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Original Research Article

Efficacy of Ruxolitinib on Clinical Improvement and Splenic Size in Lower Risk Myelofibrosis Patients

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Abstract: ***Background***: Ruxolitinib is a JAK1/JAK2 inhibitor with demonstrated success in treating MF intermediate to high-risk patients, although the implications for low-risk disease classes are not yet established. ***Objective***: To evaluate the effect of ruxolitinib on spleen size reduction and symptom burden in patients with low- and intermediate-1 risk primary myelofibrosis, and to analysis the relationship between baseline hematologic parameters and treatment response. ***Methods***: A cross-sectional study was carried out on 30 patients diagnosed with primary myelofibrosis who were treated at the Hematology consultant/Merjan teaching hospital between January and August 2025. Patients were classified according International Prognostic Scoring System (IPSS). Ruxolitinib treatment was initiated at doses of 15–20 mg twice per day and therapeutic response was assessed after a minimum of six months. The main outcomes studied were reduction in spleen size (%) (estimated by ultrasound measuring the longest axis) and alterations in the Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS). Statistical evaluations were performed using Jamovi version 2.6.44, establishing significance at $p < 0.05$. ***Results***: Among the 30 patients, 14 (46.7%) were classified as low-risk, while 16 (53.3%) were considered in the intermediate-1 risk category. The median baseline spleen sizes recorded were 20 cm for the low-risk group and 18.5 cm for the intermediate-1 group. After treatment, the median reduction in spleen size was 17.9% in low-risk compared to 15.4% in intermediate-1 group ($p = 0.16$). Moreover, an average decrease in the MPN-SAF TSS was 71.7% in the low-risk group as well as 66.4% in the intermediate-1 group ($p = 0.52$). There were no significant correlations in these data between initial hematologic parameters and treatment outcomes. ***Conclusion***: Ruxolitinib therapy resulted in reduction of splenic size and symptom severity for patients with lower-risk myelofibrosis (MF). However, the variations observed between different International Prognostic Scoring System (IPSS) categories were not statistically significant. These results underscore the possible advantages of initiating ruxolitinib therapy earlier for symptomatic low-risk MF patients and point to the necessity for larger prospective studies to confirm these findings.

Keywords: Primary Myelofibrosis, Ruxolitinib, Splenomegaly, Lower-Risk Myelofibrosis, MPN-SAF Total Symptom Score.

INTRODUCTION

Myelofibrosis (MF) is a BCR-ABL1–negative myeloproliferative neoplasm (MPN) characterized by clonal proliferation of hematopoietic stem cells, leading to progressive bone marrow fibrosis. Over time, this results in cytopenias, extramedullary hematopoiesis, and an increased risk of transformation to acute myeloid leukemia (AML) [1].

Patients with (MF) often develop a hypercatabolic state, leading to progressively debilitating symptoms such as fever, night sweats, and weight loss, as well as fatigue and lethargy. In addition, many patients present with organs- related symptoms (spleen, liver) [3, 4].

In one study, 38% of patients with PMF had splenomegaly that extended more than 10 cm below the left costal margin [5], and 23 % had massive splenomegaly that extended over 16 cm below the left costal margin [6].

The exact cause of PMF is unknown. PMF, along with the other chronic myeloproliferative disorders are considered to arise from a somatic mutation of a pluripotent hematopoietic progenitor cell [8, 9].

Ruxolitinib is a Janus kinase inhibitor (JAK1 / JAK 2), but its efficacy is independent of JAK2 mutation status, this indicates benefits in symptom relief and spleen size reduction may result from a broader suppression of kinase signaling pathways [10, 11].

The goals of management of myelofibrosis are to relieve symptoms, prevent complications, and prolong survival. The prognosis is generally poor. Most cases in PMF are associated with mutation of JAK2, CALR, or MPL genes. Some patients present with a pre fibrotic form of PMF that evolves to severely symptomatic overt fibrotic MF [7].

MATERIALS AND METHODS

Study Design and Setting

This study was designed as a cross-sectional study evaluating the clinical efficacy of ruxolitinib in patients with PMF.

Study Population

A total of 30 patients with a confirmed diagnosis of primary myelofibrosis were included.

Patients were classified according to the International Prognostic Scoring System (IPSS) into Low-risk and Intermediate-1 risk categories based on clinical and hematologic parameters at the time of diagnosis.

Treatment Protocol

Ruxolitinib therapy was initiated using a platelet-guided dosing strategy. Higher baseline platelet counts (≥200 $\times 10^9$/L) allowed initiation at 20 mg twice daily, while intermediate counts (100–199 $\times 10^9$/L) were managed with a starting dose of 15 mg twice daily. Dose escalation or reduction was subsequently determined by hematologic safety parameters and clinical efficacy.

Outcome Measures

- Primary outcome: Percentage reduction in spleen size from baseline.
- Secondary outcome: Absolute and percentage reduction in MPN-SAF TSS.

Statistical Analysis

Continuous variables were summarized as mean ± SD or median (IQR) as appropriate. Between-group comparisons were performed using independent t-test or Mann–Whitney U test, and correlations were assessed using Spearman's rank correlation coefficient, with statistical significance set at $p < 0.05$.

RESULT

1. Baseline Characteristics

There were no statistically significant differences between Low- and Intermediate-1 IPSS risk groups for most demographic and clinical characteristics at baseline.

For the Low-risk group, the median age was 59.5 years (IQR, 53.5-61.5), the median hemoglobin (Hb) level was 10 g/dL (IQR, 9-10.75), median white blood cell count (WBC) was 6500/µL (IQR, 6000-8000), the mean platelet count was 255.4 (SD 91.4), and the median baseline spleen size was 20 cm (IQR, 19.25-22).

For the Intermediate-1 risk group, the median age was 58 years (IQR, 51.25-66.5), the median Hb was 9.2 g/dL (IQR, 8.8-9.63), median WBC count was 5000/µL (IQR, 3975-7250), the mean platelet counts 286.2 (SD 134.69), and the median baseline spleen size was 18.5 cm (IQR, 17-20.25).

The mean Myeloproliferative Neoplasm Symptom Assessment from Total Symptom Score (MPN-SAF TSS) was 44.29 (SD 15,79), for the Low-risk group and 39.69 (SD 15.4) for the Intermediate-1 risk group.

Table 1: Baseline demographic and clinical Characteristics

Variables	IPSS CATEGORY		P-value
	LOW (n.=14)	Intermediate-1 (n.=16)	
Age (years)	59.5 (53.5 - 61.5)	58 (51.25 - 66.5)	0.77
Sex- n (%)			
Male	3 (21)	9 (56)	0.052
Female	11 (78)	7 (43)	
Hb (gm / dl)	10 (9 - 10.75)	9.2 (8.8 - 9.63)	0.124
Wbc (ul)	6500 (6000 - 8000)	5000 (3975 - 7250)	0.154
Platelet* (ul)	255.4 (91.4)	286.2 (134.69)	0.47
Baseline spleen size (cm)	20 (19.25 - 22)	18.5 (17 - 20.25)	0.127
MPN TSS score* (pretreatment)	44.29 (15.79)	39.69 (15.4)	0.42

2. Efficacy of Ruxolitinib

Patients in both IPSS risk categories experienced reductions in spleen size and symptom burden after receiving ruxolitinib.

Spleen Size Reduction:

- **Low-risk group:** The median reduction in spleen size was 17.9% median spleen size decreased from 20 cm (IQR, 19.25-22) at baseline to 17 cm (IQR, 15.25-18) post-treatment.
- **Intermediate-1 risk group:** The mean reduction was 15.4%, and a median spleen size decreased from 18.5 cm (IQR, 17-20.25) to 17 cm (IQR, 15-18). These reductions did not reach statistical significance (p = 0.16).

Symptom Burden Reduction:

- **Low-risk group:** A substantial decrease in symptom score was observed, with mean MPN-SAF TSS reduction of 71.7%. The median post-treatment score was 10 (IQR, 6.25-15), compared to the baseline mean score of 44.29.
- **Intermediate-1 risk:** the average reduction was 66.4%, with a post-treatment median score of 10 (IQR, 5-15) compared to a baseline mean score of 39.69.

These differences were not statistically significant (p = 0.52).

Table 2: Efficacy of Ruxolitinib Stratified by Baseline IPSS Risk Category

Outcome variable	IPSS risk category	Baseline	Post treatment	Mean reduction (%)	P* - value
Spleen size (cm)	Low	20 (19.25 - 22)	17 (15.25 -18)	17.9 (13.98 - 19)	0.16
	Intermediate-1	18.5 (17 - 20.25)	17 (15 - 18)	15.4 (8.8 - 17.8)	
MPN - SAF score	Low	44.29 (15.79)	10 (6.25 - 15)	71.7 (16.8)	0.52
	Intermediate-1	39.69 (15.4)	10 (5 -15)	66.4 (26.7)	

3. Correlation Analysis

No statistically significant correlations were found between baseline age, hemoglobin, white blood cell count, or platelet count and either the percentage change in spleen size or the absolute change in MPN-SAF TSS. (p > 0.05 for all comparisons).

Table 3: Correlation coefficient Between Baseline Variables and Treatment Outcomes

		age	Hb	Wbc	platelet
Spleen size reduction (%)	Spearman's rho	0.015	0.184	0.076	0.127
	p-value	0.938	0.330	0.690	0.504
Symptom score reduction (%) - MPN-TSS	Spearman's rho	0.168	-0.061	-0.016	-0.097
	p-value	0.374	0.750	0.933	0.610

DISCUSSION

This study provides important albeit exploratory, data on the activity of ruxolitinib in patients with lower-risk (low and intermediate-1) myelofibrosis, a group not included in the Phase III COMFORT-I or COMFORT-II studies [12].

The most impressive finding was significant reduction of symptom burden (mean reductions in MPN-SAF TSS exceeding 65% in both risk categories [13]. The observed reductions in spleen size _ 17.9% in the low-risk group and 15.4% in the intermediate-1 group _also have clinical relevance.

Although these percentages are smaller than the 35% volume reduction end-point used in the COMFORT trials, they resembled those reported in other real-world and prospective studies evaluating ruxolitinib treatment in low risk -MF patients [14]. Similar to JUMP, ROBUST studies, and several real-world evaluations have demonstrated that intermediate-1 risk MF patients derive clinical benefit from ruxolitinib in terms of spleen size reduction and symptom control, supporting its earlier use and this advocates for the utilization of ruxolitinib earlier on in the disease course [15]. In comparison with the Nanakali Hemato-Oncology Teaching Center (Erbil, Iraq), a retrospective cohort study evaluated the efficacy of ruxolitinib in patients with primary myelofibros.

The study predominantly included patients classified as intermediate-2 and high-risk according to the IPSS. The results of the present study are closely aligned with those reported by the Nanakali study, which demonstrated significant clinical benefits of ruxolitinib in terms of clinical improvement, reduction in splenic size, and improved survival rates. Notably, these benefits were observed not only in patients with advanced disease but also in symptomatic low-risk patients, as demonstrated in our study [16].

CONCLUSION

Ruxolitinib significantly improves symptoms and reduces spleen size in lower-risk myelofibrosis patients. Symptom burden decreased by ≥65% (71.7% in low-risk, 66.4% in intermediate-1), while spleen size reduced by 17.9% and 15.4%, respectively. Although spleen reductions were modest compared to COMFORT trials, the results are clinically meaningful and support ruxolitinib use for symptom and spleen control in symptomatic low-risk Myelofibrosis patients.

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