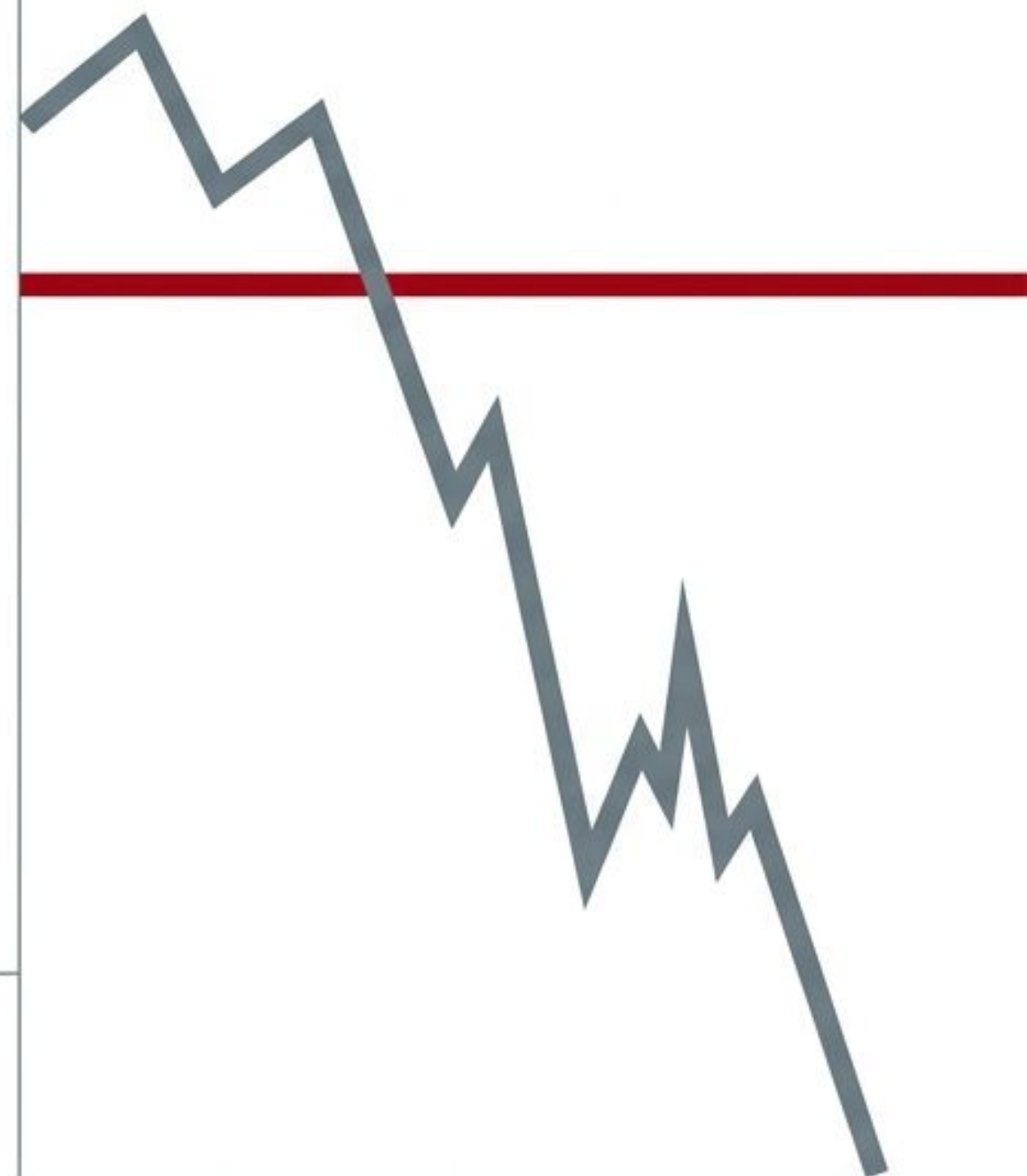


The 'Low-Risk' Paradox in Polycythemia Vera

Case Study: 51 y/o Male with increasing phlebotomy needs and escalating symptom burden.

FLASCO Clinical Oncology Series: Malignant Hematology — Precision Approaches in the Modern Era





The Patient (Baseline)

Demographics: 51 y/o Male, highly active ultra-marathon runner (history of high-altitude training).

PMHx: GERD, recurrent oral ulcers (HSV), BPH (TURP).

FHx: Mother (stroke).

Social: No smoking, no alcohol.

The Diagnosis (March 2015)

Hgb: 17 g/dL

Hct: 48%



Presentation: Incidental finding



Bone Marrow Biopsy: PV+



Molecular: JAK2+

The sheer volume of the standard-of-care strategy





2015-2021

Last 1-2 Years

Present Day

**Symptomatically
Stable**

Maintained on ASA 81mg + Q3-Month Phlebotomy. Ultra-marathon running paused, but high baseline activity maintained.

**Progressive
Functional Decline**

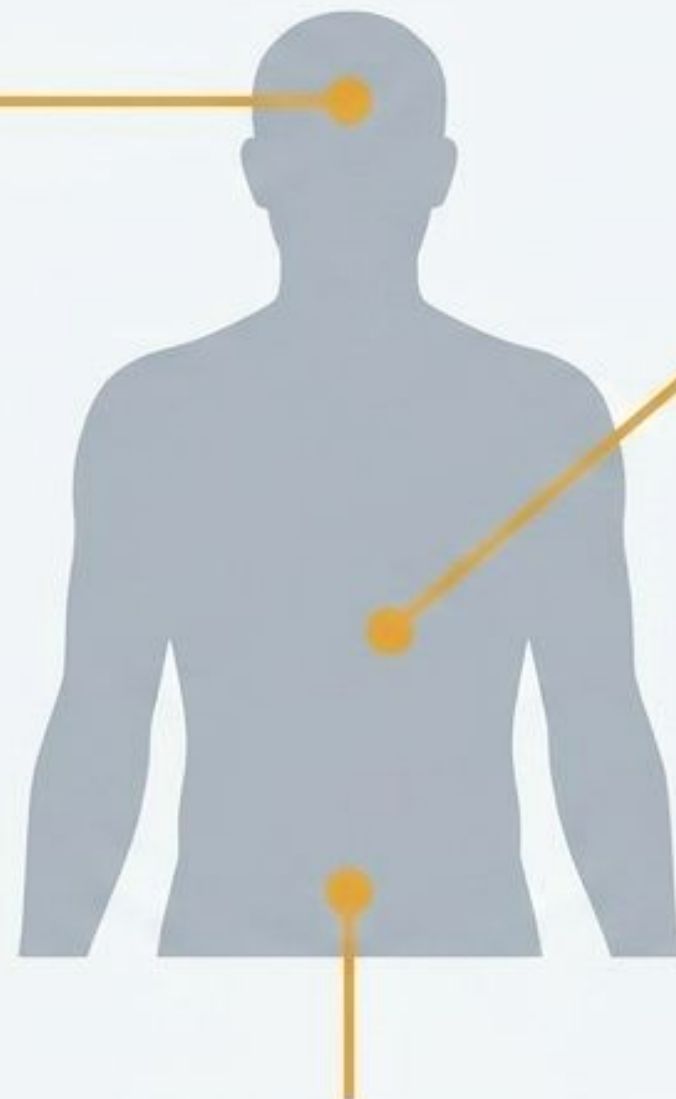
Slowly worsening fatigue and decreased exercise tolerance. Running severely limited.

**Drastic Output
Reduction**

Maximum physical output now limited to a 5K. Severe post-phlebotomy crashes (limited activity for several days post-procedure).

Neurological

Increasing headaches.
Severe brain fog
(notably worsened by
phlebotomies).



Systemic / Dermatologic

Frequent night sweats
(4-5x/week).

Aquagenic pruritus.

Musculoskeletal

Worsening fatigue; poor physical tolerance.

Objective Physical Exam

Normal PE. No splenomegaly. No early satiety.

Peripheral Blood (Recent CBC)

WBC: 7.4

Hgb: 12.4

Hct: 41 (Goal < 45% Met!)

Plt: 314

Physical Exam

No splenomegaly

No early satiety

Normal PE

Molecular & Genetics

Repeat JAK2: 22% V617F

Normal karyotype

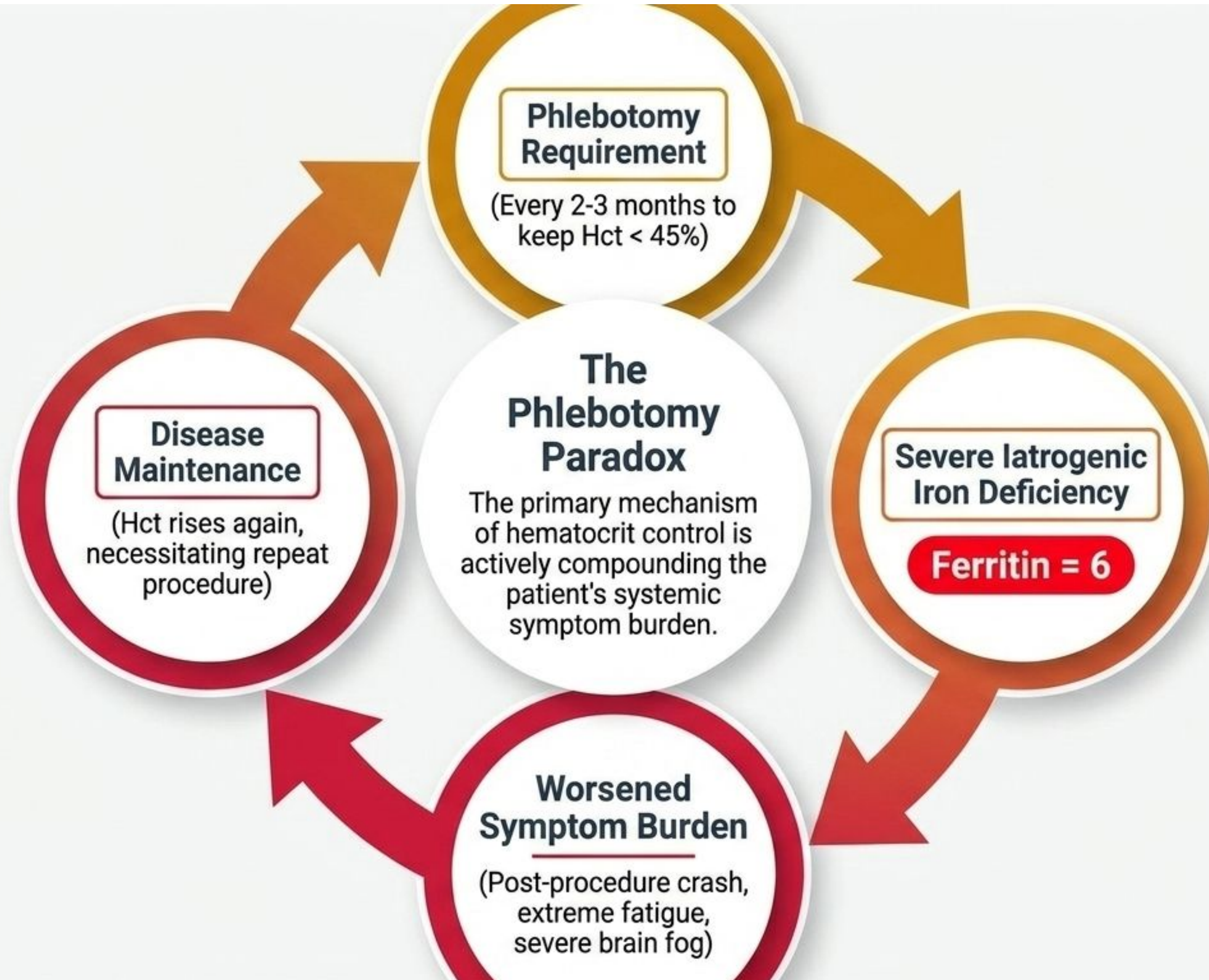
Normal cytogenetics

Bone Marrow (Repeat Biopsy)

Hypercellular marrow (70%) with trilineage hematopoiesis

Increased granulopoiesis, megakaryocytic hyperplasia and atypia

Crucially: No blasts, no reticulin fibrosis



The clinical metrics ignore a collapsing quality of life

Baseline: Ultra-Marathon Capacity

Systemic Decline

Worsening fatigue and profound brain fog, both notably exacerbated immediately following therapeutic phlebotomies.

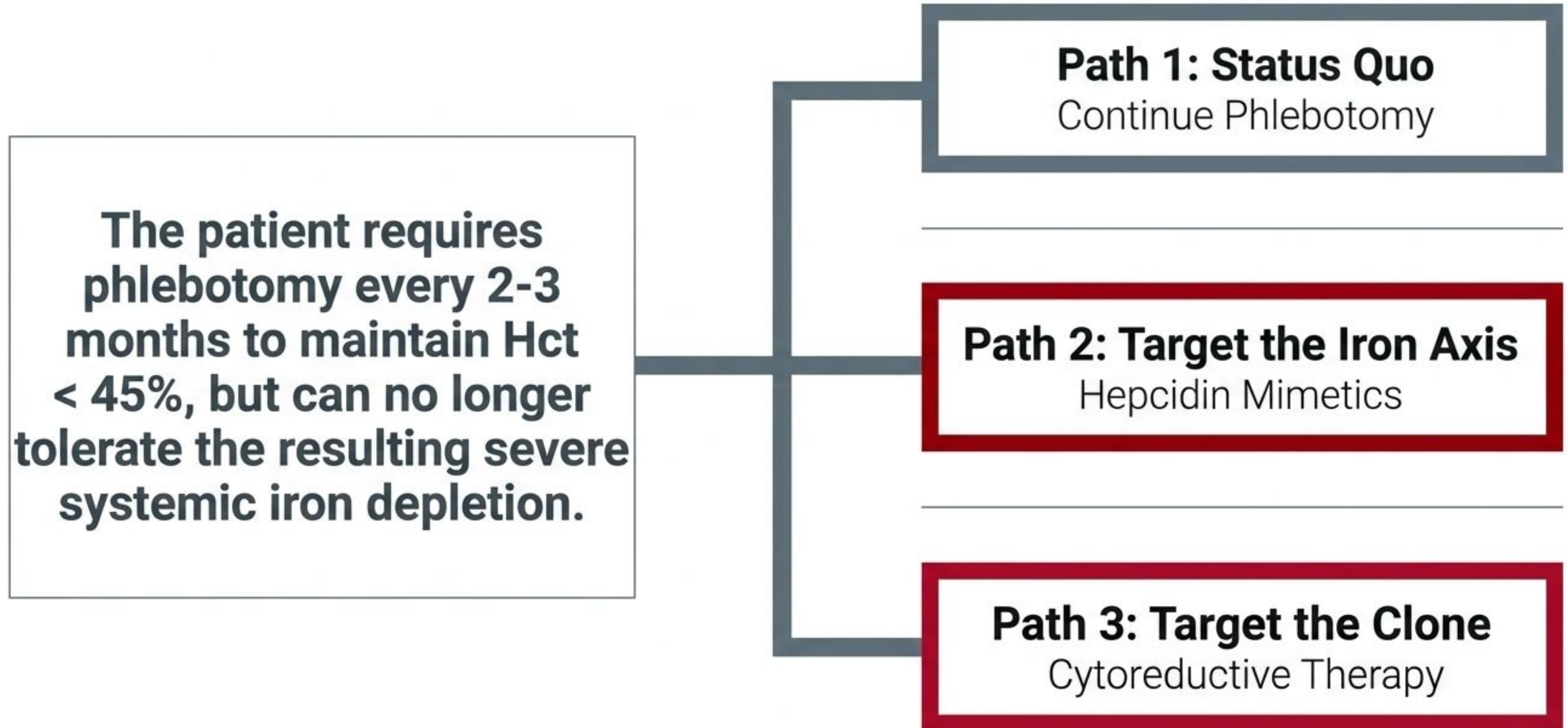
Vasomotor / Clonal Escalation

Increasing headaches, frequent night sweats (4-5x per week), and the onset of aquagenic pruritus.

Phlebotomy Intolerance

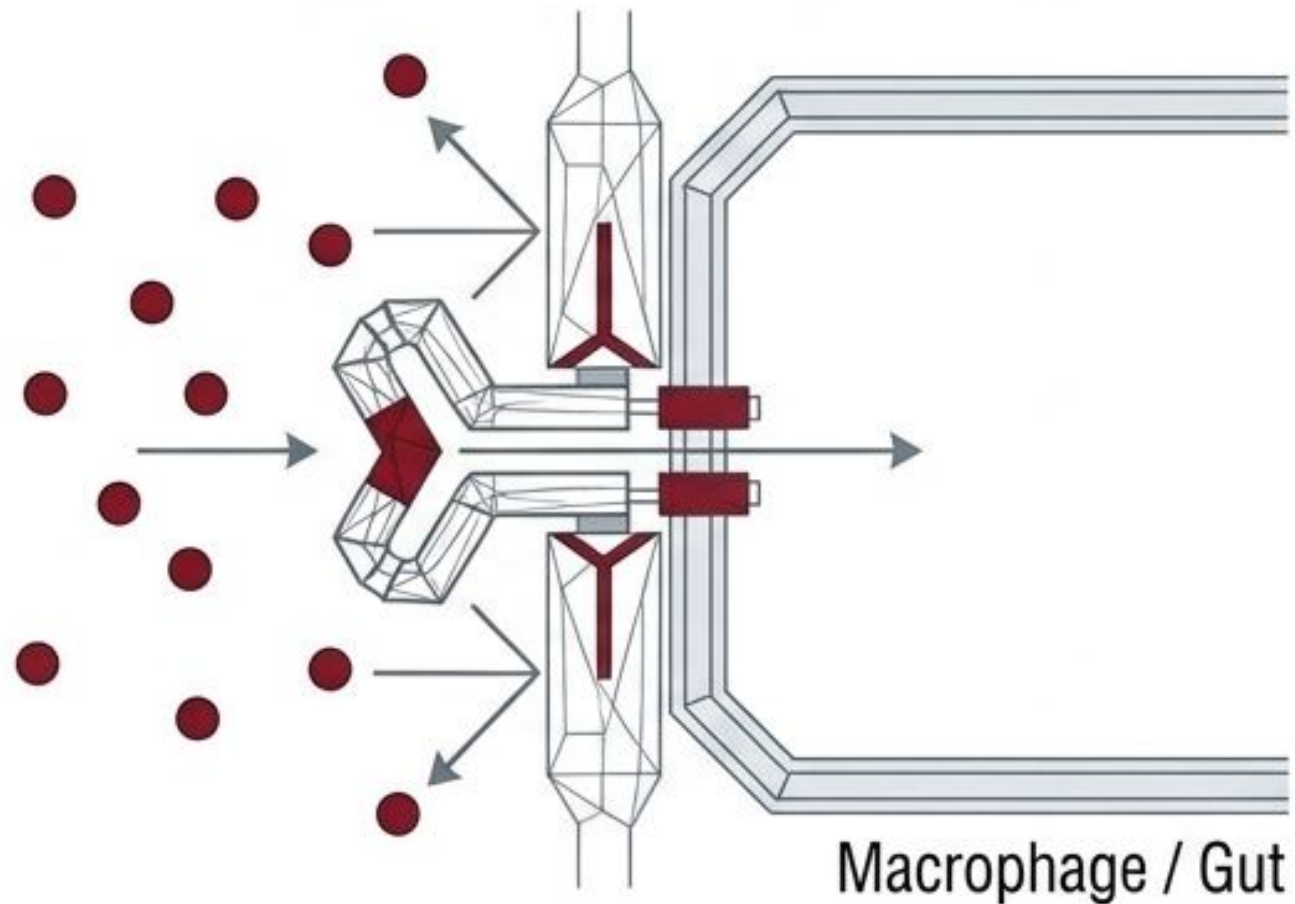
Poor recovery profile. Patient experiences worsened fatigue and heavily limited physical activity for several days post-procedure.

Current: Struggling to complete a 5K



Hepcidin Mimetics (Rusfertide)

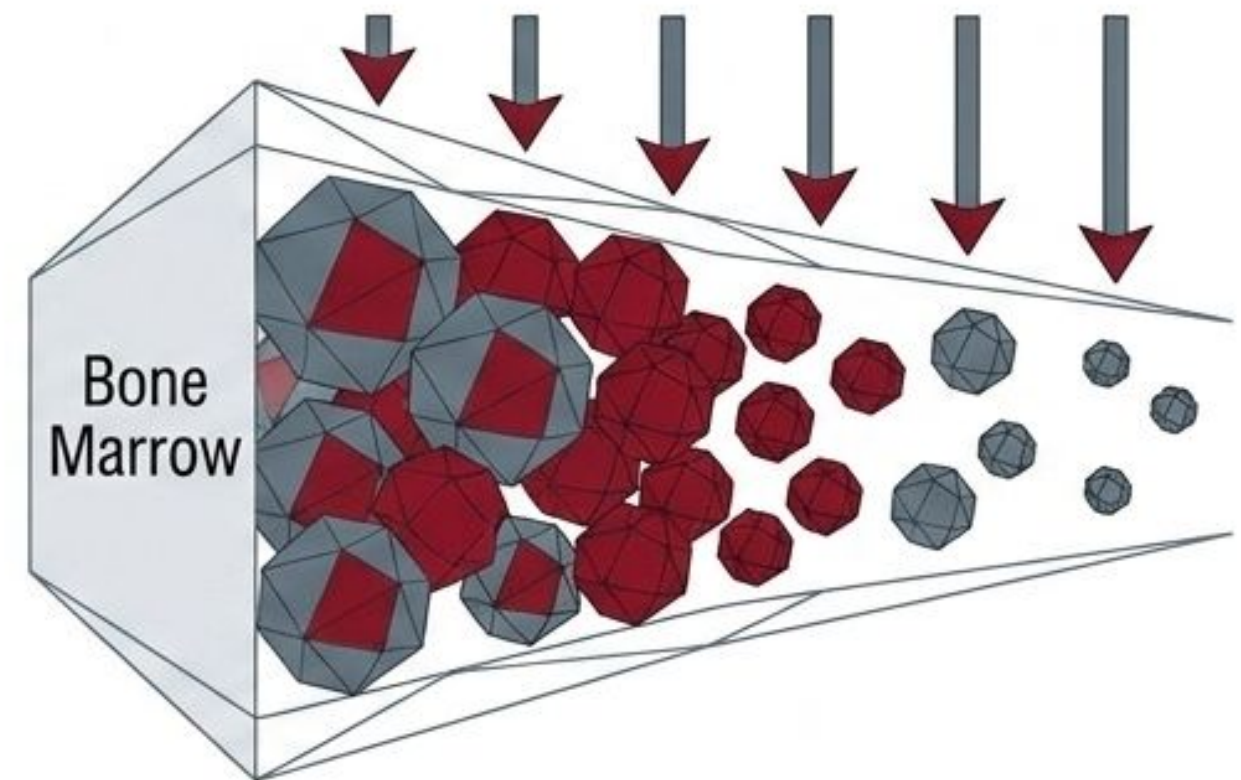
Mimics the body's master iron regulator.



- Restricts iron availability specifically to the marrow.
- Controls hematocrit without causing systemic, tissue-level iron depletion.
- Eliminates the physical need for therapeutic phlebotomy.

Cytoreductive Therapy (Interferon / Hydroxyurea)

Addresses the underlying myeloproliferation.



- Directly suppresses hypercellular bone marrow.
- Controls all blood counts simultaneously.
- Allows for gradual iron repletion and offers potential disease modification (Interferon).

Evaluating therapeutic pathways for this specific patient profile

	Controls Hct < 45%?	Repletes Systemic Iron?	Targets Disease Clone?	Resolves Vasomotor Symptoms?
Phlebotomy Only	Yes 	No 	No 	No 
Rusfertide	Yes 	Yes 	No 	Partial  resolves phleb- related fatigue
Cytoreduction (Interferon /	Yes 	Yes 	Yes 	Yes 

Are we undertreating 'low-risk' Polycythemia Vera?

Age < 60
AND

~~No prior thrombosis~~

Traditional stratification focuses exclusively on macrovascular events, ignoring the severe, compounding morbidity of iatrogenic iron deficiency and unchecked clonal symptoms.

REFERENCES

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- 3.Rumi E, Cazzola M. How I treat polycythemia vera. *Blood.* 2021;138(24):2388-2399.
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