results of an ongoing phase Ib/II study in ten centers to evaluate the safety and efficacy of the combination of paclitaxel (T), carboplatin (C) and CP-751,871 (I) in advanced NSCLC.
Methods: Phase Ib was an open-label dose-escalation study of T (200 mg/m^2), C (AUC of 6) and CP-751,871 (0.05−10 mg/kg) every 3 weeks for up to 6 cycles in patients with advanced solid malignancies; pts with response or stable disease could receive extended CP-751,871 therapy. The ongoing phase II is an open label, randomized (2:1), non-comparative study of TCI and of TC alone. Only treatment-naive NSCLC pts (stage IIIB or IV) are eligible in phase II. The statistical hypotheses are 28% (null) versus 40% (response of interest).
Results: Following informed consent and screening, 7 cohorts with a total of 30 pts, including 23 NSCLC pts, were enrolled in phase 1b. No dose limiting toxicities were identified and the recommended phase 2 dose cohort of 10 mg/kg was extended to 12 pts. One case of grade 3 GGT elevation attributed to CP-751,871 was reported. An interim analysis for futility has been conducted at 73 pts enrolled in phase II: 48 treated with TCI; 25 with TC. TCI was well tolerated. All causality grade 3, 4 toxicity included (TCI, TC): hyperglycemia (20%, 10%), fatigue (15%, 8%), neutropenia (13%, 20%) and neuropathy (10%, 4%).Twenty-two pts receiving TCI (46%) and 8 pts on TC alone (32%) had objective responses. Furthermore, 14 out of 27 TCI pts (52%) with non-adenocarcinoma responded to treatment. In addition, a PR was observed in 1 out of 4 TC pts who elected to receive single agent I after progression on TC alone.
Conclusions: CP-751,871 appears safe in combination with TC. Interim TCI activity warranted further investigation. An additional 83 pts are being enrolled in the phase II part to further assess the safety and efficacy of this combination treatment.

6509 ORAL

Management of hypertension (HTN) in patients with advanced or recurrent non-squamous non-small cell lung cancer (NSCLC) receiving first-line cisplatin and gemcitabine with bevacizumab or placebo – results from randomised phase III trial BO17704

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Background: The addition of bevacizumab (B, Avastin®) to carboplatin/paclitaxel (CP) significantly improved overall and progression-free survival (PFS) compared with CP in patients (pts) with advanced non-squamous NSCLC in a phase III trial [Sandler et al. NEJM 2006]. The incidence of grade 3−4 HTN observed in E4599 was 0.7% in the placebo-containing arm and 7.5% in B-containing arm. Study BO17704 investigated the use of B (7.5 or 15 mg/kg q3w) in addition to cisplatin/gemcitabine (CG) for the first-line treatment of pts with locally advanced, metastatic or recurrent non-squamous NSCLC.
Methods: Eligibility criteria included histologically or cytologically documented previously untreated locally advanced, metastatic or recurrent non-squamous NSCLC; ECOG PS 0–1; adequate haematological, renal and liver function; no brain metastases; no history of recent CTC grade $\geqslant$2 haemoptysis. Between 2/2005 and 8/2006, a total of 1043 pts were randomised to 3 treatment groups. All pts were to receive up to 6 cycles of C 80 mg/m^2 day 1 and G 1,250 mg/m^2 days 1 and 8 every 3 wks, plus placebo (n = 347), B 7.5 mg/kg (n = 345) or B 15 mg/kg (n = 351) every 3 wks. B was to be administered until disease progression. Data for HTN was recorded at baseline; pts were followed until resolution or stabilisation. HTN was defined by the need for anti-HTN therapy.
Results: There was an increased incidence of HTN of all grades observed in the 7.5 mg/kg (24%) and 15 mg/kg (33%) B arms compared with placebo (11%). Hypertensive crisis occurred in 2 pts in the 7.5 mg/kg B arm and 1 in the 15 mg/kg B arm. A high proportion of pts received anti-HTN therapy, including calcium channel blockers (32.7%) and ACE-inhibitors (27.6%). Few pts discontinued therapy due to HTN.
Conclusions: The incidence of severe HTN observed in this trial is consistent with that observed in the previous phase III trial in NSCLC. The incidence of worsening HTN in pts with pre-existing HTN versus the incidence of de novo HTN appeared similar with B treatment. Very few clinically relevant severe events occurred. Hypertension should be controlled to levels suggested by public health guidelines.

	CG + placebo n (%)	CG + 7.5 mg/kg B n (%)	CG + 5 mg/kg B n (%)
HTN at baseline	91/327 (27.8)	96/330 (29.1)	88/329 (26.7)
Increased baseline HTN	14/91 (15.4)	24/96 (25.0)	28/88 (31.8)
De novo HTN	18/236 (7.6)	52/234 (22.2)	74/241 (30.7)
Discontinuation due to HTN	3/32 (9.4)	6/76 (7.9)	8/102 (7.8)
Grade 3−4 HTN	6 (2)	21 (6)	29 (9)

6510 ORAL

Erlotinib in patients with advanced non-small-cell lung cancer (NSCLC): interim results from the European subpopulation of the open-label TRUST study

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Background: Erlotinib (Tarceva®) is a well tolerated oral agent that significantly improved survival, delayed symptom deterioration and improved QoL in the BR.21 study in patients (pts) with previously-treated advanced NSCLC. TRUST is a global open-label study that provides erlotinib access for pts with stage IIIb/IV advanced NSCLC. We present here interim data from European sites.
Methods: Pts are eligible for TRUST if they have failed on/are unsuitable for chemotherapy and are ineligible for other erlotinib trials. Oral erlotinib (150 mg/day) is given until progression or unacceptable toxicity. Safety parameters include: incidence/severity of erlotinib-related rash; treatment-related adverse events (AEs) leading to withdrawal; serious AEs (SAEs) and treatment-related SAEs. Other treatment-related AEs are reported if not included on a list of 15 pre-specified events. Dose reductions are permitted in 50 mg decrements, if required.
Results: At data cut-off (1/3/07), 3663 pts from 27 countries had received $\geqslant$1 dose of erlotinib and were included in the database. Median age was 63 years (range 19−91); males 64%, females 36%; stage IIIB 22%, stage IV 78%; ECOG PS 0/1 75%, PS 2/3 25%; non-smoker 21%, ever smoker 79%; adenocarcinoma 49%, squamous cell 29%, other 22%; erlotinib 1st line 13%, 2nd line 46%, 3rd line 40%, other 1%. 55% of 3615 pts experienced grade (gr) 1/2 rash; 12% gr 3/4. 54% of 3448 pts experienced $\geqslant$1 AE, and 4% had a treatment-related SAE, most commonly gastrointestinal (GI) disorders (<1% gr 1, 2% $\geqslant$ gr 3). 8% of pts had an AE that was not pre-specified in the protocol. Erlotinib was discontinued in 6% of pts due to a treatment-related AE, mainly GI disorders (1% gr 1/2, 2% gr 3/4) and rash (1% gr 1/2, 1% gr 3/4). 13% of 3446 pts required dose reduction due to a treatment-related event, mostly rash (n = 324) or diarrhoea (n = 55). The disease control rate (CR, PR + SD) was 66% at the time of interim analysis (73% in 1st line, 64.5% in 2nd/3rd line) and median time to progression (TTP) was 11.3 wks (95% CI 10.6–12.0) across all treatment lines and 15.1 wks (12.7–16.1) in 1st-line pts. TTP was also longer in pts with good PS (15.1, 11.9, 8.6 and 6.1 wks for PS 0, 1, 2 and 3). Overall survival data is not yet mature.
Conclusions: These interim data from the TRUST European subpopulation confirm the favourable safety profile of erlotinib observed in previous clinical trials and its effectiveness when used in the wider clinical setting.