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.

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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.

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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.

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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

were accrued at 32 sites between April 2004 and January 2006. Treatment consisted of VRL 25 mg/m^2 IV or 60−80 mg/m^2 oral plus GEM 1200 mg/m^2, days 1, 8 every 21 days. Activities of daily living (ADL), instrumental activities of daily living (IADL) and comorbidities were evaluated. DNA samples were collected from primary tumors for the assessment of microtubule associated protein 4 (MAP4) and from serum for checkpoint with forkhead-associated and ring finger (CHFR) methylation.
Results: Data on 130 p is available for toxicity and 95 for response. Median age 76 years (69−83); males: 86.8%; smokers: 70.5%; PS 0−1: 83.9%; adenocarcinoma: 34.4% / squamous: 48%; stage IIIB: 22.7%, IV: 77.3%. Self-sufficiency in ADL and IADL was 77.4% and 45.2% of the p analyzed. 68% of the p had comorbidities. Median cycles: 3 (1−8). 461 cycles (cy) were performed, 16.3% were delayed and 2.1% had dose reduction. Hematological toxicities: neutropenia grade 3−4, 12.5% p (4.1% cy); thrombocytopenia grade 3−4, 3.1% p (1.3% cy); grade 3 anemia, 3.1% p (0.9% cy). Efficacy in evaluable population: PR, 23.2% (95% CI, 15.1% to 32.9%); SD, 41.1%. 24 p died during the treatment period (non toxicity related) and 21 p were not evaluable. With a median follow-up of 5.8 months, median survival for the whole population was 4.97 months (mo), progression free survival 4.53 mo, event free survival 3.43 mo, 1-year survival 26.6%. Statistically significant differences in median survival were observed among subgroups: PS 0−1/2, 6.5 m vs. 2.3 mo ($p < 0.001$); gender male/female, 4.5 vs. 9.7 mo (p 0.027); ADL <6/=6, 3.4 vs. 7.1 mo (p 0.023).
Conclusions: The combination of VRL and GEM is effective, presenting a favourable response/toxicity ratio in elderly p with advanced NSCLC. A genomic analysis is ongoing.

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Level of circulating endothelial progenitor cells is a potential surrogate marker in human non-small cell lung cancer

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Vascularization is a key mechanism in non-small cell lung cancer (NSCLC) progression, and is frequently used as a prognostic factor. Until recently, it was generally accepted that the vascularization of tumors arise exclusively from the sprouting of preexisting capillaries. However, recent evidence suggests that tumor vasculature can also arise through vasculogenesis, a process by which bone marrow-derived endothelial precursor cells (EPCs) are recruited and differentiate in situ into mature endothelial cells to form new blood vessels. We assessed the quantity of circulating EPCs in the peripheral blood of 53 NSCLC patients by flow cytometry, and studied the incidence and contribution of EPCs to the vasculature of tumors. Precursor cells were detected by EPC-specific markers: CD34, vascular endothelial growth factor receptor 2 (VEGFR2, KDR), and CD133. Before therapy, no significant associations between EPC levels and standard prognostic parameters, as tumor stage, smoking history, histologic type, were detected. In NSCLC patients before anticancer treatment, the number of CD34+/VEGFR2+ EPCs in peripheral blood was significantly higher than in healthy controls (1162.4$\pm$242.4 vs. 345$\pm$54.8/mL). In the subgroup of responders to treatment (patients who achieved a tumor-free status with surgery and those with complete or partial response to chemo- or chemoradiotherapy), the mean number of EPCs/mL of blood (776.1$\pm$265) was significantly lower than in non-responders (patients with local recurrence or stable/progressive disease, 4687.9$\pm$1178.6). Our cases were also classified into two groups; EPC high or low, with a cutoff of 1000 EPCs/mL. Patients with low levels of circulating EPCs had significantly longer survival than those with high levels of EPCs (median survival: 55.5 weeks vs. 26 weeks, respectively). According to multivariate analysis, circulating EPC numbers predicted outcome independent of other variables. Our study indicated that EPCs are involved in the angiogenesis/vasculogenesis of NSCLC. However, it still remains to be determined whether EPC level can be used as a surrogate marker to monitor the efficacy of standard or antiangiogenic therapies in NSCLC.
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Influence of baseline inflammatory markers on the response to first-line chemotherapy in advanced NSCLC

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Background: Recent studies have shown that the presence and a magnitude of inflammatory response, as evidenced by concentration of circulating C-reactive protein (CRP) is a prognostic factor independent of age, stage, PS, weight loss and hypoalbuminemia in patients with NSCLC. Our retrospective analysis demonstrated that high baseline CRP and white blood cell count (WBC) correlate with a poor prognosis in NSCLC patients (ASCO, 2006).
Materials and Methods: We conducted a prospective validation study to confirm previous findings and to explore the relationship between baseline CRP and WBC with response to 1st line chemotherapy (CTX) in pts with newly diagnosed NSCLC with stages 3B, 3B pleural effusion and 4. 69 patients with non small lung cancer had CRP and WBC measured prior to their 1st treatment. Pts were enrolled between February 2005 and October 2006 and were assigned a prognostic index (PI) score of 0 if CRP $\leqslant$ 10 mg/L and WBC $\leqslant 11\times10^9$/L, 1 if one of the markers was elevated, or 2 if both were elevated. Response was measured by chest CT following two cycles of CTX.
Results: 24 (35%) pts had PI of 0; 31 (45%) patients had PI of 1, and 14 (20%) patients had PI of 2. Survival analysis demonstrated that patients with PI of 0 had a median survival of 19.9 mo (CI: 10.5−29.3); patients with PI of 1 had 10 mo (CI: 6.4−13.8) survival, while patients with PI of 2 had 3 mo (CI: 2.5−3.3) survival ($p < 0.001$). 12/32/25 pts had a PR/SD/PD after 1 (7pts) or 2 (62 pts) cycles of chemotherapy. There was a significant but fairly weak correlation between PI and disease progression. Baseline CRP level was 2 fold higher in pts who progressed compared to those who did not progress (56 mg/L vs 23 mg/L). 9/14(64%) with PI of 2 developed progressive disease, compared to 7/24(29%) with PI of 0 and 9/31 (29%) with PI of 1 ($P < 0.05$, $r = 1.3$). In the analysis of prognostic factors for survival using COX regression model the age, sex, stage, ECOG PS and PI were included. The PI had an excellent predictive power in estimating survival. The hazard for death increased 3.3 fold for each unit increase in PI value ($p < 0.001$).
Conclusion: We conclude that patients with an aberrant inflammatory response as reflected by a combination of high CRP and WBC had significantly shorter survival. Correlation with response to treatment requires further investigation.
Study was sponsored by The Angel Ball

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Analysis of the progostic value of the quantification of plasmatic epidermal growth factor receptor (EGFR) in advanced non-small cell lung cancer (NSCLC) patients

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Background: EGFR has an extracellular ligand-binding domain that can be proteolitically cleaved from the cell surface and can be accurately quantified in blood by ELISA. We have investigated the usefulness of plasma EGFR measurements as prognostic marker in advanced NSCLC.
Materials and Methods: The cohort consisted in 329 patients (p) with advanced NSCLC that received first-line therapy with cisplatin and docetaxel. The concentration levels of the EGFR extracellular binding domain were determined by a sandwich quantitative ELISA in the baseline, before therapy.
Results: Median age was 61, range [39−80], 84% males, 100% caucasian, 68% stage IIIB and 32% IV and 99% PS 0−1. The histological subtypes were: 31% squamous cell carcinoma, 49% adenocarcinoma, 15% large cell, and 5% undifferentiated. 181 p achieved complete response (CR), partial response (PR) or stable disease (SD) and 109 p progressive