Efficacy of Pacritinib for Spleen, Symptoms, and Anemia Benefit in Myelofibrosis Patients Across the Cytopenic Spectrum

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INTRODUCTION

- In patients with myelofibrosis (MF), JAK inhibitor therapy can improve both splenomegaly and disease symptoms.
- Commonly, dosing – and thus efficacy – of JAK1/2 inhibitors is limited in patients with cytopenic MF due to drug-induced exacerbation of cytopenias.[1,2]
- Pacritinib is a JAK1-sparing inhibitor of JAK2/IRAK1/ACVR1[3,4] that is approved by the Food and Drug Administration (FDA) in the United States for the treatment of adults with myelofibrosis who have a platelet count <50 x 10^9/L.
- Clinical studies of pacritinib have included patients across the cytopenic spectrum, including any grade of baseline (BL) anemia or thrombocytopenia.[5-7]

AIMS

- To describe the dosing and efficacy of pacritinib in patients with MF treated across two clinical trials (PERSIST-1 and PERSIST-2), stratified by degree of baseline thrombocytopenia and anemia.

METHODS

- Evaluable patients treated with pacritinib in the PERSIST-1 and PERSIST-2 studies were analyzed, stratified by baseline blood counts (5 subgroups):
  - Platelet count: <100 and ≥100 x10^9/L
  - Hemoglobin: <8, 8 to <10, and ≥10 g/dL
- Efficacy was assessed with the following metrics:
  - Spleen volume reduction (SVR) at week 24 based on 4 different response thresholds (>0%, ≥10%, ≥25%, and ≥35%) and median percent change in spleen volume over time
  - Total symptom score (v2.0 [excluding tiredness], TSS) response at week 24 based on 4 different response thresholds (>0%, ≥10%, ≥25%, and ≥50%) and median percent change in TSS over time
  - Anemia benefit was analyzed in the subgroup with baseline HB <8g/dL, including changes in HB over time and RBC transfusion independence (TI), defined as zero transfusion over any 12-week period.
- Median change in hemoglobin (and interquartile range) was presented by baseline hemoglobin across the study follow-up visits.

RESULTS

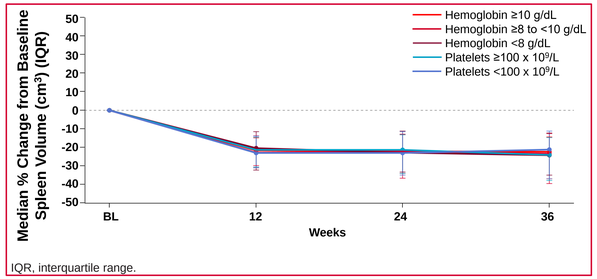
Table 1. Baseline Patient and Disease Characteristics

Characteristics	PAC (pooled) N=276
Median age, years	67
Primary myelofibrosis, n (%)	192 (70%)
Grade 3 reticulin fibrosis	142 (51.5%)
Prior JAK inhibitor, n (%)	44 (16%)
Median palpable spleen length, cm	12.00
Baseline PLT count <100 x10^9/L, n (%)	136 (49%)
Baseline PLT count ≥100 x10^9/L, n (%)	137 (50%)
Baseline HB <8 g/dL, n (%)	29 (10.5%)
Baseline HB 8 to <10 g/dL, n (%)	94 (34%)
Baseline HB ≥10 g/dL, n (%)	153 (55%)

BID, twice daily; HB, hemoglobin, JAK, Janus associated kinase; PAC, pacritinib; PLT, platelets.

- Among 276 evaluable patients, 70% had primary MF, 51.5% had grade 3 reticulin fibrosis, and 16% had prior JAK2 inhibitor exposure (**Table 1**).
- Across PLT and HB strata:
  - 75.5-82% achieved SVR≥10
  - 84-93% achieved any spleen reduction (SVR>0) (**Figure 1**).
- The depth of week 24 spleen reduction was consistent across all analyzed PLT and HB strata.
- Spleen reduction occurred by week 12 across all subgroups and remained consistent over time (**Figure 1**).

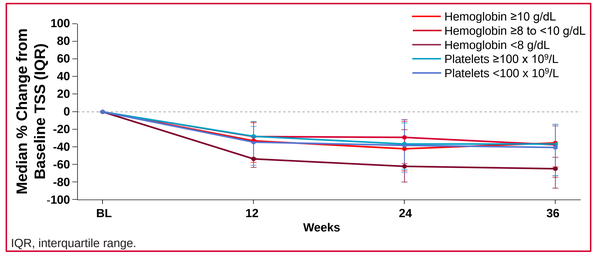
Figure 1. Spleen Volume Response Over Time by Baseline Blood Counts



IQR, interquartile range.

- Any improvement in symptoms (TSS>0) occurred in 80-87.5% of patients across all cytopenia groups.
  - TSS≥50 occurred at the highest rate (62.5%) in patients with a baseline hemoglobin <8 g/dL
  - Improvement in TSS was observed by week 12 with ongoing improvement sustained through week 36, particularly in patients with baseline hemoglobin <8 g/dL (**Figure 2**).

Figure 2. Total Symptom Score (TSS) Response Over Time by Baseline Blood Counts

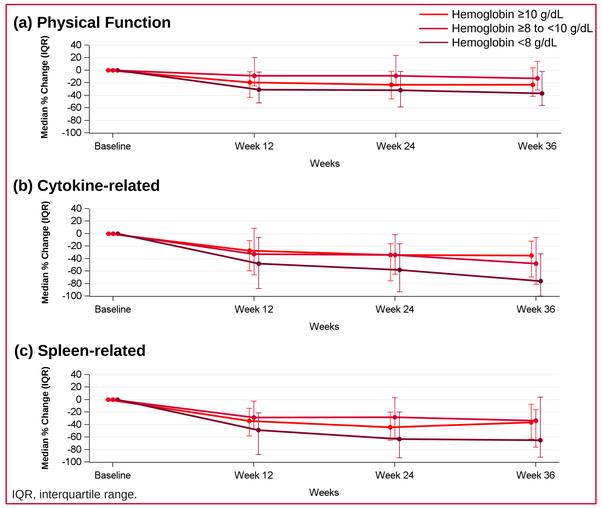


IQR, interquartile range.

- Roughly half of the patients in each subgroup reported their disease symptoms as "much" or "very much" improved at week 24.

RESULTS

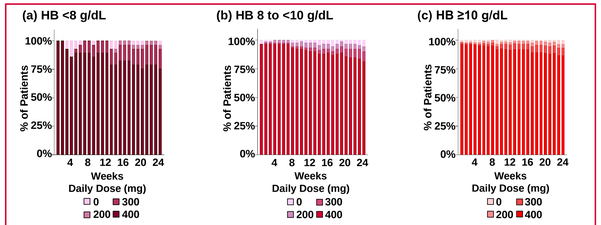
Figure 3. TSS Subscale Responses by Baseline HB Counts



IQR, interquartile range.

- All HB subgroups observed reductions in the TSS subscales (physical function, cytokine-related, and spleen-related), with the HB <8 g/dL group showing the greatest reduction (**Figure 3**).
- Patients across all hemoglobin subgroups (**Figure 4a, b, c**) maintained a median dose intensity of 100%.

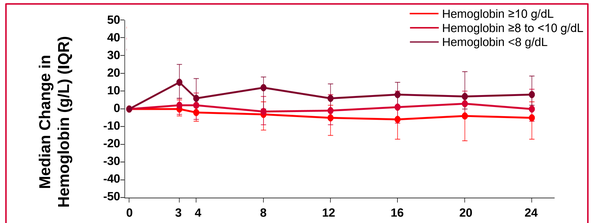
Figure 4. Dose Intensity of Patients on Pacritinib by Baseline HB Counts



HB, hemoglobin; PLT, platelet.

- Median hemoglobin remained stable through week 24 (**Figure 6**), with some improvement in the subgroup with baseline hemoglobin <8 g/dL.

Figure 5. Median Change in Hemoglobin Over Time by Baseline Hemoglobin (HB) Subgroups



N								
	0	3	4	8	12	16	20	24
HB≥10 g/dL	153	141	144	148	147	150	150	143
HB≥8 to <10 g/dL	94	85	83	90	91	91	93	82
HB<8 g/dL	29	26	26	26	27	29	27	24

IQR, interquartile range.

- Subgroups with less severe anemia had stable HB levels over time
- Of 29 patients with baseline HB <8 g/dL, 90% (n=26) were receiving RBC transfusions at baseline.
  - 35% (n=9/26) became transfusion independent (TI) on study.
- Among the patients with hemoglobin <8 g/dL who met Gale criteria for transfusion dependence at baseline, 23% (n=3/13) became TI on study.
- A modest correlation between percent improvement in hemoglobin and percent decrease in tiredness from baseline to week 24 was observed (r -0.33, *P*=0.15) in patients with baseline HB <8 g/dL.

CONCLUSIONS

- Pacritinib demonstrates consistent efficacy for spleen and symptom response in patients with MF regardless of baseline blood counts.
- Patients with more severe anemia experienced hematologic improvement and transfusion independence
- This consistent effect may be related to pacritinib's unique mechanism of action and its ability to be delivered at full dose in patients regardless of cytopenias.

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