Spleen volume reduction (SVR) predicts overall survival (OS) in myelofibrosis (MF) patients on pacritinib (PAC) but not best available therapy (BAT): PERSIST-2 landmark OS analysis

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INTRODUCTION

• Myelofibrosis (MF) is a life-limiting malignancy characterized by marrow fibrosis, splenomegaly, and progressive cytopenias.
• Pacritinib (PAC) is a JAK1-sparing inhibitor of JAK2/IRAK1/ACVR1,2 that demonstrated spleen volume response (SVR) benefit vs best available therapy (BAT; including ruxolitinib [RUX]) in MF patients with platelets ≤100 to 10% in the PERSIST-2 study.3
• JAK2 inhibitors can reduce spleen volume, which is considered a surrogate for disease response.

AIM

• To assess whether SVR on PAC or on BAT (including RUX) is associated with prolonged survival in MF patients with thrombocytenia.

METHODS

This analysis includes PERSIST-2 patients who were alive and on study at the start of the week 12 SVR window (week study week 10) on PAC 200 mg twice daily (BID) and on BAT.

• Week 12 SVR was evaluated using various volume reduction thresholds: ≥20%, ≥35%, ≥50%, and ≥10%.
• OS was evaluated among patients who achieved SVR vs. non-responders at each threshold and among patients who responded to either therapy or did not respond to therapy.
• Baseline OS was compared using the log-rank test. The impact of baseline imbalances between groups was assessed using Cox modeling.

RESULTS

• Among all tested SVR response thresholds, SVR ≥10% demonstrated the greatest separation in OS curves between responders vs. non-responders on PAC, but not on BAT (Figure 1).
• Compared to SVR ≥10% responders, non-responders had smaller spleen volumes and were more likely to require red blood cell (RBC) transfusions at baseline, shown in Table 1.

Table 1. Characteristics of SVR ≥10% Responders and Non-Responders

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>PAC 200 mg BID</th>
<th>BAT</th>
</tr>
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<tbody>
<tr>
<td>R-NeDs (N=65)</td>
<td>N-R=24</td>
<td>N-R=38</td>
</tr>
<tr>
<td>Age, median</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>DIPSS high risk</td>
<td>16%</td>
<td>18%</td>
</tr>
<tr>
<td>PLT count (≥100), median</td>
<td>68</td>
<td>67</td>
</tr>
<tr>
<td>Hemoglobin, median</td>
<td>9.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Requires RBC transfusion</td>
<td>36%</td>
<td>56%</td>
</tr>
<tr>
<td>Prior JAK2 inhibitor</td>
<td>41%</td>
<td>50%</td>
</tr>
<tr>
<td>Spleen volume (cm³), median</td>
<td>2573</td>
<td>2044.5</td>
</tr>
<tr>
<td>Palpable spleen length (cm), median</td>
<td>15.0</td>
<td>12.75</td>
</tr>
</tbody>
</table>

• As PAC can be given at full dose regardless of platelet count, it is possible that PAC may offer a unique survival advantage for MF patients with moderate or severe thrombocytopenia who achieve ≥10% spleen reduction.

CONCLUSIONS

• In MF patients with thrombocytopenia (platelets ≤100 to 10%), achieving SVR ≥10% at week 12 on full-dose PAC was associated with significant OS benefit.
• By contrast, this association was not found with BAT, including patients on RUX (most at doses of 10 mg BID or less).

DISCLOSURES:

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REFERENCES:

ABBREVIATIONS: ABO, antibody-binding platelet antibody; BID, twice daily; BAT, best available therapy; PAC, pacritinib; P, palatini; R, ruxolitinib; SB, spleen biopsy; W&W, watch and wait.

CONCLUSIONS

• On the PAC arm, median dose intensity through week 12 was 100% (200 mg BID) among SVR ≥10% responders but 78% among on RUX ≤5 mg BID at the time of the landmark analysis.
• Of the 28 patients on BAT who achieved SVR ≥10%, 23 (82%) were treated with RUX prior to the week 12 SVR assessment. 11% (3/28) of patients on BAT who achieved SVR ≥10% died compared to a similar percent (14%, 8/56) on PAC.

DISCLOSURES:

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