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. 2 Real-world evidence describing ALK TKI sequencing is limited. 2

**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 (LRK), which includes prescription transaction data from pharmacies, payers, software providers and transactional clearinghouses. 2 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. All patients ≥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 in brigatinib switch or 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.

**Methods**

**Patient Selection**

- 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 initiating brigatinib 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 at brigatinib initiation was 57.9 (12.0) years, and 58.4% were females. Most patients had third party or Medicare Part D insurance. The median number of months between initiation ofbrigatinib 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
    - 355 patients had front-line crizotinib with or without subsequent ALK TKS, 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.

**Limitations**

- Results may be limited by the fact that the database does not include all specialty pharmacies that dispense brigatinib and other ALK TKS, 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 a larger median follow up time of ALK TKI re-treatment (i.e. real world clinical effectiveness data (i.e., clinical endpoints) is warranted.

**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 lines of therapy had substantial improvement in duration and quality of life compared to previous therapies (i.e., prescribing instructions). Efficacy data were only indirectly inferred from duration of therapy.

**References**


**Funding Source**

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**Table 1. Patient characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total brigatinib patients (n=413)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>57 (9.1 ± 2.8)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>242 (58.4%)</td>
</tr>
<tr>
<td>Region, %</td>
<td>72 (17.4%)</td>
</tr>
<tr>
<td>Northeast</td>
<td>165 (105.2%)</td>
</tr>
<tr>
<td>Midwest</td>
<td>91 (22.0%)</td>
</tr>
<tr>
<td>West</td>
<td>30 (40.4%)</td>
</tr>
<tr>
<td>South</td>
<td>47 (11.4%)</td>
</tr>
<tr>
<td>Prior reg, %</td>
<td>67 (16.3%)</td>
</tr>
<tr>
<td>First line</td>
<td>267 (64.6%)</td>
</tr>
<tr>
<td>Second line</td>
<td>167 (40.4%)</td>
</tr>
<tr>
<td>Medicare</td>
<td>113 (27.1%)</td>
</tr>
<tr>
<td>Medicare Part D</td>
<td>125 (30.3%)</td>
</tr>
<tr>
<td>Cash</td>
<td>82 (19.9%)</td>
</tr>
<tr>
<td>Follow-up months, median</td>
<td>8.4</td>
</tr>
</tbody>
</table>

**Table 2. Index brigatinib therapy adherence and duration**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total brigatinib patients (n=413)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPR (mean, SD)</td>
<td>0.81 (0.2)</td>
</tr>
<tr>
<td>% Adherent</td>
<td>72.7%</td>
</tr>
<tr>
<td>DCS (mean, SD)</td>
<td>0.8 (0.5)</td>
</tr>
<tr>
<td>TTD (median, CI)</td>
<td>10.3 (8.2, 15.0)</td>
</tr>
</tbody>
</table>

**Table 3. Post-brigatinib treatment patterns and duration**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total brigatinib patients (n=413)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient status at the end of follow-up (N)</td>
<td>167 (40.4%)</td>
</tr>
<tr>
<td>Discontinued brigatinib</td>
<td>179 (43.4%)</td>
</tr>
<tr>
<td>No observed ALK TKI</td>
<td>67 (16.2%)</td>
</tr>
<tr>
<td>Number of patients who had a subsequent ALK TKI</td>
<td>100 (24.2%)</td>
</tr>
<tr>
<td>Crizotinib</td>
<td>4 (0.9%)</td>
</tr>
<tr>
<td>Alectinib</td>
<td>10 (10.0%)</td>
</tr>
<tr>
<td>Ceritinib</td>
<td>15 (13.6%)</td>
</tr>
<tr>
<td>Lorlatinib</td>
<td>17 (16.0%)</td>
</tr>
<tr>
<td>Brigatinib</td>
<td>14 (10.0%)</td>
</tr>
<tr>
<td>Continued on and off ALK TKI therapy</td>
<td>11 (2.6%)</td>
</tr>
<tr>
<td>Total duration of brigatinib therapy (months)</td>
<td>8.0 (3.6, 13.8)</td>
</tr>
</tbody>
</table>

**Figure 1. Study scheme**

**Figure 2. Treatment Sequencing and Duration of Subsequent Tyrosine Kinase Inhibitors in ALK+ Non-Small Cell Lung Cancer Patients Treated with Brigatinib in the US**

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

- Brigatinib patients with subsequent lorlatinib (n=17)
- Brigatinib patients with subsequent alectinib (n=16)
- Brigatinib patients with subsequent ceritinib (n=15)
- Brigatinib patients with subsequent crizotinib (n=10)
- Brigatinib patients with subsequent brigatinib (n=13)