

Diagnosis, Prognosis, and Treatment of Essential Thrombocythemia (ET) and Polycythemia Vera (PV): A Concise Resource for Healthcare Professionals

ET and PV are myeloproliferative neoplasms associated with prevalent *JAK2* gain-of-function mutations.^{1,2} PV is associated with *JAK2* mutations in nearly 100% of cases, but in ET, *JAK2* mutations comprise about 60% of cases with *CALR* (25%) and *MPL* (5%–7%) mutations also being prevalent drivers of the disease. Patients with ET and PV are at increased risk for thrombosis, hemorrhage, and disease transformation to myelofibrosis and acute myeloid leukemia with a reduced life expectancy compared with age-matched controls.^{1–3}



Clinical Presentation

ET¹

- More than 50% of patients are asymptomatic and diagnosed incidentally based on an abnormal platelet count on a CBC
- Approximately 30% of patients present with microcirculatory symptoms (eg, erythromelalgia, burning toes/fingers, blurred vision, migraine headaches)
- Other signs at diagnosis include palpable splenomegaly (12%), arterial thrombosis (14%), venous thrombosis (8%), major hemorrhage (4.5%)

PV²

- Similar to ET, patients may be asymptomatic with an incidental finding on a CBC (primarily erythrocytes but also leukocytes and thrombocytes) or present with microcirculatory symptoms
- Pruritus is common (48%)
- Other signs at diagnosis include palpable splenomegaly (36%), arterial thrombosis (15%–16%), venous thrombosis (8%–13%), major hemorrhage (4%)

WHO and ICC 2022 Criteria for Diagnosis of ET and PV^{4,5}

	ET	PV
Major criteria	- PLT $\geq 450 \times 10^9/L$ - BM biopsy with predominant proliferation of megakaryocytes - Not meeting WHO criteria for other MPN subtype <i>JAK2</i>, <i>CALR</i>, or <i>MPL</i> mutation	- Hgb >16.5 g/dL in men, Hgb >16.0 g/dL in women OR Hct $>49\%$ in men, Hct $>48\%$ in women OR increased red cell mass (ICC only) - BM biopsy showing trilineage proliferation (panmyelosis) <i>JAK2</i> mutation
Minor criteria	Presence of a clonal marker or absence of evidence for reactive thrombocytosis	Subnormal serum EPO level
Diagnosis	All 4 major criteria or the first 3 major criteria and 1 of the minor criteria	All 3 major criteria or the first 2 major criteria and the minor criterion

Diagnostic Pearls for ET¹

- Exclude secondary thrombocytosis (~85%–90% of cases of elevated platelets) due to inflammatory conditions such as rheumatoid arthritis and systemic lupus erythematosus, infections, splenectomy, incidental trauma or surgery, iron deficiency anemia, and solid tumors such as lung cancer
- If the initial assessment does not suggest a secondary cause of thrombocytosis, patients should undergo peripheral blood testing for *JAK2*, *CALR*, and *MPL* gene variants (Note: Up to 10% of patients with ET lack these mutations)

Diagnostic Pearls for PV²

- *JAK2* V617F and exon 12 mutations present in ~99% of patients
- Bone marrow biopsy may not be required for PV diagnosis if Hgb >18.5 g/dL in men or >16.5 g/dL in women, hematocrit >55.5% in men or >49.5% in women; however, useful to identify initial myelofibrosis in up to 20% of patients with prediction of more rapid progression to post-PV myelofibrosis and for detection of abnormal karyotype associated with worse survival
- Exclude secondary erythrocytosis which can occur commonly due to testosterone supplementation, medications (eg, aromatase inhibitors, SGLT2 inhibitors), chronic cardiopulmonary disease, bilateral renal artery stenosis, or EPO-secreting cysts; serum EPO level can be helpful in this case as it should be suppressed in PV and normal/elevated in secondary etiologies

Prognostic Scoring for ET and PV

A variety of prognostic scoring systems incorporating clinical and molecular features are available for risk assessment of ET and PV.⁶ However, no currently available therapies have been shown to prevent leukemic transformation. In addition, the ability of interferon formulations to delay fibrotic transformation is an ongoing topic of debate. Both interferon formulations and the *JAK2* inhibitor ruxolitinib have been shown to reduce *JAK2* allele fractions and improve event-free survival. To that end, prognosis and treatment are guided primarily by thrombotic risk and symptom management.^{1,2,6}

Risk of Thrombosis

ET (Revised IPSET-Thrombosis)^{7,8}

Category	Criteria
Very low risk	■ ≤60 yr ■ No history of thrombosis ■ No <i>JAK2</i> V617F mutation
Low risk	■ ≤60 yr ■ No history of thrombosis ■ <i>JAK2</i> V617F mutation present
Intermediate risk	■ >60 yr ■ No history of thrombosis ■ No <i>JAK2</i> V617F mutation
High risk	■ >60 yrs and <i>JAK2</i> V617F mutation ■ History of thrombosis

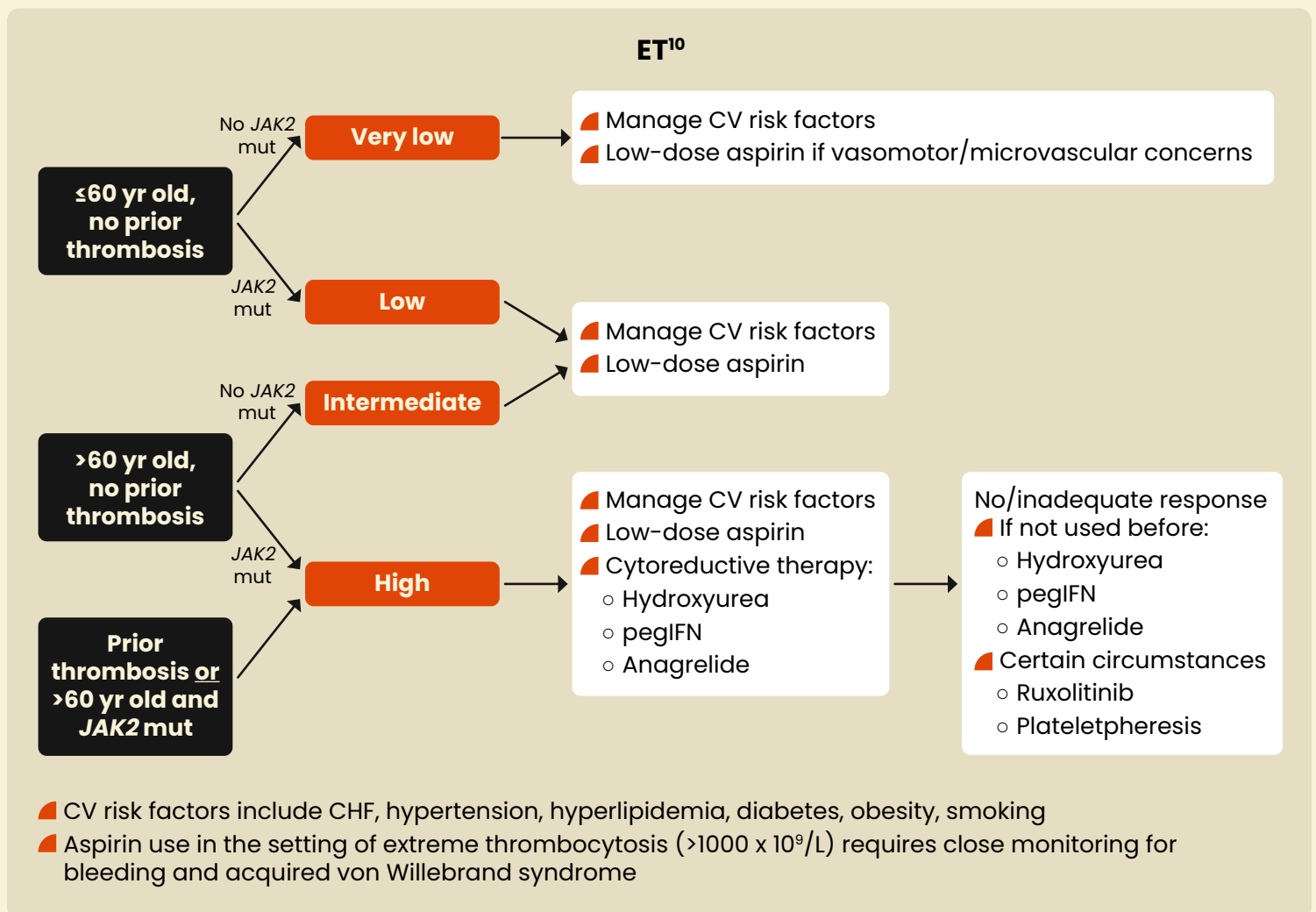
PV⁹

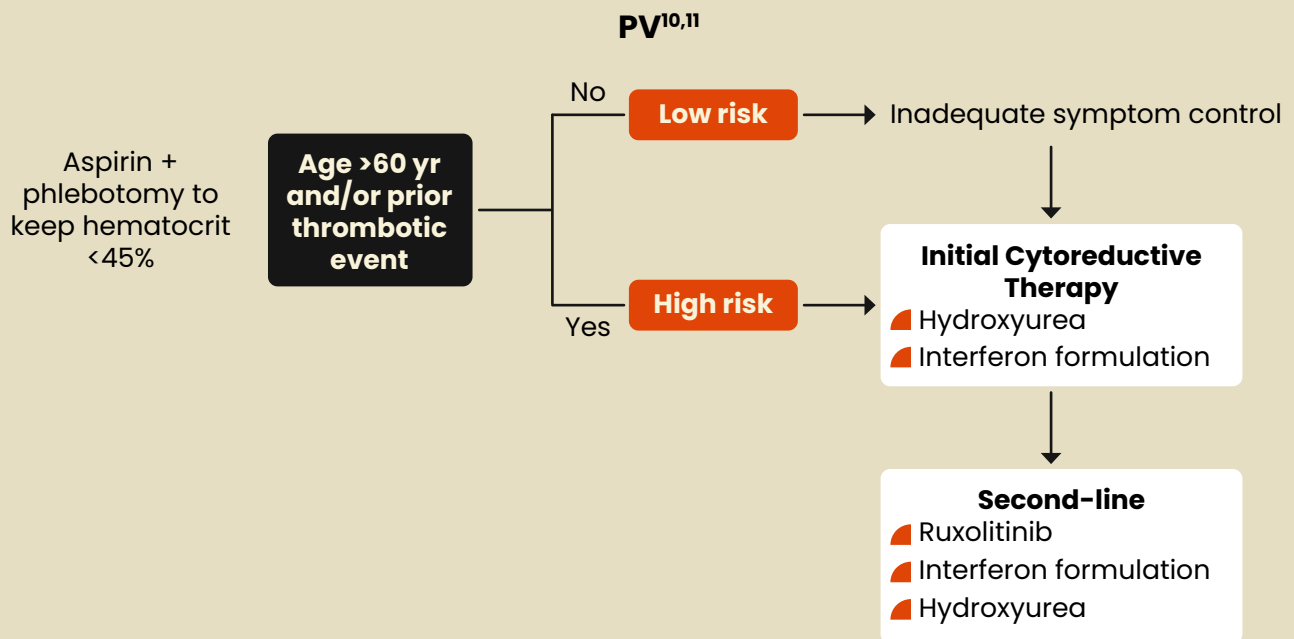
Category	Criteria
Low risk	■ ≤60 yr ■ No history of thrombosis
High risk	■ >60 yr OR ■ History of thrombosis

Clinical and Molecular Features Associated With Thrombosis⁶

Disease	Clinical Factors	Biologic Factors	Molecular Factors	Thrombosis Rate (Pt-Yr)
ET	- Age at diagnosis - Male gender - History of thrombosis - CV risk factors	WBC >15 G/L	JAK2 V617F driver mut	1.6%
PV	- Age at diagnosis - History of thrombosis - CV risk factors	- WBC >15 G/L - PNN/lymphocyte >5	JAK2 V617F VAF >50%	3%

Treatment





■ For low-risk PV

- Consider twice-daily low-dose aspirin if CV risk factors, leukocytosis, or microvascular symptoms
- Consider pegylated interferon if frequent phlebotomies or significant symptoms
- Consider ruxolitinib as treatment of choice for severe pruritus or splenomegaly

■ For high-risk PV

- In women of childbearing age planning for a pregnancy, avoid hydroxyurea because of teratogenic potential
- With a history of arterial thrombosis consider twice daily low-dose aspirin
- With a history of venous thrombosis consider systemic anticoagulation (eg, DOAC or LMWH)

References

1. Tefferi. JAMA. 2025;333:701.
2. Tefferi. Am J Hematol. 2023;98:1465.
3. Tefferi. Am J Hematol. 2024;99:697.
4. Khoury. Leukemia. 2022;36:1703.
5. Arber. Blood. 2022;140:1200.
6. Pasquer. Blood. 2025;145:257.
7. Barbui. Blood Cancer. 2015;5:e369.
8. Haider. Am J Hematol. 2016;91:390.
9. Barbui. Blood. 2014;124:3021.
10. NCCN. Clinical practice guidelines in oncology: myeloproliferative neoplasms. v.2.2025. nccn.org.
11. McMullin. Br J Haematol. 2019;184:176.