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POSTER
perspectives

(9057) Activity and safety of brigatinib (BRG) in patients (pts) with ALK+ non–small cell lung cancer (NSCLC): Phase (ph) 1/2 trial results.

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Background: BRG, an investigational oral tyrosine kinase inhibitor, has preclinical activity against ALK-rearranged NSCLC and mutants resistant to crizotinib (CRZ).

Methods: Pts with advanced malignancies, including ALK+ NSCLC, received oral BRG (30–300 mg total daily) in an ongoing ph 1/2, single-arm, open-label, multicenter trial (NCT01449461). Activity (by RECIST v1.1) and safety are reported in ALK+ NSCLC pts and all treated pts, respectively.

Results: 137 pts were enrolled. Among 79 ALK+ NSCLC pts, median age was 54 y, 49% were female, and 90% received prior CRZ. As of 15 Jun 2015, 39/79 (49%) ALK+ NSCLC pts remained on study; median duration of treatment was 15.4 mo (1 d–39.4 mo). Among ALK+ NSCLC pts with prior CRZ exposure, the objective response rate (ORR) was 72% (95% CI 60–82%; 51/71, including 44 confirmed responses); for CRZ-treated pts who received dosing regimens explored in ph 2, 90 mg qd, 90 mg qd for 7 d followed by 180 mg qd (90→180 mg qd), and 180 mg total daily, the ORR was 77% (95% CI 46–95%; 10/13, including 7 confirmed responses), 80% (95% CI 59–93%; 20/25, including 19 confirmed responses), and 65% (95% CI 43–84%; 15/23, including 14 confirmed responses), respectively. Median duration of response and median PFS were 11.2 mo (95% CI 7.8 to not reached [NR]) and 13.2 mo (95% CI 9.2–NR), respectively. All 8 CRZ-naive pts had confirmed objective responses, including 3 complete responses; median PFS was NR. In a post hoc assessment of ALK+ NSCLC pts with brain metastases at baseline, as of 9 Feb 2015, 8/15 (53%; 95% CI 27–79%) with measurable lesions (≥ 10 mm) had intracranial objective responses. Treatment-emergent adverse events (TEAEs) in ≥ 30% of all pts (generally grade 1/2): nausea 53%; fatigue 43%; diarrhea 41%; headache 33%; cough 31%. Serious TEAEs (any cause) in ≥ 2% of all pts: dyspnea 7%; pneumonia 7%; hypoxia 5%; pulmonary embolism 3%; pyrexia 2%. Of 137 pts, 13 (9%) discontinued due to an AE.

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Conclusion: BRG yielded substantial antitumor activity in ALK+ NSCLC pts both systemically and in brain metastases and had an acceptable safety profile in this population. A pivotal, randomized, ph 2 trial of BRG in CRZ-resistant ALK+ NSCLC (ALTA) evaluating 90 mg qd vs 90→180 mg qd is ongoing. Clinical trial information: NCT01449461