**NSCLC, metastatic**

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**ALK INHIBITOR AP26113 IN PATIENTS WITH ADVANCED MALIGNANCIES, INCLUDING ALK+ NON-SMALL CELL LUNG CANCER (NSCLC): UPDATED EFFICACY AND SAFETY DATA**  
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**Aim:** AP26113 is an investigational orally-active tyrosine kinase inhibitor with preclinical activity against ALK and all 9 clinically-identified crizotinib-resistant mutants tested.

**Methods:** The Phase (Ph) 2 portion of a Ph1/2 single arm, multicenter study in patients (pts) with advanced malignancies is underway. We report updated safety for all treated pts and efficacy data for ALK+ NSCLC pts previously treated with crizotinib. NCT01449461.

**Results:** As of 17 March 2014, 125 pts were enrolled: 66 in Ph1 (30-300 mg) and 59 in Ph2 (90 or 180 mg). Baseline characteristics: 58% female, median age 57 yr; diagnoses: NSCLC n = 117, other n = 8. 62 pts remain on study; median follow-up for all pts is 3.1 mo (max= 24.4 mo, ongoing). The most common treatment-emergent adverse events (≥20%) were nausea (40%), fatigue (34%), diarrhea (34%), cough (26%), headache (25%), and vomiting (21%), which were generally Grade 1/2 in severity. Early onset pulmonary symptoms (dyspnea with hypoxia and/or new findings on chest imaging) were observed in 12/125 (10%) pts: 6/44 (14%) at 180 mg qd and 1/38 (3%) at 90 mg qd. Symptoms occurred within 7 days following initiation of AP26113, required medical attention, and occurred at lower rates with lower doses. Pts continue to be enrolled at 90 mg qd. Among 51 evaluable ALK+ NSCLC pts with prior crizotinib, 35 (69%) responded. Duration of response was 1.6–14.7+ mo. Among 55 evaluable pts with ALK+ NSCLC, median progression free survival is 10.9 mo. Independent radiological review conducted on 10 pts enrolled with untreated or progressing brain metastases showed 6/10 pts with regression in brain, including 4 with undetectable brain metastases following AP26113; 2 had stable disease, 2 progressed; 7/10 remain on study (range 2.7-19.5 mo). Updated data will be presented.

**Conclusions:** AP26113 has promising anti-tumor activity in pts with crizotinib-resistant ALK+ NSCLC, including pts with brain metastases. A randomized Ph2 trial evaluating either 90 mg qd or 90mg qd escalated to 180 mg qd in crizotinib-resistant ALK+ NSCLC has been initiated.

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