There was no difference between patients with adenocarcinoma and non-adenocarcinoma histology. In 12%, the response lasted for at least a year. 79% of these patients were never-smokers with adenocarcinoma. None of the longterm responders was a current smoker, and 93% had adenocarcinoma histology.
**Survival:** Never-smokers had a median progression free survival (PFS) and overall survival (OS) of 7.5 and 13 months, respectively. Ex-smokers had a PFS and OS of 3.5 and 7.5 months, and current smokers had a PFS and OS of 2 and 5.5 months, respectively. Gender or histology had no significant effect on PFS or OS. Treatment line did not influence PFS or OS, in particular patients treated with erlotinib 1st line experienced a similar PFS and OS compared with chemotherapeutically pretreated patients. The patient on haemodialysis tolerated erlotinib well and had SD for 11 months.
**Conclusions:** The above clinical criteria may be valid for prediction of partial responses and of longterm response to erlotinib. However, except for smoking, the clinical selection criteria do not predict PFS and OS. This may be due to the significant survival advantage we found for patients with SD compared with patients progressing radiologically. Furthermore, our data indicate that erlotinib may be effective as a first-line monochemotherapy in selected patients. Our retrospective data need to be confirmed with larger patient numbers (e. g. from registries) in order to define the clinically and economically appropriate method of patient selection.

**9152** POSTER

**A population pharmacokinetic analysis for BIBF 1120, an angiokinase inhibitor, in patients with advanced non-small cell lung cancer**

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**Background:** BIBF 1120 (VargatefTM*) is a potent angiokinase inhibitor, targeting vascular endothelial, platelet-derived and fibroblast growth factor receptor tyrosine kinases. The objective of the population pharmacokinetic (PK) analysis was to describe the PK of BIBF 1120 in patients with advanced/metastatic non-small cell lung cancer (NSCLC) and to explore the impact of patient factors on the PK parameters of BIBF 1120 using data from a double-blind, randomized Phase II study.
**Methods:** In this double-blind multicenter trial, 73 patients with an Eastern Cooperative Oncology Group (ECOG) score of 0−2 with locally advanced or metastatic (stage IIIB/IV) relapsed NSCLC after failure of first- or second-line chemotherapy were randomly assigned to continuous twice-daily treatment with 150 mg or 250 mg of BIBF 1120 until disease progression or limiting toxicity. Trough samples for PK analysis were taken at various visits. Sparse absorption profiles were determined at two visits. PK data from 71 patients (736 plasma samples) were available. Demographics, laboratory values and cancer-specific covariates including baseline ECOG score were tested for their effect on PK parameters. The analysis was performed using NONMEM (Non-linear Mixed Effects Modeling).
**Results:** A one-compartment model with first-order absorption (ka) and elimination rate described the PK data adequately. The slightly delayed absorption was accounted for by a lag time of 20 minutes. Clearance (CL/F), volume of distribution (V/F) and ka were 697 L/h, 8170 L and 1.31$h^{-1}$, respectively. Interindividual and interoccasion variability estimates for CL/F and V/F were moderate to high. None of the covariates tested showed a clinically relevant effect on the PK parameters of BIBF 1120 and thus none were included in the model. A trend towards lower CL/F values with increased liver enzymes was observed but its effect was small.
**Conclusion:** BIBF 1120 plasma concentrations in NSCLC patients were described by a one-compartment model. No clinically relevant covariates influencing the PK of BIBF 1120 were detected. An international Phase III trial program investigating BIBF 1120 in NSCLC, LUME-Lung, is now recruiting patients.
*Trade name not FDA approved

**9153** POSTER

**Safety and efficacy of sunitinib in patients with non-small cell lung cancer and irradiated brain metastases**

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**Background:** The prognosis of patients (pts) with NSCLC and brain metastases (BrMs) is poor. Preclinical data suggest that VEGF signaling is essential for the growth of BrMs, thus antiangiogenic agents may have activity in this population. Sunitinib (SU) is an oral, multitargeted inhibitor of VEGFRs, PDGFRs, KIT, FLT3, CSF-1R, and RET that has single-agent antitumor activity in refractory NSCLC. This phase II study [NCT00372775: Pfizer] assessed the safety and efficacy of SU in NSCLC pts with previously irradiated BrMs.
**Materials and Methods:** NSCLC pts $\geqslant$18 years of age who had received whole brain radiation therapy (WBRT) for BrMs and $\leqslant$2 prior systemic therapies were eligible to receive SU at a starting dose of 37.5 mg with continuous daily dosing (CDD) in 4-week (wk) cycles. Antitumor efficacy was based on overall (RECIST) and intracranial bidimensional (WHO criteria) tumor assessments. Intracranial disease was assessed by MRI. Safety was assessed by monitoring AEs and focused on neurologic status. Health-related quality of life was assessed using FACT/NCCN Lung Symptom Index (FLSI) and Brain Symptom Index (FBrSI). Study termination was to occur if 3 cases of intracranial hemorrhage (ICH) associated with neurologic deficit were identified.
**Results:** Fifty-nine pts received SU for a median of 2 cycles (range: 1, 10). The median age of pts was 60 yrs (range: 35, 77), most were male (n = 36, 61%) and had good performance status (ECOG 0/1, n = 56; ECOG 2, n = 1). Most pts had adenocarcinoma (n = 37, 62.7%) or squamous cell carcinoma (n = 11, 18.6%). The most frequent AEs of any grade (G) were fatigue (n = 17, 29%), anorexia (n = 14, 24%), and nausea (n = 13, 22%). Neurologic AEs occurred in 5 pts (9%) and included increased intracranial pressure, visual hallucination, and gait disturbance (each n = 1 and G2). One pt had convulsion and peripheral motor neuropathy (both G3) and one pt had G4 mental impairment. ICH was not reported. Stable disease was reported in 12 (23%) of 53 pts via RECIST and in 10 (26%) of 39 pts with measurable BrMs via WHO. Median PFS was 9.9 wks (95% CI: 7.0, 13.4). Median OS was 19.4 wks (95% CI: 11.4, 38.6). Mean change from baseline in FLSI and FBrSI scores did not differ significantly at any time point.
**Conclusions:** Oral SU 37.5 mg on a CDD schedule had a manageable safety profile, and no cases of ICH were reported. Although not the focus of this study, preliminary data suggest SU may have antitumor activity in pts with NSCLC; further studies are warranted.

**9154** POSTER

**Clinical outcomes in patients with EGFR mutations: pooled analysis of NSCLC patients treated with either an EGFR TKI or chemotherapy**

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**Background:** NSCLC with EGFR tyrosine-kinase (TK) mutations appears to be highly sensitive to EGFR TK inhibitors (TKIs). As mutations occur in only 10−30% of patients (pts) with advanced NSCLC (which is variable according to ethnicity), it is difficult to conduct large-scale investigations in this subgroup to identify any associations between *EGFR* mutations and therapeutic outcomes. We therefore aimed to summarise published data through a pooled analysis of high-level study results.
**Materials and Methods:** Data were collated from published phase II/III studies and relevant internal, but not yet published, sources that reported PFS outcomes among pts with *EGFR* mutations, treated with either chemotherapy or EGFR TKI monotherapy (erlotinib or gefitinib). Most papers reported median PFS (time), or % PFS at a fixed time, so these data were used as the basis for our analysis. To facilitate a weighted, pooled