advanced gastric and head and neck cancers in Japan. S-1 has been shown to be active against NSCLC, producing a RR of 22.0% when given as monotherapy (Kawahara et al. Br J Cancer 2001). A combination of CDDP and S-1 is superior to S-1 alone in vivo. We evaluated the response and safety of combination chemotherapy with S-1 plus CDDP in patients with NSCLC.

Patients and Methods: The eligibility criteria were as follows: Stage IIIB or IV NSCLC, confirmed histologically or cytologically; a performance status of 0 to 2; an age of ≤74 years; adequate organ functions; and no prior chemotherapy. Written informed consent was obtained from all patients. S-1 was administered orally at 40mg/m^2 twice daily for 21 consecutive days. CDDP (60mg/m^2) was administered intravenously on day 8 of treatment with S-1. This cycle was repeated every 4 to 5 weeks, depending on toxicity.

Results: Of the 56 patients enrolled, 55 were eligible. The median number of administered cycle was 3 (range 1-12). The overall response rate was 47% (95% CI: 34%-61%, 1 CR and 25 PR). Survival has been good and is under further analysis. Toxicity was generally mild to moderate. Dose-limiting toxicity was hematological: grades 3 and 4 neutropenia (29%) and anemia (22%). Grade 3 non-hematological toxicity comprised anorexia(13%), vomiting(7%), and diarrhea(7%). There was no Grade 4 non-hematological toxicity.

Conclusions: Combination chemotherapy with S-1 plus CDDP is very effective and well tolerated in patients with advanced NSCLC. Because the need for hospitalization is minimal, this regimen is likely to improve the quality of life of patients. These results warrant further investigations of S-1 plus CDDP, including a randomized controlled trial as first-line treatment in NSCLC.

771 POSTER

Paclitaxel and carboplatin as adjuvant treatment in high-risk patients with operable non-small cell lung cancer (NSCLC): A feasibility study conducted by the Hellenic Cooperative Oncology Group (HeCOG)

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Background: The use of adjuvant chemotherapy in operable NSCLC is still under investigation. The combination of paclitaxel and carboplatin has been proved an active, safe and convenient regimen for the management of advanced disease.

Material-Methods: From 1/7/1998 to 2/9/2002, 75 patients with IB-IIIA completely resected NSCLC entered the HeCOG protocol HE 2C/98. They were treated with paclitaxel 175mg/m2 and carboplatin at an AUC of 6 every 3 weeks for 6 cycles. Patients with stage IIIA also received adjuvant RT to the mediastinum after completion of chemotherapy.

Results: There were 62 (83%) men and 13 (17%) women with a median age 63 years (range, 44 - 76) and median PS 0 (range, 0 - 2). Stage IB included 16 patients, stage II 25 patients and stage IIIA 34 patients. Fifty-eight patients (77%) completed all cycles of treatment. Median relative dose intensity of paclitaxel was 1.00 (range, 0.7 – 1.2). Median cumulative dose of carboplatin was 3305mg (range, 500 – 5640). Most commonly seen toxicities included anemia (31%), leukopenia (13%), nausea/vomiting (26%), myalgias/ arthralgias (56%), peripheral neuropathy (75%). Expression of COX-2, VEGF, cyclin D1, DDH and RCAS-1 were assessed immunohistochemically. The prognostic significance of the above mentioned markers on relapsed-free survival and overall survival will be presented at the meeting.

Conclusions: The combination of paclitaxel and carboplatin given post-operatively in high-risk patients with NSCLC is a well-tolerated, safe and convenient regimen.

772 POSTER

Comparison of two Cisplatin based doublets (Gemcitabine/ Cisplatin, Etoposide/ Cisplatin) in advanced non-small cell lung cancer

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Background: Despite the poor prognosis of patients with advanced non-small cell lung cancer (NSCLC), treatment with the new generation chemotherapy agents has improved survival and quality of life, and decreased toxicity compared to older Cisplatin based doublets. The aim of this study is to assess, in a randomized phase II trial, the results obtained in advanced stage (st) i.e. IIIB and IV NSCLC patients (pts) with a 3rd generation platinum doublet Gemcitabine/ Cisplatin (GP) versus the 2nd generation Etoposide/ Cisplatin (EP) regimen.

Methods: From 10/96 to 10/02, 88 previously untreated pts received either GP (Gemcitabine 1250 mg/m^2 d1, 8, Cisplatin 80 mg/m^2 d1), or EP (Etoposide 120 mg/m^2 d 1-3, Cisplatin 80 mg/m^2 d1) q3wks. St IIIB pts without pleural effusion had 3 cycles (cyc) followed by RT at 60 Gy; st. IV and st IIIB pts with pleural effusion had up to 6 cyc of chemotherapy (less if progressive disease).

Results: 80% males; age 57 [range 39-74]; WHO PS 0&1 in 51 pts, 2 in 37 pts; histology: squamous 56, adeno 24, large cell 4, non-small (cytology) 4 pts; AJCC st: IIIB 42, IV 46 pts; protocol GP 43, EP 45 pts. *Toxicity*: 313 cyc were given (GP 159, EP 154), with one toxic death in EP (renal failure). Febrile neutropenia (gr. 4) occurred (GP vs EP) in 2 vs 7 cycles, gr. 4 anemia 1 cyc in both arms. *Activity*: 27 pts had an objective response to CT (=31%, CI [21%-40%] at 0.05), 2 CR, 25 PR. Response rate was influenced by the PS (0-1 vs 2: 39% vs 19%, p=.04) and was not significantly different in respect with gender, clinical stage or chemotherapy regimen (GP vs EP: 26% vs 36%, p=.31). *Survival* (S): At a median (med) follow-up of 7 months (m) [1-31], overall med S is 7,6 m and 1 year S is 25%. Med S was influenced by the PS (0-1 vs 2: 10.5 vs 7.1 m, p<.01) and response to chemotherapy (CR+PR vs SD+PD: 11.2 vs 6.7 m, p<.01). A significant improvement in med S occurred with GP vs EP (10,3 vs 7.1 m, p=.04, 1-year S 39% vs 14%, p<.05). Only a trend existed among st IIIB vs st IV pts (9.7 vs 7.1 m, p=.20).

Conclusions: 1) There were no significant differences in response among the two platinum doublets. 2) Survival was significantly improved with GP over EP. 3) Prognostic factors found: for response - PS; for survival - PS, response to chemotherapy and regimen.

773 POSTER

Clinical usefulness of tumor marker CYFRA 21-1 in surgical treatment of lung cancer

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Background: Both incidence and mortality of lung cancer increase. Introduction of tumor marker CYFRA 21-1 into clinical praxis improves the inevitable surgical treatment. Aim: Intensification of clinical diagnostics in earlier recognition of tumor biological activity using tumor marker CYFRA 21-1 in both primary diagnosis and relapse; facilitate the choice whether to operate and reoperate in the same stage of disease.

Material and Methods: The sample includes 2947 patients who were surgically treated in our Clinic. 882 non small cell lung cancer (NSCLC) patients of 2947 have been controled in the Clinic for six years (adeno-carcinoma –AD and squamous cell carcinoma -SQC). In order to control disease status, CYFRA 21-1 level has been measured by ECLIA method before therapy and twelve times after the therapy, along with the clinical examinations.

Results: The sensitivity of CYFRA 21-1 in patients with primary lung cancer was 75,51%. Taking into consideration both surgical algorythm and past experience there was a need to incorporate CYFRA 21-1 into algorythm. Patients who had high values of CYFRA 21-1 before therapy (above 12 ng/mL) suffered from relapse within 1 year after the therapy (10,3%). Although CYFRA 21-1 level rises from stage IA to IIIA, we have noticed that patients in early stage with high values have also suffered from relapse earlier. In AD stage IA CYFRA 21-1 relapse has been proven between 18 and 60 months after therapy and clinical relapse between 24 and 60 months after therapy. In AD stage IIIA CYFRA 21-1 relapse was between 4 and 60 months after therapy and clinical between 10 and 60 months after therapy. The highest number of clinically proven relapses was seen between 36 and 42 months after therapy. In early stages of SQC relapses have been proven 6 to 12 months later than in AD. In late stages

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

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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.

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775 POSTER

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

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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)

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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