Health-related quality of life in patients with ALK+ non-small cell lung cancer in the phase 3 CROWN study

Background
- Lorlatinib is a third-generation ALK tyrosine kinase inhibitor designed to inhibit a variety of ALK rearrangements that develop with first- and second-generation inhibitors such as crizotinib1
- Lorlatinib is highly potent, with the ability to penetrate the blood-brain barrier to target brain metastases2

In an interim analysis of the phase 3 CROWN study (NCT03352068), lorlatinib resulted in significantly longer progression-free survival and a higher frequency of intracranial response vs crizotinib at the first-line treatment in patients with advanced ALK-positive NSCLC3,4
- Lorlatinib-treated patients had a higher incidence of grade 3/4 adverse events than patients who received crizotinib1

Here, we report patient-reported outcomes (PROs) from the CROWN study to determine the effects of lorlatinib or crizotinib on HRQoL.

Methods
- The CROWN trial is an ongoing, global, randomized, phase 3 trial comparing lorlatinib vs crizotinib in patients with ALK-positive NSCLC4
- Patients were randomized 1:1 to receive lorlatinib 100 mg orally once daily or crizotinib 250 mg orally twice daily in 28-day cycles until disease progression, death, withdrawal of consent, or unacceptable toxic effects (Figure 1).
- HRQoL was assessed using the EQ-5D-5L questionnaire, which was completed by patients at baseline and at least 1 postbaseline PRO assessment.
- The estimated minimal important differences in EQ VAS and EQ-5D-5L index scores in lung cancer are 7 to 12 points and 0.06 to 0.08, respectively
- A data cutoff of September 20, 2021, was used without adjustments for multiple comparisons

Results (data cutoff: September 20, 2021)
- Among the patients in the PRO population, 148 received lorlatinib and 140 received crizotinib
- The mean baseline EQ VAS score was 71.6 with lorlatinib and 70.4 with crizotinib, and baseline EQ-5D-5L index scores were 0.776 and 0.750, respectively (Table 1)
- Patients treated with lorlatinib had higher EQ VAS and EQ-5D-5L index scores compared with baseline (Figures 2 and 3) and there was a significant difference in EQ VAS score with lorlatinib vs crizotinib (estimated mean difference, 4.45; 95% CI, 0.94-7.96; Table 2)
- Intergroup differences in EQ VAS scores were observed at each time point during the 60-week treatment period (Figure 2).

These findings support the efficacy of lorlatinib with an additional benefit of improved HRQoL, as summarized by EuroQol 5-dimension 5-level (EQ-5D-5L) scores

Conclusions
- Improvements in health-related quality of life (HRQoL) were observed with lorlatinib treatment in patients with advanced anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) with or without brain metastases
- These findings support the efficacy of lorlatinib with an additional benefit of improved HRQoL, as summarized by EuroQol 5-dimension 5-level (EQ-5D-5L) scores

Table 1: Mean baseline scores

<table>
<thead>
<tr>
<th> </th>
<th>Lorlatinib</th>
<th>Crizotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients, n=288</td>
<td>147</td>
<td>140</td>
</tr>
<tr>
<td>EQ-5D-5L index (0-1)</td>
<td>0.776 (0.7427-0.8086)</td>
<td>0.750 (0.7102-0.7893)</td>
</tr>
<tr>
<td>EQ VAS (0-100)</td>
<td>71.6 (66.78-76.8)</td>
<td>70.4 (65.29-75.03)</td>
</tr>
</tbody>
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No difference in mean EQ-5D-5L index score was observed between treatment arms (P=0.4781) (Table 3)

Table 2: Longitudinal mixed-effects regression analysis for EQ VAS scores

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<tr>
<td>Estimated mean difference (95% CI)</td>
<td>4.45 (0.94-7.96)</td>
<td>0.02 (0.01 to 0.03)</td>
</tr>
<tr>
<td>No difference in mean EQ-5D-5L index score was observed between treatment arms (P=0.4781) (Table 3)</td>
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</tbody>
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No differences in mean EQ-5D-5L index scores between treatment arms were observed in patients with and without brain metastases (Table 3)

Figure 2: Change from baseline for EQ VAS

Figure 3: Change from baseline for EQ-5D-5L index scores

Figure 4: Absolute scores for EQ VAS

Figure 5: Absolute scores for EQ-5D-5L index