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.

6589 POSTER

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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6590 POSTER

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

6591 POSTER

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

disease (PD). Median patient's plasma levels of EGFR were 32.4 ng/ml. There were not differences in p according to histology, site of metastasis and ECOG. There were differences in response to therapy; CR+PR+SD p presented median EGFR of 31.97 ng/ml [13.2−48.6] vs 30 ng/ml [16.9−46.8] in the PD group (p = 0.024). Dividing the cohort in two sets according to EGFR median we found two significantly different groups in terms of Overall Survival (OS) and Time To Progression (TTP). Patients with EGFR32.4 ng/ml was 4.7 m [4.0−5.4], (p = 0.024). OS when EGFR32.4 ng/ml was 9.1 m [8.2−10.1], (p = 0.038).
Conclusions: Patients with PD presented significantly lower levels of serum EGFR than those patients with CR+PR+SD. There is a relationship among lower EGFR concentration in serum with a worst prognosis in advanced NSCLC p in terms of TTP and OS.

6592 POSTER

Determination of plasma K-ras mutations in codon 12 in advanced non-small cell lung cancer (NSCLC) patients. Analysis of its prognostic role

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Background: Qualitative analysis of circulating DNA in blood is a promising non-invasive diagnostic and prognostic tool. Our aim was to study the association between the presence of K-ras mutations at codon 12 and several clinical variables in advanced NSCLC patients.
Materials and Methods: We examined 451 NSCLC patients in stage IIIB and IV, treated with cisplatin and docetaxel. Blood samples were collected before chemotherapy, and circulating DNA was extracted from the plasma using commercial adsorption columns. K-ras mutational status was determined by a method based in allelic discrimination with RT-PCR.
Results: Median age was 61 years [35−82] and 84% were males. 99% had performance status 0−1. 84% were in stage IV and 16% in stage IIIB. The histological subtypes were: 32% squamous cell carcinoma, 50% adenocarcinoma, 14% anaplastic large cell, and 4% undifferentiated. 41% of the patients received second line chemotherapy. 1% achieved complete response (CR), 36% partial response (PR), 35% had stable disease (SD) and 28% progressive disease (PD). Here we present the results of the analysis of K-ras mutations in the plasma of 165 samples. 17 patients presented K-ras mutations (10.3%), being codon 12 TGT in 16 patients and GTT in 1 case. Plasmatic mutations were found either in patients presenting squamous cell carcinoma (n = 3) and in patients with adenocarcinoma (14). Patients with K-ras mutations in plasma had a median time to progression (TTP) of 2.3 months (m) [0.5−4.6] while for wild type K-ras was 4.1 m [3.3−4.8], (p = 0.9). Overall Survival (OS) in K-ras mutated patients was 10.1 m [4.1−15.8] and in wild type K-ras was 9.0 m [6.9−11.1], (p = 0.6).
Conclusions: In advanced NSCLC, there were no significant differences between patients with K-ras mutations and those with wild-type genotype with respect to baseline characteristics, response rates, TTP, or OS. Data from the rest of the cohort will be presented at the meeting.

6593 POSTER

Nerve growth factor (NGF) levels in plasma in patients with advanced non-small cell lung cancer patients (NSCLC). Is it predictive of clinical outcome?

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Background: Platinum compounds and taxanes have severe side effects in a dose and time-dependent manner, especially neurotoxicity. NGF plays an important role in growth and differentiation of neuronal components. Our goal was to study NGF levels in plasma and correlate it with patient's clinico-pathologic characteristics.
Materials and Methods: The study was performed with 451 patients with advanced NSCLC, stages IIIB-IV and treated with cisplatin and docetaxel. Peripheral blood was collected before therapy. NGF were assessed by commercial ELISA (detection limit, 5 pg/ml). Plasma from 32 age and gender-matched controls was used.
Results: 91% of males, mean age 61 y [35−82]. 86 patients in ECOG PS 0−1 and 14 PS2. 71% in stage IV and 29% in IIIB. The histological subtypes were 38% squamous cell, 37% adenocarcinoma, 5% anaplasic large cell and 20% undifferentiated. 77.5% of the metastasis was out of the lung. Patients received a median of 6 cycles of chemotherapy [1−7]. 4% presented complete response (CR), 38% partial response (PR), 25% stable disease (SD) and 30% progressive disease (PD). Patient's median plasma levels of NGF did not differ significantly from controls: 44 pg/ml [6–176] vs 31 pg/ml [14–144] respectively. There were not differences according to histology, site of metastasis and ECOG; however we could observe significant differences with stage: 25 pg/ml [10−70] in stage IIIB vs 47 pg/ml [6–176] in stage IV (p = 0.008). We could not observe any differences in response to therapy: CR+PR patients presented median NGF of 35 pg/ml [6−92] vs 39 pg/ml [10–165] in the SD+PD group. Splitting the cohort according to NGF median we found two significantly different groups in terms of Overall Survival (OS): patients with NGF44 pg/ml (p = 0.03). In the multivariate analysis, NGF levels was not predictor for time to progression (TTP) and OS.
Conclusions: NGF plasma levels did not differ in patients and controls. In our cohort with advanced NSCLC we have not found any relationship between NGF levels with histology, response, site of metastasis and TTP. By contrast NGF levels are higher in those patients in stage IV and in those presenting poorer OS.

6594 POSTER

First-line bevacizumab in combination with chemotherapy in the treatment of patients with advanced or recurrent non-squamous non-small cell lung cancer (NSCLC): an open-label safety study (MO19390)

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Background: Bevacizumab, a humanised monoclonal antibody that inhibits VEGF, improves survival of patients with advanced or recurrent NSCLC when used first-line in combination with carboplatin/paclitaxel [Sandler et al. NEJM 2006]. MO19390 is an open-label, single arm, multicentre study investigating the safety profile of bevacizumab in combination with standard first-line chemotherapy.
Methods: Approximately 2000 patients will receive bevacizumab (15 mg/kg q3w) plus standard first-line chemotherapy (investigator choice) for a maximum of 6 cycles. Non-progressing patients will receive bevacizumab monotherapy until disease progression or unacceptable toxicity. The primary endpoint is the safety profile of bevacizumab when combined with first-line chemotherapy. Secondary endpoints include time to disease progression and overall survival. Eligible patients must have histologically or cytologically documented inoperable, locally advanced, metastatic or recurrent non-squamous NSCLC, ECOG PS 0–2 and adequate haematological, liver and renal function. Patients with a history of haemoptysis, evidence of tumour invading major blood vessels or evidence of CNS metastases are excluded. During treatment, the incidence of all serious and non-serious adverse events will be monitored, irrespective of their association with bevacizumab. Information about adverse events of special interest will also be reported.
Results: As of March 2007, 306 patients have been enrolled. Safety data are available for 202 patients; 62.4% are male and the median age is 59 years. Other patient characteristics (%) include: non-smoker/ex- or current-smoker 69/31 (no data <1); ECOG PS 0/1/2 39.8/53.7/6.5 (no data <1); chemotherapy backbone: cisplatin–gemcitabine/carboplatin–paclitaxel / carboplatin–gemcitabine / cisplatin–paclitaxel / monotherapy / non-platinum doublets/other 30.2/23.8/12.9/5.9/3.5/1.5/22.2. To date, a total of 87 serious adverse events (SAEs) have been reported, 18 of which are considered by the investigator to be associated with the study drug. SAEs of special interest reported to date are 4 thromboembolic events, 1 congestive heart failure and 3 bleeding events (2 epistaxis and 1 other haemorrhage). No haemoptysis SAEs have been reported to date.
Conclusions: The large population size will provide valuable information on the safety profile of bevacizumab and will allow investigation of non-frequent adverse events. Updated safety data will be discussed.