
Polycythemia Vera in Modern Practice: Practical Treatment & Long-Term Management
Tania Jain, MD,
Johns Hopkins University

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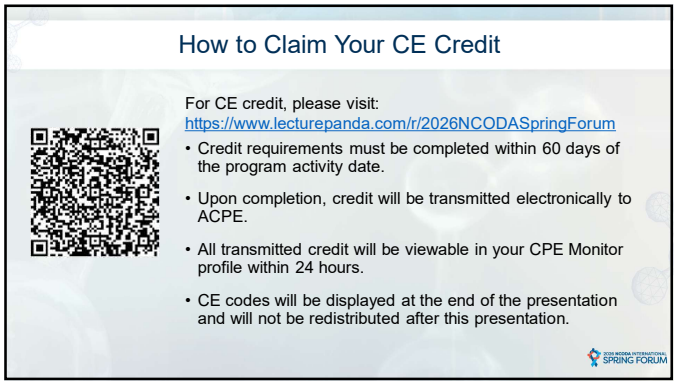
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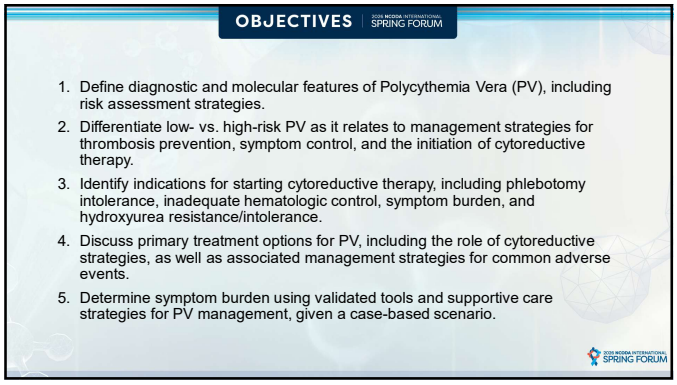
OBJECTIVES
1. Define diagnostic and molecular features of Polycythemia Vera (PV), including risk assessment strategies.
2. Differentiate low- vs. high-risk PV as it relates to management strategies for thrombosis prevention, symptom control, and the initiation of cytoreductive therapy.
3. Identify indications for starting cytoreductive therapy, including phlebotomy intolerance, inadequate hematologic control, symptom burden, and hydroxyurea resistance/intolerance.
4. Discuss primary treatment options for PV, including the role of cytoreductive strategies, as well as associated management strategies for common adverse events.
5. Determine symptom burden using validated tools and supportive care strategies for PV management, given a case-based scenario.

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DISCLOSURES

The following relevant financial relationships from the past 24 months have been identified and disclosed for the following faculty and planners of this CE activity:

- **Tania Jain, MD**
  - Institutional research support: CTI BioPharma, Kartos Therapeutics, Incyte, TScan Therapeutics, Karyopharm Therapeutics, GSK.
  - Advisory board participation: Bristol Myers Squibb, Incyte, AbbVie, CTI BioPharma, Kite Pharma, Cogent Biosciences, Blueprint Medicines, Telios Pharma, Protagonist Therapeutics, Galapagos NV, TScan Therapeutics, Karyopharm Therapeutics, MorphoSys AG, IN8bio, Calytrix Bio, Takeda Pharmaceutical.

There are no relevant conflicts of interest to disclose for this presentation for the following reviews of this CE activity:

- **Tahsin Imam, PharmD**

This continuing education activity is supported by an educational grant from PharmaEssentia

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Defining PV: Diagnostic Criteria, Molecular Features & Risk Assessment

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A Case

A **46-year-old man** is referred for new diagnosis of **polycythemia vera**.

WBC: 16, RBC: 6.03, Hgb: 18.3, Hct: 53.8, Platelet: 565

EPO: 1.2

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A Case

Bone marrow biopsy is performed and is hypercellular for age with trilineage proliferation. There is no fibrosis or dysplasia.

Cytogenetics are normal. NGS panel reveals JAK2 V617F mutation, VAF 52%.

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A Case

Other notable history: hypertension and obesity; no history of venous or arterial thrombosis

Symptoms: moderate intensity pruritus after showering

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A Case

On physical exam: well-appearing, unremarkable exam

Imaging: mild splenomegaly at 13 cm

How would you risk stratify this patient and what treatment would you recommend?

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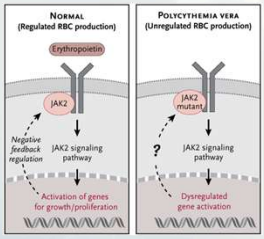
Polycythemia Vera (PV)

- Polycythemia Vera (PV) is a **myeloproliferative neoplasm**
- Characterized by clonal expansion of hematopoietic stem and progenitor cells and **elevated red blood cell mass**
- JAK-STAT signaling is the hallmark of the disease



Reekie Y. Cancer drug takes fast track to clinical trials. Harvard Medical School. April 18, 2008.

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JAK2 Molecular Features

JAK2 mutations are present in virtually all patients with PV

Mutation	Frequency	Key Features
JAK2 V617F (exon 14)	~97%	Gain-of-function point mutation; G→T substitution at nucleotide 1849; valine→phenylalanine at codon 617
JAK2 exon 12 mutations	~3%	Found in JAK2 V617F-negative patients; predominantly erythroid phenotype; younger age at diagnosis; similar prognosis to V617F

Pathophysiologic consequence:
- Constitutive activation of the JAK-STAT signaling pathway
- Normal EPO-dependent regulation is bypassed → autonomous, EPO-independent red cell production → erythrocytosis, elevated hematocrit, increased blood viscosity → thrombosis risk

Beyond JAK2 — co-occurring mutations:
- 50% of PV patients harbor additional non-JAK2 somatic mutations
- Most frequent: TET2 (~18%), ASXL1 (~15%)
- Prognostically adverse mutations: SRSF2, IDH2, RUNX1, U2AF1 (combined incidence 5–10%) — associated with inferior overall survival independent of age
- Higher JAK2 V617F allele burden associated with pruritus, fibrotic transformation, and venous thrombosis

Tefferi A, Barbui T. Polycythemia vera: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol. 2023;98:1465-1487.
NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. V.2.2026.

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Diagnosis of PV: WHO Diagnostic Criteria

1. Eythrocytosis	2. Pan-myelosis on bone marrow	3. Mutation in JAK2 gene

• Men:
  • Hgb > 16.5 g/dl
  • Hct > 49%
• Women:
  • Hgb > 16 g/dl
  • Hct > 48%
	• Age-adjusted hypercellularity with trilineage proliferation
	• Can defer BMBx for very high Hgb/Hct + JAK2 mutation
		• JAK2 V617F
		• JAK2 exon 12

Minor Criteria: subnormal EPO level

Khoury JD, et al. Leukemia. 2022;36:1703-1719
Tefferi A, Barbui T. Am J Hematol. 2023;98:1465-1487

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Diagnosis of PV: WHO & ICC Diagnostic Criteria

Diagnosis requires: ALL 3 major criteria OR the first 2 major criteria + the minor criterion

	Criteria	Details
Major 1	Elevated hemoglobin, hematocrit, OR red cell mass	Hgb >16.5 g/dL (men) or >16.0 g/dL (women) OR Hct >49% (men) or >48% (women) **OR red cell mass >25% above mean normal predicted value**
Major 2	Bone marrow biopsy: panmyelosis	Age-adjusted hypercellularity with trilineage proliferation including prominent erythroid, granulocytic, and increase in pleomorphic, mature megakaryocytes without atypia
Major 3	JAK2 mutation	JAK2 V617F or JAK2 exon 12 mutation (assay sensitivity <1% required)
Minor	Subnormal serum EPO	Below normal reference range

Arber DA, Orazi A, Hasserjian RP, et al. International Consensus Classification of myeloid neoplasms and acute leukemias: integrating morphologic, clinical, and genomic data. Blood. 2022;140:1200-1228.
Tefferi A, Barbui T. Polycythemia vera: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol. 2023;98:1465-1487.

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Traditional PV Treatment Goals

Prevent Thrombosis
+
Decrease Symptoms

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Thrombosis is Major Cause of Mortality

Table III. Causes of death

	No. of patients
Thrombosis or emboli	100
Haemorrhage	13
Leukæmia-myelofibrosis-anaemia	25
Cirrhosis of the liver	3
Urinary tract diseases (incl. cancer in 3)	20
Heart diseases (excl. coronary thrombosis)	21
Cancer (excl. cancer of the urinary tract)	9
Bronchopneumonia	14
Cerebral haemorrhage	8
Senility-debility	6
Accidents, suicide	7
Postoperative	5
Miscellaneous	7
Uncertain or unknown cause	10
Total	250

Table IV. Deaths from thrombosis

	No. of patients
Cerebral thrombosis	38
Coronary thrombosis	27
Pulmonary embolism or infarction	13
Mesenteric thrombosis	11
Extremity thrombosis	9
Generalized thrombosis	2
Total	100

Example: Aarhus Municipal Hospital. In the case of a 54-year-old man polycythaemia vera was diagnosed in 1948 after he had been suffering from headache, dizziness, and blurred vision for a couple of years. B.P. 145/70. In 1949 he had thrombosis of the left leg, in 1950 coronary thrombosis, in the same year cerebral thrombosis, in 1957 gout, in 1959 duodenal ulcer and cerebral thrombosis, and in 1960 cerebral thrombosis for the third time. The patient died in January 1961 of thrombophlebitis of the right femoral vein with gangrene of the right foot.

Chievitz and Thiede, Acta Medica Scandinavica, 1962

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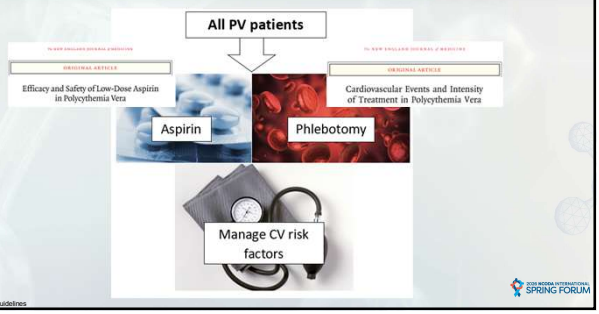
Treatment for All PV Patients



Adapted from NCCN Guidelines

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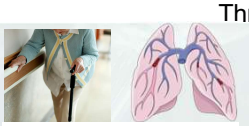
Risk Assessment for Cytoreduction Focuses on Thrombosis Risk

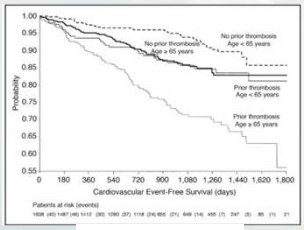


Age ≤ 60 and no history of thrombosis = **low risk; no cytoreduction**

Age > 60 and/or history of thrombosis = **high risk; recommend cytoreduction**

Previous venous event (HR, 2.6; CI, 1.5-4.4) and age ≥ 65 years (HR, 1.7; CI, 1.2-2.5) predicted venous thrombosis

Barbui et al, Blood, 2014



Marchioli et al, JCO, 2005

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Overall Survival Risk Stratification: MIPSS-PV

MIPSS-PV Scoring:

Prognostic Variable	Points
Thrombosis history	1
Leukocyte count ≥15 × 10^9/L	1
Age >67 years	2
Adverse mutations (SRSF2)	3

Risk Group Classification:

Risk Group	Total Points	Median Survival
Low	0–1	~24 years
Intermediate	2–3	~13.1–18 years
High	≥4	~3.2–5.4 years

Clinical takeaways:

- Leukocyte count ≥15 × 10^9/L, thrombosis history, age >67, and SRSF2 mutation are the four independent prognostic variables in MIPSS-PV
- SRSF2 mutation carries the highest point value (3 points) in the scoring model
- Additional prognostic information from NGS and karyotype is useful when available but not mandated in routine clinical practice

Tefferi A, Barbui T. Polycythemia vera: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol. 2023;98:1465-1487.

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Additional Risk Factors Associated with Thrombosis

- Leukocytosis (Even in Hct ≤ 45%, WBC count > 12 associated with thrombosis; HR, 1.95; 95% CI, 1.066-3.554)
- Neutrophil-to-Lymphocyte Ratio ≥ 5 (HR 2.13, p=0.001 for venous events)
- JAK2V617F allele burden ≥ 50% (HR 3.8, p=0.001 for venous thrombosis; progression to myelofibrosis)
- Hypertension, hyperlipidemia, and diabetes (HR 2.3-2.4, p=0.02 for arterial thrombosis)
- **Degree of thrombocytosis** has **not** been reliably associated with thrombotic risk…

Marchioli et al, NEJM, 2013; Gerds et al, Blood, 2024; Guglielmelli et al, Blood Cancer J, 2021

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Low- vs. High-Risk PV: Risk-Based Management Framework

RISK CATEGORY DEFINITIONS

	Low-Risk PV	High-Risk PV
Definition	Age <60 years AND no prior history of thrombosis	Age ≥60 years AND/OR prior history of thrombosis

MANAGEMENT FRAMEWORK

Management Domain	Low-Risk PV	High-Risk PV
Thrombosis Prevention	Aspirin 81–100 mg/day; phlebotomy to Hct <45%; manage CV risk factors	Aspirin 81–100 mg/day; phlebotomy to Hct <45%; manage CV risk factors; cytoreductive therapy
Symptom Control	Monitor symptom burden; evaluate for cytoreductive indications if symptoms develop (eg, pruritus, night sweats, fatigue)	Cytoreductive therapy; monitor disease-related symptoms longitudinally
Cytoreductive Therapy	Not recommended as initial treatment; indications to initiate include: frequent or intolerant phlebotomy, splenomegaly, progressive thrombocytosis and/or leukocytosis, new thrombosis, disease-related symptoms	Indicated at initiation; preferred regimens: hydroxyurea or ropeginterferon alfa-2b-njft

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms, Version 1.2026. Published January 22, 2026.
Marchioli R, Finazzi G, Specchia G, et al. Cardiovascular events and intensity of treatment in polycythemia vera. N Engl J Med. 2013;368(1):22-33.

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Recognizing when to initiate and escalate cytoreductive therapy across the spectrum of PV disease.

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ELN 2021 Recommendations to Start Cytoreduction in Low-Risk Patients

Cytoreductive drugs are recommended in patients reporting:

- A poor tolerance to phlebotomy, strictly defined as recurrent episodes of post-phlebotomy syncope despite appropriate preventive interventions or blood phobia leading to avoidance behaviour despite counselling, or severe difficulties in venous access (consensus: 100%)
- Symptomatic progressive splenomegaly (increase by >5 cm in the past year), provided that transformation to myelofibrosis has been ruled out (consensus: 85%)
- Persistent leukocytosis (leukocyte count >20 × 10^9 cells per L confirmed at 3 months (without therapy; consensus: 85%)

A trial of cytoreductive drugs can be considered:

- In patients reporting a high symptom burden (total symptom score ≥20) or severe itching (itching score ≥5) that are not ameliorated by phlebotomy, antiplatelet therapy, or antihistamines (consensus: 93%)
- On an individual basis in patients reporting a relevant cardiovascular risk (appendix p 4), provided that primary prevention strategies have been implemented (appendix p 5; consensus: 85%)

Cytoreductive drugs should be considered in patients reporting:

- Progressive (at least 100% increase if baseline count is <10 × 10^9 cells per L or at least 50% increase if baseline count is >10 × 10^9 cells per L) and persistent (leukocyte count >15 × 10^9 cells per L confirmed at 3 months) leukocytosis (consensus: 80%)
- Extreme thrombocytosis (>1500 × 10^9 platelets per L), bleeding manifestations related to the disease irrespective of the platelet count, or both (consensus: 85%)
- Inadequate haematocrit control with phlebotomies—ie, a need for at least six phlebotomies per year for at least 2 years in the maintenance phase after reaching haematocrit concentrations below 45% in the induction phase (consensus: 80%)

Recommend **interferons** as agent of choice in treatment naïve patients < 60 with no prior thrombotic events who need cytoreduction

Marchetti M, Vannucchi A, Griesshammer M et al. Appropriate management of polycythaemia vera with cytoreductive drug therapy: European LeukemiaNet 2021 recommendations The Lancet Haematology, 9, e301–e311
Marchetti et al, Lancet Hematology, 2022

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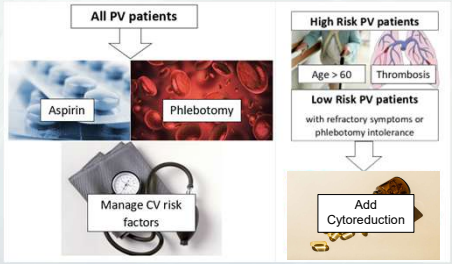
Current Landscape of PV Treatment



Adapted from NCCN Guidelines

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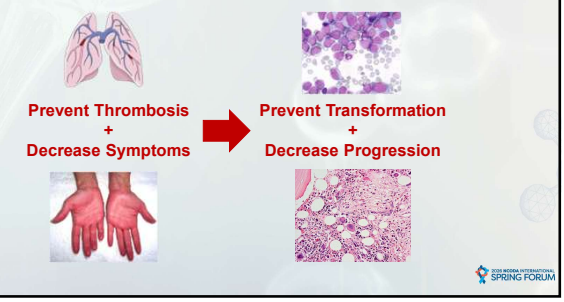
Changing Landscape of PV Treatment



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Available PV Treatments

Medication	Mechanism of Action	Route	Adverse Effects	Use	FDA Approv.
Hydroxyurea	Inhibits ribonucleotide reductase, blocks DNA synthesis, suppresses the proliferation of hematopoietic cells	PO	Bone marrow suppression, infections, and skin cancers	1st line in high risk	Used off-label in PV
Interferon-α (Ropeg-interferon-α-2b; peginterferon-α-2a)	Naturally occurring cytokine proteins; have immunomodulatory, proapoptotic, antiproliferative effects; directly targets and depletes JAK2V617F-mutated stem cells	SQ	Cytopenias, psychiatric disease, flu-like symptoms, injection-site reaction, increased serum transaminases, gastrointestinal symptoms, aggravates autoimmune disorders	1st line in high risk	Nov 2021
Ruxolitinib	Selective inhibition of JAK1 and JAK2 kinases, reducing hyperactive JAK-STAT signaling	PO	Herpes zoster infection, skin cancers, exacerbation of hepatitis B, cytopenias, hypercholesteremia, increased serum transaminases	"Useful in certain circumstances;" Preferred for hydroxyurea refractory or intolerant	Dec 2014

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Hydroxyurea Resistance/Intolerance in PV

Resistance or intolerance to hydroxyurea in PV is defined as meeting any one of the following:

1. Need for phlebotomy to keep Hct <45% after 3 months of at least 2 g/day of hydroxyurea
2. Uncontrolled myeloproliferation (platelet count >400 × 10^9/L AND WBC count >10 × 10^9/L) after 3 months of at least 2 g/day of hydroxyurea
3. Failure to reduce massive splenomegaly by >50% by palpation OR failure to completely relieve splenomegaly-related symptoms after 3 months of at least 2 g/day of hydroxyurea
4. ANC <1.0 × 10^9/L OR platelet count <100 × 10^9/L OR hemoglobin <10 g/dL at the lowest dose of hydroxyurea required to achieve a complete or partial clinicohematologic response
5. Presence of leg ulcers or other unacceptable hydroxyurea-related nonhematologic toxicities (eg, mucocutaneous manifestations, GI symptoms, pneumonitis, or fever) at any dose of hydroxyurea

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2026. Published January 22, 2026.

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Managing PV: Treatment Options & Adverse Event Considerations

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Managing Adverse Events of Cytoreductive Therapy in PV

Agent	Key Adverse Events	Management Strategies
Hydroxyurea	Bone marrow suppression; skin cancers; leg ulcers; mucocutaneous toxicities	Monitor CBC; reduce or hold dose for cytopenias per MPN-I criteria; annual dermatology exam recommended
Ropeginterferon alfa-2b-njft / Peginterferon alfa-2a	Psychiatric symptoms (depression, anxiety); autoimmune disorders; transaminase elevation; thyroid dysfunction; ophthalmologic changes	Screen for psychiatric history before initiation; monitor mood during treatment; monitor for autoimmune disorders; monitor liver enzymes at baseline and during treatment; thyroid function at baseline and annually; eye exam at baseline; periodic eye exams if preexisting ophthalmologic disorders
Ruxolitinib	Infections including viral reactivations; non-melanoma skin cancers; hypercholesterolemia; withdrawal syndrome if abruptly discontinued	Consider recombinant zoster vaccine prior to or at initiation; annual dermatology exam; lipid panel every 6 months; taper dose gradually rather than abrupt discontinuation — abrupt discontinuation may cause withdrawal syndrome including fever, hypotension, and multi-organ failure

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2026. Published January 22, 2026.

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PROUD-PV and CONTINUATION-PV

- Phase 3, randomized, controlled, open-label trial in Europe for adult patients who regardless of conventional risk status required cytoreduction with no history of therapy or < 3 years of hydroxyurea
- 257 patients randomized to ropeginterferon alfa-2b or hydroxyurea
- After 1 year, patients could enter extension, CONTINUATION-PV
- Primary outcome: complete hematological response with normal spleen size (+ improved disease burden in CONTINUATION-PV)
- Serial JAK2V617F quantitative measurements were followed

Gisslinger et al, Lancet Hematology, 2020

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PROUD-PV and CONTINUATION-PV

In PROUD-PV:

- CHR with normal spleen size was reached in **21% in the ropeginterferon alfa-2b** and **28% in hydroxyurea group** at 12 months
  - This outcome did not meet the non-inferiority threshold

In CONTINUATION-PV:

- CHR with improved disease burden was met in **53% in the ropeginterferon alfa-2b** and **38% in the hydroxyurea group**, p=0.044 at 36 months

Gisslinger et al, Lancet Hematology, 2020

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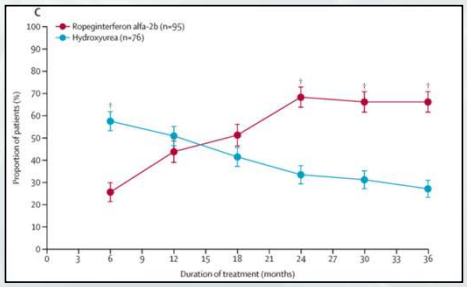
PROUD-PV and CONTINUATION-PV – Molecular Responses



Gisslinger et al, Lancet Hematology, 2020

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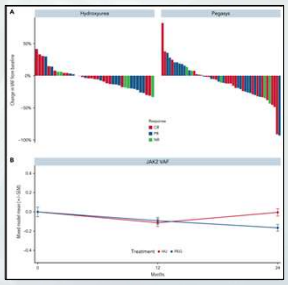
MPD-RC 112 – Molecular Response



Median change in JAK2V617F VAF observed in hydroxyurea was −5.3% and **−10.7% for peg IFN.**

Median JAK2 V617F VAF **decreased consistently from baseline through month 24 in peg IFN-α;** %V617F increased in hydroxyurea after month 12.

Mascarenhas et al, Blood, 2022

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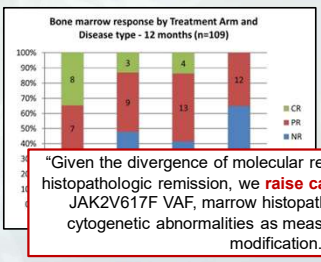
MPD-RC 112 – Bone Marrow Response



In 109 evaluable patients (pre- and post-treatment biopsy), hydroxyurea had a complete histopathologic response of 12/52 (**23%**) vs. 3/57 (**5%**) for peg IFN (*P* = .01)

"Given the divergence of molecular response and bone marrow histopathologic remission, we **raise caution** of using changes in JAK2V617F VAF, marrow histopathology, or clearance of cytogenetic abnormalities as measures of disease course modification."

Mascarenhas et al, Blood, 2022

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Five Year CONTINUATION-PV Data Shows Ongoing Molecular Responses

- Median JAK2V617F VAF declined from **37.3% to 8.5% at 60 months in interferon group** vs. **an increase from 38.1% to 44.4% at 60 months in control group**
- 54.3% of interferon patients achieved a JAK2V617F VAF < 10% and 19.6% achieved a VAF < 1% at 5 years
- Only 1 patient in control arm achieved VAF < 1%
- Disease progression in interferon arm was 0.2%-PY (1 MF case) vs 1.0%-PY in control arm (2 MF and 2 AML cases).

Kiladjian, Leukemia, 2022

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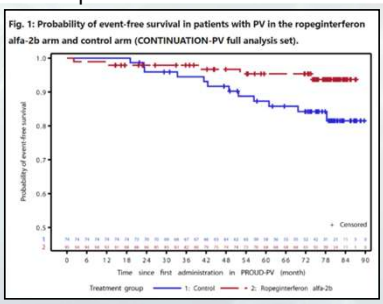
Six Year Follow Up Shows Event-Free Survival Improvement with Interferon



Gisslinger, Leukemia, 2023

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MAJIC-PV – Ruxolitinib v BAT

- Randomized, phase 2 trial evaluating safety and activity of ruxolitinib versus best available therapy (BAT) in those intolerant or resistant to hydroxyurea
- Primary outcome was complete response (CR) rate with normal spleen within 12 months
- Histologic and molecular response were secondary outcomes; as were progression-free survival, overall survival, and event-free survival
- 180 patients were included in mITT analysis

Harrison et al, J Clin Oncol, 2023

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MAJIC-PV – Outcomes

- Primary outcome of complete response was achieved in **40 (43%) patients in the ruxolitinib arm** and **23 (26%) patients in BAT arm** at 12 months
- OS did not differ, with 3-year OS of 87% (95% CI, 77 to 93) for BAT and 88% (95% CI, 79 to 93) for ruxolitinib

Harrison et al, J Clin Oncol, 2023

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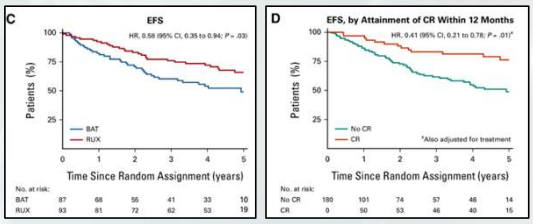
MAJIC-PV – EFS



EFS was **superior** both for ruxolitinib treatment (HR, 0.58; P=0.03), and those achieving CR within 12 months (HR, 0.41; P=0.01).

Harrison et al, J Clin Oncol, 2023

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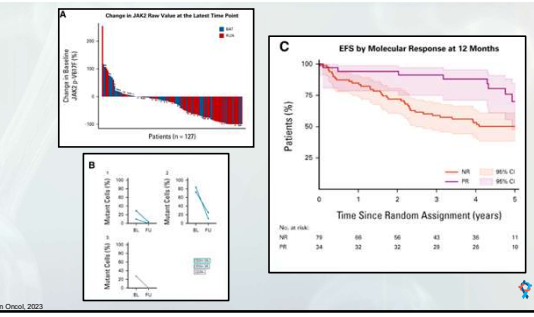
MAJIC-PV – Molecular Response



Harrison et al, J Clin Oncol, 2023

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MAJIC-PV – Molecular Response

TABLE 2. Comparison of Molecular Response (JAK2 variant allele fraction reduction of >50%) at Last Recorded Time Point With Key Trial Outcomes

Outcome	Any Treatment: Whole Trial (n = 127), Events, No. (%)	Any Treatment: NR[a] (n = 74), Events, No. (%)	Any Treatment: PR[b] (n = 53), Events, No. (%)	Any Treatment: P	Ruxolitinib: NR[a] (n = 31), Events, No. (%)	Ruxolitinib: PR[b] (n = 39), Events, No. (%)	Ruxolitinib: P	BAT: NR[a] (n = 43), Events, No. (%)	BAT: PR[b] (n = 14), Events, No. (%)
Thromboembolic event[c]	38 (30)	28 (38)	10 (19)	.02	10 (32)	7 (18)	.17	18 (42)	3 (21)
Hemorrhagic event[c]	28 (22)	23 (31)	5 (9)	.004	9 (29)	4 (10)	.04	14 (33)	1 (7)
Progression-free survival[d]	35 (28)	29 (39)	6 (11)	.001	13 (42)	3 (8)	.001	16 (37)	3 (21)
EFS[e]	53 (42)	40 (54)	13 (25)	.001	16 (52)	8 (21)	.006	24 (56)	5 (36)
OS[e]	22 (17)	18 (24)	4 (8)	.01	8 (26)	3 (8)	.04	10 (23)	1 (7)
CR achieved at 1 year	49 (39)	22 (30)	27 (51)	.02	10 (32)	22 (56)	.04	12 (28)	5 (36)

Harrison et al, J Clin Oncol, 2023

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How Does This Apply to Our Patient?

46-year-old man with newly diagnosed PV (JAK2 VAF 52%), HTN, obesity, no prior thrombosis, and mild-moderate symptom burden (pruritus + splenomegaly).

He wants to know your treatment recommendation.

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How Does This Apply to Our Patient?

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Low PV Trial

- Multicenter, phase 2, open-label, two-group, randomized trial involving adult patients with low-risk PV (< 60 years of age and no history of thrombosis)
- Patients randomly assigned 1:1 to fixed dose 100 mcg ropeginterferon + phlebotomy or phlebotomy alone
- Primary end point = maintenance of the median Hct ≤ 45% for 12 months in the absence of progressive disease at 12 months from randomization
- Also monitored JAK2V617F allele burden

Barbui et al, NEJM Evidence, 2023

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Low PV Trial

	Randomized Groups			
Core Study (12 Months)	EXP (n=64)	STD (n=63)	P Value	Effect Estimate† (95
Treatment response — n (%)	52 (81.3)	32 (50.8)	<0.001	4.20 (1.77–10.23)
Hematocrit control	52 (81.3)	37 (58.7)		3.05 (1.28–7.50)
Disease progression	0 (0.0)	8 (12.7)		—‡
No. of phlebotomies per patient year — mean (SD)	2.9 (2.4)	4.2 (3.2)		1.27 (0.27–2.26)
	EXP (n=55)	STD (n=43)		
Absolute *JAK2V617F* VAF change from baseline — %, mean (SD)	−11.9 (20.7)	1.8 (9.0)		13.73 (7.00–20.46
Partial molecular response — n (%)	16 (29.1)	0 (0.0)		—‡

Barbui et al, NEJM Evidence, 2023

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Back to Our Case

You recommend aspirin 81 mg, phlebotomy to Hct<45%, and cardiovascular risk factor management.

After further discussion, based on low PV, his thrombotic risk factors (HTN, JAK2 VAF, obesity, leukocytosis), and potential EFS benefit from CONTINUATION-PV, he elects to initiate interferon therapy.

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Back to Our Case

You have your hand on the door to leave the room, when your patient asks one last question.

I know about my thrombosis risk… but what is my overall prognosis/ chance of survival?

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Assessing & Managing Symptom Burden in PV

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Assessing Symptom Burden in PV: MPN-SAF TSS

- NCCN recommends assessment of symptoms at baseline and monitoring symptom status longitudinally during treatment for all patients with MPN.
  - The **MPN Symptom Assessment Form Total Symptom Score (MPN-SAF TSS)** is the recommended validated tool for this purpose.
- The MPN-SAF TSS is patient-reported and scores each item from 0 to 10, where 0 = absent/as good as it can be and 10 = worst imaginable/as bad as it can be.
  - The total score is the sum of all 10 items, yielding a 0–100 scale.
- The 10 MPN-SAF TSS domains are:
  - fatigue, early satiety, abdominal discomfort, inactivity, problems with concentration, night sweats, itching (pruritus), bone pain, fever, and unintentional weight loss.
- In NCCN, symptom response requires at least a 50% reduction in MPN-SAF TSS, although smaller improvements may still be clinically meaningful in some settings.
- Because changes in symptom status may signal disease progression, worsening or persistent symptoms should prompt reassessment of treatment efficacy and disease status.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2026. January 22, 2026.

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Supportive Care Strategies for Chronic PV Management

Symptom	First-Line Approach	Escalation Options
Pruritus	Sensitive skin care (short showers, mild soap, moisturizing); optimized antihistamine therapy (cetirizine, diphenhydramine); topical steroids	SSRIs; narrow-band UVB; peginterferon alfa-2a or ropeginterferon alfa-2b-njft; gabapentin; aprepitant; immunosuppressants (eg, cyclosporine, dupilumab); ruxolitinib
Headache / Vasomotor symptoms	Low-dose aspirin 80–100 mg/day; phlebotomy if Hct elevated	Twice-daily aspirin or clopidogrel 75 mg/day if aspirin-resistant; cytoreduction if aspirin ineffective; ruxolitinib; triptans or topiramate for migraine
Bone pain	NSAIDs (naproxen); loratadine	Single-fraction radiation; ruxolitinib

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2026. Published January 22, 2026.

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Back to Our Case: Assessing Symptom Burden in PV

- 46-year-old man with newly diagnosed PV
- JAK2 V617F VAF 52%, HTN, obesity, no prior thrombosis
- Moderate pruritus after showering
- Mild splenomegaly

Question

How would you use the MPN-SAF TSS to assess this patient's symptom burden, what additional symptom domains would you ask about, and what supportive care would you initiate now?

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Back to Our Case: Applying MPN-SAF TSS and Initial Supportive Care

- Use the MPN-SAF TSS at baseline to formally document this patient's symptom burden and repeat it longitudinally during treatment.
  - NCCN recommends MPN-SAF TSS for both baseline assessment and ongoing monitoring.
- The most clearly relevant symptom domain already present in this case is itching (pruritus).
  - With mild splenomegaly, the clinician should also ask about early satiety and abdominal discomfort, and review for other MPN-SAF TSS domains such as fatigue, inactivity, and concentration problems if present.
- Initial supportive care for pruritus should include:
  - Sensitive skin care
  - Optimized antihistamine therapy
  - Topical steroids
- If symptoms persist or worsen, reassess symptom burden over time and consider escalation of symptom-directed management.
  - NCCN notes that worsening symptom status may signal disease progression and should prompt reassessment of treatment efficacy and disease status.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2026. Published January 22, 2026.

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Risk Stratification for Overall Survival

MIPSS-PV

Prognostic Variable	Points
Thrombosis history	1
Leukocyte count ≥15x10⁹/L	1
Age >67	2
Adverse mutations (*SRSF2*)	3

Risk Group	Points
Low	0–1
Intermediate	2–3
High	≥4

Tefferi et al, B J Haematol, 2020

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Conclusions

- Polycythemia vera is a myeloproliferative neoplasm characterized by JAK-STAT pathway hyper-signaling and clonal expansion of hematopoietic stem/ progenitor cells, leading to elevated red cell mass
- Current landscape of treatment is focused primarily on decreasing thrombosis risk and symptom burden
- However, new treatments such as interferons and ruxolitinib may demonstrate disease modification and improved event-free survival; which may shift risk stratification and treatment landscape
- JAK2V617F VAF reduction may be a meaningful surrogate for event-free survival/ disease modification

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QUESTION & ANSWER

Polycythemia Vera in Modern Practice: Practical Treatment & Long-Term Management

Tania Jain, MD,
Johns Hopkins University

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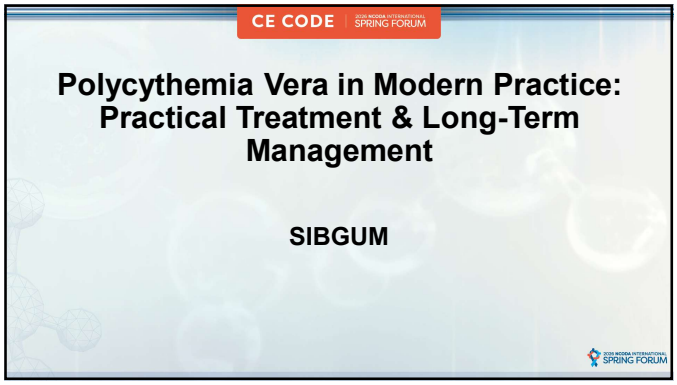
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ALIGNMENT IN ACTION
The Power of Integrated Oncology Care

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