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

A GUIDE FOR PHARMACY DIRECTORS AND CLINICAL PHARMACISTS

Help your clinicians identify the subset of patients with clinical characteristics of advanced PV

Incyte

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)

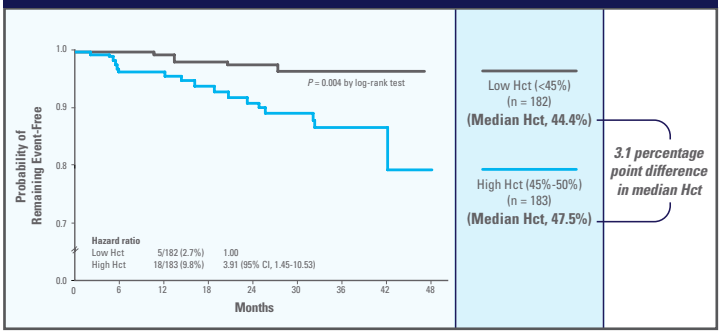
Hct, hematocrit; PV, polycythemia vera; WBC, white blood cell.

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

Evidence from the CYTO-PV study

Elevated Hct ≥45%: 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 end point. Adapted with permission from the Massachusetts Medical Society. CI, confidence interval; Hct, hematocrit.

- 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]

[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 end point was the time until cardiovascular death or major thrombosis.

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

Time-Dependent Multivariable Analysis on the Risk of Major Thrombosis in CYTO-PV Study (N = 365)[a]

WBC Count (× 10^9/L)	Events/Patients (%)	Hazard Ratio (95% CI), *P*
<7.0	4/100 (4.0)	1.0
7.0-8.4	4/84 (4.8)	1.58 (0.39-6.43), 0.52
8.5-11.0	8/88 (9.1)	2.69 (0.80-9.05), 0.11
>11.0	**12/93 (12.9)**	**3.90 (1.24-12.3), 0.02**

Adapted from Barbui T et al. *Blood*. 2015;126(4):560-561. CI, confidence interval; CYTO-PV, Cytoreductive Therapy in Polycythemia Vera; Hct, hematocrit; WBC, white blood cell.

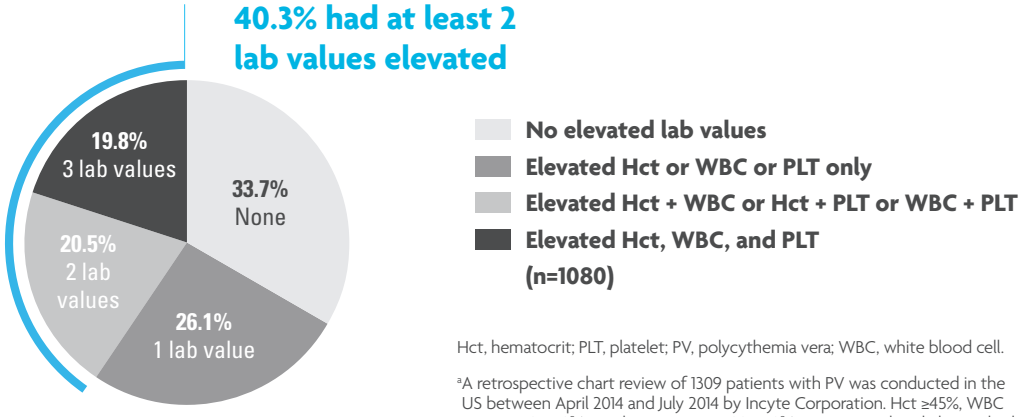
- In a multivariable time-dependent analysis, WBC counts >11 × 10^9/L were associated with increased risk of thrombosis (hazard ratio, 3.9; 95% CI, 1.24-12.3; *P* = 0.02)[7]
- These results are consistent with other literature that suggests leukocytosis may increase the risk of thrombosis[9,10]

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

In patients with PV, blood counts can remain elevated despite treatment with hydroxyurea

In a retrospective chart survey, 40.3% of patients with PV receiving hydroxyurea had at least 2 elevated lab values.[1] The purpose of this chart survey was to investigate the treatment patterns among US patients with PV in a real-world setting.

Percentage of Patients Receiving Hydroxyurea With Elevated Lab Values[1,a]

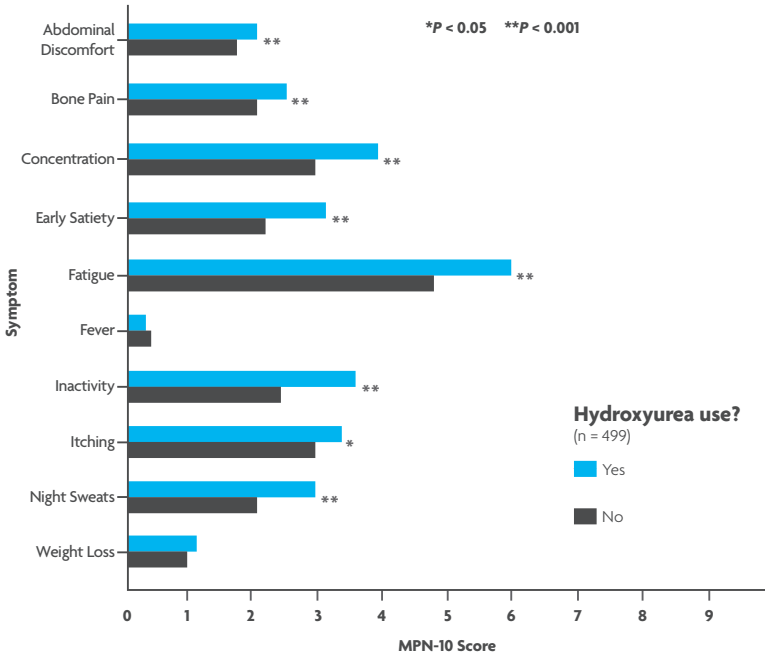


Hct, hematocrit; PLT, platelet; PV, polycythemia vera; WBC, white blood cell.

[a]A retrospective chart review of 1309 patients with PV was conducted in the US between April 2014 and July 2014 by Incyte Corporation. Hct ≥45%, WBC counts >10 × 10^9/L, and PLT counts >400 × 10^9/L were considered elevated values.

Symptom burden in patients with PV is substantial and may not be adequately controlled with hydroxyurea[11]

MPN-10 Mean Symptom Scores in Patients With Known Hydroxyurea Use[11]



In a prospective study of 1334 patients with PV, patients with known hydroxyurea use (n = 499) had, on average, a mean TSS of 29.2[11,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 (ie, known hydroxyurea use, known phlebotomy requirements, and splenomegaly). The patients had the following characteristics: known hydroxyurea use (n = 499), known phlebotomy (n = 646), palpable splenomegaly (n = 369), or all 3 features (n = 148). 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).

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.** Geyer H et al. *J Clin Oncol*. 2016;34(2):151-159.

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]
- **Symptom burden** in patients with PV is substantial and may not be adequately controlled with hydroxyurea[8]

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

Patient lists generated through electronic health record (EHR) systems can help your clinicians recognize patients who may be at risk for adverse outcomes. 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.

Create a list of 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)

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

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