Efficacy and safety of brigatinib (AP26113) in ALK+ NSCLC: phase 1/2 trial results

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Introduction: Brigatinib is an investigational oral tyrosine kinase inhibitor with preclinical activity against both rearranged ALK and clinically identified crizotinib-resistant mutant ALK.

Methods: In this ongoing phase 1/2, single-arm, open-label, multicenter study in patients with advanced malignancies (N=137; NCT01449461), patients received oral brigatinib at total doses of 30–300 mg daily. Antitumor efficacy (per RECIST v1.1) and safety data are reported in ALK+ NSCLC and all patients, respectively.

Results: Median age of ALK+ NSCLC patients (n=79) was 54 (29–83) years; 49% were female, 90% received prior crizotinib, and 47% had ≥2 prior chemotherapy regimens. As of February 17, 2015, 45/79 (57%) remained on study; median time on treatment was 12.6 months (1 day to 35.5 months). Evaluable ALK+ NSCLC patients had ORR/median PFS of 74%/13.4 months (Table). A post hoc independent radiological review of patients with brain metastases at baseline showed (as of February 9, 2015): 8/15 (53%) patients with measurable brain lesions ≥10 mm had an intracranial response; 11/31 (35%) patients with only nonmeasurable lesions had disappearance of all lesions. Treatment-emergent AEs in ≥30% of total patients (N=137), generally grades 1/2, included nausea (52%), fatigue (42%), diarrhea (40%), rash (≥10 mm had an intracranial response; 11/31 (35%) patients with only nonmeasurable lesions had disappearance of all lesions. Treatment-emergent AEs in ≥30% of total patients (N=137), generally grades 1/2, included nausea (52%), fatigue (42%), diarrhea (40%), rash (3%), cardiovascular (3%), and constipation (2%).

Conclusion: Brigatinib had antitumor activity in ALK+ NSCLC patients with (71% ORR; median PFS, 13.4 months) or without (100% ORR) prior crizotinib, including patients with brain metastases (53% ORR, measurable brain lesions). A pivotal, randomized, phase 2 trial of brigatinib in patients with crizotinib-resistant ALK+ NSCLC is on-