Poliglobulia e Policitemia

Ragusa 09/03/2024

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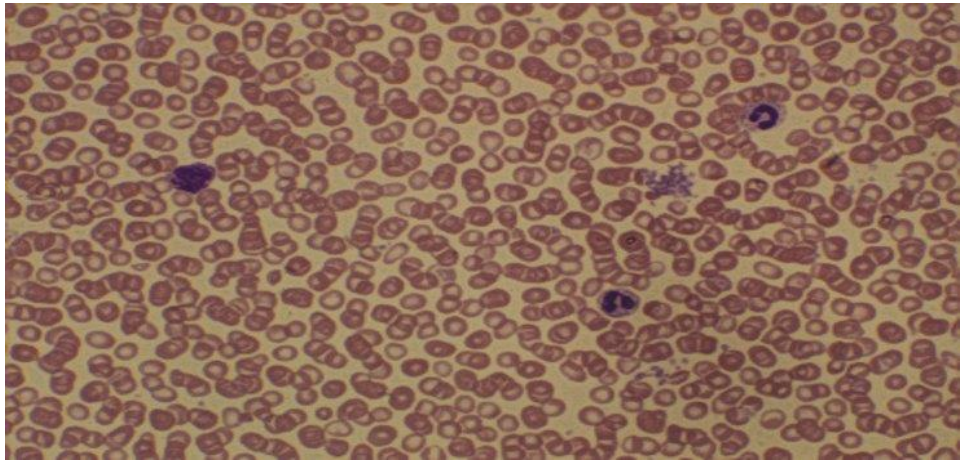
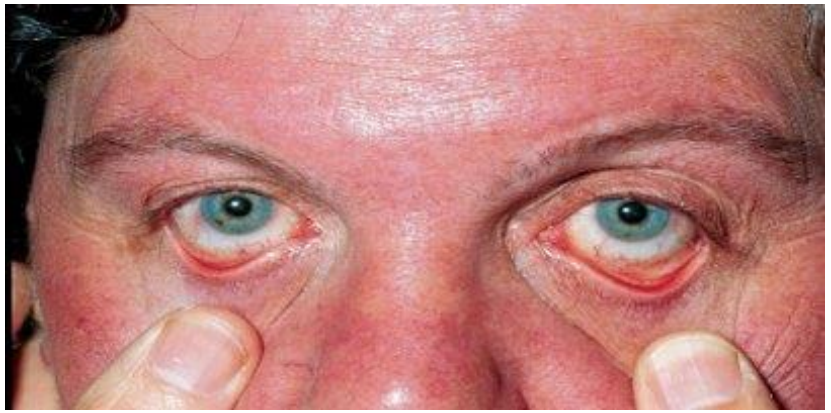
UOSD Ematologia

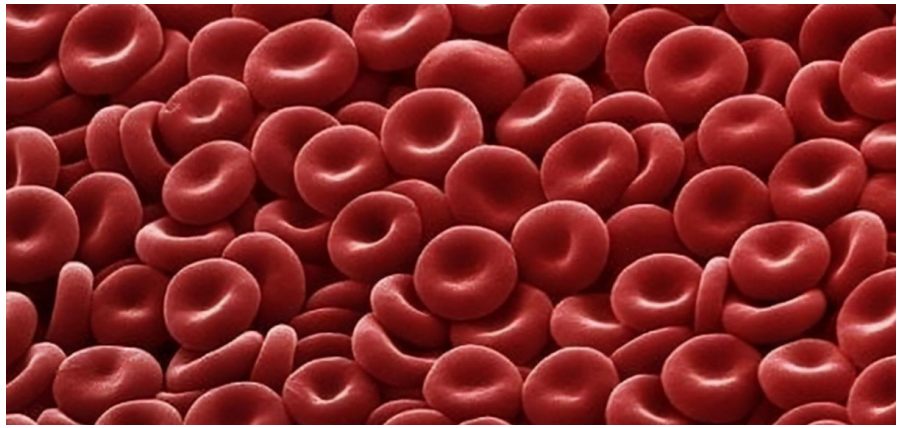
ASP Ragusa

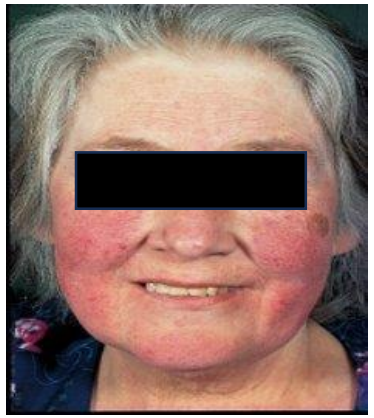
ASP RAGUSA 7

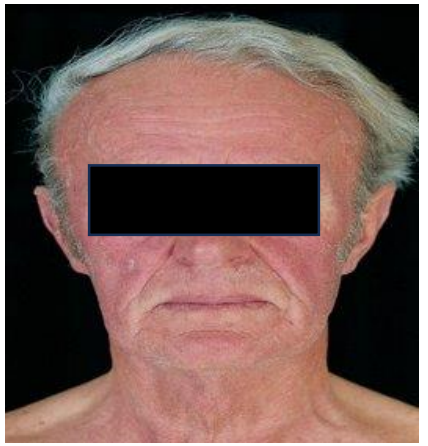
Poliglobulia o Policitemia: aumento dei Globuli Rossi, dell'Emoglobina e dell'Ematocrito.



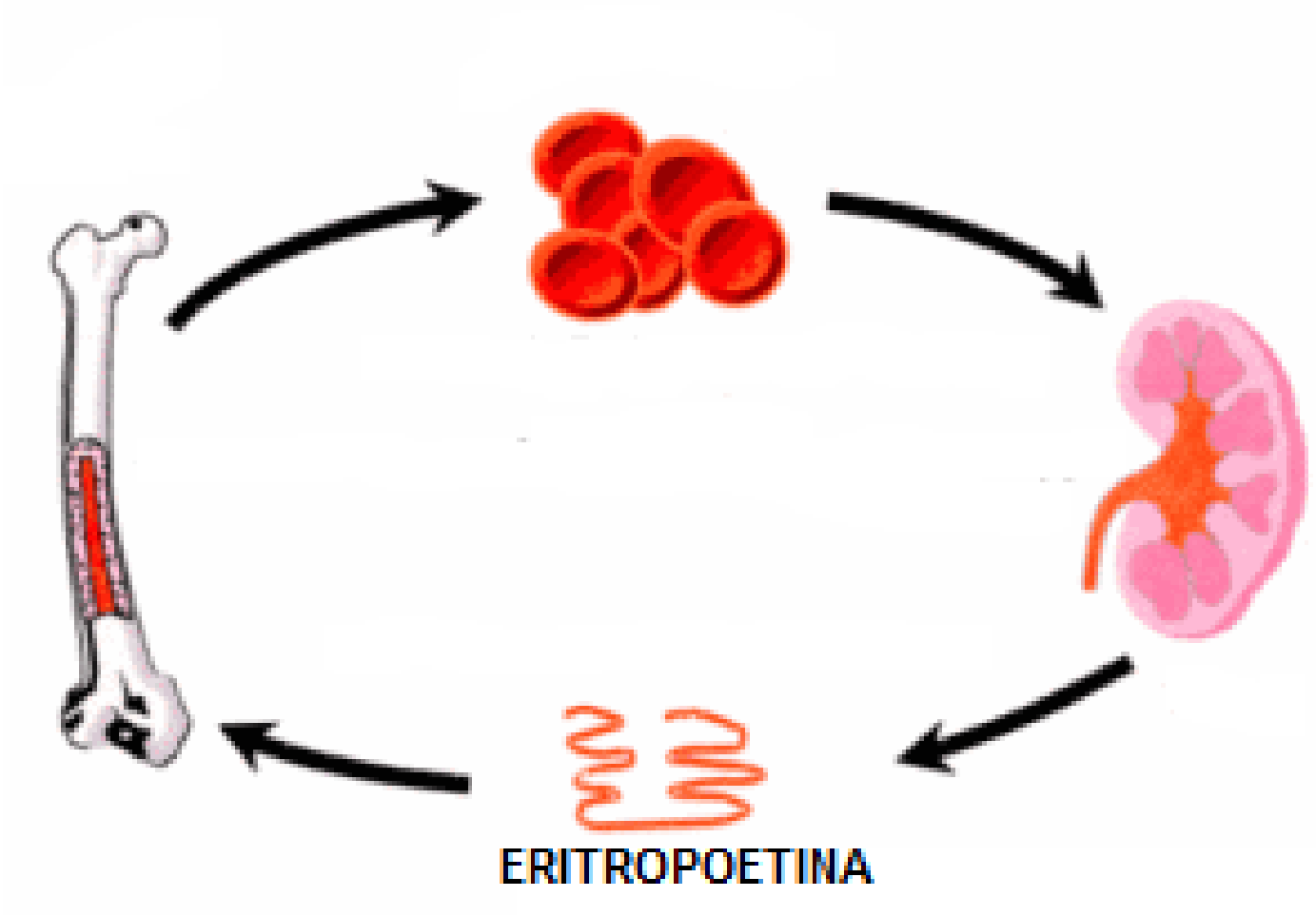




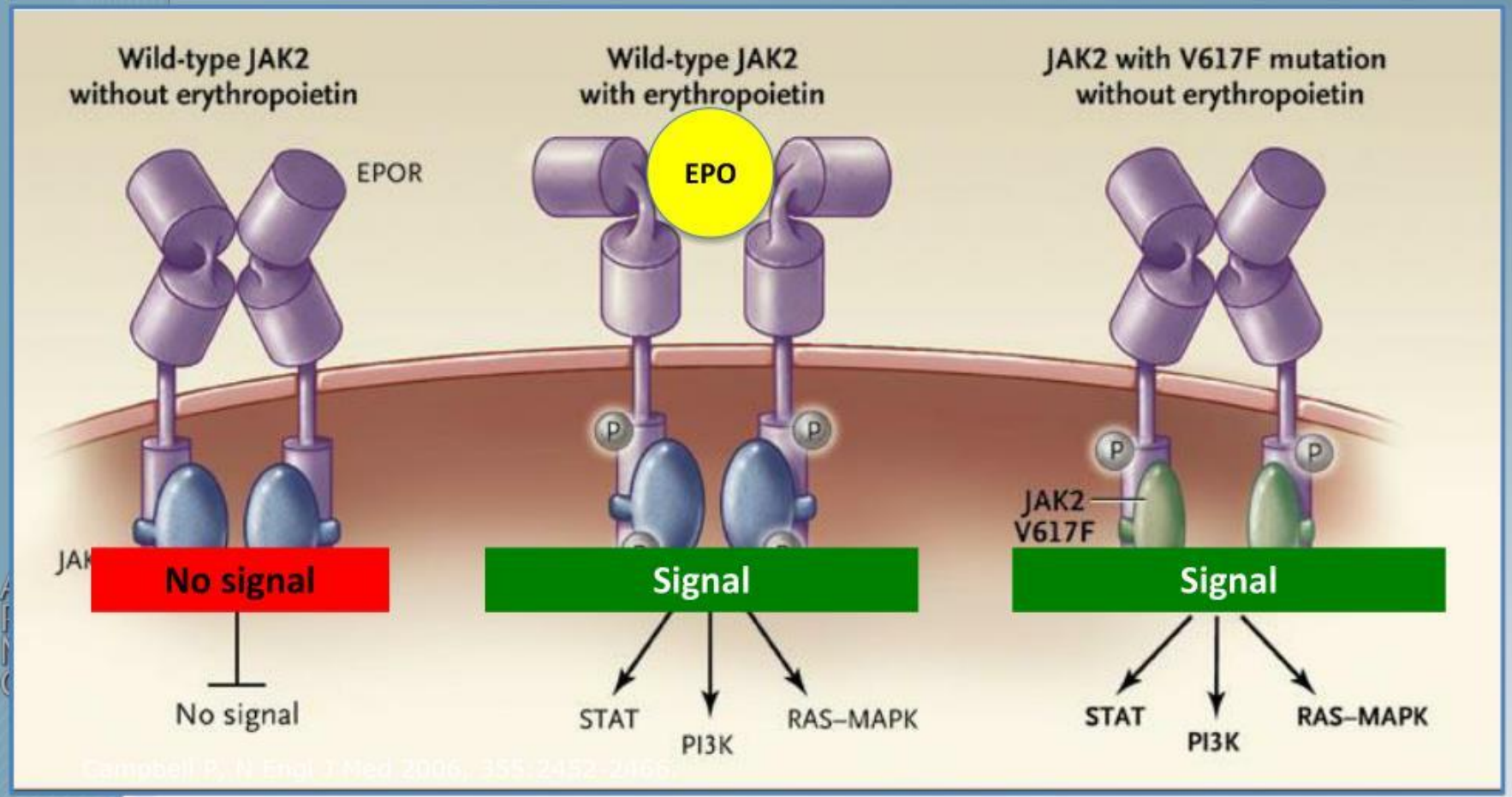




Eritropoietina: ormone che regola la produzione dei globuli rossi



JAK2: wild-type and mutant



Campbell P, N Engl J Med 2006; 355:2452-2466

Poliglobulia

- **Primaria**: l'aumento del volume percentuale dei globuli rossi è direttamente determinato ad alterazione nella produzione dei globuli rossi (mutazioni congenite o acquisite del JAK2,);

  -ERITROPOIETINA: ridotta o normale

- **Secondaria**: dipende da altri fattori o problemi di salute che influenzano la produzione dei globuli rossi

  -ERITROPOIETINA: elevata

POLICITEMIA SECONDARIA

ERITROPOITINA 

- **Ipossia cronica**: enfisema, bronchite cronica, malattie cardiovascolari croniche, apnee del sonno, alterazioni del flusso di sangue ai reni, ipertensione polmonare, difetti congeniti dell'emoglobina, vivere a lungo in alta quota ;
- **Tumori secernenti eritropoietina**: carcinoma a cellule renali, il carcinoma epatocellulare, l'adenocarcinoma e i tumori all'utero;
- **Farmaci**: aumentata assunzione di eritropoietina o di altri farmaci ad azione analoga (epoetina) sia per fini terapeutici che dopanti (nello sport);
- **Policitemia del fumatore** dovuta all'aumento dell'emoglobina legata all'anidride carbonica.

Data di Nascita: 23/05/2003
Medico: Medico Generico
Diagnosi: Diagnosi non specificata

Ingresso Laboratorio: 11/01/24 h:09:53:43
urgente: No

Ematologia

Emocromo

VALORI CRITICI EMOCROMO. SOSPETTA PATOLOGIA EMATOLOGICA. SI CONSIGLIA CONSULENZA EMATOLOGICA.

				v.n.
GLOBULI BIANCHI	**6.0**		10^3/µL	4.0 - 10.0
NE %	**52.6**		%	40.0 - 74.0
LI %	**33.1**		%	20.0 - 45.0
MO %	**10.8**		%	3.4 - 11.0
EO %	**3.0**		%	0.0 - 8.0
BA %	**0.5**		%	0.0 - 1.5
NRBC %	**0.4**	↑	%	0.0 - 0.0
GLOBULI ROSSI	**8.34**	↑↑	10^6/µL	4.40 - 5.60
HGB	**24.1**	↑↑	g/dL	13.0 - 17.5
HCT	**79.2**	↑↑	%	0.0 - 50.0
MCV	**95.0**		fL	80.0 - 100.0
MCH	**28.9**		pg	26.0 - 32.0
MCHC	**30.4**	↓	g/dL	32.0 - 36.0
RDW-CV	**24.8**	↑↑	%	10 - 16
RDW-SD	**84.1**	↑↑	%	36.8 - 46.7
PIASTRINE	**181**		10^3/µL	120 - 450

				v.n.
NE #	**3.15**		10^3/µL	1.90 - 8.00
LI #	**1.98**		10^3/µL	1.00 - 4.50
MO #	**0.65**		10^3/µL	0.20 - 1.00
EO #	**0.18**		10^3/µL	0.00 - 0.80
BA #	**0.03**		10^3/µL	0.00 - 0.20
NRBC #	**0.0**	↑	10^3/µL	0.0 - 0.0

POLIGLOBULIA SECONDARIA

Eritrocitosi Familiare di tipo 2 (ECTY2)

mutazione del gene Von Hippel-Lindau (VHL)

POLICITEMIA PRIMITIVA

ERITROPOITINA RIDOTTA O NORMALE

- **Policitemia Vera (MUTAZIONE JAK2 V617F)**
- **Policitemia Congenita.**

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2022
Myeloproliferative Neoplasms

NCCN Guidelines Index
Table of Contents
Discussion

2017 WHO DIAGNOSTIC CRITERIA FOR POLYCYTHEMIA VERA

Polycythemia Vera (PV)
(Diagnosis requires meeting either all 3 major criteria, or the first 2 major criteria and the minor criterion[2])

- **Major criteria**
  - **Hemoglobin >16.5 g/dL in men, >16.0 g/dL in women**
    OR
    Hematocrit >49% in men, >48% in women
    OR
    Increased red cell mass (RCM)[3]
  - **Bone marrow biopsy showing hypercellularity for age with trilineage growth (panmyelosis) including prominent erythroid, granulocytic, and megakaryocytic proliferation with pleomorphic, mature megakaryocytes (differences in size)**
  - **Presence of *JAK2* V617F or *JAK2* exon 12 mutation (98%)**

- **Minor criteria**
  - **Subnormal serum EPO level**

POLICITEMIA VERA

JAK2 status and thrombotic risk

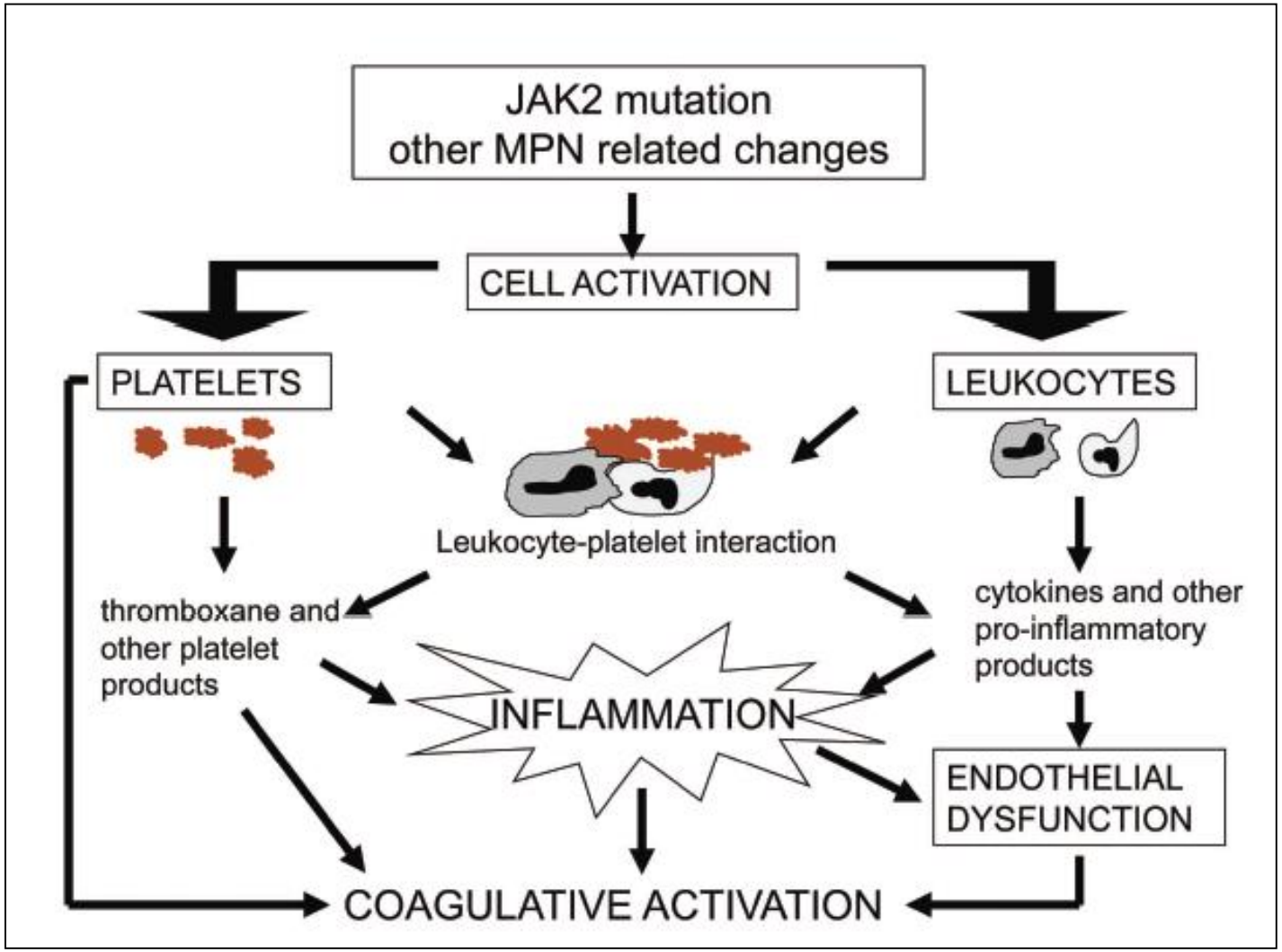
Potential role on haemostasis

- JAK2 may modify red cell adhesion molecules and promote increased adhesiveness
- JAK2 may affect platelet activation by modifying cMPL cell surface localisation and stability
- P-selectin and trombomodulin levels are higher in JAK2+ patients in comparison to JAK2- patients

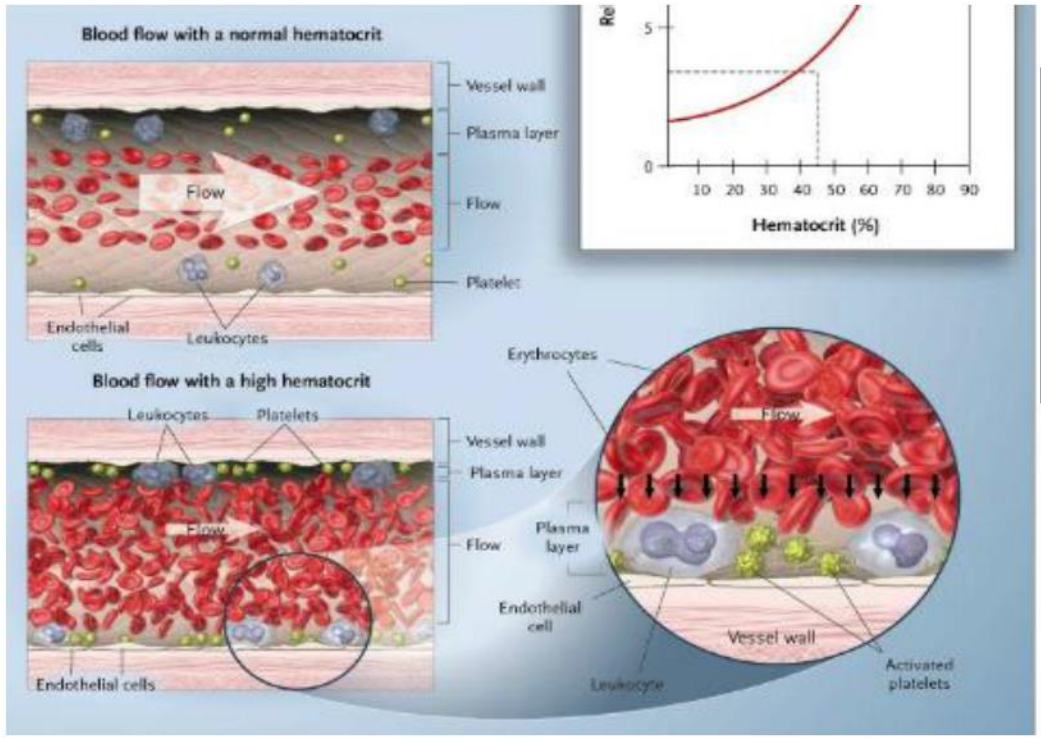
Royer et al JBC 2005

Robertson et al JTH 2007
Falanga et al Experim Hematol 2005

Inflammation and thrombosis in MPN



L'aumento della massa di globuli rossi è causa di iperviscosità che si avverte prevalentemente nella circolazione dei grossi vasi



- I globuli rossi si aggregano e in questo modo il sangue scirre più lentamente

- Come conseguenza le piastrine i globuli bianchi aderiscono all'endotelio e producono trombosi .

Spivak JNEJM. 2004 Jan 8; 350(2):99-101.

Elevato rischio di eventi tromboembolici

- Fra gli eventi ictus, embolia & angina

Complicanze Microvascolari

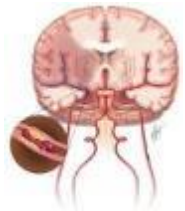
- Eritromelalgia
- Cefalea
- Vertigini
- Disturbi visivi
- Parestesie
- TIA

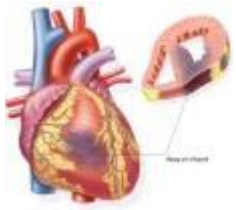
Complicanze Macrovascolari

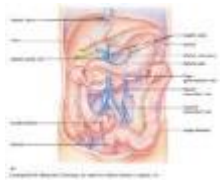
Arteriose

Infarto del miocardio
- Angina instabile
- **Ictus**
- Occlusione arteriosa periferica

Eventi trombotici venosi
- Trombosi venosa profonda
- *Embolia polmonare*
- *Trombosi venosa intra-addominale*
- Trombosi venosa cerebrale







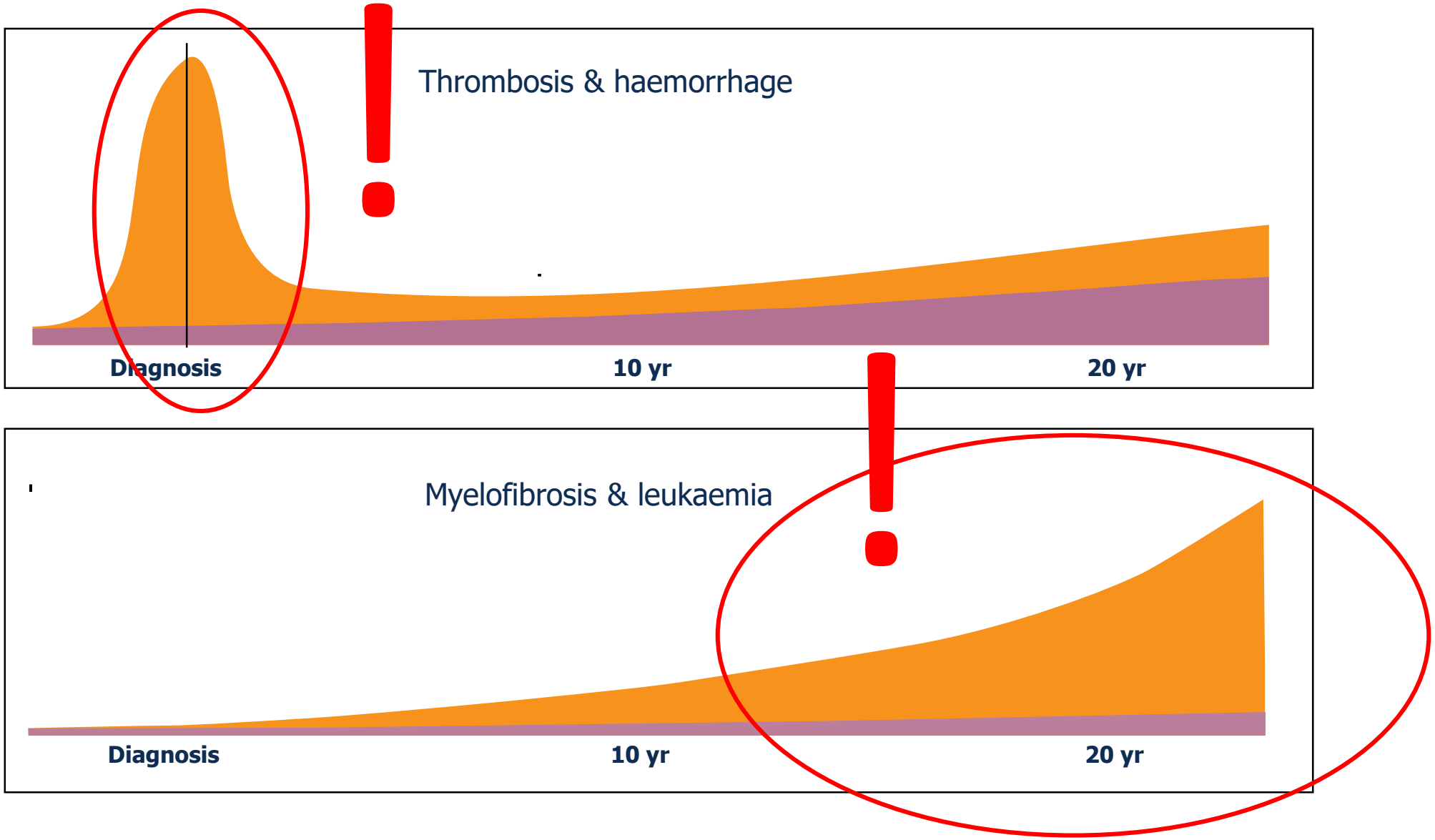
The risk of **Cardiovascular events (CV) for** PV patients is **5.5 / 100** persons per year

In patients above 65 years **with history of thrombosis**[1] the risk of **CV events goes up to 10.9 / 100 persons** per year

For PV patients the incidence of **ischemic stroke** is approximately **14.3 vs 5.3 per 1000 patient years in the general population**, over 55 years[2]

[1]Marchioli, J Clin Oncol. 2005;23(10):2224-32; [2]Zoraster and Rison, J Med Case Rep. 2013 ;7:131

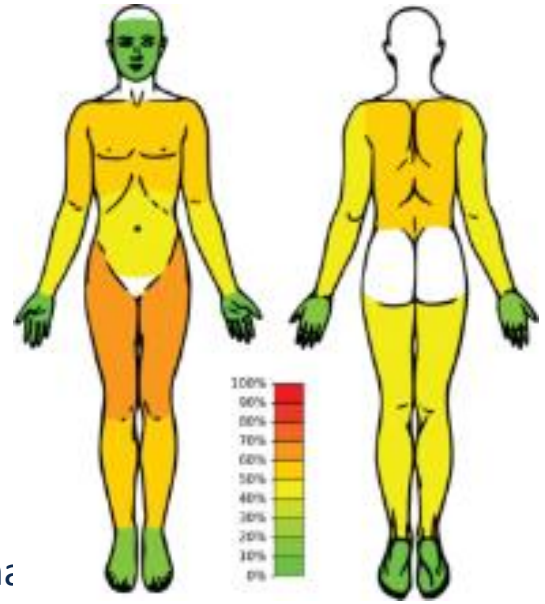
Natural history of PV



Itching is one of the most severe symptoms

Pruritus is the worst aspect of disease for many patients[1]

1. Reported in 5% up to **69% of patients**
2. Majority of patients describe the condition **as aquagenic**[1,2]
3. Associated with itching, tickling, stinging, burning, and/or "unbearable" sensations
4. Commonly experienced for **30 to 45 minutes** (range: 5–120)[1]
5. Could lead to irritability, anger, **depression and suicidal ideation**[3]
6. Associated with **significant reductions in global health** and functiona status[2]
7. **Current treatments for PV provide limited relief**[2]



Relativ

White ar

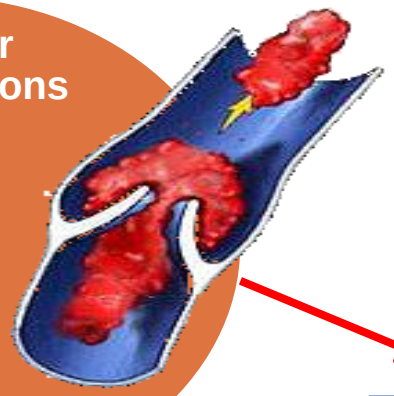
[1]Diehn & Tefferi, Br J Haematol. 2001; [2]Siegel American journal of hematology 2013; [3]Saini Europ

SMPC clinical scenario

Aumento della viscosità del sangue che ostacola la circolazione

Vascular Complications

Arterial or Venous



Risk Factors for Thrombosis

- Advanced Age
- Disease Duration
- Thrombosis History
- Novel Biomarkers
- Gender

Symptoms

Independent of Risk Factors

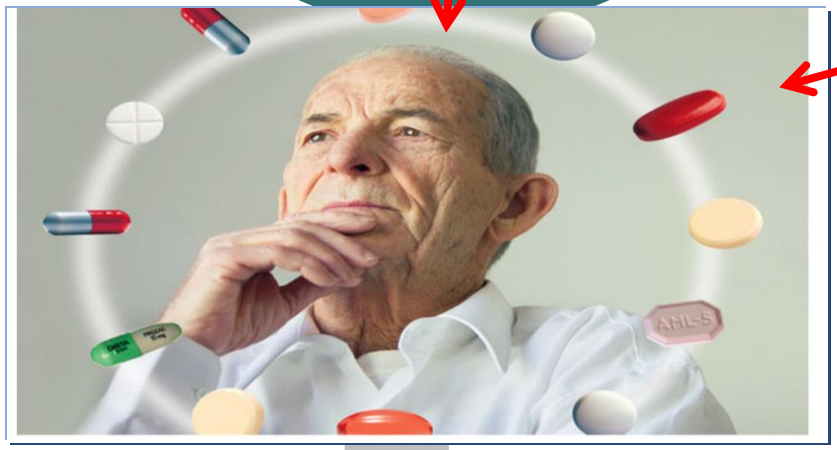
- Fatigue
- Pruritus
- Splenomegaly

Disease Transformation

MF or AML

Risk Factors for Transformation

- Advanced Age
- Disease Duration
- Baseline BM Fibrosis
- Leukocytosis

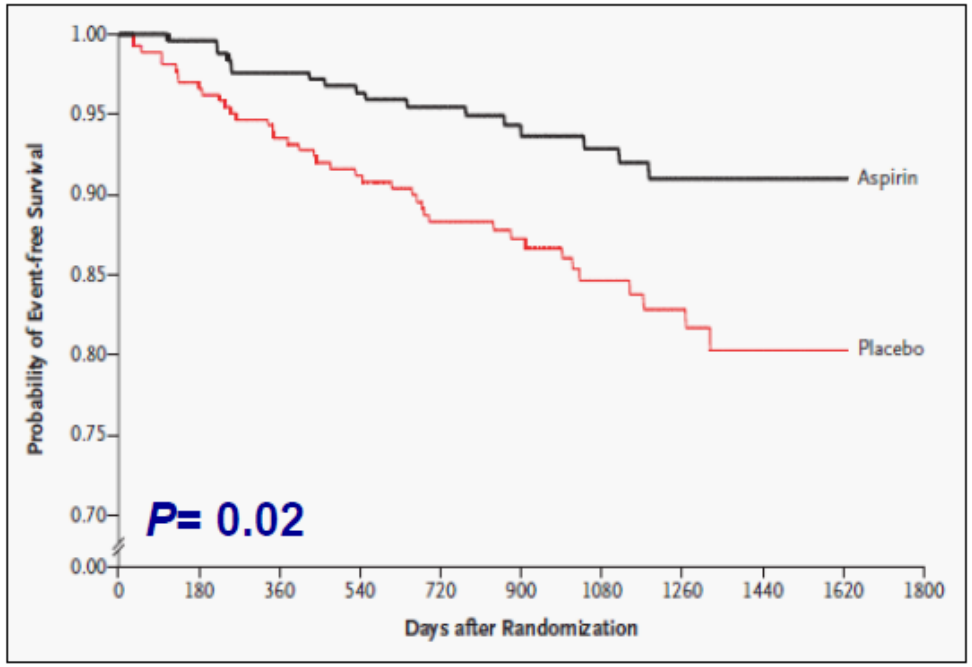


Decreased Quality of Life and Life Expectancy

Studio ECLAP **ASA 100mg/die** riduzione significativa di mortalità totale, morte cardiovascolare, trombosi non fatale

(senza significativo aumento del rischio di complicanze emorragiche)

ASA 100 mg/die a tutti i pazienti con PV



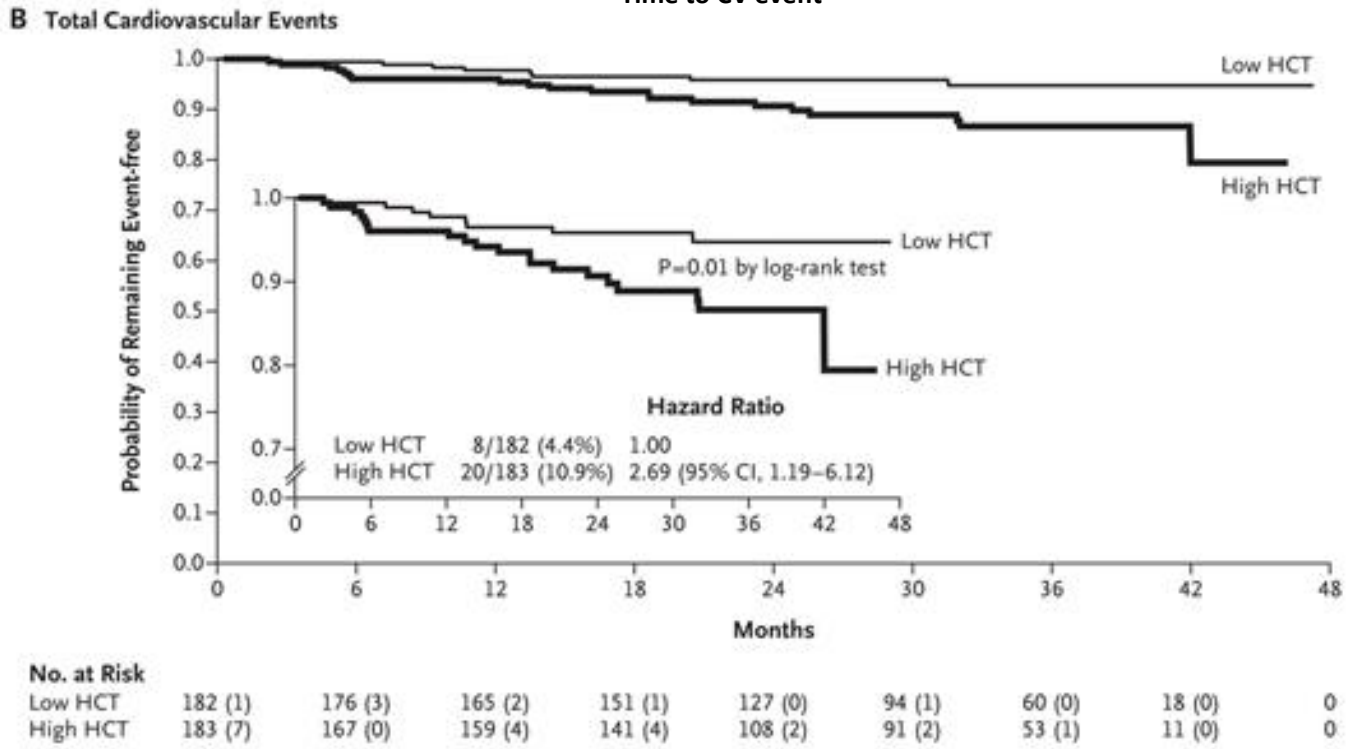
Marchioli R et al. JCO. 2005; 23(10):2224-32

Finazzi G, Barbui T. Blood. 2007(109): 5104-11 Barbui T. Haematologica. 2006;2(6):32-35

CYTO-PV study: A HCT < 45% is associated with a significantly lower risk of thrombosis compared with HCT at 45%–50%

The risk of CV events is reduced by approximately 3-fold in patients with HCT < 45%

Time to CV event



Marchioli R, et al. *N Engl J Med.* 2013;368:22-33.

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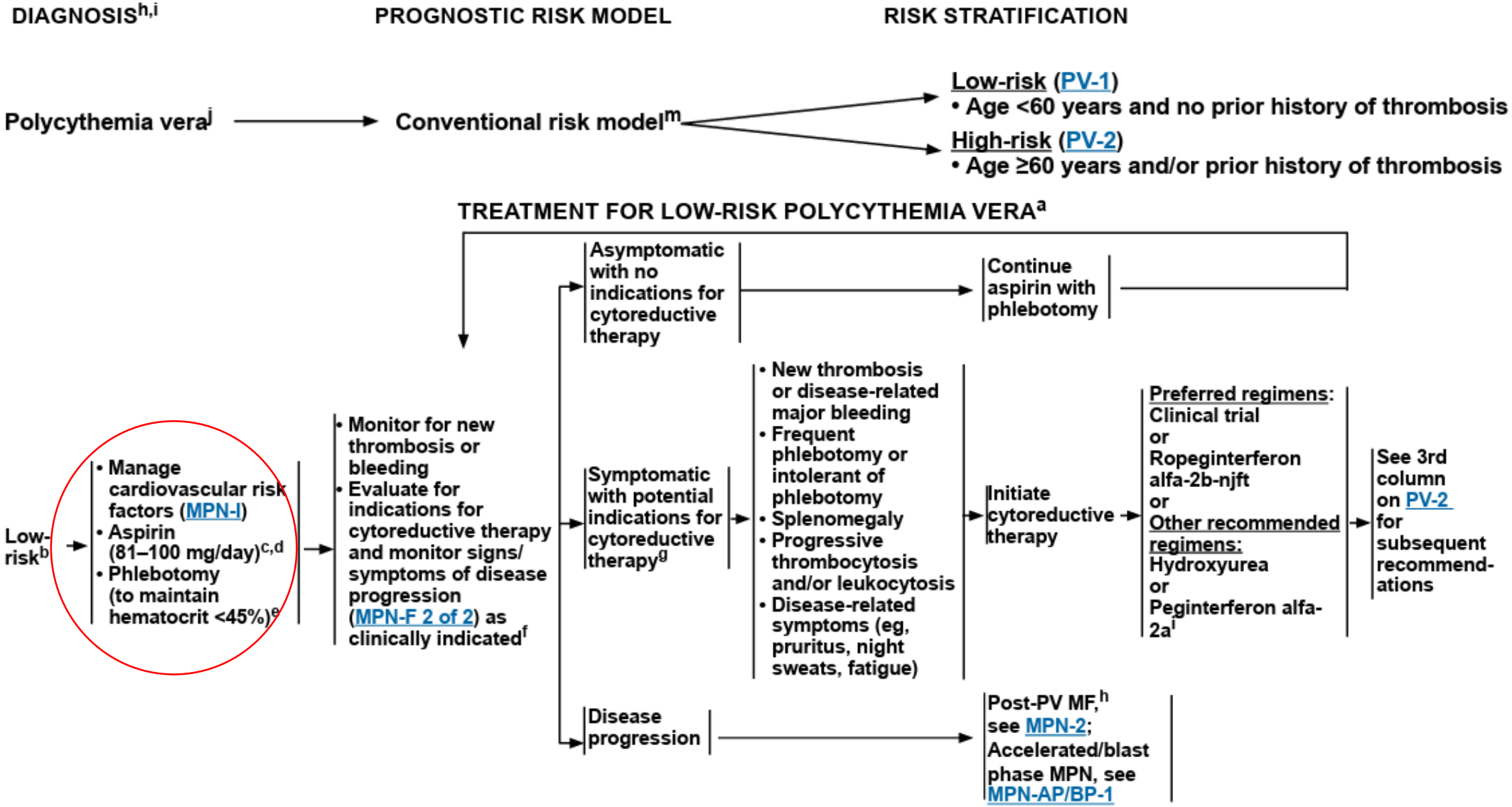

DIAGNOSIS[h,i]
PROGNOSTIC RISK MODEL
RISK STRATIFICATION
Polycythemia vera[j]
Conventional risk model[m]
Low-risk (PV-1)
• Age <60 years and no prior history of thrombosis
High-risk (PV-2)
• Age ≥60 years and/or prior history of thrombosis
TREATMENT FOR LOW-RISK POLYCYTHEMIA VERA[a]
Low-risk[b]
• Manage cardiovascular risk factors (MPN-I)
• Aspirin (81–100 mg/day)[c,d]
• Phlebotomy (to maintain hematocrit <45%)[e]
• Monitor for new thrombosis or bleeding
• Evaluate for indications for cytoreductive therapy and monitor signs/symptoms of disease progression (MPN-F 2 of 2) as clinically indicated[f]
Asymptomatic with no indications for cytoreductive therapy
Continue aspirin with phlebotomy
Symptomatic with potential indications for cytoreductive therapy[g]
• New thrombosis or disease-related major bleeding
• Frequent phlebotomy or intolerant of phlebotomy
• Splenomegaly
• Progressive thrombocytosis and/or leukocytosis
• Disease-related symptoms (eg, pruritus, night sweats, fatigue)
Initiate cytoreductive therapy
Preferred regimens:
Clinical trial
or
Ropeginterferon alfa-2b-njft
or
Other recommended regimens:
Hydroxyurea
or
Peginterferon alfa-2a[i]
See 3rd column on PV-2 for subsequent recommend-ations
Disease progression
Post-PV MF,[h] see MPN-2;
Accelerated/blast phase MPN, see MPN-AP/BP-1

Evidence- and consensus-based recommendations for phlebotomy in polycythemia vera

Tiziano Barbui,[1] Francesco Passamonti,[2,] Patrizia Accorsi,[3] Fabrizio Pane,[4] Alessandro M. Vannucchi,[5]

Claudio Velati,[6] Robert Peter Gale,[7] Sante Tura,[8] Giovanni Barosi.[9]

SIdEM
Società Italiana di Emaferesi e Manipolazione Cellulare

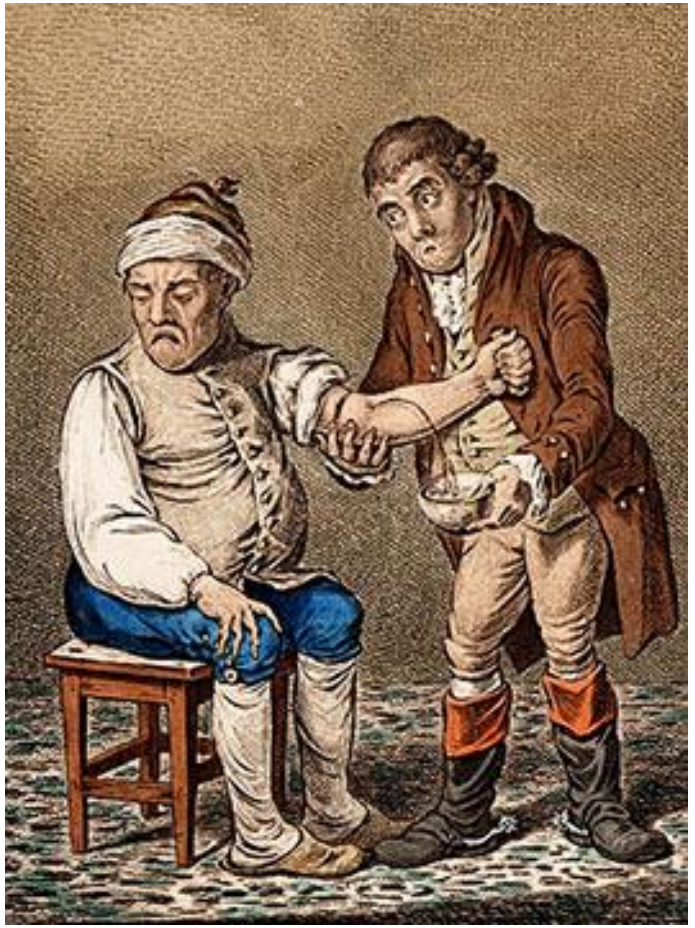
SIMTI
Società Italiana di Medicina Trasfusionale e Immunoematologia

Barbui T et al, Leukemia 2018;

Recommendations: Phlebotomy

INDICATIONS FOR PHLEBOTOMY

The Panel considered phlebotomy is appropriate to reduce the excess RBC mass induce iron deficiency, and achieve a target hemoglobin level judged appropriate for a person with PV. There are **no absolute or relative contraindications to phlebotomy** in this setting.



TARGET HAEMATOCRIT FOR PHLEBOTOMY

The target of phlebotomy in PV should be a **haematocrit < 45%** (strong recommendation).

Definition of special situations

PHLEBOTOMY-ASSOCIATED IRON DEFICIENCY

Routine monitoring of serum ferritin and transferrin saturation during phlebotomy is not recommended **except** in persons with symptoms potentially attributed to severe tissue iron deficiency such as pica, mouth paresthesia, esophagitis and restless legs. The panel **recommends iron supplementation in this instance**. Subsequent loss of control of the target hematocrit should be treated with cytoreductive drugs.

Phlebotomy strategy

Indication

- Phlebotomy begin **as soon as possible after the diagnosis of PV or even earlier** in persons with recent, active vascular complications and a high likelihood of PV.

Induction

- Phlebotomy regimen should **consider a person's weight** and should remove **300 to 450 mL** of blood **every other day** or **twice a week** until the target hematocrit is achieved.

Maintenance

- The **maintenance phase** should have the same volume of blood as in the induction phase. **Phlebotomy intervals** should be determined by **measuring hematocrit levels monthly** in the **1st 6 months and ≤2 months thereafter**.

Fluid reintegration: to be or not to be?

Endovenous reintegration

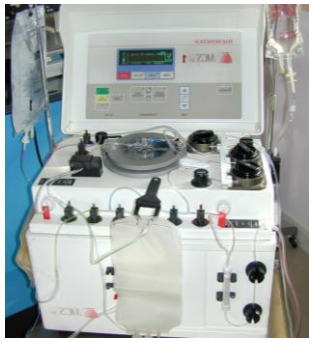
- The small volume of plasma removed by phlebotomy **does not require replacement**.

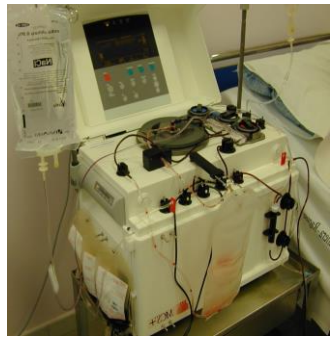
Oral intake

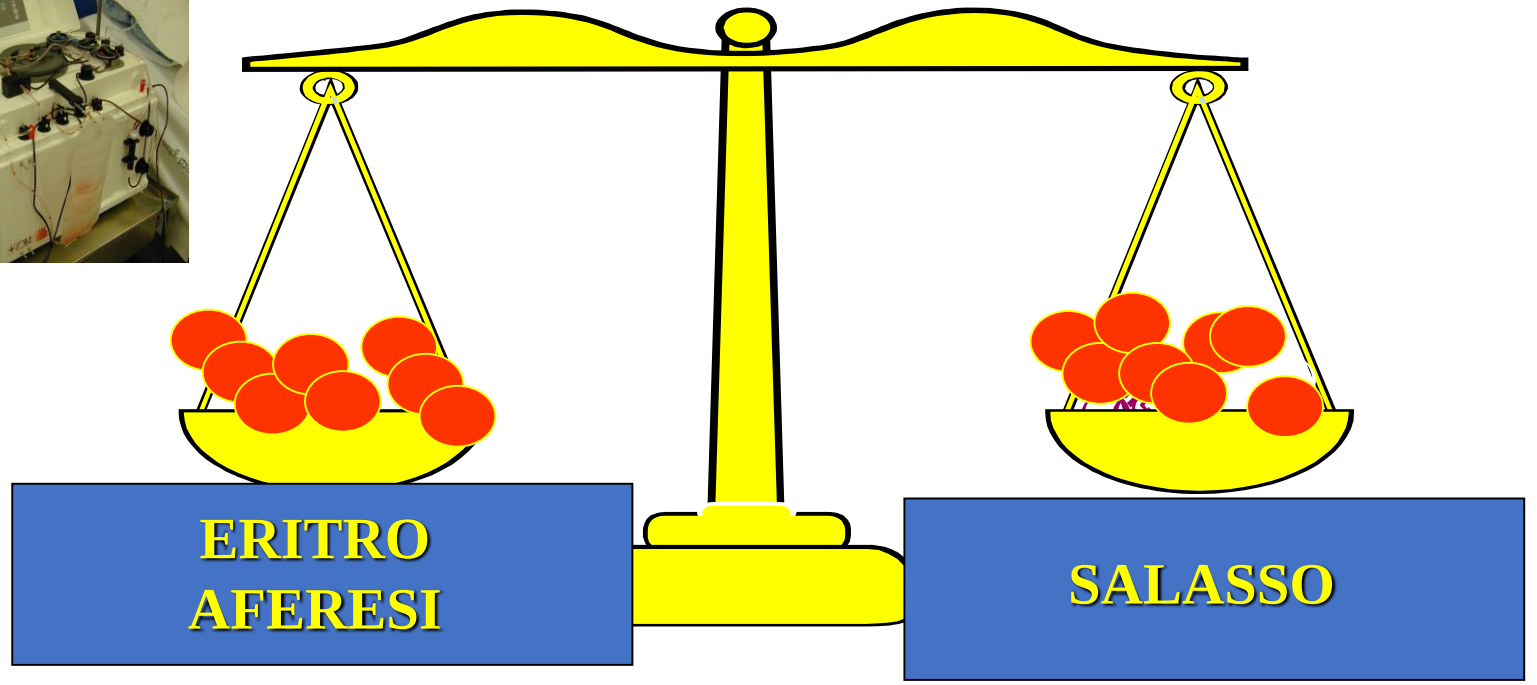
- **Oral intake** of liquids of **about 1 L before and after phlebotomy** is recommended as is continuous blood **pressure monitoring** during phlebotomy.

ERITROAFERESI

Come rimuoverli ?







L'estrazione di 10 ML di emazie per Kg di peso corporeo con separatore cellulare produce una riduzione di ca il 13% dell' Ht iniziale con una singola procedura

Per ottenere lo stesso risultato con la salassoterapia tradizionale occorre fare N.3 PRELIEVI DA 450 ML

Red blood Cell Apheresis

RBC-APHERESIS

- The panel recommended RBC-apheresis **as an alternative to phlebotomy** in persons with severe vascular complications when **rapid attainment of a target hematocrit is needed** or before emergency surgery in persons with an extremely high hematocrit value to reduce the risk of peri-operative vascular complications.
- The panel agreed that **RBC-apheresis is not a remedy for phlebotomy-intolerance**.

POLIGLOBULIE

PROTOCOLLO «RAGUSA»

Patologia	Salasso terapia	Preferibilmente Terapia aferetica	Terapia aferetica	Target
Policitemia vera	Ht > 45 ≤ 48	Ht > 48 ≤ 51	Ht > 51	Ht < 45
Policitemia secondaria a broncopatia	Ht >52-55 ≤ 58	Ht > 58 ≤ 61	Ht > 61	Ht < 52-55
Policitemia secondaria a cardiopatia cianogena congenita	Ht > 55-60 ≤ 63	Ht> 63 ≤66	Ht>66	Ht < 55-60

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Original article

Evaluation of erythrocytapheresis compared to phlebotomy in polycythaemia vera patients

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Phlebotomy

ABSTRACT

Introduction: Polycythaemia vera patients can present with arterial or venous vascular occlusive events such as thrombosis or cardiovascular disease; disease-related symptoms may significantly impact on the quality of life. The aim of this study was to evaluate the efficacy and safety of erythrocytapheresis compared to [illegible] polycythaemia patients.

Methods: This study reports the findings of a retrospecti[illegible] vera patients diagnosed according to published guidelines[illegible] cytapheresis or phlebotomy over a four-year period. The [illegible] blood volume and red blood cell count to near normal lev[illegible] ate the symptoms and complications associated with poly[illegible] ly applying a mathematical model.

Results: Using the model, 20 erythrocytapheresis procedur[illegible] tory values (red blood cell count, haemoglobin count and [illegible] cantly reduced in patients treated with erythrocytaphe[illegible] patients, erythrocytapheresis resulted in less work absen[illegible] lost production, with a lower overall procedure cost in com[illegible]

Conclusion: This model can assist in selecting the proper t[illegible] patients. Especially for those with high blood volumes a[illegible] levels (delta), erythrocytapheresis offers a more efficient w[illegible] compared to phlebotomy thereby, potentially reducing t[illegible] dures required for the induction of polycythaemia vera [illegible] between procedures during the maintenance phase.

* Corresponding author at: C.Da Pantanazzi, Ragusa, RG 97100, Italy.
E-mail address: sergio.cabibbo@asp.rg.it (S. Cabibbo).

PROTOCOLLO «RAGUSA»

Table 2 – Characteristics of the patients submitted to phlebotomy and erythrocytapheresis between 2018 and 2021.

Type of procedure	phlebotomy	Erythrocytapheresis
N° of patients	20 patients	20 patients
Median age	61.5	63
Gender (%)	Male 35 / Female 30	Male 35 / Female 30
Clinical symptom	Splenomegaly 55%	Splenomegaly 55%
Mean RBC collection time	10 min (range: 5–15 min)	25.7 ± 4.5 min (range: 10–37 min)
Mean collection volume	400 mL (range: 390–410 mL)	534 ± 144 mL (range: 244–793 mL)
Total Number of procedures	320	28
Pre-treatment vs. post treatment		
Mean red blood cell (x 10^{12} mm³)	7.9 vs. 6.5	7.9 vs. 6.5
Mean haemoglobin (g/dL)	15 vs. 13	20 vs. 13
Mean haematocrit (%)	48 vs. 45	55 vs. 45
Hypocalcaemia	–	2.76%
Hypovolaemia	–	–
Vascular complications	–	–
Interval between procedures	20 days 4 months	6–7 months
Work absenteeism per patient	12 (days/year)	3 (days/year)
Cost per procedure (Euros)	45.80	375.40
Overall cost/patient/year (Euros)	2900	1800

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Polycythemia Vera

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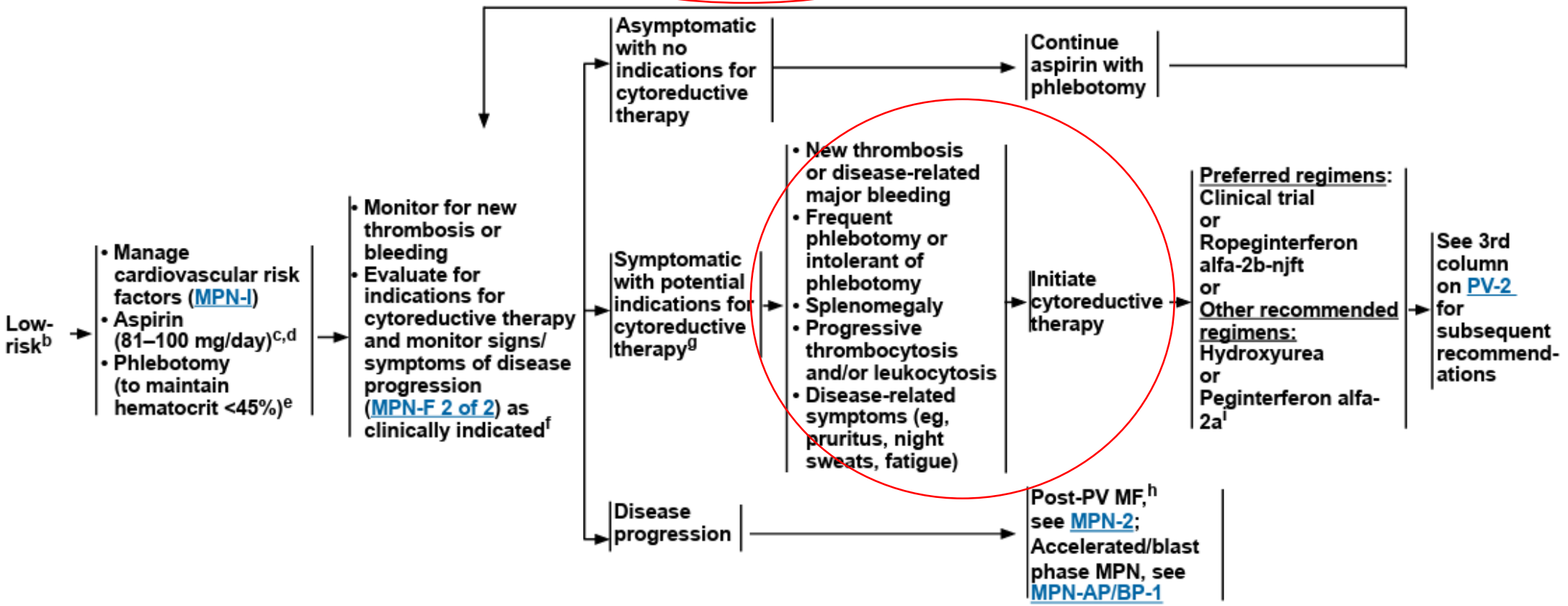
TREATMENT FOR LOW-RISK POLYCYTHEMIA VERA[a]



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TREATMENT FOR HIGH-RISK POLYCYTHEMIA VERA[a]

High-risk →

- Manage cardiovascular risk factors (MPN-I)
- Aspirin (81–100 mg/day)[c,d]
- Phlebotomy (to maintain hematocrit <45%)[e]

Regimens for cytoreductive therapy:

Preferred regimens:
Hydroxyurea
or
Ropeginterferon alfa-2b-njft
or
Other recommended regimen:
Peginterferon alfa-2a[i]
or
Useful in certain circumstances:
Ruxolitinib

→

- Monitor for new thrombosis or bleeding
- Monitor response and signs/symptoms of disease progression (MPN-F 2 of 2) as clinically indicated[f,j,k,]

→

Adequate response → Continue treatment

Inadequate response or Loss of response →

Potential indications for change of cytoreductive therapy:[g]
- Intolerance or resistance to prior cytoreductive treatment[l]
- New thrombosis or disease-related major bleeding
- Frequent phlebotomy or intolerant of phlebotomy
- Splenomegaly
- Progressive thrombocytosis and/or leukocytosis
- Disease-related symptoms (eg, pruritus, night sweats, fatigue)

→

Preferred regimens:
Clinical trial
or
Ruxolitinib[m] (category 1 for high-risk PV for hydroxyurea resistance or intolerance)
or
Other recommended regimens:
Ropeginterferon alfa-2b-njft if not previously used
or
Hydroxyurea if not previously used
or
Peginterferon alfa-2a[i] if not previously used

Disease progression →

Post-PV MF,[h] see MPN-2; Accelerated/blast phase MPN, see MPN-AP/BP-1

Hydroxyurea in PV

- Use cytoreduction in **high-risk patients (age ≥ 60 yr and/or previous thrombosis)**
- Use cytoreduction in **low-risk patients in case of** hyperleukocytosis, thrombocytosis (>1000-1500x10^9/l), symptomatic splenomegaly, symptoms

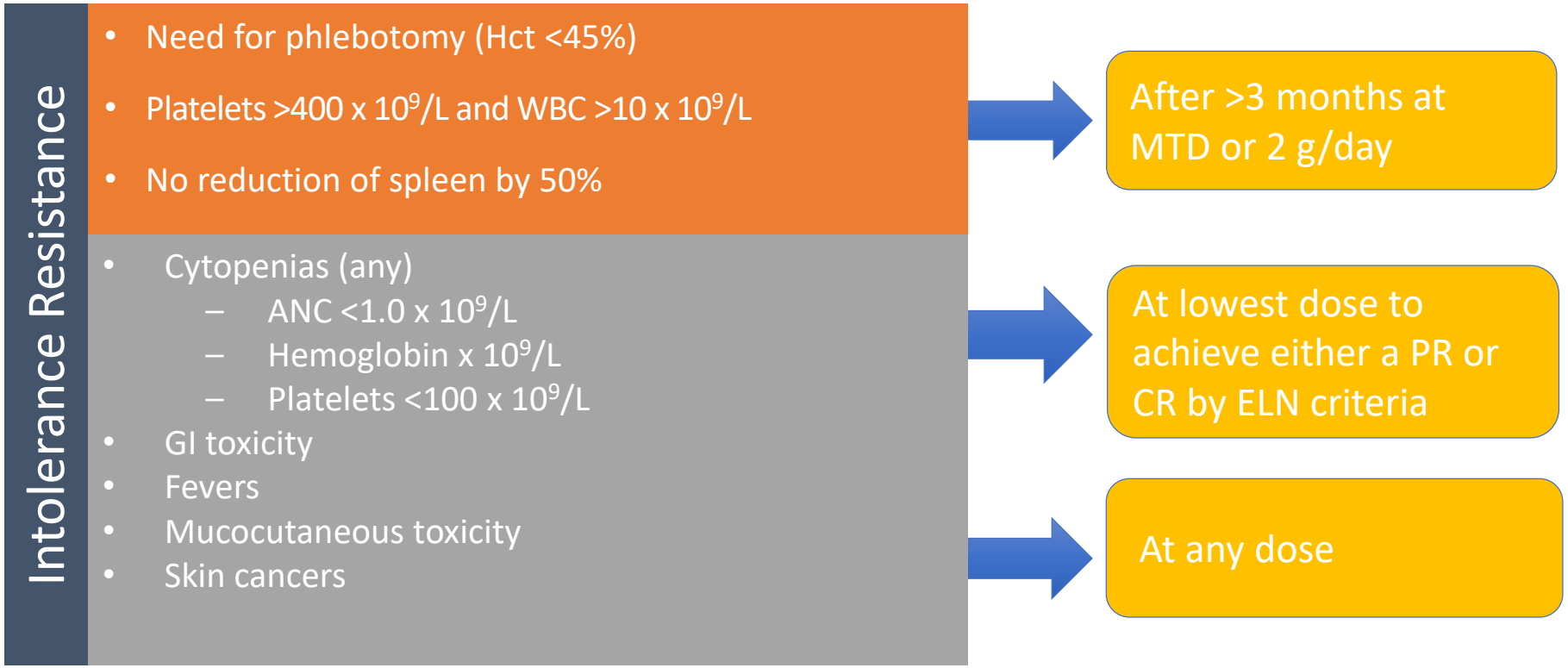
- Hydroxyurea is the recommended front-line therapy in PV (ESMO/ELN)
  - In high-risk pts, HU significantly reduces CV events (5.8 vs 3x100 p/y in PHL vs HU)

Results of HU in large retrospective cohorts:

- **Responses in 90% of patients (CR 24%, PR 66%)**
- **Discontinuation in 15.4% of patients**:
  - Need for phlebotomies (3.3%)
  - Uncontrolled myeloproliferation (1.6%)
  - Failure to reduce massive splenomegaly (0.8%)
  - Cytopenia at the lowest HU-dose to achieve response (1.7%)
  - Extra-haematological toxicity (9%)
- **Cytopenia affected survival, progression to MF, AML**
- **Splenomegaly affected MF**

Alvarez-Larrán et al, Blood 2012;119(6):1363-9.; Barosi G et al. Blood. 2009;113:4829-4833. Alvarez-Larran et al; Br J Haematol. 2016 Mar;172(5):786-93; Barbui et al, J Clin Oncol 2011;29:761. Vannucchi AM et al, Ann Oncol 2015;26 Suppl 5;85; Vannucchi AM, Haematologica. 2017 Jan;102(1):18-29.

ELN Consensus Criteria for Hydroxyurea Resistance and Intolerance in PV



Barosi G et al. *Br J Haematol*. 2010;148:961-963.

HU mucocutaneous toxicity in PV patients

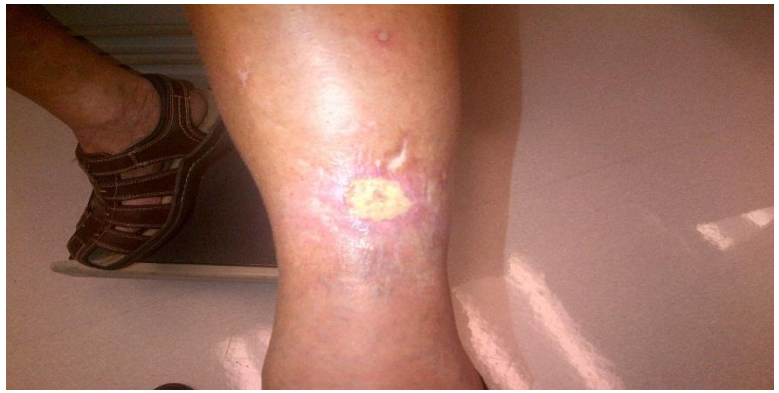
Cutaneous Adverse Events in 110 Patients

Category	At Baseline	During Follow-Up	
	No. of patients (%)	No. of patients (%)	Total No. of events
Actinic keratoses	13 (11.8)	32 (29)	103
Aphthous ulcers & mucositis	–	24 (21.8)	26
Alopecia	–	15 (13.6)	15
Hyperpigmentation of skin & nails	–	10 (9.1)	11
Squamous cell carcinoma*	3 (2.7)	8 (7.3)	15
Basal cell carcinoma*	8 (7.3)	9 (8.2)	9
Leg ulcers	4 (3.6)	7 (6.4)	8
Others	–	7 (6.4)	8

* 9 patients presented 11 NMSC; 2 patients presented simultaneously SCC and BCC.

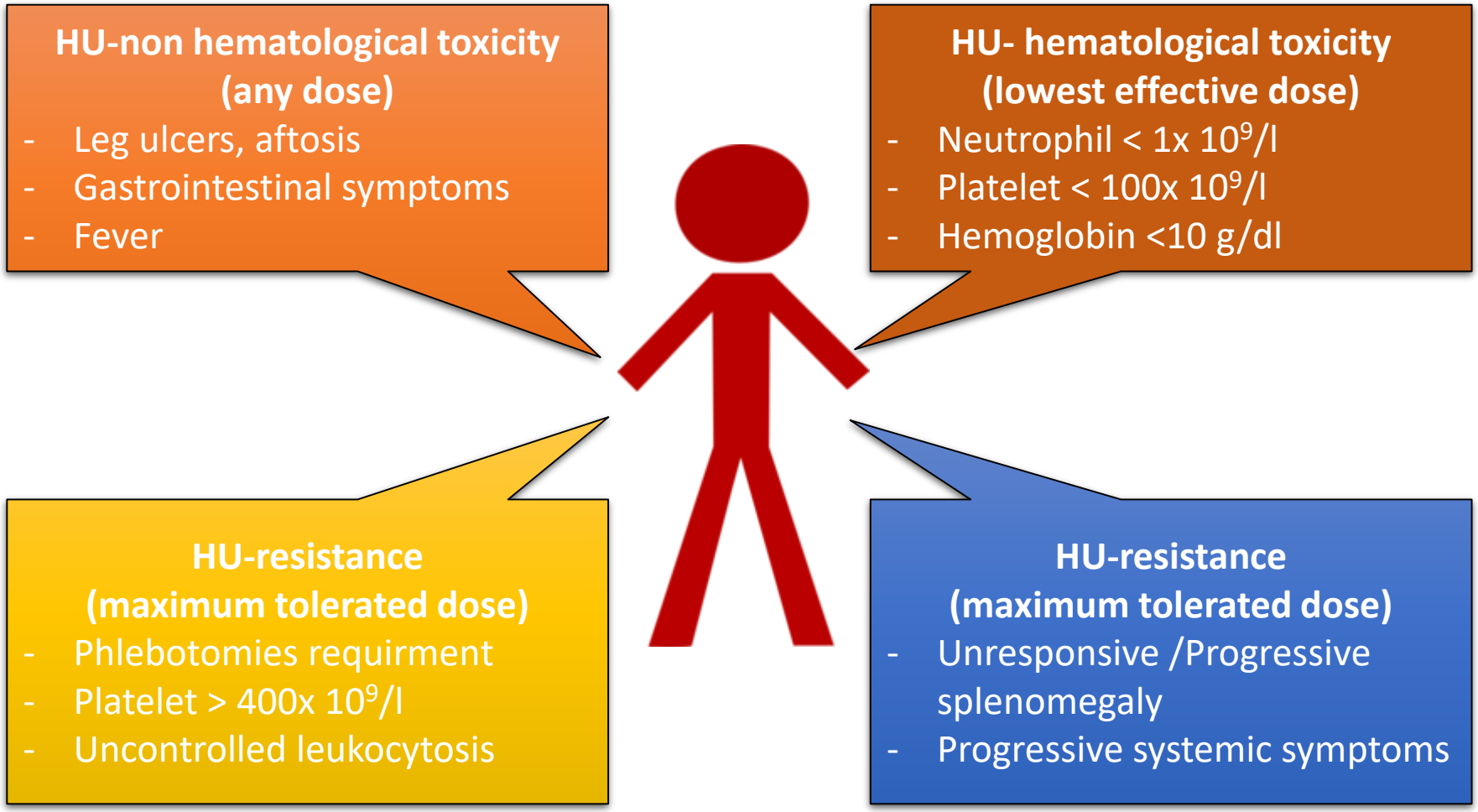
- **66/110 (60%) patients developed any cutaneous adverse event (CAE)**
- **14/66 (21%) patients with CAE developed serious CAE**

From Besses C, et al. In: Proceedings from the American Society of Hematology; December 9-12, 2017; Atlanta, GA [abstract 4208].



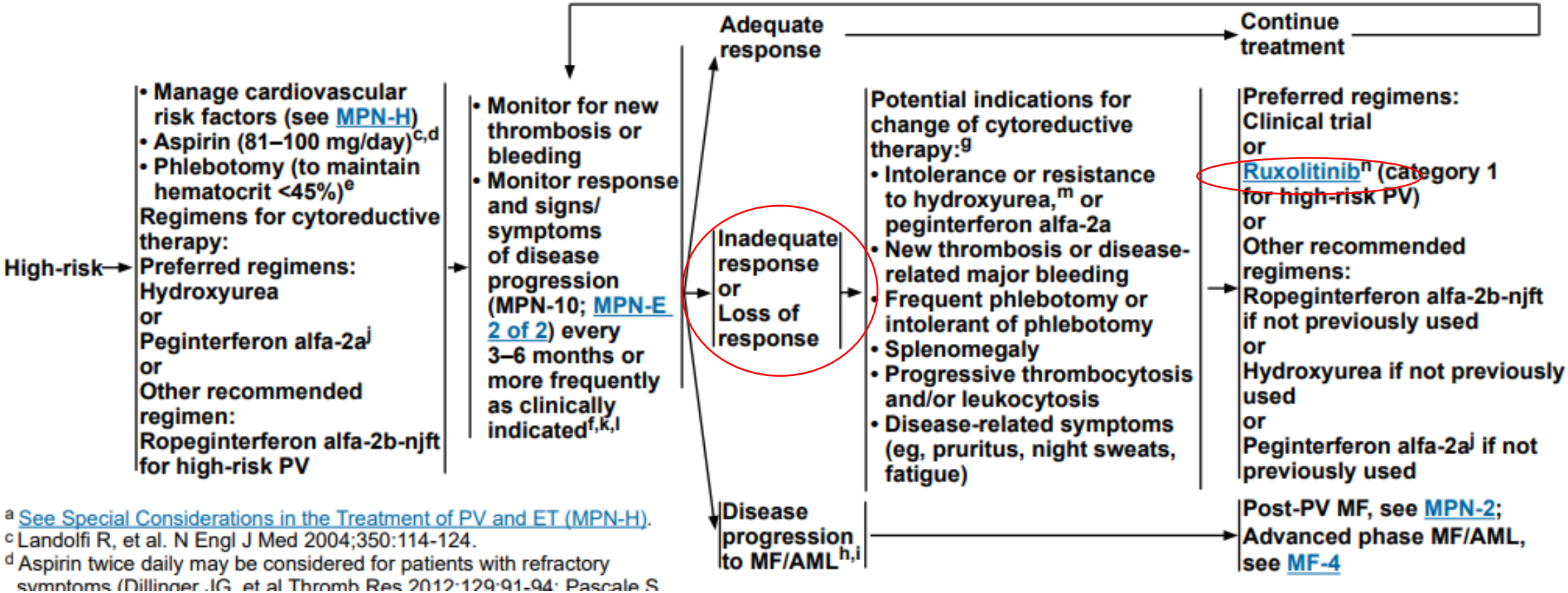
Inadequately controlled PV

when switching to a second-line therapy



Marchioli R, et al. N Engl J Med. 2013;368:22-33. Prchal JT, et al. Polycythemia vera. Williams Hematology. 8th edition. Najean Y, et al. Blood. 1997;90(9):3370-3377. Mesa RA. Blood. 2009;113:5697-5698. Alvarez-Larrán A, et al. Blood. 2012;119(6):1363-1369. Barosi G et al, Br j Hematol. 2010;148(6)961-63.

TREATMENT FOR HIGH-RISK POLYCYTHEMIA VERA[a]



[a] See Special Considerations in the Treatment of PV and ET (MPN-H).

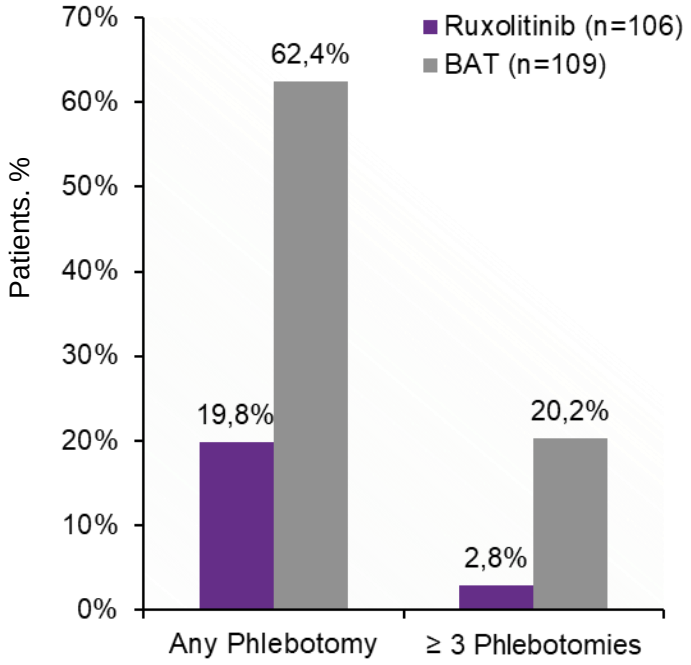
[c] Landolfi R, et al. N Engl J Med 2004;350:114-124.

[d] Aspirin twice daily may be considered for patients with refractory symptoms (Dillinger JG, et al Thromb Res 2012;129:91-94; Pascale S

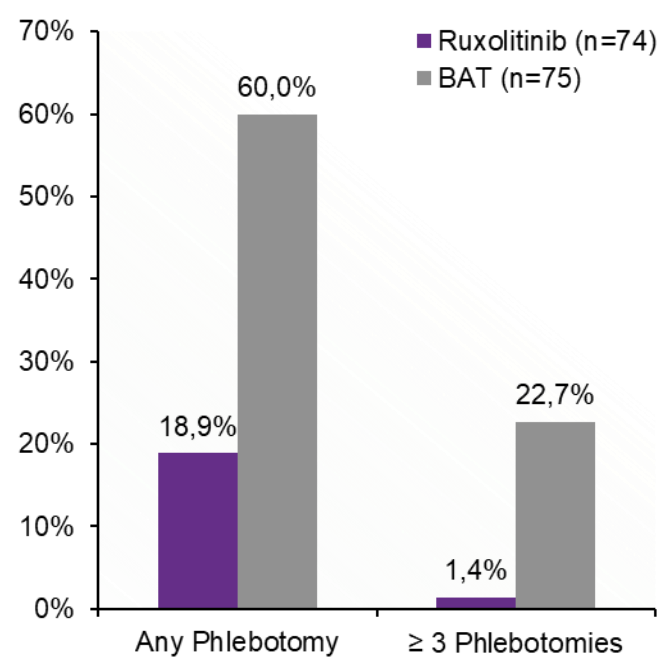
Rate of phlebotomy procedure

Ruxolitinib lowers the need for phlebotomy and ameliorates markers of iron deficiency

- **RESPONSE:** Up to Week 32[1]



- **RESPONSE 2:** Up to Week 28[2]

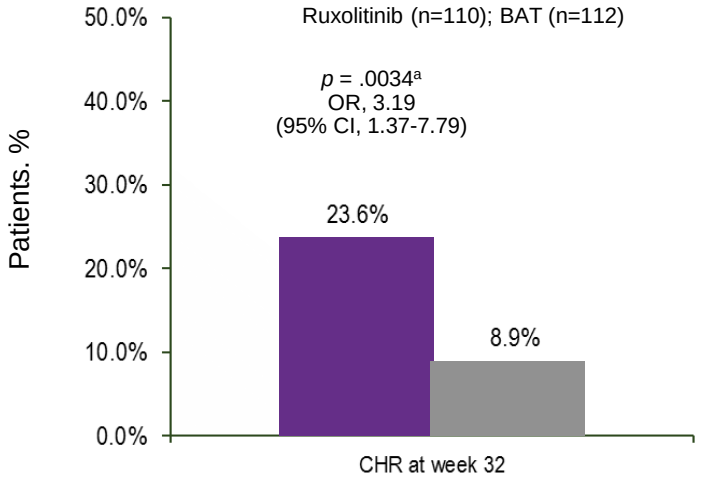


1. From Vannucchi AM, et al. *N Engl J Med*. 2015;372(5):426-435. Copyright © 2015 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.
2. Reprinted from Passamonti F, et al. *Lancet Oncol*. 2017;18(1):88-99 Copyright 2017, with permission from Elsevier.

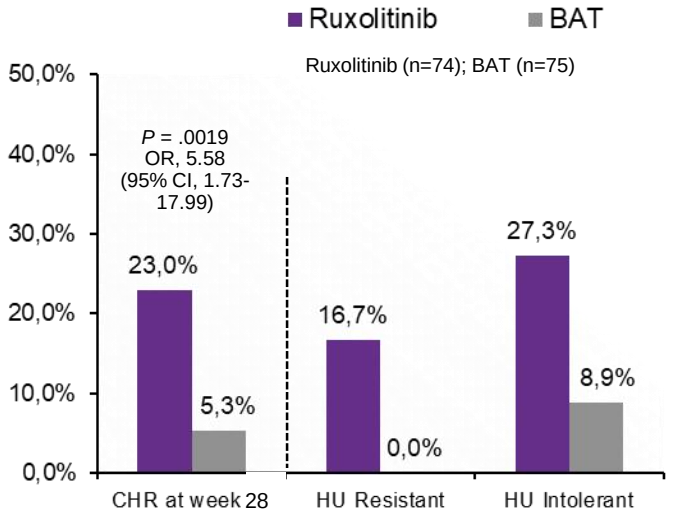
Secondary endpoint
Complete hematologic remission

- CHR is defined as HCT control, PLT count ≤ 400 x 10^9/L, and WBC count ≤ 10 x 10^9/L.

- **RESPONSE**[1] at Week 32
  - 88.5% of patients (23/26) who achieved CHR maintained it at week 48



- **RESPONSE 2**[2] at Week 28
  - Significantly more patients randomized to ruxolitinib achieved CHR compared with those randomized to BAT



CHR, complete hematological remission. [a] *p* value, odds ratio, and 95% CI were calculated using stratified exact Cochran-Mantel-Haenszel test; CHR is defined as Hct control, PLT count ≤ 400 × 10^9/l, and WBC count ≤ 10 × 10^9/l

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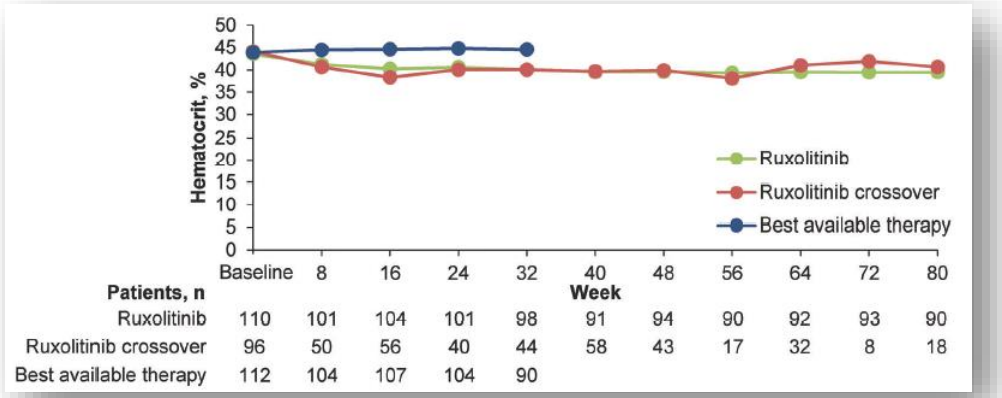
Ruxolitinib provide more consistent control of HCT to ≤ 45% than those who received BAT over time



The mean change from baseline in HCT ranged from:

- −3.12% to −4.36% in the RUX arm (from wk 12 to 80)
- +0.06% and +1.03% in the BAT arm (from wk 12 to 32).

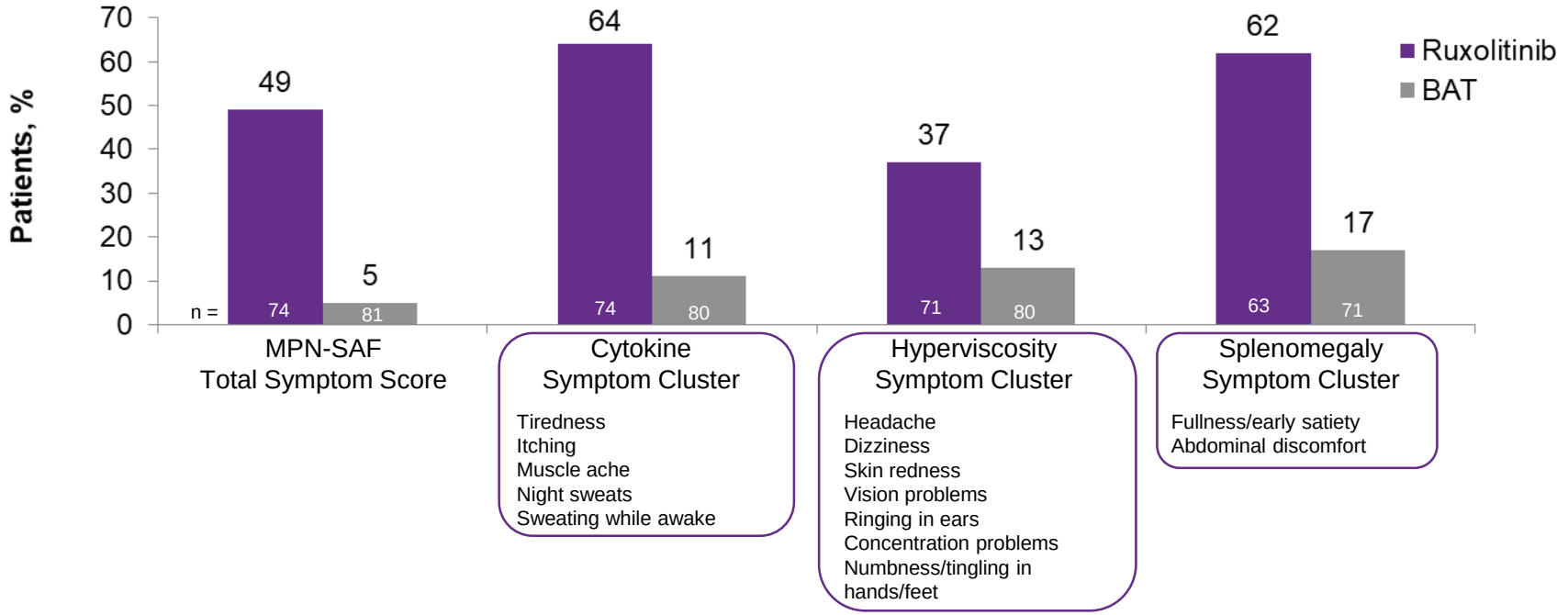
- **Patients in the BAT arm spent 12 times more time (in percentage of time) with an HCT > 45% than patients in the ruxolitinib arm** (median, 39.1% [quartile (Q) 1-Q3, 12.9%-65.9%] vs 3.0% [Q1-Q3, 0.0%-16.7%])

Griesshammer M Abstract EHA #P670 2015
Verstovsek et al. Haematologica 2016 Volume 101(7):821-829

Improvement in symptoms

RESPONSE at Week 32

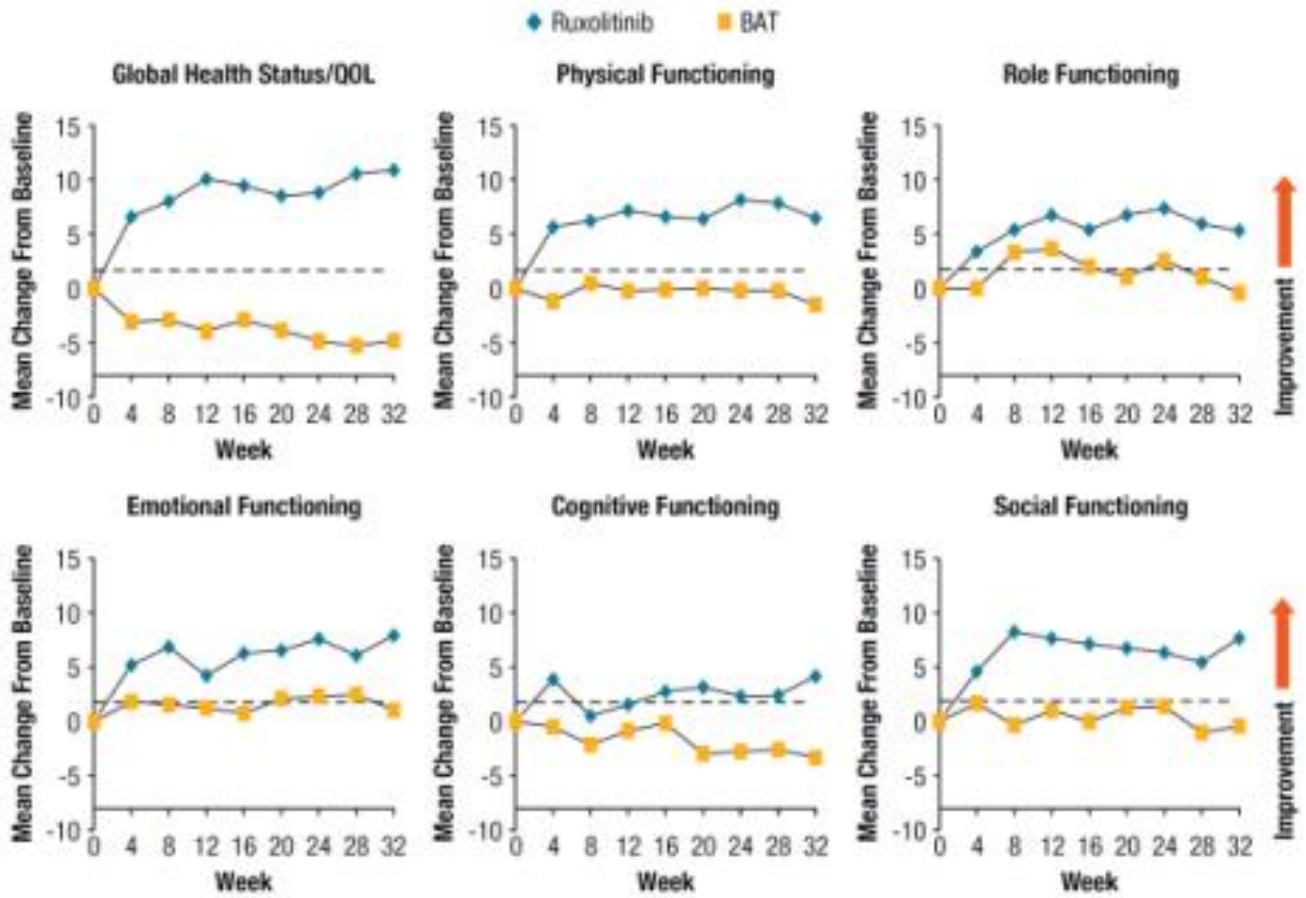
Percentage of Patients with a ≥ 50% Improvement in MPN-SAF Symptom Score at Week 32[a]



[a] In patients with scores at both baseline and week 32.
MPN-SAF, Myeloproliferative Neoplasm Symptom Assessment Form.

Ruxolitinib significantly improves patients Quality of Life

Mean change from baseline to Week 32 in EORTC QLQ-C30* HRQoL and functional domain scores (Response study)



Vannucchi AM, et al. NEJM, 2015; 372:426-35

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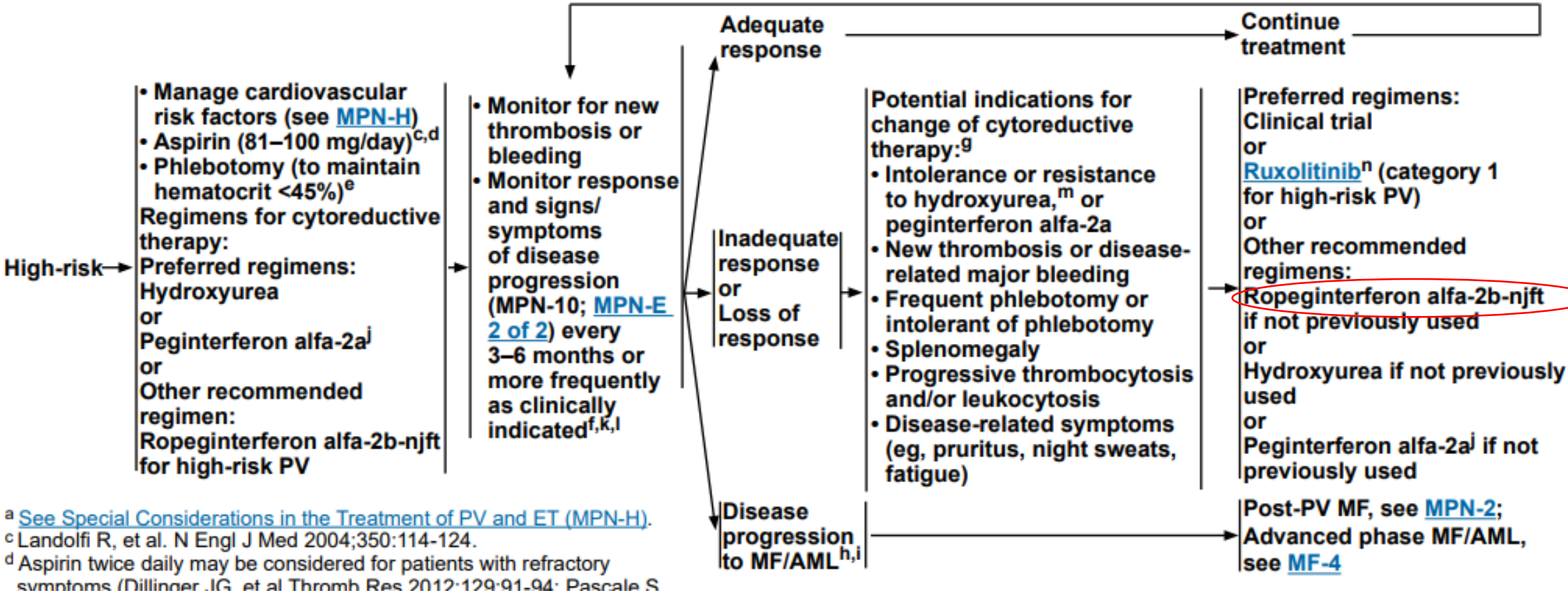
TREATMENT FOR HIGH-RISK POLYCYTHEMIA VERA[a]



[a] See Special Considerations in the Treatment of PV and ET (MPN-H).
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[d] Aspirin twice daily may be considered for patients with refractory symptoms (Dillinger JG, et al Thromb Res 2012;129:91-94; Pascale S

Take home messages

- La diagnosi precoce può ridurre il rischio trombotico
- La stratificazione del rischio trombotico è il driver dell'inizio del trattamento
- Controllo aggressivo dei fattore di rischio cardiovascolare e aspirina in tutti i pazienti
- Flebotomia per mantenere l'HCT <45%

- **Citoriduzione**
  - L'Idrossiurea è il gold standard come terapia di prima linea
  - Alcuni pazienti hanno una risposta inadeguata basata sulla resistenza o sull'intolleranza (10-20% dei pazienti)
    - La resistenza comprende un sottogruppo di pazienti con prognosi infausta
    - L'intolleranza è un'indicazione di cambiamento terapeutico e può avere un significato prognostico
  - L'interferfone può essere un opzione in particolare nei pazienti più giovani
  - Ruxolitinib è approvato per i pazienti con PV che hanno una risposta inadeguata o sono intolleranti all'idrossiurea ed è efficace nel raggiungere l'HCT, la splenomegalia e il controllo dei sintomi sistemici