Primary results of ALESIA: A randomised, phase III, open-label study of alectinib vs crizotinib in Asian patients with treatment-naive ALK+ advanced NSCLC

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Background: Alectinib (ALC), a highly selective CNS-active ALK inhibitor, showed superior efficacy vs crizotinib (CRZ) in treatment-naive ALK+ NSCLC in the global phase III ALEX study (PFS HR 0.47, 95% CI 0.34–0.65, p < 0.001). At an updated data cutoff, the PFS HR was 0.43, 95% CI 0.32–0.58, median PFS 34.8 months ALC vs 10.9 months CRZ. We report primary results from the phase III ALESIA study of first-line ALC vs CRZ in Asian patients with advanced ALK+ NSCLC using the global ALC dose (NCT02838420).

Methods: Patients had ALK+ stage IIIIB/IV NSCLC (by central IHC testing) and ECOG PS 0–2. Asymptomatic CNS metastases were allowed. Patients were randomised 2:1 to receive ALC 600mg BID (n = 125) or CRZ 250mg BID (n = 62). Regular tumour/CNS imaging was performed. Primary endpoint: PFS by INV (RECIST v1.1). Primary objective consistency: with the PFS benefit seen in ALEX. Secondary endpoints: PFS by IRC, time to CNS progression, ORR, DOR, OS, CNS ORR, QoL and safety.

Results: Median duration of follow-up was 16.2 months ALC vs 15.0 months CRZ. At the primary data cutoff (May 31, 2018), ALC significantly reduced the risk of progression/death (INV PFS) vs CRZ: HR 0.22, 95% CI 0.13–0.38, p < 0.0001; median PFS not estimable (NE) ALC vs 11.1 months CRZ. Secondary endpoints supported the primary endpoint: IRC PFS, HR 0.37 (95% CI 0.22–0.61; p < 0.0001); median PFS NE ALC vs 10.7 months CRZ; time to CNS progression (IRC) cause-specific HR 0.14 (95% CI 0.06–0.30; p < 0.0001); ORR (INV), 91.2% ALC vs 77.4% CRZ, p = 0.0095; DOR (INV), HR 0.22 (95% CI 0.12–0.40); p < 0.0001; median DOR NE ALC vs 9.3 months CRZ; OS data immature: HR 0.28 (95% CI 0.12–0.68); p = 0.0027; event rate ALC 6.4% vs CRZ 21.0%; median OS NE both arms; CNS ORR (IRC) in patients with measurable/non-measurable CNS baseline lesions, 72.7% ALC vs 21.7% CRZ (50.0% vs 13.0% complete response). Despite longer treatment duration (14.7 ALC vs 12.6 months CRZ), fewer ALC patients had grade 3–5 AEs (29% vs 48% CRZ), serious AEs (15% vs 26%) or AEs leading to treatment discontinuation (7% vs 10%).

Conclusions: ALESIA study results are consistent with the global ALEX study and confirm the clinical benefit of ALC in Asian patients with advanced ALK+ NSCLC.

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