

Retrospective Comparison of Patient Outcomes on Pacritinib Versus Ruxolitinib in Patients with Myelofibrosis and Thrombocytopenia

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BACKGROUND

- Pacritinib is a JAK2/IRAK1 inhibitor¹ approved by the Food and Drug Administration (FDA) in the United States for patients with myelofibrosis (MF) and thrombocytopenia.
- Unlike the JAK1/2 inhibitor ruxolitinib, which must be dose-reduced or held in patients with thrombocytopenia, pacritinib has been studied at full dose regardless of platelet count.

OBJECTIVE

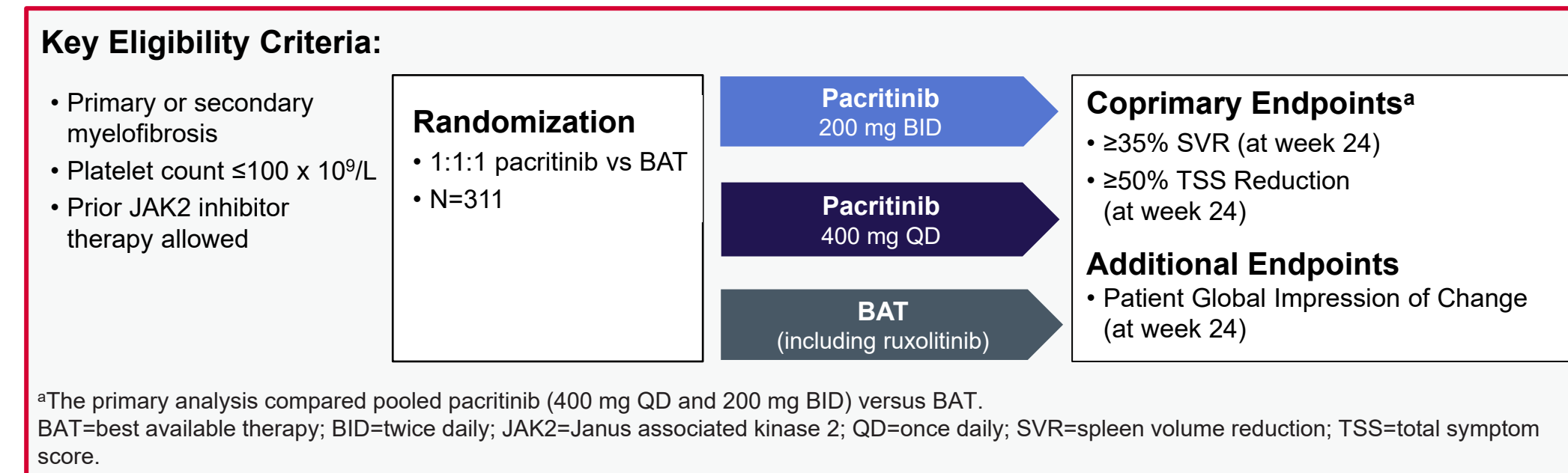
- To retrospectively analyze outcomes in patients treated with pacritinib versus ruxolitinib as part of the phase 3 PERSIST-2 study.

METHODS

Study Design

- In PERSIST-2, patients were randomized 1:1:1 to pacritinib 200 mg twice daily (BID), pacritinib 400 mg once daily (QD), or best available therapy (BAT)², as shown in **Figure 1**.
- 45% of patients on BAT received ruxolitinib.

Figure 1. PERSIST 2 Study Design



- This analysis focuses on the approved dose of 200 mg BID dose for pacritinib and on patients who received ruxolitinib as BAT (BAT=RUX) prior to week 24.
- Safety analyses were based on all treated patients.
- Efficacy analyses were based on the intention-to-treat (ITT) population randomized at least 22 weeks prior to study end. The modified Total Symptom Score (mTSS) was used to assess MF symptoms.³
- Survival analysis was based on ITT for the pacritinib arm and treated patients for the ruxolitinib group.
- The Fisher's Exact test was used to describe response differences. Logistic or Cox proportional hazard regression models were used to adjust for baseline differences.

RESULTS

Patient Characteristics

- Safety analysis included 106 patients on pacritinib and 44 on ruxolitinib.
- ITT efficacy analysis (patients randomized ≥ 22 weeks prior to study end) included 74 on pacritinib and 32 on ruxolitinib.
- Baseline characteristics were similar between groups, including median platelet count (55 vs 61 $\times 10^9/L$) and percentage receiving RBC transfusion (46% vs 43%).
- Patients in the ruxolitinib group were more likely to have prior JAK inhibitor exposure and PS ≥ 2 .

Table 1. Baseline Patient and Disease Characteristics

Characteristics	PAC n=106	BAT=RUX n=44
Age (years), median	67	68
Female gender, n (%)	44 (42%)	15 (34%)
ECOG PS ≥ 2 , n (%)	12 (11%)	10 (23%)
Platelets ^a ($\times 10^9/L$), median	55	61
Platelets $< 50 \times 10^9/L$, n (%)	47 (44%)	17 (39%)
Hemoglobin (g/dL), median	9.7	9.9
Receives RBC transfusions, n (%)	49 (46%)	19 (43%)
Peripheral blasts $\geq 1\%$, n (%)	48 (45%)	27 (61%)
Primary myelofibrosis, n (%)	82 (77%)	22 (50%)
DIPSS high risk, n (%)	29 (27%)	12 (27%)
Prior JAKi exposure, n (%)	51 (48%)	32 (73%)

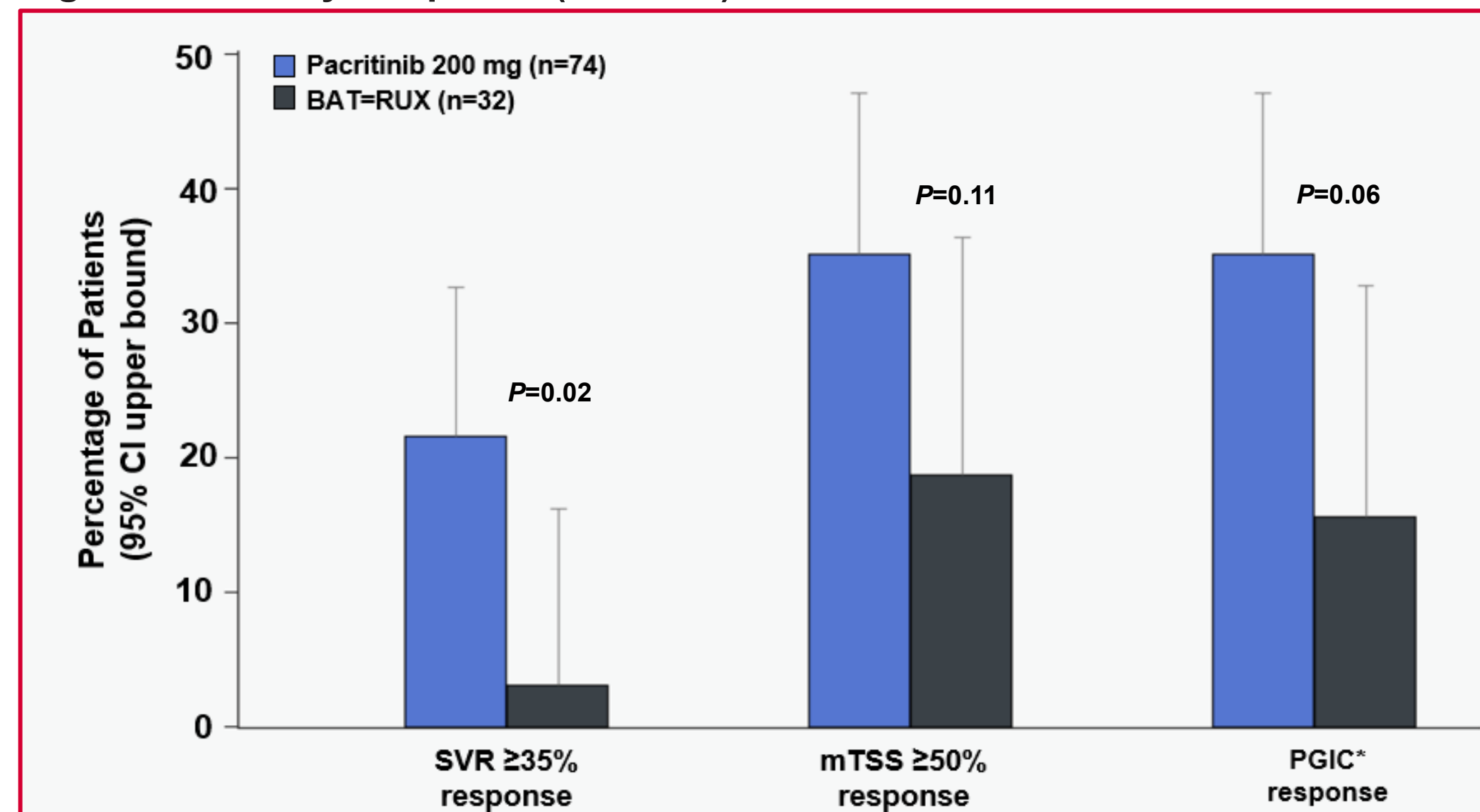
^aBaseline platelet information was not available for all patients in the safety population. DIPSS=Dynamic International Prognostic Scoring System; EGOC=Eastern Cooperative Oncology Group; JAKi=Janus associated kinase inhibitor; PAC=pacritinib; PS=performance status; RBC=red blood cell; RUX=ruxolitinib.

- The following differences in baseline characteristics were accounted for in the multiple regression model: percentage with grade 3 fibrosis, percentage with primary MF, percentage with $\geq 1\%$ peripheral blasts, and percentage with prior JAK2 inhibitor use.
- Median total daily dose of pacritinib was 400 mg [interquartile range (IQR): 400 – 400 mg] and ruxolitinib was 10 mg (IQR: 10 – 20 mg).

Efficacy

- Patients treated with pacritinib vs ruxolitinib achieved higher rates of spleen volume reduction (SVR) (22% vs 3%, $P=0.02$) and mTSS response (35% vs 19%; $P=0.11$) at week 24 (**Figure 2**).
- A greater percentage of patients on pacritinib reported “much” or “very much” improved symptoms (35% vs 16%, $P=0.06$); (**Figure 2**).

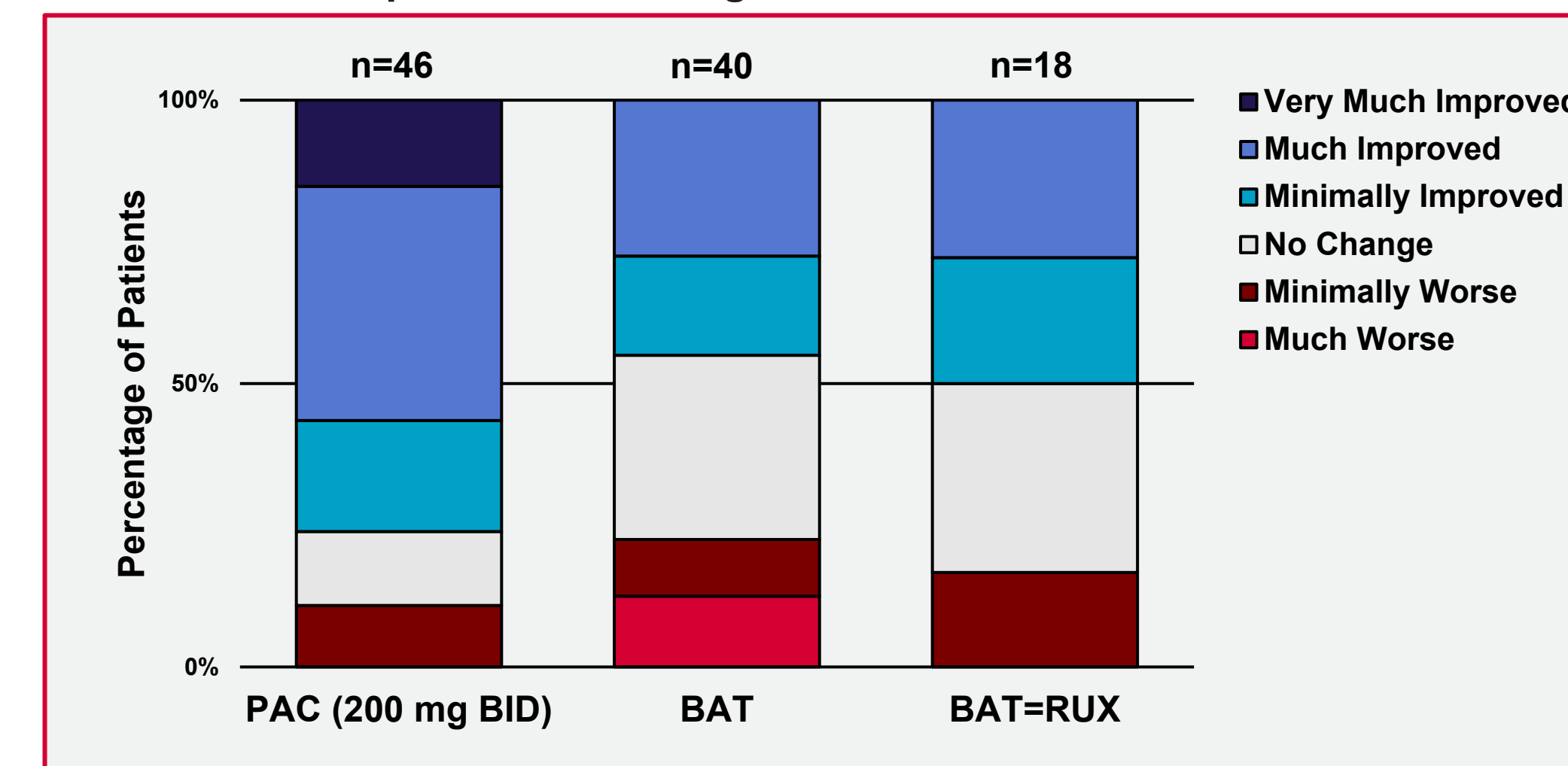
Figure 2. Efficacy Endpoints (Week 24)



RESULTS

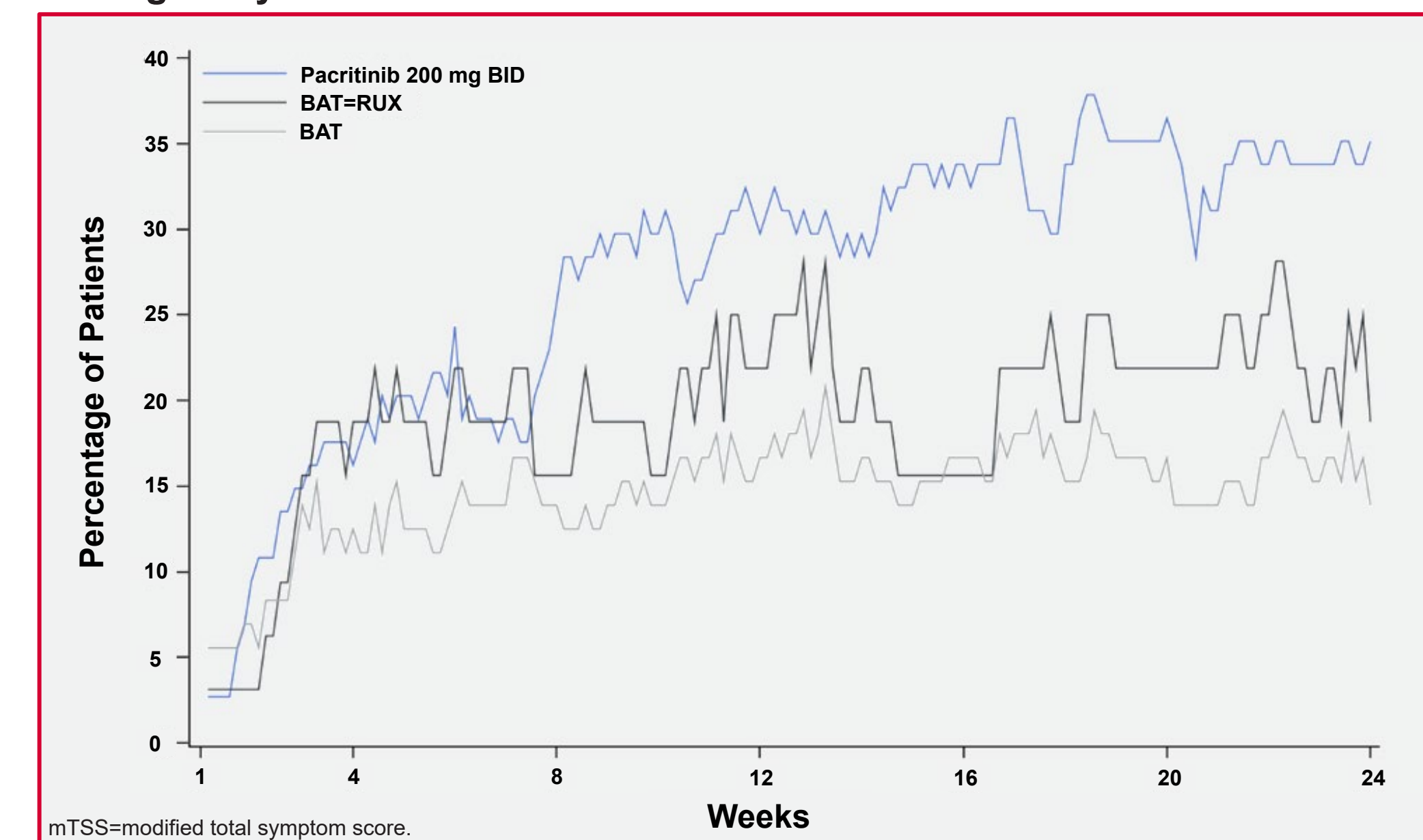
- Among ruxolitinib-treated patients with an available Patients' Global Impression of Change measure at week 24, 50% reported either no improvement or worsening symptoms, while 76% of pacritinib-treated patients reported improvement (**Figure 3**).

Figure 3. Patient-reported Change in MF Symptoms at Week 24 Based on Patient Global Impression of Change



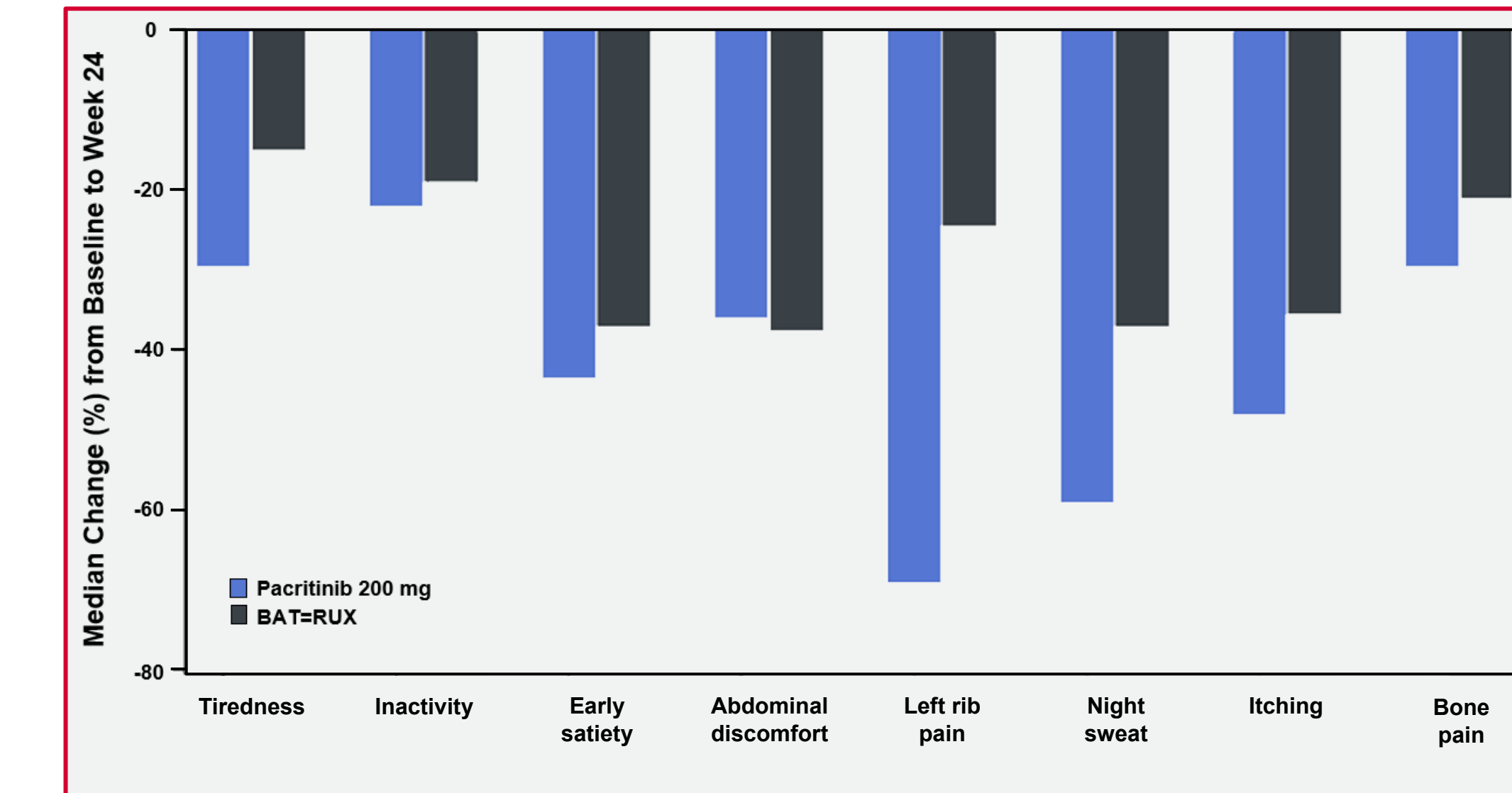
- Rolling 7-day mTSS data shows rapid onset of symptom response by week 4, with ongoing improvement through weeks 12-24 (**Figure 4**).

Figure 4. Percentage of Patients with $\geq 50\%$ Reduction in mTSS Score Based on Rolling 7-day Assessment



- After adjusting for imbalances in baseline characteristics, there was no diminution of treatment effect on SVR or mTSS.
- The hazard ratio for survival on pacritinib vs ruxolitinib was 0.71 (95% CI: 0.26-1.96). After adjusting for baseline imbalances between groups, the hazard ratio for survival on pacritinib vs ruxolitinib was 0.46 (95% CI: 0.15-1.43).
- Patients on the pacritinib arm had greater percentage reduction in most MF symptoms compared to patients who received ruxolitinib as BAT (**Figure 5**).

Figure 5. Individual Symptom Change from Baseline



- The greatest observed differences between treatment groups were in tiredness, left rib pain, night sweats, and itching.

Safety

- Overall and fatal adverse events occurred at similar rates on pacritinib vs ruxolitinib, as did bleeding events (**Table 2**).
- Cardiac events occurred more commonly on pacritinib, though the difference was largely due to higher rates of grade 1 peripheral edema on pacritinib.
- There were low rates of herpes zoster reactivation (n=0 vs 1), fungal skin infection (n=0 vs 1), pulmonary aspergillosis (n=1 vs 0), deep venous thrombosis (n=0 vs 1), and pulmonary embolism (n=1 vs 0) on pacritinib and ruxolitinib, respectively.

Table 2. Adverse event (AE) Overview by Treatment Group

Patients with ≥ 1 AE, n (%)	PAC n=106	BAT=RUX n=44
Any AE	100 (94%)	41 (93%)
Fatal AE	8 (8%)	5 (11%)
AE requiring dose reduction	13 (12%)	5 (11%)
AE requiring drug withdrawal	16 (15%)	7 (16%)
Withdrawal due to thrombocytopenia	2 (2%)	1 (2%)
Withdrawal due to anemia	3 (3%)	0
Hemorrhagic AE	45 (43%)	18 (41%)
Cardiac AE	34 (32%)	10 (23%)

Additional comparative safety data on pacritinib and ruxolitinib has been previously presented.⁴

CONCLUSIONS

- Pacritinib, administered at the full dose of 200 mg BID, yielded higher response rates and a similar safety profile compared to lower-dose ruxolitinib in patients with MF who have moderate or severe thrombocytopenia.**

ACKNOWLEDGEMENTS: This study was supported by CTI BioPharma and was initially presented at EHA 2022 by Professor Claire Harrison and additional data was presented at SOHO 2022 by Dr. Prithviraj Bose.

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