inhibit IGF-1R without inhibiting closely related receptors such as the insulin receptor. AXL1717 is presently studied in phase II setting.
**Materials and Methods:** Advanced-stage cancer patients with progressive solid tumours and no remaining treatment options were included in the Phase I/II clinical trial. The primary objective of the study was to identify and confirm a recommended Phase II dose (RP2D). AXL1717 has been administered every third week as a single-day BID oral treatment in consecutively increasing doses as the only treatment with anti-tumour efficacy. Doses have been increased both within and between patients. In the recently completed phase I multidose part of the study, consecutive cohorts of advanced-stage cancer patients were given 7−28 days of increasing BID doses of AXL1717. A total of 35 patients (median age 63) were included in phase I and they were given approximately 1192 doses of AXL1717. A total of 178 of full-day pharmacokinetic assessments were performed. An additional 7 patients have been treated as confirmation of RP2D.
**Results:** The single-day dosing part of the study was successfully concluded. The results showed that AXL1717 could be administered as a single-day BID treatment in very high doses with excellent tolerability. Dose-limiting toxicity was not been reported in single day dosing. 390 mg BID were identified as recommended phase II dose (RP2D) following 28 days of dosing. Reversible, dose-related and probably mechanism-driven neutropenia was identified as the only dose-limiting adverse event in multidosing. No neutropenias have been reported within the study in connection to 28 days dosing of RP2D. 12 out of 42 patients had non-small cell lung cancer (NSCLC) and were treated with single agent AXL1717 longer than 7 days in the study resulting in a median survival of 45 weeks and of the 7 patients with RECIST confirmed progression, the median time to progression was 37 weeks as of 2011−04−05.
**Conclusion:** Phase I/II study of AXL1717 has shown that the agent can be administrated safely orally to advanced-stage cancer patients resulting in good bioavailability and tolerability. Even though the study was not designed to assess anti-tumour effects, encouraging signs suggesting clinical activity were seen in patients with NSCLC.

**9014** POSTER DISCUSSION

**Randomized Phase II Trial of NGR-hTNF and Chemotherapy in Chemo-naive Patients With Non-small Cell Lung Cancer (NSCLC) − Preliminary Results**

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**Background:** NGR-hTNF is a vascular targeting agent obtained by fusing the NGR peptide, that binds to CD13 overexpressed on tumour blood vessels, to the tumour necrosis factor (hTNF). By selective damaging tumour vasculature and decreasing interstitial pressure, NGR-hTNF improves the intratumoral penetration of cytotoxic agents.
**Methods:** Chemo-naive, stage IIIb-IV NSCLC patients, including patients with brain metastasis, stratified by histology (nonsquamous vs squamous) and PS (0 vs 1), were randomly assigned to receive cisplatin 80 mg/m$^2$ day 1 plus either gemcitabine 1,250 mg/m$^2$ days 1, 8 for squamous histology or pemetrexed 500 mg/m$^2$ day 1 for nonsquamous histology for up to 6 cycles plus NGR-hTNF 0.8 μg/m$^2$ day 1 until progression (arm A) or chemotherapy alone (arm B). Primary study objective was progression-free survival (PFS). Assuming a 15% absolute increase in PFS rate ($\beta = 20\%$ and 1-sided $\alpha = 10\%$), a sample size of 102 patients was calculated.
**Results:** Of the 98 patients recruited so far, 64 patients (32 in each arm) were presently assessed for safety and preliminary activity. Baseline characteristics were (arm A/B): median age: 63/62 years; PS of 1: 11/9; squamous histology: 8/8. A total of 180 cycles (range 1−17) were administered in arm A and 133 cycles (range 1−6) in arm B. Treatment-related grade 3−4 toxicities for arm A vs B were 23% vs 34% for all adverse events and included: neutropenia 13% vs 15%; thrombocytopenia 3% vs 6%; fatigue 3% vs 12%; renal or respiratory failures 0% vs 6%; thromboembolism 6% vs 0%. Grade 1−2 hypertension was 3% in arm A and 11% in arm B. No grade 3 or 4 toxicities related to NGR-hTNF were observed, while 31% of patients experienced NGR-hTNF-infusion related grade 1 transient chills. Neither pulmonary hemorrhage nor bleeding were reported in both arms. Median follow-up time was 8.6 months in arm A and 5.5 in arm B. In patients with nonsquamous histology (n = 48), PFS rates at eight months were 38% in arm A and 18% in arm B. In nonsquamous patients who achieved disease control (partial response plus stable disease; n = 36), PFS rates at eight months were 51% in arm A and 21% in arm B. Among patients with squamous histology (n = 16), 2 partial responses, 5 stable diseases and 1 progressive disease in arm A and 1 partial response, 4 stable diseases and 3 progressive diseases in arm B were observed.
**Conclusion:** NGR-hTNF and chemotherapy can be safely combined in NSCLC, regardless of histology, showing promising antitumour activity.

**9015** POSTER DISCUSSION

**EGFR Mutation Status in NSCLC Patients Stage IIIB/IV in Germany − Initial Results From a German Registry**

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**Background:** Lung cancer is the leading cause of cancer deaths worldwide. In Germany, each year approximately 47,000 patients are newly diagnosed with lung cancer and 41,000 die of the disease. Mutations in the EGFR gene are known to predict for sensitivity to EGFR tyrosine kinase inhibitors (TKI) in patients with advanced non-small-cell lung cancer (NSCLC). Clinico-pathological characteristics associated with a higher prevalence of EGFR mutations are adenocarcinoma histology, Asian origin, non-smoking history, and female gender; however, most of this information comes from Asian studies. REASON was set up to investigate the prevalence of EGFR mutations in German patients with advanced NSCLC and the association between mutations and clinico-pathological parameters, thus generating data from a predominantly Caucasian population.
**Methods:** REASON is an AstraZeneca sponsored registry (ClinTrials ID: NCT00997230). Patients with stage IIIB/IV NSCLC for whom EGFR mutation testing was planned were enrolled at approximately 150 participating sites The primary objective was to collect incidence data on the EGFR mutation status in the German patient population and correlate the EGFR mutation status with patient characteristics. Secondary objectives include clinical outcome of EGFR mutation positive patients, clinical management and pharmaco-economic data associated with diagnosis and first-line treatment options of EGFR mutation positive patients.
**Results:** To date, information covering the period up to the first-line treatment is available on 3155 patients. The majority of patients (89%) were newly diagnosed with NSCLC and presented with symptomatic (89%) stage IV disease (86%). Baseline data is displayed in Table 1.

Table 1. Baseline data

| | | n | % |
|---|---|---|---|
| Gender | Male | 1967 | 62.3 |
| | Female | 1188 | 37.7 |
| Smoking status | Ever-smoker | 2571 | 81.5 |
| | Non-smoker | 584 | 18.5 |
| Histology | Adenocarcinoma | 2146 | 68.0 |
| | Squamous cell carcinoma | 616 | 19.5 |
| | Others | 393 | 12.4 |
| EGFR mutation all histologies | Negative | 2716 | 86.1 |
| | Positive | 310 | 9.8 |
| | Positive, but not TKI sensitive | 14 | 0.4 |
| | Not evaluable for mutation | 115 | 3.6 |
| | Positive | 310 | 9.8 |
| | Positive, but not TKI sensitive | 14 | 0.4 |
| | Not evaluable for mutation | 115 | 3.6 |
| EGFR mutation adenocarcinoma | Positive | 274 | 12.8 |
| Total number | | 3155 | 100 |

The study is currently ongoing and follow up data will be available soon.
**Conclusion:** REASON aims to provide the largest data base yet on baseline epide-mio-logical and clinico-pathological characteristics of patients with newly diagnosed stage IIIB/IV NSCLC in a predominantly Caucasian population. Additionally, information on treatment decisions for patients with stage IIIB/IV EGFR mutation positive NSCLC, clinical outcomes and their pharmaco-economic impact, will help to build an enhanced knowledge base for improved patient care.