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 Of 9 pts withdrawn, 2 had disease progression, 5 toxicity or treatment delay, 1 patient decision, 1 death unrelated to treatment. 3 of 13 pts (23%) have confirmed partial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.

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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.

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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.

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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.