Impact of Pacritinib on Symptoms in Thrombocytopenic Myelofibrosis Patients Who Require RBC Transfusion

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Conclusions

- Pacritinib has previously demonstrated improvement in symptoms in patients with myelofibrosis (MF)
- This retrospective analysis shows that pacritinib provides substantial symptom benefit compared with best available therapy (BAT) or low-dose ruxolitinib, specifically in patients who require red blood cell (RBC) transfusion
- Pacritinib could therefore be a potential option to address an unmet need for patients with MF who are transfusion-dependent

Introduction

- Patients with MF and anemia experience a negative impact on both quality of life and prognosis[1]
- Clinical and economic burden is higher in patients with transfusion-dependent MF, thereby highlighting the need for therapeutic options that help limit transfusion dependence[2]
- Pacritinib, a JAK2/IRAK1/ACVR1 inhibitor, has demonstrated a clinical and statistically significant improvement in transfusion requirements in patients with MF who required RBC transfusion at baseline in the phase 3 PERSIST-2 study[3]

Aim

- To retrospectively evaluate the impact of pacritinib 200 mg twice daily (BID) versus BAT, including ruxolitinib, on symptom burden in patients requiring RBC transfusion in the phase 3 PERSIST-2 study

Methods

- This analysis focused on patients enrolled in PERSIST-2 who were randomized ≥12 weeks (≥22 weeks for efficacy analyses) prior to study termination, received pacritinib 200 mg BID or BAT (including ruxolitinib), and were RBC transfusion-dependent at baseline
- Symptom improvement was measured by Total Symptom Score (TSS; version 2.0, excluding tiredness) and Patient Global Impression of Change (PGIC) at week 24
- The proportion of patients in each group who achieved a transfusion independence response (TI-R; any 12-week interval with no RBC transfusions) by week 24 was determined
- Treatment arm comparisons (pacritinib versus BAT) were performed using Fisher's exact test

Results

- Baseline characteristics for the intention-to-treat efficacy population were similar between patients who received pacritinib (n=35), all BAT (including ruxolitinib; n=34), or ruxolitinib as BAT (n=13), including median platelet count (45 vs 45 vs 43 × 10^9/L) and hemoglobin (8.5 vs 8.7 vs 8.6 g/dL), respectively
- ≥50% of patients in each group had prior JAK inhibitor exposure and all patients required RBC transfusion at baseline
  - The median units per month of RBCs transfused over the past 90 days were 1.51 for the pacritinib group, 1.71 for the any BAT group, and 1.70 for the ruxolitinib as BAT group

Results

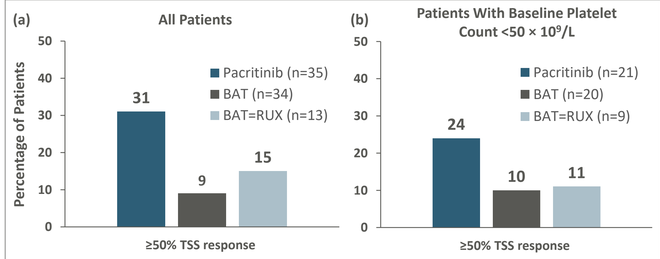
Pacritinib Maintains Full Dose Intensity

- The median dose intensity for pacritinib was 100% (median daily dose of 400 mg)
- The median total daily ruxolitinib dose was 10 mg at week 24

Efficacy Outcomes: TSS Response Greater With Pacritinib

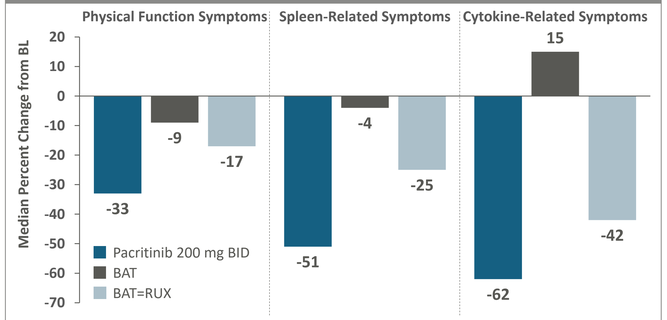
- A significantly greater proportion of patients treated with pacritinib versus BAT achieved a ≥50% TSS reduction (31% vs 9%; *P*=0.034), while 15% of patients achieved TSS reduction on ruxolitinib (**Figure 1a**)
- A similar trend for ≥50% TSS reduction was observed in patients with baseline platelets <50 × 10^9/L treated with pacritinib (24%) versus BAT (10%) or ruxolitinib (11%) (**Figure 1b**)

Figure 1. All Patients (a) and Patients with Baseline Platelet Count <50 × 10^9/L (b) Achieving ≥50% TSS Reduction



BAT, best available therapy; RUX, ruxolitinib; TSS, total symptom score (version 2.0, excluding tiredness).

Figure 2. Median Percent Change of Subscale Symptoms* from Baseline to Week 24



*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'). BAT, best available therapy; BID, twice daily; BL, baseline; RUX, ruxolitinib.

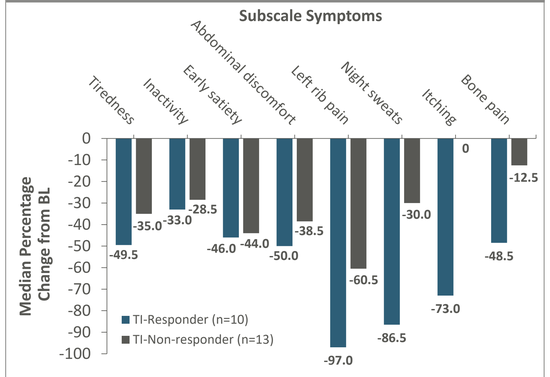
Reduction in Subscale Symptoms with Pacritinib

- TSS reduction on pacritinib was primarily due to reductions in both spleen- and cytokine-related symptoms (**Figure 2**)
- Physical function-related symptoms (excluded from the total score) also showed a higher median percent reduction for the pacritinib arm compared with BAT (tiredness: 37% vs 13%; inactivity: 30% vs 4%)
- In addition, a higher proportion of patients at week 24 reported symptoms as "very much" or "much" improved (PGIC) with pacritinib (37%) compared with BAT (9%, *P*=0.009), including ruxolitinib (8%)

A Greater Proportion of Patients on Pacritinib Achieved ≥50% TSS Reduction and TI-R

- Of the 11 patients on pacritinib with a TSS response, 6 (54.5%) also achieved TI-R. In contrast, no TSS responders on BAT achieved TI-R
- Greater individual symptom reduction was observed in TI-responders on pacritinib than TI-non-responders on pacritinib (**Figure 3**)

Figure 3. Individual Symptom Reduction by TI-Responders versus TI-Non-Responders

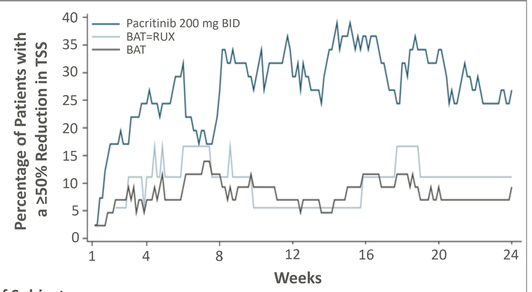


BL, baseline; TI, transfusion independent.

Rolling TSS Response Greater and More Consistent with Pacritinib

- Patients who were non-TI at baseline treated with pacritinib had a greater TSS response based on a 7-day moving average than those treated with BAT (including ruxolitinib), or ruxolitinib as BAT (**Figure 4**)

Figure 4. TSS Response Rate Based on 7-Day Moving Average per MPN-SAF TSS 2.0 Over Time



No. of Subjects							
Pacritinib 200 mg BID	39	37	32	32	31	25	22
BAT=RUX	16	14	14	12	12	9	7
BAT	40	36	36	33	29	22	18

BAT, best available therapy; BID, twice daily; RUX, ruxolitinib; TSS, total symptom score (version 2.0, excluding tiredness).

Safety

- In the safety population, the percentage of patients experiencing ≥1 treatment-emergent adverse event (TEAE) of grade ≥3 anemia was similar in the pacritinib (17.1%) and BAT (16.3%) arms
- A similar percentage of patients on pacritinib and BAT had a TEAE of fatigue (14.6% vs 14.0%)
- Fatigue TEAEs on pacritinib were reported by patients to be entirely low-grade (no grade ≥3 events) and did not require dose modification
- In contrast, 2 patients (4.7%) experienced ≥1 TEAE of grade ≥3 fatigue on BAT
  - One patient (2.3%) experienced a TEAE of fatigue that required dose reduction

References

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3. Oh S, et al. *Blood Adv* 2023;7:5835–5842.

Disclosures

SO: Consultancy: CTI BioPharma Corp., a Sobi company; **JM:** Speakers Bureau: Sobi, GSK, Incyte; **MS:** Lectures: Novartis, MDS, AOP Orphan, CTI BioPharma Corp., a Sobi company; **SB, PS, KRT:** employed by and received payment of unvested equity awards as an employee as part of an overall compensation package from CTI BioPharma Corp., A Sobi company; **AG:** Consultancy: GSK, Rain Oncology, AbbVie, and Disc Medicine.

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