Abstract: P1037

Title: CONSISTENCY OF PACRITINIB FOR SPLEEN AND SYMPTOM REDUCTION IN PATIENTS WITH MYELOFIBROSIS REGARDLESS OF CYTOPENIAS

Abstract Type: Poster Presentation

Session Title: Myeloproliferative neoplasms - Clinical

Background:

In patients with myelofibrosis (MF), JAK inhibitor therapy can improve both splenomegaly and disease symptoms. Unfortunately, dosing – and thus efficacy – of the available JAK1/2 inhibitors ruxolitinib and fedratinib is frequently limited in patients with cytopenic MF due to drug-induced exacerbation of cytopenias. Pacritinib is a JAK1-sparing inhibitor of JAK2/IRAK1/ACVR1 that has been studied at full dose in patients with MF regardless of cytopenias.

Aims:

To present data on spleen and symptom benefit in pacritinib-treated patients stratified by both baseline platelet (PLT) count and hemoglobin (HB) level.

Methods:

Evaluable patients treated with pacritinib (200 mg twice daily or 400 mg daily) in the PERSIST-1 and PERSIST-2 studies were analyzed, stratified by baseline PLT count (<100, ≥100x10^9/L) and HB level (<8, 8 to <10, ≥10 g/dL). Groups were analyzed for depth of spleen volume response (SVR), total symptom score (TSS; version 2.0 excluding tiredness) response, patient global impression of change (PGIC), and dose intensity.

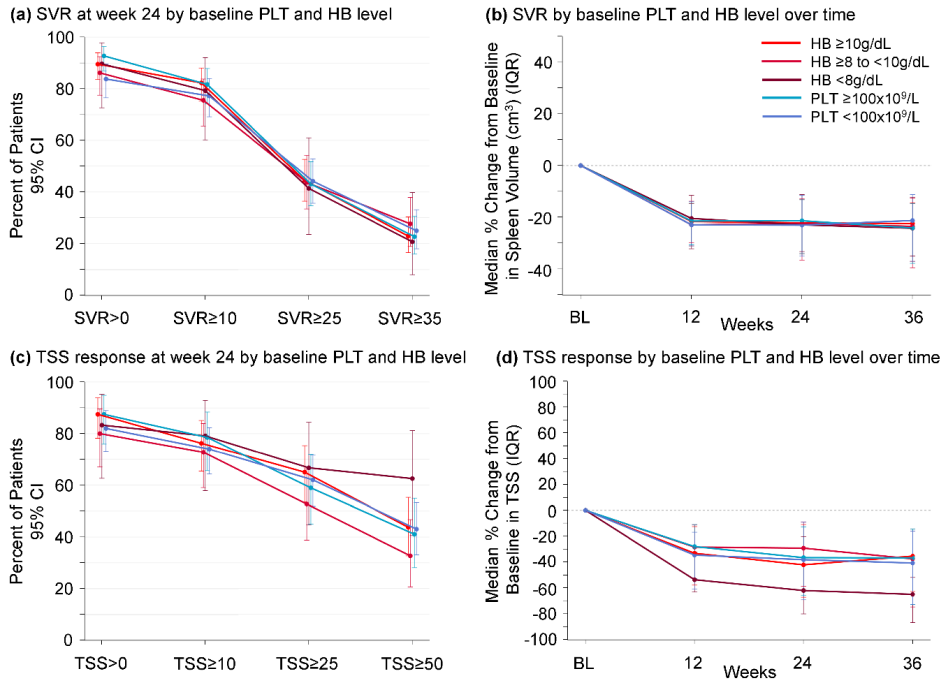
Results:

Of 276 patients evaluable for spleen response, median age at baseline was 67 years, 51.5% had grade 3 bone marrow fibrosis, 70% had primary MF, and 16% had prior JAK2 inhibitor exposure. Median pacritinib dose intensity was >99.7% for the duration of the study across PLT and HB subgroups. Overall, 80% of patients achieved ≥10% SVR, 75.5% had ≥10% TSS reduction, and 78% reported that their symptoms were "improved" at week 24. Week 24 spleen reduction occurred consistently across PLT and HB strata (**Figure 1a**), with 84-93% experiencing clinical improvement (any spleen reduction) and 21-28% achieving spleen response (≥35% SVR). Spleen response occurred at similar rates regardless of baseline PLT or HB strata, with most patients achieving full benefit by Week 12 (**Figure 1b**). Symptom response was also consistent across strata, though TSS response (≥50% TSS reduction) occurred at highest rates (62.5%) in patients with HB <8 g/dL (**Figure 1c**). There was no diminution in TSS reduction in patients with thrombocytopenia compared to those with higher PLT counts. Unlike spleen reduction, symptom benefit continued to occur beyond week 12, particularly in patients with baseline HB <8 g/dL (**Figure 1d**). Across all analyzed cytopenia subgroups, at least three-quarters of patients (75-81%) reported symptoms were "improved" at week 24, with 37-55% reporting that their symptoms were "much" or "very much improved".

Summary/Conclusion:

Pacritinib demonstrates consistent efficacy for spleen and symptom response in patients with MF regardless of blood counts. This consistent effect may be related to pacritinib's unique kinome profile and its ability to be delivered at full dose in patients with MF regardless of cytopenias.

Figure 1. Spleen volume response (SVR) and total symptom score (TSS) response on pacritinib stratified by baseline platelet (PLT) or hemoglobin (HB) level



Abbreviations: BL, baseline; CI, confidence interval; HB, Hemoglobin; IQR, interquartile range; PLT, Platelet; SVR, spleen volume response; TSS, modified total symptom score.
[a] Clinical Improvement is defined as any spleen reduction.
[b] Only scores from TSS v2.0 were included in this analysis.

Keywords: Spleen, Myelofibrosis, Janus Kinase inhibitor