Bone Marrow Fibrosis by WHO Grade and Quantitative Image Analysis is Reduced by PRM-151 in Patients with Myelofibrosis and Associated with Improved Bone Marrow Morphology and Increased Platelet Counts


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Background

PRM-151: Recombinant Human Pentraxin-2 (PTX-2)

- PTX-2 is an endogenous regulator of tissue repair.
- PTX-2 binds to damaged tissue (e.g., monocytes/macrophages).
- PTX-2 prevents and reverses fibrosis in pre-clinical models.
- PTX-2 levels are low in myelofibrosis (MF) patients.

- Also low in patients with renal, pulmonary, and liver fibrosis

PRM-151 Adaptive Phase 2 Trial Design: Myelofibrosis

Stage 1: 27 Patients Enrolled

- Weekly PRM-151 10 mg/kg IV
- Monthly PRM-151 15 mg/kg IV

Stage 2: 120 Patients

- Any treatment arm from Stage 1 with 2 patients may be included
- Arms can be adapted for Stage 2

Results

11/23 Patients with Grade 2 or Grade 3 MF at Baseline Had Reduction ≥ 1 Grade During the 36-week Period

<table>
<thead>
<tr>
<th>Patients (N)</th>
<th>Best BM Fibrosis Grade After Baseline</th>
<th>BM Fibrosis Grade at Baseline</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Grade 3 (n=15)</td>
<td>7</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 2 (n=8)</td>
<td>0</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 1 (n=9)</td>
<td>0</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

Morphologic and CIA Evaluations Both Show Increase in BM Response Rate Over Time, with CIA Being More Sensitive than Morphology

- PLT responses to PRM-151 were correlated with decreased BM fibrosis by CIA.
- Trends were observed toward other indicators of improvement in the bone marrow microenvironment.
- CIA was performed on whole slide scans for objective quantification of fibrosis.
- Values of bone and reticulin fibers were compared across serial sections of each patient to determine the trend.
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Summary

- PRM-151 treatment in Stage 1 of this Phase 2 adaptive clinical trial resulted in:
  - Decreased BM fibrosis by WHO grade in 11/23 patients with Grade 2 or 3 fibrosis
  - Improvements in hemoglobin and platelets, including transfusion independence, in 10/21 patients with baseline Hgb < 100 g/L and/or platelets < 100 x 10^11/L
  - Reductions in symptoms in most patients, with 4 IWG symptom responses
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Conclusions

- Reduction in reticulin fibrosis in patients treated with PRM-151 was associated with reduction in collagen.
- Trends were observed toward other indicators of improvement in the bone marrow microenvironment.
- CIA was correlated with morphologic analysis and confirmed reduction in bone marrow fibrosis.
- CIA was more sensitive and quantitative with 72% of PRM-151 treated patients showing decreased BM fibrosis.
- PLT responses to PRM-151 were correlated with reduced BM fibrosis by CIA.
- BM responses in patients treated with PRM-151 in Stage 2 of this ongoing adaptive Phase 2 clinical trial will be assessed by Morphology, CIA, and PET-CT.