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

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INTRODUCTION

Myelofibrosis with Severe Thrombocytopenia

- Patients with myelofibrosis (MF) and severe thrombocytopenia (platelet count <50,000/µL) have advanced disease[1] 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).[2,3]
- Approved treatment options are limited for these patients, and they are often excluded from clinical trials due to the risk of treatment-related cytopenias.
- 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.[4]
- Pacritinib demonstrated efficacy vs. best available therapy (BAT) in two Phase 3 studies (PERSIST-1[5] and PERSIST-2[6]), both of which included patients with severe thrombocytopenia.

PERSIST-1

Key Eligibility
- Primary or secondary MF
- Any platelet count
- No prior treatment with JAK2 inhibitors

Randomization
- 2:1 pacritinib vs. BAT
- N=327

Pacritinib 400mg QD

BAT (excluding ruxolitinib)

Primary Endpoint
- ≥35% SVR at Week 24

PERSIST-2

Key Eligibility
- Primary or secondary MF
- Platelet count <100,000/µL
- Prior JAK2 inhibitor therapy allowed

Randomization
- 1:1:1 pacritinib vs. pacritinib vs. BAT
- N=311 (211 completed 24 weeks on study)

Pacritinib 400mg QD

Pacritinib 200mg BID

BAT (including ruxolitinib)

Co-Primary Endpoints*
- ≥35% SVR at Week 24
- ≥50% TSS reduction at Week 24

BAT, best available therapy; **SVR,** spleen volume response; **TSS**, total symptom score
* Primary analysis compared pooled pacritinib (400mg QD and 200mg BID) vs. BAT

Study Objective

- As clinical trial outcomes for patients with MF and severe thrombocytopenia have not been previously reported, a retrospective pooled analysis was performed on data from PERSIST-1 and -2 to better evaluate outcomes in this high-risk patient population.

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, pruritis, 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**.

Table 1: Key Demographic and Baseline Characteristics (Safety Population)

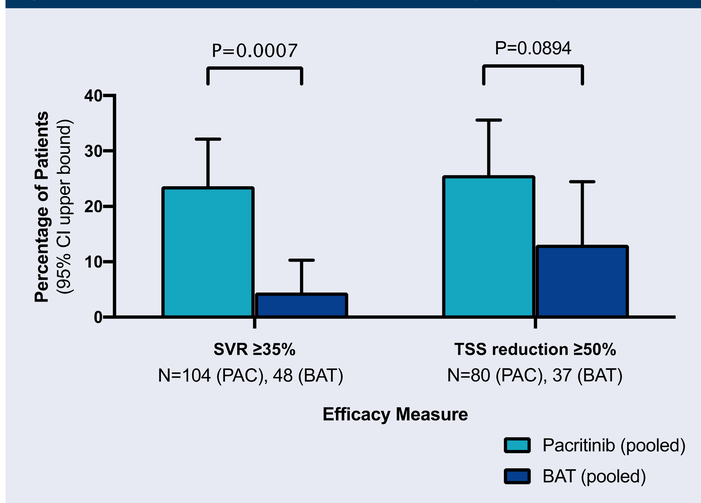
Characteristic	All Pooled Pacritinib Patients (n=132)	Pooled Pacritinib 400 mg QD (n=85)	Pacritinib 200 mg BID (n=47)	Pooled BAT (n=57)
Mean age, y	68.7	69.1	67.9	68.6
Female, %	39.4	37.6	42.6	50.9
≥65 years of age, %	71.2	71.8	70.2	68.4
Platelet count at baseline, /µL Median (Range)	 28,500 (6,000-49,000)	 28,000 (6,000-49,000)	 32,000 (6,000-49,000)	 25,000 (5,000-49,000)
Hemoglobin <10 g/dL, %	64.4	64.7	63.8	61.4
Marrow fibrosis grade 3, %	50.8	48.2	55.3	45.6

BAT=best available therapy, **BID**=twice daily, **MF**=myelofibrosis, **QD**=once daily.

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**).

Figure 1: Pacritinib vs. BAT Efficacy Outcomes (Week 24)



BAT=best available therapy, **SVR**=spleen volume response, **TSS**=total symptom score.

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]).

Table 2: Most Common (>15% in Any Group) Treatment-Emergent Adverse Events

Adverse Event, %	All Pooled Pacritinib (n=132)		Pooled BAT (n=57)	
	All Grade	Grade 3/4	All Grade	Grade 3/4
Diarrhea	60.6	5.3	12.3	1.8
Anemia	31.8	31.8	21.1	19.3
Nausea	29.5	1.5	12.3	1.8
Thrombocytopenia	34.1	34.1	21.1	21.1
Vomiting	26.5	0.8	5.3	1.8
Epistaxis	15.9	6.8	24.6	1.8
Peripheral edema	15.9	1.5	21.1	0
Abdominal pain	11.4	1.5	17.5	1.8

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.
- PACIFICA, 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.

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PosterCast