112 chemotherapy-naïve patients were randomized to receive four to six 3-week cycles of taxane and platinum alone (n = 37) or taxane and platinum plus 0.20 mg/kg subcutaneous CPG 7909 on weeks 2 and 3 of each cycle (n = 75). Baseline demographics were similar for the treatment arms; however, 85% of patients in the CPG 7909 arm had stage IV NSCLC, vs. 65% in the chemotherapy-only arm. The phase II trial was conducted at 23 sites, and patients received study treatment until disease progression or unacceptable toxicity occurred. Primary endpoint was objective response rate (ORR), which was evaluated after cycles 2, 4, and 6 using Response Evaluation Criteria in Solid Tumors guidelines. Coded and blinded CT scans from 91 of 112 patients underwent retrospective independent radiological review. Ongoing secondary efficacy analyses include clinical benefit, time to response, duration of response, and survival; biomarker responses to CPG 7909 will be compared for responders and nonresponders in both arms.
Results: Data were available on all 112 patients for intention-to-treat response analysis. Investigator-evaluated ORR was 19% in the chemotherapy-only arm and 37% in the CPG 7909 arm; independent radiological review ORR was 25% vs. 32%, respectively. Median overall survival was 6.8 months in the chemotherapy-only arm and 11.7 months in the CPG 7909 arm, and Kaplan-Meier curves showed a trend toward improved overall survival in the latter arm. One-year survival rates were 36% vs. 47% in the chemotherapy-only and CPG 7909 arms, respectively. Survival analysis is ongoing.
Conclusions: The data suggest that addition of weekly CPG 7909 to a taxane/platinum regimen for first-line treatment of NSCLC improves objective response. Confirmatory phase III trials are warranted to further document the clinical benefit of this new agent.

1132 POSTER

Neoadjuvant and adjuvant chemotherapy in a radical treatment protocol for malignant mesothelioma with extrapleural pneumonectomy

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Background: To evaluate the feasibility and effects of neoadjuvant and adjuvant chemotherapy as part of a radical surgery protocol for malignant mesothelioma (MM).
Materials and Methods: Case notes were analysed from 95 consecutive patients undergoing extrapleural pneumonectomy (EPP) for MM. Patients with non-sarcomatoid mesothelioma, clinically staged T1–3, N0–1, were resected if they were medically operable by standard criteria. Case notes were reviewed to determine how many successfully completed the planned tri-modality treatment programme, including chemotherapy and radiotherapy. The reasons for non-compliance were recorded. Differences in survival between groups were estimated using Kaplan-Meier analysis and the Log Rank test.
Results: Referrals were received from 28 oncology centres nationwide. Overall median survival from diagnosis was 14.7 months for all patients and 28.9 months for epithelioid node negative cases. Neoadjuvant chemotherapy was administered to 20 patients, all of whom underwent successful EPP. Referral to an oncologist to consider adjuvant chemotherapy was made in 41 patients; treatment within 3 months was received by 8 patients. 8 died prior to assessment for adjuvant therapy and a further 7 were considered too unwell. However adjuvant chemotherapy was not offered to 10 patients as there was no residual disease. 3 patients refused adjuvant therapy and 2 were refused therapy as it was too long post operation. Overall survival in the patients receiving neoadjuvant or adjuvant chemotherapy was greater than those not receiving chemotherapy ($p = 0.005$). In multivariate analysis, significant independent prognostic factors were the receipt of neoadjuvant or adjuvant chemotherapy ($p = 0.02$) and preoperative haemoglobin >14 g/dL ($p = 0.04$).
Conclusions: Survival in patients receiving chemotherapy as well as EPP was greater than surgery alone. The success rate at achieving adjuvant chemotherapy was low, therefore we advocate incorporation of neoadjuvant chemotherapy in future trials.

1133 POSTER

Phase I/II dose-escalation trial of patupilone every 3 weeks in patients with non-small cell lung cancer

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Background: Although the current standard of care for patients with newly diagnosed advanced non-small cell lung cancer (NSCLC) is a platinum-containing doublet, these regimens are associated with cumulative toxicity and suboptimal survival. Patupilone, a natural epothilone, is a microtubule-targeting cytotoxic agent that is active in a variety of tumors, including those that are resistant to taxanes. We are investigating the safety, efficacy, and maximum tolerated dose of patupilone in patients with stage IIIB/IV NSCLC.
Material and Methods: Patients who did not have brain metastases, who had relapsed after 1 prior platinum-containing regimen, and who had good performance status were enrolled. Patients received patupilone at a starting dose of 6.5 mg/m^2 via 20-minute IV infusion once every 3 weeks, with dose escalation in 0.5 mg/m^2 increments and proactive diarrhea management in the phase I study. Any grade 3 or 4 toxicities occurring in cycle 1 were considered dose-limiting toxicities.
Results: To date, 50 patients have been enrolled in 13 cohorts receiving 6.5 (n = 3), 7.0 (n = 3), 7.5 (n = 6), 8.0 (n = 6), 8.5 (n = 6), 9.0 (n = 3), 9.5 (n = 3), 10.0 (n = 3), 10.5 (n = 3), 11.0 (n = 3), 11.5 (n = 3), 12.0 (n = 3), and 13.0 (n = 5) mg/m^2 patupilone. All patients had received platinum therapy and 30% had been treated with a taxane. Median age was 59 years (range, 33 to 77 years) and median performance status was 1. Dose-limiting toxicities were observed in 4 patients: 1 patient in the 7.5 mg/m^2 cohort reported grade 3 asthenia and 3 patients (1 patient each in the 8.0-, 8.5-, and 13.0 mg/m^2 cohorts) reported grade 3 diarrheoa. The most frequently reported adverse events were diarrhea (60%), nausea (40%), and abdominal pain (34%). Of 17 patients who had grade 3 adverse events; 7 had grade 3 diarrheoa. Grade 1 or 2 peripheral neuropathy occurred in 12 patients and grade 3 peripheral neuropathy occurred in 3 patients. Grade 1 alopecia occurred in 6 patients. Grade 3 hematologic toxicity was rare, and there were no grade 4 adverse events. Based on acute and chronic toxicities, the recommended phase II dose is 10 mg/m^2 patupilone. Five patients had a partial response (including 1 prior taxane-treated patient) and 14 patients had stable disease according to Response Evaluation Criteria in Solid Tumors.
Conclusion: Patupilone is safe and well tolerated and may have antitumor activity in patients with advanced NSCLC. Updated data will be presented.

1134 POSTER

A randomized phase II trial of irinotecan plus carboplatin versus etoposide plus carboplatin in patients with extensive disease small cell lung cancer

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Background: Superiority of irinotecan/cisplatin over etoposide/cisplatin has been demonstrated in a small phase III trial in extensive disease small cell lung cancer (SCLC). Since carboplatin is as effective as cisplatin with a favourable toxicity profile, many oncologists prefer carboplatin. The trial presented here analyzed the efficacy of irinotecan/carboplatin (IP) versus the standard regimen etoposide/carboplatin (EP).
Patients and Methods: Extensive disease SCLC patients were randomly assigned to receive carboplatin AUC 5 mg x min/mL either in combination with 50 mg/m^2 of irinotecan on days 1, 8 and 15 (IP) or with etoposide 140 mg/m^2 days 1–3 (EP). Cycles were repeated on day 29 in arm A (IP) and on day 22 in arm B (EP). The trial was designed as a phase III study with OS as primary endpoint. After a first step of 70 patients it was planned to perform a phase II analysis to determine response rate and toxicity before extension into phase III.

Results: 70 patients were randomized. Complete remissions (CR) were observed in 4 of 33 evaluable patients in the IP arm. No CR occurred in the EP arm. Overall response rate was 67% and 59% in the IP and EP arm. Three patients (2 in the IP arm and 1 in the EP arm) were not evaluable for response assessment due to early death. Significant differences in grade 3 and 4 thrombopenia (17% IP vs 48% EP, $p = 0.01$) and neutropenia (26% IP vs 51% PE, $p < 0.01$) were found. Grade 2–4 diarrheoa was more frequent with IP (17%) than with EP (6%) ($p = 0.16$). Median progression-free survival (PFS) was 9 months (95% CI 7.1 – 10.9) in the IP arm and 6 months (95% CI 4.1 – 7.9) in the EP arm ($p = 0.03$).
Conclusion: IP is less toxic and improves PFS. This phase II analysis justifies the extension into phase III to assess the impact on survival. The phase III trial will be performed.

1135 POSTER

Skip mediastinal nodal metastases in the IIIA/N2 non-small cell lung cancer

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Objectives: To study the incidence and characteristics of mediastinal nodal metasteses without N1 nodal metasteses ("skip-N2 metastases") in patients with resected pIII/A/N2 non-small cell lung cancer (NSCLC).
Methods: A total of 322 NSCLC patients who underwnt RO surgical resection with a systemic mediastinal nodal dissection in four years time period (2000–2003) were retrospectively reviewed. The 85 patients (26%) at stage IIIA/N2 (pN2+) were grouped according to their skip metastases status. Patient's data were statistically analyzed.
Results: Skip N2 metastses were found in 21 patients (25%) without N1 nodal involvement. The postoperative survival for skip-N2 desease was almost the same as that for pN2 desease with N1 nodal involvement. The incidence of N2 metastses seemed to be more frequent in adenocarcinoma patients ($p > 0.005$), but skip N2 metastses were significantelly higher ($p > 0.001$) in squamous cell carcinoma patients. Altough skip metastases involved more often upper mediastinal lymph nodes and one station level, the difference was not found statsitically significant ($p > 0.227$). Complications rate showed no difference between anlyzed groups of patients.
Conclusion: Sample mediastinal lymphadenectomy may not be appropriate in surgery for NSCLC, because skip metastases were found in 25% of patients without N1 nodal involvement. Role of intraoperatively sentinel node lymph dissection has yet to be proven.

1136 POSTER

Preoperative concurrent chemotherapy with accelerated hyperfractionated radiotherapy in non-small-cell lung cancer; feasibility, toxicity and long-term results of a phase II study

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Purpose: We carried out a phase II trial to evaluate the feasibility, toxicity and effect on survival of polychemotherapy delivered concurrently with accelerated modified hyperfracctionated radiotherapy (AMHR) in non-small-cell lung cancer stage III patients.
Methods: Thirty eight patients with locally advanced stage III NSCLC received neoadjuvant therapy consisting of two cycles of polychemotherapy using cisplatin 80 ml/m^2 on day 1, ifosfamide 1.5 gr/m^2 on day 1 and VP-16 100 mg/m^2 for 3 days and concurrent with the second cycle of chemotherapy AMHR 40.2 Gy (1.8 Gy+0.88 Gy) in 3 weeks.
Results: From October 1997 to October 2001, 38 patients were entered into the study. There were 37 IIIA and 1 IIIB. All the patient were pathologically staged (mediatinoscopy or node punction). The most frequent cell type was squamous cell carcinoma, 20 (52.6%), and adenocarcinoma 12, (31.6%). PS was 0 in 3 patients (8%), PS 1: 31 (81%) and PS 2: 4 (11%). The prominent grade 3–4 side-effect was leucopenia 22%, trombopenia 13.5% and anemia 11%. Other toxicity grade 3–4 was esophagitis in 3%. There was 1 surgically related death. The response rate was one complete response (3%), 16 PR (42%), 13 (34%) with stable disease and 8 (21%) with progressive disease. Surgical-pathological staging showed downstaging in 20 patients including complete sterilization of the tumor in 14 patients (36.8%). The median survival for all 38 patients was 21.85 months with 71.05%, 49.19% and 21.39% 1 year, 2 and 5-years survivors respectivally. On univariate analysis about overall survival were significant; surgical technique, pneumectomy versus lobectomy and others ($p = 0.0028$), postoperative tumor viability, non versus yes ($p = 0.0005$), and downstaging ($p < 0.0001$). On multivariate analysis were only significative the surgery (no versus yes) ($p < 0.0001$)
Conclusions: This neoadjuvant chemoradiotherapy treatment is a tolerable and survival-enhancing multimodality approach to stage III NSCLC.

1137 POSTER

Phase II study of carboplatin and irinotecan (CPT-11) in patients with limited disease small cell lung cancer (SCLC)

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Background: To evaluate the efficacy and safety of combination chemotherapy containing carboplatin and irinotecan (CPT-11) in the first-line treatment of limited disease small cell lung cancer (VALG classification).
Patients and methods: From December 2002 to May 2004 61 patients (pts) were enrolled. 40 pts (66%) were male, 21 pts (34%) female. Median age was 63 years (range 41–77) and median ECOG performance status was 1. Patients received carboplatin AUC 5 on day 1 and irinotecan (CPT-11) 50 mg/m^2 on days 1, 8 and 15, every 4 weeks, followed by standard irradiation (irradiation of the chest with 56 Gy after complete or partial remission, irradiation of the brain with 30 Gy after complete remission).
Results: A total of 233 chemotherapy cycles were administered. The median number of cycles per patient was 4. The overall response rate (ORR) to chemotherapy was 64% (15 CR (24.6%), 24 PR (39.4%), 13 SD (21.3%), PD (3.3%), 7 not evaluable (11.4%)). The median overall survival was 12.6 months (95% confidence intervall 11.6 months – inf.), the median disease-free survival 10.9 months (95% confidence intervall 7.88 – 11.89 months), and the 1-year survival rate 53.5%. Hematological and non-hematogical toxicity was low (CTC-grade 3 neutropenia 14.8%, grade 3 thrombocytopenia 5.4%, grade 3/4 anemia 5.1%, grade 3 vomiting 5.1%, grade 3 emesis 3.6%, grade 3 diarrhoea 3.6%, grade 3 alopecia 3.6% of pts).
Conclusions: The results suggest that the combination of carboplatin and irinotecan (CPT-11) is active and well tolerable in patients with limited disease small cell lung cancer. We recommend to compare carboplatin and irinotecan (CPT-11) with standard chemotherapy cisplatin and etoposide in a randomized phase III study.

1138 POSTER

How accurate is the RTOG/EORTC scoring schema (RESS) in reflecting the late radiation morbidity in lung cancer patients?

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Introduction/Purpose: The increasing use of dose escalation and altered fractionation regimens in the definitive treatment of lung cancer patients emphasizes the importance to accurate grading of late lung toxicity. RESS, the most frequently used grading tool, combines clinical symptoms and radiological abnormality making it confusing and potentially inaccurate. We compared the late lung toxicity using the RESS to a Symptom Only Scale and report the results.
Materials/Methods: The medical records and chest x-rays (CXR) of patients with NSCLC who received curative radiation with doses of 52.5 Gy/15 fractions or 60 Gy/30 fractions were reviewed. All patients had a minimum follow-up of 12 months with no signs of local relapse. Patients' symptoms and CXR findings between 6–12 months post-radiation were recorded. They were scored as per the RESS and the following Symptom Only Scale: *grade 0*: no increase in lung symptoms, *grade 1*: increase in lung symptoms due to RT but not requiring steroids, *grade 2*: same but steroids are required, *grade 3*: oxygen is needed, *grade 4*: assisted ventilation is required and *grade 5*: death related to radiation.
Results: 50 patients were analyzed. All had radiographic changes (Fig. 1). There were 0, 28, 49, and 23% grade 0, 1, 2 and 3 toxicity respectively according to RESS, mostly on the basis of radiographic abnormalities. Most patients had no or mild symptoms only. According to the Symptom Only Scale they were scored 86, 7, 7 and 0% grade 0, 1, 2 and 3 toxicity