Symptom Burden in Patients with Myelofibrosis who Have Moderate or Severe Thrombocytopenia: a Retrospective Analysis of Patients Enrolled in the PERSIST-2 Study

JNCCN 21-774

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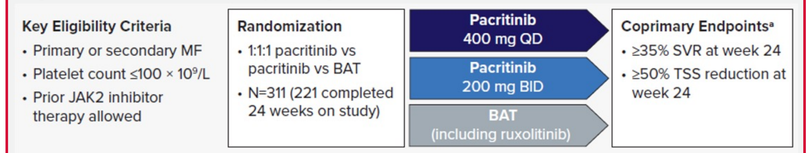
INTRODUCTION

Symptom Burden in Patients with Myelofibrosis and Thrombocytopenia

- With multiple new treatments entering the myelofibrosis space, but in the absence of curative treatments beyond stem cell transplantation, improving, stabilizing and prolonging good quality of life for patients becomes a central consideration for health care providers. Improvements in platelet counts have been rare, even in recent trials that have included patients with cytopenias.[1]
- Moderate (50-100 x 10^9/L) to severe (<50 x 10^9/L) thrombocytopenia is a recognized marker of poor prognosis in patients with myelofibrosis. However, patients with moderate to severe thrombocytopenia are often excluded from clinical trials, so there is a lack of data on symptom burden in this population.
- Data from the MPN-QOL study group showed that patients with platelet counts <100 x 10^9/L have more severe symptomatology compared to those without thrombocytopenia. Physical function symptoms (fatigue and inactivity) are particularly severe in these patients.[2]
- Symptom burden data was evaluated for the 311 patients with myelofibrosis and platelet counts ≤100 x 10^9/L enrolled in the phase 3 PERSIST-2 study of pacritinib vs Best Available Therapy (**Figure 1**).
- Pacritinib is an oral Janus kinase (JAK) 2/interleukin-1 receptor–associated kinase 1 (IRAK1) inhibitor that does not inhibit JAK1.[3]

Figure 1. PERSIST-2 Study Design



[a]The primary analysis compared pooled pacritinib (400 mg QD and 200 mg BID) versus BAT.
BAT=best available therapy; BID=twice daily; MF=myelofibrosis; QD=once daily; SVR=spleen volume response; TSS=total symptom score.

OBJECTIVE

- To retrospectively evaluate the severity, prevalence, and overall symptom burden in patients treated in PERSIST-2 with moderate or severe thrombocytopenia.

METHODS

- The analysis included all patients in the PERSIST-2 study with moderate or severe baseline thrombocytopenia, which was stratified by baseline platelet count:
  - There were 118 patients with baseline platelet count of 50-100 x 10^9/L.
  - There were 141 patients with baseline platelet count of <50 x 10^9/L.
- Symptom scores were evaluated using total symptom score (TSS) v2.0 and averaged for the 7 days prior to randomization. The overall TSS score was the sum of individual symptom scores, including tiredness, early satiety, abdominal discomfort, rib pain, night sweats, itching, and bone pain (excluding inactivity) for a total score of 70.
- Symptom prevalence was defined by a symptom score of ≥1 on a scale of 0-10.
- The Wilcoxon test was used to compare differences in scores between patients with moderate and severe thrombocytopenia.

RESULTS

Baseline Characteristics

- Baseline symptom burden was high in both platelet stratum:
  - Patients with moderate thrombocytopenia had a median TSS score of 22; the mean (min, max) TSS score was 23.7 (4.0, 58.4).
  - Patients with severe thrombocytopenia has a median TSS score of 23; the mean (min, max) TSS score was 25.7 (3.0, 64.3).
- Key baseline characteristics for this study population are shown in **Table 1**.

Table 1. Key Baseline Characteristics

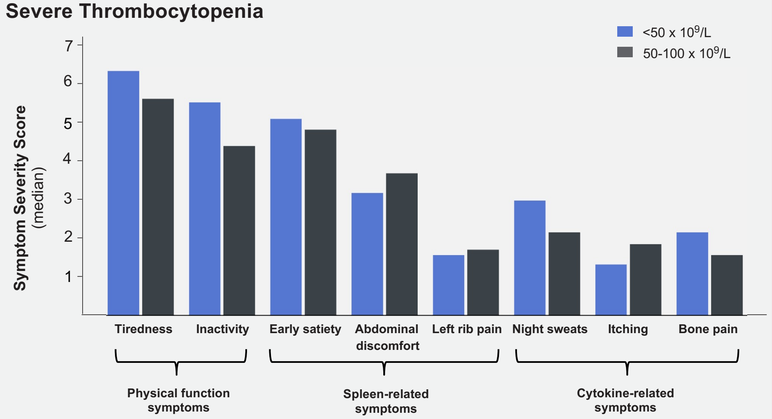
	Platelet count of <50 x 10^9/L	Platelet count of 50-100 x 10^9/L
Number of patients, n	141	118
Median age (IQR), years	69 (64-74)	67 (62-74)
Platelet count x 10^9/L, median (IQR)	28 (18-40)	70 (58-82)
Hemoglobin, g/dL, median (IQR)	9.2 (8.2-10.6)	9.4 (8.4-11.0)
Peripheral blasts ≥1%, n (%)	68 (48.2)	48 (40.7)
DIPSS, n (% with high risk)	51 (36.2)	26 (22)
RBC transfusions, unit/month (IQR)	2.27 (1.21-4.44)	1.64 (0.83-3.50)
Reticulin fibrosis, n (% with marrow fibrosis 3[a])	72 (51.4)	72 (61.5)
Primary myelofibrosis diagnosis, n (%)	100 (70.9)	79 (66.9)

[a]Advanced collagen fibrosis with or without osteosclerosis.
DIPSS=Dynamic International Prognostic Scoring System; IQR=interquartile range; RBC=red blood cell.

Symptom Severity and Prevalence

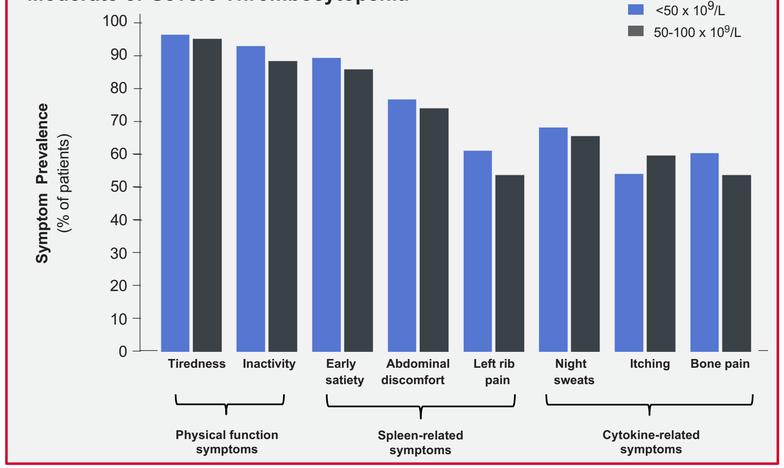
- Tiredness was the most severe symptom, regardless of platelet stratum, with a median score of 6 out of 10 (**Figure 2**).

Figure 2. Symptom Severity in Patients with Myelofibrosis and Moderate or Severe Thrombocytopenia



- Patients with severe thrombocytopenia reported higher median scores for physical function-related symptoms (tiredness plus inactivity) when compared to those with moderate: 12 vs 10, *P*=0.014.
- The severity of spleen-related symptoms inclusive of early satiety, abdominal discomfort, and left rib pain were similar between patients with moderate and severe thrombocytopenia (**Figure 2**).
- The severity of cytokine-related symptoms inclusive of night sweats, itching, and bone pain were fairly similar between patients with moderate and severe thrombocytopenia (**Figure 2**).
- Tiredness and inactivity were the most severe and prevalent reported symptoms in patients with moderate and severe thrombocytopenia (**Figure 3**).
- All symptoms as seen in **Figure 3** had a prevalence of >50% in both platelet strata.

Figure 3. Symptom Prevalence in Patients with Myelofibrosis and Moderate or Severe Thrombocytopenia



CONCLUSIONS

- **Physical function symptoms (tiredness and inactivity) represent the most prevalent burden for myelofibrosis with moderate or severe thrombocytopenia.**
- **As pivotal studies for the JAK1/2 inhibitors, ruxolitinib and fedratinib, excluded patients based on lower platelet counts (<50 and <100 x 10^9/L), an unmet need remains for therapies that can improve symptomatic disease for patients with myelofibrosis and limits impact to their platelet count; pacritinib, may fill this role.**

REFERENCES: 1. Bankar A, Gupta V. *Expert Opin Investig Drugs.* 2020;29(5):461-474. **2.** Scotch AH, et al. *Leuk Res.* 2017;63:34-40. **3.** Singer JW, et al. *J Exp Pharmacol.* 2016;8:11-19.

ACKNOWLEDGMENTS: This poster was presented at the 2022 National Comprehensive Cancer Network. This study was supported by CTI BioPharma.

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