1/76; hypokalemia 1/76. Nine patients were discontinued from study due to toxicity. There was one treatment-related death (pneumonitis). Response: CR 0, PR 8 (12%; 95% CI 5–23%), SD 32 (48%; 95% CI 37–60%), and PD 26 (39%; 95% CI 28–51%). Median duration of PR has not been reached. Median duration of SD was 6 months. Survival: Median overall survival was 11.0 months (95% CI 8–14 mo). Median survival by response: PR: median survival not yet reached; SD: 12 mo (95% CI 10–16 mo); PD: 7 mo (95%CI 4–11 mo). In 28 pts with available tissue, EGFR mutations were found only in 3/5 responders. K-ras mutations were found in 2/9 with disease progression and 2/13 with stable disease. EGFR CN did not correlate with treatment outcome.
Conclusions: Erlotinib appears to be relatively well tolerated and demonstrates encouraging activity and median survival in patients $\geqslant$70 years of age with previously untreated advanced NSCLC. We have recently completed accrual, and results will be updated.

1129 POSTER

Sequential versus concomitant administration of docetaxel and gemcitabine as first-line treatment of advanced non-small cell lung cancer (NSCLC): results of a phase II/III randomised study

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Background: Docetaxel (D) and gemcitabine (G) – alone or in combination – have shown encouraging activity and relatively favourable toxicity in patients (pts) with advanced NSCLC. However, the optimum schedule requires definition. This Phase II/III study evaluated the clinically relevant haematological toxicity (CRHT) of first-line treatment with G and D given either concomitantly or sequentially. Interim results have been presented previously (J Clin Oncol 2005; 23: 634S [abstract 7057]).
Methods: Pts were randomised to receive 3-weekly cycles of G 1000 mg/m^{2}and D 75 mg/m^2 either concomitantly (Arm A: G, Days 1, 8 and D, Day 8 for 6 cycles) or sequentially (Arm B: G, Days 1, 8 for 3 cycles followed by D, Day 1 for 3 cycles). CRHT was defined as NCI-CTC Grade 3–4 thrombocytopenia requiring platelet transfusion, anaemia requiring red blood cell transfusion or febrile neutropenia requiring intravenous (iv.) antibiotics.

	Arm A, G + D (N = 166) n (%)	Arm B, G → D (N = 160) n (%)
CRHT		
At least one event	26 (16)	8 (5)
Anaemia + transfusion	19 (11)	8 (5)
Thrombocytopenia + transfusion	2 (1)	1 (1)
Febrile neutropenia + iv antibiotics	7 (4)	1 (1)
Overall Grade 3–4 haematological toxicity		
At least one event	67 (40)	46 (29)
Anaemia	7 (4)	3 (2)
Thrombocytopenia	10 (6)	4 (3)
Neutropenia	61 (37)	42 (26)

Results: The Phase II study included 339 pts; data from 336 pts are reported in this abstract (Arms A/B: 174/162 pts; median age 62.1/64.9 years). Arms were well matched for standard demographics. At baseline, 87% of pts had stage IV disease; 85% had WHO PS $\leqslant$ 1. Median survival was 7.1 and 7.2 months in Arms A and B, respectively ($p > 0.05$); overall response was 32% and 23%, respectively ($\div^2$ test, $p = 0.097$) and median time to progression was 6.2 and 4.7 months, respectively (log-rank test, $p = 0.016$). Arm B received 64% and 44% of the total doses of G and D, respectively, given in Arm A. CRHT occurred less often in Arm B ($p = 0.002$): the proportion of patients with CRHT was 31% of those with CRHT in Arm A. Transfusions and iv antibiotic treatment days were less common in Arm B (Table, 326 evaluable pts). QoL (EORTC-LC13 and SS14 measurements) also favoured Arm B. Final Phase II analysis results for 339 patients will be presented.
Conclusion: G and D given sequentially is as effective as concomitant administration of G and D as first-line treatment for advanced NSCLC, and is associated with significantly reduced CRHT, less iv antibiotic use and a trend towards improved QoL.

1130 POSTER

Docetaxel/gemcitabine vs. a sequential protocol comprising cisplatin/gemcitabine/docetaxel in the first-line treatment of patients with stage IV non-small cell lung cancer (NSCLC): results of a randomised phase II trial

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Background: Patients with metastatic non-small cell lung cancer (NSCLC) are most frequently treated with a platinum-based chemotherapy doublet combination. However, recent studies have demonstrated that triple-agent therapies allow improvement in the treatment response but can be associated with frequent intolerability. A sequential triple-agent schedule may combine acceptable tolerability and good efficacy. We therefore conducted a multicentric, prospectively randomised study that evaluates a sequential three-drug schedule and a platinum-free doublet regimen.
Methods: Patients with histologically confirmed metastatic (UICC stage IV) NSCLC were randomised to one of two protocols: gemcitabine (900 mg/m^2, 30 min. infusion) on days 1 and 8, and docetaxel (75 mg/m^2, 1 hour infusion) on day 1, repeated every three weeks up to six cycles (DOC-GEM). In regimen CIS-GEM-DOC, gemcitabine (900 mg/m^2, days 1 and 8) and cisplatin (70 mg/m^2, 1 hour infusion, day 1) were given for three cycles, followed by three cycles of docetaxel (100 mg/m^2, day 1, every three weeks).
Results: 113 patients (pts.) were totally included. 55/58 pts. were randomised to DOC-GEM and CIS-GEM-DOC, respectively. One patient was excluded from analysis due to violation of inclusion criteria. 20.4% of the pts. responded in the DOC-GEM arm whereas 31.0% responded in the CIS-GEM-DOC protocol (intent-to-treat, WHO criteria, difference not significant). The median time to progression was 3.6 months for patients receiving DOC-GEM (95% confidence interval 1.4 to 5.9) and 5.2 months in the CIS-GEM-DOC schedule (95% confidence interval 3.1 to 7.3, $p = 0.06$). The median survival was 8.7 months with DOC-GEM (95% confidence interval 5.7 to 11.6) and 9.4 months for patients receiving CIS-GEM-DOC (95% confidence interval 7.8 to 11.0, difference not significant). The 1-year survival rates were 34% and 35%, respectively. Mild to moderate leukopenia was frequently seen in both schedules. Other frequent adverse effects were nausea/vomiting, thrombocytopenia, anemia, diarrhea, and skin toxicity.
Conclusions: In the present study, both schedules demonstrated good efficacy and acceptable toxicity. No significant differences were demonstrated in terms of response rate or survival. However, the sequential triple-agent schedule approached statistical significance in response duration.

1131 POSTER

Addition of CPG 7909 to taxane/platinum regimen for first-line treatment of unresectable NSCLC improves objective response in phase II clinical trial

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Background: A taxane/platinum regimen remains first-line treatment of stage IIIb/IV (unresectable) non–small cell lung cancer (NSCLC), yet expected partial response is only 20%-30%. Tumor response and survival have been significantly improved in many preclinical models with the addition of synthetic oligodeoxynucleotide CPG 7909, a Toll-like receptor 9 agonist with immunostimulatory activity. Previous trials have established the dosing ranges, biologic response, and safety of weekly subcutaneous CPG 7909.
Materials and Methods: To investigate the effect of adding CPG 7909 to standard chemotherapy for first-line treatment of stage IIIb/IV NSCLC,

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.