106O 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–naive, 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–naive ALK+ NSCLC.

Clinical trial identification: NCT02737501.

Editorial acknowledgement: Professional medical writing assistance was provided by Lauren Gallagher, PhD, (Peloton Advantage, Parsippany, NJ) and funded by Millennium Pharmaceuticals, Inc.

Legal entity responsible for the study: ARIAD Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

Funding: ARIAD Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

Disclosure: R. Califano: Honoraria, consulting/advisory role: AstraZeneca, BMS, Roche, MSD, Boehringer Ingelheim, Takeda, Novartis, Pfizer, Lilly Oncology. C. Gridelli: Speakers bureau, advisory role: Pfizer, Roche. A. Delmonte: Consulting/advisory role: AstraZeneca, Boehringer Ingelheim. M.R. Garcia Campelo: Honoraria: ARIAD, AstraZeneca, Roche, Pfizer, BMS, Boehringer Ingelheim; Speakers bureau, advisory role: ARIAD, AstraZeneca, Roche, Pfizer, BMS, Boehringer Ingelheim. A. Bearz: Speakers bureau, advisory role: AstraZeneca, Pfizer, Eli Lilly, BMS, Novartis, Roche, MSD, Boehringer Ingelheim, Takeda. F. Griesinger: Research funding to institution: AstraZeneca, Boehringer Ingelheim, BMS, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, Takeda, Siemens; Consulting or advisory role: ARIAD, AstraZeneca, Boehringer Ingelheim, BMS, Celgene, Lilly, MSD, Novartis, Pfizer, Roche, Takeda, ARIAD, AbbVie, Siemens. E. Felip: Consulting/advisory role: AbbVie, AstraZeneca, Blue Print Medicines, Boehringer Ingelheim, BMS, Celgene, Eli Lilly, Guardant Health, Janssen, Merck KGaA, MSD, Novartis, Pfizer, Roche, Takeda; Speakers bureau: AbbVie, AstraZeneca, Boehringer Ingelheim, BMS, Eli Lilly, Merck KGaA, MSD, Novartis, Pfizer, Roche, Takeda. S. Popat: Research funding to institution: Boehringer Ingelheim, Epizyme, BMS, Clovis Oncology, Roche, Lilly, Takeda; Honoraria: Boehringer Ingelheim, AstraZeneca, Roche, Takeda, Chugai Pharma; Consulting or advisory role: Boehringer Ingelheim, Roche, Novartis, Pfizer, AstraZeneca, BMS, MSD, Guardant Health, AbbVie; Travel, accommodations, expenses: Boehringer Ingelheim, BMS, Merck Sharp & Dohme. A. Morabito: Honoraria: AstraZeneca, Roche, Boehringer Ingelheim, Pfizer, MSD, BMS. S. Ghosh: Honoraria/speakers bureau: Pfizer. M. Tiseo: Speakers bureau, advisory role: AstraZeneca, BMS, Boehringer Ingelheim, Eli Lilly, MSD, Novartis, Otsuka, Pfizer, Pierre Fabre, Roche. J. Haney, D. Kerstein: Employment, stock and other ownership interests: Arîad. D.R. Camidge: Honoraria: AstraZeneca, Takeda, Arrys/Kyn, Genoptix, G1 Therapeutics (DSMB), Mersana Therapeutics, Roche/Genentech, Ignyta, Daichii Sankyo (ILD adjudication committee), Hansoh SRC, Bio-Thera DSMB, Lycera, Revolution Med, Orion, Clovis, Celgene, Novartis); Research funding (ARIAD/Takeda). All other authors have declared no conflicts of interest.

Table: 106O

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

[a]Response, ≥1 assessment;
[b]95% CI;
[c]Log-rank