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E4303**Granulocyte colony-stimulating factor enhances the anticancer effects of cisplatin against lung cancer by promoting angiogenesis**

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Background: In spite of the common use of the G-CSF for chemotherapy, there were few reports that showed the effects of G-CSF and the combination effects of G-CSF and anticancer drugs against lung cancer.

Methods: In the present study, we investigated the effects of G-CSF and the combination effects of G-CSF and cisplatin on lung cancer growth. First we investigated the effect of G-CSF against the LL-2 and KLN-205 cells by MTT assay and tried to detect the G-CSF receptor by RT-PCR. Next, to analyze the G-CSF effects in vivo, we transplanted the LL-2 into C57BL/6 mice, intraperitoneally administered G-CSF (30 µg/kg/day) with or without cisplatin (5 mg/kg), measured the tumor size and analyzed pathologically by HE and immunostaining.

Results: In vitro analyses, G-CSF showed no effects in LL-2 and KLN-205 cells, and RT-PCR revealed no G-CSF receptor mRNA. In vivo analyses, G-CSF alone did not significantly suppress tumor growth. However, concurrent G-CSF administration with cisplatin significantly enhanced the tumor suppressing effect of cisplatin in early stage of tumor growth.

The analysis data of vWF immunostaining indicated that the neovascularization in the peripheral region of the tumors was more enhanced in G-CSF treatment mice. ELISA assay revealed that G-CSF did not influence the serum concentration of TNF-alpha and IL-12 in tumor-bearing mice.

Conclusion: This study suggests that concurrent (combination) administration of cisplatin with G-CSF is a safe and effective method for enhancing anticancer effects and reducing chemotherapeutic agent-induced myelosuppression.

E4304**Systemic inflammatory reaction following pleurodesis with talk surrury**

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Aim: The occurrence of systemic inflammatory reaction in neoplastic pleurisy following pleurodesis with talk surrury

Material and method: 85 patients, 64 males aged 68±8 and 21 females aged 56±12. Body temperature, white blood cell count and type, c-reactive protein (CRP) were documented before and 48 hours following pleurodesis. Antipyretic and anti-inflammatory medication was not administered. Only opiates were given during the procedure. All patients were followed up for 3 months.

Results: 12% of patients presented with fever more than 38°C, increase in white blood cell count (p<0.005) with an increase in neutrophils (p<0.001) and an increase in CRP (p<0.001). Antibiotics were not administered and the above findings subsided within 48 hours, except for CRP which remained elevated. Pleurodesis was successful in all patients with the above findings, whereas the success rate was diminished in the remaining patients.

Conclusion: Pleurodesis with talc surrury may present with a systemic inflammatory reaction which subsides without the administration of antibiotics and non steroid anti-inflammatory drugs.

E4305**A phase II trial of lipoplatin-gemcitabine in patients with advanced NSCLC: preliminary results**

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Background: Lipoplatin is a new liposomal cisplatin already tested in solid tumors with encouraging results. Recently, we reported the results of a phase I study of a combination of lipoplatin with gemcitabine. The purpose of this phase II trial was to evaluate response and toxicity in patients (pts) with advanced NSCLC.

Patients and methods: We are planning to include 40 pts with PS < 2, in this phase II study, combining lipoplatin 120mg/m² d1,8 to gemcitabine 1000mg/m² d1,8 every three weeks, as suggested by our results of the phase I trial. To this day 27 pts (21 males, 77.8%) are assessable for response and toxicity according to the WHO criteria. Patients median age is 70 years (41-78). Stage IV at diagnosis have 22 pts (81.5%). Carcinomas histological type is adenocarcinoma in 14 (51.8%) and squamous-cell in 13 (48.2%).

Results: From the 27 assessable pts, PR have 6 pts (22.2%), SD 5 (18.5%) and PD 16 (59.2%). Hematological toxicity is: Grade 3-4 neutropenia in 6 pts (22.2%), Grade 3 thrombocytopenia 1pts (3.7%) and grade 3 anemia in 1 (3.7%). Grade 3-4 nausea/emetis have 9pts (33.3%), Grade 3 hyperthermia 9pts (33.3%) and Grade 3 nephrotoxicity 1pts (3.7%). Other toxicity, such as rash, constipation, peripheral neuropathy, is rare and/or mild. To this day only TTP has been evaluated: median overall TTP is 14 weeks (3-50). Significant different TTP is observed between pts PR vs PD (p=.0001), SD vs PD (p=.001), but not between PR vs SD (p=0.3).

421. Therapy of thoracic tumours

E4302**Analysis of clinical factors in relationship to treatment effects of erlotinib in non small cell lung cancer (NSCLC) patients**

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Background: Our study evaluates the outcome of the first 47 patients with advanced NSCLC (stage III/IV) treated with erlotinib. We tried to find parameters that could predict efficacy of erlotinib treatment in this patients.

Patients and Methods: There were 53.2% men and 46.8% women. Mean age was 58.4 years. Never-smokers were 21.3%, former-smokers 61.7% and 17.0% were smokers. Adenocarcinoma was diagnosed in 59.6%, BAC in 6.4%, squamous cell carcinoma in 21.3%, NSCLC without further details in 10.6% and large cell carcinoma in 2.1%. PS at the start of treatment was 0 in 2.1%, 1 in 70.2% and 2 in 27.7% patients.

Results: Best objective response was PR in 21.3% and SD in 36.2% patients. PD was found in 23.4% and the treatment was stopped until 1 month in 19.2% patients. Average duration of treatment in patients with PR was 9.4 months and in patients with PD 3.4 months. PR was significantly more frequent in women than in men (p<0.001). There was a trend to better response in the former one (p=0.067) in patients with adenocarcinoma. Better response was in never smokers (PR 40%) than in former-smokers and smokers (PR 21.4%), but this difference was not statistically significant. 2nd line treatment was with significantly better response (PR 40.9%) than 3rd line (PR 6.7%). Median survival in patients with PR was statistically significant (p<0.001) longer than those with SD a PD.

Conclusions: Erlotinib was well tolerated with evidence of antitumor activity in 2nd and 3rd line of antitumor therapy in patients with advanced NSCLC. We found female sex, histology of adenocarcinoma, never smoker status and 2nd line treatment as potential factors of better response.

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Conclusion: Although our phase II trial is still on going, our preliminary results are encouraging in terms of response rate and toxicity.

E4306**Clinical characteristic of lung cancer patients with interstitial pneumonia treated with chemotherapy or radiotherapy**

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Objective: Lung cancer associated with interstitial pneumonia (IP) has poor prognosis, and its clinical characteristics were not well documented. Standard therapy for lung cancer associated with IP has not established. Therefore, we evaluated the clinical characteristics of lung cancer patients with IP who treated with chemotherapy or radiotherapy(RT).

Material and Methods: We enrolled 47 lung cancer patients with IP who treated with chemotherapy or RT at Kurume University Hospital from 1999 to 2007. These patients were divided into four groups; operative therapy (n=10), chemotherapy alone (n=18), radiochemotherapy (n=7), and RT alone (n=2). We analyzed the relationship between clinical characteristics and survival time. We investigated the correlation between acute exacerbation and chemotherapy or RT in lung cancer patients with IP.

Result: Median age of patients is 71(54 to 82). Forty-two patients were men and 5 were women. Twenty-three patients were current smoker, 21 were ex-smoker and 3 were never-smoker. Histological examination showed that 17 patients were adenocarcinoma, 18 squamous cell carcinoma, 1 large cell carcinoma, 9 small cell carcinoma, and 2 were unknown histology. Twenty five patients (53.2%) were treated with chemotherapy showed significant better prognosis than patients who did not receive chemotherapy. Only 3 (6.3%) patients suffered from acute exacerbation due to chemotherapy.

Conclusion: Our study showed that lung cancer patients with IP treated with chemotherapy or RT had better prognosis than those who had no treatment. These results suggest that chemotherapy is efficient for good performance status of lung cancer patients with IP.

E4307**Treatment of patients with advanced non-small-cell lung cancer (NSCLC) with erlotinib: results from clinical practice**

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Background: It is not entirely clear who benefits from therapy with the EGFR-tyrosine kinase inhibitor erlotinib. Post-hoc subgroup analyses of randomized phase II and III studies suggest that nonsmokers, women, and patients with adenocarcinoma may have a superior response to treatment.

Aim: We performed a retrospective analysis to answer the question, whether these 3 response criteria can be used in routine clinical practice for patient selection for therapy with erlotinib.

Methods: 26 consecutive patients with inoperable pretreated NSCLC who were treated with erlotinib (150 mg/d) were analysed. In addition, a patient on hemodialysis unfit for conventional chemotherapy was treated with erlotinib 1st line.

Results: 11 patients had an objective response, another 5 showed stable disease. The patient on hemodialysis tolerated erlotinib well with stable disease after 4 months. In 4 patients – never-smoking women with adenocarcinoma – the response lasted for more than a year. None of the current smokers responded to erlotinib.

Conclusion: The physicians had performed a clinical preselection: 12 patients were never smokers, whereas only 5 were current smokers. 21 patients had an adenocarcinoma, only 5 had squamous cell carcinoma. In contrast to our results, in the randomized clinical trial (BR.21), which was performed without this patient selection, erlotinib showed an objective remission of only 8.9%. Thus, the above clinical criteria may be valid for response prediction to erlotinib. Our retrospective data need to be confirmed with larger patient numbers (e. g. from registries) in order to define the clinically and economically appropriate method of patient selection.

E4308**Mutations of EGFR and k-ras genes and TK inhibitors. Are there differences between gefitinib and erlotinib?**

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Background: NSCLC patients should profit from therapy by TK inhibitors. Clinical predictors of efficacy are non-smoking status, female sex, good performance status and adenocarcinoma type. Molecular predictors are EGFR mutations and gene amplifications, eventually EGFR overexpression.

Aim of study: We investigated mutations of EGFR and k-ras genes in gefitinib and erlotinib patients and its correlation to response and survival. In a subset, we have also performed analysis of EGFR amplification.

Patients and methods: We analyzed a total of 294 patients (223 gefitinib, 71 erlotinib). Mutations were detected from histologic and cytologic specimens processed by laser microdissection. Exon 19 deletions and exon 21 mutations (L858R) were analyzed by fragment and analysis and temperature-gradient CE, respectively.

Results: In gefitinib, EGFR mutations were at 14,9% (in 75% ex.19 del. vs. 25% L858R). K-ras mutations found in 13,6%, mostly codon 12 GGT>TGT. In erlotinib, we found 8,4% EGFR mutated and 11,2% K-ras mutated. In both groups EGFR mutated adenocarcinomas have better TTP and MOS than other EGFR mutated types (412 vs 117 days, $p=0.00045$, and 534 vs 207 days, $p=0.00473$) and also better TTP and MOS than non-mutated adenocarcinomas (429 days vs 85, $p=0.00013$, and 534 vs 244 days, $p=0.00028$). Erlotinib longer than 6 months, had EGFR mutations in 83.3%, while K-ras mutated, non-mutated and cases without analysis were at 17%, 15,2% and 17%.

Conclusions: The results suggest that EGFR mutations should be examined in prior to TKI therapy of adenocarcinomas. Neither K-ras mutations or EGFR amplifications showed effect for therapy outcome.

E4309**Prophylactic cranial irradiation in small-cell lung cancer patients**

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Introduction: Despite the evidence-based medicine, prophylactic cranial irradiation (PCI) is still a debatable issue of the small-cell lung cancer (SCLC) treatment approach.

Objective: The study is aimed at establishing the survival of SCLC pts whose treatment protocol included PCI.

Methods: The results obtained from 455 SCLC pts treated in our Institute over the period Jan. 1999-Dec. 2003.

Results: The examined cohort included 362 (79.5%) males and 93 (20.5%) females, at the mean 57.5 (21-81) years of age.

The disease was staged as limited (LD) or extensive (ED) in 333(73.2%) and 122 (26.8%) pts respectively.

The LD pts achieved the following radiological response: CR-9(2.7%) pts, PR-138 (41.4%) pts, SD-78(23.4%) pts, and PD -108 (32.5%) subjects. The response rate (RR) of 44.1% and 8.2-mts mean survival were obtained.

The ED pts achieved the following radiological response: CR-1 (0,8%) pt, PR-37(30,3%) pts, SD-19(15,6%) pts, and PD- 65(53,3%) pts. The response rate (RR) of 31.1.1% and 5-mts mean survival were obtained. The LD pts received a combined chemo-irradiation treatment (cisplatin-etoposide and irradiation 40 Gy), while the ED pts received only chemotherapy.

Twenty-two pts of the LD Group who received PCI (36 Gy) achieved the overall mean survival of 15.9 mts. Of them, 5 (22.7%) and 17 (77.3%) achieved a complete or partial treatment response respectively. The subgroup with a PR had the mean survival of 17.5 mts, while the one with a CR achieved the mean survival of 8.2 mts.

Conclusion: The results of our study suggest that even the SCLC pts with partial response may achieve a significantly longer survival with PCI, so this treatment option should be routinely offered to these pts in the future.

E4310**Topotecan in combination with carboplatin and etoposide as first line treatment in SCLC patients: a phase I/II study – final results**

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The inhibition of Topoisomerase-I by Topotecan(T) results in increased *in vitro* sensitivity of the tumor to Etoposide(E). Carboplatin(C) when combined with Camptothecin in preclinical studies had a synergistic effect without any cross resistance. We used the combination of these 3 agents in 44 chemotherapy-naive male patients with SCLC (median age 63.5, PS 0-1 and adequate renal, liver & bone marrow function). ED was present in 28 (64%) pts. Each treatment cycle consisted of T (1 mg/m² on days 1, 2 & 3), C (AUC=5.5 on day 3) and an oral dose of E (100 mg on days 15, 16 & 17) for up to 8 cycles and every 32 days. Responders received radiotherapy to the primary site (50 Gy) after the 4th cycle and complete responders also received PCI. Palliative radiotherapy and hematopoietic growth factors were used as appropriate. Due to grade 3/4 neutropenia at the initial stages the dose of T was decreased to 0.8 mg/m² and of C to AUC=5 for all patients for the subsequent cycles. CR was achieved in 4 pts (9%), PR in 18 (40.9%), SD in 8 and PD in 14. Median survival was 280(95%CI 208-352) days (LD: 455days) and median time to progression 137 days. 11 pts developed grade 3/4 neutropenia and 3pts grade 3/4 anemia. Non-hematological toxicity was mild. 15 pts (34%) were alive during the 1st year, 3 (6.8%) in the 2nd year and 2 (4.5%) in the 4th year. In contrast to ORR, TTP and survival were quite similar to those of SCLC

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pts suffering from ED treated by a Platinum-E regimen. The T/C/E combination was active and well tolerated, but with lower toxicity. This regimen could be tried in the future for SCLC pts with poor prognosis to minimize side effects.

E4311**Timing of radiotherapy and possible survival benefit in limited disease SCLC patients**

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Background: It is standard clinical practice to combine chemotherapy and chest radiotherapy in treating patients with Limited-Disease (LD) SCLC. However, the best way to integrate both modalities is still unclear.

Purpose: To evaluate if the timing of chest irradiation with respect to chemotherapy would influence survival in pts with LD SCLC.

Patients and methods: In this multicenter study 493 pts with LD SCLC and PS 0-1 were retrospectively analyzed. 161 (Group A) of them received early radiotherapy (20+20 Gy) concurrent with the first 2 cycles of platinum chemotherapy and 332 pts (Group B) received radiotherapy after 6 cycles of platinum chemotherapy followed by 1 or 2 further cycles.

Results: A significantly higher survival was observed when chest radiotherapy was applied after the end of chemotherapy (Group A: Md: 270days, 95% CI 238-301, p=0.02 Breslow, Group B: Md 319, 95% CI 298-339).

Conclusions: In our study, results show that late radiotherapy had better influence on survival in comparison to early radiotherapy in LD SCLC pts. Nevertheless, the small number of pts impedes meaningful conclusions and further prospective studies are required.

E4312**Phase II open-label trial of Erlotinib in progressive pretreated advanced non-small cell lung cancer (NSCLC)**

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Background: Erlotinib is an oral tyrosine kinase inhibitor, targeting the human epidermal receptor type 1/EGFR, approved for treatment of patients with locally advanced or metastatic non-small-cell lung cancer (NSCLC) after failure of more than 1 or 2 previous chemotherapeutic regimens.

Method: An open-label trial of daily oral Erlotinib in inoperable stage III B/IV NSCLC progressed following standard chemotherapy has been designed. Primary endpoints were overall response rate (ORR) and overall survival (OS); secondary objectives were safety assessment, ORR and OS in sub-groups of patients clustered by histological type, gender, smoking history, PS, skin rash.

Patients and treatment: 102 patients were enrolled from Oct 2005 to July 2007; M/F 75/27; average age 63.2 (range 31-79); ECOG PS 0/1/2/3: 25/41/21/15; Stage III B: 32, IV: 70. Squamous: 20, adenocarcinoma: 40, non small cell: 39, mixed histology: 3. Smoking history: never smoked 10%, previous smokers 60%, current smokers 30%. 82 out of the 102 patients entered into the study were evaluable for response.

In 18% of patients erlotinib was tested as second-line chemotherapy, in 73% as third-line, 9% as forth-line. Erlotinib was given at standard dose of 150 mg once daily. In rash G3, erlotinib was reduced to 100 mg.

Results: ORR was 55% (PR: 21 pts, SD: 23 pts, RC: 1 pts); PD: 45%; skin rash in 42% (G1: 13 pts, G2: 16 pts, G3: 10 pts). Diarrhea in 13% (G1: 6 pts, G2: 4 pts, G3: 2 pts). OS and cluster analysis will be presented at the meeting.

Conclusions: Erlotinib demonstrated efficacy in NSCLC patients in progression after standard chemotherapy. The regimen was well tolerated and safely administered.

E4313**Study on coagulation abnormality and effect of anticoagulation on prognosis in advanced cases of non-small cell lung cancer**

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Objective: To investigate the alteration of coagulation factors and the effect of anticoagulation on prognosis in advanced cases of non-small cell lung cancer (NSCLC).

Methods: Plasma levels of D-dimer (DD), thrombomodulin (TM), tissue plasminogen activator (tPA), plasminogen activator inhibitor 1 (PAI-1), protein C (PC), protein S (PS), antithrombin III (AT-III), and serum total homocysteine (tHCY), were measured by ELISA in 82 cases of stage IIIB-IV NSCLC (NSCLC group) and 30 normal subjects (control group). Then 35 patients were treated by

chemotherapy(CT) plus low molecular weight heparin (LMWH, Nadroparin 0.1 ml/15kg,b.i.d, i.h) (CT +LMWH group); other 34 patients were only treated by CT(CT group). Finally, all patients were followed up.

Results: the levels of DD, TM, PAI-1, tHCY, in NSCLC group were significantly elevated ($P < 0.05$), while the levels of PS, AT-III were greatly decreased ($P < 0.05$), compared with control group. But there was no significant difference in levels of PC, tPA. The follow-up results: there were 5 cases (14.3%) complicated with deep venous thrombosis (DVT) in CT + LMWH group, while there were 10 cases (29.4%) with DVT or/and pulmonary thromboembolism (PTE) in CT group. Kaplan-Meier survival analysis showed that median overall survival were longer CT plus LMWH group than CT group (12 months vs. 8 months) ($P < 0.05$). Toxicity from LMWH was few.

Conclusions: Hypercoagulable state in advanced cases of NSCLC was related to activation of coagulation and fibrinolytic system, as well as endotheliocyte. LMWH may reduce occurrence of thrombosis and prolong survival time.

E4314**Targeting neuropeptide receptors by substance-P analogues identifies a strategy to develop novel anti-cancer therapies**

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Lung cancer is the most common fatal malignancy in the developed world and small cell lung cancer (SCLC) accounts for 25% of all lung cancer. Despite initial sensitivity to chemotherapy and radiotherapy patients relapse with resistant disease and survival rarely exceeds 2 years. Multiple neuropeptide growth factors including gastrin releasing peptide (GRP) and arginine vasopressin (AVP) stimulate mitogenic signalling in small cell lung cancer (SCLC) and the expression of their cognate receptors correlates with chemoresistance. We have identified several analogues of substance P which block mitogenic signalling by GRP and AVP but activate receptor mediated cell death by acting as "biased agonists" at neuropeptide receptors. These analogues are antiproliferative in vitro and inhibit growth of SCLC xenografts in vivo. Our work has provided a proof of concept for the development of pathway selective agonists as anticancer agents for SCLC. One of these agents [Arg6,D-Trp7,9,NmePhe8]-substance P (6-11) (SP-G), has completed a Phase 1 clinical trial where therapeutic plasma levels were achieved with minimal acute toxicity. Future work aimed at developing more efficacious analogues with better bioavailability will provide a novel therapeutic utility for SCLC and other neuroendocrine tumours expressing neuropeptide receptors.

E4315**Non-small cell lung cancer with single brain metastasis: the role of surgical treatment**

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The prognosis of NSCLC with brain metastasis is very poor, with median survival rate below 6 months, even if treated with palliative radio and/or chemotherapy.

Methods: 32 patients with NSCLC and single brain metastasis underwent surgical treatment of both primary lung cancer and secondary cerebral lesion. Patients (pts) were divided into two major groups. In group 1 (G1) 20 pts presented a synchronous brain metastasis. In group 2 (G2) 12 pts presented a metachronous brain metastasis during the follow-up period (range 4-22 months since the primary tumor). Patients selected in G1 had T1-2, N0-1 clinical staging, good performance status (ECOG 0-1), age < 75 years. Craniotomy has always been the first approach. In G2 also patients with locally advanced tumors (T3 and/or N2) were included. Whole brain radiotherapy and/or chemotherapy was the post-operative choice treatment.

Results: Histologic findings have shown: adenocarcinoma in 17 cases, squamous cell carcinoma in 12 cases, large cell carcinoma in 2 and large cell neuroendocrine carcinoma in one. Survival analysis has shown an overall value of 78% at 1 year (90% in G1; 42% in G2), 44% at 2 years (47% in G1; 25% in G2), and 3 years (15% in G1; 17% in G2). According to univariate analysis prognosis is definitively better in N0 tumors compared to N1-2 tumors and in adenocarcinoma cases compared to other histotypes ($p < 0.05$).

Conclusions: We can conclude that combined surgical therapy is, nowadays, the choice treatment for this kind of patients, even though restricted to selected cases. The knowledge of prognostic factors may optimize indications for surgery.

E4316**Thoracic radiotherapy as retreatment for locally recurrent symptomatic non small cell lung cancer**

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Background: Locally recurrent is common event after treatment of non small cell lung cancer (NSCLC). Symptoms from local recurrence after radiotherapy for NSCLC are often difficult to palliate

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Purpose: To evaluate the efficacy and safety of the reirradiation for locally recurrent symptomatic NSCLC previously treated with radiotherapy.

Material and Method: 22 patients (17 male, 5 female) with history of previous thoracic radiation therapy, underwent thoracic reirradiation for locally recurrent non small cell lung cancer. 91% patients had Performance status ≥ 2 . Median age was 62.5 years (range 38- 72). Patients had at least one of the respiratory symptoms related to locally recurrent non small cell lung cancer. 45% patients had received a radical dose at the first course of radiotherapy. The median time from the initial course to the re-irradiation was 11 month. Patients reirradiated with total dose 20Gy in 5 fractions. The field included the tumor volume with margin of not more than 1cm.

Results: The thoracic reirradiation was achieved effective palliation of intrathoracic symptoms related to locally recurrent non small cell lung cancer, 80% for haemoptysis, 75% for chest pain, 38,8% for dyspnea and 43,7% for cough. Treatment was well tolerated. Reirradiation –induced toxicity included symptomatic radiation pneumonitis in 2 patients and symptomatic radiation esophagitis in 6 patients. These toxicities were not fatal. No radiation myelopathy was observed. The median survival time after reirradiation was 3 month.

Conclusion: Thoracic reirradiation can provide good palliation and should be considered as a treatment option for locally recurrent symptomatic non small cell lung cancer.

E4318

A phase III randomised study comparing concomitant standard cisplatin (P) – etoposide (E) and chest irradiation to concomitant etoposide plus daily cisplatin and chest irradiation as induction therapy for limited (LD) small cell lung cancer (SCLC)

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Background: Early concomitant chemoradiotherapy is a standard of care in LD SCLC. We evaluated if the daily administration of cisplatin during radiotherapy gives an advantage in term of survival in comparison to the standard approach.

Methods: Patients with previously untreated LD SCLC, Karnofsky performance status ≥ 60 , adequate haematological, hepatic, renal, lung and cardiac functions were eligible. Patients were randomised between a first course of E (100 mg/m² D1-3) plus P given either at 90 mg/m² on D1 (arm A) or at 6 mg/m² (D1-5, D8-12, D15-19) (arm B) one hour prior to chest irradiation (15 fractions of 2.66 Gy). Afterwards, all patients received P (90 mg/m² D1) plus E (100 mg/m² D1-3) up to 6 cycles.

Results: 204 eligible patients (arm A 104, arm B 100) were randomised without any significant imbalance between both arms. Best response rates were similar: 84% in arm A and 80% in arm B (p = 0.59). Seventy-nine deaths occurred in each arm. Median, 2- and 5-years survivals were 15.5 m, 35%, 18% (arm A) and 17 m, 38%, 21% (arm B) (p = 0.48). There was more leucopenia in arm A and more thrombopenia in arm B.

Conclusions: Overall results were very good. Patients with LD SCLC obtained similar survival including long-term survival with early concurrent chemoradiotherapy whatever the cisplatin administration regimen during radiotherapy.

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Early and late immunological effects of radio-frequency ablation in lung cancer patients

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Radio-frequency ablation (RFA) is an effective technique to destroy lung tumor in patients without surgical prospects. Tumor destruction could be an antigen source for the immune system to develop a response against the tumor.

We assessed whether RFA could induce a systemic inflammatory response and/or modulate T-cell reactivity in lung tumor patients not suitable for resective surgery. We considered leukocyte counts and plasma levels of chemokines, cytokines and acute phase reactants (APRs) as inflammatory parameters. The number of peripheral T regulatory (Treg) cells, the degree of proliferation of un-fractionated CD4+ T cells and the number of IFN- γ secreting cells were assessed to evaluate T-cell reactivity.

Early after RFA there was a significant systemic inflammatory reaction, as demonstrated by the increase of neutrophils and monocytes, and levels of multiple chemokines and APRs. However, a concomitant secretion of IL-10 was observed. Later after treatment, we demonstrated a significant and persistent reduction of CD4+ Treg cells, that was accompanied by an increase of non antigen-specific proliferation of un-fractionated CD4+ T cells and of IFN- γ secreting cells. RFA may influence immune responses, by inducing early a systemic inflammatory reaction and later a reduction of Treg cell pool. IL-10 release might represent a self-regulatory mechanism controlling the entity of the inflammatory response. The reduction of Treg pool might improve patient's immunocompetence and at least partially overcome tumor tolerance.

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Randomized phase II study of adjuvant cisplatin/docetaxel (Cis-Doc) or cisplatin/vinorelbine (Cis-VRB) in patients (pts) with resected stage IB-II NSCLC: interim analysis

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Background: Several randomized phase III trials in early-stage NSCLC, showed that Cis-VRB adjuvant chemotherapy (CT) improves survival; however, compliance with adjuvant CT remains problematic.

A recent meta-analysis in pts with advanced NSCLC found a significant survival benefit for docetaxel-based CT compared to vinca alkaloid-based CT

Methods: Pts with completely resected stage pIB-II NSCLC, good performance status and planned start of chemotherapy within 60 d of resection were included. Pts were randomized (2:1) to adjuvant CT with Cis-Doc (Cis and Doc both 75 mg/m² on day 1) or Cis-VRB (Cis 80 mg/m² on day 1; VRB 25 mg/m² on days 1 and 8) every 3 weeks for 4 cycles. Primary endpoint was success of treatment delivery (defined as ≥ 3 cycles of chemo with a relative dose intensity (RDI) of $\geq 80\%$). A two-stage design with pre-planned interim analysis was used (total sample size 99 pts).

Results: From 12/2005 to 09/2007, 45 pts (33 males, 12 females) were randomized (Cis-Doc 35/Cis-VRB 10). Pathological stages included stage IB (n=32), stage IIA (n=6), stage IIB (n=7). Resection consisted of segmentectomy (n=1), (bi-)lobectomy (n=34), sleeve lobectomy (n=2) and pneumonectomy (n=8).

In arm Cis-Doc 25 and 23 pts and in arm Cis-VRB 15 and 9 pts completed 3 and 4 cycles resp. Dose intensity (mg/m².wk) was: Cis 24.4 and Doc 24.5 in Cis-Doc arm and Cis 23.7 and VRB 15.0 in Cis-VRB arm. RDI was Cis-Doc 98%/98% and Cis-VRB 89%/90%. No treatment-related deaths were observed.

Conclusions: Adjuvant CT with 3-weekly schedules of Cis-Doc or Cis-VRB results in a good CT compliance and dose intensity.

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Palliative radiotherapy and quality of life of elderly lung cancer patients

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Purpose: more than 50% of patients with non-small cell lung carcinoma are above 65 years of age. Due to comorbidity and fragility some of them are unfit for surgery or chemotherapy. The purpose of the study is to evaluate palliative effects and quality of life of elderly lung cancer patients undergoing only palliative radiotherapy.

Material and methods: in the period January 2002 – October 2007 there were 167 patients aged from 68-87 years (Me 74 years) with pathohistologically confirmed non-small cell lung carcinoma who were treated with radiotherapy dose of 30Gy in 10 fractions. All the patients were diagnosed based on radiography, CT scan, bronchoscopy. The majority of 133(79,64%) pts had lung cancer with mediastinal lymph node metastases while 34(20,35%) of them also had suprarenal metastases. Patients with bone, brain and liver metastases were excluded from the study. The main symptoms were hemoptysis, cough, chest pain and dyspnea. Two thirds of them were outpatients

Results: radiotherapy was more effective in relief of hemoptysis and chest pain than dyspnea to be the least effective in cough relief. Only 7 patients did not finish radiotherapy. Radiotherapy was well tolerated by the majority of the patients with minor side effects like dysphagia G1-2 and cough. No blood count disorders were evidenced.

Conclusion: the results of this retrospective study recommend radiotherapy as an effective palliative method for elderly lung cancer patients free of distant metastases who are not candidates for surgery or chemotherapy. The effect of the treatment leading to diminishing of the symptoms such as hemoptysis, dyspnea, and chest pain improve the quality of life.