WHEN MANAGING POLYCYTHEMIA VERA (PV)

IT'S A FINE LINE BETWEEN CONTROL AND RISK

Polycythemia vera (PV) is a rare MPN that can lead to far-reaching outcomes due to uncontrolled HCT, persistent symptom burden, and iron dysregulation[1-7]

Risks of Uncontrolled HCT

Even slight elevations in HCT (45%-50%) can increase the risk of major thrombotic events or CV death

People with PV who consistently maintained HCT levels ≥45%, specifically within 45%-50%, were 4x more likely to experience major thrombotic events or CV death compared to those whose HCT was tightly controlled below the 45% threshold.[8*]

*In an Italian randomized controlled trial study (CYTO-PV) of 365 PV patients being treated with phlebotomy, hydroxyurea, or both, 2.7% (n=5/182) with HCT <45% died from CV causes or had major thrombotic events vs 9.8% (n=18/183) with HCT 45%-50%, after a median follow-up of 31 months (HR, 3.91; 95% CI, 1.45-10.53; *P*=0.007).[8]

4x

MORE LIKELY TO EXPERIENCE MAJOR THROMBOTIC EVENTS OR CV DEATH

Current PV treatment guidelines are focused on keeping HCT below the 45% threshold and monitoring disease progression, but may not capture fluctuating HCT and associated risks.[5,8,9]

Learn more about the risk of uncontrolled HCT at RethinkPVpro.com/Managing-PV.

Persistent Symptom Burden

Recent data suggest an association with increased symptom burden and reduced overall survival in people with PV[4†‡]

Nearly 80% of patients with MPNs, including PV, report emotional strain, including anxiety and stress related to symptom burden and disease uncertainty (N=117).[10]

Symptom burden also has a profound impact on patients' personal lives, as 63% had to adjust family or social plans and 48% had to adjust their daily activities (N=380).[11§] Employment was similarly impacted, with 27% leaving a job and 22% going on disability leave (N=248).[12‖]

Explore the underlying symptom burden that people with PV are struggling with at RethinkPVpro.com/Symptom-Burden.

†Based on an analysis of PV patients with high symptom burden (defined as Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score [MPN-SAF TSS] >35) [n=24] vs those with low symptom burden (n=256).[13]
‡A multicenter, retrospective, observational study comprising patients from 13 academic and community centers. Eligibility criteria were patients >18 years old, enrolled with a diagnosis of PV, ET or MF (primary or post-PV/ET) according to WHO and/or International Consensus criteria, and having completed at least one MPN-SAF TSS questionnaire between April 2013 and August 2022.[4]
§Based on an online survey of 813 US adults (median age 62–66) diagnosed with ET, MF, or PV, conducted from May to July 2014 (MPN Landmark survey).[11]
‖Based on a cross-sectional online survey of 904 US adults aged 18–70 diagnosed with ET, MF, or PV, conducted from April to November 2016.[12]

Mechanism of Disease and the Role of Iron

Erythrocytosis disrupts iron homeostasis through hepcidin suppression

Erythrocytosis leads to iron dysregulation and increased TE risk in PV

PV is universally characterized by erythrocytosis, which drives iron dysregulation. In return, iron dysregulation exacerbates erythrocytosis, increasing the TE risk in people with PV.[8,14,15]

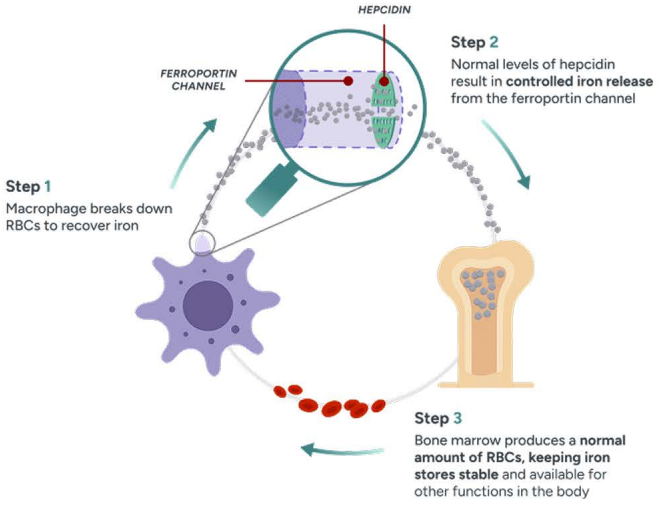
The hepcidin-ferroportin axis

The hepcidin-ferroportin axis balances iron absorption, recycling, and utilization for erythropoiesis. Since the hallmark of PV is erythrocytosis, imbalance in this axis can further impact RBC production.[5,7,16,17]

Dysregulated iron metabolism plays a central role in PV due to continued erythrocytosis despite iron deficiency caused by hepcidin suppression, since under normal physiological conditions hepcidin would be downregulated to recover from systemic iron deficiency.[7]

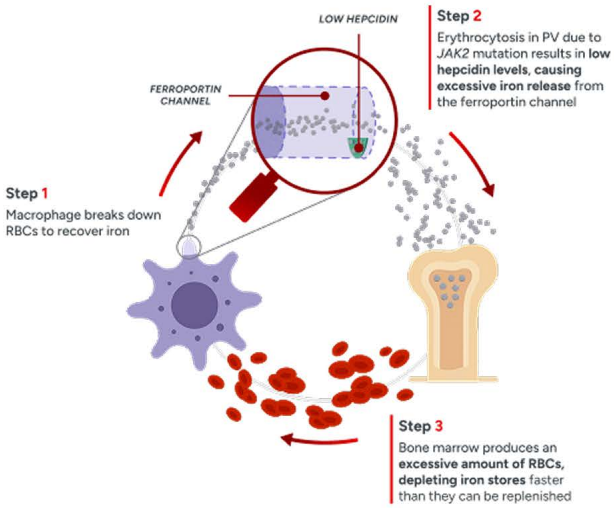
Normal physiology vs PV pathophysiology

Regulated iron metabolism



In normal homeostasis, binding of hepcidin to ferroportin blocks iron exportation, maintaining a feedback loop that effectively recycles unused iron from RBCs for erythropoiesis.[7,17]

Dysregulated iron metabolism



Erythrocytosis in PV leads to persistently low hepcidin levels, disrupting the iron feedback loop and thus increasing ferroportin activity. This leads to increased iron export from storage for erythrocytosis, contributing to systemic iron deficiency.[7]

Iron deficiency may persist or worsen with ongoing therapeutic phlebotomy, especially as erythrocytosis continues, and can lead to debilitating symptoms such as: fatigue, problems with concentration (brain fog), physical inactivity, and weakness and dizziness.[14,16,18,19]

These symptoms are often driven or exacerbated by systemic iron deficiency, even in the absence of anemia.[5,14]

Learn more about the mechanism of disease and the role of iron in PV at RethinkPVpro.com/Iron-Dysregulation.

CI=confidence interval; CV=cardiovascular; CYTO-PV=cytoreductive therapy in polycythemia vera; ET=essential thrombocythemia; HCT=hematocrit; HR=hazard ratio; JAK2=Janus kinase 2; MF=myelofibrosis; MPN=myeloproliferative neoplasm; MPN-SAF=Myeloproliferative Neoplasm Symptom Assessment Form; PV=polycythemia vera; RBC=red blood cell; TE=thromboembolic event; TSS=total symptom score; WHO=World Health Organization.

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