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Real-World Assessment of Clinical Outcomes in Lower-Risk Myelofibrosis Patients Receiving Treatment With Ruxolitinib

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INTRODUCTION

- Published trial data shows that ruxolitinib reduces splenomegaly and improves both splenomegaly-related and nonsplenomegaly-related symptoms in patients with intermediate-2– and high-risk myelofibrosis (MF)[1-3]
- However, few trial-based assessments of ruxolitinib in patients with lower-risk (ie, low- and intermediate-1–risk) MF have been conducted to understand whether they too would benefit from ruxolitinib treatment, and no studies to date have made such assessments in a real-world population
- In this study, we assessed changes in spleen size and symptoms during ruxolitinib treatment for lower-risk MF patients in real-world clinical settings

METHODS

- This was a retrospective, observational review of anonymized medical record data collected in January 2014 by 49 hematologists and oncologists in the United States
- Patient inclusion criteria were:
  1. Diagnosed with lower-risk MF (International Prognostic Scoring System [IPSS] score of 0 or 1)
  2. First treated with ruxolitinib ≥ 3 months before the medical record abstraction date
  3. ≥ 18 years of age at ruxolitinib initiation
  4. Complete medical history from MF diagnosis until the medical record abstraction date
  5. Never enrolled in an MF-related interventional trial
- Minimum quotas of n = 50 and n = 25 were set for patients with intermediate-1– and low-risk MF, respectively, with a predetermined maximum of 110 patients in the combined total
- Spleen size and symptoms were retrospectively observed at MF diagnosis, at ruxolitinib initiation, and at best response while on ruxolitinib
  - "At best response" defined as the time at which the patient's disease manifestation reached its most improved status during the time the patient was observed on ruxolitinib, even if ruxolitinib treatment was continuing at the time the medical record abstraction was performed
- Spleen size was captured via predefined categories of no splenomegaly (spleen not palpable), very mild or mild splenomegaly (< 10 cm palpated), moderate splenomegaly (10-20 cm palpated), or severe splenomegaly (> 20 cm palpated)
- Symptoms of interest included those captured in the Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF; general fatigue, night sweats, early satiety, abdominal pain, weight loss, itching/pruritus, and bone pain), which were categorized as mild, moderate, or severe based on medical notes recorded at each time point[4]
- The study was descriptive in nature, and so only univariate statistics were presented

RESULTS

Patient Characteristics

- A total of 108 patients were included in the study (25 with low-risk MF and 83 with intermediate-1–risk MF; **Table 1**)
- Ruxolitinib start dates spanned January 2012 to November 2013
- All low-risk MF patients were ≤ 65 years of age, and nearly 80% of intermediate-1–risk MF patients were ≤ 65 years of age
- The majority of patients in both risk groups (60% and 69%, respectively) were male
- A higher proportion of intermediate-1–risk patients were positive for the *JAK2* V617F mutation (72%) than low-risk patients (56%)
- Hypertension was the most common comorbidity (from the Charlson comorbidity index[5]) in both risk groups: 24% in low-risk patients, 35% in intermediate-1–risk patients
- Most patients (low-risk, 92%; intermediate-1–risk, 77%) were still receiving ruxolitinib treatment at the medical record abstraction date
- Median observed ruxolitinib exposure time was approximately 8 months in both risk groups

Splenomegaly

- In low-risk patients, the combined proportion of patients with moderate or severe splenomegaly (≥ 10 cm palpated spleen) decreased from 64% at MF diagnosis to 16% at best response during ruxolitinib treatment (**Figure 1A**)
- Similar findings were observed for intermediate-1–risk patients: The proportion with moderate or severe splenomegaly decreased from 53% at MF diagnosis to 10% at best response (**Figure 1B**)

Symptoms

- In low-risk patients (**Figure 2A**), general fatigue, night sweats, and early satiety were the 3 most commonly reported symptoms, experienced by one-third to nearly one-half of patients, depending on the observation point and symptom examined
- In intermediate-1–risk patients (**Figure 2B**), general fatigue, night sweats, and weight loss were the 3 most commonly reported symptoms, experienced by approximately one-half to two-thirds of patients, depending on the observation point and symptom examined
- For most symptoms, distinct shifts in symptom severity from more severe to less severe were observed in both low-risk and intermediate-1–risk patients, proceeding from MF diagnosis through best response while on ruxolitinib
  - In low-risk patients with fatigue, for example, the proportion with moderate or severe fatigue decreased from 90% at MF diagnosis to 37% at best ruxolitinib response; in intermediate-1–risk patients, the decrease was from 76% at MF diagnosis to 42% at best response. For most other symptoms, similar improvements in severity distribution were observed

RESULTS (cont)

Table 1. Patient Characteristics

	All Patients (N = 108)		IPSS Category: Low Risk (n = 25)		IPSS Category: Intermediate-1 Risk (n = 83)	
	n	%	n	%	n	%
Age						
≤ 65 years	91	84.3	25	100.0	66	79.5
> 65 years	17	15.7	0	0.0	17	20.5
Sex						
Male	72	66.7	15	60.0	57	68.7
Female	36	33.3	10	40.0	26	31.3
Race/ethnicity						
White	79	73.1	21	84.0	58	69.9
Black	16	14.8	2	8.0	14	16.9
Hispanic	10	9.3	0	0.0	10	12.0
Other	2	1.9	1	4.0	1	1.2
Don't know	1	0.9	1	4.0	0	0.0
MF type at diagnosis						
Primary MF	88	81.5	20	80.0	68	81.9
Post–polycythemia vera MF	10	9.3	3	12.0	7	8.4
Post–essential thrombocythemia MF	9	8.3	2	8.0	7	8.4
Don't know	1	0.9	0	0.0	1	1.2
***JAK2* V617F mutation test result**						
Positive	74	68.5	14	56.0	60	72.3
Negative	21	19.4	7	28.0	14	16.9
Test not done	3	2.8	1	4.0	2	2.4
Don't know	10	9.3	3	12.0	7	8.4
Charlson comorbidities at ruxolitinib initiation						
Human immunodeficiency virus/AIDS	2	1.9	0	0.0	2	2.4
Cerebrovascular disease	5	4.6	1	4.0	4	4.8
Chronic pulmonary disease	9	8.3	1	4.0	8	9.6
Congestive heart failure	0	0.0	0	0.0	0	0.0
Connective tissue disease	4	3.7	1	4.0	3	3.6
Dementia	3	2.8	0	0.0	3	3.6
Hemiplegia	2	1.9	0	0.0	2	2.4
Malignant lymphoma	1	0.9	0	0.0	1	1.2
Malignant solid tumor	3	2.8	1	4.0	2	2.4
Liver disease	7	6.5	1	4.0	6	7.2
Mild	6	5.6	1	4.0	5	6.0
Moderate or severe	1	0.9	0	0.0	1	1.2
Myocardial infarction	2	1.9	0	0.0	2	2.4
Peripheral vascular disease	1	0.9	0	0.0	1	1.2
Ulcer disease	1	0.9	1	4.0	0	0.0
Diabetes	17	15.7	2	8.0	15	18.1
With end-organ damage	2	1.9	1	4.0	1	1.2
Without end-organ damage	15	13.9	1	4.0	14	16.9
Hypertension	35	32.4	6	24.0	29	34.9
Depression	7	6.5	0	0.0	7	8.4
None of these	36	33.3	11	44.0	25	30.1
Other	0	0.0	0	0.0	0	0.0
Don't know	8	7.4	4	16.0	4	4.8
Still on ruxolitinib at last available follow-up						
Yes	87	80.6	23	92.0	64	77.1
No	15	13.9	2	8.0	13	15.7
Don't know	6	5.6	0	0.0	6	7.2

IPSS, International Prognostic Scoring System; **MF**, myelofibrosis.

Figure 1. Spleen Size Distribution

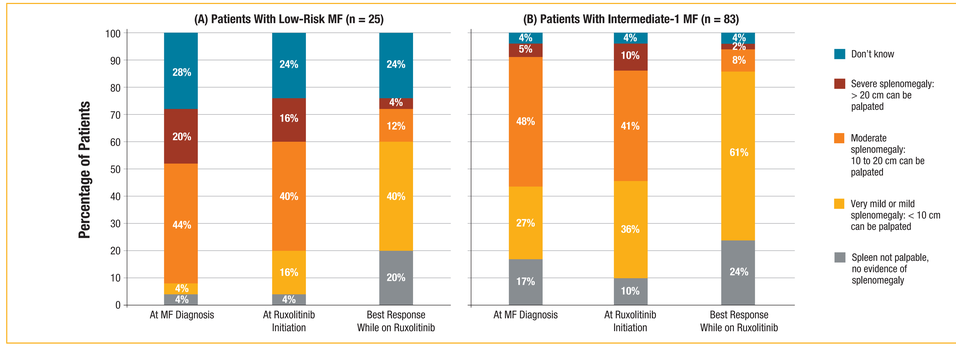
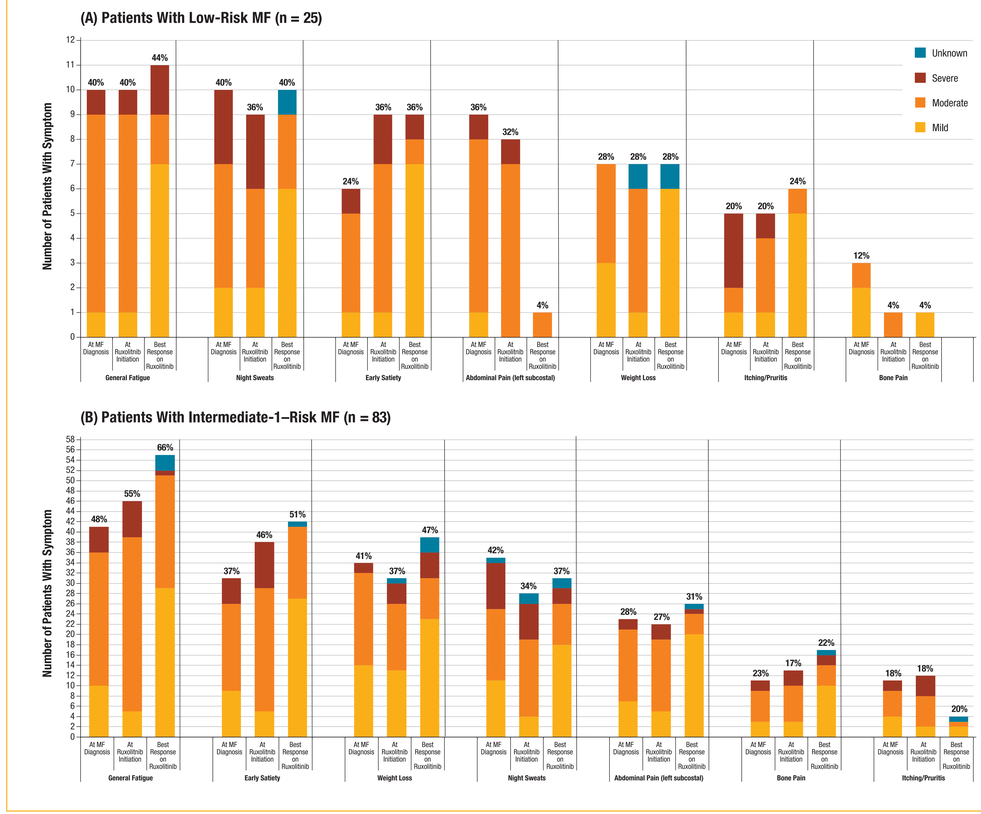


Figure 2. Symptom Prevalence and Severity Distribution



LIMITATIONS

- As in many retrospective medical record abstraction studies, in our study, the patients selected were those who were convenient to sample; therefore, our study findings may not be generalizable to the overall low- or intermediate-1–risk MF populations in the United States
- Only physicians who agreed to participate in the study contributed data; therefore, these physicians may not be representative of all physicians treating low- or intermediate-1–risk MF in the United States
- Finally, while no time limit was imposed on physicians for the completion of individual case report forms (CRFs), the CRF was designed to limit the time burden its use imposed; therefore, the scope of information that could be collected in this study was limited and it is possible that additional information could have contributed further to the study findings

DISCUSSION AND CONCLUSIONS

- **Results presented here indicate that lower-risk MF patients may indeed benefit from treatment with ruxolitinib, particularly in splenomegaly reduction and improvement in both splenomegaly-related and non–splenomegaly-related symptoms**
- **Reductions in spleen size reported here may be a conservative estimate of the maximum spleen size reduction that each patient experienced during ruxolitinib treatment, since the majority of patients were still on ruxolitinib at last follow-up; with longer follow-up, it is possible that an even more favorable response would have been observed**
- **For the same reasons noted above, symptom improvements reported in this study may also represent conservative estimates of the maximum improvements that each patient experienced during ruxolitinib treatment**
- **Only 1 previous study (the ROBUST trial), published by Mead et al in 2014,[6] has sought to assess in a clinical trial setting the possible therapeutic benefits of ruxolitinib in patients with lower-risk MF. This study showed that half of patients with intermediate-1–risk MF who received ruxolitinib achieved a reduction in spleen size of at least 50% at week 48 (vs baseline) after initiation of ruxolitinib**
- **Mead et al also reported improvements in disease-related symptoms, as assessed using the Myelofibrosis Symptom Assessment Form (MFSAF), for more than half (57%) of intermediate-1–risk patients treated with ruxolitinib**
- **Taken together, the findings reported by Mead et al and the data that our study collected from a real-world setting are consistent**

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DISCLOSURES

Davis: Employee of RTI Health Solutions, which received research funding for this work from Novartis Pharmaceuticals Corporation. **Kaye:** Employee of RTI Health Solutions, which received research funding for this work from Novartis Pharmaceuticals Corporation. **Côté:** *Novartis:* employment. **Gao:** *Novartis:* employment. **Ronco:** *Novartis:* employment. **Seifeldin:** *Novartis:* employment. **Mendelson:** *Novartis:* employment. **Off-Label Use:** The study discusses use of ruxolitinib in patients with lower-risk (IPSS 0 or 1) MF in real-world practice; currently, ruxolitinib is indicated in the United States only for the treatment of higher-risk MF (IPSS >1).

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Poster Presentation at the 56th ASH Annual Meeting, December 6-9, 2014, San Francisco, California.

This study was funded by Novartis Pharmaceuticals Corporation.