LBA58 Intracranial efficacy of brigatinib (BRG) vs crizotinib (CRZ) in the phase III ALTA-1L trial

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Background: BRG, a next-generation ALK inhibitor, has robust efficacy in CRZ-resistant ALK+ NSCLC. ALTA-1L evaluated the efficacy of BRG vs CRZ in TKI-naive ALK+ NSCLC patients (pts). The primary endpoint of blinded independent review committee (BIRC)-assessed PFS was met at first interim analysis (IA) and previously reported (HR, 0.49; P = 0.0007). Here we report detailed intracranial efficacy from the first IA of ALTA-1L (NCT02737501).

Methods: The open-label, multicenter study enrolled pts with ALK inhibitor-naive stage IIIB/IV ALK+ NSCLC. Pts were stratified by presence of baseline (BL) brain metastases and history of chemotherapy for advanced disease and randomized 1:1 to BRG 180 mg qd with 7-day lead-in at 90 mg or CRZ 250 mg bid. Primary endpoint: BIRC–assessed PFS (RECIST v1.1). IAs were planned at ~50% and ~75% of 198 expected PFS events. Secondary endpoints included intracranial ORR (iORR) and intracranial PFS (iPFS). An exploratory competing risks analysis of intracranial progression (per CNS BIRC), systemic progression (per systemic BIRC), and death was also performed.

Results: Of 275 randomized pts (BRG/CRZ, n = 137/138), 31%/34% had BL brain metastases (BIRC-assessed); 13%/14% had prior brain radiotherapy. At data cut-off (19 February 2018; median follow-up, 11/9.3 mo), iPFS in ITT population was significantly improved with BRG (HR, 0.42 [95% CI, 0.24–0.70]; P = 0.0006). In the ITT population competing risks analysis, time to intracranial progression without prior systemic progression was significantly improved with BRG (HR, 0.30 [95% CI, 0.15–0.60]; P < 0.001); 1-year cumulative incidence (BRG vs CRZ): 12% (95% CI, 6–20) vs 23% (95% CI, 15–31). Time to systemic progression without prior intracranial progression was also improved with BRG (HR, 0.51 [95% CI, 0.30–0.86]; P = 0.017). Additional intracranial efficacy results are presented in the table.

Conclusions: BRG has superior intracranial activity vs CRZ in ALK TKI-naive pts with ALK+ NSCLC.

Table: LBA58

BIRC-Assessed Endpoint	BRG	CRZ	P Value
All patients (ITT), n	137	138	
iPFS events, n (%)	22 (16)	39 (28)	
Median iPFS, mo	NR (NR[a])	NR (11–NR[a])	
1-y iPFS, %	78 (68–85[a])	61 (50–71[a])	
iPFS hazard ratio (95% CI)	0.42 (0.24–0.70[a])		0.0006[b]
Any baseline brain metastases, n	43	47	
iPFS events, n (%)	11 (26)	28 (60)	
Median iPFS, mo	NR (11–NR[a])	6 (4–9[a])	
1-y iPFS, %	67 (47–80[a])	21 (6–42[a])	
iPFS hazard ratio (95% CI)	0.27 (0.13–0.54[a])		<0.0001[b]
iORR[c], %	79 (64–90[a])	23 (12–38[a])	<0.0001[d]
Confirmed iORR, %	67 (51–81[a])	17 (8–31[a])	<0.0001[d]
Measurable brain metastases, n	18	21	
iORR[c], %	83 (59–96[a])	33 (15–57[a])	0.0023[d]
Confirmed iORR, %	78 (52–94[a])	29 (11–52[a])	0.0028[d]

NR, not reached
[a]95% CI;
[b]Log-rank;
[c]Response, ≥1 assessment;
[d]Cochran-Mantel-Haenszel test

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