of SQC relapses have been found 6 moths later than in AD. Clinical relapse has been proven 6 to 18 months after CYFRA relapse. The increase of CYFRA 21-1 level has required more extensive and frequent bronchological examination which provided the reoperation of 4,2% patients in the same stage of the disease.

Conclusions: These results show that tumor marker CYFRA 21-1 has prognostic and predictive value in surgical treatment of primary lung neoplasms.

774 POSTER

Quality of life assessment and final results of a randomised Phase II Study with single-agent Gemcitabine and Docetaxel given sequentially every 3 weeks show effective treatment in advanced NSCLC

L.R. Pilz[1], G. Koschel[2], J. Mezger[3], K. Schott[4], W. Spengler[5], C. Manegold[6]. [1] *German Cancer Research Center (DKFZ), Biostatistics C060, Heidelberg, Germany;* [2] *AKH Hamburg, Lungenabteilung, Hamburg, Germany;* [3] *KH Sankt Vincentius, Innere Medizin Onkologie, Karlruhe, Germany;* [4] *Thoraxklinik, Innere Medizin Onkologie, Heidelberg, Germany;* [5] *KH Schillerhöhe, Pneumologie Onkologie, Gerlingen, Germany;* [6] *Thoraxklinik, Innere Medizin Onkologie, Heidelberg, Germany*

Gemcitabine (G) and Docetaxel (D) have been shown to be effective in chemotherapy-naïve and pretreated patients (pts) and are not cross-resistant. We have tested G/D in doses of 1250 mg/m^2 /100 mg/m^2 and a q3w schedule G: day 1,8 / D: day 1 (Proc ASCO 2001; 20: 337a [Abstract 1346]) giving G or D initially up to 6 cycles and in case of tumor progression switching to D and G, respectively, (up to 6 cycles). 330 patients with median age of 64 (range 29-85) entered the study (stage at study entry IIIB/IV 11%/89%; WHO performance status 0 or 1/>1: 81%/19%; histology adenomatous/squamous/miscellanous 48%/26%/26%), and all 321 evaluable patients have been analyzed. In median survival, no statistical significant difference can be seen between the treatment arms A/B 6.3/8.6 mos (KaplanMeier: log-rank p=0.206). The corresponding confidence intervals (CI) are A/B [5.2;7.2]/[7.1;10.3]. The 1-Year-Survival-Rate of A/B is 28%/31% with 12(7.5%)/17(10.5%) censored observations. So far the treatment arms A and B can be statistically considered as equally effective. The quality of life (QoL) evaluation was measured by using the EORTC QLQ-C30 with annexed LC13 questionnaire. 88%/96% (A/B) of pts participated in the QoL evaluation (a total of 1346 forms (QLF)). Compliance of pts was high: in the first 6 interrogations (till 5th cycle) the rate was varying between 68%/70% and 86%/86% (A/B). 57%/50% pts were evaluable per protocol for baseline data (1st QLF) and after the 2nd cycle (3rd QoL evaluation). The individual tolerance toward the treatment was measured by the weighted sum score of the individual difference of the first 13 questions: There was no statistical significant difference between A and B (p-value is 0.3913 in the Wilcoxon rank sum test with an estimate of -0.077 and a CI of [-0.154;0.077]). Missing values and different scales have been adjusted by recalculating the mean scores for every patient and sub-number. Additionally scores of question 1-7, 8-28, 29-30 of EORTC-QLQ-C30, and 31- 42, and the two parts of question 43 of LC13, symptom scale ss14, scores of EORTC-QLQ-C30 and LC13 have been analyzed by the Wilcoxon rank sum test (base-line vs 3rd QLF). For all tests only a statistical significant difference between arm A/B can be seen for the score of LC13 (p-value of 0,0001) and for the Score 31-42. Question 43 alone is not different. The result is that in part LC13 pts of arm A feel as good as at base-line and pts in arm B do not so (M(A)=0,00 and M(B)=0,22). The same test was used for the base-line vs 6th QLF (28/37 pts in arm A/B, respectively). At this time point no differences in any of the scores can be seen. The use of G and D as carried out in the two arms is effective. Only a significant difference in QoL assessment in the annexed part of LC13 (baseline vs 3rd QLF) can be seen between the two drugs; in the main measurement of QoL there is no difference.

Sponsored by Aventis Pharma Deutschland and Lilly Deutschland, Germany.

775 POSTER

Standards of care for patients with small cell lung cancer (SCLC): a survey of clinical practice within the European Union (EU)

P.E. Postmus[1], G. Dane[2], G.A. Ross[2]. [1] *Vrije Universiteit Medical Center, Dept. of Pulmonary Diseases, Amsterdam, The Netherlands;* [2] *GlaxoSmithKline, Harlow, UK*

To assess the actual chemotherapeutic regimens currently employed for the management of SCLC in Europe, a survey of cancer treatment centres across the EU was conducted by GlaxoSmithKline clinical development during 2002. The survey comprised a series of questions based on theoretical clinical cases regarding the choice of first- and second-line therapies. One hundred and seventy-two cancer treatment centres were identified and numbered questionnaires were sent to each. One hundred and one replies were received by the deadline for database entry. Of the respondents, 90% were from university hospitals or secondary referral centres.

The percentage of SCLC patients treated with each of the major first-line treatment regimens within the EU are as follows:

Treatment Regimen	% of SCLC Patients Treated	
	Limited Disease	Extensive Disease
cisplatin/etoposide	59	38
carboplatin/etoposide	28	38
platin not otherwise specified	11	10
doxorubicin-based	2	11

At relapse of the SCLC, treatment of patients who are of adequate performance status is clearly based on treatment-free interval, and recovery from treatment-specific toxicities. For a patient with a short treatment-free interval (6 weeks), 78% of clinicians would use chemotherapy and all of them would use a cross-over regimen. For a patient with a longer treatment-free interval (3 months), at least 93% of clinicians would use chemotherapy and the majority would use a cross-over regimen. When the treatment-free interval is even longer (2 years), the management is most likely to be re-treatment with the first-line regimen. If there is residual toxicity from the first-line regimen, cross-over is the common practice, even after a long treatment-free interval. The primary basis for the decision-making in relapsed SCLC is the published literature in the light of the local clinical experience. Details of the survey results will be presented.

776 POSTER

An economic analysis of the TAX 326 trial: a multicenter randomized study of docetaxel + cisplatin (DC) or docetaxel + carboplatin (DCb) vs. vinorelbine + cisplatin (VC) as first-line therapy in advanced non-small cell lung cancer (NSCLC)

N. Leighl[1], F.A. Shepherd[2], W.S. Tsao[3], P. Lindgren[4], C.B. Belani[5], F.V. Fossella[6], P.G. Goodwin[7]. [1] *Princess Margaret Hospital/University of Toronto, Medical Oncology, Toronto, Canada;* [2] *Princess Margaret Hospital/University of Toronto, Medical Oncology, Toronto, Canada;* [3] *Princess Margaret Hospital/University of Toronto, Medical Oncology, Toronto, Canada;* [4] *Stockholm Health Economics Consulting, Uppsala, Sweden;* [5] *University of Pittsburgh Cancer Institute, Medical Oncology, Pittsburgh, USA;* [6] *University of Texas M.D. Anderson Cancer Center, Medical Oncology, Houston, USA;* [7] *Mount Sinai Hospital/University of Toronto, Medical Oncology, Toronto, Canada*

Lung cancer is a leading cause of cancer mortality in North America. The annual direct costs of lung cancer care in the United States are estimated at over $5 billion US. Systemic therapy in patients with advanced NSCLC has been shown to prolong survival and improve symptom control in the first- and second-line setting. TAX 326, a randomized trial, compared DC or DCb with a current standard, VC. Patients treated with DC had longer median survival than those treated with VC (11.3 vs. 10.1 months, p=0.044) and better quality of life scores. Patients treated with DCb had similar survival to those treated with VC (9.4 months). Consequently the DCb arm was not included in this analysis. A retrospective cost-effectiveness analysis was performed of the DC and VC arms of the TAX 326 trial, evaluating direct medical costs of therapy from the viewpoint of Canada's public healthcare system. Costs were derived from the Princess Margaret Hospital/University Health Network, a tertiary cancer center, in 2002 Canadian dollars. Resource use was determined through prospective trial data provided by Aventis Pharma. Of the 1218 patients in the intent-to-treat TAX 326 population, 1203 received protocol treatment and were included in this cost analysis. The mean incremental survival benefit in the DC arm over VC was 30 days. Docetaxel use was more costly, and the cost-effectiveness (CE) of DC over VC was $48,933 CAD (approximately $30,583 USD) per year of life gained (LYG). The largest cost in the DC arm was chemotherapy (46%), and in the VC arm was hospitalization (46%). In univariate sensitivity analyses, CE estimates were most sensitive to changes in survival and chemotherapy cost. Variation in total chemotherapy cost (±20%) yielded CE estimates of $31,616 to $66,251 CAD per LYG. Variation in survival (± 2 SD) yielded CE estimates of $24,467 to $734,000 CAD per LYG. Treatment with DC first-line in advanced NSCLC significantly improves survival, quality of life and symptom control compared with VC. While cost should not be

a major factor in treatment decisions, our CE estimate of $48,933 CAD (approximately $30,583 USD) per LYG shows that treatment with DC in this setting is within an acceptable range of cost-effectiveness compared with other healthcare interventions.

777 POSTER

A multi-institutional trial comparing survival of patients with brain metastases from lung cancer treated with temozolomide plus radiotherapy versus radiotherapy alone

D. Antonadou[1], N. Coliarakis[2], M. Paraskevaidis[2], H. Athanasiou[3], G. Sarris[1], M. Synodinou[1], G. Georgakopoulos[1], C. Beroukas[3], P. Karageorgis[3], N. Throuvalas[1]. [1]*Metaxa Cancer Hospital, 1st Radiation Oncol Dept, Athens, Greece;* [2]*Metaxa Cancer Hospital, 2st Radiation Oncol Dept, Athens, Greece;* [3]*Ag. Savas Cancer Hospital, 2st Radiation Oncol Dept, Athens, Greece*

Background: This randomized study evaluated the efficacy and safety of concurrent administration of Temozolomide (TMZ) and WBRT compared to WBRT alone in patients with previously untreated brain metastases from lung cancer.

Material and Methods: Patients with histologically or cytologically proven lung cancer and brain metastases were randomly assigned to treatment with TMZ 75mg/m^2 per day during conventional WBRT 3 Gy /5days per week (total dose 30Gy) or with WBRT alone. Beginning one month post WBRT, patients in WBRT + TMZ received 200mg/m^2 per day for five consecutive days every 28 days for 6 cycles. The primary endpoint was radiological response assessed by CT scan or MRI at 3 months post WBRT.A survival analysis by treatment arm was also performed by different prognostic factors as number of lesions, first diagnosis brain metastases, recursive partitioning analysis (RPA) classes and cause of death (primary site and/or brain).

Results: To date 108 evaluable patients have been enrolled. The groups were similar with respect to age, gender, performance status neurological function score and RPA classes.103 patients have been evaluated for response by radiological assessment (52 in the TMZ and WBRT group; 51 in the WBRT alone group). In the TMZ and WBRT group 48% of patients achieved complete and partial response compared to 27.5% respectively in WBRT alone group(p=0.031)Median follow up was 5.56 months (range0.426-20.79). Median survival was 7.9 months in the TMZ plus WBRT and 4.3 in the control arm (p=0.06) . The median survival in patients with multiple lesions in the study group was 7.3 months versus 4 months in the control group (p=0.1248). The median survival in patients with first diagnosis brain metastases and then lung was 7.4 months in the study group and 4 months in the control group (p=0.013). The median survival in RPA class I was 8 months in the TMZ and WBRT group compared to 8 months in the control group (p=0.78) and in Class II 3.8 months in the study group versus 3.31 in the control group (p=0.05). No grade 3 toxicities were noted.

Conclusion: These data indicate that combination treatment with TMZ and WBRT improves the efficacy of WBRT alone in brain metastases especially in chemotherapy naive patients.

778 POSTER

UPA and PAI-1 are associated with angiogenesis but not prognosis in non-small cell lung carcinoma

B. Offersen[1], P. Pfeiffer[2], P. Andreasen[3], J. Overgaard[1]. [1]*Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus, Denmark;* [2]*Odense University Hospital, Department of Oncology, Odense, Denmark;* [3]*Aarhus University, Department of Molecular Biology, Aarhus, Denmark*

Background. Urokinase Plasminogen Activator (uPA) and Plasminogen Activator Inhibitor type 1 (PAI-1) has been suggested as a prognostic marker in nonsmall-cell lung carcinomas (NSCLC). This study investigates the levels of uPA and PAI-1 in 124 NSCLC, where estimates of tumour angiogenesis have been presented previously.

Materials and methods. UPA and PAI-1 levels were assessed in 119 and 123 frozen tumours, respectively, using a sandwich ELISA method.

Results. Median uPA was 30 ng/mg protein (range, 5-163 ng/mg protein), and median PAI-1 was 34 ng/mg protein (range, 3-286 ng/mg protein). UPA and PAI-1 were significantly correlated, P<0.0001. Both factors were independent of histological type, T and N classification, malignancy grade, stage, age and vascular scores. Evaluated as continuous parameters or in tertiles, neither of the factors were markers of poor prognosis in univariate analysis. Significantly higher levels of uPA and PAI-1, respectively, were seen in tumours with an angiogenic vascular pattern as compared to tumours with an alveolar vascular pattern. In multivariate analysis using overall death as endpoint, high disease stage (P<0.0001), old age (P=0.05) and adenocarcinoma (P=0.002) were identified as the only independent markers of poor prognosis, whereas the angiogenic vascular pattern was borderline significant (P=0.06).

Conclusions. In this study, significantly high uPA and PAI-1 levels were seen in tumours with an angiogenic vascular pattern as compared to tumours with an alveolar vascular pattern. However, neither uPA nor PAI-1 were prognostic markers in univariate or multivariate analyses. We conclude that uPA and PAI-1 are not prognostic markers in NSCLC, but may be involved in angiogenic processes in NSCLC.

779 POSTER

A pilot study of hyperfractionated accelerated radiotherapy (HART) following induction cisplatin and vinorelbine for stage III non-small cell lung cancer (NSCLC).

S. Ishikura[1], Y. Ohe[2], K. Nihei[1], K. Kubota[2], R. Kakinuma[2], H. Ohmatsu[2], K. Goto[2], S. Niho[2], Y. Nishiwaki[2], T. Ogino[1]. [1]*National Cancer Center Hospital East, Radiation Oncology, Kashiwa, Japan;* [2]*National Cancer Center Hospital East, Thoracic Oncology, Kashiwa, Japan*

Background: Continuous hyperfractionated accelerated radiotherapy (CHART) is superior to radiotherapy alone for inoperable NSCLC. The purpose of this study is to assess the feasibility and efficacy of HART (modified CHART) following induction chemotherapy for stage III NSCLC.

Material and Methods: Thirty patients with stage IIIA/B NSCLC were enrolled between July 1999 and March 2001. The treatment consisted of 2 cycles of cisplatin 80 mg/m^2 on day 1 and vinorelbine 25 mg/m^2 on day 1 and 8 every 3 weeks followed by HART; three times a day (1.5-1.8-1.5 Gy, 4-hour interval) for a total dose of 57.6 Gy in 36 fractions over 2.5 weeks. Patient characteristics: median age 64 (range 46-73), male/female: 24/6, performance status 0/1: 8/22, < 5% weight loss/5% or greater: 25/5, T1/2/3/4: 4/10/1/15, N0/1/2/3: 1/4/18/7, IIIA/B: 9/21, squamous/non-squamous: 13/17.

Results: All patients received 2 cycles of chemotherapy and all but one patient completed HART. Grade 3 or greater toxicities included neutropenia: 25, anemia: 3, thrombocytopenia: 2, infection: 5, esophagitis: 5, nausea: 3, radiation pneumonitis: 3, and dermatitis: 1. There were 2 early deaths due to radiation pneumonitis. The overall objective response rate was 83% (25/30, 95% CI: [65%, 94%]). With a median follow-up period of 33 months in surviving patients, the median survival time was 22 months (95% CI: [13, 34$^+$]) and the 2-year overall survival was 50% (95% CI: [32%, 68%]). The median progression-free survival time was 10 months (95% CI: [8, 20]) and the 1-year progression-free survival was 47% (95% CI: [29%, 65%]). To date we have observed 2 cases with grade 3 subcutaneous tissue toxicity.

Conclusions: HART following induction cisplatin and vinorelbine was feasible and promising. Future investigation employing dose-intensified radiotherapy in combination with chemotherapy is warranted.

780 POSTER

A phase II study of cisplatin (CDDP) and epirubicin (EPI) in malignant pleural mesothelioma (MPM). A study by the European Lung Cancer Working Party (ELCWP).

T. Berghmans[1], J.J. Lafitte[2], B. Stach[3], P. Recloux[4], J. Lecomte[5], C. Collon[6], V. Ninane[1], J. Klastersky[1], J.P. Sculier[1]. [1]*Institut Jules Bordet, Medicine, Bruxelles, Belgium;* [2]*CHU Calmette, Pneumology, Lille, France;* [3]*Cabinet Médical Dampierre, Pneumology, Anzin, France;* [4]*Clinique Saint Joseph, Medicine, Mons, Belgium;* [5]*CHU Charleroi, Pneumology, Charleroi, Belgium;* [6]*CHI. le Raincy-Montfermeil, Pneumology, Montfermeil, France*

Background: A meta-analysis of chemotherapy and immunotherapy in MPM showed that the most active chemotherapy regimen in term of response rate (RR) is a combination including CDDP and adriamycin (ADR) (Berghmans et al, Lung Cancer 2002; 38: 111). EPI demonstrated an activity similar to ADR (9% versus 11% RR) in regimens without CDDP. The aim of this study was to assess the RR and toxicity of CDDP plus EPI in MPM, a combination not reported in the literature.

Material and methods: Eligibility criteria included untreated unresectable MPM, adequate cardiac, renal, haematological and hepatic functions, absence of active infection and presence of assessable lesion(s). After central registration, patients received CDDP and EPI (both at 90 mg/m^2), every 3 weeks for 3 cycles. Stable and responding (WHO criteria) patients were treated until best response or unacceptable toxicity. We used a two-stage optimal design of Simon to determine the number of patients to be