RT in 8 patients who completed the planned treatment (C. Gridelli, Lung Cancer 2000); the Maximum Tolerated Dose (MTD) was 5 mg/m^2/day.
Oral vinorelbine (NVBo) has produced similar results in advanced NSCLC when compared to IV NVB. Based on the bioavailability of NVBo (40%) and the available marketed dosages (20−30 mg), a feasibility study has been implemented in patients (pts) with locally advanced or inoperable stage III NSCLC.
Material and Methods: Three to 6 pts between 18 and 70 years, with histologically proven untreated locally advanced inoperable stage IIIAN2/IIIB (supraclavicular lymph nodes and pleural effusion excluded) NSCLC, adequate bone marrow, hepatic and renal function, KPS $\geqslant$ 80%, were expected at each dose level. Eight levels were planned with NVBo given concomitantly with 60 Gy RT (2 Gy/day; 5 days a week) from 20 mg total dose up to 60 mg total dose on days (D) 1, 3 and 5 each week during 6 weeks. Here we report the analysis of the first 5 dose levels.
Results: Between 06/02 and 07/06, 12 men and 3 women were enrolled with stages IIIA N2 (2 pts) or IIIB (13 pts). Median age 61.2 years [49.3−71.3], median KPS 100% [80–100%]. The first 5 levels were completed without the occurrence of dose-limiting toxicity (3 pts per dose level). Overall, 11 pts received 100% of the planned NVBo dose during the 6 weeks treatment period and 4 pts missed only one intake for other reason than toxicity.
Neither grade $\geqslant$3 haematological/ non-haematological toxicity nor treatment interruption >2 weeks occured. Only 2 pts experienced grade 2 radiation-induced oesophagitis and constipation. Objective response was observed in 4 pts (27%) and 2 additional pts had confirmed partial response during follow-up.
Conclusion: NVBo with this new original schedule of 3 times a week intake concomitantly with RT for 6 weeks, is still well tolerated with dosages up to 50 mg on D1, 40 mg D3 and 40 mg D5, each week, without MTD. Additional dose escalation is ongoing to determine the recommended dose for phase II trials.

6583 POSTER

The prognostic value of hemoglobin concentration and WBC count in sequential radio-chemotherapy or radiotherapy alone for locally advanced non-small cell lung cancer

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Background: The aim of this study was to evaluate the prognostic value of hemoglobin concentration at the beginning (Hb1) and at the end (Hb2) of sequential radio-chemotherapy or radiotherapy alone for lung cancer. The analysis accounted for WBC count, platelets count, as well as tumor and treatment related variables.
Material and Methods: The retrospective study included 224 patients treated between 1998 and 2003 for stage IIIB non-small cell lung cancer: 118 patients received cisplatine-based induction chemotherapy (2−6 cycles) followed by conventionally fractionated 3-D conformal radiotherapy (median total dose 66 Gy, dose per fraction 2.0 Gy), while 106 patients were treated with radiotherapy alone (median dose 66 Gy). The variables used in the analysis included Hb, WBC and platelets counts at the beginning and at the end of radiotherapy, as well as 8 tumor and treatment related variables (general performance status, age, sex, TN stage, number of chemotherapy cycles, total radiation dose, overall radiation treatment time). A multivariate Cox proportional hazard regression analysis was performed to identify the variables that significantly affected overall survival (OS). Backward stepwise regression was used to optimize the model.
Results: Several of the parameters studied (e.g. platelets count, $p = 0.02$) appeared to have a significant influence on OS of 224 patients when univariate model was used, but only Hb2 remained significant ($p < 0.00001$) in a multivariate model. Likewise, only Hb2 appeared significant ($p = 0.00004$) when multivariate analysis was restricted to subgroup of the patients treated with radiotherapy alone. By contrast, not only low Hb2, but also the above-average WBC count at the end of radiotherapy (WBC2), low number of chemotherapy courses, and advanced N stage appeared as significant and independent predictor of impaired OS among the patients treated with radio-chemotherapy.
Conclusion: Hemoglobin concentration at the end of radiation treatment appear to be the strongest predictor of long-term survival among the patients with non-small cell lung cancer treated with radiotherapy alone. In patients treated with induction chemotherapy the above-average WBC count at the end of radiotherapy was also a predictor of an impaired survival. This may suggest that the above-average WBC2 may be considered as one of the surrogate markers of individual resistance to cytotoxic therapy, and/or a sign of a deficient systemic treatment.

6584 POSTER

Induction chemotherapy with vinorelbine and a platinum compound followed by concurrent chemoradiotherapy and consolidation chemotherapy with the same drugs for stage III non-small-cell lung cancer (NSCLC) – a phase II study

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Purpose: to determine the response rate (RR), toxicity, time to progression (TTP) and survival (S) of induction Chemotherapy (ChT) with Vinorelbine (Vrb) and Cisplatin (Cis) or Carboplatin (Carbo) followed by concurrent chemoradiotherapy (ChRT) and consolidation ChT with the same drugs, for stage III NSCLC.
Methods and Materials: 53 patients (pts) were included from 05.02.2004 to 20.12.2006: median age 57(39–73), M/F=50/3, PS 1/2=31/22, stage IIIA/IIIB=6/47, squamous cell cc 43, large cell cc 5, adenocc 1, "non-small" carcinoma 4. Treatment consisted of 2 cycles (c) of induction ChT with Vrb (25 mg/sqm, d1, 8, q21) and Cis (100 mg/sqm, d1, q21), or Carbo (AUC 5, d1, q21), followed by 2 more c (with reduced doses: Vrb 15 mg/sqm, d1, 8, q21, Cis 80 mg/sqm, d1, q21 or Carbo AUC 2.5, d1, q21) given concurrently with RT and 2 c of consolidation ChT with the same drugs. RT (15MV) has been administrated to a total dose of 60−68 Gy/30−34 fractions. The last 17 pts benefited of conformal-3DRT. 86% of pts completed at least 4 c, 70% completed 5 or 6 c of ChT. The optimal doses of RT have been received by 75% of pts.
Results: 53 pts were evaluable for toxicity. Severe grade (gr) 3 or 4 neutropenia occured in 5 pts, anemia in 4.One pt had gr 3 trombocitopenia and also 2 pts had gr 3 gastro-intestinal toxicity. Gr 3 neuropathy occured in 1 pt.
Two pts stopped treatment after 2 c of induction ChT (one because of gr 3 neuropathy, gr 2 febrile neutropenia and evolution of the disease, and the other because of gr 4 neutropenia and decompensation of diabetes melitus). Other 2 pts didn't receive cycle 3 of chemotherapy because of toxicities or evolution of the disease. Of the 53 pts. evaluable after induction ChT, 5.7% obtained CR, 37.8% PR, 52.8% had SD and 3.7% PD. Of the 49 pts evaluable for response after ChRT, 33% achieved CR, 37% PR for an overall RR of 70% (CI:58−82), 18% of pts had SD, and 12% had PD.
Progression-free-S at 1 year was 38% (CI:24−53%) with a mTTP of 9 months (CI:6.9−17.9). The disease specific S at 1 year was 60% (CI:44%-73%) and the mS was not reached yet. For the 27 pts still alive the median follow-up was 9.6 months.
Conclusions: Preliminary results indicate that induction ChT followed by concurrent ChRT with Vrb and a Platinum compound, followed by consolidation ChT with the same drugs given for advanced stage III NSCLC is feasible, well tolerated and has a positive effect on the RR and survival

6585 POSTER

Accelerated radical radiotherapy for non-small cell lung cancer (NSCLC) using two common regimens: a single centre audit of outcome

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Background: Radical radiotherapy (RT) regimens for NSCLC vary considerably. Our centre uses both continuous hyperfractionated accelerated radiotherapy (CHART) and accelerated hypofractionated RT using 55 Gy in 20 fractions over 4 weeks. This audit reports outcome according to RT regimen.
Materials and Methods: All case notes and RT records of radically treated patients between 1999 and 2004 were retrospectively reviewed. Basic patient demographics, tumours, characteristics, RT and survival data were collected. Patients treated with CHART received 54 Gy in 36 fractions over 12 days.
Results: One hundred and thirty-seven patients received CHART and 140 received hypofractionated RT. Median age was 65 (41−83) in CHART and 73 (33−87) in hypofractionated group respectively. Sixty-five percent were male in CHART compared to 61% in hypofractionated group. Histological confirmation was obtained in 90% of CHART and 76% of hypofractionated patients. For CHART patients, stages 1, 2, 3 and unclassified were 12%, 8.0%, 68% and 12% and the staging for the hypofractionated regimen was 54%, 11%, 34%, 2% respectively. WHO performance status was 0/1, 2/3 and undocumented in 88%, 6%, and 7% of CHART patients and 78%, 22%, and 0% of the hypofractionated patients. Prior chemotherapy was given in 34% CHART and 19% of hypofractionated patients. Median overall survival (OS) from time of diagnosis was 16.6 months and 21.4 months in

the CHART and hypofractionated groups respectively. Two-year OS (2YS) from diagnosis was 34% for CHART and 45% in the hypofractionated group.
Conclusion: This single centre audit reflects outcome of unselected consecutively treated NSCLC patients. Patient selection for the two radiotherapy regimens was largely down to the timely availability of the next CHART session, though only CHART patients received prophylactic nodal irradiation (PNI), so smaller peripheral lesions were selected for the hypofractionated schedule when PNI was not felt to be indicated. This helps to explain the demographic differences in the two groups and means direct comparison is not possible.
Encouragingly, CHART outcome demonstrates reproducibility, with the original CHART paper (Saunders M et al 1999). Our hypofractionated outcome is similar to that previously reported (Lester et al, 2004), but despite this being the UK's most common regime, 55 Gy in 20 daily fractions remains un-validated by phase III trial data.

6586 POSTER

Cisplatin (CDDP) plus vinorelbine (VRB) as first-line treatment for patients with advanced non-small-cell lung cancer (NSCLC): molecular correlates

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Background: The combination of cisplatin plus vinorelbine is a commonly used regimen for first-line therapy in advanced NSCLC. The correlation between predictive genetic markers and clinical endpoints may improve the prediction of treatment success and thereby the tailoring of chemotherapy. In this trial, predictive genetic markers of response to CDDP/VRB were examined in genomic DNA and cDNA derived from tumors and circulating tumors.
Materials: From April 2004 to January 2006, 238 chemonaive patients (pts) with stage IIIB (pleural effusion or supraclavicular lymph nodes)–IV or recurrent NSCLC were accrued at 35 sites. Treatment consisted of CDDP 75 mg/m^2 IV day 1 plus VRB 25 mg/m^2 IV or 60−80 mg/m^2 oral, days 1, 8 every 21 days. DNA samples were collected from primary tumors for the assessment of microtubule associated protein 4 (MAP4) and from serum for the checkpoint forkhead-associated and ring finger (CHFR) methylation.
Results: Data on 198 pts is available. Median age 62 years (38−80); males: 83.8%; smokers: 77.8%; PS 0−1: 95.3%; adenocarcinoma, 48.9%/ squamous 32.8%; stage IIIB: 16.7%, IV: 83.3%. Median cycles: 4 (1−12). Hematological toxicities (%pts): neutropenia grade 3−4, 17.2%; thrombocytopenia grade 3−4, 1%; anemia grade 3, 2%. Febrile neutropenia appeared in 14 cycles/10 pts (1.8%/5.1%). Non-hematological toxicities (%pts): pulmonary grade 3−4, 5.5%; nausea/vomiting grade 3−4, 8.1%; asthenia grade 3, 13.2%; pain grade 3, 6.6%; infection grade 3, 4.1%; neurotoxicity grade 3, 0.5%. Efficacy in evaluable population: CR, 2.3%; PR, 30.8%; ORR, 33.1% (95% CI 26.1−40.2%); SD, 39.7%. Median follow up of 6.7 months, median survival for the whole population was 9 months (mo), progression free survival 5.07 mo, event free survival 4.8 mo, 1-year survival 39.9%.
Conclusions: This trial confirms that CDDP/VRB is effective as first-line therapy, presenting a favourable toxicity profile in p with advanced NSCLC. A complete genomic analysis is ongoing.

6587 POSTER

A phase IB, dose-finding study of erlotinib in combination with pemetrexed in patients with advanced (stage IIIB/IV) non-small-cell lung cancer (NSCLC): a preliminary analysis of the BP18193 study

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Background: Erlotinib (Tarceva®) monotherapy has shown significantly improved survival, delayed symptom deterioration and improved QoL in patients (pts) with advanced NSCLC. This study was designed to determine the maximum tolerated dose (MTD) of the erlotinib/pemetrexed (Alimta®) combination (E/P) and to collect preliminary evidence of anti-tumour activity.
Methods: Pts were enrolled into this non-randomised open-label study if they had either failed first-line, platinum-based chemotherapy or were considered suitable for the E/P regimen. Pts received P 500–700 mg/m^2 i.v. every 21 days; E 100–150 mg/day p.o. MTD was defined as the dose below that which led to dose-limiting toxicities (DLTs) in $\geqslant$1/3 pts. The MTD cohort was then to be expanded to 12 pts for confirmation of tolerability.
Results: A total of 20 pts, median age 59 yrs, were entered into 4 cohorts: 3 (1 female) in cohort 1 (E100/P500), 6 (1 female) in cohort 2 (E150/P500), 6 (2 female) in cohort 3 (E150/P600) and 5 (2 female) in cohort 4 (E150/P700). No DLTs were reported in cohorts 1–3, but each pt reported at least one adverse event (AE). 3 pts in cohort 4 had DLTs (one skin rash with secondary infection, one grade 2 skin rash and one neutropenia, anaemia, thrombocytopenia and rash). Frequently reported AEs (any grade) included diarrhoea (in 17 pts), rash (16 pts), fatigue (13 pts), anorexia (11 pts), neutropenia (6 pts) and dyspnoea (4 pts). Serious AEs were experienced by 5 pts (33%) in cohorts 1–3 and by 3 pts (60%) in cohort 4. Following results from a separate study examining doses of P >500 mg, which did not improve efficacy over the standard 500 mg dose, it was decided to discontinue using P doses >500 mg in ongoing studies. Thus, enrolment in higher-dose cohorts for this study was prematurely discontinued and MTD could not be confirmed in an expanded cohort. Two partial responses were reported, one each in cohorts 1 and 4. Pharmacokinetic (PK) evaluation for E, its metabolite OSI-420, and for P, showed no drug–drug interaction. PK parameters were comparable when given in E/P combination and alone.
Conclusions: The data suggest that the E/P combination is well-tolerated. Full, standard, single-agent doses of both drugs were given concurrently in cohort 2 and did not lead to DLTs. Discontinuation of enrolment meant that MTD could not be confirmed but the E/P regimen warrants further investigation.

6588 POSTER

Vinorelbine (VRL) plus gemcitabine (GEM) as first-line treatment for elderly patients with advanced non-small-cell lung cancer (NSCLC): molecular correlates

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Background: The clinical benefit of non-cisplatin doublets vs single-agent therapy in elderly or unfit p is still controversial. The present study focuses on the clinical outcome of VRL/GEM in elderly p and the role of functional status and comorbidities. Predictive genetic markers of response to VRL/GEM will also be examined in genomic and cDNA from tumor and circulating tumor DNA.
Materials: 145 chemonaive p with stage IIIB (pleural effusion or supraclavicular lymph nodes)-IV or recurrent NSCLC and age >70 years