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Consistency of pacritinib for spleen and symptom reduction in patients with myelofibrosis regardless of cytopenias

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BACKGROUND

- 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]

OBJECTIVE

- To describe the dosing and efficacy of pacritinib in MF patients 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 x 10^9/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
  - Patient-reported change in disease symptoms, as measured by the Patient Global Impression of Change (PGIC) at week 24
- Median change in hemoglobin (and interquartile range) was presented by baseline hemoglobin across the study follow-up visits.

RESULTS

- Among 276 evaluable patients, 70% had primary MF, and 16% had prior JAK2 inhibitor exposure (**Table 1**).

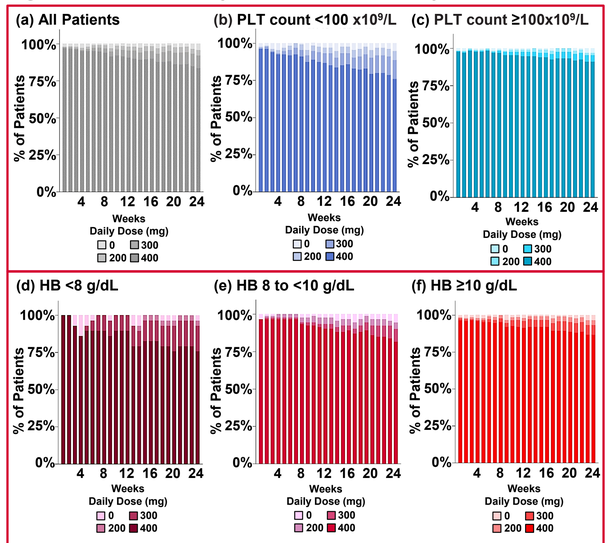
Table 1. Baseline Patient and Disease Characteristics

Characteristics	PAC (pooled) N=276
Median age, years	67
Primary myelofibrosis, n (%)	192 (70%)
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.

- Patients across all baseline platelet subgroups (**Figure 1b, c**) and hemoglobin subgroups (**Figure 1c, d, e**) maintained a median dose intensity of 100%.

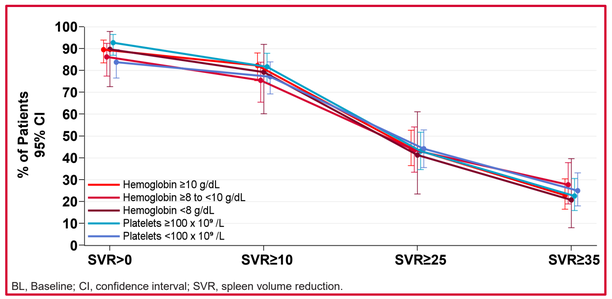
Figure 1. Dose Intensity of Patients on PAC by BL Blood Counts



BL, baseline; HB, hemoglobin; PAC, pacritinib; PLT, platelet.

- Across PLT and HB strata, 21-28% achieved ≥35% SVR (SVR≥35), 39-44% achieved SVR≥25, 75.5-82% achieved SVR≥10, and 84-93% achieved any spleen reduction (SVR>0) (**Figure 2**).
- The depth of week 24 spleen reduction was consistent across all analyzed PLT and HB strata.

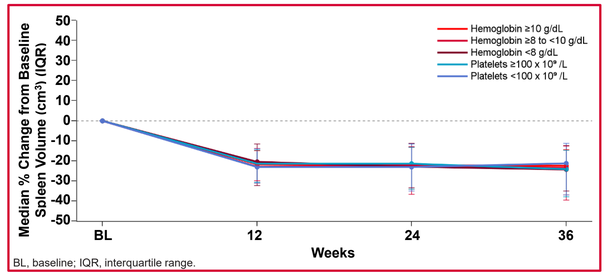
Figure 2. Spleen Response by BL Blood Counts at Week 24



BL, Baseline; CI, confidence interval; SVR, spleen volume reduction.

- Spleen reduction occurred by week 12 across all subgroups and remained consistent over time (**Figure 3**).

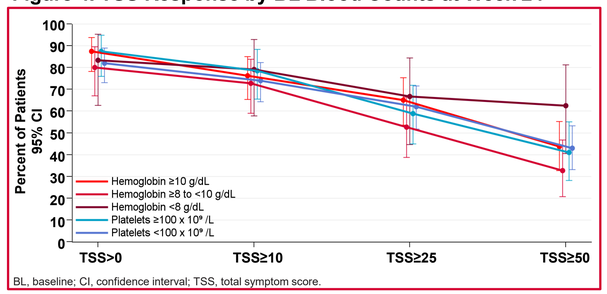
Figure 3. Spleen Response Over Time by BL Blood Counts



BL, baseline; IQR, interquartile range.

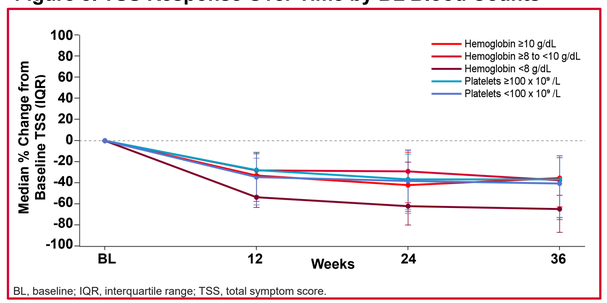
- Any improvement in symptoms (TSS>0) occurred in 80-87.5% of patients across all cytopenia groups.
  - TSS≥50 occurred at the highest rate (62.5%) in patients with a baseline hemoglobin <8 g/dL (**Figure 4**).
- Improvement in TSS was observed by week 12 with ongoing improvement sustained through week 36, particularly in patients with baseline hemoglobin <8 g/dL (**Figure 5**).

Figure 4. TSS Response by BL Blood Counts at Week 24



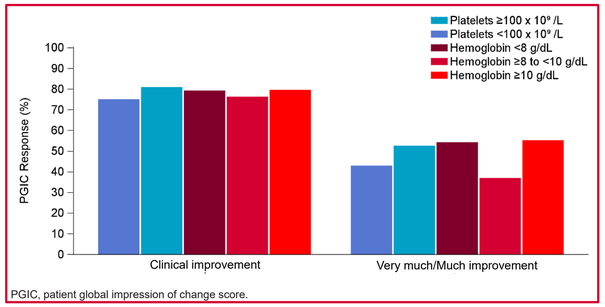
BL, baseline; CI, confidence interval; TSS, total symptom score.

Figure 5. TSS Response Over Time by BL Blood Counts



BL, baseline; IQR, interquartile range; TSS, total symptom score.

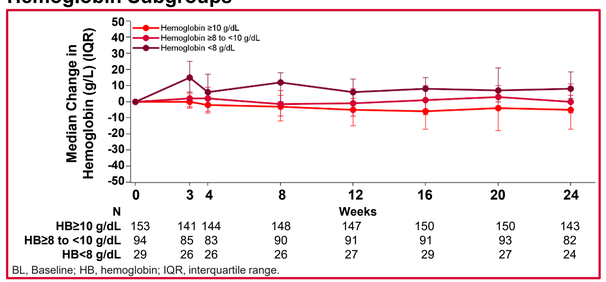
Figure 6. PGIC Response by BL Blood Counts at Week 24



PGIC, patient global impression of change score.

- Clinical improvement in disease symptoms, defined as any improvement based on PGIC response, was reported in approximately 80% across all blood count subgroups (**Figure 6**).
- Roughly half of the patients in each subgroup reported their disease symptoms as "much" or "very much" improved at week 24.

Figure 7. Median Change in Hemoglobin Over Time by BL Hemoglobin Subgroups



N							
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

BL, Baseline; HB, hemoglobin; IQR, interquartile range.

- Median hemoglobin remained stable through week 24 (**Figure 7**), with some improvement in the subgroup with baseline hemoglobin <8 g/dL.

CONCLUSIONS

- Pacritinib demonstrates consistent efficacy for spleen and symptom response in patients with MF regardless of baseline blood counts.
- 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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