Pacritinib in patients with intermediate-1-risk myelofibrosis: outcomes from post-hoc analysis of two phase 3 studies

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CONCLUSIONS

- Patients with intermediate-1 (INT-1)-risk myelofibrosis (MF), treated with pacritinib, had improvements in spleen size and symptom burden
- Toxicity was acceptable in this subgroup and the safety profile was similar to what has already been reported in primary analysis with pacritinib
- These data suggest pacritinib may be a treatment option for patients with INT-1-risk MF who have splenomegaly and symptomatic disease, including those with platelet count >50 × 10^9/L

INTRODUCTION

- Although patients with INT-1-risk MF have a better prognosis compared to those with higher-risk disease, they may experience signs and symptoms of the disease that could benefit from treatment
- Pivotal studies of ruxolitinib and fedratinib only enrolled patients with intermediate-2 or high-risk MF
- A Dynamic International Prognostic Scoring System (DIPSS) score of 1–2 is considered INT-1-risk with a median survival of 14.1 years (from the time of diagnosis)[1]
- Phase 3 trials for pacritinib, a JAK1-sparing inhibitor of JAK2/IRAK1/ACVR1, included patients with INT-1-risk according to DIPSS scoring[2,3]
- Patients with severe thrombocytopenia may have worse prognosis compared to less cytopenic patients with INT-1-risk MF

AIM

- To present treatment outcomes for pacritinib versus best available therapy (BAT) in patients with INT-1-risk MF

METHODS

- This post-hoc INT-1-risk subgroup analysis evaluated efficacy outcomes at week 24 in the intention-to-treat (ITT) PERSIST-1 (NCT01773187) and PERSIST-2 (NCT02055781) patients who were randomized ≥22 weeks prior to study end
- Outcomes included ≥35% spleen volume response (SVR), ≥50% 6-symptom Total Symptom Score (TSS) response, and Patient Global Impression of Change (PGIC) response, reporting symptoms as "very much" or "much" improved
- As TSS instrument version was amended from v1.0 to v2.0 part-way through PERSIST-1, results only included patients completing the Myeloproliferative Neoplasm-Symptom Assessment Form (MPN-SAF) TSS, version 2.0 (excluding tiredness)
- Treatment comparisons of pacritinib versus BAT were performed using the Fisher exact test
- A subgroup analysis in patients with baseline platelet count >50 × 10^9/L was performed
- Adverse events were analyzed from the safety population
- Hematological endpoints included median platelet counts and hemoglobin levels, summarized over time

RESULTS

- This analysis included 150 patients randomized to pacritinib and 62 to BAT
- Age, gender, platelet count, and hemoglobin were similar between groups at baseline (**Table 1**)
- Over 90% of patients in both groups had no prior JAK inhibitor exposure (**Table 1**)

Table 1. Baseline characteristics

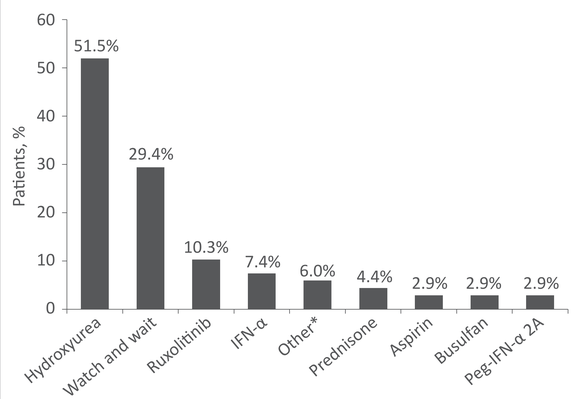
	Pooled pacritinib (n=150)	Pooled BAT (n=62)
Age, years, median (IQR)	65 (58, 71)	62 (57, 67)
Male, n (%)	87 (58)	32 (52)
Race, White, n (%)	132 (88)	57 (92)
Primary MF diagnosis, n (%)	90 (61)	28 (45)
Time since current MF diagnosis, years, median (IQR)	1 (0.2, 3.6)	1.7 (0.2, 5.9)
Spleen length, cm (IQR)	11 (7, 16)	14 (9, 17)
Platelet count (× 10^9/L), median (IQR)	182 (89, 343)	219 (96, 404)
Hemoglobin (g/dL), median (IQR)	11.8 (10.5, 13.3)	11.9 (10.9, 13.2)
Prior JAK inhibitor, n (%)	5 (3.3)	5 (8.1)

BAT, best available therapy; IQR, interquartile range; JAK, Janus kinase; MF, myelofibrosis.

Breakdown of pooled BAT treatments

- Among the 68 patients who were treated with BAT group (safety population), the most common treatment was hydroxyurea (51.5%), followed by watch and wait (29.4%) (**Figure 1**)

Figure 1. BAT treatments

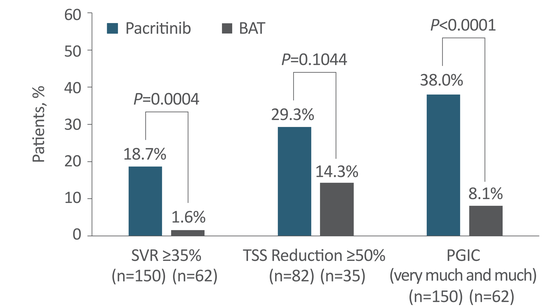


*(n=1 each): anagrelide, cytarabine, lenalidomide, and thalidomide.
BAT, best available therapy; IFN-α, interferon alpha; peg-IFN-α, pegylated interferon alpha.

Greater treatment response with pacritinib for all patients

- Among patients with INT-1-risk MF at baseline, the proportion of patients who achieved SVR ≥35% was higher in the pacritinib group versus the BAT group (*P*=0.0004) (**Figure 2**)
- Similarly, the proportion of patients who achieved TSS reduction ≥50% was numerically greater in the pacritinib group (29.3%) versus the BAT group (14.3%; *P*=0.1044) (**Figure 2**)
- Additionally, the proportion of patients who achieved a PGIC response of "very much" or "much" improved was 38.0% for the pacritinib group versus 8.1% for the BAT group (*P*<0.0001) (**Figure 2**)

Figure 2. Efficacy outcomes of pacritinib vs BAT in all patients with INT-1-risk MF DIPSS

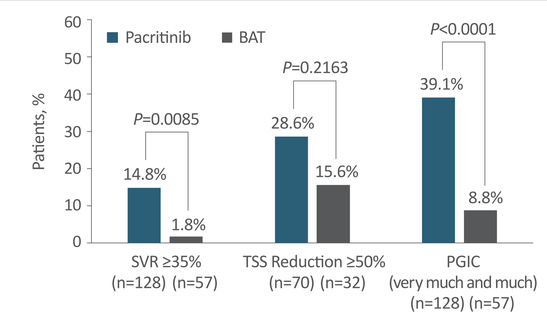


BAT, best available therapy; DIPSS, Dynamic International Prognostic Scoring System; INT-1, intermediate-1; MF, myelofibrosis; PGIC, Patient Global Impression of Change; SVR, spleen volume response; TSS, Total Symptom Score.

Greater treatment response with pacritinib in patients with platelet counts >50 × 10^9/L

- In the subgroup of patients with a baseline platelet count >50 × 10^9/L, the proportion of patients who achieved SVR ≥35% was higher in the pacritinib group versus BAT (*P*=0.0085) (**Figure 3**)
- Similarly, in the subgroup of patients with a baseline platelet count >50 × 10^9/L, the proportion of patients who achieved TSS ≥50% was 28.6% on pacritinib versus 15.6% on BAT (*P*=0.2163) (**Figure 3**)
- Similar efficacy results favoring pacritinib versus BAT in achieving PGIC response of "very much" or "much" improved were noted (*P*<0.0001) (**Figure 3**)

Figure 3. Efficacy outcomes of pacritinib vs BAT in patients with INT-1 risk-MF DIPSS and baseline platelet count >50 × 10^9/L



BAT, best available therapy; DIPSS, Dynamic International Prognostic Scoring System; INT-1, intermediate-1; MF, myelofibrosis; PGIC, Patient Global Impression of Change; SVR, spleen volume response; TSS, Total Symptom Score.

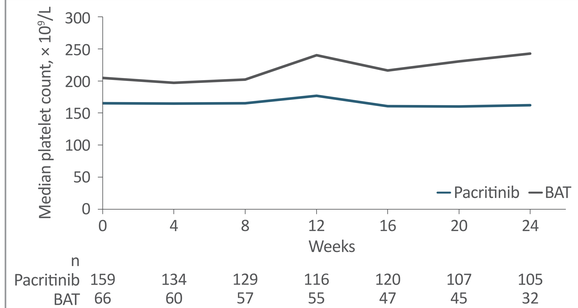
Safety

- The safety population included 164 patients in the pacritinib group and 68 patients in the BAT group
- Common Terminology Criteria for Adverse Events grade ≥3 treatment-emergent adverse events reported in ≥10% included anemia (19.5% vs 11.8%) and thrombocytopenia (16.5% vs 7.4%)

Stability in platelet counts

- Median platelet count remained stable from baseline to week 24 in both groups (**Figure 4**)

Figure 4. Median platelet count over time

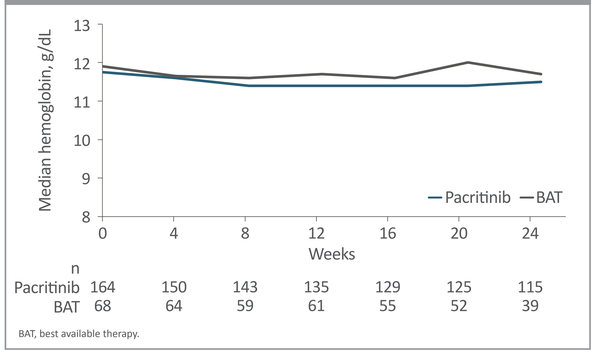


BAT, best available therapy.

Stability in hemoglobin

- Median hemoglobin remained stable from baseline to week 24 in both groups (**Figure 5**)

Figure 5. Median hemoglobin over time



BAT, best available therapy.

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