Efficacy of Pacritinib in Patients With Myelofibrosis Who Have Both Thrombocytopenia and Anemia

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CONCLUSIONS

- In patients with myelofibrosis who have both thrombocytopenia and anemia (bicytopenia), pacritinib demonstrates increased clinical efficacy for spleen volume reduction, symptom benefit, and red blood cell (RBC) transfusion response compared with best available therapy (BAT)
- Pacritinib is well-tolerated at full dose in patients with bicytopenia
- These findings suggest pacritinib may be an effective option to address the unmet need for patients with myelofibrosis who have both thrombocytopenia and anemia

BACKGROUND

- Both thrombocytopenia and anemia pose treatment challenges in patients with myelofibrosis
- RBC transfusion dependency and platelet count <100 × 10^9/L are associated with worse overall survival in patients with myelofibrosis[1]
- When these two cytopenias co-occur ("bicytopenia"), management becomes particularly challenging, and appropriate treatment selection is critical to optimize efficacy while minimizing myelosuppressive adverse events in patients with myelofibrosis
- Pacritinib is a JAK1-sparing inhibitor of JAK2/IRAK1/ACVR1[2,3] that has been studied at full dose in patients with myelofibrosis, regardless of baseline thrombocytopenia or anemia

AIM

- To present efficacy data on spleen volume reduction, symptom benefit, and RBC transfusion response in pacritinib-treated patients with moderate or severe bicytopenia

METHODS

- Patients treated with pacritinib 200 mg twice daily (BID) or BAT in PERSIST-2 with baseline bicytopenia (platelet count <100 × 10^9/L and hemoglobin <10 g/dL) were included in this retrospective analysis
- Outcomes of interest included spleen volume reduction (SVR) ≥35%, total symptom score (TSS; version 2.0, excluding tiredness) reduction ≥50%, Patient Global Impression of Change (PGIC), and transfusion independence response (TI-R) at week 24
  - TI-R was assessed among patients requiring RBC transfusion at baseline (within 90 days), with response defined as the absence of RBC transfusions over any 12-week period through 24 weeks (Gale criteria)
- Baseline characteristics are presented in the safety population (all treated); efficacy is presented in the intention-to-treat efficacy population (patients randomized ≥22 weeks prior to end of study)
- Overall survival was assessed in all randomized patients with baseline bicytopenia
- Statistical testing of efficacy endpoints was performed using Fisher's exact test

RESULTS

- Among 46 patients on pacritinib and 47 on BAT, baseline characteristics were generally similar between groups, respectively: median age (65 vs 68 years), platelet count (46 vs 46 × 10^9/L), and hemoglobin (8.4 vs 8.6 g/dL) (**Table 1**)
- A lower percentage of patients treated with pacritinib compared with BAT were receiving RBC transfusions (59% vs 77%) and had prior JAK inhibitor exposure (43% vs 55%) (**Table 1**)
- Most patients treated with pacritinib were able to maintain full doses over time
  - The median actual dose intensity for pacritinib was 400 mg/day
- A total of 21 out of 47 (45%) of patients in the BAT group received ruxolitinib
  - The median last total dose of ruxolitinib was 10 mg/day

RESULTS

Table 1. Patient Characteristics

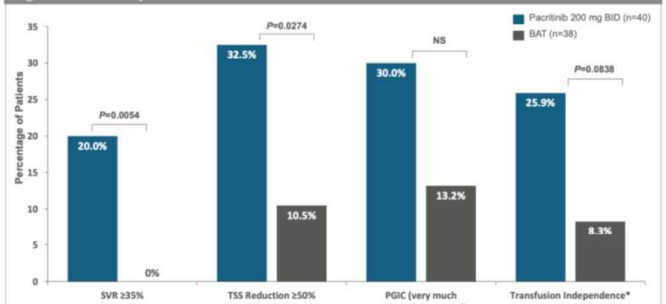
Baseline Characteristics	Pacritinib 200 mg BID n=46	BAT n=47
Age, years, median	65	68
DIPSS high risk, n (%)	14 (30.4)	20 (42.6)
Platelet count, × 10^9/L, median	46	46
Hemoglobin, g/dL, median	8.4	8.6
Patients with baseline RBC transfusions, n (%)	27 (58.7)	36 (76.6)
Prior JAK2 inhibitor, n (%)	20 (43.5)	26 (55.3)
Spleen volume, cm^3, median	2420.0	2392.9
Palpable spleen length, cm, median	15.5	14

BAT, best available therapy; BID, twice daily; DIPSS, Dynamic International Prognostic Scoring System; RBC, red blood count.

Efficacy Outcomes: Spleen and Symptoms at Week 24

- In the pacritinib group, 20% (8 of 40 patients) had SVR ≥35% compared with 0% (0 of 38 patients) in the BAT group (*P*=0.0054; **Figure 1**)
- Similarly, 32.5% of the patients in the pacritinib group had a ≥50% reduction in TSS compared with 10.5% of patients in the BAT group (*P*=0.0274; **Figure 1**)
- PGIC response (patient-reported symptoms "very much" or "much" improved) at week 24 was greater in the pacritinib group (30%) compared with BAT (13.2%; *P*=NS; **Figure 1**)

Figure 1. Efficacy Outcomes for Pacritinib vs BAT at Week 24



*TI-R was assessed among 27 patients treated with pacritinib and 36 patients treated with BAT who required RBC transfusion at baseline (within 90 days), with response defined as the absence of RBC transfusions over any 12-week period through 24 weeks (Gale criteria).
BAT, best available therapy; NS, not significant; PGIC, Patient Global Impression of Change; SVR, spleen volume reduction; TI-R, transfusion independence response; TSS, total symptom score (version 2.0, excluding tiredness).

- Similar efficacy results were noted in patients with baseline platelets <50 × 10^9/L:
  - In the pacritinib group, 19% (4 of 21 patients) had SVR ≥35% compared with 0% (0 of 21 patients) in the BAT group
  - Similarly, 23.8% of the patients in the pacritinib group had a ≥50% reduction in TSS compared with 9.5% of patients in the BAT group
  - PGIC response (patient-reported symptoms "very much" or "much" improved) at week 24 was greater in the pacritinib group (28.6%) compared with BAT (9.5%)

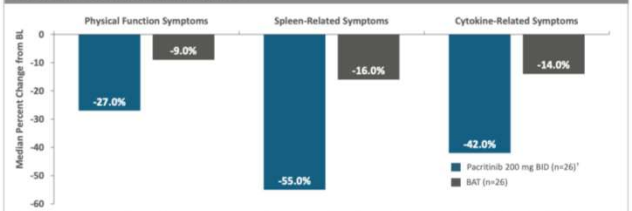
Efficacy Outcomes: Transfusion Independence

- Among the 27 patients on pacritinib and 36 on BAT who received RBC transfusions at baseline, 25.9% of patients on pacritinib and 8.3% of patients on BAT achieved TI-R (*P*=0.083; **Figure 1**)
- Additionally, 40.7% of patients on pacritinib compared with 11.1% on BAT achieved a >50% reduction in transfusions (*P*=0.0083)

Pacritinib Reduces All Subscale Symptoms

- Physical function-related, spleen-related, and cytokine-related symptoms showed a higher median percentage reduction in the pacritinib group compared with BAT (**Figure 2**)
  - Treatment effect was greatest for spleen-related symptoms

Figure 2. Median Percent Change in Subscale Symptoms* From Baseline to Week 24 for Pacritinib vs BAT



*Physical function scores (sum of 'tiredness' and 'inactivity'), spleen-related symptom scores (sum of 'abdominal discomfort', 'early satiety', and 'left rib pain'), and cytokine-related symptom scores (sum of 'itching', 'night sweats', and 'bone pain').
†Except for the spleen-related symptoms subscale, n=25.
BAT, best available therapy; BID, twice daily; BL, baseline.

Overall Survival

- The unadjusted hazard ratio for overall survival for pacritinib versus BAT was 0.74 (95% confidence interval, 0.27–1.98)

Safety

- A total of 22% patients in the pacritinib group reported at least one treatment-emergent adverse event (TEAE) leading to study drug discontinuation compared with 19% in the BAT group
- TEAEs that resulted in death were reported in 5 of 46 patients (11%) on pacritinib versus 8 of 47 patients (17%) on BAT

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DISCLOSURES

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