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

respectively (P value 0.046), indicating that the inclusion of radiographic abnormalities significantly upgrade the toxicity scores.
Conclusion: All patients developed radiographic abnormalities post curative radiotherapy, the extent/severity of which did not correlate with the symptoms. The use of the Symptom Only Scale seems to be more clinically relevant and may be a better tool to evaluate long-term toxicity after curative radiation in the lung.

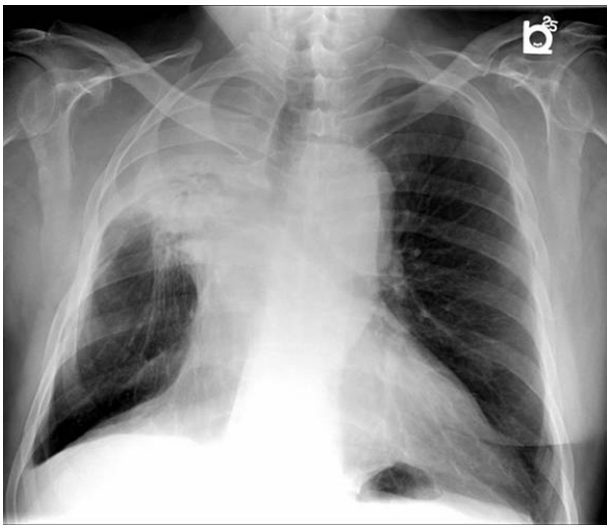

Fig 1. 74 year old male, 16 months post curative radiation, asymptomatic, scoring grade 3 according to RESS and grade 0 according to symptom only system

1139 POSTER

Economic impact of adopting pemetrexed plus cisplatin for malignant pleural mesothelioma into Scottish clinical practice

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Background: The efficacy of pemetrexed + cisplatin (pem/cis) versus cisplatin alone (cis) was evaluated in the largest-ever randomised phase III trial in patients with unresectable malignant pleural mesothelioma (Vogelzang 2003). Emergent data early in the trial led to a decision that all patients be fully supplemented with folic acid and vitamin B12. Survival benefit was assessed in all fully vitamin-supplemented patients (FS) and in those FS patients with advanced disease (stage III/IV). A cost-effectiveness evaluation of pem/cis compared to cis in the treatment of all FS patients and in the FS patients with advanced mesothelioma was conducted for Scotland.
Method: A cost per life-year saved (LYS) analysis using the median survival gain from the clinical trial was undertaken. The above cohorts were chosen because either one could reflect clinical practice in Scotland: vitamin supplementation is mandatory with pemetrexed treatment (ALIMTA* SPC) and most patients treated for mesothelioma in Scotland have advanced disease at presentation (Aziz 2002). Specific unit costs were applied to drug acquisition, administration, supportive care medication, hospitalisations for serious adverse events and post-study chemotherapy, with incidence derived directly from the clinical trial. A discount rate of 3.5% per annum was applied to all outcomes.
Results: The incremental per patient cost for pem/cis compared to cis was £8,196 and the results of the analyses are shown in the table.
The robustness of the model was tested using one-way sensitivity analyses on key variables affecting both cost and outcomes estimates in the cost-effectiveness model. Little variation in the incremental cost/LYS was found with the variables tested for the FS with advanced disease patients (£17,500-£25,000).
Conclusions: The trial demonstrated clear survival gain for the combination therapy, particularly in the cohort of fully supplemented patients with advanced disease. This analysis demonstrates that the pemetrexed/cisplatin combination is a cost-effective treatment for patients with advanced maligant pleural mesothelioma.

	Pem/cis	cis	*P*	Hazard Ratio (95% CI)	Cost/LYS
Fully supplemented (n)	168	163	0.051	0.75 (0.57–1.00)	£30,355
Median survival (months)	13.3	10.0			
Fully supplemented (Stage II/IV) (n)	125	122	0.003	0.63 (0.46–0.86)	£20,844
Median survival (months)	13.2	8.4			

1140 POSTER

First results of long term outcome in patients with inoperable or irresectable Non-small cell lung cancer (NSCLC) treated with high-dose accelerated radiotherapy with or without concurrent or sequential chemotherapy

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Background: Results of high dose radiotherapy (RT) +/− chemotherapy (CT) with curative intent were analyzed in all patients (pts) with NSCLC treated in our department from 1995–2004.
Material: Included are 131 pts with medically inoperable or irresectable NSCLC (TNM stage I: 15 pts, IIB: 15 pts, IIIA: 67 pts, IIIB: 32 pts, X: 2 pts). ECOG performance score was 0, 1 or 2 in 28 pts, 76 pts and 27 pts respectively. Sex distribution: male 89 pts, female 42 pts. Pathology: adenocarcinoma: 18 pts, squamous cell carcinoma (ca): 39 pts, large cell ca: 60 pts, undifferentiated carcinoma 8 pts. No pathologic confirmation could be obtained in 6 pts.
Treatment: Standard curative treatment in our department is 66 Gy /2.75 Gy/ 24 fx/ 33days combined with daily administration of Cisplatin 6 mg/m^2 after completion of the phase II EORTC 08912 study in 1997. If pts fulfilled the inclusion criteria of the EORTC phase III study 08972/22973 they were randomised to either our standard arm or the sequential treatment arm consisting of two courses of a 21-day schedule of CT(Gemcitabin 1250 mg/m^2 d1, Cisplatin 75 mg/m^2 d2) followed by the same RT without daily Cisplatin. Concurrent chemo-radiotherapy was given to 56 pts, 26 pts were treated with sequential chemo-radiotherapy. If administration of CT was not possible, pts received RT only (49 pts).
Results: The 1, 2 and 5 yr actuarial overall survival (OVS) are 46%, 24% and 15%. Factors with a significant influence on OVS are concurrent administration of Cisplatin (1, 2 and 5 yrs OVS 56%, 33% and 24% respectively) and performance status. Older patients (>58 yr) show a trend for a poorer survival, as does advanced stage, but this is apparent only for patients not receiving chemotherapy. The incidence of local recurrence is 36%, the incidence of distant metastases 46%. No late complications are seen in 65 pts, grade 1 or 2 in 22 pts, grade 3 in 19 pts (lung 16x, oes 2x, heart 1x) and grade 4 in 5 pts (spinal cord 1x, lung 2x, oes 2x). One patient had a lethal complication (oes). In 20 patients no sufficient data are present to assess late complications.
Conclusion: In patients with inoperable or irresectable NSCLC radiotherapy 66 Gy/ 24 fx/ 33 days combined with concurrent chemotherapy of daily Cisplatin 6 mg/m^2 results in excellent treatment outcome with a 1, 2 and 5 yr OVS of 56%, 33% and 24%.

1141 POSTER

Postoperative radiotherapy (PORT) for non-small-cell lung cancer (NSCLC): Results of the 1999–2001 patterns of care study (PCS) nationwide process survey in Japan

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Background: Results of the PORT meta-analysis have considerable impact on the practice pattern for NSCLC after surgery. This study was undertaken to investigate the practice process of PORT for NSCLC in Japan.
Material and Methods: The PCS conducted a nationwide survey of PORT for NSCLC in Japan. The PCS randomly sampled institutions and patients from academic and non-academic institutions (A1: academic, treating ⩾430 patients/year, A2: <430 patients, B1: non-academic, ⩾130 patients/year,