Putting Knowledge Into Practice:

Self-guided learning in polycythemia vera and myelofibrosis for advanced practice providers

Assessing Splenomegaly and Disease-Related Symptoms in Myelofibrosis

Overview

The* Putting Knowledge Into Practice *self-guided learning modules have been developed specifically for advanced practice providers (APPs) to help provide education and resources to help manage patients with polycythemia vera (PV) and myelofibrosis (MF).

Assessing Splenomegaly and Disease-Related Symptoms in Myelofibrosis provides information about including these factors in management plans for patients with MF.

Topics include

- Causes and implications of splenomegaly
- Presence of splenomegaly and MF-related symptoms at diagnosis and throughout the course of disease
- Importance of ongoing monitoring of splenomegaly and symptoms, and their impact on patient quality of life

How to Use This Module

This is a self-guided learning module that gives you the flexibility to

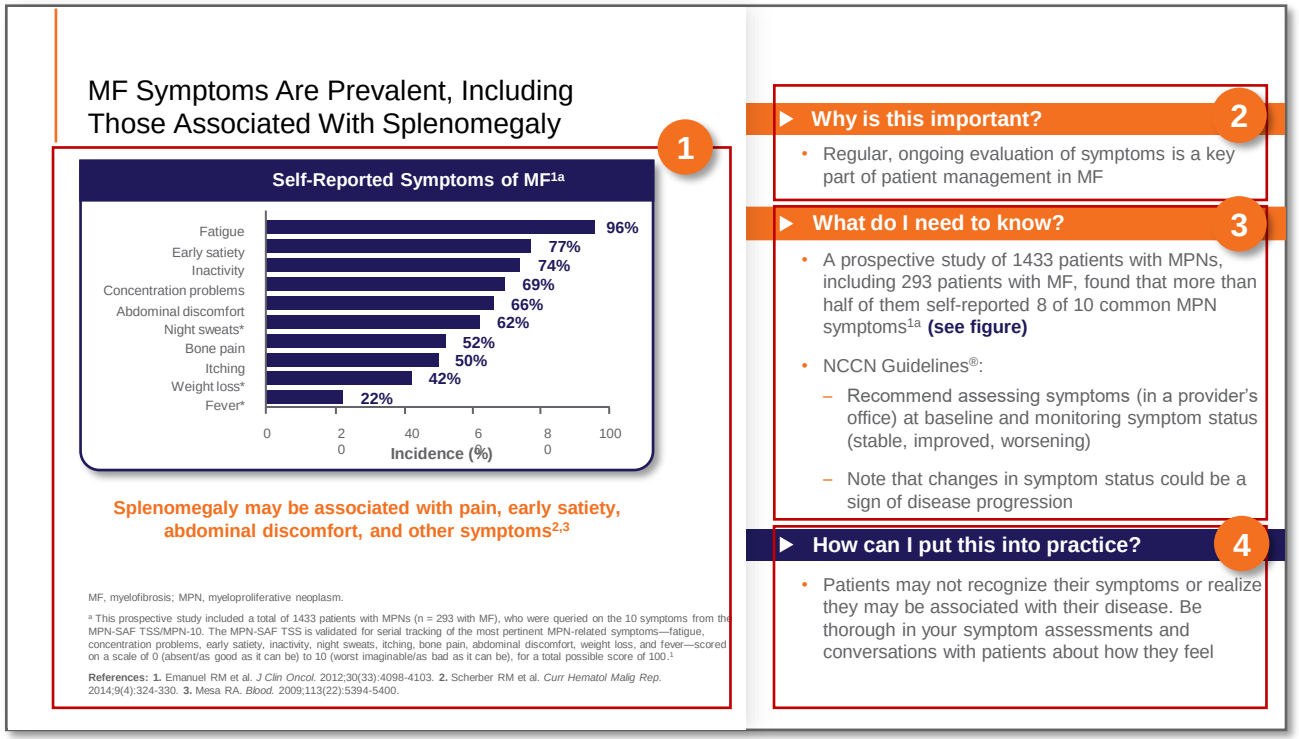
- Proceed through the topic at your own pace
- Return to important points for clarity or reinforcement

Each slide in the module is designed to

- Explain a specific point
- Make the information relevant to your practice

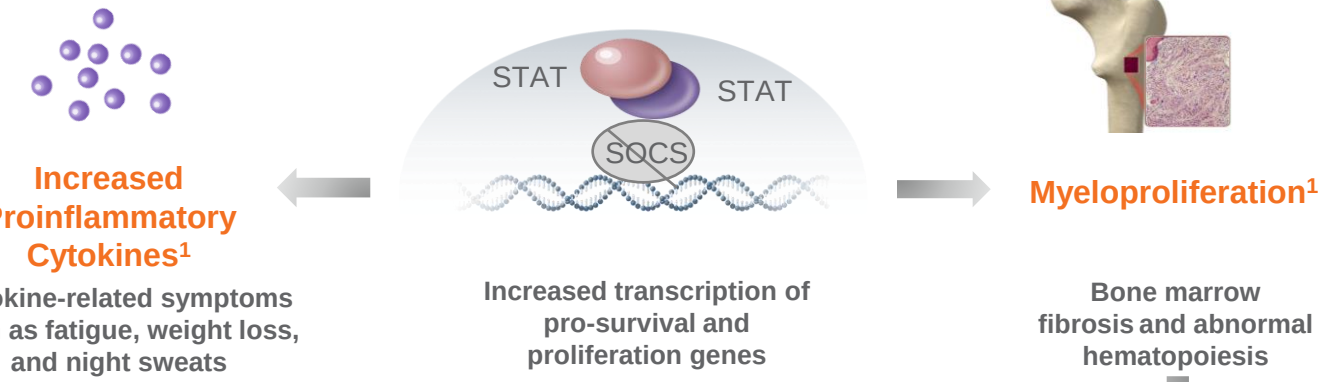
Links to additional resources for APPs can be found at the end of this presentation.

▶ Each slide has 4 sections:



1. Provides key data and contextual information
2. Summarizes the key learning point
3. Expands on the key learning point
4. Reviews ways to implement in practice

Overactive JAK Pathway Signaling Is a Key Driver of Myelofibrosis



Increased Proinflammatory Cytokines[1]

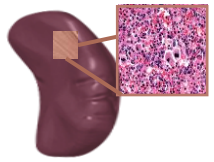
Cytokine-related symptoms such as fatigue, weight loss, and night sweats

Increased transcription of pro-survival and proliferation genes

Myeloproliferation[1]

Bone marrow fibrosis and abnormal hematopoiesis

Extramedullary Hematopoiesis[1-3]



Splenomegaly and its associated symptoms, such as pain, early satiety, abdominal discomfort

Factors that impact JAK signaling[4-6]:

- *JAK2* mutations
- *MPL* mutations
- *CALR* mutations
- Excess cytokines
- Increased JAK1 signaling
- Impaired negative signaling mechanisms (eg, those involving SOCS)

JAK1
plays a major role in signaling of key proinflammatory cytokines[7]

JAK2
mediates signals for hematopoietic growth factors[7]

CALR, calreticulin; JAK, Janus-associated kinase; MPL, myeloproliferative leukemia virus oncogene (TPO receptor); SOCS, suppressor of cytokine signaling; STAT, signal transducer and activator of transcription.

References: 1. Spivak JL. *N Engl J Med.* 2017;376(22):2168-2181. **2.** Mesa RA. *Blood.* 2009;113(22):5394-5400. **3.** Scherber RM et al. *Curr Hematol Malig Rep*. 2014;9(4):324-330. **4.** Quintás-Cardama A et al. *Nat Rev Drug Discov.* 2011;10(2):127-140. **5.** Klampfl T et al. *N Engl J Med*. 2013;369(25):2379-2390. **6.** Vainchenker W et al. *Blood*. 2011;118(7):1723-1735. **7.** Quintás-Cardama A et al. *Blood*. 2010;115(15):3109-3117.

Why is this important?

- Overactive JAK pathway signaling can contribute to the clinical manifestations of MF, including splenomegaly due to extramedullary hematopoiesis[1,7]

What do I need to know?

- In MF, JAK-pathway mutations, such as *JAK2*, *CALR*, and *MPL*, lead to dysregulated signaling[4-6]
- This may result in abnormal blood counts, bone marrow fibrosis, extramedullary hematopoiesis (eg, splenomegaly), and MF-associated symptom burden[1] **(see figure)**

How can I put this into practice?

- Educating your patients on their disease can help them better understand how MF affects them physiologically and can cause symptom burden

Splenomegaly Is Prevalent in MF and Often Is Present at Diagnosis

Approximately 90%

of patients with MF had palpable splenomegaly at diagnosis[1]

Based on a study of 1054 patients with primary MF; data were available for 768 patients, 681 of whom had palpable splenomegaly[1]

- **NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms recommend palpating the spleen at diagnosis in all patients[2]**
- Imaging, including ultrasound, may be appropriate for patients with a body habitus which precludes palpation[3]

MF, myelofibrosis; NCCN, National Comprehensive Cancer Network.

References: 1. Cervantes F et al. *Blood*. 2009;113(13):2895-2901. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms V.1.2020. © National Comprehensive Cancer Network, Inc 2020. All rights reserved. Accessed May 21, 2020. 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. **3.** Tremblay D et al. *Ann Hematol.* 2020;99(7):1441-1451**. 4.** Arber DA et al. *Blood*. 2016;127(20):2391-2405.

Why is this important?

- Splenomegaly is an important clinical indicator in MF, and spleen assessment should be part of a diagnostic work up[2,4]

What do I need to know?

- In one study of patients with primary MF, 681 of 768 evaluable patients had splenomegaly at diagnosis[1] **(see figure)**

How can I put this into practice?

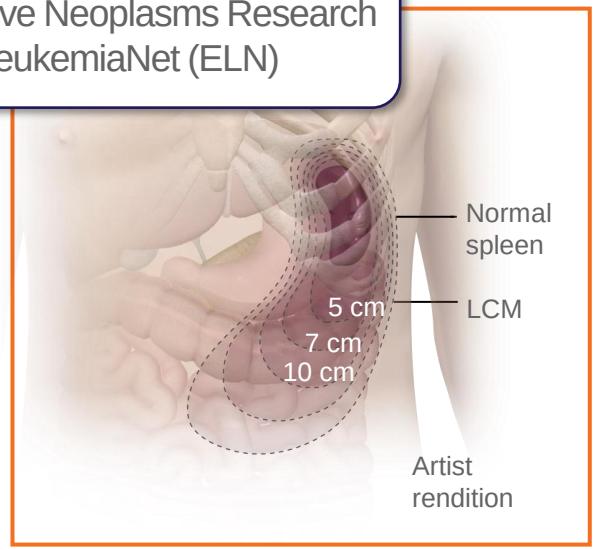
- Conduct spleen assessments in newly diagnosed patients with MF
- Be sure your patients understand that an enlarged spleen is a commonly observed characteristic of MF that may be present at the time of their diagnosis
- It is also important to continue to monitor for splenomegaly throughout the course of disease

New or Increasing Splenomegaly May Indicate Disease Progression

A palpable spleen of ≥5 cm

below the left costal margin
constitutes progressive disease[a]

According to current response criteria in MF developed by the International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN)



LCM, left costal margin; MF, myelofibrosis.

[a] Progressive disease assignment for splenomegaly requires confirmation by CT or MRI showing a ≥25% increase in spleen volume from baseline. Baseline values for both physical examination and imaging studies refer to pretreatment (baseline) and not to post-treatment measurements.

Reference: Tefferi A et al. *Blood*. 2013;122(8):1395-1398.

▶ Why is this important?

- Splenomegaly can occur or increase throughout the course of a patient's disease

▶ What do I need to know?

- New or increasing splenomegaly is considered to be a marker of disease progression in MF[a] **(see figure)**
- These IWG-MRT and ELN criteria were developed to account for the potentially significant impact of disease-related symptoms, including those associated with splenomegaly, on quality of life

▶ How can I put this into practice?

- Consider including spleen assessments in appropriate patients as part of your regular monitoring and management protocol

A Majority of Patients With MF Report Symptom Burden at Diagnosis[1,2]

95%

of patients reported 2+ MF-related symptoms at diagnosis[2a]

Based on a retrospective chart review of 180 patients with MF[2a]

MF, myelofibrosis; MPN, myeloproliferative neoplasm.

[a] Retrospective observational study of symptom burden and splenomegaly in 180 patients with MF; data were collected at the time of diagnosis of MF in patients without splenomegaly (n=78) or at the time of detection of splenomegaly in patients with splenomegaly (n=102). In patients with splenomegaly, splenomegaly was most often recorded at the time of diagnosis (median time from MF diagnosis to reported splenomegaly was 1 day).[2]

[b] The MPN Landmark Survey, funded by Incyte Corporation, was a web-based questionnaire composed of 65 multiple-choice questions intended to help evaluate the patient's perception of disease burden in the MPN disease setting. A total of 813 patients in the United States with a previous diagnosis of polycythemia vera (n = 380), MF (n = 207), or essential thrombocythemia (n = 226) participated.[1]

References: 1. Mesa R et al. *BMC Cancer*. 2016;16:167. **2.** Mitra D et al. *Cancer Med*. 2013;2(6):889-898.

▶ Why is this important?

- Symptom burden is a hallmark of MF, including in patients with earlier disease, and symptoms may be present at diagnosis[1,2]

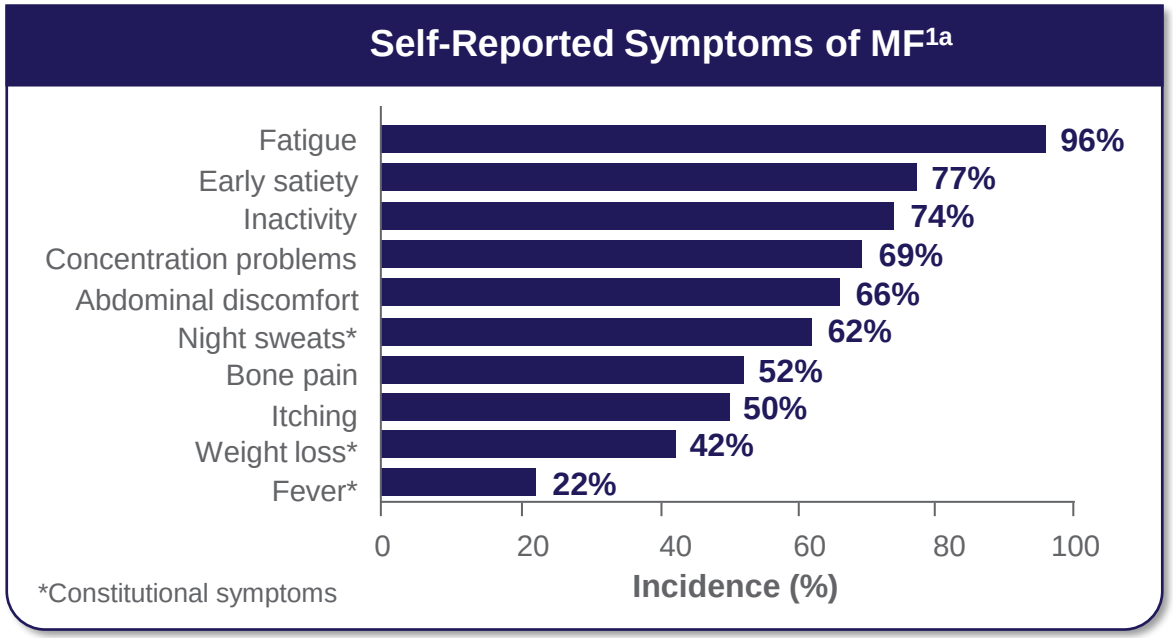
▶ What do I need to know?

- In a retrospective chart review of 180 patients with MF, 95% of patients reported 2+ MF-related symptoms at diagnosis[2a] **(see figure)**
- In the MPN Landmark survey, a web-based questionnaire intended to help evaluate patient perceptions of disease burden in the MPN disease setting, 49% of patients with MF reported experiencing symptoms at least 1 year before diagnosis[1b]

▶ How can I put this into practice?

- Newly diagnosed patients with MF may have symptoms so it may be helpful to consider disease-related symptoms in your diagnostic work up
- Patients with MF may experience symptoms for some time and they may not consider them significant or have learned to accommodate them, so probe diligently about symptom burden

MF-Related Symptoms Are Prevalent, Including Those Associated With Splenomegaly



Splenomegaly may be associated with pain, early satiety, abdominal discomfort, and other symptoms[2,3]

MF, myelofibrosis; MPN, myeloproliferative neoplasm.

[a] This prospective study included a total of 1433 patients with MPNs (n = 293 with MF), who were queried on the 10 symptoms from the MPN-SAF TSS/MPN-10. The MPN-SAF TSS is validated for serial tracking of the most pertinent MPN-related symptoms—fatigue, concentration problems, early satiety, inactivity, night sweats, itching, bone pain, abdominal discomfort, weight loss, and fever—scored on a scale of 0 (absent/as good as it can be) to 10 (worst imaginable/as bad as it can be), for a total possible score of 100.[1]

References: 1. Emanuel RM et al. *J Clin Oncol*. 2012;30(33):4098-4103. **2.** Scherber RM et al. *Curr Hematol Malig Rep*. 2014;9(4):324-330. **3.** Mesa RA. *Blood.* 2009;113(22):5394-5400. **4.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms V.1.2020. © National Comprehensive Cancer Network, Inc 2020. All rights reserved. Accessed May 21, 2020. 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.

▶ Why is this important?

- Regular, ongoing evaluation of symptoms should be part of patient management in MF

▶ What do I need to know?

- A prospective study of 1433 patients with MPNs, including 293 patients with MF, found that at least half of them self-reported 8 of 10 common MPN symptoms[1a] **(see figure)**
- NCCN Guidelines®:
  - Recommend assessing symptoms (in a provider's office) at baseline and monitoring symptom status (stable, improved, worsening)[4]
  - Note that changes in symptom status could be a sign of disease progression[4]

▶ How can I put this into practice?

- Patients may not recognize their symptoms or realize they may be associated with their disease. Be thorough in your symptom assessments and conversations with patients about how they feel

MF-Related Symptoms Can Impact Quality of Life for Some Patients

Patient-reported results from the MPN Landmark Survey[a]:

81% of patients with MF reported that their symptoms reduced their quality of life[b]

79% reported that MF interfered with family or social life[c]

MF, myelofibrosis; MPN, myeloproliferative neoplasm.

[a] The MPN Landmark Survey, funded by Incyte Corporation, was a web-based questionnaire composed of 65 multiple-choice questions intended to help evaluate the patient's perception of disease burden in the MPN disease setting. A total of 813 patients in the United States with a previous diagnosis of polycythemia vera (n = 380), MF (n = 207), or essential thrombocythemia (n = 226) participated.
[b] Patients reported whether they strongly agreed, somewhat agreed, somewhat disagreed, or strongly disagreed with the following statement: MF symptoms reduce my quality of life.
[c] Patients reported impact on their family or social life on a scale that ranged from 1 (not at all) to 5 (a great deal). The patient was included as having interference with family or social life if they had ever experienced the issue and reported a score >1.

Reference: Mesa R et al. *BMC Cancer*. 2016;16:167.

▶ Why is this important?

- Addressing and helping maintain quality of life is an important management goal for some patients with MF

▶ What do I need to know?

- Results from The MPN Landmark Survey, a web-based questionnaire intended to help evaluate patient perceptions of disease burden in the MPN disease setting, found that **(see figure)**
  - 81% of patients with MF (n=207) reported their symptoms reduced their quality of life[b]
  - 79% (n=163) reported that MF interfered with family or social life[c]

▶ How can I put this into practice?

- Ask patients questions about their ability to perform daily activities in order to help identify
  - Disease-related symptoms that may be new, becoming more frequent, worsening, or improving
  - How these symptoms may be affecting their quality of life

Enhance Your Conversations About Symptoms With Contextual Questions

Early Satiety
- Do you feel full quickly after meals?
- Have you lost weight in the past 6 months, without intentionally trying to?

Fatigue and Inactivity
- Do you feel tired even after getting enough sleep, or do you tire quickly during the day?
- How many normal waking hours each day do you spend in a bed or chair?
- Are there activities that you were able to do 3 months ago that you struggle with now?

Abdominal Discomfort
- Do you have abdominal discomfort, particularly after eating?
- Do you experience any dull or sharp pains in your abdomen?
- Do you experience abdominal discomfort at any other time?
- Do you find it difficult to get into a comfortable position for sleeping?

Concentration Problems
- How often have you felt a “brain fog”—memory lapses, inability to pay attention for long periods, or generally having problems concentrating that interfere with your ability to work?
- How has this impacted your life? Have you had to change school plans, work, or how you function at home?

Caregivers can be a valuable source of information. They often see the impact of MF-related symptoms on a patient’s quality of life or daily activity.

▶ Why is this important?

- Patients with MF may not fully discuss their symptoms with their healthcare team

▶ What do I need to know?

- Symptoms such as fatigue and concentration problems may be overlooked as being due to aging
- Contextual questions can be helpful for identifying a patient’s MF-related symptom burden
- A caregiver’s observations can also provide valuable insights about changes in a patient’s daily activities and quality of life

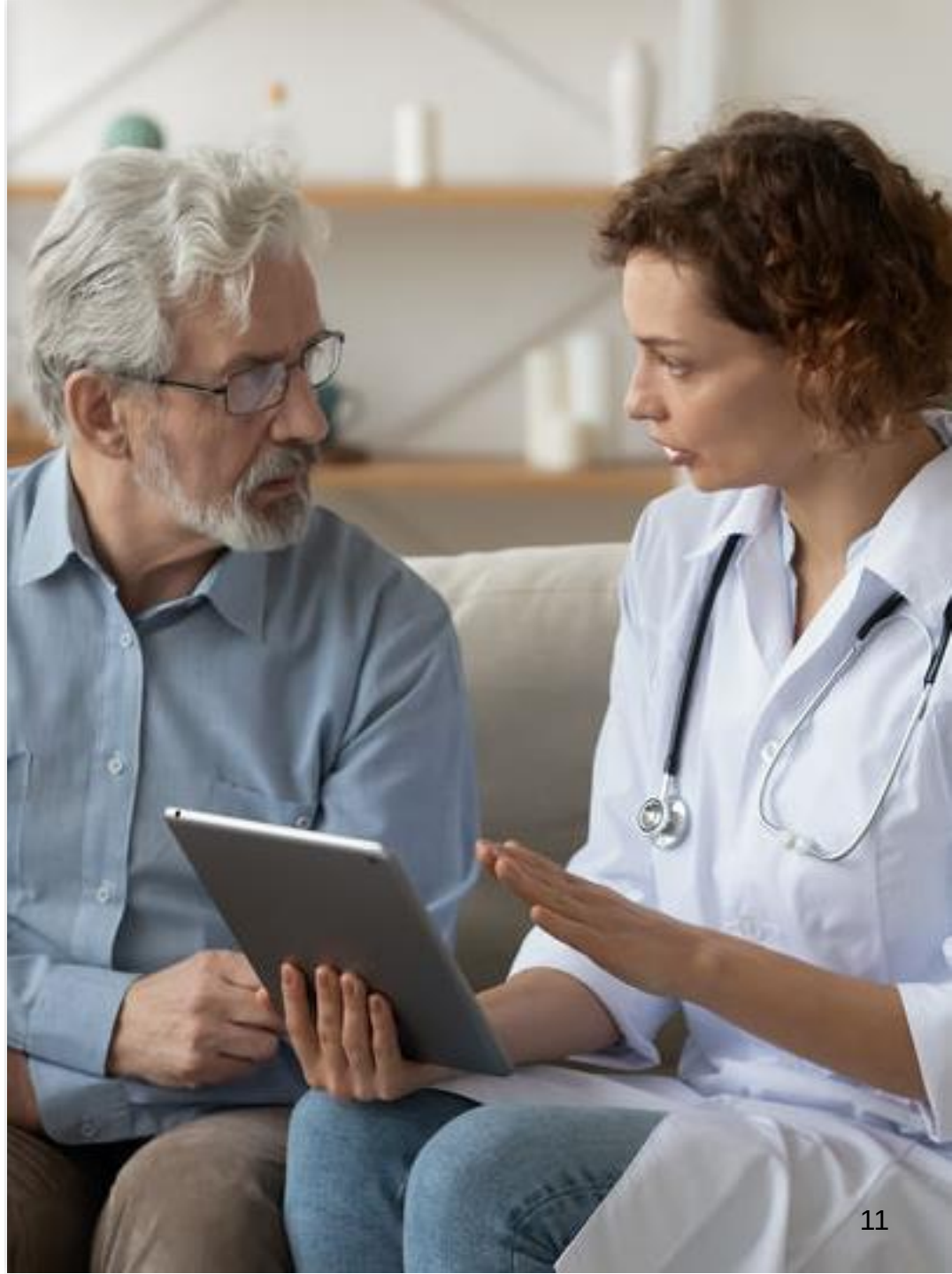
▶ How can I put this into practice?

- Use open-ended contextual questions to help encourage your patients to express their symptom burden and severity based on what they experience in daily life
- These questions can also help support symptom assessments during telehealth calls

MF, myelofibrosis.

Key Considerations for Monitoring Splenomegaly and MF-Related Symptoms

- **Assess the spleen** by palpation—and imaging (eg, ultrasound) if appropriate for an accurate assessment—**at diagnosis and consistently throughout the course of disease**
- Obtain a detailed picture of the patient's symptom burden by asking open-ended questions about **specific symptoms known to be associated with MF**
- **Empower patients and caregivers** to take an active role in symptom identification by educating them about MF-related symptoms



MF, myelofibrosis.

Summary

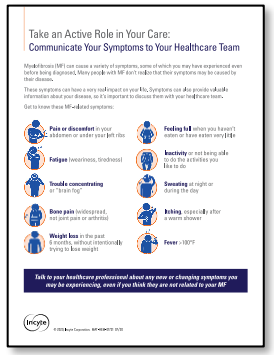
- MF is a serious hematologic malignancy that arises from overactive JAK/STAT signaling and is characterized by splenomegaly and substantial symptom burden
- Splenomegaly is an important clinical indicator that should be assessed at diagnosis and as part of ongoing patient management
- Symptoms should be monitored at baseline and during the course of disease, as changes in symptom status could be a sign of disease progression
- Changes in symptom status can be challenging to identify because patients may not recognize their symptoms or realize they may be associated with their disease
- Use of contextual questions in patient conversations may help patients more accurately describe their symptom burden and severity in terms of how it impacts their quality of life

JAK/STAT, Janus kinase-signal transducer and activator of transcription; MF, myelofibrosis.

Additional Resources

▶ Click to Explore

Download


Take an Active Role in Your Care:
Communicate Your Symptoms to Your Healthcare Team
Talk to your healthcare professional about any new or changing symptoms you may be experiencing, even if you think they are not related to your MF

[Symptom assessment conversation aid]

Video

[Watch a physician discuss spleen assessment]

Contact Incyte

[Meet with an Oncology Clinical Nurse Educator]