Insights from the MPN Practice Perspectives Survey of hematologists/oncologists (N=1550)

Presented by **Prithviraj Bose, MD,** MPN Expert

MYELOFIBROSIS (MF)

THE IMPORTANCE OF ACTIVELY MANAGING PATIENTS WITH MF AT DIAGNOSIS

MPN
Practice Perspectives Survey

MPN=myeloproliferative neoplasm.

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Introduction

In partnership with Incyte, we recently conducted the MPN Practice Perspectives Survey over 6 months to gain real-world perspectives on the management of patients with MF. Practicing hematologists/oncologists across the United States were invited to participate, to collect comprehensive insights that could inform best practices to optimize the management of patients with MF.

From the survey, we learned that OS is not the primary treatment goal for many physicians and that many are continuing to watch and wait, despite the potential benefits of OS that early treatment initiation offers.

In my practice, I actively manage MF at diagnosis, including managing cytopenias. In my opinion, timely initiation of treatment is key to mitigating disease progression (including splenomegaly and debilitating symptoms), which may help to achieve OS.[1-3] In this review, I will provide my perspectives on ways we can optimize the management of patients with MF.

Key points

- MF treatment goals include spleen volume reduction/symptom control and **the ultimate goal of OS**
- Importance of **actively managing** patients at diagnosis
- Importance of **managing cytopenias**

OS=overall survival.

Establishing OS as a treatment goal in MF

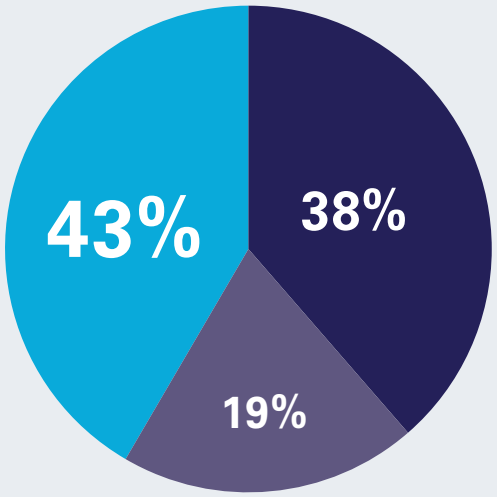
Our first survey question asked physicians to identify their primary treatment goals. As shown in the survey results below, SVR/symptom control was selected the most often at 43%, with OS being second at 38%. The remaining physicians selected cytopenia management as their primary goal.

I was a bit surprised that OS came in second, as this is something we are often able to achieve, and in my practice OS is my ultimate treatment goal. I initiate treatment early instead of watching and waiting because, in my experience, 90% of patients are candidates for active treatment upon diagnosis.[4,5] If cytopenias occur, I manage them as necessary to reach my treatment goals. As clinicians, we must prioritize therapies that can help meet the goal of maximizing OS.

MPN Practice Perspectives MF Survey—Question 1

What is your primary goal when treating patients with MF?

- Spleen volume reduction/symptom control
- Overall survival
- Cytopenia management



Only **38%** of respondents state that OS is their primary treatment goal

"In my practice, **OS is my ultimate treatment goal,** so I initiate treatment early in the course of the disease."

Prithviraj Bose, MD, MPN Expert

SVR=spleen volume reduction.

The importance of actively managing patients at diagnosis for the ultimate goal of OS

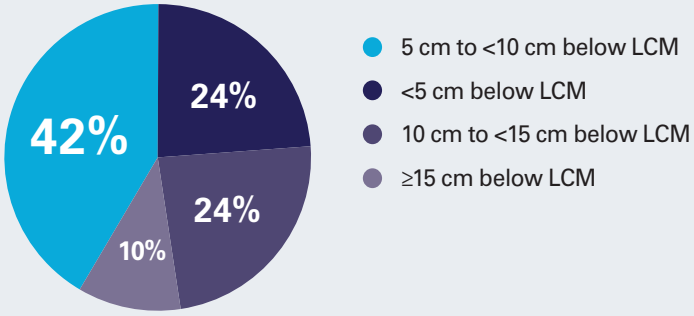
Approximately 90% of patients have a palpable spleen at diagnosis. Since the spleen serves as a critical prognostic indicator in MF and is a surrogate marker for OS, early management of palpable splenomegaly is vital to improving patient outcomes.[2,4,5]

When presented with a patient with mild to moderate symptoms, 42% of respondents indicated they would initiate treatment if they had a palpable spleen of 5 cm to 10 cm below the LCM. This is in line with the IWG-MRT and ELN response criteria, which state that a palpable spleen of ≥5 cm below LCM constitutes progressive disease and requires intervention.[2]

However, approximately one-third of the survey respondents would only consider initiating treatment if the spleen size were ≥10 cm below LCM. A post hoc pooled analysis of the COMFORT trials (N=528) showed a 14% increase in the risk of death over 3 years for each additional 5 dL in spleen volume at baseline **(Figure 1)**.[5] Based on these data, in my practice I actively manage my patients with MF who have any degree of palpable splenomegaly at diagnosis and regularly monitor throughout the course of treatment.

MPN Practice Perspectives MF Survey—Question 2

At what baseline spleen size do you typically consider initiating treatment for a patient with MF who presents with mild to moderate symptoms?

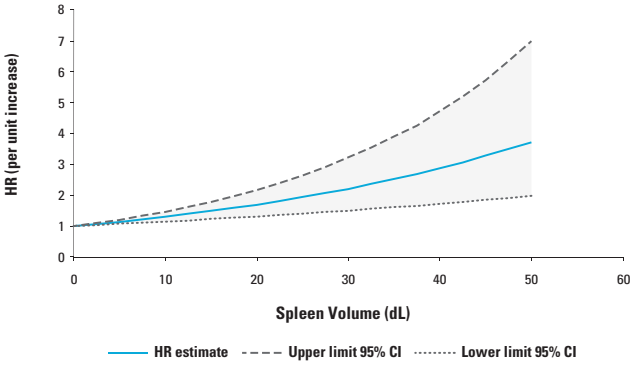


>75% of respondents allow the spleen to be >5 cm below LCM before intervening

Figure 1

Palpable spleen is a marker of disease progression and is associated with poor overall survival[5]

Relationship Between Spleen Volume and Risk of Death in the COMFORT Studies[5]



- 14% increase in the risk of death over 3 years for each additional 5 dL in spleen volume at baseline (HR, 1.14; 95% CI, 1.07-1.21)[5]

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"Since the spleen serves as a critical prognostic indicator in MF and is a **surrogate marker for OS, early management of palpable splenomegaly** is vital to **improving patient outcomes.**"

Prithviraj Bose, MD, MPN Expert

CI=confidence interval; COMFORT=COntrolled MyeloFibrosis study with ORal JAK inhibitor Treatment; ELN=European LeukemiaNet; HR=hazard ratio; IWG-MRT=International Working Group-Myeloproliferative Neoplasms Research and Treatment; LCM=left costal margin.

The importance of active management for patients early in the course of disease

In the next question, we probed physicians on whether they would act earlier in the course of disease for patients with MF and characteristics such as a palpable spleen 5 cm below LCM, mild MF symptoms, and no presentation of anemia or thrombocytopenia.

As shown below, approximately half of survey respondents opted to initiate ruxolitinib; however, the other ~50% stated that they would watch and wait or initiate hydroxyurea. Based on my experience in my practice, patients who are earlier in the course of their disease have a higher chance of achieving SVR. Therefore, I tend to initiate treatment as early as possible for the ultimate goal of OS.

Click here for information on primary and secondary endpoints and safety data for ruxolitinib.

"The benefits of initiating treatment earlier in the course of the disease are clear. **Watching and waiting is not a strategy I use in my practice.**"

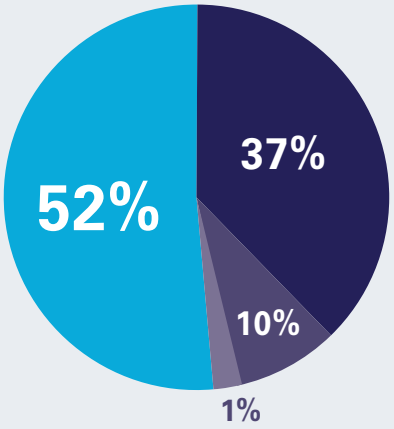
Prithviraj Bose, MD, MPN Expert

MPN Practice Perspectives MF Survey—Question 3

You just diagnosed your patient with intermediate-1 primary MF.

The patient has a spleen that is palpable 5 cm below the LCM; has mild disease-related symptoms; and has no anemia and no thrombocytopenia. What would you typically do next for a patient like this?

- Initiate ruxolitinib
- Watch and wait
- Initiate hydroxyurea
- Other



48% of respondents delay treatment with ruxolitinib for patients with MF early in the course of their disease

Ruxolitinib is available in 5mg, 10mg, 15mg, 20mg, and 25mg tablets.

INDICATIONS AND USAGE

Jakafi® (ruxolitinib) is indicated for treatment of intermediate or high-risk myelofibrosis (MF), including primary MF, post–polycythemia vera MF and post–essential thrombocythemia MF in adults.

IMPORTANT SAFETY INFORMATION

- Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia, which are each dose-related effects. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated
- Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary

Please see additional Important Safety Information on the following pages and see Full Prescribing Information for Jakafi.

Treatment strategies for patients with MF and anemia

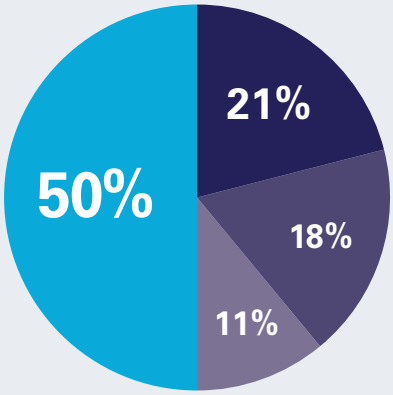
Responses to questions about treatment approaches for patients with MF and anemia were split. 50% of participants stated that they would not initiate ruxolitinib at diagnosis for patients with MF and anemia. In my clinical practice, I am confident in treating my patients with ruxolitinib at diagnosis and managing their anemia. We have always been able to manage cytopenias to achieve our goals. There are ways to manage through anemia. For instance, there are dosing strategies that help to effectively manage these patients.[6] I initiate treatment regardless of anemia, and initiate treatment early in order to have the best chance of improving OS.

"There are strategies to manage anemia. I **initiate treatment early** to have the best chance of achieving my **ultimate goal of overall survival.**"

Prithviraj Bose, MD, MPN Expert

MPN Practice Perspectives MF Survey—Question 4

For your appropriate patients with MF and anemia, which of the following would preclude you from initiating ruxolitinib at diagnosis?



- Nothing precludes me from initiating ruxolitinib at diagnosis
- Transfusion dependent regardless of Hb
- Hb 8 g/dL to ≤10 g/dL and not transfusion dependent
- Hb ≤8 g/dL and not transfusion dependent

50% of respondents are hesitant to initiate ruxolitinib for patients with anemia

Hb=hemoglobin.

IMPORTANT SAFETY INFORMATION (continued)

- Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi® (ruxolitinib)
- Severe neutropenia (ANC <0.5 × 10^9/L) was generally reversible by withholding Jakafi until recovery
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines

Please see additional Important Safety Information on the following pages and see Full Prescribing Information for Jakafi.

Conclusion

Thank you to my colleagues who took the time to participate in the MPN Practice Perspectives Survey. I thoroughly enjoyed reviewing the results and providing my perspectives on active management at diagnosis in order to achieve OS.

To optimize the management of patients with MF, we must prioritize OS as a treatment goal, actively manage MF at diagnosis, including managing cytopenias, and initiate treatment early in the course of the disease to strive toward that ultimate goal of OS.

The actions we take early in the course of the disease can impact long-term outcomes. Following a watch-and-wait approach may not allow us to achieve the ultimate goal of OS, which is why in my practice I actively manage patients with MF at the point of diagnosis.[7]

Key recommendations

- Make **OS** the primary treatment goal in MF[1-3]
- Initiate treatment **early** in the course of the disease[1-3]
- **Manage cytopenias**[6]

Find more expert perspectives

about MF treatment goals and OS.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms V1.2024. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed August 6, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2.** Tefferi A, Rumi E, Finazzi G, et al. Survival and prognosis among 1545 patients with contemporary polycythemia vera: an international study. *Leukemia*. 2013;27(9):1874-1881. **3.** Barbui T, Barosi G, Birgegard G, et al. Philadelphia-negative classical myeloproliferative neoplasms: critical concepts and management recommendations from European LeukemiaNet. *J Clin Oncol*. 2011;29(6):761-770. **4.** Cervantes F, Dupriez B, Pereira A, et al. New prognostic scoring system for primary myelofibrosis based on a study of the International Working Group for Myelofibrosis Research and Treatment. *Blood*. 2009;113(13):2895-2901. **5.** Vannucchi AM, Kantarjian HM, Kiladjian J-J, et al. A pooled analysis of overall survival in COMFORT-I and COMFORT-II, 2 randomized phase III trials of ruxolitinib for the treatment of myelofibrosis. *Haematologica*. 2015;100(9):1139-1145. Supplemental information available at: https://doi.org/10.3324/haematol.2014.119545. **6.** Cervantes F, Ross DM, Radinoff A, et al. Efficacy and safety of a novel dosing strategy for ruxolitinib in the treatment of patients with myelofibrosis and anemia: the REALISE phase 2 study. *Leukemia*. 2021;35(12):3455-3465. **7.** Bose P. Management of patients with early myelofibrosis: a discussion of best practices. *Curr Hematol Malig Rep*. 2024;19(3):111-119.

IMPORTANT SAFETY INFORMATION (continued)

- Tuberculosis (TB) infection has been reported. Observe patients taking Jakafi® (ruxolitinib) for signs and symptoms of active TB and manage promptly. Prior to initiating Jakafi, evaluate patients for TB risk factors and test those at higher risk for latent infection. Consult a physician with expertise in the treatment of TB before starting Jakafi in patients with evidence of active or latent TB. Continuation of Jakafi during treatment of active TB should be based on the overall risk-benefit determination

Please see additional Important Safety Information on the following page and see Full Prescribing Information for Jakafi.

IMPORTANT SAFETY INFORMATION (continued)

- Progressive multifocal leukoencephalopathy (PML) has occurred with Jakafi® (ruxolitinib) treatment. If PML is suspected, stop Jakafi and evaluate
- Herpes zoster infection has been reported in patients receiving Jakafi. Advise patients about early signs and symptoms of herpes zoster and to seek early treatment. Herpes simplex virus reactivation and/or dissemination has been reported in patients receiving Jakafi. Monitor patients for the development of herpes simplex infections. If a patient develops evidence of dissemination of herpes simplex, consider interrupting treatment with Jakafi; patients should be promptly treated and monitored according to clinical guidelines
- Increases in hepatitis B viral load with or without associated elevations in alanine aminotransferase and aspartate aminotransferase have been reported in patients with chronic hepatitis B virus (HBV) infections. Monitor and treat patients with chronic HBV infection according to clinical guidelines
- When discontinuing Jakafi, myeloproliferative neoplasm-related symptoms may return within one week. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, DIC, or multi-organ failure. If any of these occur after discontinuation or while tapering Jakafi, evaluate and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi without consulting their physician. When discontinuing or interrupting Jakafi for reasons other than thrombocytopenia or neutropenia, consider gradual tapering rather than abrupt discontinuation
- Non-melanoma skin cancers (NMSC) including basal cell, squamous cell, and Merkel cell carcinoma have occurred. Perform periodic skin examinations
- Treatment with Jakafi has been associated with increases in total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Assess lipid parameters 8-12 weeks after initiating Jakafi. Monitor and treat according to clinical guidelines for the management of hyperlipidemia
- Another JAK-inhibitor has increased the risk of major adverse cardiovascular events (MACE), including cardiovascular death, myocardial infarction, and stroke (compared to those treated with tumor TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur
- Another JAK-inhibitor has increased the risk of thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. In patients with myelofibrosis (MF) and polycythemia vera (PV) treated with Jakafi in clinical trials, the rates of thromboembolic events were similar in Jakafi and control treated patients. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately
- Another JAK-inhibitor has increased the risk of lymphoma and other malignancies excluding NMSC (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi, particularly in patients with a known secondary malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers
- In myelofibrosis and polycythemia vera, the most common nonhematologic adverse reactions (incidence ≥15%) were bruising, dizziness, headache, and diarrhea. In acute graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >50%) were infections (pathogen not specified) and edema. In chronic graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >20%) were infections (pathogen not specified) and viral infections
- Avoid concomitant use with fluconazole doses greater than 200 mg. Dose modifications may be required when administering Jakafi with fluconazole doses of 200 mg or less, or with strong CYP3A4 inhibitors, or in patients with renal or hepatic impairment. Patients should be closely monitored and the dose titrated based on safety and efficacy
- Use of Jakafi during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking Jakafi should not breastfeed during treatment and for 2 weeks after the final dose

INDICATIONS AND USAGE

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