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Updated efficacy and safety data from the global phase III ALEX study of alectinib (ALC) vs crizotinib (CZ) in untreated advanced ALK+ NSCLC.

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Abstract Disclosures

Abstract:

Background: The primary ALEX (NCT02075840) analysis showed superior investigator (INV)-assessed PFS with ALC vs CZ (HR 0.47, 95% CI 0.34–0.65, p<0.001; median 11.1 months [m] CZ, not estimable [NE] ALC) in untreated ALK+ NSCLC. We report updated data (cutoff Dec 1 2017). **Methods:** ALEX enrolled patients (pts) with stage IIIB/IV ALK+ NSCLC (by central IHC) and no prior systemic therapy for advanced NSCLC; asymptomatic CNS metastases (mets) were allowed. Pts were randomized 1:1 to receive ALC 600mg BID (n = 152) or CZ 250mg BID (n = 151). Primary endpoint: PFS (INV, RECIST v1.1), with q8w CNS imaging in all pts. Secondary endpoints: ORR, time to CNS progression, DOR, OS, and safety. **Results:** With 10m longer follow-up (median 22.8m CZ vs 27.8m ALC), ALC significantly reduced risk of disease progression/death by 57% vs CZ (ITT; stratified HR 0.43, 95% CI 0.32–0.58): median PFS (INV) was 34.8m ALC vs 10.9m CZ. Median PFS by baseline (BL) CNS mets status was 27.7m ALC vs 7.4m CZ (HR 0.35, 95% CI 0.22–0.56) in pts with, and 34.8m vs 14.7m (HR 0.47, 95% CI 0.32–0.71) in pts w/out BL CNS mets. In the BL CNS mets group, the number of pts who received WBRT (n = 16 ALC, n = 17 CZ) or SRS (n = 4 ALC, n = 6 CZ) was balanced, as was the number of BL lesions (median 2 per arm). Updated secondary endpoint data (INV): ORR 82.9% ALC (95% CI 75.95–88.51; n = 152) vs 75.5% CZ (95% CI 67.84–82.12; n = 151); median DOR 33.3m ALC (95% CI 31.1–NE; n = 126) vs 11.1m CZ (95% CI 7.5–13.0; n = 114), stratified HR 0.33, 95% CI 0.23–0.48. OS data are still immature (events ALC 28.3%, CZ 31.8%; stratified HR 0.76, 95% CI 0.50–1.15). Despite significantly longer treatment (Tx) duration with ALC (27.0m vs 10.8m), proportion of pts with grade 3–5 AEs (44.7% vs 51.0%), AEs leading to dose reduction (16.4% vs 20.5%) or interruption (22.4% vs 25.2%) were lower with ALC vs CZ. Proportion of pts with AEs leading to discontinuation: 13.2% each arm. Fatal AEs: 5% CZ (2 Tx-related AEs) and 4% ALC pts (0 Tx related). **Conclusions:** ALC 600mg BID showed superior efficacy vs CZ (PFS HR 0.43, median 34.8m ALC vs 10.9m CZ) in untreated ALK+ NSCLC, regardless of BL CNS mets, and favorable and durable tolerability despite longer Tx duration, consolidating ALC as the new standard of care. Clinical trial information: NCT02075840