day until disease progression or unacceptable toxicity. Dose reductions (50mg increments) were allowed as required. The NCI-CTC v3.0 was used to assess toxicities, including: incidence and grade of erlotinib-related rash; serious AEs (SAEs) and treatment-related SAEs; and AEs leading to treatment withdrawal. Other treatment-related AEs were reported if they were not included on a list of 15 pre-specified AEs in the study protocol (rash; pruritis; dry skin; diarrhea; nausea; vomiting; stomatitis; abdominal pain; fatigue; dyspnoea; cough; anorexia; infection; conjunctivitis; and keratoconjunctivitis sicca).

Results: 885 patients were included in the analysis at the data cut-off (20/11/06) from Taiwan (n=297), mainland China (n=248), Hong Kong (n=160), South Korea (n=146), Thailand (n=30), Indonesia (n=2) and Malaysia (n=2). The median age was 61 years (range 22-95). Patient characteristics included: male 55%, female 45%; stage IIB 20%, stage IV 79% (no data 1%); ECOG PS 0 15%, PS 1 67%, PS 2 14%, PS 3 4%; non-smoker 52%, ever-smoker 48% (no data <1%); adenocarcinoma 68%, squamous-cell carcinoma 19%, other 13%; erlotinib 1st line 11%, 2nd line 55%, 3rd line 33%, other <1%. Data on the occurrence of rash were available for 882 patients, 83% of whom experienced rash, mostly grade 1/2 (88% of those with rash). Adverse event (AE) safety data were available for 598 patients, 54% of whom experienced at least one AE. 19 patients (3%) had treatment-related SAEs, most commonly gastrointestinal (GI) disorders (1%), including abdominal pain (n=2), diarrhoea (n=5) and gastric ulcer haemorrhage (n=1). 17% of patients had at least one other treatment-related AE that was not pre-specified (3% had at least one grade 3/4 event); mucosal inflammation occurred in 3% of patients (<1% grade 3/4), but no other single event occurred in more than 2% of patients. Treatment-related interstitial lung disease (ILD; grade 2) was suspected in one patient, but this event was not reported as an SAE and did not lead to treatment withdrawal; the patient continued on erlotinib until disease progression. 18 patients (3%) had at least one treatment-related AE leading to withdrawal of erlotinib; the most common such events were rash (4 patients), diarrhoea (3 patients) and pneumonitis (3 patients). Among 589 patients with available data, 76 (13%) required dose reduction due to a treatment-related event, mainly rash (n=57). Efficacy data will be presented.

Conclusions: Safety data for the E/SE Asian patient population in TRUST support the safety profile of erlotinib seen in clinical trials. The incidence of ILD and ILD-like events is <1%, which is in-keeping with what has been seen with erlotinib universally. In the ‘real-life’ clinical setting, erlotinib is well tolerated, with full therapeutic doses administered to the majority of patients.

Introduction: Inhibition of angiogenesis has shown promise in a variety of solid tumours. In NSCLC, the addition of bevacizumab to platinum-based doublet chemotherapy has led to a modest improvement in survival in highly selected patients (pts). Antiangiogenic agents may be associated with cavitation of tumours, felt possibly due to ischemic necrosis; in the lung, this may lead to air-trapping and subsequent enlargement of the target lesion, which may lead to difficulties with assigning overall best response as well as date of progression. The NCIC CTG has conducted a number of studies of VEGFR inhibitors as single agent or in conjunction with standard chemotherapy regimens in a number of tumour types, including NSCLC.

Methods: Two phase I studies enrolled first line NSCLC patients to escalating doses of a VEGFR inhibitor in combination with either standard carboplatin/paclitaxel or cisplatin/gemcitabine regimens. The control arm of a large phase II/III study of the same regimen of carboplatin and paclitaxel with identical entry criteria was used as a historical control. In all trials, response was assessed by RECIST every second cycle, radiology reports were reviewed centrally confirming response, progression and evidence of cavitation, while an independent response review has been conducted for one phase I study, where possible for all patients with cavitation noted in radiology reports, and is ongoing for the second phase I study. Pts showing cavitation had, in addition, an ‘exploratory’ response assessment in which the longest diameter of the cavity was subtracted from the total size of the measured lesion.

Results: As expected, when independent radiology review was conducted using RECIST criteria, similar overall response rates were confirmed, although individual patients’ response may have changed. Significant cavitation of pulmonary lesions was seen in approximately 20% of patients treated with VEGFR inhibitors. The use of the ‘exploratory’ response assessment did not significantly increase the overall number of responses but did lead to an earlier designation of response and/or progression in 10% of patients.

Conclusions: The addition of VEGFR inhibitors to platinum-based chemotherapy leads to encouraging antitumour activity, sometimes with cavitation. The cavitation noted with the use of antiangiogenic agents may have implications for response assessment and trial endpoints that rely upon determination of time to disease progression.

PD3-2-8 Molecular Targeted Therapy: EGFR inhibitors, Thu, 12:30 - 14:15

Phase II Trial of Cetuximab (C225) in Combination with Monthly Carboplatin (Cb) and Weekly Paclitaxel (Pac) in Patients with Advanced NSCLC: Promising Early Results

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Background: C225 is a unique monoclonal antibody targeting epidermal growth factor receptor. Weekly C225 in combination with standard q 3 week PacCb yielded a median survival of nearly 11 months in a large phase II trial of SWOG (Kelly, ASCO 2006), and is currently being tested in combination with bevacizumab and PacCb. We mounted a phase II trial of this agent in combination with monthly Cb and weekly Pac, in an effort to capitalize on potential synergy between taxane and C225, and to mitigate taxane-induced neuropathy and myalgia/arthritis.
Materials and Methods: Enrollees received Cb AUC 6 day 1 in combination with Pac 100 mg/m² days 1, 8, and 15 every 4 weeks, and C225 at a loading dose of 400 mg/m² day 1, then 250 mg/m² weekly thereafter. C225 was continued as a single agent after 6 full cycles of therapy in patients without disease progression or limiting toxicity. Eligibility stipulated advanced NSCLC (Stage IV, “wet” and IIIB or recurrence after prior surgery/radiation); ECOG performance status 0-1; measurable tumor, and adequate physiologic indices.

Results: 53 patients were accrued at FCCC and its OPN partners. Amongst the first 32 patients enrolled, 53% were male; median age was 63 years (range 41-86), 47% were PS-0; 6% had received prior RT. Overall response rate was 55% (16/29) including one CR; 3 patients were not evaluable for response: one was found to have brain mets during week 1 and two experienced immediate HSRs. With median potential F/U of ≥ 1 yr, median event-free survival was 5.3 months (n=30) and median survival 11.1 months (n=32). 25% (8/32) received 6 cycles of chemotherapy with 19% (6/32) going onto maintenance C225. Chief grade ≥ 3 attributable adverse events included neutropenia (28%); anemia (6%); HSR (9%) acniform rash (28%) and hypomagnesemia (19%). Overall inc. (any grade) of rash was 84% and hypomagnesemia 47%. Other significant toxicities included grade 1-2 paronychia, with nail lysis and digital fissures (19%), which tended to be cumulative.

Conclusions: C225 in combination with monthly Cb and weekly Pac is highly active in advanced NSCLC. Response and survival data to date are promising. Toxicities match those seen with this PacCb alone, but also include persistent hypomagnesemia, and cumulative paronychia and nail changes, the latter troublesome, if not treatment-limiting. We will report the full results in 9/07.

PD3-3-2 Molecular Targeted Therapy: Beyond EGFR Inhibitors, Thu, 12:30 - 14:15
A randomized double-blind Phase IIa dose-finding study of vandetanib in Japanese patients with NSCLC

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Methods: Eligible patients had locally advanced or metastatic (stage IIIB/IV) or recurrent NSCLC, after failure of one or two platinum-based chemotherapy regimens. Patients were randomized to receive once-daily oral vandetanib 100, 200 or 300 mg (1:1:1), with stratification according to sex, histology (adenocarcinoma vs other histology) and smoking status (smoker vs non-smoker). Tumor response was assessed by RECIST every 4 weeks for the first 24 weeks of treatment and then every 8 weeks until progressive disease (PD) or any other withdrawal criteria was met. The primary objective was to determine the objective response rate (ORR) for each vandetanib dose. Secondary assessments included disease control rate (DCR), safety and tolerability. Exploratory assessments included analysis of tumor samples for amplification of EGFR gene copy number (fluorescence in situ hybridization [FISH]) and somatic mutations of the EGFR gene, and measurement of plasma VEGF levels.

Results: Fifty-three patients (34 males/19 females, median age 60 years, range 30–78) received vandetanib (100 mg, n=17; 200 mg, n=18; 300 mg, n=18). The overall ORR was 13.2% (7/53; all partial responses [PRs]). The ORR in the vandetanib 100, 200 and 300 mg/day arms were 17.6% (3/17), 5.6% (1/18) and 16.7% (3/18), respectively. There...