Real-World Treatment Patterns and Effectiveness of Subsequent Treatments Following First-line (1L) Brigatinib for Patients with Anaplastic Lymphoma Kinase Positive (*ALK*+) Non-Small Cell Lung Cancer (NSCLC) from ALTA-1L

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Background

- Anaplastic lymphoma kinase-positive (*ALK*+) non-small cell lung cancer (NSCLC) occurs in approximately 5% of all NSCLC cases.[1,2]
- Targeted therapies for *ALK*+ NSCLC include first-generation (i.e., crizotinib) and next-generation tyrosine kinase inhibitors (TKIs).[3]
- Brigatinib is a next-generation ALK TKI, which showed superior clinical efficacy versus crizotinib for first-line (1L) treatment of patients with *ALK*+ NSCLC in the phase III ALTA-1L trial.[4]
- There is a lack of data on treatment patterns and outcomes post-1L brigatinib and limited information on subsequent anticancer therapies was collected under the trial protocol for ALTA-1L.

Objective

- To investigate the real-world treatment patterns and outcomes of subsequent treatments following discontinuation of 1L brigatinib in the ALTA-1L trial.

Methods

Study design and patients

- This was a retrospective, longitudinal, non-interventional, multinational, multisite-based chart review study.
- Eligible patients had received 1L brigatinib at participating sites in the ALTA-1L trial, who then discontinued 1L brigatinib during or after completion of the ALTA-1L trial (Figure 1).
- Patients were followed from the final dose of brigatinib (index date) until end of follow-up or death.
- Data were extracted from patient medical records (electronic case report forms), between November 4, 2022 and October 18, 2023 (database lock).

Study outcomes and statistical analyses

- Real-world time to treatment discontinuation (rwTTD) was defined as time from initiation to discontinuation of 2L treatment for any reason.
- Real-world progression-free survival (rwPFS) was defined as time elapsed from initiation of 2L treatment to disease progression or death.
- Real-world PFS2 (rwPFS2) was defined as time from randomization in ALTA-1L trial to first documented disease progression on 2L treatment or death due to any cause among those patients who initiated subsequent systemic anticancer treatments.
- Overall survival (OS) was defined as time from the date of randomization in the ALTA-1L trial until date of death.
- Patient characteristics and treatment patterns were summarized using descriptive statistics.
- Time-to-event analysis was performed using the Kaplan-Meier method. Analyses were performed using Statistical Analysis System version 9.4.
- Subgroups of interest included patients initiating 2L ALK TKIs or 2L lorlatinib.

Results

Patients

- Twenty sites enrolled eligible patients across 10 countries (Hong Kong, South Korea, Taiwan, United Kingdom, Spain, Italy, Netherlands, France, Denmark, and Austria).
- A total of 48 patients met the inclusion criteria and were included in the enrolled set (ENR); median follow-up was 12.4 months (**Table 1**).
- Median age in the ENR was 58 years, and the majority were female (54.2%), identified as Asian (54.2%), or were never smokers (62.5%) (**Table 1**).
- Of the 48 patients in the ENR, most common reason for 1L brigatinib discontinuation was progressive disease (PD) [34 (70.9%)]; median time from index date to start of 2L (95% confidence interval [CI]) was 4.0 (3.0-9.0) days.

Question What are the real-world treatment patterns and outcomes of subsequent systemic anticancer therapies post 1L brigatinib in patients with *ALK*+ NSCLC?

Study Design

Figure 1. Study design flow chart

Results

Figure 2. rwTTD for 2L ALK TKIs and 2L lorlatinib

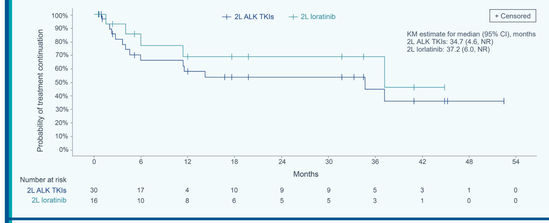
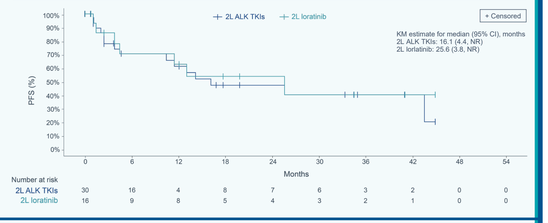


Figure 3. rwPFS for 2L ALK TKIs and 2L lorlatinib



Key takeaway Patients who received subsequent ALK TKIs (including lorlatinib) after 1L brigatinib had prolonged clinical benefit.

Results

Table 1. Baseline patient characteristics at index date

	ENR (n=48)	2L ALK TKI (n=30)	2L lorlatinib (n=16)
Age (years), median (range)	58 (33 – 85)	57.5 (34 – 82)	52.5 (40 – 77)
Female sex, n (%)	26 (54.2)	18 (60.0)	10 (62.5)
Race, n(%)			
Native Asian	26 (54.2)	15 (50.0)	7 (43.8)
White	21 (43.8)	14 (46.7)	8 (50.0)
Unknown	1 (2.1)	1 (3.3)	1 (6.3)
Geographic region, n (%)			
Asia Pacific	25 (52.1)	15 (50.0)	7 (43.8)
Europe	23 (47.9)	15 (50.0)	9 (56.3)
Cigarette smoking, n (%)			
Never	30 (62.5)	20 (66.7)	12 (75.0)
Current	2 (4.2)	0	0
Former	13 (27.1)	8 (26.7)	3 (18.8)
Unknown	3 (6.3)	2 (6.7)	1 (6.3)
Brain metastasis, n (%)	20 (41.7)	16 (53.3)	10 (62.5)
Follow-up (months), median (IQR)	12.4 (3.7, 27.0)	17.0 (6.1, 36.0)	14.8 (2.7, 33.2)

2L, second-line; ALK, anaplastic lymphoma kinase; ENR, enrolled set; IQR, inter-quartile range; TKI, tyrosine kinase inhibitor.

Treatment patterns

- A total of 40 (83.3%) out of the 48 patients in the ENR had received a subsequent systemic anticancer therapy (**Table 2**).
  - Thirty (75.0%) patients received an ALK TKI as first subsequent therapy; the most common were lorlatinib [16 (53.3%)], then alectinib [8 (26.7%)], and crizotinib [6 (20.0%)].

Table 2. First subsequent systemic anticancer therapies

	n (%)
Alectinib	7 (17.5)
Alectinib + chemotherapy	1 (2.5)
Chemotherapy	9 (22.5)
Chemotherapy + immunotherapy	1 (2.5)
Crizotinib	6 (15.0)
Lorlatinib	15 (37.5)
Lorlatinib + ramucirumab	1 (2.5)
Total	40 (100)

rwTTD

- Discontinuation of 2L ALK TKIs was reported for 14 (46.7%) patients; median rwTTD (95% CI) was 34.7 (4.6, not reached [NR]) months.
  - Probability of treatment continuation at 24 months was 53.1% (95% CI: 32.2, 70.2) (**Figure 2**).
- Discontinuation of 2L lorlatinib was reported for 5 (31.3%) patients; median rwTTD (95% CI) was 37.2 (6.0, NR) months.
  - Probability of treatment continuation at 24 months was 68.1% (95% CI: 35.4, 86.8) (**Figure 2**).

Tumor response

- Of 30 patients who received 2L ALK TKIs, 1 achieved a complete response (CR), 7 achieved a partial response (PR), 9 had stable disease (SD), 7 had PD, and 6 had no reported value. Real-world overall response rate (rwORR) (95% CI) was 33.3% (15.6, 55.3) and real-world disease control rate (rwDCR) (95% CI) was 70.8% (48.9, 87.4).
- Of 16 patients who received 2L lorlatinib, 1 achieved CR, 3 achieved PR, 6 had SD, 3 had PD and 3 had no reported value. rwORR (95% CI) was 30.8% (9.1, 61.4) and rwDCR (95% CI) was 76.9% (46.2, 95.0).

rwPFS, rwPFS2, and OS

- Median rwPFS (95% CI) was 16.1 (4.4, NR) months for 2L ALK TKIs and 25.6 (3.8, NR) months for 2L lorlatinib (**Figure 3**).
  - Estimated 24-month rwPFS (95% CI) was 47.0% (26.2, 65.3) for 2L ALK TKIs and 53.4% (23.9, 76.0) for 2L lorlatinib (**Figure 3**).
- Median rwPFS2 (95% CI) was 51.6 (25.9, NR) for 2L ALK TKIs and 74.7 (25.9, NR) for 2L lorlatinib (**Table 3**).
  - Estimated 24-month rwPFS2 (95% CI) was 78.4% (58.1, 89.7) for 2L ALK TKIs and 86.7% (56.4, 96.5) for 2L lorlatinib (**Table 3**).
- Median OS (95% CI) was 74.7 (30.0, NR) months for both 2L ALK TKIs and 2L lorlatinib (**Table 3**).
  - Estimated 36-month OS (95% CI) was 66.7% (46.9, 80.5) for 2L ALK TKIs and 75.0% (46.3, 89.8) for 2L lorlatinib (**Table 3**).

Table 3. rwPFS2 and OS for 2L ALK TKIs and 2L lorlatinib

	2L ALK TKI (n=30)	2L lorlatinib (n=16)
rwPFS		
Median rwPFS, months (95% CI)	16.1 (4.4, NR)	25.6 (3.8, NR)
24-month rwPFS, % (95% CI)	47.0 (26.2, 65.3)	53.4 (23.9, 76.0)
36-month rwPFS, % (95% CI)	40.3 (19.7, 60.1)	40.1 (12.1, 67.4)
rwPFS2		
Median rwPFS2, months (95% CI)	51.6 (25.9, NR)	74.7 (25.9, NR)
24-month rwPFS2, % (95% CI)	78.4 (58.1, 89.7)	86.7 (56.4, 96.5)
36-month rwPFS2, % (95% CI)	66.7 (45.5, 81.1)	73.3 (43.6, 89.1)
OS		
Median OS, months (95% CI)	74.7 (30.0, NR)	74.7 (30.0, NR)
24-month OS, % (95% CI)	73.3 (53.7, 85.7)	81.3 (52.5, 93.5)
36-month OS, % (95% CI)	66.7 (46.9, 80.5)	75.0 (46.3, 89.8)

2L, second-line; ALK, anaplastic lymphoma kinase; CI, confidence interval; NR, not reached; OS, overall survival; rwPFS, real-world progression-free survival; TKIs, tyrosine kinase inhibitors.

Limitations

- Subset of included sites may have differed from brigatinib arm or overall ALTA-1L trial population; sites may not be representative of all sites in a given country.
- Patients who discontinued 1L brigatinib and received subsequent therapies may have differed from overall cohort of patients enrolled in brigatinib arm of ALTA-1L.
- The timing between patients discontinuing 1L brigatinib and receiving subsequent therapies may have differed within the cohort of patients included in the study.
- Use of retrospective chart review data may be associated with systematic under-reporting of information.
- Due to small sample size, KM estimates of median require cautious interpretation, particularly given the wide confidence intervals; study was not powered to detect differences between subgroups.

Conclusions

- Most patients started subsequent systemic anticancer therapy after the discontinuation of 1L brigatinib.
- Most common first subsequent therapies were ALK TKIs; lorlatinib was the most common targeted therapy.
- Patients treated with 1L brigatinib, followed by subsequent ALK TKIs (including lorlatinib), experienced prolonged clinical benefits.

References

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Disclosures

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