Male to female ratio was 17:29, mean age was 52.7 years (ranged from 31 to 74 years). Relapse free time varied from 6 months to 5 years. All patients had abnormal radiographic finding. Radiography was done on routine control examination in 60% of patients, who had no symptoms. The most common primary malignancy was laryngeal carcinoma (22pts-47.8%), breast carcinoma (6pts-13%), adenocarcinoma of the colon (5pts-10.8%), thyroid gland carcinoma (5pts-10.8%) cervical carcinoma of the uterus (3pts-6.52%) and other, less common tumors (stomach, esophagus, prostate, tongue). Bronchoscopic finding revealed that endoluminal metastases were more common in right lung (in 31 pts-67.4%). Most of the metastases were seen in upper lobe bronchi (52%). Biopsy was performed and pathohistological verification was obtained in all patients. In more then 1/2 of the patients histologic type was squamocellular carcinoma.

We can conclude that fiberoptic bronchoscopy with biopsy is simple, cheap technique in diagnosis of endobronchial metastases. Histological verification is 100% in centrally localized lesions.

P1-157 **Mesothelioma and Other Thoracic Malignancy Posters, Mon, Sept 3**

Mediastinal adenosquamous carcinoma with involved the left subclavian artery

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I would like to present the mediastinal adenosuamous cell carcinoma involved the left subclavian artery, left brachiocepharic vein, left recurrent nerve and left phrenic nerve.

A 48-year-old male visited our institute with abnormal findings of left upper mediastinal on chest X ray. The left subclavian artery was involved with the tumor of 5.0 X 4.5 cm in diameter on chest CT scan. However, there were no left shoulder pain and lower arterial pressure of the left upper extremities than the right upper extremities. VATS (video-assisted thoracoscopic surgery) was performed for pathological diagnosis, and the pathological diagnosis was adenosquamous cell carcinoma. PET (positron emission tomography) scan revealed the just uptake of the tumor site. So, we performed the mediastinal tumor resection and the combined resection of the left subclavian artery, the left brachiocepharic vein, left recurrent nerve and left phrenic nerve. The left subclavian artery reconstructed with Gelwaeve 8mm, and the left brachiocepharic vein reconstructed with ringed e-PTFE 10mm. The postoperative course was smooth and not eventful, he was discharge on the 10 days after operation.

P1-281 **Mesothelioma and Other Thoracic Malignancy Posters, Mon, Sept 3**

Clinical features of bronchial carcinoid tumor- 10 years experience (1996-2006)

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The aim of the study was to analyse clinical features and 1-yr survival rate of bronchial carcinoid patients diagnosed at the Institute of Lung Diseases and TB in Belgrade 1996-2006.

The group consists of 58 pts (30 females and 28 males), the average age of 48 ys (17 - 75). 57 of them underwent operation: lobectomy in 34pts (58.6.%), pneumonectomy in 11pts(19%), atypical resection in 9pts (15.5%), bilobectomy in 3pts (5.2%). Hystologic finding of typical carcinoid tumor was in 39pts (67.2%), while atypical in 19pts (32.8%). Central tumor type was noted in 30pts(51.7%) and peripheral in 28pts (48.3%). CT scan showed that majority of peripheral tumors were 3-3.5cmX4-4.5cm in diameter, with the exception of 1 case with the tumor size 8x7cm and 2 of size 6x5cm.

The most frequent symptoms were cough -30pts (51.7%), chest pain-25pts (43.1%), dyspnoea -20pts (34.5%), haemoptysis-19pts (32.7%), fever-18pts(31.0%), weight loss-13pts (22.4%) and fatigue-12pts (20.7%). Majority of pts had disease symptoms lasting either 1 year and longer-25pts (43.1%) or less than 3 months -16pts (27.6%).

Five pts (8.6%) had associated neuroendocrine disorder or tumor either in the previous history or at the same time of bronchial carcinoid tumor diagnosis. Only one pt with Kushing Sy persisting after operation of gonadotropic adenoma of pituitary gland, has shown to have hormonal activity of the peripheral bronchial carcinoid tumor since this Sy resolved after lung operation.

The 1-year follow-up analysis shows 1-year survival rate of 86.2% (50pts): 8pts died within the first year after diagnosis or operation. One pt died 6th day after operation due to fatal pulmonary embolism, and other 7 pts died due to metastatic disease relapse

Novel Therapeutics: Cytotoxic Chemotherapy

P3-016 **NT: Cytotoxic Chemotherapy Posters, Wed, Sept 5 – Thur, Sept 6**

In vitro activity of picropodophyllin in lung cancer cell lines and association to the insulin-like Growth Factor-1 receptor

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Background: Insulin-like Growth Factor-1 (IGF-1) and its receptor (IGF-1R) are important for transformation and growth of malignant cells and for the prevention of apoptosis. IGF-1R is often over-expressed in malignant tumors and several oncogenes depend on intact IGF-1R to achieve their transforming activity.

Recently, members of the cyclolignan family were identified as potential inhibitors of the IGF-1 receptor tyrosine kinase. Picropodophyllin (PPP), in particular, shows promise since it demonstrates selectivity for IGF-1R without inhibiting activity of the insulin receptor or other more distantly related receptors. There is, however, on ongoing debate if inhibition of microtubule assembly contributes to the cytotoxic effects of PPP as this is the major mechanism of action for its epimer podophyllotoxin, PPT. Tumor cells of lung cancer also express IGF-1-receptors, but their role in the malignant phenotype is still not clear. The aim of this study was to investigate the role of IGF-1R in lung cancer and to evaluate its potential as a therapeutic target through use of PPP, a specific tyrosine kinase inhibitor of IGF-1R. We also investigated the relation between IGF-1 receptor status in cells and sensitivity to conventional and experimental chemotherapeutic agents, including PPT and other microtubule inhibiting agents.

Methods: Expression levels of IGF-1R was evaluated by immunoprecipitation using antibodies directed against IGF-1R, followed by SDS-Polyacrylamide Gel Electrophoresis (SDS-PAGE) and Western blotting. 9 different cell lines, including both non-small cell and small cell lung cancer, were used in the analyses. Using the panel of IGF-1R expressing cell lines, we studied PPP-induced cell death by means of Fluorometric Microculture Cytotoxicity Assay (FMCA). We also combined PPP treatment with a panel of various cytotoxic drugs in order to study potentially additive or synergistic effects. Gene expression profiling using the microarray technique on an Affymetrix platform was used to characterize the cell lines. Quantitative real-time RT-PCR was used to validate gene expression levels.

Results: The sensitivity to PPP differed between the various cell lines, yielding IC50-values ranging from below 1 to almost 100 μM. Within the tested concentration range PPP-effects were nicely dose-dependent, and the shapes of the concentration-response curves differed from those of PPT which were much shallower. However both drugs shared cell lines in which the highest and lowest activity was seen, and correlation analysis of endpoints yielded moderate correlation coefficients. In addition, a panel of various cytotoxic drugs was tested in its effect on the lung cancer cells and a wide variation in sensitivity was noted between the cell lines. The gene expression profiles of the cells were examined using microarray technique and by statistical analyses, the profiles were evaluated for correlation with sensitivity to PPP. Further data on these analyses will be presented at the meeting. We also plan to study the effect of PPP on IGF-R signaling in the aforementioned cell lines from lung cancer and its importance to tumor biology, elucidating which signal proteins and pathways are affected by the treatment.

Conclusions: IGF-1R constitutes a potential therapeutic target in lung cancer and since regulation of the IGF-1R signal pathway is disrupted in a variety of tumors, inhibitors may be useful in various diagnoses. The cyclolignan picropodophyllin (PPP) significantly decreased cell viability in a concentration dependent manner in all lung cancer cell lines. PPP has been described as a specific inhibitor of IGF-1R, but in these experiments effects appear affected also by other, additional, mechanisms.

P3-017 **NT: Cytotoxic Chemotherapy Posters, Wed, Sept 5 – Thur, Sept 6**

Characterization of efficacy and cellular signalling induced the novel melphalan pro-drug J1 and J3 in NSCLC cells

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Background: Previous characterization of the novel melphalan containing pro-drugs J1 and J3 have revealed an increased cytotoxicity in human tumour cells of various origins compared to the parental substance melphalan (Gullbo et al., 2003). J1 is now in a Phase I trial. In order to get increased knowledge about the cellular signalling triggered by the melphalan-containing pro-drugs and trying to understand possible synergies with conventional chemotherapies, we have here compared the effects of J1, J3 and melphalan in NSCLC cell lines.

Methods: NSCLC cells have been treated with either J1, J3 or melphalan alone or in combination with standard chemotherapy. Cell viability upon treatments have been assessed using FMCA or MTT methods. Apoptotic signalling parameters (caspase-3 activation, mitochondrial depolarization, Bcl-2 family protein activation, Mitogen activated protein kinase (MAPK) activation) have been examined at various time points post treatment using a combination of flow cytometry, western blotting and immunoflurescence microscopy analysis.

Results and Conclusion: We report here that the melphalan pro-drug J1 causes a more rapid induction of apoptosis compared to melphalan in NSCLC cells. Moreover, our data show that J1-induced apoptotic signalling involves activation of Bak and Bax, depolarisation of mitochondria and activation of caspase-3. We report here that J1 causes an increased and more sustained activation of the MAPK JNK compared to melphalan. A role for JNK in J1-mediated cytotoxicity is shown by using pharmacological inhibitors. The importance of various cellular compartments for J1-mediated apoptotic signalling and the possible synergy with standard chemotherapy will also be discussed.

Reference:

Gullbo J, Tullberg M, Vabeno J, Ehrsson H, Lewensohn R, Nygren P, Larsson R, Luthman K. (2003) Structure-activity relationship for alkylating dipeptide nitrogen mustard derivatives.Oncol Res. 14(3):113-32.

P3-018 **NT: Cytotoxic Chemotherapy Posters, Wed, Sept 5 – Thur, Sept 6**

Comparison of vinorelbine plus oxaliplatin or cisplatin for treatment of advanced lung adenocarcinoma

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Objective: To observe and compare the effect and side reaction of two kinds of combined chemotherapy in treating patients with advanced lung adenocarcinoma. One is Vinorelbine plus Oxaliplatin (NO) AND THE OTHER IS Vinorelbine plus Cisplatin (NP).

Methods: 120 patients with advanced lung adenocarcinoma were divided into two groups. One group was treated with NO and the other was treated with NP,. Patients in two groups were well-matched in basic characteristics. All of them were treated by the two regimens responsively for 2 or 3 cycles.

Results: The reponse rate was 43.3% in group NO and 45.0% in group NP. The median survival duration, one-year survival rate and three-year survival rate in NO group were eleven months, 38.3% and 8.3%; and in group NP they were ten months, 38.3% and 10.0%. There was no statistics difference in the curative effect of the two groups($P<0.05$). Bone marrow inhibition was dose-limited toxicity of the two groups. The rates of III degree-IV degree neutropenia in group NO and NP were 22.2% and 21.6% ($P<0.05$). The rate of alimentary canal reaction in group NP was higher than the rate in group NO ($P<0.05$).The rate of renal disfunction in group NP was higher than the rate in group NO ($P<0.05$). The rate of neurotoxicity in group NO is higher the rate in group NP ($P<0.05$),but all patients, neurotoxicity can be renewed after chemotherapy. The rate of other unwanted reactions in two groups is similar. All side reactions can be endured.

Conclusion: Both NO and NP are effective and safe in treating patients with advanced lung adenocarcinoma. The two regimens have the close curative effect. And the side reactions are similar. However, NO regimen has slighter toxicity in gastrointestin and renal function, so patients can endure better.