Allied healthcare professional guide to polycythemia vera

Overview of polycythemia vera

Polycythemia vera is a chronic, progressive myeloproliferative neoplasm that affects about 100,000 people in the United States.[1-3] Polycythemia vera is slightly more prevalent in men than women and occurs mostly in older people, with a median age at diagnosis of approximately 60 years.[2]

Unlike hemochromatosis,[4] polycythemia vera is characterized by an overproduction of red blood cells, white blood cells (WBCs), and platelets[5] without significant bone marrow fibrosis.[6]

Erythrocytosis (elevated total red cell mass) is the most prominent clinical expression of polycythemia vera, and it distinguishes polycythemia vera from all other myeloproliferative neoplasms, including essential thrombocythemia and primary myelofibrosis.[7]

Diagnosing polycythemia vera: WHO criteria[8]

The World Health Organization (WHO) has established major and minor criteria to diagnose polycythemia vera. The criteria are:

Major Criteria	Minor Criteria
1. Hb >18.5 g/dL in men and >16.5 g/dL in women or other evidence of increased red cell volume[a]	1. Bone marrow biopsy showing hypercellularity for age with trilineage growth (pan-myelosis) with prominent erythroid, granulocytic, and megakaryocytic proliferation
2. Presence of *JAK2*V617F mutation or other functionally similar mutation, such as *JAK2* exon 12 mutation	2. Serum erythropoietin level below reference range of normal
	3. Endogenous erythroid colony formation in vitro

Hb, hemoglobin; JAK, Janus-associated kinase.

[a] Hb or hematocrit (Hct) >99th percentile of method-specific reference range for age, sex, altitude of residence **or**

Hb >17 g/dL in men or >15 g/dL in women if associated with a documented and sustained increase of ≥2 g/dL from baseline value that cannot be attributed to correction of iron deficiency **or**

Elevated red cell mass >25% above mean normal predicted value.

Diagnosis of polycythemia vera requires the presence of both major criteria and 1 minor criterion or the presence of the first major criterion together with 2 minor criteria.

Assessing disease control in managing polycythemia vera

Major Risk Stratification Criteria That May Call for Cytoreductive Therapy in Polycythemia Vera[9]

- History of thrombosis (arterial or venous thrombosis; microcirculatory disturbances)
- Age >60 years

For many patients, polycythemia vera remains well managed with hydroxyurea.

However, disease control may be inadequate in patients with any of the following clinical characteristics:

Assessing the Need for Additional Control:
Adapted from ELN Consensus Criteria for Hydroxyurea Failure in Polycythemia Vera[9,10]

Complete blood count (CBC) values to monitor

- Hct ≥45%

→ Have your patients developed a need for phlebotomy, or require increasingly frequent phlebotomies, to control Hct?

- Platelet count >400 × 10^9/L
- WBC count >10 × 10^9/L

→ Must you frequently modify the dose of hydroxyurea, or have you reached the maximum tolerated dose, and counts remain elevated?

Do you see unacceptable adverse reactions that require attention?

→ **Hematologic:** neutropenia, thrombocytopenia, anemia, or other hematologic toxicity

Non-hematologic: leg ulcers, gastrointestinal symptoms, pneumonitis, fever, or toxicity at any dose of hydroxyurea

Do your patients have increasing disease-related signs and symptoms (eg, splenomegaly)?

ELN, European LeukemiaNet.

Identifying patients with polycythemia vera whose disease is inadequately controlled by hydroxyurea

Characteristics of patients with polycythemia vera who have an inadequate response to hydroxyurea despite maximum tolerated dose[10]

- Need for phlebotomy to maintain Hct <45% **or**
- Elevated WBC count (>10 × 10^9/L) and elevated platelet count (>400 × 10^9/L) **or**
- Failure to reduce splenomegaly

Adapted from modified ELN criteria for hydroxyurea resistance and intolerance.

Patient case example: Inadequate response to hydroxyurea

60-year-old female diagnosed with polycythemia vera at age 55

Initial treatment: Hydroxyurea initiated because of elevated Hct level and WBC and platelet counts

- Titrated to maximum tolerated dose of hydroxyurea
- Hct level continues to fluctuate above 45% and requires phlebotomy 4-6 times per year

Clinical presentation:

- Hct level: 48%
- Elevated WBC count
- Normal platelet count
- Increase in symptoms

Characteristics of patients with polycythemia vera who have an intolerance to hydroxyurea[10]

- Cutaneous vasculitic toxicities **or**
- Presence of hydroxyurea-related non-hematologic toxicities, such as gastrointestinal symptoms, pneumonitis, or fever

Adapted from modified ELN criteria for hydroxyurea resistance and intolerance.

Patient case example: Intolerant of hydroxyurea

70-year-old male diagnosed with polycythemia vera at age 57

Initial treatment: Phlebotomy alone for 8 years

- Hydroxyurea initiated because of increasing symptoms and frequency of phlebotomy to maintain Hct level <45%
- Titrated hydroxyurea to 1 g twice daily

Clinical presentation: After 4 years, patient experienced problematic leg ulcers requiring office visits for wound care

- Hydroxyurea discontinued
- Phlebotomy frequency increased
- Spleen size: 5 cm below costal margin

Patient resources

Several organizations maintain online resources that may be useful for your patients with polycythemia vera. Please share these websites offering support, education, and awareness with them:

MPNResearchFoundation.org
Patient resources, community activities, research and treatment news, and information on living with a myeloproliferative neoplasm

LLS.org
Information and support services from The Leukemia & Lymphoma Society (LLS), the world's largest voluntary health agency dedicated to blood cancer

NIH.gov
Community resources, news, and health information from the National Institutes of Health, part of the US Department of Health and Human Services

Assessment for inadequate response to or intolerance of hydroxyurea in patients with polycythemia vera

Clinical checklist

Use this checklist to help assess whether hydroxyurea is providing adequate control in your patients with polycythemia vera.[1]

Patient is taking or has taken hydroxyurea for polycythemia vera	Yes	No
Phlebotomy is required to maintain hematocrit <45%	Yes	No
Treatment has failed to reduce splenomegaly, ie, >50%	Yes	No
Both platelet and white blood cell (WBC) counts are elevated: platelet >400 × 10^9/L, WBC >10 × 10^9/L	Yes	No

Patient checklist

Is your patient currently taking or has he or she previously taken hydroxyurea for polycythemia vera? If so, ask your patient the following questions to determine whether he or she may be having an inadequate response to or intolerance of hydroxyurea.

While taking hydroxyurea, did you develop any skin issues such as leg ulcers?	Yes	No
While taking hydroxyurea, did you develop unacceptable toxicities such as fever, lung inflammation, constipation, diarrhea, nausea, or vomiting?	Yes	No
While taking hydroxyurea, did you continue to have symptoms related to an enlarged spleen such as stomach pain or a feeling of fullness?	Yes	No

Based on the responses above, your patient may be having an inadequate response to or intolerance of hydroxyurea. Treatment options should be discussed.

Notes: _____

Reference: 1. Barosi G et al. *Br J Haematol.* 2009;148(6):961-963.

References: 1. Marchioli R et al; CYTO-PV Collaborative Group. *N Engl J Med.* 2013;368(1):22-33. **2.** Tefferi A. *Mayo Clin Proc.* 2003;78(2):174-194. **3.** Data on file. Incyte Corporation. Wilmington, DE. **4.** Leitman SF. *Hematology Am Soc Hematol Educ Program.* 2013;2013:645-650. **5.** Spivak JL. *Blood.* 2002;100(13):4272-4290. **6.** Michiels JJ. *Hematol J.* 2004;5(2):93-102. **7.** Spivak JL. *Ann Intern Med.* 2010;152(5):300-306. **8.** Vardiman JW et al. *Blood.* 2009;114(5):937-951. **9.** Barbui T et al. *J Clin Oncol.* 2011;29(6): 761-770. **10.** Barosi G et al. *Br J Haematol.* 2009;148(6):961-963.