73%, squamous histology 48%, WHO performance status 0 55%, stage I 61%, stage II 32% and stage III 7%. In the CT-S group 75% patients received all 3 prescribed cycles of chemotherapy, 13% received 2 cycles, 7% 1 cycle and 4% no chemotherapy. Pre-chemotherapy the proportions of patients reported as having cough, breathlessness, haemoptysis, and chest pain were 62%, 46%, 21%, and 20% and post-chemotherapy the proportions were 39%, 33%, 2%, and 9% respectively. During chemotherapy the following proportions of patients were reported as experiencing moderate/severe symptoms: 29% lethargy, 28% nausea, 17% alopecia, 12% anorexia, 11% vomiting, 11% sore mouth and 6% ototoxicity. Three patients died within 30 days of a cycle of chemotherapy (2 myocardial infarctions, 1 lung cancer). Post-chemotherapy and pre-surgery 47% patients were reported as having responded (3% CR, 44% PR), 27% patients had stable disease, only 2% showed progressive disease, and 23% were not assessable. In the S group the median time from randomisation to surgery was 16 days, compared to 84 days in the CT-S group (medians of 7 days from randomisation to start of chemotherapy, 63 days on chemotherapy, and 14 days from the end of chemotherapy to surgery). Disease stage based on clinical TNM reported at randomisation and pathological TNM reported at surgery were compared, for 175 S and 172 CT-S patients with data at both timepoints. In the S group 19% were reported as having a lower (better) pathological stage, 45% the same, and 36% a worse stage. In the CT-S group the respective proportions were 31%, 41% and 28%. The extent of surgery was similar in the 2 treatment groups: lobectomy 50% S, 53% CT-S, pneumonectomy 29% S, 27% CT-S, other resections 9% S, 8% CT-S, thoracotomy with no resection 4% S, 3% CT-S, and no surgery 7% S, 10% CT-S.
Conclusions: In this trial, giving 3 cycles of cisplatin-based chemotherapy appeared to be feasible and generally well tolerated and few patients progressed on chemotherapy.

1122 ORAL

Paclitaxel poliglumex vs. gemcitabine or vinorelbine for the treatment of performance status (PS) 2 patients with chemotherapy-naïve advanced non-small cell lung cancer (NSCLC): the STELLAR 4 phase III study

M. O'Brien[1], F. Oldham[2]. [1]*Royal Marsden Hospital, London, United Kingdom;* [2]*CTI, Seattle, USA*

Background: Platinum-based chemotherapy is standard of care for patients with advanced NSCLC; however, this treatment is usually avoided in patients with poor PS due to the associated toxicities that can exacerbate pre-existing co-morbidities. These patients are usually treated with single agents and no standard treatment has been established. Paclitaxel poliglumex (PPX; XYOTAX™) is a macromolecular drug conjugate linking paclitaxel with a biodegradable polymer, poly-L-glutamic acid. Phase I/II studies indicated that PPX is active and generally well-tolerated in high-risk patients (PS2 or >70 years). This study compares PPX vs. gemcitabine or vinorelbine in chemotherapy-naïve PS2 patients with advanced NSCLC.
Patients and methods: This randomized, open-label, multinational, phase III study included chemo-naïve PS2 pts with locally-advanced or metastatic NSCLC not amenable to combined modality therapy with curative intent or recurrent disease previously treated with radiation and/or surgery. Pts were randomized equally to either: (A) PPX 175 mg/m^2 Q3W (210 mg/m^2 before Amendment 3); or (B) gemcitabine 1000 mg/m^2 (days 1, 8, 15 Q4W) or vinorelbine 30 mg/m^2 (days 1, 8, 15 Q3W). Stratifications included gender, geographic location, disease stage, history of brain metastases. Treatment continued until completion of 6 cycles, disease progression or intolerable toxicity. The primary endpoint was overall survival (OS). Secondary endpoints included RR, TTP, toxicity, and QOL.
Results: A total of 477 pts enrolled; median age was 63 (range: 30–90), 72% were male, and 68% had stage IV disease. Treatment with PPX resulted in a median survival of 7.3 months and a 1-year and 2-year survival of 26% and 15%, respectively. The control arm showed a median survival of 6.6 months, and 1-year and 2-year survival of 13% and 10%, respectively. The difference in survival was not statistically significant. When PPX was compared to gemcitabine, the survivals were comparable; PPX compared to vinorelbine showed a significant improvement in survival, gemcitabine also showed a survival benefit over vinorelbine ($p < 0.02$ for both). More pts ($p = 0.003$) completed full 6 courses of therapy on the PPX arm compared to the control arm. In the PPX arm, there were fewer cardiac toxicities ($p = 0.013$), gastrointestinal side effects ($p = 0.004$), nausea ($p = 0.041$), and vomiting ($p = 0.013$). PPX pts also had a significant reduction in severe hematologic toxicities including anemia ($p < 0.001$), neutropenia ($p = 0.006$), and thrombocytopenia ($p = 0.003$). Hair loss was uncommon on both arms. Grade 3/4 neuropathy was observed more frequently on the PPX arm (4% vs. 0%).
Conclusions: Compared to the current single-agent standards in NSCLC, gemcitabine and vinorelbine, PPX is less toxic, and provides a more convenient treatment schedule. PPX has a comparable efficacy compared to gemcitabine and a survival benefit compared to vinorelbine.

1123 ORAL

Panitumumab, a fully human antibody, combined with paclitaxel and carboplatin versus paclitaxel and carboplatin alone for first line advanced non-small cell lung cancer (NSCLC): a primary analysis

J. Crawford[1], P. Swanson[2], D. Prager[3], P. Schwarzenberger[4], A. Sandler[5], J. Schiller[6], D. Johnson[5], L. Navale[7], S. Moss[7], S. Jerian[7]. [1]*Duke University Medical Center, Durham, NC, USA;* [2]*Hematology Oncology Associates, Port S Lucie, FL, USA;* [3]*UCLA Medical Center, Los Angeles, CA, USA;* [4]*Louisiana State University Health Science Center, New Orleans, LA, USA;* [5]*Vanderbilt-Ingram Cancer Center, Nashville, TN, USA;* [6]*University of Wisconsin School of Medicine, Madison, WI, USA;* [7]*Amgen Inc., Thousand Oaks, CA, USA*

Background: Panitumumab is a fully human monoclonal antibody directed against the epidermal growth factor receptor (EGFr). In part 1 of this 2-part phase 2 trial in patients (pts) with advanced NSCLC, panitumumab could be safely combined with standard paclitaxel (P; 200 mg/m^2) and carboplatin (C; 6 mg/min/mL) (Crawford, ASCO 2004).
Methods: In Part 2, pts (stage IIIB or IV NSCLC, EGFr expression $\geqslant$1+ in 10% of tumor cells, ECOG <2) were randomized 2:1 to receive panitumumab 2.5 mg/kg QW plus PC Q3W (Arm 1) or PC alone Q3W (Arm 2). PC was continued until PD or up to a maximum of 6 cycles, panitumumab was continued until PD or intolerability. Tumor response (RECIST) was evaluated Q6W. The primary study objective was to compre time to PD (TTP) with panitumumab + PC vs PC alone; secondary objectives were to compare additional measures of efficacy and safety. The primary analysis was performed when 113 PD events occurred and had 65% power at the $p = 0.10$ level to detect a 50% improvement in TTP.
Results: of 175 pts enrolled, 166 treated pts (112 in Arm 1; 54 in Arm 2) were included in this analysis. Baseline demographics and disease characteristics were similar between arms. The study included 94 men and 72 women (mean [SD] age of 61.5 [10.4] yrs, ECOG of 0 [n = 52] or 1 [n = 112]). Two percent were Asian; 10% never smoked. Most (62%) had adenocarcinoma; 21% had squamous cell carcinoma. Median TTP (95% CI) was 4.2 (3.1, 5.4) mos for Arm 1 and 5.3 (3.6, 5.6) mos for Arm 2 (log-rank $p = 0.55$). Objective response rates were 15.2% for Arm 1 and 11.1% for Arm 2 ($p = 0.63$). Median (95% CI) survival times were 8.5 (7.1, 12.0) mos for Arm 1 and 8.0 (6.7, 11.8) mos for Arm 2 ($p = 0.81$). Adverse events (Arm 1 vs Arm 2) more frequently seen in the panitumumab arm included rash (59% vs 17%), dry skin (20% vs 4%) dermatitis acneiform (21% vs 0%), pruritus (18% vs 6%), diarrhea (48% vs 26%), vomiting (44% vs 31%), stomatitis (33% vs 9%), dizziness (21% vs 11%). Neutropenia was not significantly different (24% vs 28%). No panitumumab-induced human anti-human antibodies were detected in 110 pts tested post baseline.
Conclusions: Results from this phase 2 study indicate that panitumumab + PC is well tolerated with similar efficacy as PC alone in an unselected NSCLC population. Retrospective assessment of tumors for biomarkers may define subpopulations more likely to benefit from panitumumab. Clinical studies of panitumumab in NSCLC are ongoing with other novel combinations of targeted agents.

1124 ORAL

Results of a randomized, double-blind Phase II trial of ZD6474 versus gefitinib in patients with NSCLC

M. Ranson[1], D. Bodkin[2], R. Govindan[3], B. Sleckman[4], N. Rizvi[5], A. Capo[6], P. Germonpré[7], I. Dimery[8], A. Webster[9], R. Natale[10]. [1]*University of Manchester, Department of Medical Oncology, Manchester, United Kingdom;* [2]*Sharp Memorial Hospital, San Diego, USA;* [3]*Washington University Medical School, St Louis, USA;* [4]*St John's Mercy Medical Center, St Louis, USA;* [5]*Memorial Sloan-Kettering Cancer Center, New York, USA;* [6]*Centro Oncológico de Integración Regional (COIR), Mendoza, Argentina;* [7]*University Hospital of Antwerp, Antwerp, Belgium;* [8]*AstraZeneca, Wilmington, USA;* [9]*AstraZeneca, Macclesfield, United Kingdom;* [10]*Cedars-Sinai Outpatient Cancer Center, Los Angeles, USA*

Background: ZD6474 is an orally available inhibitor of two key pathways in tumour growth: vascular endothelial growth factor receptor (VEGFR)-dependent tumour angiogenesis and epidermal growth factor receptor (EGFR)-dependent tumour cell proliferation and survival. In this ongoing two-part Phase II study, the efficacy and safety of ZD6474 is compared with that of gefitinib (IRESSA), an EGFR tyrosine kinase inhibitor approved for the treatment of advanced non-small-cell lung cancer (NSCLC).
Methods: Patients with locally advanced or metastatic (IIIB/IV) NSCLC, after failure of first-line and/or second-line platinum-based chemotherapy