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Final overall survival (OS) and safety analysis of the phase III ALEX study of alectinib vs crizotinib in patients with previously untreated, advanced ALK-positive (ALK+) non-small cell lung cancer (NSCLC)

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Background

Results from ALEX (NCT02075840), a randomised phase 3 study, led to the global approval of first-line (1L) alectinib in patients (pts) with advanced *ALK*+ NSCLC. Final PFS data from ALEX were previously published (median 34.8 months alectinib; 10.9 months crizotinib); OS was immature. Here, we report final OS, duration of response (DoR) and safety data from ALEX.

Methods

Eligible patients ≥18 years old with previously untreated, advanced *ALK*+ NSCLC were randomised 1:1 to receive alectinib (600 mg; BID) or crizotinib (250 mg; BID) until disease progression (PD), toxicity, withdrawal or death; no crossover was permitted before PD. Stratification factors: ECOG performance status (0/1 vs 2); race (Asian vs non-Asian); baseline CNS mets (yes vs no). Key secondary endpoints: OS; DoR; safety.

Results

At data cutoff (April 28, 2025), 303 patients were enrolled (alectinib, n=152; crizotinib, n=151). After median follow-ups of 53.5 (alectinib) and 23.3 months (crizotinib), median OS (mOS) was 81.1 (95% CI 62.3–not estimable) and 54.2 months (95% CI 34.6–75.6), respectively (Table). In pts with baseline CNS mets and prior radiation, mOS was 92.0 months with alectinib vs 39.5 months with crizotinib; in pts with baseline CNS mets and no prior radiation, mOS was 46.9 vs 23.7 months, and in pts without baseline CNS mets, mOS was 94.0 vs 69.8 months, respectively. Median DoR was 42.3 months (alectinib) vs 11.1 months (crizotinib). No new or unexpected safety concerns were reported.Table: LBA73

	Alectinib (n=152)	Crizotinib (n=151)
OS, median months (95% CI)	81.1 (62.3–NE)	54.2 (34.6–75.6)
No. of events, n (%)	76 (50.0)	73 (48.3)
HR*	0.78 (0.56–1.08)	
DoR†, median months (95% CI)	*n=126* 42.3 (31.3– 51.3)	*n=115* 11.1 (7.9– 13.0)
HR*	0.41 (0.30–0.56)	
Safety		
Median treatment duration, months	28.1	10.8

	Alectinib (n=152)	Crizotinib (n=151)
≥1 Adverse event, n (%)	147 (96.7)	148 (98.0)
Related	125 (82.2)	135 (89.4)
Grade 3–5	88 (57.9)	87 (57.6)
Grade 5	10 (6.6)	7 (4.6)
Serious	70 (46.1)	48 (31.8)
Leading to dose interruption	49 (32.2)	43 (28.5)
Leading to dose reduction	35 (23.0)	30 (19.9)
Leading to treatment discontinuation	27 (17.8)	22 (14.6)

*Stratified; †By investigator; DoR, duration of response; HR, hazard ratio; NE, not estimable

Conclusions

Final data from ALEX show 1L alectinib induced a clinically meaningful OS benefit (regardless of baseline CNS mets status) and DoR compared with crizotinib in pts with previously untreated, advanced *ALK*+ NSCLC. Safety data were in line with the known safety profile of alectinib. These data continue to support 1L alectinib as a standard of care in pts with advanced *ALK*+ NSCLC.

Clinical trial identification

NCT02075840.

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