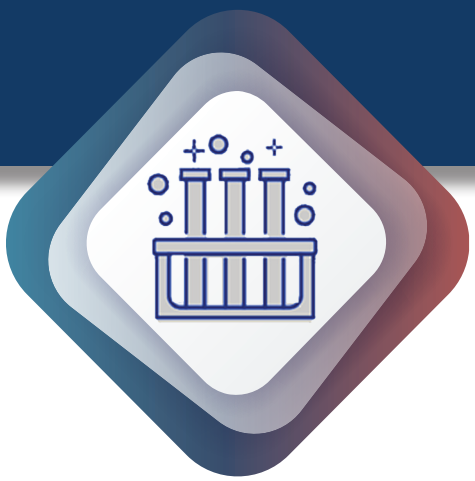

Goals of Treatment, Expectations, and Adverse Events (Cytopenias)

How should patients participate in their own care, monitoring of symptoms, and reporting of symptoms?

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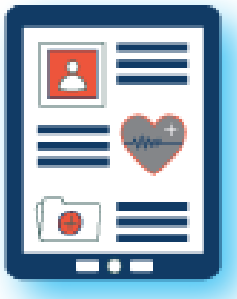
"The goal is to create alignment with the patient at every juncture and to meet the patient where they are to improve engagement in the care process."

Shared decision-making (SDM) is a tool to set individualized goals of care. Patient-centered communication (PCC) is critical to building a foundation of trust, essential to ongoing patient and caregiver engagement in discussing goals of care, participating in treatment decision-making, setting expectations, and tracking and reporting disease and treatment related symptoms. This is critically important in effectively managing patients with myelofibrosis (MF) where symptom burden impact, mitigation and management are the preferred primary outcomes in most clinical trials and are essential for improving quality of life.

PCC requires a bidirectional and dynamic exchange of information across the continuum of care.[1] Although many clinicians believe they consistently apply these principles in interactions with patients and caregivers, discordance between clinician and MF patient perspectives of clear and effective communication indicate there are gaps and barriers to SDM and PCC.[2,3] Differing views among patients and clinicians emphasize the need to deploy a more intentional process for supporting patients and caregiver health literacy, learning style, and decision-making preferences.



Understanding common barriers and those specific to the patient with MF is necessary to overcome them. There are general barriers inherent in the health care system, including a lack of training and education for PCC and SDM, time limitations, challenges within the electronic health record (EHR), staff turnover and shortages limiting continuity, and inefficient workflows.[4] The increased use of telehealth during the COVID-19 pandemic, although allowing patients to continue their care, has disrupted the important face-to-face communications and evaluation of physical findings and symptom burden critical to managing MF. For those patients that prefer telehealth options, alternating visits with in-person and

virtual options may offer a better way to adequately evaluate symptom burden and physical findings (weight loss, wasting, splenomegaly, hepatomegaly, frailty, etc.). Including the caregiver, if possible, in telehealth visits may improve virtual evaluation of symptom severity and identification of any new concerns for the patient and the caregiver.

The rapidly evolving science with expanded treatment options and continuously updated treatment guidelines, along with modification of criteria for response and progression or ruxolitinib failure, pose challenges to the clinician, including their ability to effectively explain these using PCC and SDM to the patient. There are many unknowns as much of the data is in its nascent phase. Acknowledging the strengths and limitations of the data and any alternative treatment options, including clinical trials, is recommended.

"Setting expectations for the patient and their caregivers when presenting treatment options is critical to optimal outcomes."

Maximizing each treatment option requires a proactive approach to symptom assessment and mitigation.

Information specific to each treatment option including schedule, dosing, administration, missed dose management, drug-drug and drug-food interactions, common and rare adverse events (AEs), self-management strategies, and when, who and how to call to seek assistance, including emergent management, are core components of informed consent and setting expectations. Using simple language, printed or online information, and when possible visual aids will improve understanding.[5,6]

With most treatment options being either all oral or combination therapies, the time patients spend with the infusion nursing staff and support staff in general is more limited. Oral adherence continues to pose a challenge to the patient and to practices with an estimated adherence rate ranging from 50 to 65% in most studies of patient reported outcomes.[7,8] Taking drugs as prescribed is essential to achieving the desired outcomes.

Moderate to severe AEs are one of the most common reasons for early discontinuation of oral therapies for MF.[7]

The most common disease related symptoms and treatment related adverse events for patients living with MF are well described. Translating that into

language that the patient and caregivers can understand is essential to building self-care and self-advocacy strategies and to making informed decisions about AE management and any dose modifications. Encouraging the use of journals, calendars, patient portals in the EHR, and other tools or decision aids can improve patient-provider communication. Emulating practices used in clinical trials for symptom tracking and self-report including reviewing pill counts or asking about missed doses may provide the best option to tailor discussions about AE management and the importance of adherence.

"Establishing oral adherence programs within each practice, leveraging assistance and support programs for oral antineoplastics, and providing pre-treatment and follow-up education similar to that provided for injectable agents is essential to optimize oral adherence and limit AE severity."[9]

With the expanded options for treatment, some of the disease or treatment related AEs now direct therapy. For example, MF patients with thrombocytopenia (platelets <50k × 10^9/L) may benefit most from treatment with pacritinib, an oral therapy which has shown to cause less thrombocytopenia, allowing continuation of therapy in this patient population.[10-13] Similarly, MF patients who are either intolerant of or are losing benefit from ruxolitinib that have platelet counts >50k × 10^9/L, may continue to benefit from fedratinib, a JAK2-selective kinase inhibitor. In the JAKARTA1 and JAKARTA-2 trials, ~35% to 40% of patients in the JAKARTA1 trial and 25% to 30% of patients (JAKARTA-2) met the primary endpoints of spleen volume reduction (SVR) ≥35% and >50% reduction in total symptom score (TSS), respectively, indicating that one can still salvage spleen and symptom burden, even with a drug from the same class that differs from the original JAK inhibitor.[14,15]

"Interdisciplinary collaboration and coordination of resources to address and overcome barriers (e.g., social needs, financial barriers, language barriers, transportation, cost of care etc.) will improve patient engagement and treatment continuity."

Fedratinib is also now approved for use in adults with intermediate-2 or high-risk MF in the frontline setting. In patients that may continue to benefit from ruxolitinib, but who become transfusion dependent for red blood cells, may benefit from the addition of luspatercept*, an activin ligand trap, which is part of the TGF-beta superfamily, that down-regulates SMAD signaling allowing for red cell maturation.[16]

*Luspatercept is not FDA approved for any use in patients with myelofibrosis who have become transfusion dependent. The safety and efficacy of luspatercept-aamt is currently being studied in patients with myeloproliferative neoplasm (MPN)-associated myelofibrosis who are receiving concomitant JAK2 inhibitor therapy and who require red blood cell transfusions (RBCs), as part of a clinical trial.

Referrals to social services, nutrition, physical therapy, psychiatry, palliative and supportive care, and integrative oncology based on individual patient needs will optimize wellness and may reduce symptom burden and distress.[17]
The patient and their caregivers are an extension of the clinical team and must assume a large part of managing their illness and wellness. How can we empower patients and caregivers to become partners in their care?[17,18]

1) Build trust:
   a. Listen, individualize SDM and PCC strategies, provide reassurance, reinforce learning, reflect on what you know about the patient's individual situation.

2) Support self-efficacy:
   a. Encourage patient-caregiver to leverage support networks.
      i. List current sources of support – consider how each source might assist with specific tasks.
      ii. Build strategies to support the knowledge and skills necessary to mitigate stressors and decrease symptom burden.
      ii. Attend/join support group for MF survivors.
   b. Discuss how to prepare for each provider visit and what is expected between visits to improve outcomes (give homework).
   c. Foster communication skills.

3) Support health literacy using a continuum-based, interdisciplinary, individualized approach:
   a. Provide education relevant to patient needs at each point in time.
   b. Refer or recommend vetted information sources and professional resources.
   c. Begin the discussion of palliative and supportive care early in the diagnosis.

4) Take action to reduce barriers to care:
   a. Maximize interdisciplinary resources.
   b. Build a consistent approach to care and communication with the patient, caregiver, and other clinicians.
   c. Be prepared to shift based on changing goals of care.
   d. Develop or optimize an oral antineoplastic therapy program.

5) Promote wellness:
   a. Referral to integrative oncology.
   b. Discuss diet and exercise as tools to improve wellness.
   c. Discuss alternative and complimentary medicines and therapies. Patients will use them and may not self-disclose. It is important to understand their role in the patient's tolerance to therapy and any potential contraindications.

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