Conclusion: Our MA suggests that SUV max measured on primary tumour is of prognostic value for survival in NSCLC; the next step is to confirm these results in a MA based on individual patients data allowing to perform multivariate analysis taking into account well known prognostic factors.

6525 POSTER

Phase II study investigating the efficacy and safety of continuous daily sunitinib dosing in previously treated advanced non-small cell lung cancer (NSCLC)

R. Govindan[1], J.R. Brahmer[2], S. Novello[3], R. Rosell[4], C.P. Belani[5], J.N. Atkins[6], H.H. Gillenwater[7], L. Tye[8], R.C. Chao[8], M.A. Socinski[9].
[1]Washington University School of Medicine, Division of Oncology, St Louis, USA; [2]Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins, Cockeysville, USA; [3]University of Turin, San Luigi Hospital Regione Gonzole, Orbassano, Italy; [4]Catalan Institute of Oncology, Medical Oncology Service, Barcelona, Spain; [5]UPMC Cancer Pavilion, University of Pittsburgh, Pittsburgh, USA; [6]Southeastern Medical Oncology Center, Cox Blvd, Goldsboro, USA; [7]University of Virginia Health Services, Clinical Internal Medicine, Charlottesville, USA; [8]Pfizer Inc, Global Research and Development, La Jolla, USA; [9]University of North Carolina, Lineberger Comprehensive Cancer Center, Chapel Hill, USA

Background: Overexpression of the vascular endothelial growth factor receptor (VEGFR) and VEGF expression in NSCLC are associated with increased tumor angiogenesis and reduced survival in NSCLC patients (pts). Sunitinib malate (SUTENT®; SU) is an oral, multitargeted tyrosine kinase inhibitor of VEGFRs, PDGFRs, KIT, RET and FLT3. In the first pt cohort of this study, SU on a 4/2 schedule (4 wks on, 2 wks off treatment) demonstrated a partial response (PR) rate of 11% in pts with recurrent advanced NSCLC (Socinski, ESMO 2006). In the second pt cohort of this phase II, multicenter study, a continuous dosing (CD) schedule of SU was evaluated for efficacy and safety.
Patients and Methods: Eligible pts had stage IIIB/IV NSCLC previously treated with $\leqslant$2 chemotherapy regimens, ECOG PS $\leqslant$1 and adequate organ function. Pts received SU 37.5 mg/d continuously in 4-wk cycles. The primary endpoint was RECIST-defined objective response rate. Secondary endpoints included duration of response, progression-free survival (PFS), overall survival (OS) and safety.
Results: 47 pts were treated with SU 37.5 mg/d on the CD schedule. Baseline characteristics included: median age 60 yrs (range 37–81); male 57%; ECOG PS 0/1/2 49%/49%/2%; adenocarcinoma 53%, squamous cell carcinoma 15%, other 32%. A median of 3 (range 1–12) SU cycles were initiated. SU was generally well tolerated. Frequently reported adverse events (AEs) included fatigue/asthenia, pain/myalgia, nausea/vomiting, dyspnea, diarrhea and stomatitis/mucosal inflammation, and most were Grade (Gr) 1/2 in severity. Gr $\geqslant$3 AEs included fatigue/asthenia (17%), dyspnea (9%), hypertension (6%), hypoxia (6%), and pleural effusion (6%). Treatment-related serious AEs included (n = 1, each): hypoxic respiratory failure (Gr 3), congestive heart failure (Gr 4), worsening of toxic shock syndrome (Gr 5) and abdominal pain (Gr 2). 1 pt (2%) achieved a confirmed PR. 8 pts (17%) had stable disease for >3 months, of whom 4 had SD for >6 months. Median PFS was 12.3 wks (95% CI: 8.9–16.0). Median OS has not yet been reached.
Conclusions: SU 37.5 mg/d on a CD schedule has an acceptable safety profile in previously treated NSCLC pts and is associated with promising antitumor activity. Further study of CD SU in combination with other treatments for NSCLC is warranted.

6526 POSTER

Review of pulmonary haemorrhage (PH) in non-small cell lung cancer (NSCLC) subjects receiving bevacizumab and cisplatin plus gemcitabine on protocol BO17704

V. Hirsh[1], J. Bennouna[2], H. Kuo[3], B. Szima[4], M. Gottfried[5], A. Kunitsyn[6], J. Trigo[7], G.C. Chang[8], J. Cosaert[9], C. Manegold[10]. *[1]MUCH, Department of Oncology, Montreal, Canada; [2]Centre Rene Gauducheau, Medical Oncology, Saint Herblain, France; [3]Chang Gung Memorial Hospital, Department of Thorax II, Taoyuan, Taiwan; [4]Markusovszky Korhaz, Pulmonologiai Osztaly, Szombathely, Hungary; [5]Sapir Medical Center Meir Hospital, The Oncology Department, Kefar Saba, Israel; [6]Moscow Regional Oncology Hospital, Department of Thoracic Surgery, Moscow Region, Russian Federation; [7]Hospital Clinico Universitario Virgen Victoria, Servicio de Oncologia, Malaga, Spain; [8]Taichung Veterans General Hospital, Chest Department, Taichung, Taiwan; [9]F. Hoffmann-La Roche, Clinical Science, Basil, Switzerland; [10]Klinikum Mannheim gGmbH Universitatsklinikum, Chirurgische Klinik, Mannheim, Germany*

Background: Bevacizumab, (Avastin®, B), in combination with cisplatin/gemcitabine, prolongs progression-free survival (PFS) in the first-line treatment of advanced NSCLC. Pulmonary haemorrhage (PH) was reported in a phase II study of B plus chemotherapy in NSCLC, leading to the exclusion of predominantly squamous cell carcinoma in subsequent NSCLC trials.
Methods: Subjects were treated on protocol BO17704, a randomised, double-blind phase III study of cisplatin/gemcitabine (CG) +/− B (7.5 or 15 mg/kg) for up to 6 cycles followed by B until disease progression, for first-line treatment of advanced/recurrent non-squamous NSCLC. Patients with prior grade $\geqslant$2 haemoptysis, or with lesions abutting or invading major blood vessels, were excluded. PH cases were identified by reported Adverse Event (AE) MedDRA Preferred Terms (PT). The following PTs associated with PH were found in the BO17704 database: haemoptysis, respiratory tract haemorrhage, bronchial haemorrhage. In addition, a clinical review of all serious bleeding on BO17704 reported to the Roche Databases (RDB) was performed to identify possible additional cases of PH.
Results: Central lesions, exclusive of lymph nodes, were reported in 381/1043 (36.5%) of subjects overall.

Pulmonary haemorrhage grade 3–5 adverse events on BO17704 and ECOG 4599

	BO17704			E4599
	Placebo arm n = 327 n/%	7.5 mg/kg B arm n = 330 n/%	15 mg/kg B arm n = 329 n/%	15 mg/kg B arm n = 427 n/%
Grade 3–5 PH	2* (0.6)	5 (1.5)	3* (0.9)	10 (2.3)

Events in the table were as reported through the AE case report form (8 cases) or via clinical review of the RDB* (2 cases). There was 1 fatal event in the placebo arm and 1 fatal event in the 15 mg/kg B arm; 4 of 5 grade 3–5 events in the 7.5 mg/kg B arm were fatal; and all grade 3–5 events in the 15 mg/kg B arm were fatal at the time of clinical data cut-off. Of grade 3–5 PH events identified, 2 of 10 were associated with thrombocytopenia (grade 1 and 3). Grade 3–4 thrombocytopenia occurred at a rate of 23–27% across treatment arms.
Conclusions: The incidence of severe PH in BO17704 (1.2% across both B-containing arms) was lower than in E4599 (2.3%). Most PH events in BO17704 occurred in the 7.5 mg/kg B arm, although study treatment duration was slightly longer in the 7.5 mg/kg B arm (mean 4.94 cycles) than in the 15 mg/kg B arm (mean 4.63 cycles).

6527 POSTER

Intravenous administration of PLK-1 siRNA with atelocollagen as an in vivo drug delivery system (DDS) inhibits the growth of murine liver metastasis of lung cancer

E. Kawata[1], E. Ashihara[1], S. Kimura[1], J. Kuroda[2], T. Maekawa[1].
[1]Kyoto University Hospital, Department of Transfusion Medicine and Cell Therapy, Kyoto, Japan; [2]Kyoto Prefectural University of Medicine, Division of Hematology and Oncology Department of Medicine, Kyoto, Japan

Background and Purpose: Despite advances in medical oncology, about a million have died of lung cancer worldwide. The current treatments are insufficient, making a more effective novel therapy necessary. PLK-1 is a family of polo-like kinases (PLKs) and is crucial for the regulation of cell division. It has been reported to overexpress in many cancer types, and its elevated expression is positively correlated with malignancy and a poor prognosis for the patient. We investigated in vitro effects of PLK-1