Quality of life (QoL) and self-reported function with ripretinib in ≥4-line therapy for patients with gastrointestinal stromal tumors (GIST): Analyses from INVICTUS

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INTRODUCTION

• Gastrointestinal stromal tumor (GIST) is a rare sarcoma accounting for 1%–2% of all malignancies.
• Primary mutations in receptor tyrosine kinase (RTK) or platelet-derived growth factor receptor alpha (PDGFRα) occur in 90% of patients with GIST.

• In May 2020, the US FDA approved ripretinib for the treatment of adult patients with advanced GIST who have received prior treatment with ≥3 or ≥4 kinase inhibitors, including imatinib.

• Ripretinib is a novel switch-inhibitor tyrosine kinase inhibitor (TKI) that is designed to broadly inhibit cKIT and PDGFRα signaling through a dual mechanism of action.

• INVICTUS (NCT03393755) is a randomized, double-blind, placebo-controlled phase 3 trial of ripretinib in advanced GIST patients who received at least imatinib, sunitinib, and regorafenib.

• Patients demonstrating a significant improvement in median progression-free survival vs placebo (6.3 vs 1 month, respectively; hazard ratio [HR] = 0.15 [95% CI 0.06–0.35]; P < 0.0001) and clinically meaningful median overall survival vs placebo (15.1 vs 6.4 months; HR = 0.36 [95% CI 0.21–0.59]; nominally P = 0.004, with a well-tolerated safety profile.

• Here, we summarize patient-reported outcomes (PROs) from patients receiving ripretinib or patients receiving placebo from the INVICTUS trial.

METHODS

• In INVICTUS, 129 patients were randomized 2:1 to receive ripretinib 150 mg once daily (n = 85) or placebo (n = 44; one patient did not receive drug).

• PROs were assessed using questions from the EuroQol 5D (EQ-5D-5L) and the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), Table 1.

• All analyses compared the change from baseline on cycle 1 day 1 (C1D1) to cycle 2 day 1 (C2D1) between ripretinib and placebo.

• Comparisons were only made out to cycle 2 day 1 due to the low number of patients in the placebo group.

RESULTS

• Ripretinib was associated with a significant increase in the patients’ self-reported health status on the EQ-5D-5L VAS while placebo was associated with a decline (P = 0.004; Figure 3A).

• Patients receiving ripretinib reported better physical and role functioning on the EORTC QLQ-C30 compared with the decline observed in patients receiving placebo (P = 0.004; P < 0.001; Figure 3A).

• Patients receiving ripretinib had higher perceptions of their overall health and quality of life compared with patients receiving placebo (both P < 0.001; Figure 3B).

• Differences between treatment arms were clinically significant (using threshold for meaningful change).

• Patients receiving ripretinib reported stable PROs on min PRO measures out to cycle 10 (Figure 4).

CONCLUSIONS

• In the INVICTUS phase 3 study, ripretinib demonstrated a significant improvement in PFS and a clinically meaningful overall survival benefit compared with placebo; five key quality of life measures tested showed improvement in patients with ≥4-line advanced GIST receiving ripretinib compared with declining measures in patients receiving placebo.

• Patients in the ripretinib arm had consistently stable PROs and the measures suggest these patients were able to maintain quality of life while PRs declined sharply in the placebo arm.

• The differences in PRO measurements between patients receiving ripretinib and those receiving placebo were clinically significant.

Table 1. Patient reported outcomes assessments

<table>
<thead>
<tr>
<th>Question</th>
<th>Cycle 1 D1 (baseline)</th>
<th>C1D1</th>
<th>Cycle 2 Day 1 (Baseline)</th>
<th>C2D1</th>
<th>Change C1D1 to C2D1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall quality of life C30</td>
<td>70.1 ± 24.1</td>
<td>−16.1</td>
<td>66.4 ± 28.9</td>
<td>−22.7</td>
<td>−5.7</td>
</tr>
<tr>
<td>Physical function C30</td>
<td>42.9 ± 24.8</td>
<td>−7.1</td>
<td>49.1 ± 26.7</td>
<td>0.0</td>
<td>6.2</td>
</tr>
<tr>
<td>Role function C30</td>
<td>46.4 ± 30.1</td>
<td>−12.2</td>
<td>58.6 ± 30.0</td>
<td>16.3</td>
<td>12.5</td>
</tr>
<tr>
<td>Social function C30</td>
<td>48.6 ± 29.2</td>
<td>−6.9</td>
<td>41.8 ± 27.7</td>
<td>−6.8</td>
<td>−11.7</td>
</tr>
<tr>
<td>Emotional function C30</td>
<td>50.2 ± 28.6</td>
<td>0.8</td>
<td>50.5 ± 29.8</td>
<td>0.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Global health perceptions C30</td>
<td>70.0 ± 27.1</td>
<td>−5.7</td>
<td>64.3 ± 29.0</td>
<td>−5.7</td>
<td>−5.7</td>
</tr>
</tbody>
</table>

Figure 4. Longitudinal change in PRO scores from baseline in the ripretinib arm.

A) EQ-5D-5L VAS

B) EORTC QLQ-C30

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References


2. References in support of this article, and all author disclosures can be found in the Supporting Information.

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