

1060 Brigatinib (BRG) vs crizotinib (CRZ) in the phase III ALTA-1L trial

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Background: We report results of the first interim analysis (IA) from the ALTA-1L study of BRG vs CRZ in anaplastic lymphoma kinase (ALK) inhibitor-naïve, ALK-positive non-small cell lung cancer (ALK+ NSCLC; NCT02737501).

Methods: This open-label, multicenter study enrolled patients (pts) with advanced ALK+ NSCLC. Eligible pts had ≤1 prior systemic therapy for advanced NSCLC. Asymptomatic central nervous system (CNS) metastases were allowed. Pts were randomized 1:1 to BRG 180 mg QD with 7-day lead-in at 90 mg or CRZ 250 mg BID. Primary endpoint was blinded independent review committee (BIRC)-assessed progression-free survival (PFS; RECIST v1.1); secondary efficacy endpoints included BIRC-assessed objective response rate (ORR), intracranial ORR (iORR), and intracranial PFS (iPFS). IAs were planned at 50% and 75% of 198 expected PFS events.

Results: 275 pts were randomized (BRG/CRZ, n = 137/138); median age (years) 58/60. 26%/27% received prior chemotherapy for advanced disease, and 29%/30% had baseline brain metastases. At data cutoff (19 Feb 2018), with a median follow-up of 11.0/9.3 months (BRG/CRZ) and 99 PFS events, BRG met the prespecified threshold for statistical superiority vs CRZ in the primary endpoint of BIRC-assessed PFS (HR 0.49; 95% CI, 0.33–0.74; log-rank P = 0.0007); BRG median PFS was not reached (NR; 95% CI, NR) vs CRZ 9.8 months (95% CI, 9.0–12.9). Investigator-assessed PFS HR 0.45 (95% CI, 0.30–0.68); log-rank P = 0.0001. Table shows additional efficacy data. Most common grade ≥3 treatment-emergent adverse events (AEs): BRG: increased blood creatine phosphokinase (16.2%) and lipase (13.2%), hypertension (9.6%); CRZ: increased alanine aminotransferase (9.5%), aspartate aminotransferase (5.8%), and lipase (5.1%). Any grade interstitial lung disease/pneumonitis: BRG, 3.7%; CRZ, 2.2%. Discontinuations due to AE (BRG/CRZ): 11.8%/8.8%.

Conclusions: BRG showed a statistically and clinically significant improvement in PFS vs CRZ in ALK inhibitor-naïve ALK+ NSCLC.

Clinical trial identification: NCT02737501.

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Table: 1060

BIRC-Assessed Endpoint, %	BRG (n = 137)	CRZ (n = 138)	P Value
All pts			
ORR ^a	76 (68–83 ^b)	73 (65–80 ^b)	
Confirmed ORR	71 (62–78 ^b)	60 (51–68 ^b)	0.0678
With any intracranial CNS metastases	(n = 43)	(n = 47)	
iORR ^a	79 (64–90 ^b)	23 (12–38 ^b)	
Confirmed iORR	67 (51–81 ^b)	17 (8–31 ^b)	<0.0001
Median iPFS, months	NR (11–NR ^b)	6 (4–9 ^b)	
1-year iPFS	67 (47–80 ^b)	21 (6–42 ^b)	
HR	0.27 (0.13–0.54)		<0.0001 ^c
With measurable intracranial CNS metastases	(n = 18)	(n = 21)	
iORR ^a	83 (59–96 ^b)	33 (15–57 ^b)	
Confirmed iORR	78 (52–94 ^b)	29 (11–52 ^b)	0.0028

^aResponse, ≥1 assessment;

^b95% CI;

^cLog-rank