The Oral JAK2/IRAK1 Inhibitor Pacritinib Demonstrates Spleen Volume Reduction in Myelofibrosis Patients Independent of JAK2 V617F Allele Burden

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BACKGROUND

JAK2 Allele Burden in Myelofibrosis

- In patients with primary JAK2-mutated MF, lower JAK2 allele burden is associated with poor prognosis and poor response to treatment.1,3
- Patients with low allele burden (variant allele frequency <50%) have:
  - More anemia and leukopenia
  - Shorter overall survival
  - 5.5-fold lower chance of achieving a spleen volume response (SVR) with ruxolitinib2
- Patients with low JAK2 allele burden represent an area of unmet medical need as they are high-risk and underserved by available therapies.

Pacritinib as Therapy for Myelofibrosis

- Pacritinib is an oral JAK2/IRAK1 inhibitor6
- Unlike other JAK2 inhibitors, pacritinib does not inhibit JAK15
- Pacritinib leads to significant improvements in spleen volume response (SVR) compared to best available therapy (BAT) in two Phase 3 studies (PERSIST-1 and -2).6,7

METHODS

- A retrospective analysis of PERSIST-1 and PERSIST-2 was performed in which outcomes were stratified by JAK2 V617F mutation status and allele burden
- Baseline JAK2 V617F was quantified by PCR, and variant allele frequencies were binned by quartile
- The efficacy endpoint was the percentage of patients achieving ≥35% SVR (by MRI or CT scan) at Week 24 based on an intention-to-treat analysis
- Analysis was based on pooled results across the two studies for patients treated with pacritinib and those treated with BAT.

RESULTS

Table 1: Baseline Characteristics by JAK2 Mutation Status and Allele Burden

<table>
<thead>
<tr>
<th>JAK2 V617F</th>
<th>Allele Burden&lt;50%</th>
<th>Allele Burden≥50%</th>
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<tbody>
<tr>
<td>Positive</td>
<td>N=311 (211 1:1:1 pacritinib vs. BAT; 50% BID vs. BAT)</td>
<td>N=256 (170 2:1 pacritinib vs. BAT; 50% BID vs. BAT)</td>
</tr>
<tr>
<td>Age (median, range)</td>
<td>66.0 (33-84) years</td>
<td>67.0 (23-87) years</td>
</tr>
<tr>
<td>Platelets (median, µL)</td>
<td>97,000 (41-181,000)</td>
<td>75,000 (41-180,000)</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>≥80,000 µL</td>
<td>31%</td>
</tr>
<tr>
<td>RBC transf. dependent (%)</td>
<td>61%</td>
<td>53%</td>
</tr>
<tr>
<td>Spleen length (median)</td>
<td>10.0 cm</td>
<td>19.5 cm</td>
</tr>
<tr>
<td>Spleen volume (median)</td>
<td>1817 cm³</td>
<td>1904 cm³</td>
</tr>
<tr>
<td>Primary myelofibrosis (%)</td>
<td>76%</td>
<td>80%</td>
</tr>
</tbody>
</table>

Figure 1: Percent Change in Spleen Volume (Week 24) on Pacritinib vs. BAT Stratified by JAK2 Mutation Status and Allele Burden Quartile

CONCLUSIONS

- Pacritinib demonstrated clinical efficacy regardless of JAK2 allele burden or JAK2 mutation status
- No SVR response was observed for patients treated with best available therapy (including ruxolitinib) who had low JAK2 allele burden or JAK2 V617F-negative disease
- Pacritinib was associated with higher rates of SVR response than BAT among patients will low JAK2 allele burden (<50%):
  - Allele burden >0 to 25% response rate for pacritinib vs. BAT = 21% vs. 0% (P<0.001)
  - Allele burden >25 to 50% response rate for pacritinib vs. BAT = 15% vs. 0% (P=0.02)
- No SVR response was observed for patients treated with BAT (including ruxolitinib) who had low JAK2 allele burden or JAK2 V617F-negative disease.

REFERENCES


POSTER INFORMATION

This poster was presented at the 2019 American Society of Hematology Annual Meeting.