic value of SUVmax in surgically treated patients with lung cancer.
Methods: The patients included were selected from a database of patients with lung cancer, between 2007 and 2010, who underwent surgical resection with performance of PET with quantification of SUVmax prior to surgery.
Results: 26 patients underwent surgical resection of lung lesion, with mean age 64±12.2 years, 16 (61.5%) were male. 23 underwent pre-surgical PET. The value of SUVmax was accessed in 21: 9 (42.9%) adenocarcinoma, 8 (38.1%) carcinoid tumors, 2 (9.5%) squamous cell carcinoma and 2 (9.5%) NSCLC. The mean SUVmax was 5.4±4.4. In carcinoid tumors the mean SUVmax was 3 and in NSCLC 6.9: adenocarcinoma 7.3 and squamous cell carcinoma 5.5. The pre-surgical stage was IA 6 (28.6%), IB 12 (57.1%), IIB 1 (4.8%) and III in 2 (9.5%). After surgery, staging was distributed as follows: IA 8 (38.1%), IB 7 (33.3%), IIA 1 (4.8%), IIB 1 (4.8%) IIIA 4 (19%). Downstaging occurred in 4 and upstaging in 4, with mean SUVmax of 2.2 and 3.2, respectively. With respect to surgical stage, the average SUVmax was 6.1 in stage III, 5.2 in stage II and 5.3 in stage I. Recurrence was observed in 2 (9.5%), with SUVmax of 15.6 and 1.9. The median follow-up was 23.4 months and no deaths were reported.
Conclusion: Although limited by a small sample size, higher values of SUVmax in patients with post-surgery upstaging, in adenocarcinoma and in more advanced stages was observed in this study.

P4180

Outcomes of NSCLC patients with positive EGFR mutation

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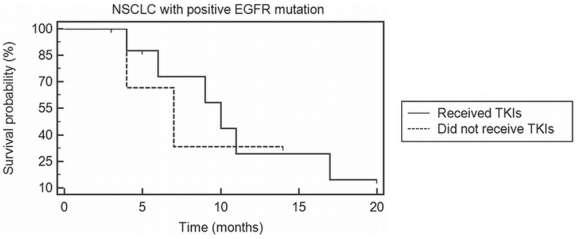
Background: Tyrosine kinase inhibitors (TKIs) have been shown to offer an increased progression-free survival and response rate in non small cell lung cancer (NSCLC) patients with epidermal growth factor receptor (EGFR) activating mutations. Screening is recommended in patients with advanced NSCLC, particularly in those with adenocarcinoma.
Aims: To evaluate the outcomes of NSCLC patients who underwent EGFR mutation testing.
Methods: Retrospective of 135 patients between Jan 2010 and Dec 2011.
Results: Of the 135 patients, 13(10%) had positive EGFR mutation. Further information was not available for 1 and hence excluded from analysis. 9 had stage IV, 2 had stage IIIb and 1 had stage IIa. All had adenocarcinoma except 1, adenosquamous. Performance status (n=11), median (IQR), 2(1-2).
Of the 12 patients with positive mutation, 8 received TKIs; mean duration of treatment was 7 months (SD 4). 1 had an insertion in exon 20 usually regarded as resistant to TKI. 1 had palliative chemotherapy and 1 had metastatic brain lesion resected with palliative radiotherapy prior to receiving TKI. Median survival was 10 months in those who received TKIs and 7 in those who did not; there was no survival difference in both groups (p=0.785, 95% CI 0.23-6.74).



Conclusion: Most of our patients had advanced disease and despite the use of TKIs in selected patients the prognosis remained poor. Common mutations were deletions in exon 19 and point mutations in exon 21.

P4181

One year survival differences of EGFR- and KRAS-mutated advanced non-small cell lung cancer (NSCLC) compared to the wildtype population

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Introduction: With investigation of the complex relationship between EGFR-related biomarkers and response to tyrosine kinase inhibitor (TKI) novel therapies for NSCLC have been established. In numerous clinical studies the effect of TKIs in patients with activating EGFR mutations is proven by a better progression free survival (PFS) while the prognostic value of KRAS mutations remain vague. The current study in our clinic retrospectively analysed the one year survival of patients with NSCLC and an activating EGFR- or KRAS-mutation.
Methods: Within 15 months until Dec 2010, all subsequent biopsies of newly diagnosed NSCLC (n=753) were tested for the ability to be analysed by Sanger- and Pyrosequencing for the presence of EGFR mutations and by LightCycler Real-time PCR for the presence of KRAS mutations. The obtained data were correlated with the centre-bound tumour registry for survival data and analysed by Kaplan-Meier estimator.
Results: In a total of 552 cases with NSCLC, EGFR mutation was present in 27/552 (4,9%, male n=10) and KRAS mutation in 85/552 cases (15,8%, male n=43). In advanced NSCLC (IIIB/IV), 16/27 patients had an EGFR mutation and 46/85 had KRAS mutation. The one year survival of advanced NSCLC and EGFR mutation was 11/16 (68,8%) vs. 5/16 (31,3%) without mutation. Stratifying according to KRAS it was 15/46 (34,8%) with vs. 30/46 (65,2%) without mutation.
Conclusion: Comparable with previous reports, the one year survival of NSCLC with EGFR mutation is improved whereas the the one year survival with KRAS mutations seems to be poorer.

P4182

Recruitment of podoplanin positive cancer-associated fibroblasts in metastatic lymph nodes predicts poor prognosis in pathological N2 stage III lung adenocarcinoma

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Background: Cancer-associated fibroblasts (CAFs) directly communicate with cancer cells and play important roles in cancer progression. Recent studies have reported that primary cancer tissue with podoplanin-expressing CAFs predicted a poorer outcome among stage I lung adenocarcinoma patients. However, whether podoplanin(+)-CAFs can also be recruited into metastatic lymph nodes and influence the prognosis remains unclear.
Methods: We selected 112 patients with pathological N2 stage III lung adenocarcinoma and examined the podoplanin expression of CAFs and their prognostic impact in primary and metastatic N2 lesions.
Results: A significant positive correlation was found in podoplanin expression in CAFs between pairs of primary and metastatic lesions ($P < 0.001$). The difference in the overall survival of patients with podoplanin-positive/negative CAFs in their primary lesion was not correlated ($P = 0.927$). In contrast, patients with podoplanin(+)-CAFs in metastatic lymph nodes had a shorter overall survival than those without podoplanin(+)-CAFs ($P = 0.003$). In multivariate analyses, podoplanin(+)-CAFs in metastatic lymph nodes were a significantly independent risk factor for a poor outcome ($P = 0.007$).
Conclusions: Our study indicated podoplanin(+)-CAFs in metastatic lymph nodes was a significant prognostic factor for overall survival among pathological N2 stage III adenocarcinoma patients.

P4183

Immunohistochemical expression of Bcl-2 and p53 in patients with lung cancer: Correlation with survival time

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Background and aim: Bcl-2 and mutated p53 genes are the most relevant proteins involved in apoptosis and tumor development. The aim of this study was to determine the Bcl-2, p53 and Ki-67 expression and their impacts on survival time in patients with lung cancer.
Material and methods: 127 patients with lung cancer (LC), 87 with non-small cell lung cancer (NSCLC) and 40 with small cell lung cancer (SCLC) were stained immunohistochemically on paraffin-embedded tissue, using specific monoclonal antibody for Bcl-2 and p53.
Results: The differences in apoptotic marker expression between NSCLC and SCLC were revealed: p53 expression is seen more frequently in NSCLC patients (46/87; 52,87%). Bcl-2 expression is seen in 26/40 (65,0%) SCLC patients, and only in 27/87 (31,03%) with NSCLC (p=0,000). The Kaplan-Meier survival analysis demonstrated that Bcl-2 positive SCLC patients had poor survival status (Log Rank=20,137 p=0,000). In NSCLC patients only p53 immunoreactivity was associated with shortened survival (log Rank=6,534 p=0,011). Multivariate analysis showed that over-expression of Bcl-2 and p53 were independent prognostic marker for poor survival in the patients with SCLC (HR=6,02 p=0,000), and NSCLC (HR=1,547 p=0,049), respectively.
Conclusions: The results indicated that aberrant expression of p53 and Bcl-2 have a strong effect on survival and prognosis in patients with NSCLC and SCLC and reflect their different pathogenesis.