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Integrated Efficacy and Safety of Brigatinib Following Alectinib Treatment in the ALTA-2 and J-ALTA Studies

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DISCLOSURES

Commercial Interest	Relationship(s)
Turning Point Therapeutics	Ownership or Stock Interest
Elevation Oncology	Ownership or Stock Interest
Pfizer	Honorarium, Research Funding
Roche Pharma AG	Honorarium, Research Funding
Genentech/Roche	Honorarium, Speaker's Bureau, Research Funding
ARIAD/Takeda	Honorarium, Research Funding
AstraZeneca	Honorarium, Speaker's Bureau, Research Funding
Janssen/Johnson & Johnson	Honorarium, Research Funding
Revolution Medicines	Research Funding
Mirati Therapeutics	Research Funding

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Background

- Alectinib is a standard-of-care anaplastic lymphoma kinase inhibitor for patients with advanced or metastatic *ALK*-positive non–small cell lung cancer; however, most patients eventually develop disease progression
- Subsequent ALK inhibitor therapy can be beneficial in these patients, but few studies have evaluated ALK inhibitors in patients with *ALK*+ NSCLC following progression on alectinib
- We conducted an integrated efficacy and safety analysis of two phase 2 studies of brigatinib treatment in patients with *ALK*+ NSCLC with disease progression on alectinib

Overview of Integrated Study Design

ALTA-2 (NCT03535740), post-alectinib cohort (n=86)[1]

Single arm, open-label study conducted in Asia, Europe, North America, and Australia

- Locally advanced or metastatic *ALK*+ NSCLC[a]
- Disease progression on alectinib
- ≤3 lines of systemic therapy for metastatic disease (included crizotinib prior to alectinib)

Brigatinib 180 mg QD (7-day lead-in at 90 mg QD)

Primary endpoint:
Confirmed BIRC-assessed ORR
Secondary endpoints:
DoR, PFS, OS, safety

J-ALTA (NCT03410108), main cohort (n=47)[2]

Single arm, open-label study conducted in Japanese patients

- Locally advanced or metastatic *ALK*+ NSCLC[a]
- Disease progression on alectinib ± prior crizotinib

[a] Patients with asymptomatic brain metastases at screening were eligible for enrollment

ALK, anaplastic lymphoma kinase; *ALK*+, *ALK* gene rearranged; BIRC, blinded independent review committee; DoR, duration of response; NSCLC, non–small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QD, once daily.

1. Ou SI, Nishio M, Ahn MJ, et al. *J Thorac Oncol.* 2021 (submitted); 2. Nishio M, Yoshida T, Kumagai T, et al. *J Thorac Oncol.* 2021;16(3):452-463.

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Baseline Patient Characteristics

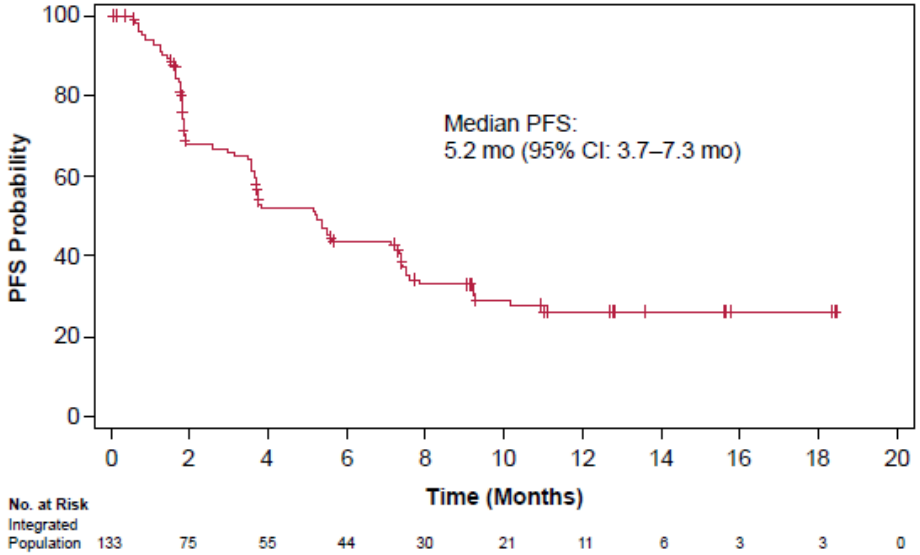
Characteristic, n (%)	Integrated Population N = 133
Age, median (range), years	54 (22–82)
Female, n (%)	68 (51)
Brain metastases at baseline by BIRC	66 (50)
Stage IV disease at study entry	131 (98)
Prior anticancer therapies	
Alectinib only	77 (58)
Crizotinib and alectinib	56 (42)
Chemotherapy for metastatic disease	41 (31)
2 prior therapies	53 (40)
3 prior therapies	24 (18)
Duration of prior alectinib, median (range), mo	15 (1–65)
Best response to prior alectinib as CR/PR	96 (72)

CR, complete response; CI, confidence interval; CNS, central nervous system; DCR, disease control rate; iORR, intracranial objective response rate; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

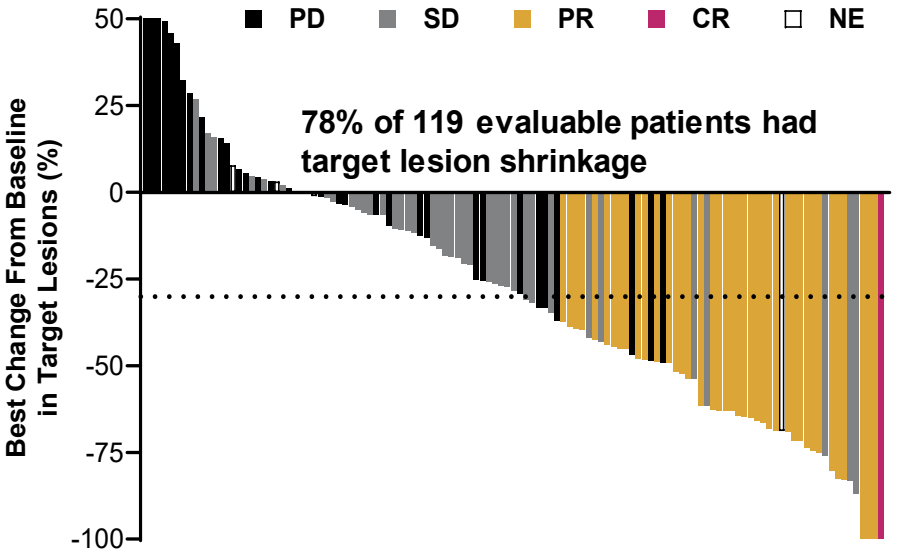
BIRC-Assessed Efficacy

Parameters	Integrated Population N = 133
Confirmed ORR, n (%) [95% CI]	41 (31) [23–39]
CR	1 (1)
PR	40 (30)
SD	42 (32)
PD	33 (25)
Not Evaluable/Not Reported	17 (13)
DCR, n (%) [95% CI]	83 (62) [54–71]
Median DoR, mo (95% CI)	9.2 (5.5–NE)
Median PFS, mo (95% CI)	5.2 (3.7–7.3)
Median OS, mo (95% CI)	NE (16.2–NE)
Patients with baseline CNS metastases, n (%)	66 (50)
Confirmed iORR, n (%) [95% CI]	9 (14) [6–24]
Intracranial CR/PR	6 (9) / 3 (5)

BIRC-Assessed Progression-Free Survival



Best Target Lesion Response



Note: The dotted line at -30% represents the threshold for partial response per RECIST v1.1.
RECIST, Response Evaluation Criteria in Solid Tumors.

- Data cut-off: J-ALTA, January 22, 2020; ALTA-2, September 30, 2020
- Median follow-up for the integrated population: 11 months
- Thirty-four patients (26%) were still receiving brigatinib treatment at the data cut-off

Safety Overview, Integrated Population

TEAEs, n (%)	N = 133
Any-grade TEAEs	133 (100)
Treatment related	117 (88)
Leading to dose interruption	63 (47)
Leading to dose reduction	23 (17)
Leading to discontinuation	16 (12)
Grade 3–4 TEAEs	87 (65)
Grade 5 TEAEs	12 (9)
Treatment related	0

TEAE Overview, Integrated Population

TEAEs, n (%)	N = 133
Any grade, >25% of patients	
Increased blood creatine phosphokinase	65 (49)
Diarrhea	53 (40)
Nausea	42 (32)
Hypertension	37 (28)
Any grade ILD/pneumonitis	8 (6)
Early onset[a]	2 (2)
Grade 3–4, >5% of patients	
Increased blood creatine phosphokinase	15 (11)
Hypertension	14 (11)
Increased lipase	10 (8)
Pneumonia	7 (5)

[a] Occurring within 14 days of brigatinib initiation.
ILD; interstitial lung disease; TEAE, treatment-emergent adverse event.

- Brigatinib treatment demonstrated clinically meaningful efficacy in this integrated analysis of patients with advanced or metastatic *ALK*+ NSCLC who progressed on prior alectinib in the ALTA-2 or J-ALTA trials

- Safety results were consistent with the known profile of brigatinib, with no new safety findings observed

- Final manuscripts for both studies are in preparation