evaluable for response according to RECIST criteria: PR 29.4% and SD 41.2%. With a median follow-up of 3.9 months (range 0.7−11.1), median PFS was 4.6 months (95% CI: 2.6−6.6) and median OS has not been reached yet. Hematological toxicities were: 1 p gr. 3 anemia; 2 p gr. 3 and 2 p gr. 4 leucopenia; 10 p gr. 3, 1 p gr. 4 neutropenia and 3 p febrile neutropenia. Most common grade 3/4 non hematological toxicities were: vomiting (1p gr. 4), high blood pressure, asthenia and hyperglycemia. 1 p experienced gr. 4 abdominal pain, 1 p. gr. 4 constipation, 1 p. gr. 4 nausea and 1 p gr. 4 respiratory infection. No grade 3/4 hemoptysis were reported.
Conclusions: This interim analysis shows that B in combination with cisplatin and vinorelbine is safe and well tolerated and has a promising activity in chemo-naïve p with non squamous NSCLC. Survival data will be updated.

9146 POSTER

Long term benefit from erlotinib treatment is independent of prognostic factors and therapeutic response

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Background: Erlotinib (Tarceva®) is an orally-active targeted inhibitor of the epidermal growth factor receptor. In the TRUST study, a single arm open-label phase IV trial assessing Erlotinib treatment in over 7,000 patients with advanced non small-cell lung cancer (NSCLC), the median progression-free survival was 14.3 weeks. 20% of the TRUST study patient population had a progression free survival of more than 12 months. Based on these findings we have initiated this retrospective study, performed in Germany, in order to analyze the profile of long term survivors, thus optimizing the selection of NSCLC patients which will benefit the most from Erlotinib treatment.
Materials and Methods: Questionnaires were retrospectively filled in by attending physicians of patients surviving over one year from the TRUST cohort in Germany. Information of patients' demographics, disease and treatment characteristics were evaluated.
Results: Data from 301 patients were collected. The average age of long term survivors was 66 years (range 23−87). 75% of patients were in good or moderately restricted conditions (Eastern Cooperative Oncology Group score 0 or 1). 50% of the patients received Erlotinib as second line therapy; 52% had been treated with Erlotinib for at least 18 months, and 25% were treated for over 24 months. 43% of patients were male, 14% were smokers and 33% were past smokers. Histology type was adenocarcinoma and squamous cell in 67% and 15% of patients, respectively. 56% of patients had a stable disease over the course of treatment, while 44% had partial or full response. Although 78% of patients developed a typical skin reaction, the tolerability of Erlotinib was considered good or very good by 80% of treating physicians.
Conclusions: The long-term benefit of this target-oriented therapy, which was predominantly very well or well tolerated, was not limited to groups with good prognostic characteristics By contrast to conventional chemotherapy, long-term therapeutic success with Erlotinib was not restricted to patients in which complete or partial remission was induced. In summary, these data confirm Erlotinib to be effective in the long term treatment of NSCLC.

9147 POSTER

Bevacizumab and erlotinib as first-line therapy in advanced (stage IIIB/IV) non-squamous non-small-cell lung cancer (NSCLC) followed by platinum-based chemotherapy (CT) at disease progression - a multicenter phase II trial of SAKK

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Background: Standard platinum-based CT for the treatment of advanced NSCLC is toxic and yields unsatisfactory results. This phase II trial aimed at evaluating the feasibility and efficacy of a first-line combination of two targeted therapies (TT), Bevacizumab (B) and Erlotinib (E), followed by standard platinum-based CT.
Methods: Inoperable patients (pts) with confirmed non-squamous stage IIIB or stage IV NSCLC, WHO performance status (PS) 0−1, without immediate need of CT, without large, centrally located tumors, pre-existing tumor cavitations and brain metastases were eligible. B was given at 15 mg/kg i.v. on day 1 of each 21-day cycle and E 150 mg p.o. daily until PD or unacceptable toxicity. Upon PD, patients received standard CT: gemcitabine 1250 mg/m^2 i.v. on days 1 and 8 q3w and either cisplatin 80 mg/m^2 or carboplatin AUC 5 i.v. on day 1 for a maximum of six cycles or until PD. Primary endpoint is disease stabilization (CR + PR + SD) at 12 weeks under B+E. Secondary endpoints are OS, RR, TTP, disease stabilization at 6 and 18 weeks, safety and QoL, response to subsequent CT and gene expression analysis.
Results: 101 eligible pts were accrued from January 9, 2006 to April 1, 2009. Median age 61y, 52.5% females, 85% stage IV, 49% PS 1, 29% never smokers. Among the 79 pts having stopped B+E, 70% continued to CT. Among 95 patients, the most frequent worst G3 toxicities during B+E were rash (3), acne (2), pruritus (2), hypertension (2), dyspnea (2, incl. one fatal) and diarrhea (2). There were 2 fatal hemorrhages and 1 cardiac failure. The median OS is 13.4 months (95% CI: 10.5−19.4 m) at a median follow-up of 17.5 m. Up to now, tumor assessments are available for 92 patients during B+E and for 53 during CT. Corresponding best RECIST-responses to first line B+E were 17.4% PR, 55.4% SD, 26.1% PD, and 1.1% early death. Best responses to 2nd line CT were 11.3% PR, 47.2% SD, 22.6% PD, and 18.9% not assessable.
Conclusions: Combined TT in first-line non-squamous NSCLC is feasible with acceptable toxicity and very good median OS. As the last patient was recruited on April 1, 2009, mature results of the primary endpoint and specific secondary endpoints will be available at the 2009 ESMO/ECCO meeting.

9148 POSTER

Phase 1 study of the toll-like receptor 9 (TLR9) agonist, IMO-2055, combined with erlotinib (E) and bevacizumab (B) in patients (pts) with advanced or metastatic non-small cell lung cancer (NSCLC)

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Introduction: IMO-2055, a novel synthetic TLR9 agonist, induces Th-1 type immune responses and has shown promise in providing a potential means to control tumor growth. IMO-2055 has shown additive or synergistic antitumor activity in a number of tumor models in combination with cytotoxics, targeted therapies and monoclonal antibodies, including in lung cancer xenograft studies of IMO-2055, E, and B in triple combination. Clinical trials have shown IMO-2055 monotherapy is generally well tolerated given weekly for > 1 year. We report initial results of an open label 3+3 dose finding study of the combination of IMO-2055 with E and B.
Methods: IMO-2055 SC is given on days (d) 1, 8, and 15 of a 3-week (w) cycle. Dosages range from 0.08 to 0.48 mg/kg/w. B is given as 15 mg/kg IV on d1 and E as 150 mg PO daily. Pts have AJCC stage 3−4 histologically proven NSCLC not amenable to curative therapy, progression during or after 1st-line treatment, with ECOG score <2. Pts with intrathoracic

squamous disease are excluded. DLTs are defined as grade 3−4 clinical AEs or prolonged grade 3−4 lab results for cycle 1 only.
Results: 14 pts (7 male; 7 female) have been treated from Dec 2007 to Mar 2009 for a median of 6 cycles (range 1−20). 14 pts are evaluable for safety and 13 for efficacy. Median ECOG PS is 1. Grade 3 anorexia, dehydration and acneiform rash (face) have been identified as DLT in 1 patient at 0.16 mg/kg/week. Enrollment continues in cohort 4 at 0.48 mg/kg/w. Most common adverse events have been diarrhea (79%), fatigue (64%), injection site reaction (57%), rash (57%), anorexia (50%) and nausea (50%) with 1 treatment-related SAE (the above-cited DLT). Of 9 pts withdrawn, 2 had disease progression, 5 toxicity or treatment delay, 1 patient decision, 1 death unrelated to treatment. 3 of 13 pts (23%) have confirmed partial response. 5 patients are currently on treatment for a median of 9 cycles (range 5−21 cycles).
Conclusions: IMO-2055 appears to be well tolerated at dosages up to 0.32 mg/kg in combination with E and B. Pending completion of cohort 4, enrollment of additional pts will continue at a recommended Phase 2 dose level. Anti-tumor activity has been seen in pts with advanced, pretreated NSCLC. Controlled trials should be feasible to evaluate the promising combination of IMO-2055 plus E and B.

9149 POSTER

Phase II study of bevacizumab in combination with cisplatin and docetaxel as first line treatment of patients (p) with metastatic non squamous non-small-cell lung cancer (NSCLC)

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Background: Bevacizumab (B), in addition to platinum-based chemotherapy, is indicated for 1st line treatment of p with advanced NSCLC other than predominantly squamous cell histology. B has been shown to improve progression free survival (PFS) and overall survival (OS) when combined with cisplatin/gemcitabine and carboplatin/paclitaxel, respectively. However, there are limited data on the safety and efficacy of B in combination with other widely used chemotherapy doublets for NSCLC. This is a single-arm, open-labeled, single-stage phase II trial of cisplatin (C), docetaxel (D) and B for NSCLC.
Methods: Eligibility criteria: chemo-naïve, stage IIIB wet or IV, non-squamous NSCLC, PS 0−1, no brain metastases and no history of gross hemoptysis. P received D (75 mg/m^2), C (75 mg/m^2), and B (15 mg/kg iv) on day 1 every 3 weeks for up to 6 cycles, followed by B 15 mg/kg alone every 3 weeks until disease progression or toxicity. Primary endpoint: PFS.
Results: 50 p were enrolled (enrollment completed): 24% female, median age 60 (36−74), PS 1: 64%, adenocarcinoma: 72%; stage IV: 92%. Two p did not start treatment. Median follow-up is 5.3 months (range 0−13.6). Median number of cycles of B was 7 (range 0−18). 56% completed 6 cycles of treatment; 24% received $\geqslant$ 12 cycles of B. Most frequent grade $\geqslant$ 3 toxicities: diarrhea (14.6%), fatigue (14.6%), dyspnea (9.8%), anorexia (4.9%), alopecia (4.9%), esophagitis (4.9%), constipation (4.9%), mucositis (12.2%), proteinuria (4.9%); hematological toxicities: neutropenia (22%), febrile neutropenia (9.8%), leucopenia (14.6%), lymphopenia (4.9%). Of interest, 41.5% developed grade <3 epistaxis and 17% hypertension (1 p grade 3). One p died due to hemoptysis. 46 p were evaluable for response: 29 PRs (ORR: 63%). 18 of 48 p have experienced progression or death with a median SLP of 7.8 months (95% CI: 6.6-NR). Median OS is 13.5 months (95% CI: 12.7−13.6; 81.2% p censored); 1-year survival is 83.9% (95% CI: 67.4%-92.5%).
Conclusions: Treatment with C, D and B, followed by maintenance B in 1st line of advanced nonsquamous NSCLC shows an acceptable toxicity profile and promising efficacy. Final results will be presented.

9150 POSTER

Phase I trial of vorinostat in combination with erlotinib for advanced non-small cell lung cancer (NSCLC) patients (pts) with EGFR mutations after erlotinib progression (NCT00503971): The TARZO trial

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Background: We treated 217 pts with EGFR mutations with first- or second-line erlotinib, attaining a response of 70% and progression-free survival of 14 months. EGFR mutations are associated with Hsp90 for stability, and inhibition of Hsp90 may represent a novel strategy for the treatment of EGFR-mutant NSCLCs that become resistant to EGFR tyrosine kinase inhibitors. Vorinostat inhibits histone deacetylase (HDAC), inducing acetylation of Hsp90 and increases levels of E-cadherin. These findings prompted us to initiate a phase I study in erlotinib-treated pts with EGFR mutations progressing to erlotinib. At the time of progression, instead of stopping erlotinib, we added vorinostat, with the aim of defining the maximum tolerated dose (MTD) and attaining disease stabilization.
Methods: A 3+3 rule dose escalation was used to determine the maximum tolerated dose (MTD) of oral erlotinib 150 mg QD in combination with oral vorinostat (dose level 1 [DL1], 300 mg QD on days 1−7 every 21 days; DL2, 400 mg QD on days 1−7 every 21 days, and; DL3, 400 mg QD on days 1−7 and 15−21 in a 28-day cycle). Cycles were repeated for a maximum of 6 until progressive disease or intolerable toxicity. Pts with advanced NSCLC with EGFR mutations (exon 19 del and L858R) after erlotinib progression and ECOG $\leqslant$2 were eligible.
Results: The combination was administered to 12 pts (median age, 59 years; range 41−77) at 3 dose levels. One pt remains on treatment. The MTD of the combination was reached at erlotinib 150 mg QD plus vorinostat 400 mg QD on days 1−7 and 15−21 in a 28-day cycle. There was a single DLT in the third cohort (Grade 3 diarrhea). The most common drug-related toxicities of any grade in the first cycle of treatment were anemia (77.8%), skin alterations (66.7%), diarrhea (66.7%), xerostomy (55.6%), asymptomatic changes in liver function tests (55.6%), and asthenia (55.6%). There were no Grade $\geqslant$3 drug-related adverse events during the first cycle of treatment and the overall analysis of cycles showed asthenia (11.1%), somnolence (11.1%) and hyporexia (11.1%). No accumulated toxicity was observed. Of 10 pts evaluable for efficacy, seven had stable disease as best response (median duration of treatment 6.0 cycles, range 3−12).
Conclusion: The combination of vorinostat and erlotinib appears to be well tolerated in this group of advanced NSCLC pts with EGFR mutations after erlotinib progression; the combination demonstrated prolonged disease stabilization. A phase II trial will be initiated.

9151 POSTER

Treatment of patients with advanced non-small-cell lung cancer (NSCLC) with erlotinib: results from clinical practice

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Background: The EGFR-TKI erlotinib has shown benefit in pretreated NSCLC. Post-hoc subgroup analyses of randomized studies suggest that nonsmokers, women, and patients with adenocarcinoma histology may have a superior response to treatment. We performed a retrospective analysis to answer the question, whether these 3 response criteria can be used in routine clinical practice for selection of patients.
Methods: We analyzed all consecutive patients with NSCLC starting treatment with erlotinib between May 2005 and January 2009. Response was assessed radiologically using RECIST criteria.
Results: 121 caucasian patients were analysed. 9 patients who were unfit to receive conventional chemotherapy including one patient on chronic haemodialysis were treated with erlotinib 1st line.
Response: 16.5% of patients demonstrated a partial remission, 33.9% experienced stable disease. Partial remissions were seen more frequently in never-smokers, in females, and in patients with adenocarcinoma histology. The disease control rate (PR + SD) was higher in non-smokers than in ex-smokers or smokers, and in male than in female patients.