

Treatment Sequencing and Duration of Subsequent Tyrosine Kinase Inhibitors in ALK+ Non-Small Cell Lung Cancer Patients Treated with Brigatinib in the US

Mohammad Jahanzeb¹, Huamao Mark Lin², Yanyu Wu², Magdaliz Gorritz³, Catherine McGuinness³, Kainan Sun³, Chi-Chang Chen³, Pingkuan Zhang², D. Ross Camidge⁴

¹Florida Precision Oncology, a division of GenesisCare, Boca Raton, FL; ²Millennium Pharmaceuticals, Inc., Cambridge, MA, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA; ³IQVIA, Inc., Plymouth Meeting, PA; ⁴University of Colorado, Aurora, CO



Background

- Anaplastic lymphoma kinase (ALK) mutations occur in 3-5% of non-small cell lung cancer (NSCLC) cases.¹
- Though next-generation targeted therapies for ALK+ NSCLC are associated with improved clinical outcomes, tumors develop resistance and require subsequent therapies.
- Real-world evidence describing ALK TKI sequencing is limited.

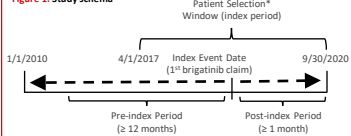
Objectives

- To understand post-brigatinib treatment patterns and duration of post-brigatinib ALK TKI therapy in the real-world setting.

Study design

- This retrospective cohort study utilized IQVIA's US-based Longitudinal Patient-Centric Pharmacy Claims Database (LRx), which includes prescription transaction data from pharmacies, payers, software providers and transactional clearinghouses.
- All patients with ≥1 claim for brigatinib between 01-Apr-2017 and 30-Sep-2020 were identified for analysis. Patients were indexed on their first brigatinib claim.
- Patients were ≥18 years of age on the index date, had at least 12 months of pre-index observation, and were continuously followed post-index until brigatinib discontinuation (≥ 90-day gap in brigatinib therapy or switch to another ALK TKI) or the end of follow-up. **Figure 1**
- All available data prior to the index date was used to identify prior ALK TKI therapies.
- This study complied with all applicable laws regarding patient privacy. No direct subject contact or primary collection of individual human subject data occurred. Informed consent, ethics committee or IRB approval were not required

Figure 1. Study schema



*Patient selection window based on date of US approval of brigatinib

Methods

Time to treatment discontinuation (TTD)

- Treatment was considered discontinued if:
 - There was a ≥ 90-day gap in brigatinib therapy
 - A new ALK TKI therapy was initiated

- Patients who did not meet this definition were censored at the end of available follow-up.
- Time to treatment discontinuation was defined as the number of months between the start of brigatinib treatment to the earliest of: last day of supply, switch date, or end of follow-up.

Adherence

- Medication possession ratio (MPR) was defined as the sum of the days' supply for all brigatinib claims while on treatment, divided by the treatment duration (i.e., time to treatment discontinuation defined above).
- Adherence was defined as MPR ≥ 80%.
- Dose compliance scores (DCS) were calculated as the sum of doses received from the first to the last prescription of brigatinib prior to discontinuation, divided by the perfect compliance dose (per label; 7 days at a dose of 90 mg/day followed by a maintenance dose of 180 mg/day for the duration of therapy).

Data analysis

- Mean, median, standard deviation (SD) and 95% confidence intervals (CI) were generated as measures of central tendency and variance for continuous variables; frequencies and percentages for categorical variables.
- Time to treatment discontinuation and the proportion of patients on therapy at 3, 6, and 12-months post-index were estimated using Kaplan-Meier analysis.

Results

- In total, 413 brigatinib patients were included in the study.

Patient characteristics

- The (mean [SD]) age was 57.9 (12.9) years, and 58.4% were females. Most patients had third party or Medicare Part D insurance. The median follow up time from initiation of brigatinib was 8.4 months. **Table 1**

Brigatinib treatment patterns

- Adherence to therapy and DCS were high across brigatinib cohorts.
- Median (95% CI) time to brigatinib discontinuation was 10.3 (8.2-15.0) months. **Table 2**

Treatment sequencing

- 195 patients had front-line crizotinib with or without subsequent ALK TKIs, 133 had crizotinib followed by alectinib and/or ceritinib, 62 had only crizotinib, 99 had only alectinib, and 80 had no observed ALK TKI.
- The most commonly received therapy immediately prior to initiating brigatinib was alectinib, received by 212 (51.3%) patients.

- 167 (40.4%) of brigatinib patients discontinued or switched to another ALK TKI.
- Among patients who discontinued brigatinib, 100 (59.9%) received subsequent ALK TKIs.
- Lorlatinib was the most common next ALK TKI (57%), followed by brigatinib retreatment (16%), alectinib (13%), ceritinib (10%), and crizotinib (4%). **Table 3**

Table 1. Patient characteristics

	Total brigatinib patients N=413
Age, mean (SD)	57.9 (12.9)
Female sex, n (%)	241 (58.4%)
Region, %	
Northeast	72 (17.4%)
Midwest	91 (22.0%)
South	99 (24.0%)
West	104 (25.2%)
Unknown	47 (11.4%)
Payer type, %	
Third Party	267 (64.6%)
Medicaid	13 (3.1%)
Medicare Part D	125 (30.3%)
Cash	8 (1.9%)
Follow-up months, median	8.4

Table 2. Index brigatinib therapy adherence and duration

	Total brigatinib patients N=413
MPR (mean, SD)	1.1 (0.4)
% Adherent	92.7%
DCS (mean, SD)	1.0 (0.5)
TTD (median, 95% CI)	10.3 (8.2, 15.0)

MPR: Medication possession ratio; DCS: dose compliance score; SD: standard deviation; CI: confidence interval

Table 3. Post-brigatinib treatment patterns and duration

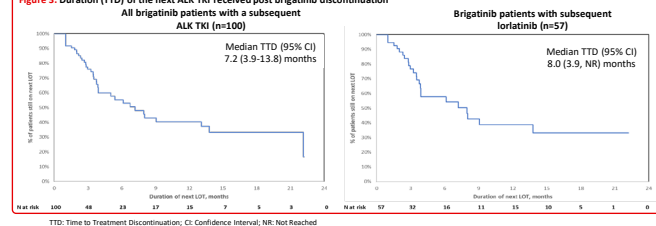
Characteristic	Total brigatinib patients N=413
Patient status at the end of follow up (N)	
Discontinued brigatinib	167 40.4%
Still on index brigatinib	179 43.4%
Unknown	67 16.2%
Number of patients had a subsequent ALK TKI	100 24.2%
Crizotinib	4 4.0%
Alectinib	10 10.0%
Ceritinib	13 13.0%
Lorlatinib	57 57.0%
Brigatinib	16 16.0%
Duration of next ALK-TKI therapy, Median (95% CI)	7.2 (3.9, 13.8)
Survival probability of next ALK-TKI therapy at: (%)	
3 months	75.9%
6 months	55.3%
12 months	40.4%
Duration of lorlatinib post brigatinib, months	
Median TTD (95% CI)	8.0 (3.9, NR)

NR: not reached; TTD: time to treatment discontinuation

Duration of subsequent ALK TKIs **Figure 3**

- The median (95% CI) TTD of the post-brigatinib ALK TKI was 7.2 (3.9-13.8) months
- In patients who received lorlatinib after brigatinib was discontinued, median (95% CI) lorlatinib TTD was 8.0 (3.9-not reached) months

Figure 3. Duration (TTD) of the next ALK TKI received post brigatinib discontinuation



Conclusions

- This US-based real-world study provides early insight into ALK TKI treatment sequencing and duration following brigatinib therapy in NSCLC.
- Results suggest that brigatinib has real-world durable clinical benefits for patients. Patients using brigatinib in later line settings stayed on therapy for a significant duration of time with high adherence.
- Treatment with subsequent ALK TKIs can still bring benefit to patients after discontinuing brigatinib, suggesting that brigatinib could be used in earlier lines.
- More formalized prospective data are needed to establish sequencing recommendations.

Limitations

- Results may be limited by the fact that the database does not include all specialty pharmacies that dispense brigatinib and other ALK TKIs, potentially yielding a data set that does not contain all treatment history and is not necessarily representative of all brigatinib/ALK TKI patients.
- A study of larger sample sizes and longer follow up periods, as well as real-world clinical effectiveness data (i.e., clinical endpoints) is warranted.
- Dosing data may be limited by the fact that it was derived from days of supply, tablet strength, and quantity dispensed (vs. prescribing instructions). Efficacy data were only indirectly inferred from duration of therapy.

References

- Camidge DR, Kim HR, Ahn M, et al. (2020) Journal of Clinical Oncology. doi: 10.1200/JCO.20.00505

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Disclosures

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