Putting Knowledge Into Practice:

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

Identifying and Monitoring Symptoms in Polycythemia Vera

Incyte

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).

Identifying and Monitoring Symptoms in Polycythemia Vera provides information on disease-related symptoms in patients with PV and guidance on how to manage them.

Topics include:

- Prevalence and causes of PV-related symptoms

- Monitoring symptom burden in patients with PV

- Practical approaches to symptom assessment in patients with PV

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:**

Patients Can Experience Symptoms Despite Adequate Blood Count Control

1

Mean Total Symptom Score According to Blood Count Control Status (Hct, WBC, PLT)[1]

	TSS
All 3 uncontrolled	20.2
≥1 controlled	18.7
≥1 controlled	18.7
All 3 controlled (CHR)	19.1

0 4 8 12 16 20 24
TSS

Total Symptom Score Key[2,3]
0-7: Low symptom burden
8-17: Intermediate symptom burden
18-31: Moderately high symptom burden
>32: High symptom burden

CHR, complete hematologic response; Hct, hematocrit; HU, hydroxyurea; MPN, myeloproliferative neoplasm; MPN-SAF TSS, Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score; PLT, platelet; PV, polycythemia vera; TSS, total symptom score; WBC, white blood cell.

[a] REVEAL was a prospective, observational study that collected contemporary data regarding burden of disease, clinical management, patient-reported outcomes, and healthcare resource utilization from 2510 adult patients with PV in the United States and was sponsored by Incyte. Patients were enrolled over an approximate 2-year period (July 2014 to August 2016). This analysis included 1813 (72.2%) evaluable patients who had a complete blood count within 30 days before completion of the at-enrollment MPN-SAF TSS. At the time of enrollment, most patients (n = 1714; 94.5%) were being managed with cytoreductive therapy; 1581 patients (87.2%) were managed with phlebotomy, HU, or a combination thereof. CHR was defined as Hct <45%, WBC count <10 × 10^{9}/L, and PLT count ≤400 × 10^{9}/L; these same criteria were used to determine if Hct, WBC, and PLT were controlled.[1]
References: 1. Grunwald MR et al. *Clin Lymphoma Myeloma Leuk.* 2019;19(9):579-584. **2.** Emanuel RM et al. *Blood.* 2013;122:4067. **3.** Geyer H et al. *J Clin Oncol.* 2016;34(2):151-159.

▶ **Why is this important?**   **2**
- The burden of symptoms that patients with PV experience is not correlated with how effectively their blood counts are being controlled

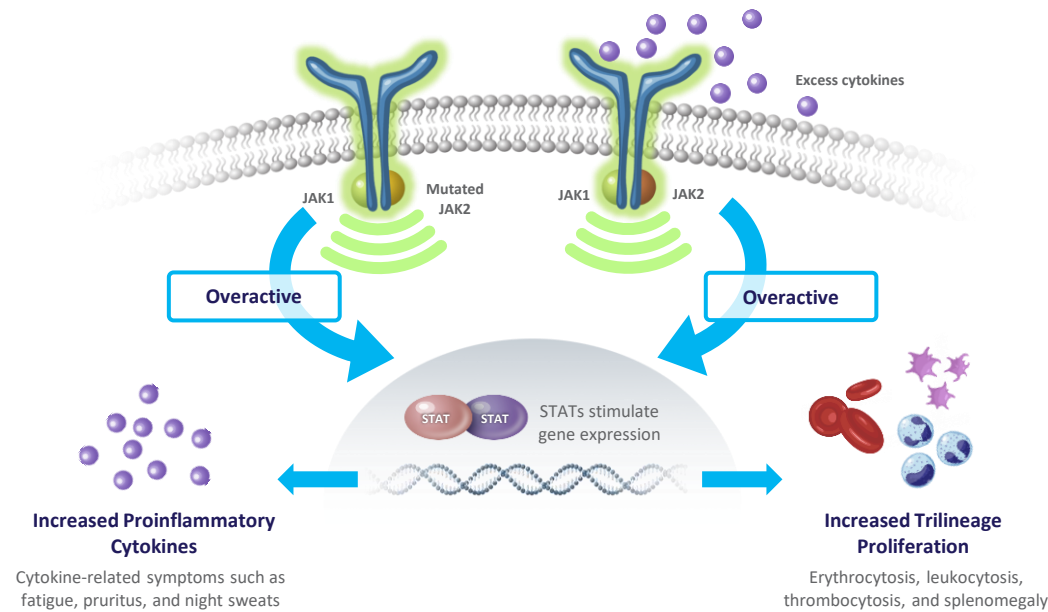▶ **What do I need to know?**   **3**
- Patients with PV in one prospective, observational study on average reported a moderately high symptom burden regardless of the number of blood counts controlled[1] **(see figure)**
- Most patients were managed with cytoreductive therapy at enrollment, 87.2% of whom were managed with phlebotomy, HU, or a combination of the two
- Remember that factors other than blood hyperviscosity, such as increased proinflammatory cytokines and splenomegaly, can also contribute to symptom burden

▶ **How can I put this into practice?**   **4**
- Probe your patients about their symptoms even if they are maintaining adequate blood count control, and be sure they understand that the two are not necessarily related

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

Proinflammatory Cytokine Activity and Blood Cell Proliferation Can Drive Symptoms[1-6]

Excess cytokines

JAK1 | Mutated JAK2 | JAK1 | JAK2

Overactive | Overactive

STATs stimulate gene expression

Increased Proinflammatory Cytokines
Cytokine-related symptoms such as fatigue, pruritus, and night sweats

Increased Trilineage Proliferation
Erythrocytosis, leukocytosis, thrombocytosis, and splenomegaly

JAK1 plays an important role in signaling of key proinflammatory cytokines[1]

JAK2 mediates signals for hematopoietic growth factors (eg, EPO, TPO, G-CSF)[1]

▶ Why is this important?

- Symptoms of PV are associated with blood hyperviscosity due to elevated blood cell counts, increased cytokine activity, and splenomegaly[4,6-8]

▶ What do I need to know?

- Overactive JAK/STAT pathway signaling may result in elevated blood cell counts, including hematocrit (erythrocytosis), white blood cells (leukocytosis), and platelets (thrombocytosis)[3,4] **(see figure)**

- Increased proinflammatory cytokines contribute to symptoms such as fatigue, pruritus, and night sweats[6]

▶ How can I put this into practice?

- Educate patients on their disease to help them better recognize and understand PV-related symptoms

EPO, erythropoietin; G-CSF, granulocyte colony-stimulating factor; JAK, Janus kinase; PV, polycythemia vera; STAT, signal transducer and activator of transcription; TPO, thrombopoietin.

References: 1. Quintás-Cardama A et al. *Blood.* 2010;115(15):3109-3117. **2.** Vainchenker W et al. *Blood.* 2017;129(6):667-679. **3.** Arber DA et al. *Blood.* 2016;127(20):2391-2405. **4.** Verstovsek S et al. *Expert Rev Hematol.* 2015;8(1):101-113. **5.** Quintás-Cardama A et al. *Nature Rev.* 2011;10:127-140. **6.** Geyer HL et al. *Mediators Inflamm.* 2015;2015:284706. **7.** Craver BM et al. *Cancers (Basel).* 2018;10(4):1-18. **8.** Scherber R et al. *Blood.* 2011;118(2):401-408.

PV Symptoms May Persist Despite Interventions Such as HU

MPN-10 Mean Symptom Scores in Patients With Known HU Use

■ HU use (n = 499)
■ No HU use (n = 807)

† $P < 0.05$ ‡ $P < 0.001$
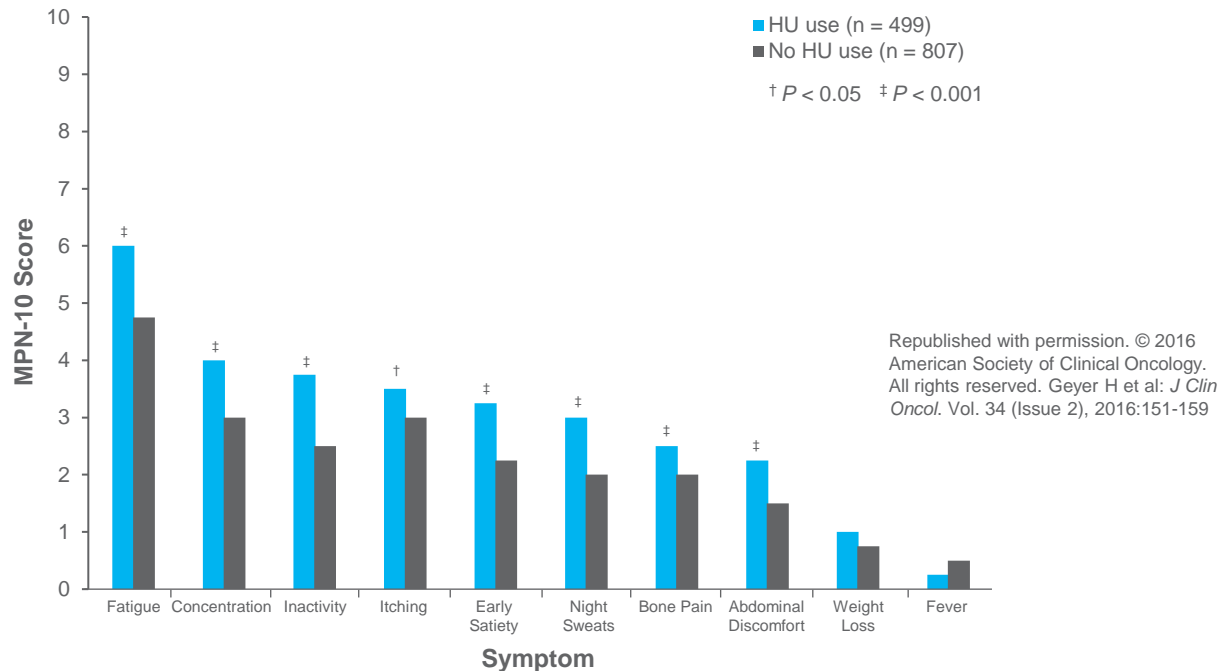
HU, hydroxyurea; MPN, myeloproliferative neoplasm; PV, polycythemia vera; TSS, total symptom score.
[a] In this prospective study of 1334 patients with PV, patients were stratified by known HU use (n = 499), known phlebotomy (n = 646), palpable splenomegaly (n = 369), or all 3 features (n = 148) and compared to a control group of patients who lacked the specified feature. Assessment of MPN symptoms was performed by using the MPN-Symptom Assessment Form Total Symptom Score (MPN-SAF TSS; MPN-10). All items were evaluated on a 0 (absent) to 10 (worst imaginable) scale for a possible range of 0 to 100, with 100 representing the highest level of symptom severity. The TSS for each patient was analyzed to place the patient into the quartiles of low symptom burden (TSS, 0 to 7), intermediate symptom burden (TSS, 8 to 17), moderately high symptom burden (TSS, 18 to 31), or high symptom burden (TSS, ≥32).
Reference: Geyer H et al. *J Clin Oncol.* 2016;34(2):151-159.

► Why is this important?

- Patients receiving hydroxyurea may continue to experience symptoms
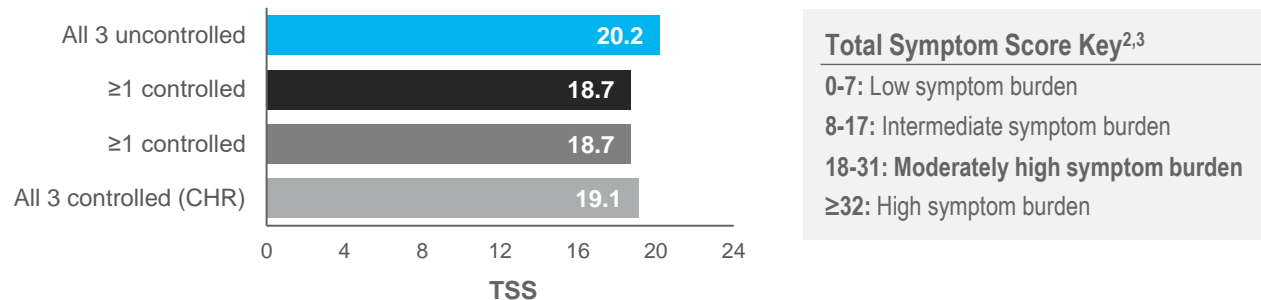
► What do I need to know?

- One prospective study evaluated mean self-reported total symptom scores (TSS) across 1334 patients with PV where a subset of patients received HU (n = 499)[a] **(see figure)**

- Patients with known HU use reported a 29.2 average TSS, indicating a moderately high symptom burden

- Patients with known HU use had the highest mean symptom scores for microvascular and cytokine-related symptoms, including fatigue, inactivity, concentration problems, night sweats, and bone pain

► How can I put this into practice?

- Be vigilant about symptom severity and impact on quality of life among your patients receiving HU

- Be sure patients understand that they may still experience symptoms despite treatment with HU

Patients Can Experience Symptoms Despite Adequate Blood Count Control

Mean Total Symptom Score According to Blood Count Control Status (Hct, WBC, PLT)[1]

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All 3 uncontrolled	20.2
≥1 controlled	18.7
≥1 controlled	18.7
All 3 controlled (CHR)	19.1

Total Symptom Score Key[2,3]

0-7: Low symptom burden

8-17: Intermediate symptom burden

18-31: Moderately high symptom burden

≥32: High symptom burden

Reprinted from *Clinical Lymphoma Myeloma & Leukemia*, 19(9), Grunwald MR, Burke JM, Kuter DJ, et al, Symptom burden and blood counts in patients with polycythemia vera in the United States: an analysis from the REVEAL Study, 579-584, Copyright 2019, with permission from Elsevier.

CHR, complete hematologic response; Hct, hematocrit; HU, hydroxyurea; MPN, myeloproliferative neoplasm; MPN-SAF TSS, Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score; PLT, platelet; PV, polycythemia vera; TSS, total symptom score; WBC, white blood cell.

[a] REVEAL was a prospective, observational study that collected contemporary data regarding burden of disease, clinical management, patient-reported outcomes, and healthcare resource utilization from 2510 adult patients with PV in the United States and was sponsored by Incyte. Patients were enrolled over an approximate 2-year period (July 2014 to August 2016). This analysis included 1813 (72.2%) evaluable patients who had a complete blood count within 30 days before completion of the at-enrollment MPN-SAF TSS. At the time of enrollment, most patients (n = 1714; 94.5%) were being managed with cytoreductive therapy; 1581 patients (87.2%) were managed with phlebotomy, HU, or a combination thereof. CHR was defined as Hct <45%, WBC count <10 × 10^9/L, and PLT count ≤400 × 10^9/L; these same criteria were used to determine if Hct, WBC, and PLT were controlled.[1]

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▶ Why is this important?

- The burden of symptoms that patients with PV may experience can occur even with effective blood count control[1]
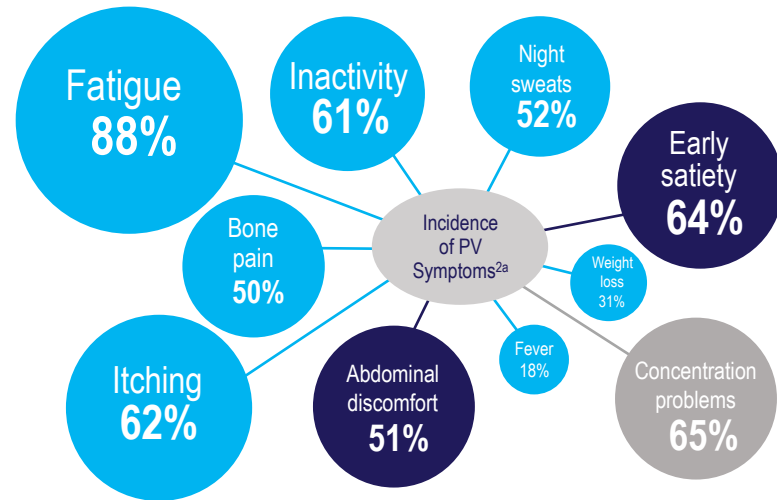
▶ What do I need to know?

- Evaluable patients with PV (n = 1813) in the prospective, observational REVEAL study on average reported a moderately high symptom burden regardless of the number of blood counts controlled[1a] **(see figure)**

- Most patients (n = 1714; 94.5%) were managed with cytoreductive therapy at enrollment, 87.2% of whom were managed with phlebotomy, HU, or a combination of the two[1]

- Remember that factors other than blood hyperviscosity, such as increased proinflammatory cytokines and splenomegaly, can also contribute to symptom burden[4,5]

▶ How can I put this into practice?

- Probe your patients about their symptoms even if they are maintaining adequate blood count control, and be sure they understand that the two are not necessarily related

A Majority of Patients With PV Reported That Symptoms Impact Quality of Life[1-3]

In the MPN Landmark Survey,[b]

66% of patients with PV reported that their symptoms diminished their quality of life[3c]

Fatigue 88%

Inactivity 61%

Night sweats 52%

Early satiety 64%

Bone pain 50%

Incidence of PV Symptoms[2a]

Weight loss 31%

Itching 62%

Abdominal discomfort 51%

Fever 18%

Concentration problems 65%

Type of symptom — Cytokine-related — Hyperviscosity-related — Splenomegaly-related

MPN, myeloproliferative neoplasm; MPN-SAF TSS/MPN-10, Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score; PV, polycythemia vera.

[a] This prospective study included a total of 1433 patients with MPNs (n = 538 with PV), 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.[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 disease burden in the MPN disease setting. A total of 813 patients in the United States with a previous diagnosis of PV (n = 380), myelofibrosis (n = 207), or essential thrombocythemia (n = 226) completed the survey.[3]

[c] Patients reported whether they strongly agreed, somewhat agreed, somewhat disagreed, or strongly disagreed with the following statement: PV symptoms reduce my quality of life.[3]

References: 1. Scherber R et al. *Blood.* 2011;118(2):401-408. **2.** Emanuel RM et al. *J Clin Oncol.* 2012;30(33):4098-4103. **3.** Mesa R et al. *BMC Cancer.* 2016;16:167.

▶ **Why is this important?**

- PV-related symptoms are prevalent and may impact your patient's quality of life[1-3]

▶ **What do I need to know?**

- In a prospective study that included 538 patients with PV, 8 of 10 clinically relevant symptoms were reported in 50% or more of patients[2a] **(see figure)**
- Symptoms related to cytokine activity, hyperviscosity, and splenomegaly are shown
- In the MPN Landmark Survey, two-thirds of patients with PV reported their symptoms diminished their quality of life[3c]

▶ **How can I put this into practice?**

- Implement a process to assess symptom frequency, severity, and impact on quality of life in all of your patients with PV

Obtain a Detailed Picture of How a Patient Is Feeling

Open-ended questions can encourage your patients to express their symptom burden and severity based on what they experience in daily life

Fatigue and Inactivity
- Are there activities that you were able to do 3 months ago that you struggle with now?
- How much does your fatigue or inactivity influence your day-to-day activities? Your enjoyment of life?

Day or Night Sweats
- Do you experience sweating, particularly at night or in the evenings?
- Does this require you to change your sheets or clothing?
- Does this wake you up or impact your sleep?
- How often did this happen in the past month?

Itching
- Have you noticed changes in your skin, particularly itching?
- When you shower, do you ever feel itchy afterwards? How often?
- Have you found yourself taking shorter/fewer/cooler showers to try to avoid itchiness?

Concentration Problems
- How often have you felt a "brain fog"—memory lapses (such as problems remembering words or dates) or generally having problems concentrating?
- 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 PV-related symptoms on a patient's quality of life or daily activity.

PV, polycythemia vera.
Reference: Mesa RA et al. *Cancer.* 2017;123(3):449-458.

▶ Why is this important?
- Patients with PV may not recognize that their symptoms are related to their disease or fully discuss them with their healthcare team[1]

▶ What do I need to know?
- Symptoms such as fatigue and concentration problems may be overlooked as being due to aging, or night sweats may be attributed to menopause
- Contextual questions can be helpful for identifying a patient's PV-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 contextual questions to help detect subtle changes in a patient's symptom status and determine how their quality of life may be affected

Regular Symptom Monitoring Could Help Identify Signs of Disease Progression

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms recommend

- Assessing symptoms (in a provider's office) at baseline
- Monitoring symptom status (stable, improved, or worsening)

▶ Why is this important?

- Along with impacting patient quality of life, changes in symptom status could be a sign of disease progression in some patients. Therefore, change in symptom status should prompt evaluation

▶ What do I need to know?

- NCCN Guidelines® recognize the importance of monitoring patients' response and signs and symptoms of disease progression as part of comprehensive care for patients with PV
- The presence of disease-related symptoms may indicate a need to consider a change in a patient's management plan

▶ How can I put this into practice?

- Share changes in symptom status that could be a sign of disease progression with appropriate care team members

Key Considerations for Symptom Monitoring

Actively monitor symptoms over the course of disease, **even if blood counts are not elevated**

Ask open-ended questions about **specific symptoms known to be associated with PV**

Engage patients and caregivers by educating them about PV-related symptoms

PV, polycythemia vera.

Summary

- PV-related symptoms are driven by 3 clinical manifestations of overactive JAK/STAT pathway signaling:
  - Increased proinflammatory cytokine activity
  - Blood hyperviscosity due to elevated blood cell counts
  - Splenomegaly

- Symptom burden can be substantial in some patients with PV and may persist despite
  - Treatment with HU
  - Adequately controlled blood counts

- The majority of patients with PV experience disease-related symptoms that may impact their quality of life

- Symptoms should be monitored at baseline and during the course of disease
  - Changes in symptom status could be a sign of disease progression

- Contextual questions in patient conversations can help detect changes in symptom burden

Additional Resources

Downloads
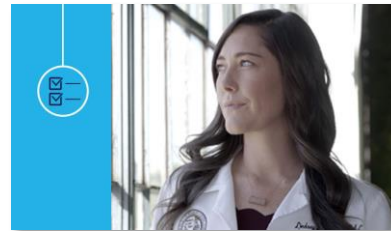

[Symptom assessment conversation aid](#)

[White paper on optimizing the management of PV](#)

Videos

[Watch a patient with PV talk about her symptoms](#)

[Watch a physician assistant discuss symptom monitoring and management](#)

Contact Incyte

[Order a PV blood model](#)

[Meet with an Oncology Clinical Nurse Educator](#)