Results. Pts were divided into two groups according to GTV: < 100 cc (13 pts) and > 100 cc (12 pts). Kaplan-Meier survival analysis showed significant differences between the groups considering both TTP and OS (Logrank p = 0.03 and 0.01 respectively). There were no statistical differences in the two groups regarding age, stage or sex distribution. 9/25 pts (36%) developed RP grade 2 or higher. None of the variables examined correlated significantly to the development of lung toxicity.

Conclusions. Our preliminary results indicate that in NSCLC, GTV plays a prognostic role even in pts at the same clinical stage and receiving the same treatment combination of CRT. None of the dose parameters was a predictor of development of RP. In addition, there was no difference regarding mean lung dose among the pts who developed lung toxicity when compared to those who did not.

825 POSTER

Statistical analysis of survival in patients with advanced non-small-cell lung cancer (NSCLC) treated with gefitinib ('Iressa', ZD1839) in an expanded access program (EAP): preliminary results

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Background: In patients (pts) with refractory NSCLC for whom no other treatment options are available, there is an unmet clinical need for effective treatments which prolong survival. As part of a global EAP gefitinib ('Iressa', ZD1839), an orally active EGFR-TKI (epidermal growth factor receptor tyrosine kinase inhibitor) has been used to treat pts with NSCLC.

Methods: Of those pts eligible for entry, the majority had received and failed chemotherapy for advanced incurable stage III/IV NSCLC; a small minority were chemo-naïve pts for whom no other treatment options were available due to co-morbidity or low performance status. Pts received 250 mg/day gefitinib orally. Data collection was limited as the EAP was not designed to provide efficacy data. Duration of therapy and survival were measured from the start of initial therapy or earliest resupply date (if date of initial therapy was unavailable), to the last resupply date for ongoing pts or date of last dose for withdrawn pts. Periodic follow-up data for surviving pts after withdrawal was not collected and pts were censored for survival at withdrawal until death was reported.

Results: As of 28 February 2003, data were available on 18,245 pts; 1,093 pts were excluded (missing start or resupply dates) and follow-up was unavailable for 3,504 pts. The earliest resupply date was used as start of therapy for 76 pts. Results for all evaluable pts (confirmed to have started therapy) and for those who entered 1 or more years prior to analysis are shown.

	All evaluable pts (n=17,152)	Pts entered 1 or more years prior to analysis (n=5,755)
Mean duration of treatment, mths	2.61	4.1
No. pts treated for >6 mths	1564	1169
No. pts treated for >12 mths	378	373
Median survival, mths (CI)	5.1 (4.9–5.3)	5.9 (5.6–6.2)
1-year survival, % (CI)	29 (28–30)	33 (31–34)

These data are comparable to those obtained from pretreated pts with advanced NSCLC who received 250 mg/day gefitinib in 2 large Phase II trials (IDEAL 1 and 2) (Fukuoka et al. JCO 2003; in press; Kris et al. Proc ASCO 2002; 21:292a); mean durations of treatment were 2.8 and 2.5 months, median survival was 7.6 and 6.5 months, and 1-year survival rates were 35 and 27%, respectively.

Conclusion: An ad-hoc retrospective analysis has found that gefitinib provides unprecedented, clinically meaningful and durable antitumor activity in a group of pts with incurable NSCLC for whom no other treatment options are available. 'Iressa' is a trademark of the AstraZeneca group of companies

826 POSTER

The role of Her-2/neu expression on the survival of patients with non-small cell lung cancer (NSCLC). A systematic review of the literature with meta-analysis.

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Background: Neu prognostic value for survival in patients with lung cancer remains controversial. We performed a systematic review of the literature to clarify its impact.

Material and methods: Studies related to the assessment of neu in lung cancer patients were identified after an extensive review of the literature by an electronic search, completed by the references found in the selected articles. A team of nine investigators performed a methodological evaluation of each trial by using the European Lung Cancer Working Party scale, as previously described (Eur Respir J 2001; 18: 705). A study was called positive or negative if neu was respectively a significant favourable or unfavourable prognostic factor for survival (significant studies). Otherwise, a study was considered as non-significant. Combined hazard ratio (HR) for survival was obtained by the Peto method.

Results: Thirty studies were eligible: 24 dealt with NSCLC, 5 with adenocarcinoma and 1 with small cell carcinoma. Thirty-one % of the 4582 patients were positive for neu, without difference according to disease extent or histological type. According to neu expression, 13 studies were "negative", 1 "positive" and 16 not significant. The median quality score for the pooled trials was 57.6% (range: 37.4% to 82.6%). Significant studies had a statistically significant better quality score than non-significant studies (61.2% vs 52.6%, p = 0.03). Respectively 86% and 56% of the significant and non-significant studies were evaluable for the meta-analysis. This suggested a potential bias favouring significant studies, when aggregating survival results. We calculated a HR by a random-effect method, including 20 studies assessing the role of neu in NSCLC (test of heterogeneity p = 0.001). The HR was 1.55 (95% CI: 1.29-1.86), meaning that tumours without neu expression had a better prognosis. When we compared the studies with a quality score above and below the median quality score, we found respectively HR = 1.59 (95% CI: 1.23-2.04) and 1.50 (95% CI: 1.13-2.00).

Conclusion: Overexpression of neu might be a factor of poor prognosis for survival in NSCLC. Nevertheless, the potential bias in favour of the significant studies that we observed justified further prospective large size confirmatory study

827 POSTER

A phase II randomized study comparing docetaxel/cisplatin induction therapy followed by thoracic radiotherapy with or without weekly docetaxel in unresectable stage IIIA–IIIB non-small cell lung cancer

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A phase II randomized study comparing docetaxel/cisplatin induction therapy followed by thoracic radiotherapy with or without weekly docetaxel in unresectable stage IIIAIIIB non-small cell lung cancer

Background: This study evaluated the efficacy and safety of induction chemotherapy (docetaxelcisplatin) followed by either concomitant docetaxel-based chemotherapy plus radiotherapy or radiotherapy alone in locally advanced NSCLC.

Material and methods: 108 chemoradiotherapy-naïve patients with unresectable Stage IIIA or IIIB NSCLC, and WHO performance status ≤1, received 2 cycles of induction chemotherapy (docetaxel 85 mg/m^2 d1 + cisplatin 40 mg/m^2 d1, 2 q3w). In cases of complete response, partial response or no change following 2 cycles of induction chemotherapy, patients were randomized to either thoracic radiotherapy (2 Gy for 5 d/w, total 60 Gy) with weekly docetaxel (20 mg/m^2) [Group A] or radiotherapy alone (total 60 Gy) [Group B] q6w.

Results: An overall response rate (ORR) of 44% [95% CI: 34.252.9] was achieved after induction chemotherapy, with disease control reported in 86% of patients (PR 44%, SD 42%, progressive disease [PD] 12%, early death 2% [lung haemorrhage, sudden death]). Although NCI-CTC-defined grade 34 neutropenia occurred in 46% of patients, febrile neutropenia occurred in only 4%. Characteristics of the 89 patients randomized to local therapy were well balanced between the treatment arms. In the 89 treated patients (n=43 [A], n=46 [B]), a higher ORR of 58% was achieved for Group A (CR 5%, PR 53%, SD 7%, PD 26%) versus 48% for Group B (CR 2%, PR 46%, SD 9%, PD 35%). Despite a high incidence of grade 3-4 lymphocytopenia in the chemoradiotherapy arm (80% in Group A and 20% in Group B), infection only occurred in 5% of patients in Group A. Grade 34 neutropenia was low in both groups with no patient receiving radiotherapy plus docetaxel experiencing this toxicity; 2% of patients experienced grade 3 neutropenia in Group B. Since the cutoff date of 1 March 2002, 70%

of patients in Group A and 65% in Group B were alive. Corresponding numbers of progression-free patients were 53% and 50%.

Conclusions: The administration of chemoradiotherapy incorporating weekly docetaxel after induction chemotherapy is a feasible approach in unresectable locally advanced NSCLC, achieving a high ORR with a manageable toxicity profile. Final study results will be presented at the meeting.

Melanoma and sarcoma

828 POSTER

cKIT expression in adult primitive neuroectodermal tumor (PNET) and Ewing's sarcoma: a retrospective immunohistochemical study

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Background: The stem cell factor/c-kit tyrosine kinase receptor pathway has been shown to be important for tumor growth and progression in several cancers, including mast cell diseases, gastrointestinal stromal tumor, acute myeloid leukemia, small cell lung carcinoma, and Ewing sarcoma. We performed immunohistochemical analysis for KIT in 28 of 16 PNET and 12 Ewing's sarcoma.

Methods: Formalin-fixed, paraffin-embedded sections were stained with rabbit polyclonal anti-human c-kit (CD117, Dako) using standard avidin-biotin-peroxidase complex technique, antigen retrieval, and an automated stainer.

Results: Cytoplasmic c-kit expression was showed immunorecativity of % 50 (6/12) for Ewing's sarcoma group and % 50 (8/16) for primitive neuroectodermal tumor (PNET). Within the each group 2 sections were stained both for cytoplasmic and membranous component.

Conclusion: Our results were indicate that target therapy tyrosine kinase receptor inhibitor may be an additional methods to cytotoxic drugs for c-kit positive Ewing's sarcoma and PNET.

828A POSTER

Vascular endothelial growth factor levels in melanoma. relationship with coagulation and platelet activation markers

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Background: Vascular endothelial growth factor (VEGF) is a potent angiogenic factor essential for tumor growth and metastasis. Lately, it was shown that thrombin activation of platelets causes VEGF release, and that VEGF-stimulated endothelial cells promote adhesion and activation of platelets through the generation of thrombin. Thus, the present study was aimed at analyzing whether VEGF levels are increased in patients with various stages of melanoma as a result of platelet and/or coagulation activation.

Patients and Methods: Plasma samples were obtained from 95 patients with nodular (30%), superficial spreading (68%) or acral (2%) melanoma [61 males, mean age ± SD: 52 ± 15 years] and 61 healthy donors [14 males, mean age ± SD: 55 ± 14 years). Stage I (n=63) disease was defined as the presence of the primary tumor with no clinically detectable metastatic lesion. Stage II (n=14) disease was defined as the presence of regional lymph node metastasis. Stage III (n=18) disease was defined as widespread disease with metastatic involvement at distant sites. Plasma sP-selectin and VEGF levels were measured by ELISA (both by R&D Systems). Coagulation tests and complete and differential blood cell counts were routinely assayed in each recruited subject.

Results: Median plasma VEGF levels were higher in melanoma patients (19.0 pg/ml) compared to control subjects (2.2 pg/ml; $p<0.001$). In particular, median VEGF levels were higher in stage III compared to stages II and I melanoma (27.9 pg/ml *vs.*, 22.9 pg/ml, *vs.*, 14.1, Anova test: $F=3.2$, $p<0.05$). Similarly, metastatic patients had higher levels of sP-selectin ($F=4.7$, $p< 0.02$) and a prolonged International Normalized Ratio (INR)($F=17.0$, $p< 0.0001$) than stage I and II melanoma. Correlation analysis showed that VEGF levels strongly correlated with sP-selectin ($r=0.57$, $p<0.0001$) in melanoma patients. Thus, to further analyze the relationship between VEGF and clinical and laboratory variables of melanoma, a multiple regression analysis including age, sex, stage, diagnosis, VEGF and sP-selectin levels, blood cell counts and coagulation tests was performed. Final model by stepwise analysis showed that only sP-selectin (beta=0.27, $p<0.05$) and INR (beta=0.29, $p<0.05$) were independently related to VEGF.

Conclusions: These results suggest that elevated plasma VEGF levels are strictly related to the presence of haemostatic activation in patients with advanced stage of melanoma.

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829 POSTER

Adults with Ewing's sarcoma/PNET: is it possible to improve survival (Phase II trial: induction chemotherapy adriablastin-cisplatin)

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Background: Ewing's sarcoma/PNET is a disease rarely seen in adults. The literature data regarding outcome of adults with this disease, are insufficient.

Purpose: to assess outcome and survival of adults Ewing's sarcoma/PNET treated with neoadjuvant and adjuvant adriamycin-cisplatin chemotherapy (CT) combination.

Patients and methods: Since November 1998, fourteen adults with non-metastatic Ewing's sarcoma (12 pts.) and PNET (2 pts.) have been treated at our institute. Twelve pts. were male and 2 were female. The median age was 24.5 years (range 20-44). Nine pts. had tumor located in the central axis skeleton (3 in the pelvic bones, 3 in the spine and 3 in the chest wall). In 5 pts., sites of primary tumor were distal parts of the leg. Nine pts. had locally advanced disease (tumor volume greater than 150 ml) and 5 pts. had small volume localized disease (less than 150 ml).

Treatment consisted of 4-6 cycles neoadjuvant CT with doxorubicin 25 mg/sqm D1-3 and cisplatin 30 mg/sqm D2-5, followed by local treatment and adjuvant CT with EVAIA regimens. In three pts. CT was used with adjuvant intention.

Local treatment was: surgery (6 pts.), surgery followed by radiotherapy (3 pts.), radiotherapy followed by surgery (2 pts.) or radiotherapy alone (1 pt.). One patient was not treated locally.

Results: At completion of induction CT, the response, as assessed by NMR imaging, was: 10 PR and 1 SD. Radiological response of the soft tissue mass, separately, was: 6 CR, 4 PR and 1 SD. Histological response to induction CT was evaluated in 7 of 9 pts. who underwent surgery immediately after induction CT. Five of seven pts. were good responders with viable tumor cells of 10% or less.

The median of follow-up was 20 months. For all pts., the median probability of overall survival and median probability of time to progression were, at the moment, 38 months (range 7-42) and 24 months (range 6-42), respectively.

The chemotherapy was well tolerated. No cases of adriamycin cardiotoxicity were seen. Seven pts. experienced transitory grade 4 granulocytopenia at least in one cycle, without febrile episodes.

Conclusion: These preliminary results showed very promising activity of adriamycin-cisplatin regimen, and further testing is needed.

830 POSTER

A clinicopathologic review of uncommon vascular hemangiopericytomas with follow up and analysis of outcome: a 12 year study

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Background: Having a pericytic origin, hemangiopericytoma(HPC) is an uncommon vascular tumor of adults and shared histology with synovial sarcoma, mesenchymal chondrosarcoma and solitary fibrous tumor stems the long lasted diagnostic dilemma. Along with endeavour to solve this problem, this study also defines clinical nature and prognosis of affected patients.

Methods: A total of 51 patients with documented diagnosis of primary, recurrent or metastatic HPC were selected from a prospectively main-