**BACKGROUND**

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 that demonstrated spleen volume response (SVR) benefit vs best available therapy (BAT, including RUX) in MF patients with platelets ≤100 × 10^9/L in the PERSIST-2 study. 1,2

- JAK2 inhibitors can reduce spleen volume, which is considered a surrogate for disease response.

**OBJECTIVE**

To assess whether spleen volume response (SVR) on PAC or on BAT (including RUX) is associated with prolonged survival in MF patients with thrombocytopenia.

**METHODS**

This analysis includes PERSIST-2 patients who were alive and on study at the start of the week 12 SVR window (study week 10) on PAC 200 mg twice daily (BID) and on BAT. 1,2

- Week 12 SVR was evaluated using various volume reduction thresholds: ≥35%, ≥20%, ≥10%, and >0%.

- OS was evaluated among SVR responders vs. non-responders at each threshold based on landmark analysis methodology. Survival 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 ≤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.

- Achieving ≥20% reduction in palpable spleen length on PAC is associated with OS benefit (HR = 0.14 [95% CI: 0.07, 0.30], P = 0.0007), though the separation between responder and non-responder survival curves was not as great as at the SVR ≥10% threshold.

- Figure 1A, B

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PAC 200 mg BID</th>
<th>BAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>N=65</td>
<td>N=28</td>
</tr>
<tr>
<td>Age, median</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>DIPSS high risk</td>
<td>18.5%</td>
<td>46%</td>
</tr>
<tr>
<td>PLT count (×10^11/L), median</td>
<td>58</td>
<td>68</td>
</tr>
<tr>
<td>Hemoglobin (g/dL), median</td>
<td>9.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Requires RBC transfusion</td>
<td>38%</td>
<td>58%</td>
</tr>
<tr>
<td>Prior JAK2 inhibitor</td>
<td>45%</td>
<td>50%</td>
</tr>
<tr>
<td>Spleen volume (cm^3), median</td>
<td>2573</td>
<td>2094.5</td>
</tr>
<tr>
<td>Palpable spleen length (cm), median</td>
<td>15.00</td>
<td>12.75</td>
</tr>
</tbody>
</table>

**CONCLUSIONS**

- In MF patients with thrombocytopenia (platelets ≤100 × 10^9/L), 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).

**ACKNOWLEDGEMENTS**

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REFERENCES: