Quality-adjusted survival with brigatinib versus crizotinib in ALK-positive (ALK+) non-small cell lung cancer (NSCLC): Results from the ALTA-1L trial


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Background
• Anaplastic lymphoma kinase (ALK) gene rearrangements occur in 3-5% of patients with NSCLC.1-3 Tumors harboring ALK gene rearrangements are sensitive to ALK kinase inhibitors (TKIs).

• Brigatinib was approved by the US Food and Drug Administration for the treatment of ALK-positive NSCLC in November 2019.

• The ALTA-1L trial randomized 150 ALK+ NSCLC treatment-naïve patients to brigatinib 90 mg or crizotinib 250 mg once daily.

• Both BIRC- and INV-assessed progression were used for this post-hoc analysis.

• Quality-adjusted survival (Q-TWiST) is a commonly used method for comparing health outcomes that takes into account both health-related quality of life (HRQoL) and survival.

Methods
• Both BIRC- and INV-assessed progression were used for this post-hoc analysis.

• Quality-TWiST (% improvement) > 10% was considered clinically important at baseline.

• A subgroup analysis was performed for patients without or with brain metastasis at baseline, respectively.

• All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results
• Partitioned survival curves at 50 months of follow-up are shown in Figure 1.

• Among patients with brain metastases, differences in Q-TWiST and QA-PFS between brigatinib and crizotinib were statistically significant at all time points.

• Differences in Q-TWiST and QA-PFS were consistent with the results of the randomized phase II trial.

• A subgroup analysis was performed in patients without or with brain metastasis at baseline, respectively.

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• All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC, USA).

Table 1: Mean Duration in Health State and Q-TWiST at 50 Months of Follow-up (overall population)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (SE)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brigatinib</td>
<td>22.54 (1.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Crizotinib</td>
<td>23.60 (1.13)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2: Subgroup Analysis of Q-TWiST and QA-PFS Among Patients With Brain Metastasis at Baseline

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (SE)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brigatinib</td>
<td>21.90 (1.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Crizotinib</td>
<td>22.68 (1.98)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Discussion
• There were significant benefits of brigatinib vs. crizotinib in quality-adjusted survival time measured by the Q-TWiST method in overall population.

• There were significant improvements in Q-TWiST and QA-PFS for brigatinib vs. crizotinib among all patients and those without and with brain metastases at baseline.

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• The study was associated with a few limitations:

• All endpoints were measured by the Q-TWiST method in overall population.

• Only grade 3/4 adverse events were included, and the same utility value was assigned to the different adverse events.

• The current analysis was not designed to compare the length of grade 3/4 adverse events owing to limited data availability. This could lead to overestimation of time spent in TOX.

Conclusion
• In patients with advanced ALK+ NSCLC, frontline treatment with brigatinib was associated with significant and clinically important gains in Q-TWiST and QA-PFS compared to crizotinib.

• The Q-TWiST assessment result is supportive of the study’s primary endpoint.

• These results further support brigatinib as a frontline treatment for ALK+ NSCLC.

References


Disclosures

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