Implementing a Quality Intervention* for Patients with Clinical Characteristics of Advanced Polycythemia Vera

A guide for US healthcare professionals responsible for population-based decision making

Help clinicians identify the subset of patients with clinical characteristics of advanced polycythemia vera (PV)

*The elements of the quality intervention described have not been validated or approved for securing accreditation or reimbursement, nor has the information been supported or endorsed by any entity for these purposes.

Clinical characteristics of advanced PV

PV is a hematologic malignancy that *may become advanced in a subset of patients despite treatment with hydroxyurea and phlebotomy, resulting in ineffective disease control.*[1-4]

Hct+ | **Elevated Hct levels ≥45% *plus one* additional factor—despite treatment with maximum tolerated dose of HU[5] and phlebotomy**

Elevated Hct levels[6] **≥45%**

+

Elevated WBC counts[7] **>11 × 10^9/L**

OR

Burdensome disease-related symptoms[8] (such as fatigue, early satiety, inactivity, concentration problems, and itching)

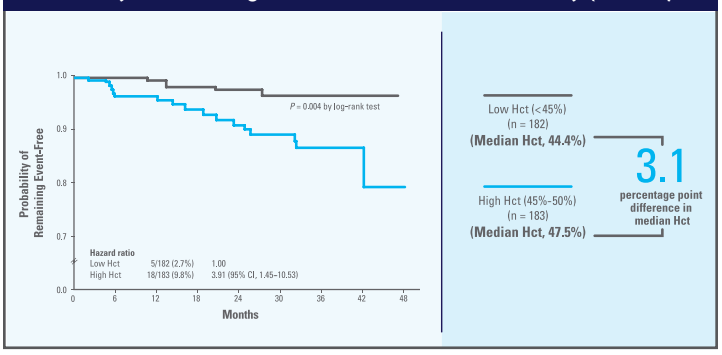
Hct, hematocrit; PV, polycythemia vera; WBC, white blood cell.

Patients with clinical characteristics of advanced PV are at increased risk of thrombosis

CYTO-PV study

Elevated Hct of 45% to 50%: 4-fold higher rate of cardiovascular death and major thrombosis[6]

Probability of remaining event-free in the CYTO-PV study (N = 365)[6]



Kaplan-Meier curves for primary composite endpoint. From *New Engl J Med*, Marchioli R, Finazzi G, Specchia G, et al; CYTO-PV Collaborative Group,Cardiovascular events and intensity of treatment in polycythemia vera, 368, Page No. Copyright © 2013 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

- Managing Hct levels between 45% and 50% significantly increased the risk of cardiovascular death and major thrombosis compared with an Hct level managed to <45% (hazard ratio, 3.91; 95% CI, 1.45 to 10.53; $P = 0.007$)[6,a]

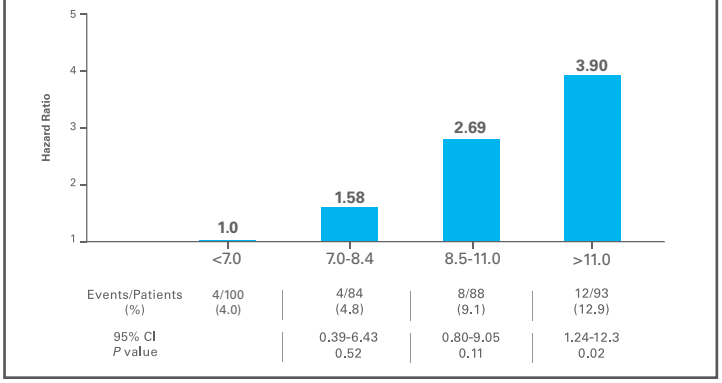
CI, confidence interval; Hct, hematocrit.

[a]In the Cytoreductive Therapy in Polycythemia Vera (CYTO-PV) study of 365 adult patients with PV treated with phlebotomy, hydroxyurea, or both, patients were randomized to 1 of 2 groups—either the low-Hct group (n = 182; with more intensive therapy to maintain a target Hct level <45%) or the high-Hct group (n = 183; with less intensive therapy to maintain a target Hct level of 45% to 50%). Baseline characteristics were balanced between the groups. Approximately 50% of patients had received an initial diagnosis of PV within 2 years prior to randomization. 67.1% of patients (n = 245) were at high risk because of age ≥65 years or previous thrombosis. The composite primary endpoint was the time until cardiovascular death or major thrombosis.[6]

Additional analysis from the CYTO-PV study

Elevated WBC counts >11 × 10^9/L increased the risk of thrombosis[7]

Time-dependent multivariable analysis on the risk of major thrombosis in the CYTO-PV study (N = 365)[7,a]



- In a multivariable time-dependent analysis, WBC counts >11 × 10^9/L were associated with increased risk of thrombosis (hazard ratio, 3.9; 95% CI, 1.24-12.3; $P = 0.02$)[7]
- In this analysis, there was a trend for increased risk of thrombosis with WBC count >7 x 10^9/L (ie, HR >1) that became statistically significant in patients with WBC counts >11 x 10^9/L[7]
- These results are consistent with other literature that suggests leukocytosis may increase the risk of thrombosis[9,10]

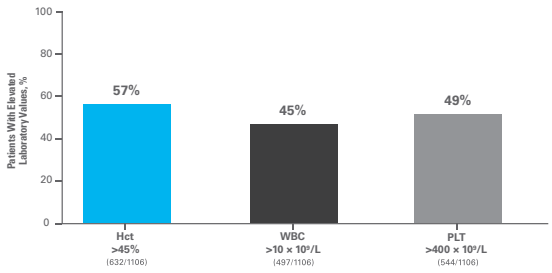
CI, confidence interval; CYTO-PV, Cytoreductive Therapy in Polycythemia Vera; Hct, hematocrit; WBC, white blood cell.

[a]Adjusted for age, gender, cardiovascular risk factors, previous thrombosis, and Hct levels.

Some patients with PV continued to have elevated blood counts, despite treatment with hydroxyurea[11]

REVEAL study

Elevated laboratory values in patients who received HU for ≥3 months in the REVEAL study[11]



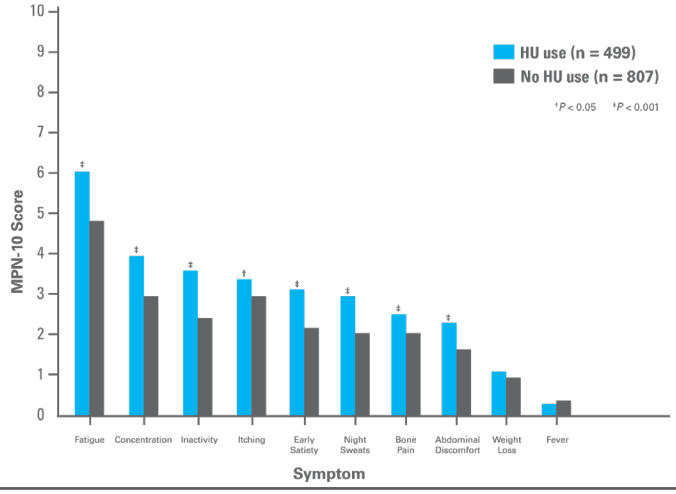
Reprinted from Grunwald MR, Kuter DJ, Altomare I, et al. Treatment patterns and blood counts in patients with polycythemia vera treated with hydroxyurea in the United States: an analysis from the REVEAL Study. *Clin Lymphoma Myeloma Leuk*. 2020 Apr;20(4):219-225. doi: 10.1016/j.clml.2019.09.601. Copyright 2020, with permission from Elsevier.

- REVEAL was a prospective, observational study of 2510 patients with PV in the United States, sponsored by Incyte. This analysis included 1432 patients who received HU, of whom 1381 had received HU for ≥3 months[11,12]
- The median of the maximum Hct value among evaluable patients (n = 1106) who received HU for ≥3 months was[12]:
  - 48.3% for those who reported a value >45%
  - 42% for those who reported a value ≤45%

Hct, hematocrit; HU, hydroxyurea; PLT, platelet; PV, polycythemia vera; WBC, white blood cell.

On average, patients with known hydroxyurea use had moderately high symptom burden[13]

MPN-10 mean symptom scores in patients with known HU use[13]



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- In a prospective study of 1334 patients with PV, patients with known hydroxyurea use (n = 499) had a mean TSS of 29.2[13,a]

MPN-10, Myeloproliferative Neoplasm Symptom Assessment Form; TSS, Total Symptom Score.

[a]A prospective study of 1334 patients with PV was conducted to assess baseline symptoms with certain disease features: known hydroxyurea 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 that lacked the specified feature. Assessment of myeloproliferative neoplasm (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. The MPN-10 TSS has 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).[13]

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

recommend assessing symptoms (in a provider's office) at baseline and monitoring symptom status (stable, improved, or worsening)[14]

Changes in symptom status could be a sign of disease progression[14]

NCCN, National Comprehensive Cancer Network.

References: 1. Parasuraman S et al. *Exp Hematol Oncol*. 2016;5:3. **2.** Mascarenhas J. *Clin Lymphoma Myeloma Leuk*. 2016;16suppl:S124-S129. **3.** Rumi E, Cazzola M. *Blood*. 2017;129(6):680-692. **4.** Spivak JL et al. *N Engl J Med*. 2014;371(9):808-817. **5.** Barosi G et al. *Br J Haematol*. 2010;148(6):961-963. **6.** Marchioli R et al. *N Engl J Med*. 2013:368(1):22-33. **7.** Barbui T et al. *Blood*. 2015;126(4):560-561. **8**. Emanuel RM et al. *J Clin Oncol*. 2012;30(33):4098-4103. **9.** Gangat N et al. *Br J Haematol*. 2007;138:354-358. **10.** Landolfi R et al. *Blood*. 2007;109(6):2446-2452. **11.** Grunwald MR et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(4):219-225. **12.** Grunwald MR et al. Poster presented at: 59th Annual Meeting and Exposition of the American Society of Hematology; December 9–12, 2017; Atlanta, GA. **13.** Geyer H et al. *J Clin Oncol*. 2016;34(2):151-159. **14.** 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.

Actively monitor patients for **Hct+**

Proactively identify the subset of patients with clinical characteristics of advanced PV

Hct+

Elevated Hct levels ≥45% *plus one* additional factor—despite treatment with maximum tolerated dose of hydroxyurea[5] and phlebotomy

- In the CYTO-PV study, **managing Hct** between 45% and 50% was associated with a 4-fold higher rate of cardiovascular death and major thrombosis compared with Hct <45%[6]
- In an additional analysis from the same study, **elevated WBC counts** >11 × 10^9/L increased the risk of thrombosis[7]
- On average, patients with known hydroxyurea use had **moderately high symptom burden**[13]

Use EHR systems to identify patients with clinical characteristics of advanced PV

1. Select the ***query, report, or list tab*** within your system
2. **Enter ICD-10 Code *D45*** for PV
3. Select drug: ***Hydroxyurea***

Review the list for patients with **Hct+:**

Elevated Hct ≥45%, phlebotomy, *plus one* additional factor:

- **WBC count >11 × 10^9/L**, *or*
- **Burdensome symptoms** (eg, fatigue, early satiety, inactivity, concentration problems, or itching)

Clinical criteria such as diagnosis, medication, and blood counts can be used proactively to identify the subset of patients with clinical characteristics of advanced PV.

These patients may require a different management approach. Monitor your EHR system regularly and notify clinicians of patients who have the clinical characteristics of advanced disease.

Incyte