Pacritinib Demonstrates Efficacy Versus Best Available Therapy in Myelofibrosis Patients with Severe Thrombocytopenia in Two Phase 3 Studies

Ruben A. Mesa1, Moshe Talpaz2,3, Jean-Jacques Kiladjian4, Claire Harrison5, Srdan Verstovsek6, Sarah A. Buckley7, Karisse Roman-Torres7, John O. Mascarenhas8

INTRODUCTION

Myelofibrosis with Severe Thrombocytopenia

- Patients with myelofibrosis (MF) and severe thrombocytopenia (platelet count <50,000/µL) have advanced disease1 and poor prognosis.2,3
- Median survival for such MF patients is only 15 months vs. 4-7 years for patients with normal platelet counts.1,2
- Approved treatment options are limited for these patients, and they are often excluded from clinical trials due to the risk of treatment-related cytopenias.3
- These patients represent an area of serious unmet medical need.

Pacritinib Therapy for Myelofibrosis

- Pacritinib is an oral JAK2/IRAK1 inhibitor with minimal activity against JAK1.1
- Pacritinib demonstrated efficacy vs. best available therapy (BAT) in two Phase 3 studies (PERSIST-1 and PERSIST-2), both of which included patients with severe thrombocytopenia.

METHODS

- Patients from PERSIST-1 and PERSIST-2 with baseline platelet counts <50,000/µL were included in the analyses.
- Study design overviews are presented above. Notably, neither study had a lower limit on platelet count for eligibility.
- Efficacy analyses were performed on an intention-to-treat (ITT) population and included
  - The percentage of patients with SVR ≥35% at Week 24 on pacritinib vs. BAT.
  - The percentage of patients with TSS v2.0 reduction ≥50% at Week 24 on pacritinib vs. BAT. TSS scores were based on the 6-symptom score (early satiety, abdominal discomfort, night sweats, pruritus, bone pain, and pain under the ribs on the left side).
- Safety analyses were performed on all patients who received study drug.
- Cardiac and hemorrhagic events were defined using Standardized MedDRA Queries.

RESULTS

Baseline Patient Characteristics

- A total of 189 patients were included in the safety population, with 152 included in the ITT efficacy population for SVR and 117 in the ITT efficacy population for TSS.
- Key characteristics for the safety population are in Table 1.

Efficacy of Pacritinib vs. BAT

- Significantly more patients had an SVR ≥35% with pacritinib vs. BAT (23% vs. 2%, Figure 1).
- More patients had a TSS reduction ≥50% with pacritinib vs. BAT (25% vs. 11%, Figure 1).

Safety

- The most common treatment-emergent adverse events in this severely thrombocytopenic patient population were consistent with the overall Phase 3 study results and were generally manageable and lower grade (Table 2).
- There were similar high-grade (3/4) and fatal (grade 5) hemorrhagic events in pacritinib-treated patients:
  - Pacritinib: 14% Grade 3/4; 2% Grade 5
  - BAT: 14% Grade 3/4; 4% Grade 5
- There was similar high-grade (3 or 4) and fatal (grade 5) cardiac events in pacritinib-treated patients:
  - Pacritinib: 8% Grade 3/4; 3% Grade 5
  - BAT: 12% Grade 3/4; 7% Grade 5
- There was no excess in mortality in pacritinib-treated patients (HR 1.01 [95% CI 0.57-1.80]).

CONCLUSIONS

- Pacritinib demonstrates clinical efficacy in patients with myelofibrosis and severe thrombocytopenia, a patient population with serious unmet medical need.
- Pacritinib’s safety profile in this patient population is consistent with that seen in the general MF population, including patients treated with BAT.
- PACIFIC, a randomized phase 3 study, was designed to confirm the benefits of pacritinib in patients with MF and severe thrombocytopenia. This study has recently started enrollment and is ongoing.

REFERENCES


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