



Strategie condivise
per la Mielofibrosi

23 giugno 2025 • Milano

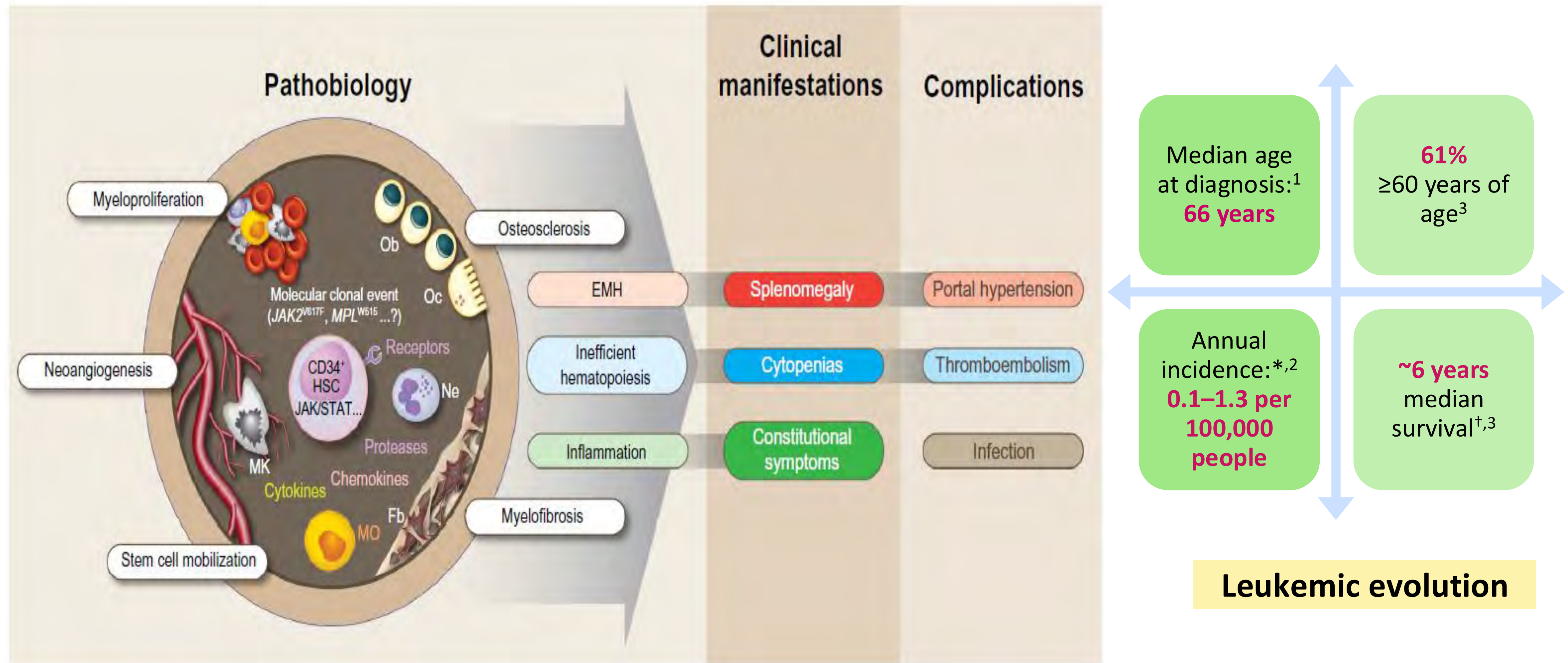
MIELOFIBROSI: DIAGNOSI E PROGNOSI ATTUALE CON FOCUS SUL PAZIENTE ANEMICO

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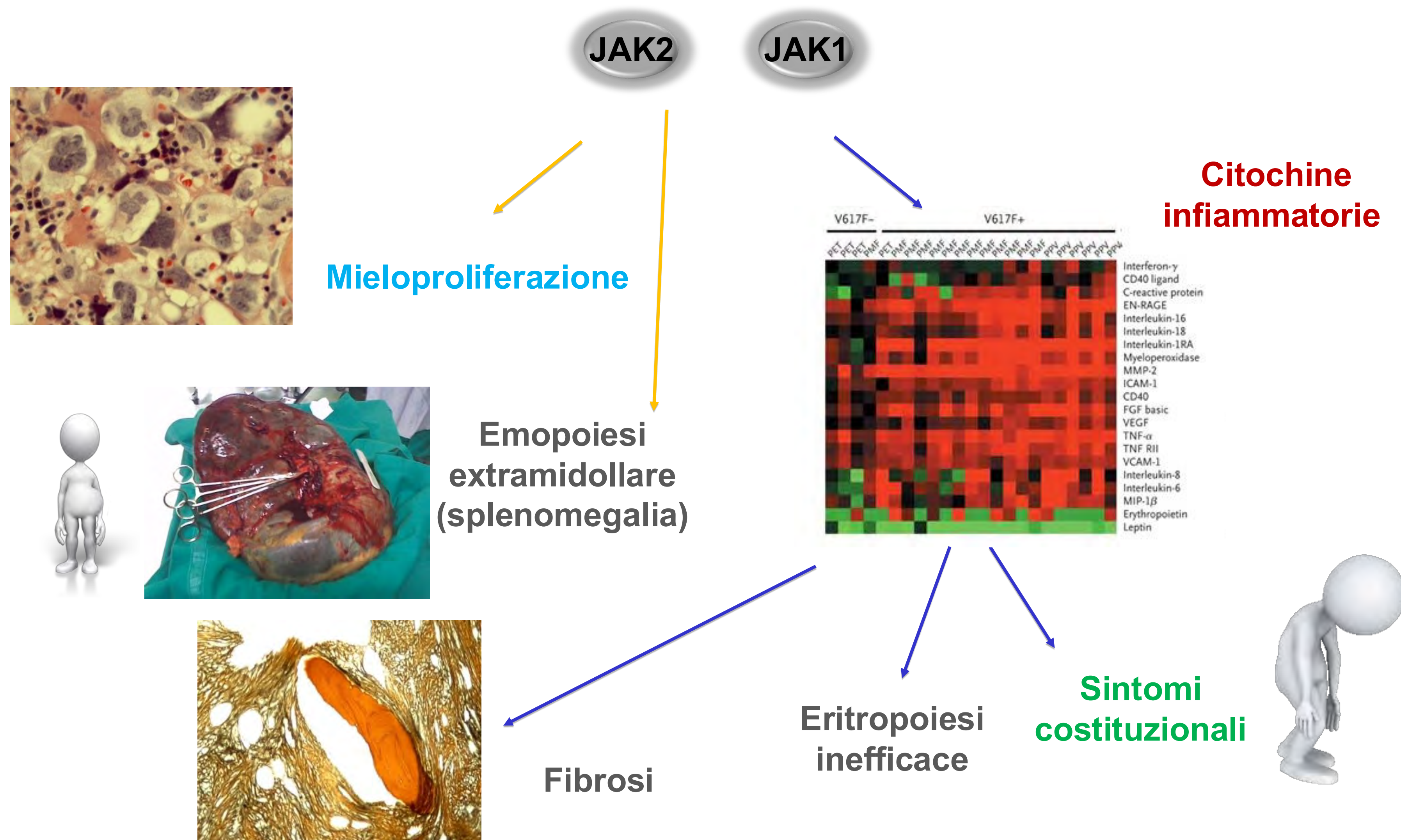
Myelofibrosis: epidemiology and clinical features



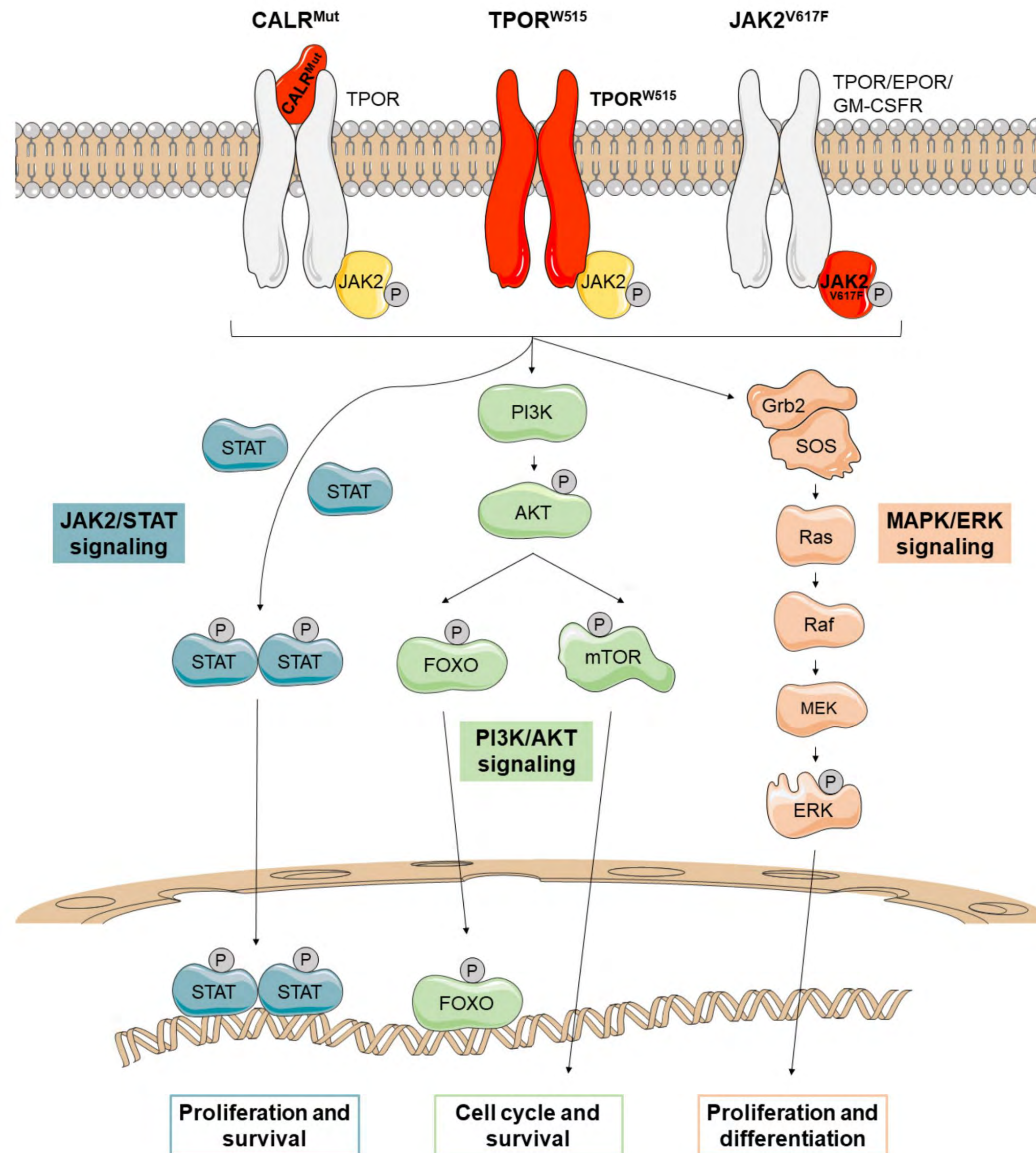
* Europe; † Survival varies depending on risk.⁶

1. Tefferi A, et al. *Mayo Clin Proc* 2012; 87:25–33; 2. Moulard O, et al. *Eur J Haematol* 2014; 92:289–297; 3. Tefferi A, et al. *Blood* 2014; 124:2507–2513; 4. Caocci G, et al. *Blood* 2019; 134(suppl 1):4186; 5. Harrison CN, et al. *Ann Hematol* 2017; 96:1653–1665; 6. Tefferi A. *Am J Hematol* 2016; 91:1262–1271.

La deregolazione del pathway JAK-STAT è responsabile delle manifestazioni della MF

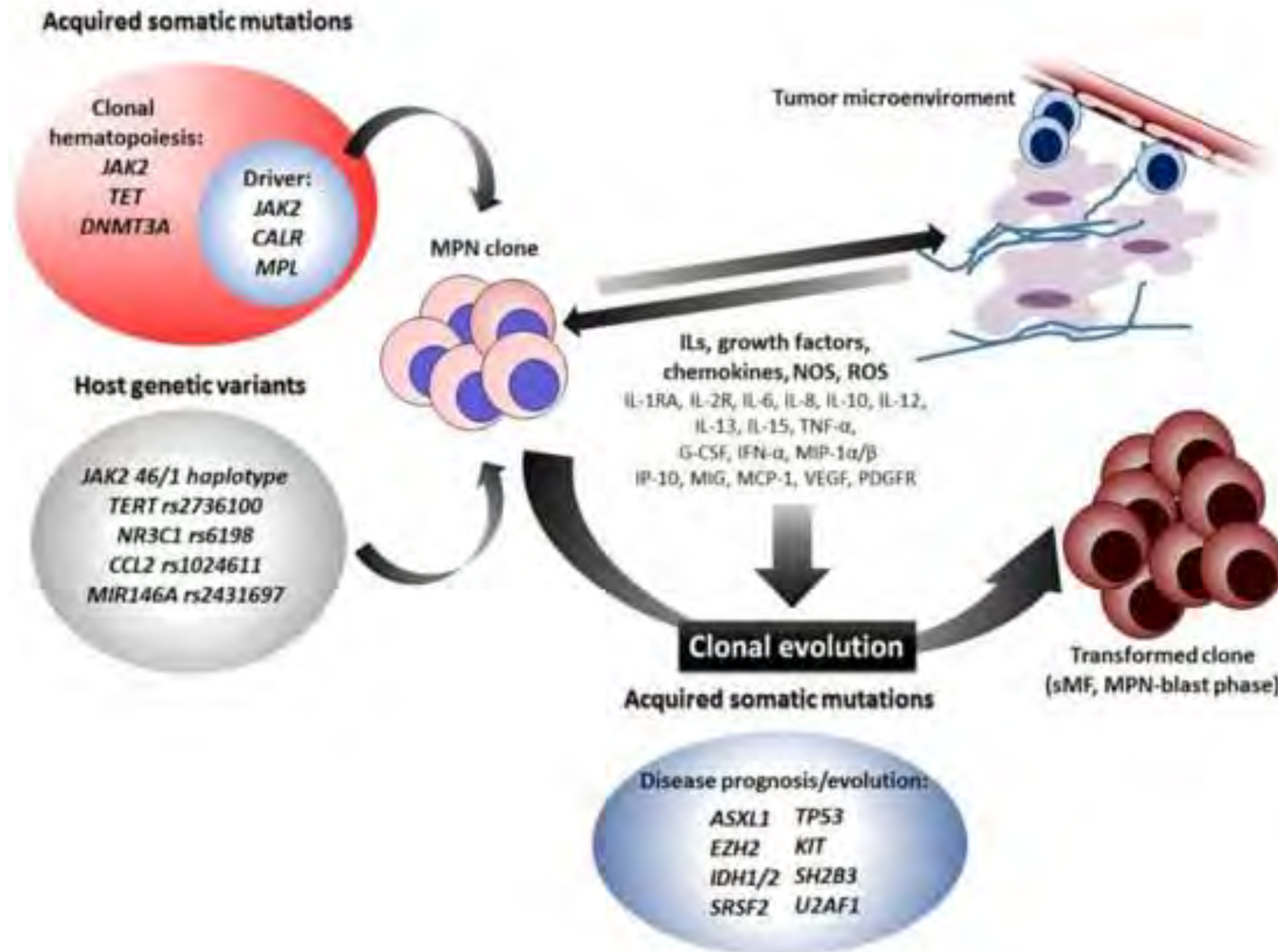


JAK2-related signaling pathways active in *Ph*-MPNs

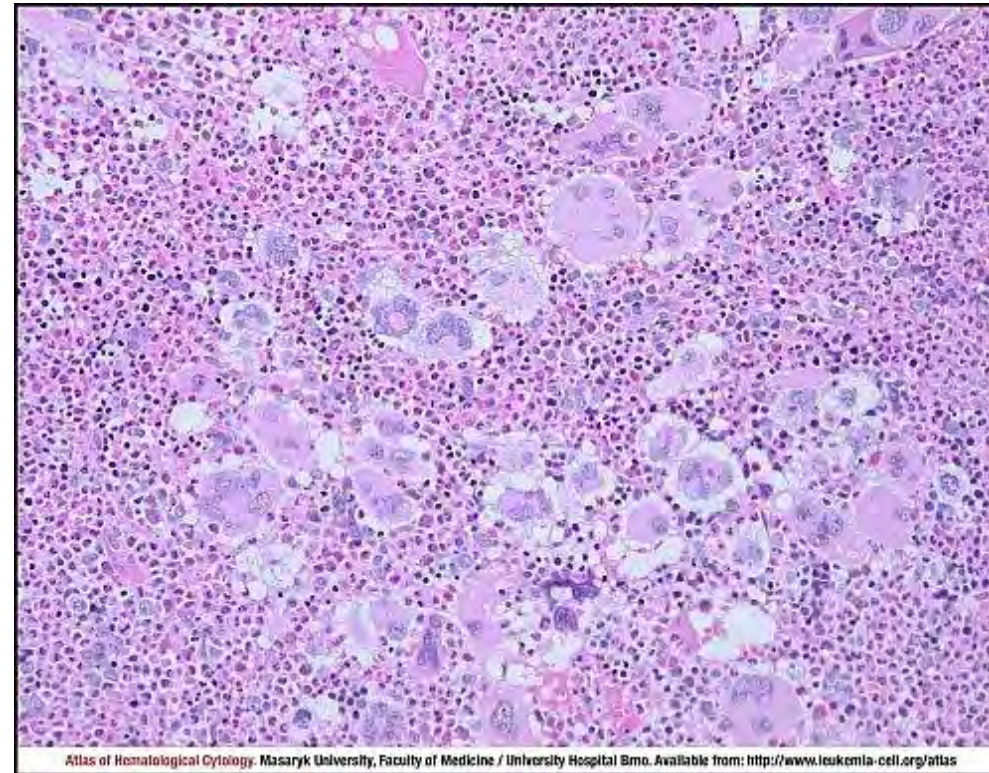


Mutations in *CALR*, *JAK2* (*JAK2*^{V617F}), and *MPL* (TPOR^{W515}) lead to the constitutive activation not only of JAK2/STAT, but also PI3K/AKT, and MAPK/ERK signaling that promotes the transport to the nucleus of several transcription factors such as STATs and FOXO. There, they regulate transcription of their target genes, causing increased proliferation and survival of mutant cells.

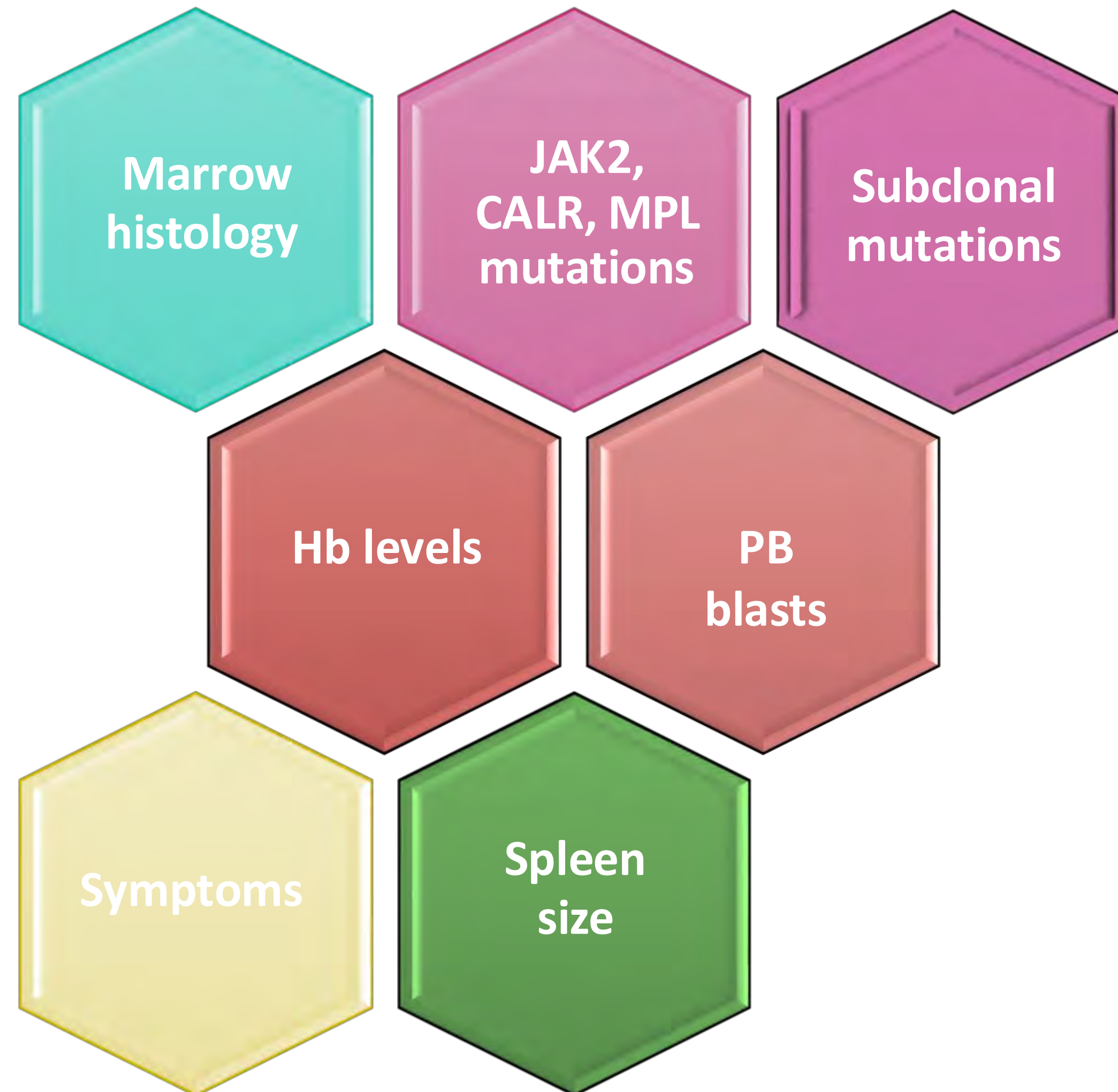
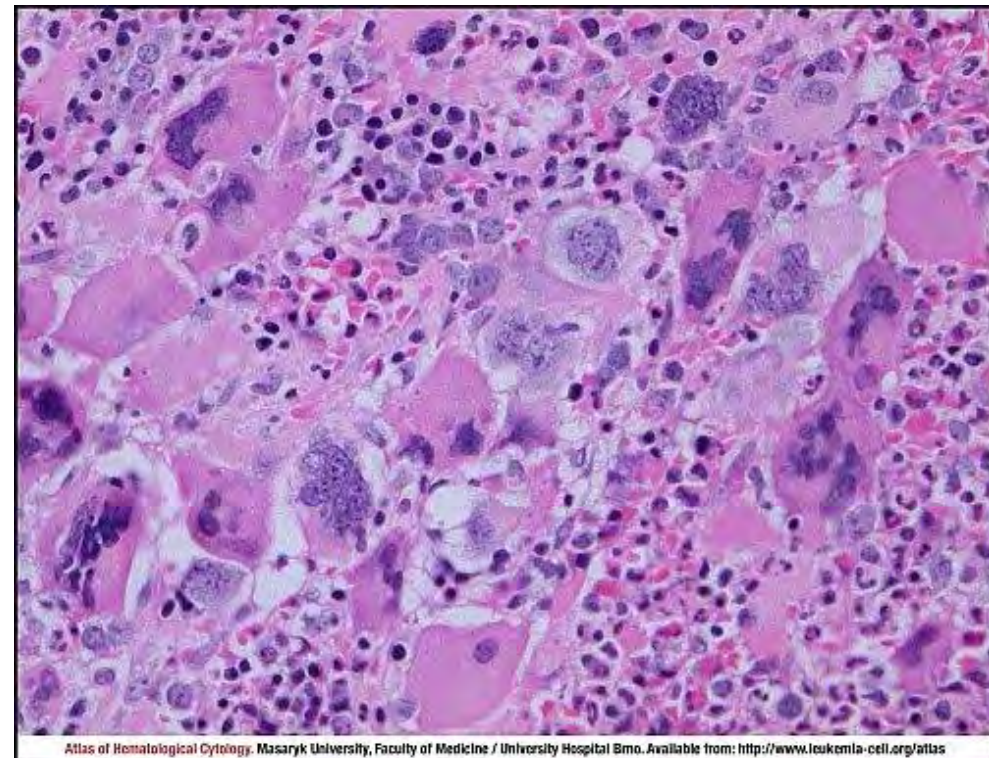
There is much more that JAK2 STAT in PMF pathogenesis ?



MF: Diagnostic Criteria



**Early & overt
MF PPV/PET-MF**



REVIEW ARTICLE **OPEN**

The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms

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Khoury JD, et al. *Leukemia* 2022; 36: 1703-1719

International Consensus Classification of Myeloid

The two classification are **not conflicting**

- In both classification diagnosis is still based on the **integration of clinical, molecular and morphological features**
- In both classification proposals **histopathology has a major role**

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Arber DA, et al. *Blood* 2022; 140: 1200-1228

Diagnosi PMF secondo ICC 2022

Primary myelofibrosis (Overtly fibrotic stage) (*Diagnosis requires meeting all 3 major criteria and one minor criterion*)

Major criteria:

1. Megakaryocyte proliferation and atypia,^a accompanied by $\geq$ grade 2 reticulin/collagen fibrosis^b
2. Presence of *JAK2*, *CALR* or *MPL* mutations, or presence of other clonal markers, or absence of evidence for reactive bone marrow fibrosis
3. Not meeting ICC criteria for other myeloid neoplasms

Minor criteria:

Anemia not otherwise explained
Leukocytosis $\geq 11 \times 10^9/L$
Palpable splenomegaly
Increased serum lactate dehydrogenase
A leukoerythroblastic blood smear

Primary myelofibrosis (Pre-fibrotic/early stage) (*Diagnosis requires meeting all 3 major criteria and one minor criterion*)

Major criteria:

1. Megakaryocyte proliferation and atypia,^a accompanied by $\leq$ grade 1 reticulin/collagen fibrosis, granulocyte proliferation/decreased erythropoiesis
2. Presence of *JAK2*, *CALR* or *MPL* mutations, or presence of other clonal markers, or absence of evidence for reactive bone marrow fibrosis
3. Not meeting ICC criteria for other myeloid neoplasms

Minor criteria:

Anemia not otherwise explained
Leukocytosis $\geq 11 \times 10^9/L$
Palpable splenomegaly
Increased serum lactate dehydrogenase

^bDiffuse often coarse fiber network with or without evidence of collagenization (trichrome stain).

^aAberrant nuclear/cytoplasmic ratio; hyperchromatic and irregularly folded nuclei; dense megakaryocyte clustering; these changes are often accompanied by increased cellularity, granulocytic proliferation and decreased erythropoiesis.

Diagnosi prePMF e overt PMF:
-Tutti e tre i criteri maggiori
- Almeno un criterio minore

Khoury JD, et al. Leukemia 2022; 36: 1703-1719
Arber DA, et al. Blood 2022; 140: 1200-1228

PMF pre fibrotica: criteri per la diagnosi

	Pre-PMF
Major criteria	Bone marrow biopsy showing megakaryocytic proliferation and atypia, bone marrow fibrosis grade <2, increased age-adjusted BM cellularity, granulocytic proliferation, and (often) decreased erythropoiesis JAK2, CALR, or MPL mutation⁽¹⁾ or presence of another clonal marker ⁽²⁾ or absence of reactive bone marrow reticulin fibrosis⁽³⁾ Diagnostic criteria for BCR::ABL1 positive chronic myeloid leukemia, polycythemia vera, essential thrombocythemia, myelodysplastic syndromes, or other myeloid neoplasms are not met
Minor criteria	Anemia not attributed to a comorbid condition Leukocytosis $\geq 11 \times 10^9/L$ Palpable splenomegaly Lactate dehydrogenase level above the reference range

- The diagnosis of pre-PMF requires all 3 major criteria and at least 1 minor criterion confirmed in 2 consecutive determinations

(1) It is recommended to use highly sensitive assays for JAK2 V617F (sensitivity level <1%) and CALR and MPL (sensitivity level 1–3%) — in negative cases, consider searching for non-canonical JAK2 and MPL mutations

(2) Assessed by cytogenetics or sensitive NGS techniques; detection of mutations associated with myeloid neoplasms (e.g., ASXL1, EZH2, IDH1, IDH2, SF3B1, SRSF2, and TET2 mutations) supports the clonal nature of the disease

(3) Minimal reticulin fibrosis (grade 1) secondary to infection, autoimmune disorder or other chronic inflammatory conditions, hairy cell leukemia or another lymphoid neoplasm, metastatic malignancy, or toxic (chronic) myelopathies

Khoury JD, et al. *Leukemia* 2022; 36:1703-1719

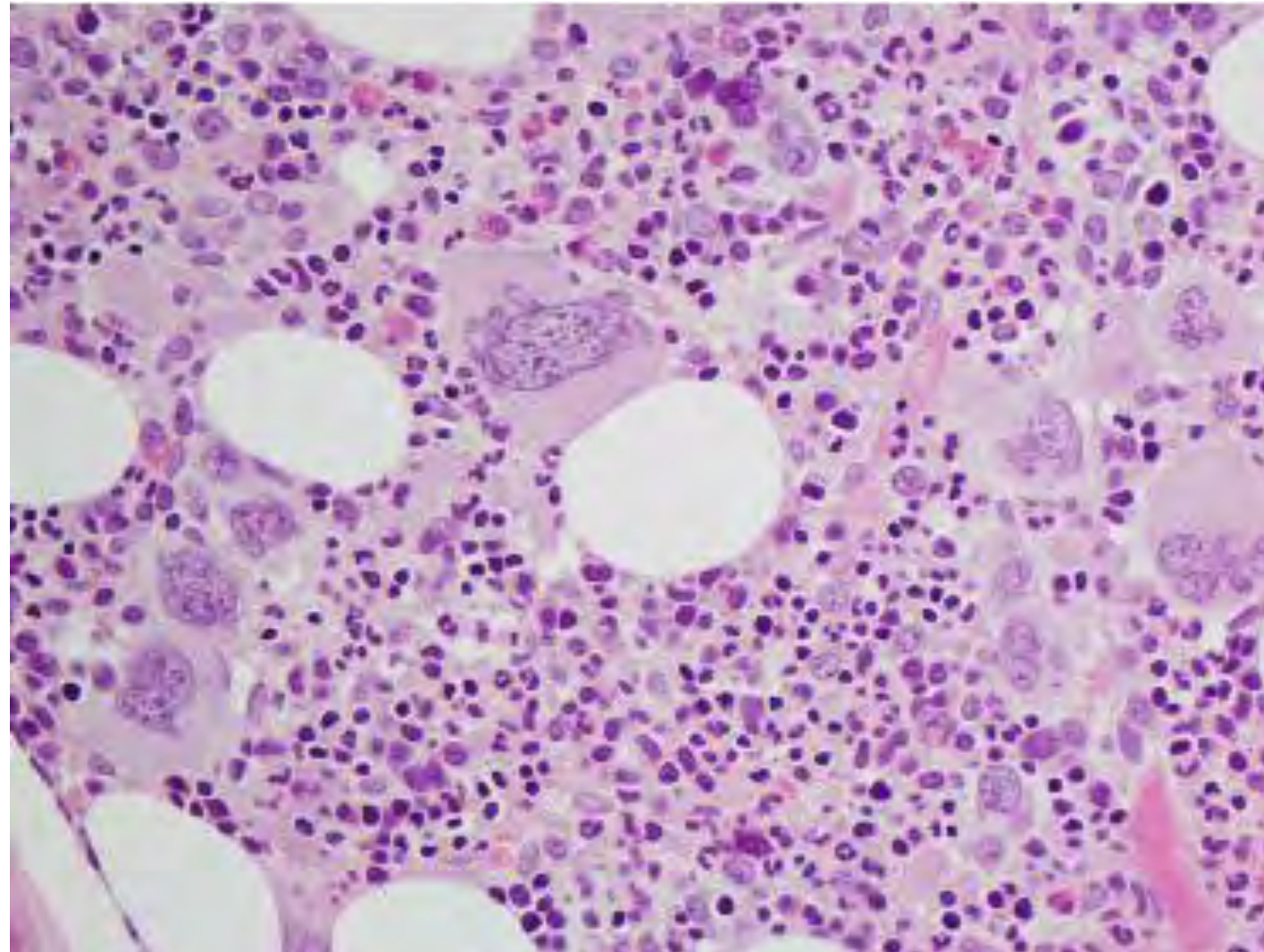
Arber DA, et al. *Blood* 2022; 140: 1200-1228

Thiele J, et al. *Am J Hematol* 2023; 98:166-179

Gianelli U, et al. *Virchows Arch* 2023; 482:53-68

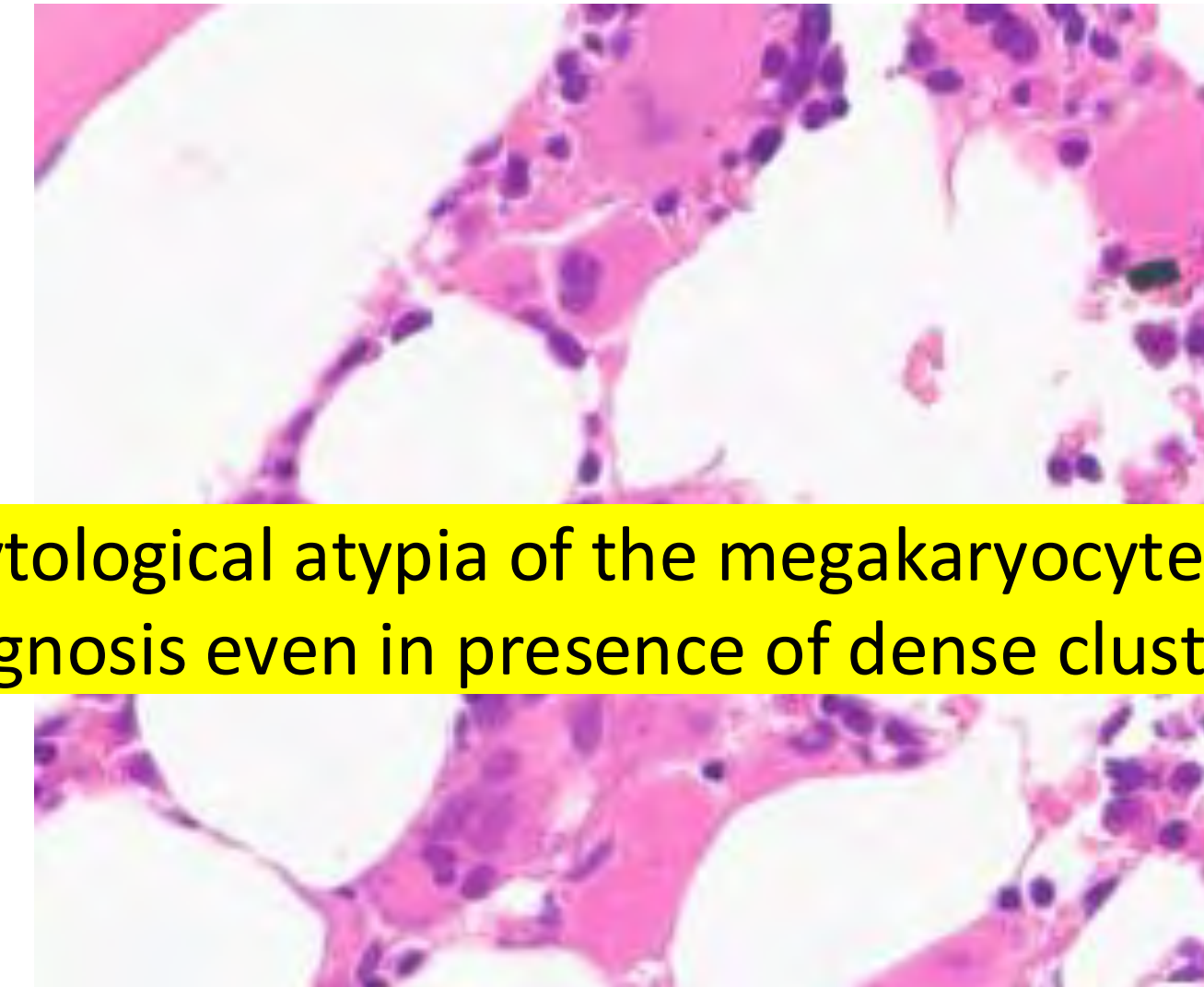
Pre-MF e diagnosi differenziale ET: ruolo anatomopatologo fondamentale

PRE-MF



- **Cellularity:** increased
- **Erythropoiesis:** normal or decreased
- **Granulopoiesis:** increased (left shifting)
- **M/E:** increased
- **Megakaryocytes:** increased, **dense clusters (often), atypia** (increased N/C, abnormal pattern of chromatin clumping – bulbous or hyperchromatic nuclei)
- **Reticulin fibers:** MF-0 or MF-1

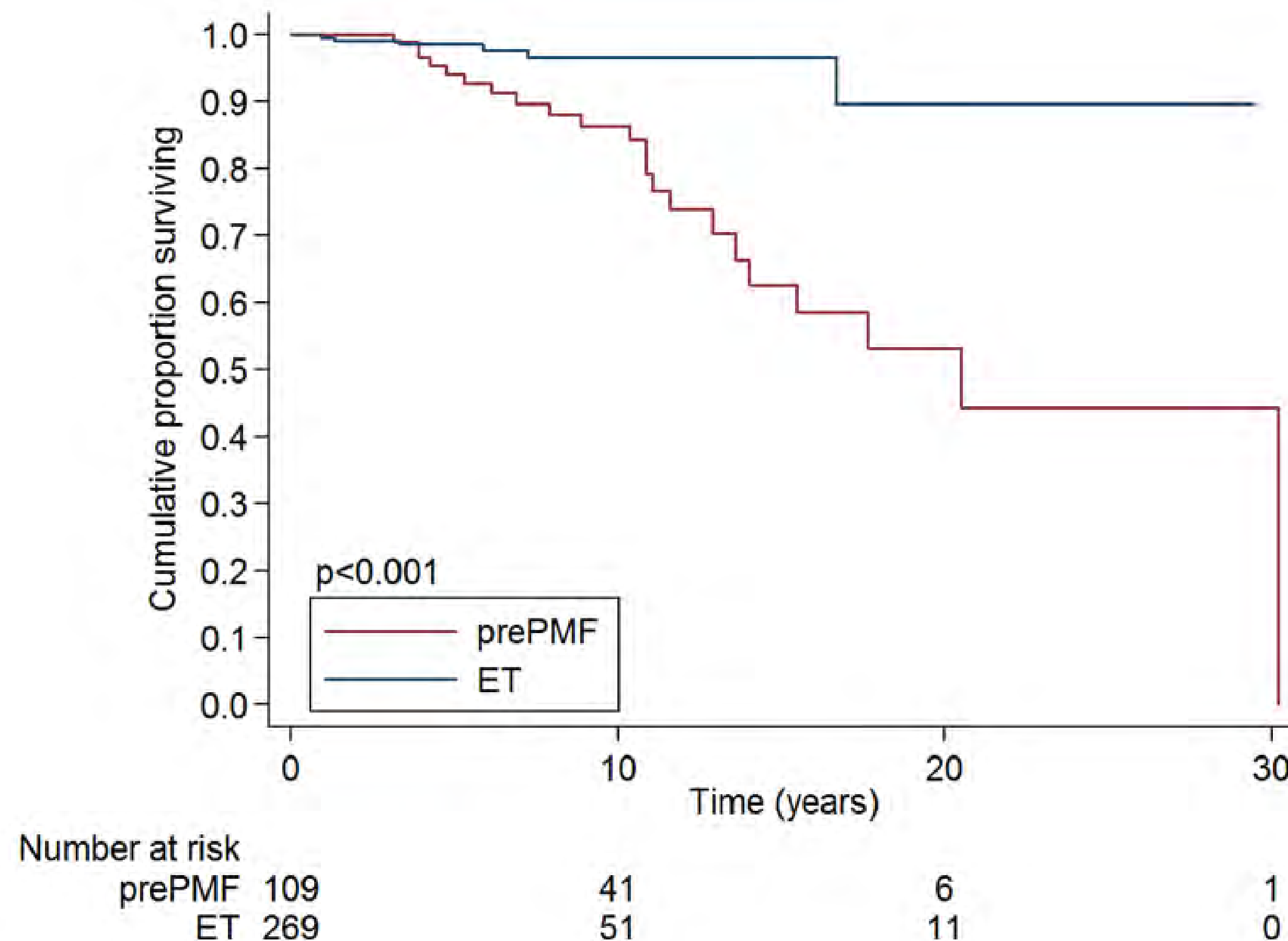
ET



Absence of cytological atypia of the megakaryocytes support ET diagnosis even in presence of dense cluster

- **Cellularity:** normal or slightly increased
- **Erythropoiesis:** normal
- **Granulopoiesis:** normal
- **M/E:** 3/1
- **Megakaryocytes:** increased, loose clusters, large to giant, **infrequently dense**, with mature cytoplasm and heperlobulated nuclei
- **Reticulin fibers:** MF-0, rarely MF-1

OS diversa in ET vs PMF

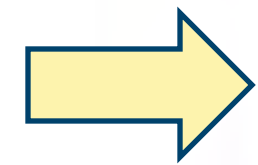


10 y OS:

- pre-MF:86.4%
- ET: 96.6%

ET has a lower risk for major hemorrhagic events, a significantly lower risk of myelofibrotic progression ranging between 0.8% to 4.5 % at 10 years, as well as a very low risk of transformation to BP with a reported 10-year cumulative incidence between 0.7% and 1.9%

PMF pre fibrotica: criteri per la diagnosi



	Pre-PMF
Major criteria	Bone marrow biopsy showing megakaryocytic proliferation and atypia, bone marrow fibrosis grade <2, increased age-adjusted BM cellularity, granulocytic proliferation, and (often) decreased erythropoiesis
	JAK2, CALR, or MPL mutation ⁽¹⁾ or presence of another clonal marker ⁽²⁾ or absence of reactive bone marrow reticulin fibrosis ⁽³⁾
	Diagnostic criteria for BCR::ABL1 positive chronic myeloid leukemia, polycythemia vera, essential thrombocythemia, myelodysplastic syndromes, or other myeloid neoplasms are not met
Minor criteria	Anemia not attributed to a comorbid condition
	Leukocytosis $\geq 11 \times 10^9/L$
	Palpable splenomegaly
	Lactate dehydrogenase level above the reference range

- The diagnosis of pre-PMF requires all 3 major criteria and at least 1 minor criterion confirmed in 2 consecutive determinations

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Khoury JD, et al. *Leukemia* 2022; 36:1703-1719

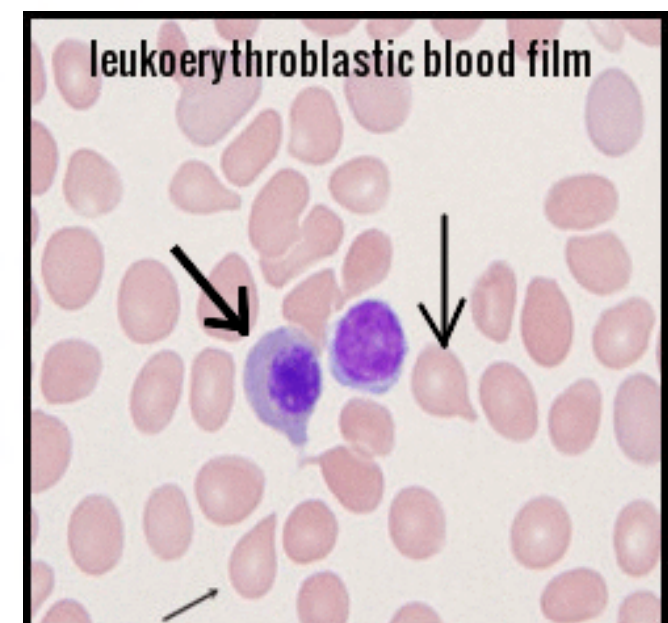
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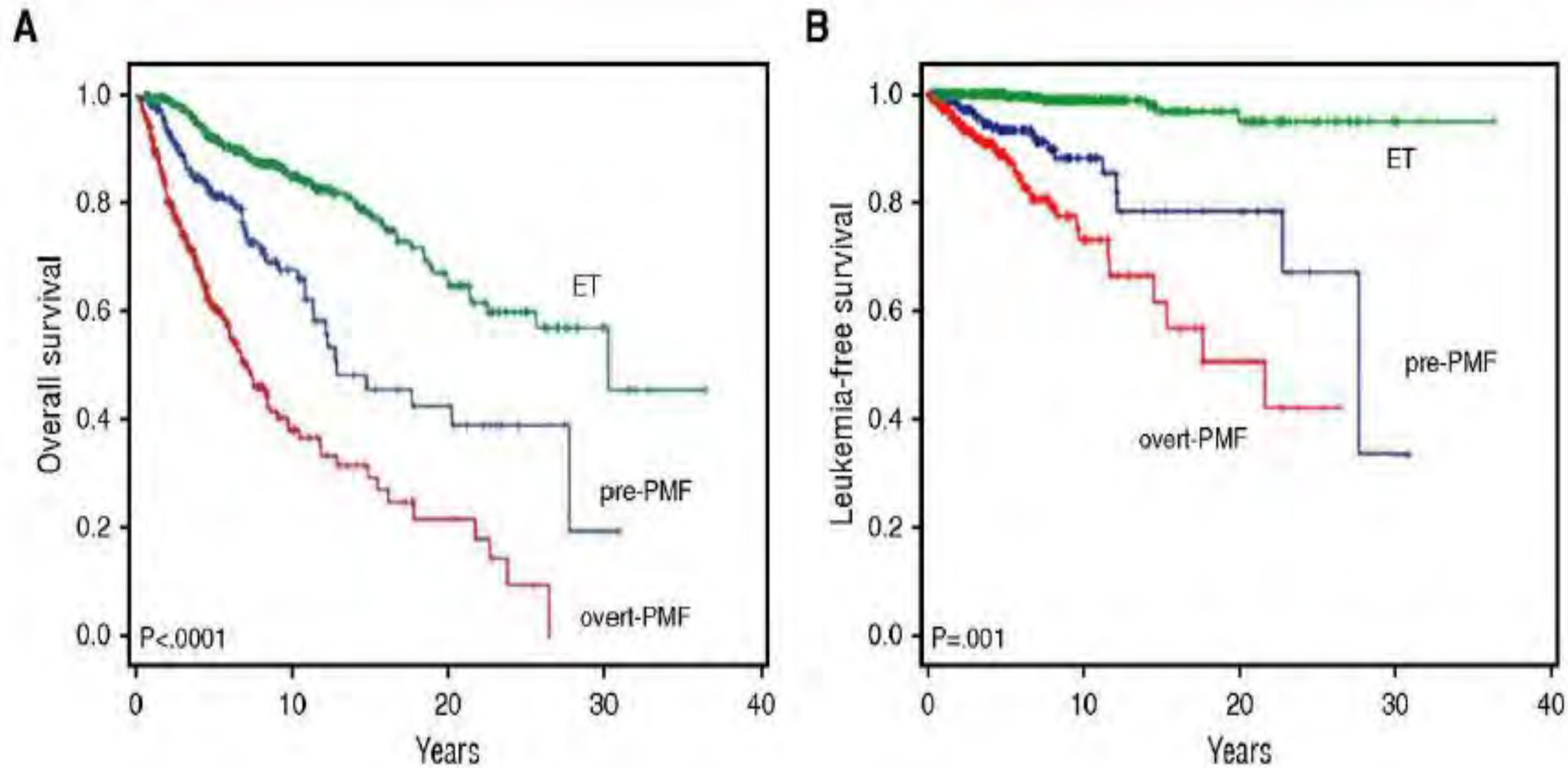
PMF overt: criteri per la diagnosi

Overt-PMF	
Major criteria	Bone marrow biopsy showing megakaryocytic proliferation and atypia, accompanied by reticulin and/or collagen fibrosis grades 2 or 3
	JAK2, CALR, or MPL mutation or presence of another clonal marker or absence of reactive bone marrow reticulin fibrosis
	Diagnostic criteria for BCR::ABL1 positive chronic myeloid leukemia, polycythemia vera, essential thrombocythemia, myelodysplastic syndromes, or other myeloid neoplasms are not met
Minor criteria	Anemia not attributed to a comorbid condition
	Leukocytosis $\geq 11 \times 10^9/L$
	Palpable splenomegaly
	Lactate dehydrogenase level above the reference range
	Leukoerythroblastosis

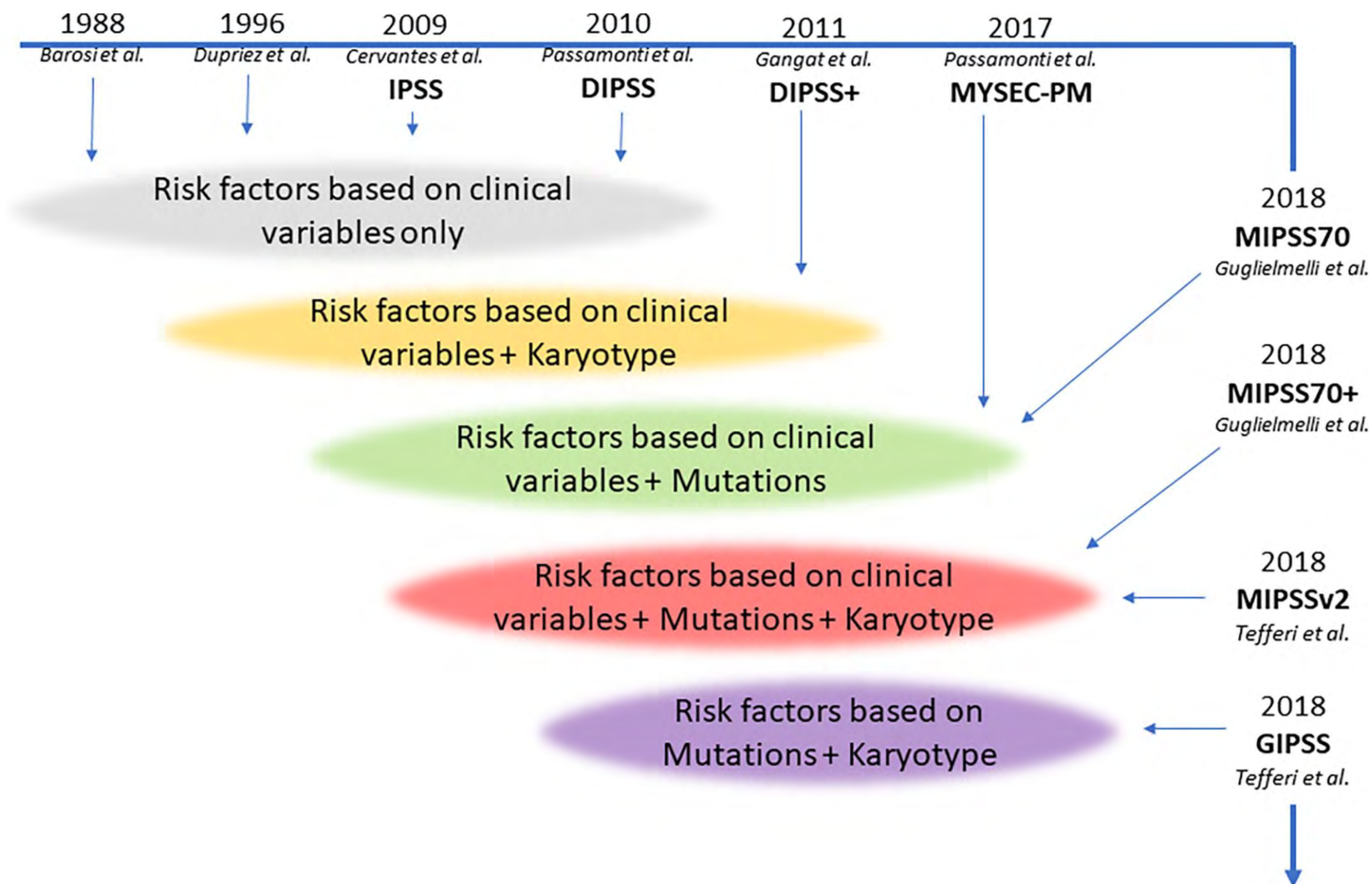


- The diagnosis of pre-PMF requires all 3 major criteria and at least 1 minor criterion confirmed in 2 consecutive determinations
 - It is recommended to use highly sensitive assays for JAK2 V617F (sensitivity level <1%) and CALR and MPL (sensitivity level 1–3%) — in negative cases, consider searching for non-canonical JAK2 and MPL mutations
 - Assessed by cytogenetics or sensitive NGS techniques; detection of mutations associated with myeloid neoplasms (e.g., ASXL1, EZH2, IDH1, IDH2, SF3B1, SRSF2, and TET2 mutations) supports the clonal nature of the disease
 - Minimal reticulin fibrosis (grade 1) secondary to infection, autoimmune disorder or other chronic inflammatory conditions, hairy cell leukemia or another lymphoid neoplasm, metastatic malignancy, or toxic (chronic) myelopathies

Prognostic Impact of Prefibrotic versus Overt PMF Diagnosis



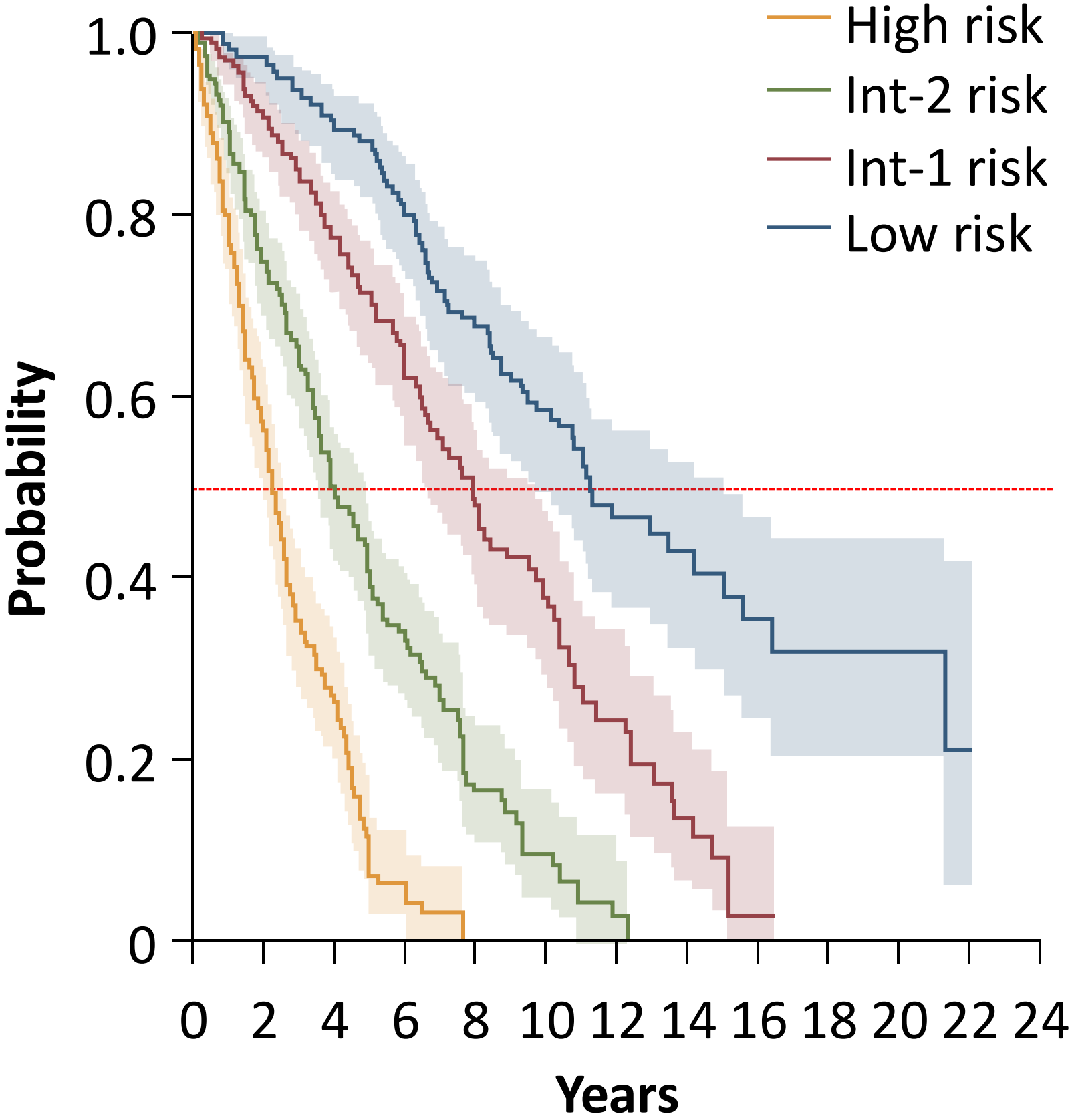
Classificazione ed evoluzione dei modelli prognostici in MF



Modelli prognostici classici in MF

Variable	IPSS ¹	DIPSS ²	DIPSS-plus ³
Age >65 years	✓	✓	✓
Constitutional symptoms	✓	✓	✓
Hemoglobin <10 g/dL	✓	✓	✓
Leukocyte count >25×10 ⁹ /L	✓	✓	✓
Circulating blasts ≥1%	✓	✓	✓
Platelet count <100×10 ⁹ /L			✓
RBC transfusion need			✓
Unfavorable karyotype +8,-7/7q-, i(17q), inv(3), -5/5q-, 12p-, 11q23 rearr.			✓
Scoring system	1 point each	1 point each but Hb=2	1 point each
Risk categories			
Low risk	0	0	0
Intermediate-1 risk	1	1–2	1
Intermediate-2 risk	2	3–4	2–3
High risk	≥3	5–6	4–6

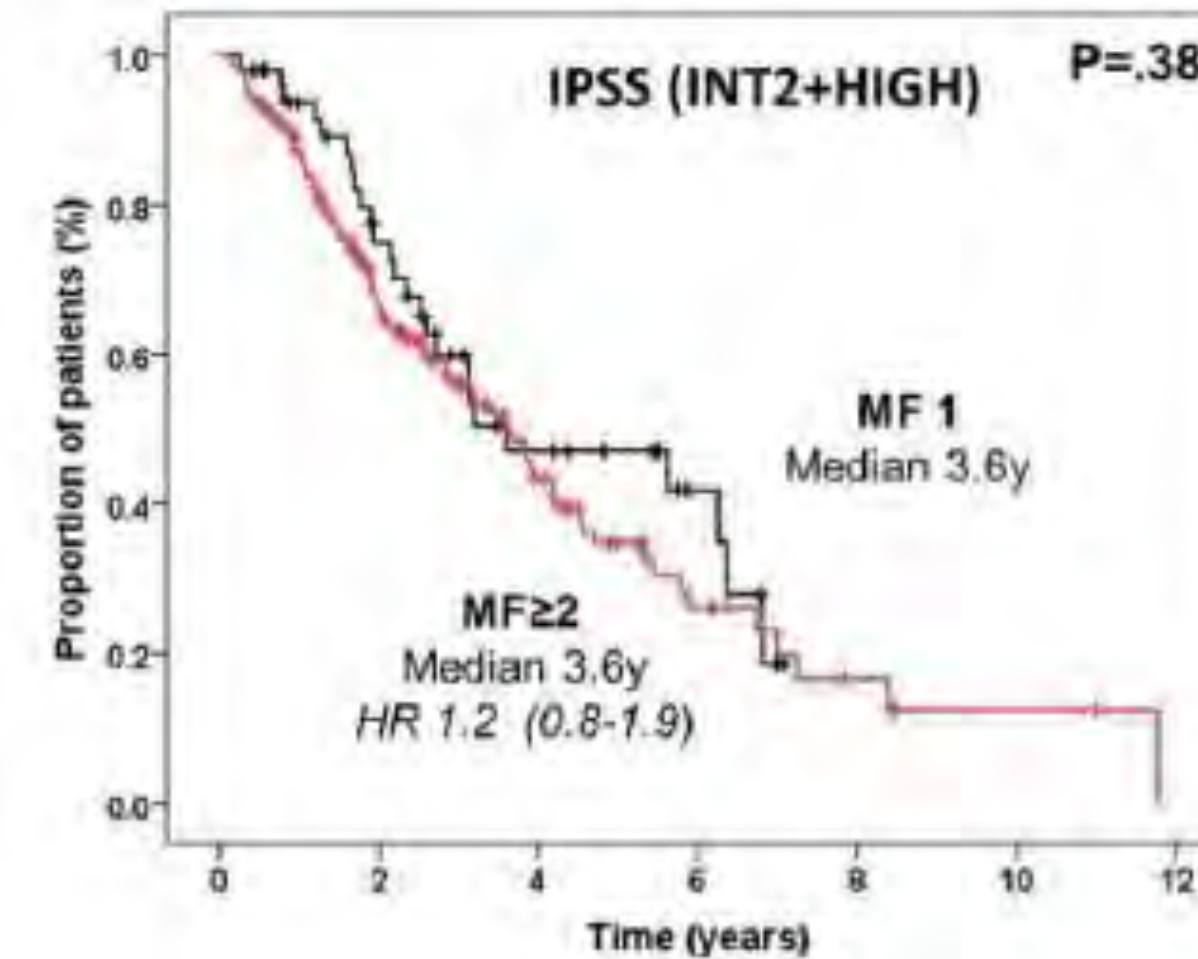
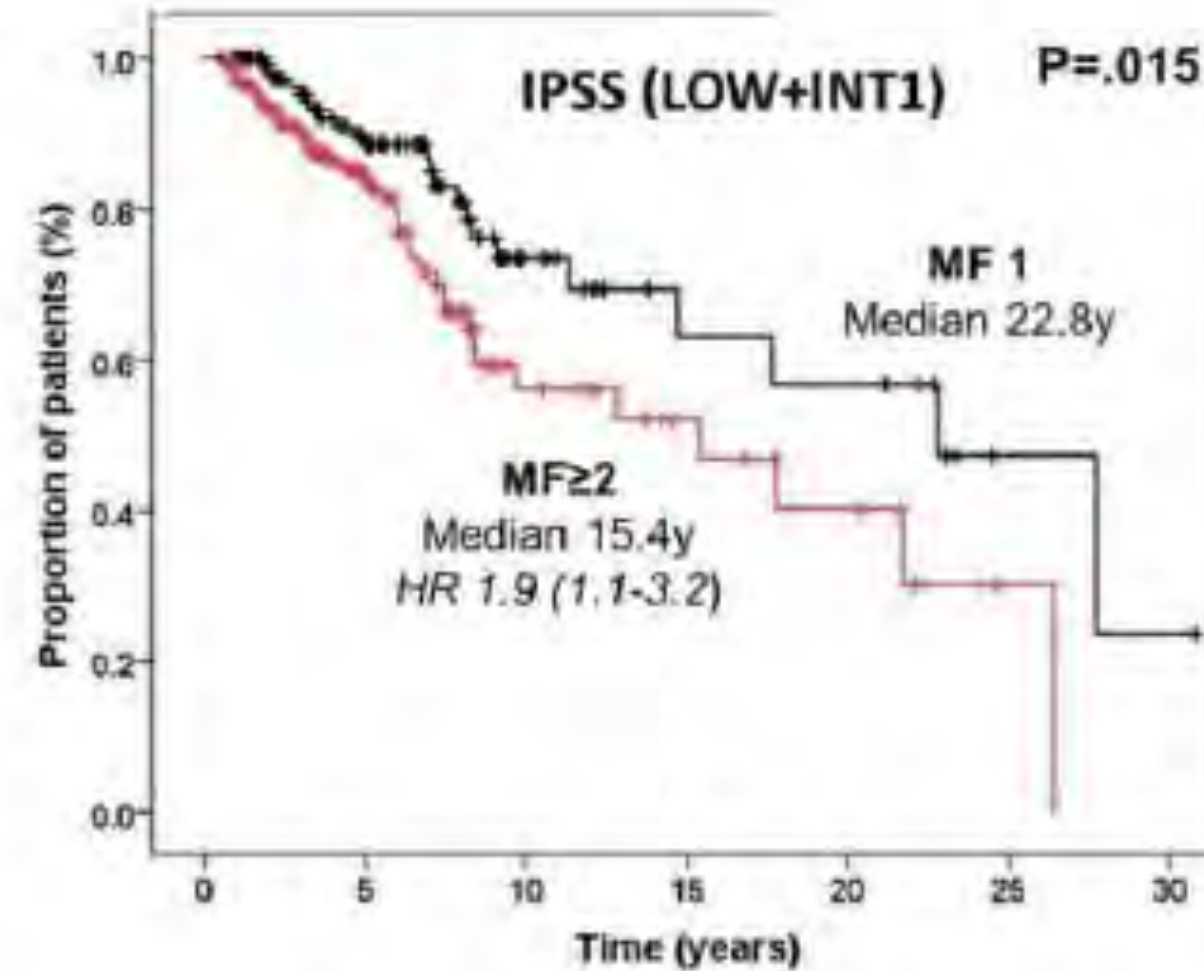
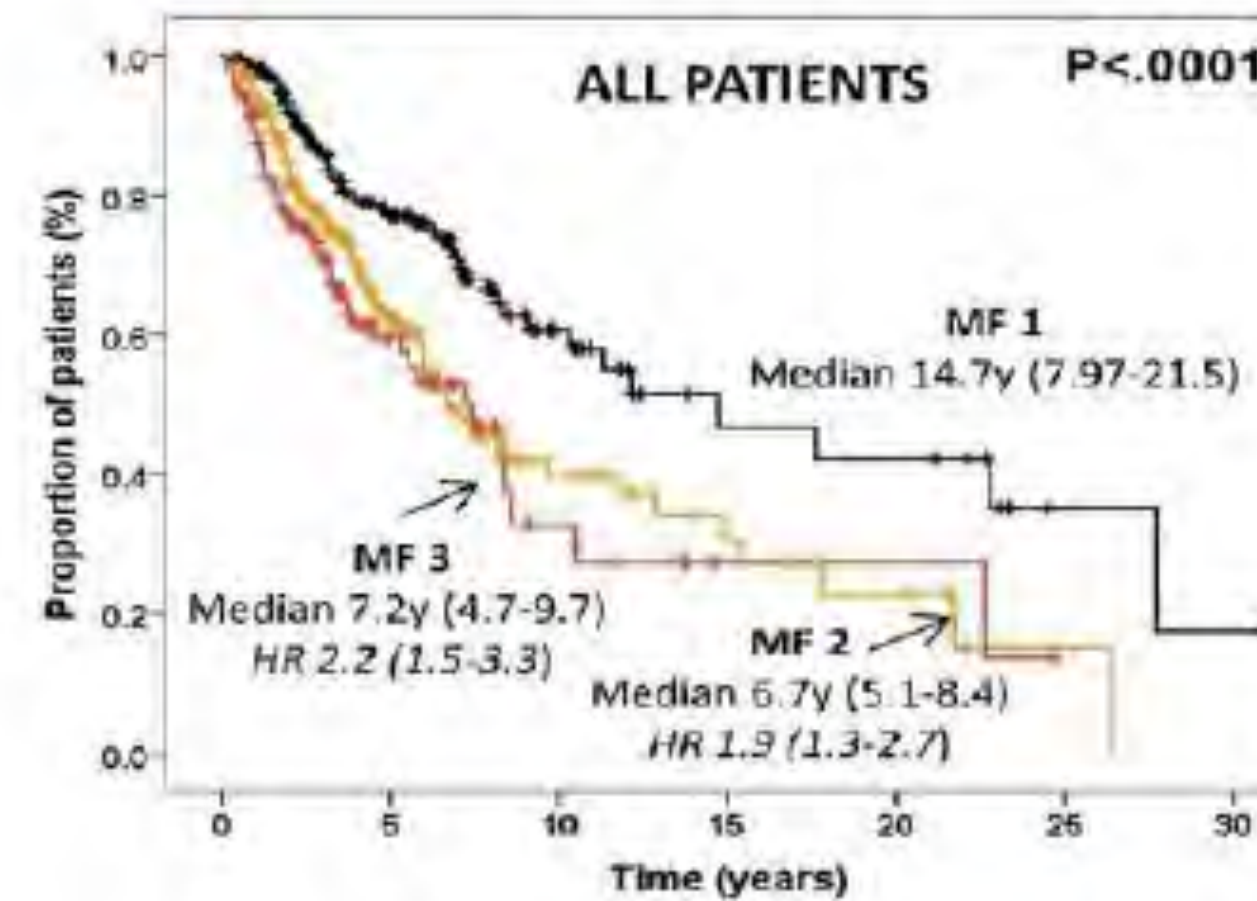
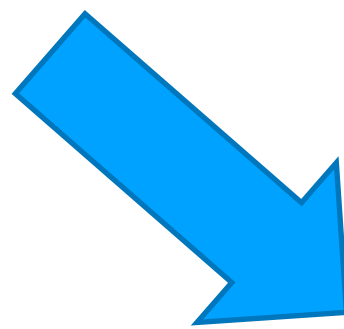
Actuarial survival curves of the 4 risk groups of patients according to IPSS^{1*}



DIPSS, Dynamic International Prognostic Scoring System; IPSS, International Prognostic Scoring System; RBC, red blood cell.
1. Cervantes F, et al. *Blood* 2009; **113**:2895–2901; 2. Passamonti F, et al. *Blood* 2010; **115**:1703–1708; 3. Gangat N, et al. *J Clin Oncol* 2011; **29**:392–397.

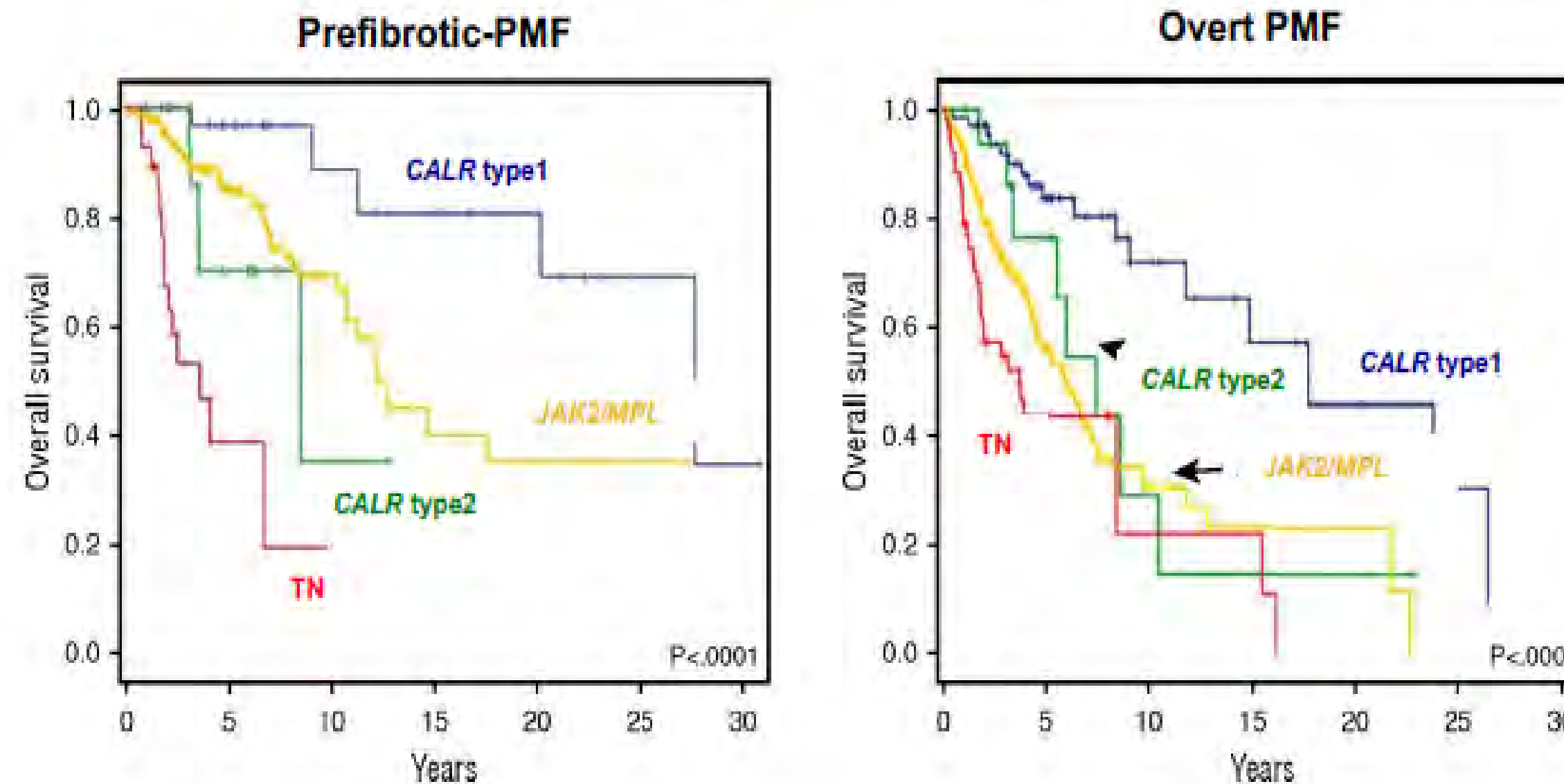


Prognostic impact of BM fibrosis grade in PMF



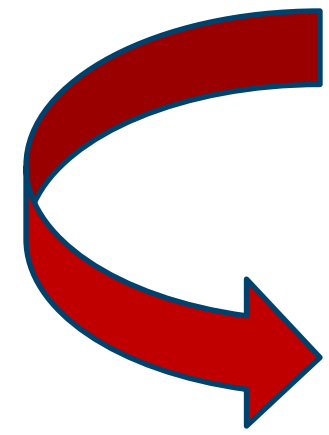
Guglielmelli, et al. Am J Hematol. 2016;91:918-922

Prognostic impact of driver mutations in PMF



- In pre-PMF and overt-PMF, *CALR* type 1 mutation was the most favorable, with median survival of 27.7 years and 17.8 years, respectively
- In pre-PMF, TN had the worst outcome while an intermediate outcome was associated with *JAK2V617F* and *MPLW515*
- In overt PMF, *CALR* type 1/like differed significantly from the other three mutation assets

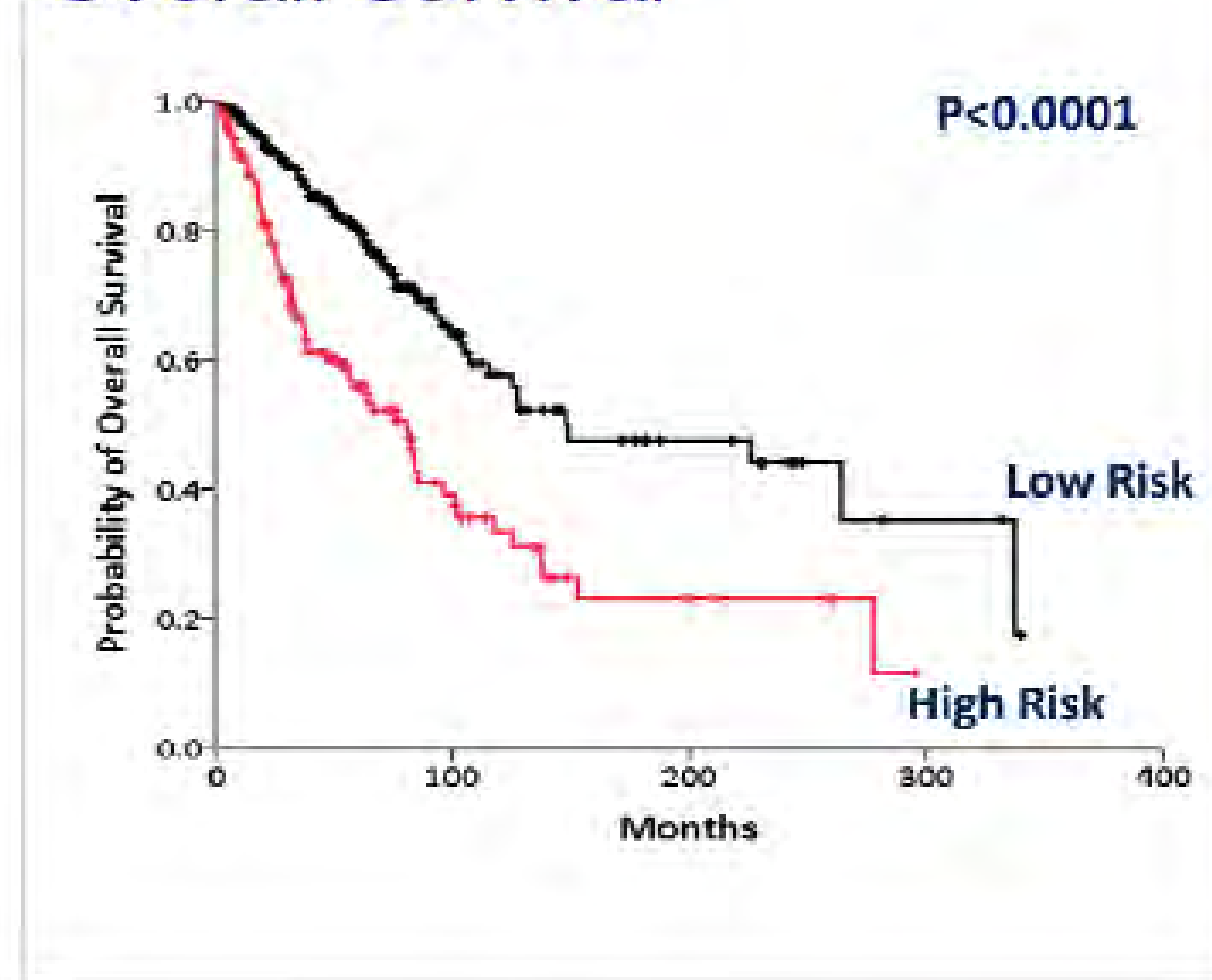
Prognostic impact of additional mutations in PMF



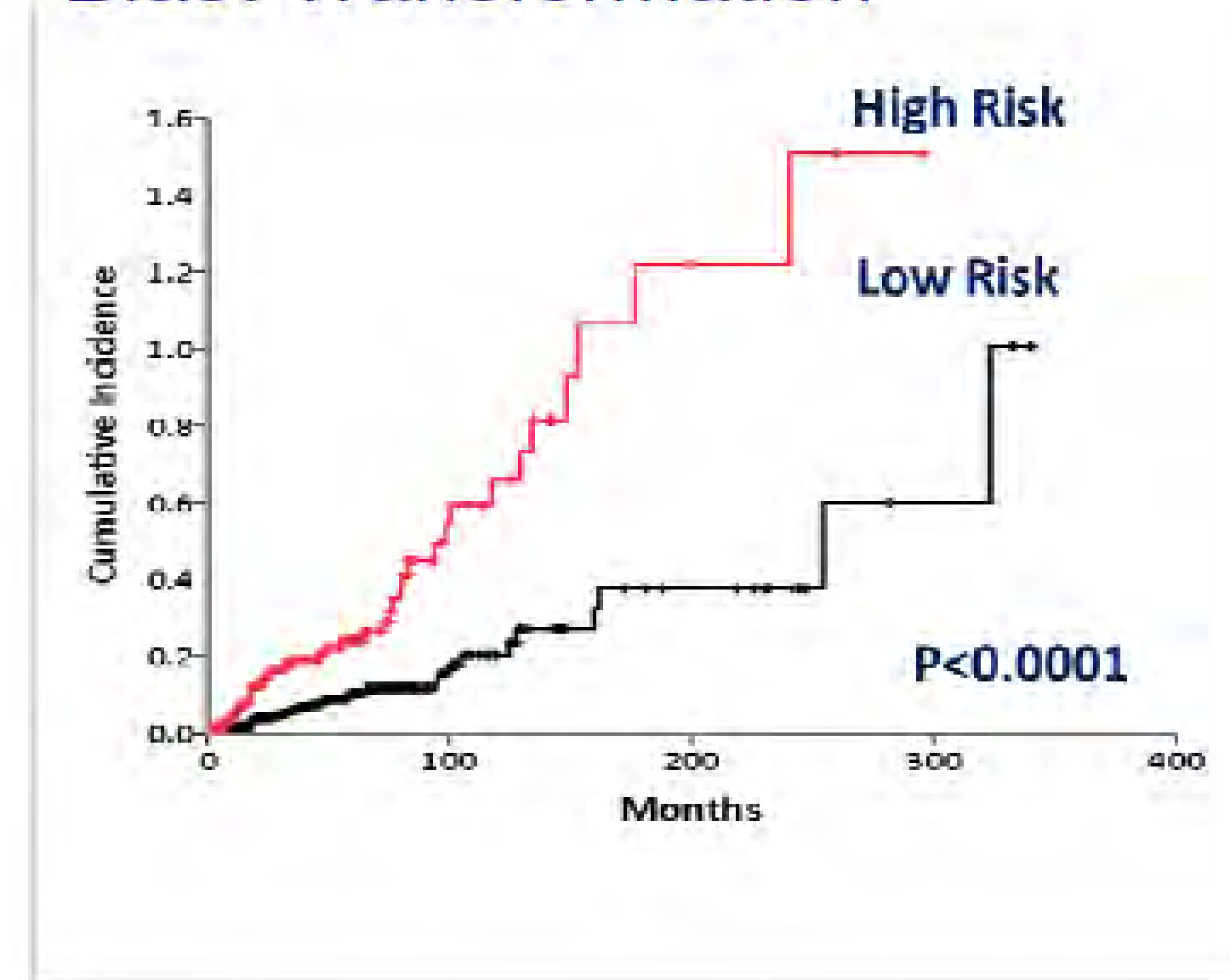
High Molecular Risk Prognostic Category

harboring ≥ 1 mutation in any one of *ASXL1*, *EZH2*, *SRSF2*, *IDH1/2*

Overall Survival

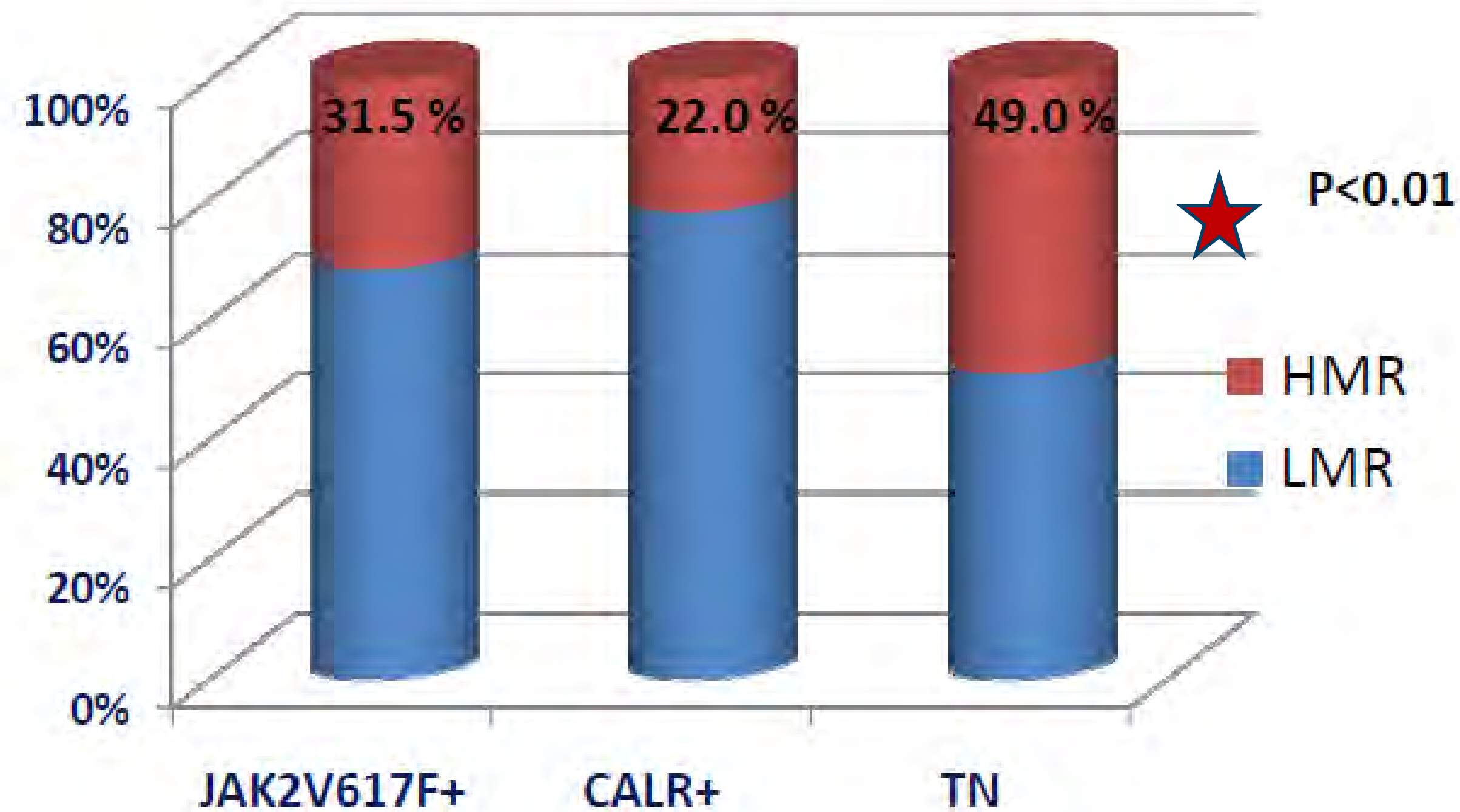


Blast Transformation



- A HMR status is associated with reduced OS and increased risk of blast transformation in PMF patients independent of IPSS/DIPPS-plus scores

Prognostically Detrimental HMR Mutations Are More Represented Among Triple Negative Patients

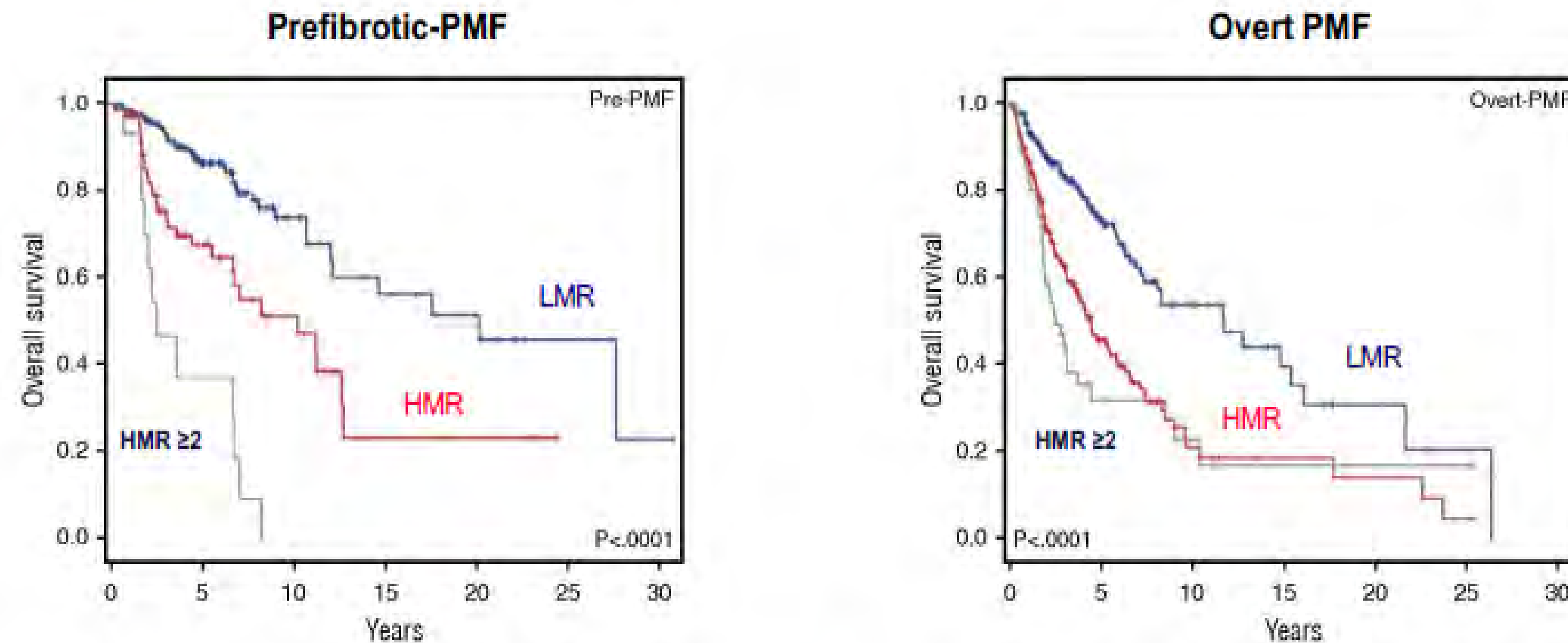


- Spliceosome mutations (SRSF2, SF3B1, U2AF1) are infrequent in CALR+ patients compared with JAK2V617F, MPL+ and triple negative

Guglielmelli P et al; abstract 4540. EHA 2014; Tefferi A et al, Leukemia 2014; 28:1472-7

Prognostic impact of HRM in prefibrotic and overt PMF

Harboring ≥ 2 mutation in any one of ASXL1, EZH2, SRSF2, IDH1/2 (+ U2AF1)



- The HMR category was associated with significantly shorter survival in pre-PMF and overt PMF independent of IPSS/DIPPS-plus score
- NGS for testing for variants in other myeloid neoplasm-associated genes is suggested

MIPSS70 risk score for transplantation-age patients

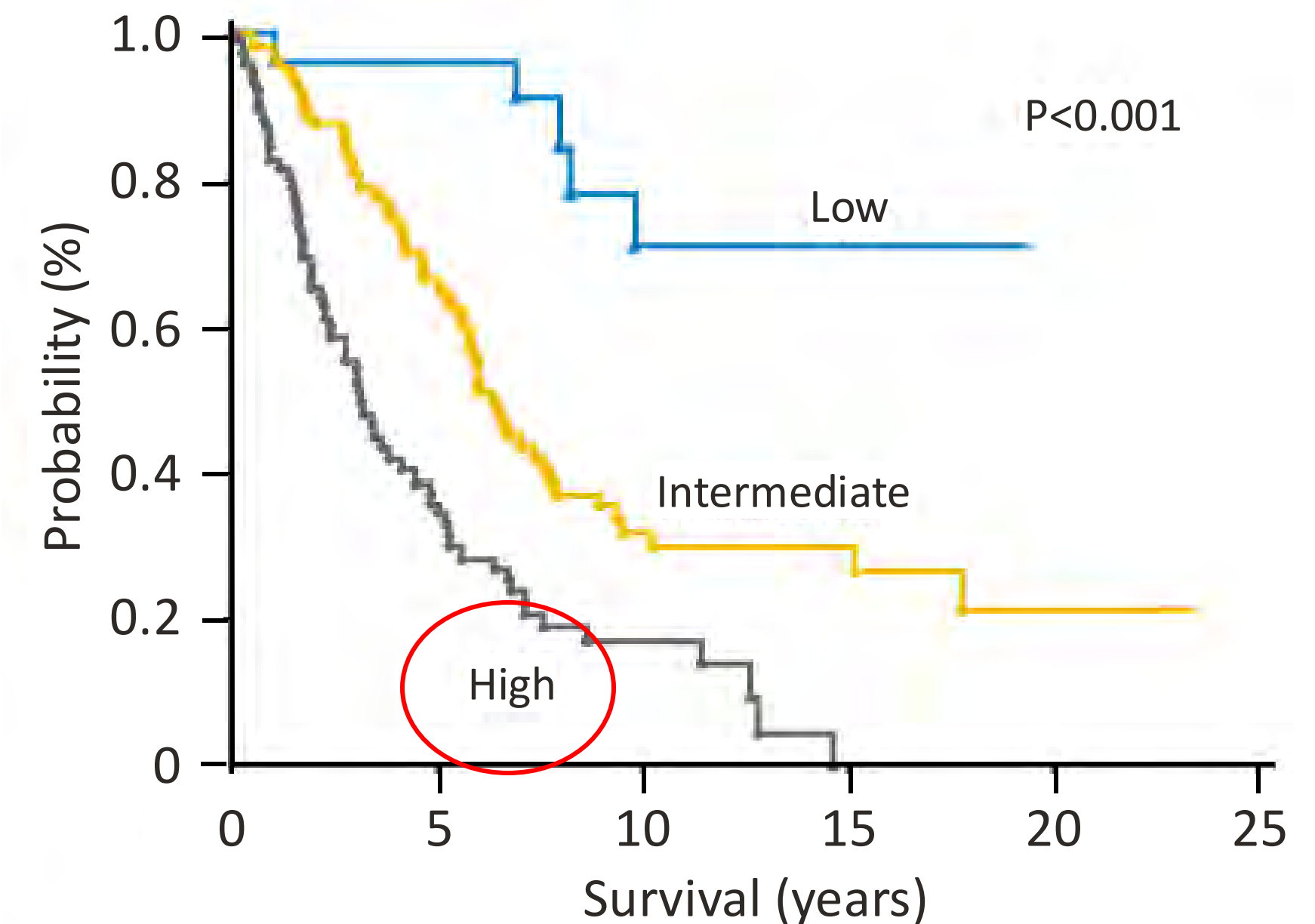
Variables associated with reduced OS

Variables	HR (95% CI)	Score
Hb <100 g/L	1.9 (1.32–2.71)	1
WBC >25×10 ⁹ /L	3.8 (2.21–6.64)	2
PLT <100×10 ⁹ /L	3.2 (2.09–4.77)	2
PB blasts ≥2%	1.7 (1.17–2.54)	1
Constitutional symptoms	2.2 (1.57–3.03)	1
BM fibrosis	1.9 (1.34–2.71)	1
Absence of <i>CALR</i> type 1	1.9 (1.21–2.96)	1
HMR category*	1.8 (1.26–2.49)	1
≥2 HMR mutations†	4.0 (2.43–6.40)	2

Risk categories

Low	0–1
Intermediate	2–4
High	≥5

Overall survival by MIPSS70 classification

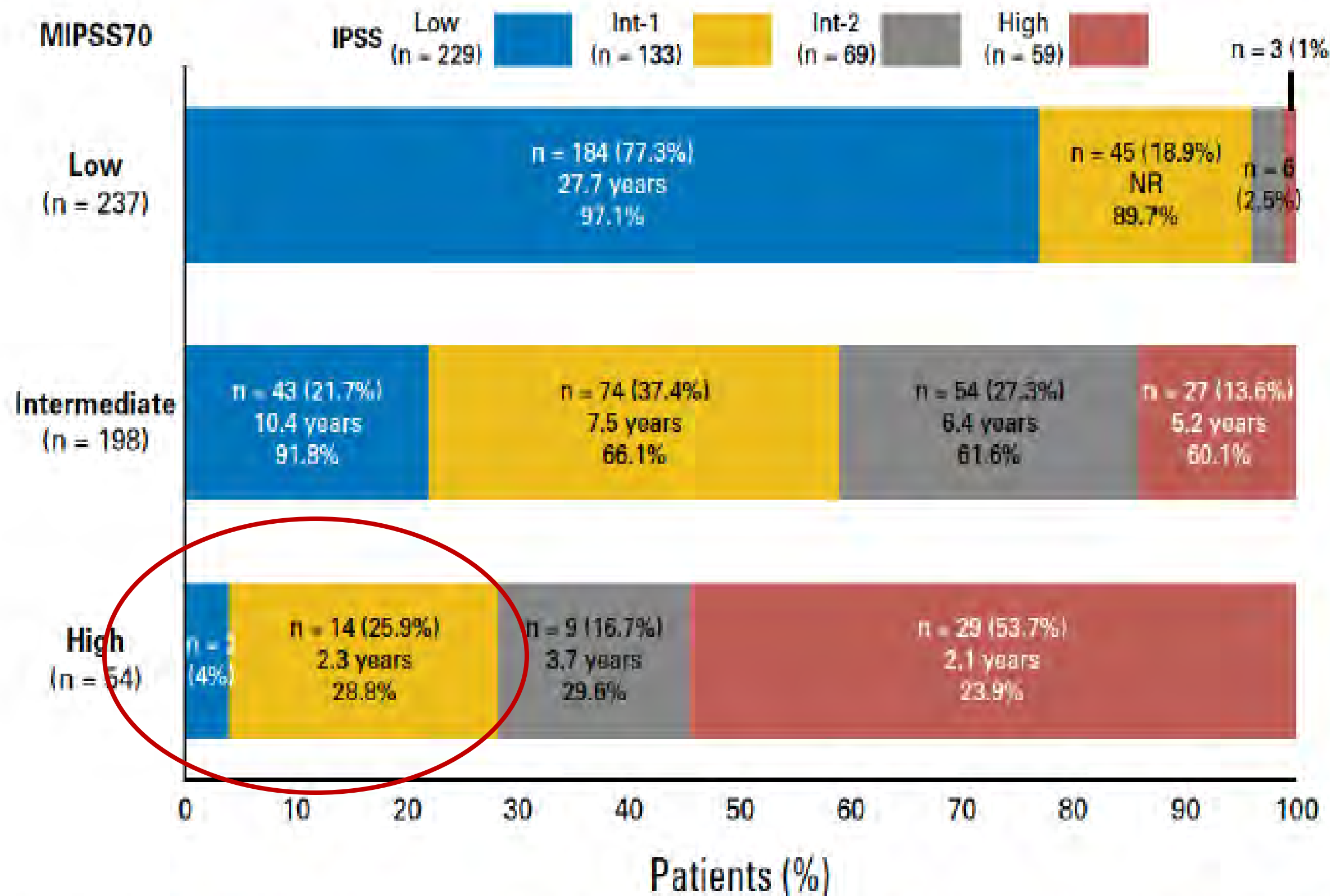


* Any mutation in: *ASXL1*, *EZH2*, *SRSF2*, *IDH1/2*, *U2AF1*; † Two or more mutated genes among: *ASXL1*, *EZH2*, *SRSF2*, *IDH1/2*.

≥2 mutations in the same gene are counted as one. MIPSS, Mutation-Enhanced International Prognostic Score System.

Guglielmelli P, et al. *J Clin Oncol* 2018; **36**:310–318.

MIPSS70 is more performant for predicting survival in PMF than IPSS

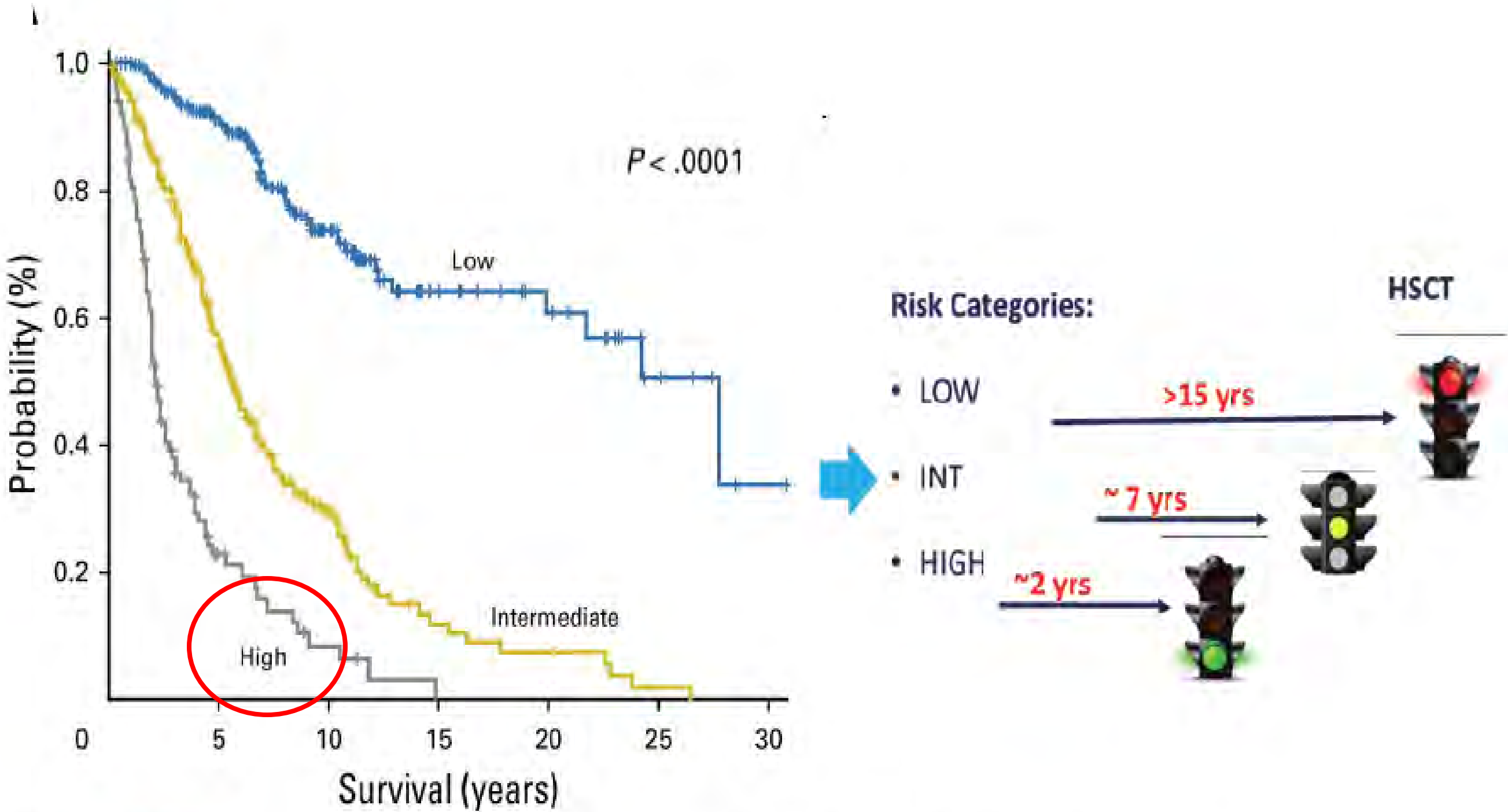


The higher categories included 30% of patients originally classified as low or intermediate IPSS risk; conversely, 6 patients (3.5%) included in intermediate-2 IPSS group were downgraded to the lowest risk categories of MIPSS70.

MIPSS70: mutation enhanced prognostic score system for transplant-age patients PMF

Variables	Weighted value
Hb <100g/L	1
WBC >25x10 ⁹ /L	
PLT <100x10 ⁹ /L	2
PB blasts ≥2%	
Constitutional Symptoms	1
Grade ≥2 BM fibrosis	
Absence CALR Type1	1
HMR category*	
≥2 HMR mutations	2

Risk category	Score	OS (y)	HR
Low	0-1	27.7	1
Intermediate	2-4	7.1	5.5(3.8-8.0)
High	>5	2.3	16.0(10.2-25.1)



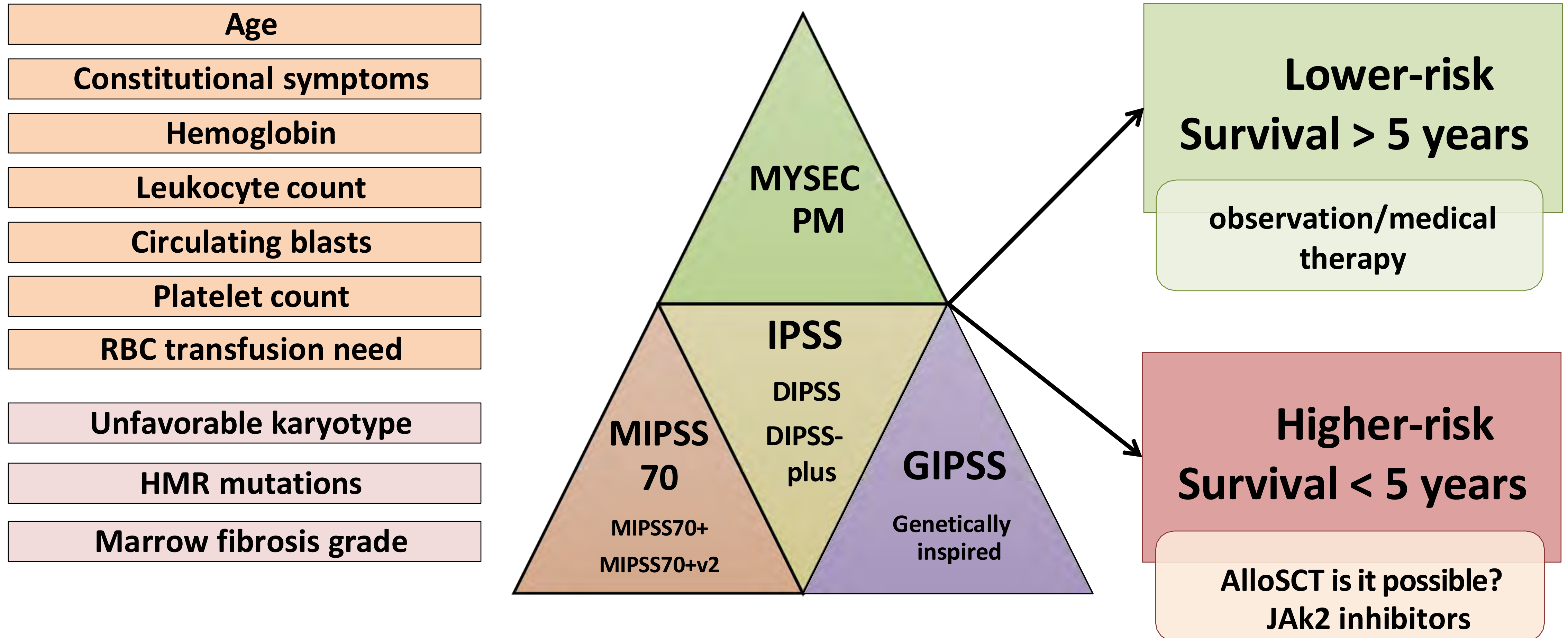
*HMR category= any mutation in: ASXL1, EZH2, SRSF2, IDH1/2, U2AF1 Q157

Learning cohort: italian cohort

Version 2.0

The higher categories included 30% of patients originally classified as low or intermediate IPSS risk; conversely, 6 patients (3.5%) included in intermediate-2 IPSS group were downgraded to the lowest risk categories of MIPSS70

Prognostic scores in MF

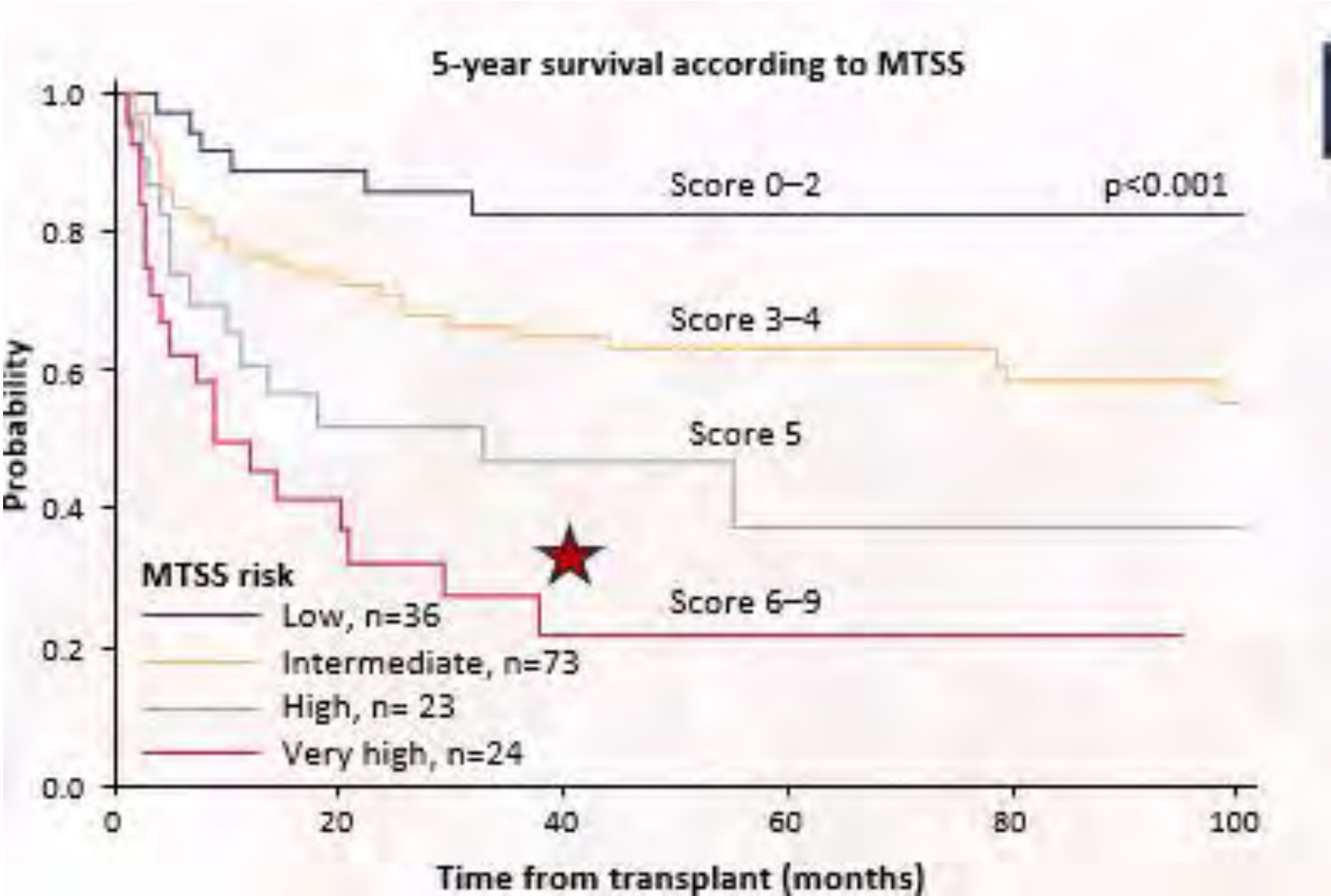


Tefferi, BCJ 2018; Cervantes, Blood 2009; Passamonti, Blood 2010;
Gangat, JCO 2011; Passamonti, Leukemia 2017; Guglielmelli, JCO 2018;
Tefferi, JCO 2018; Tefferi, Leukemia 2018

Thanks Palandri F (modified)

MTSS determines prognosis after allogeneic HSCT

Clinical-molecular myelofibrosis transplant scoring system validated in 156 patients

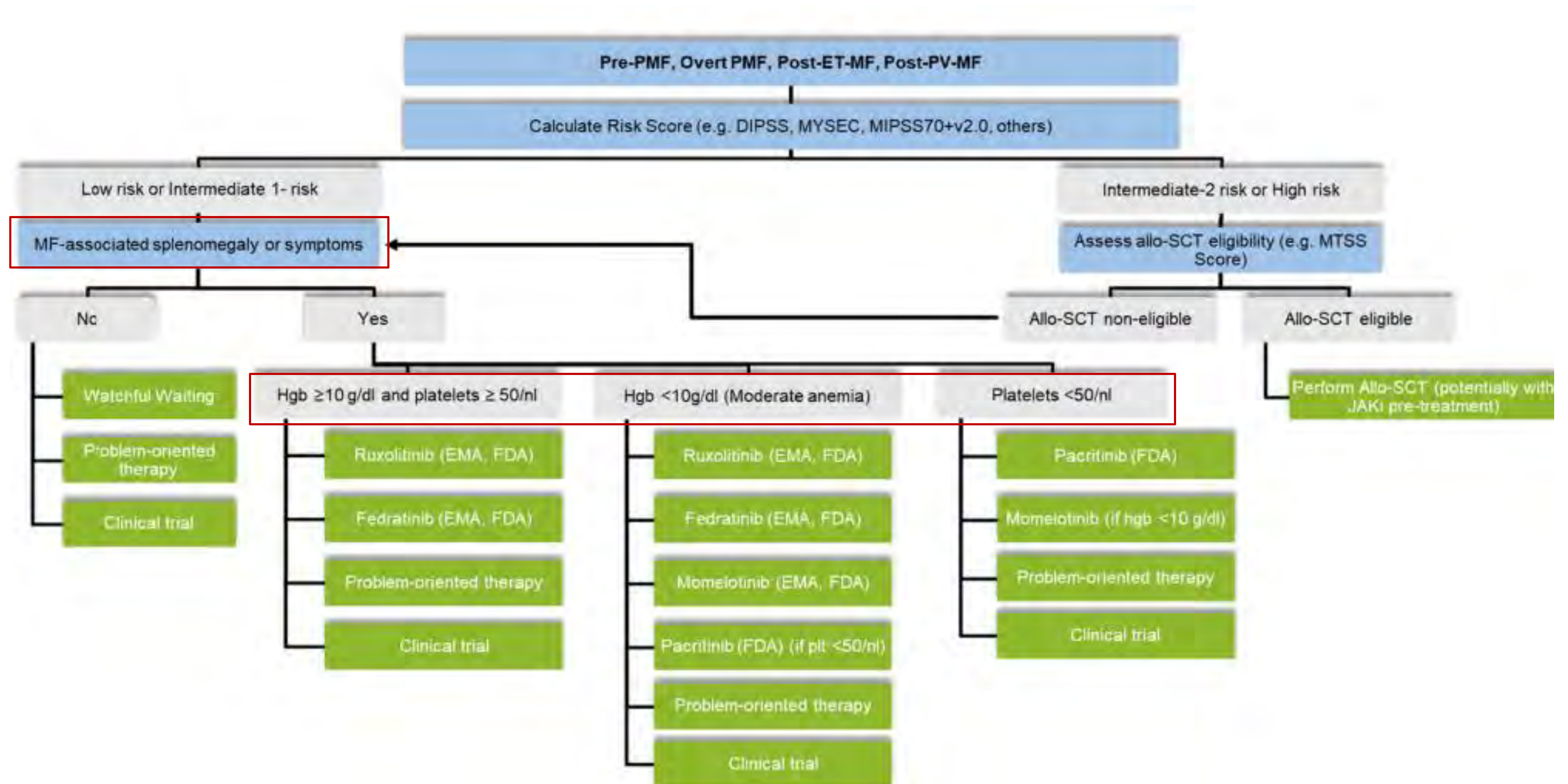


Variable	HR*	Score
Platelet count <150×10 ⁹ /L	1.67	1
Leukocyte count >25×10 ⁹ /L	1.57	1
KPS <90%	1.50	1
Age ≥57 years	1.65	1
Non-CALR/MPL driver mutation genotype	2.40	2
ASXL1 mutation	1.42	1
HLA-mismatched unrelated donor	2.08	2

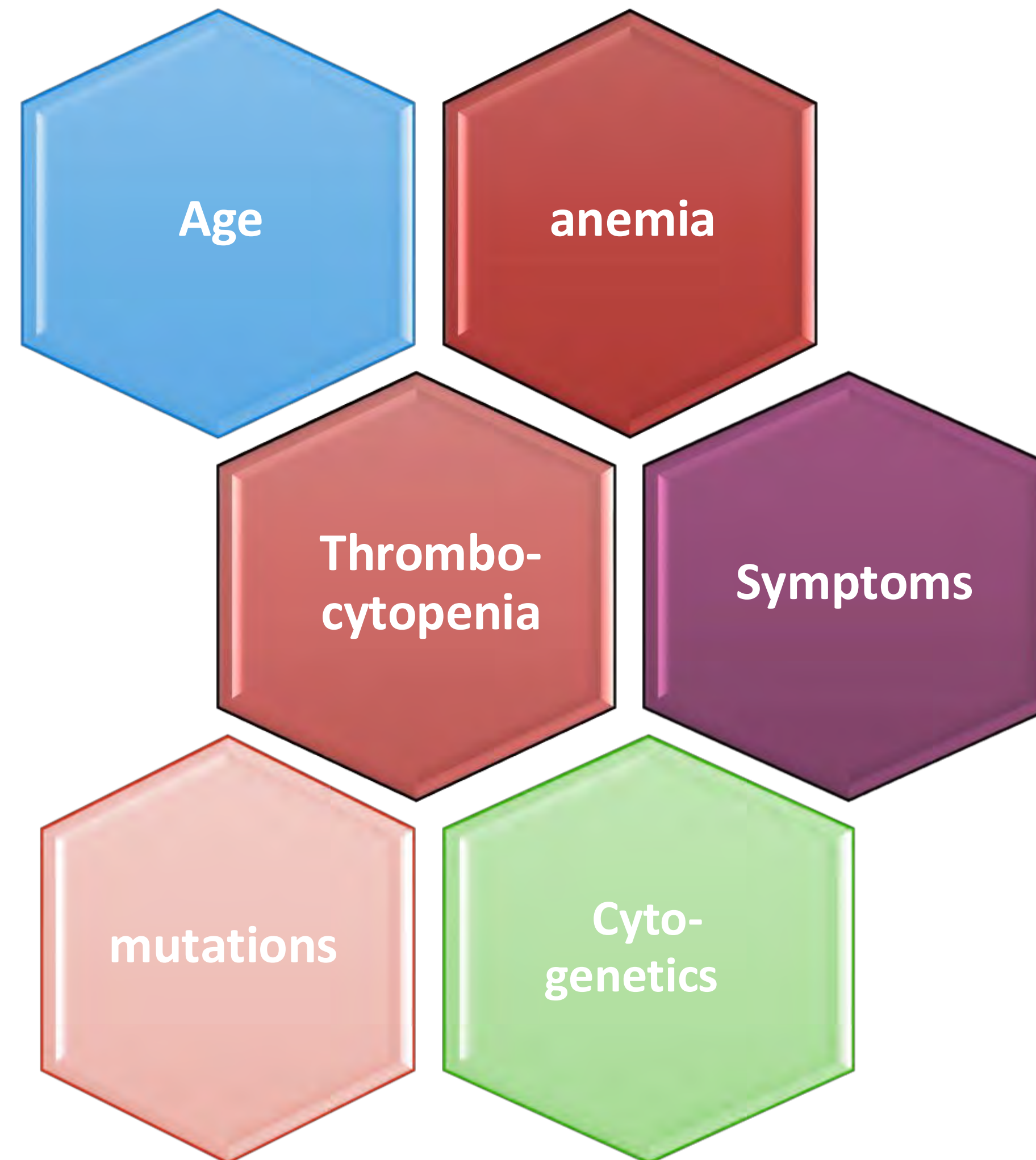
*Multivariate analysis.
HLA, human leukocyte antigen; HSCT, hematopoietic stem cell transplantation ; KPS, Karnofsky performance status; MTSS, myelofibrosis transplant scoring system.
Gagelmann N, *et al. Blood* 2019; 133:2233–2242.



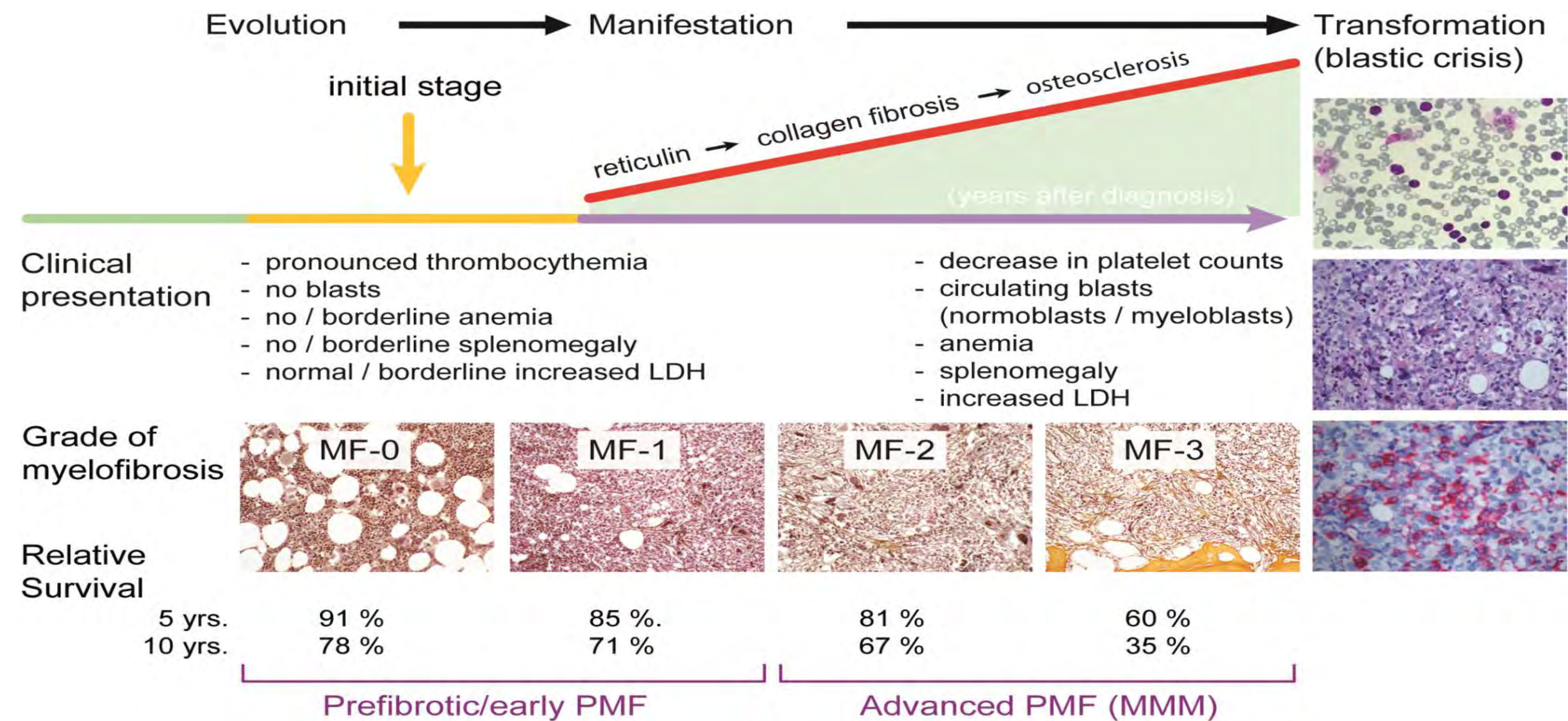
Treatment strategy in MF – transplant eligible or not



MF: prognosi e ruolo dell'anemia



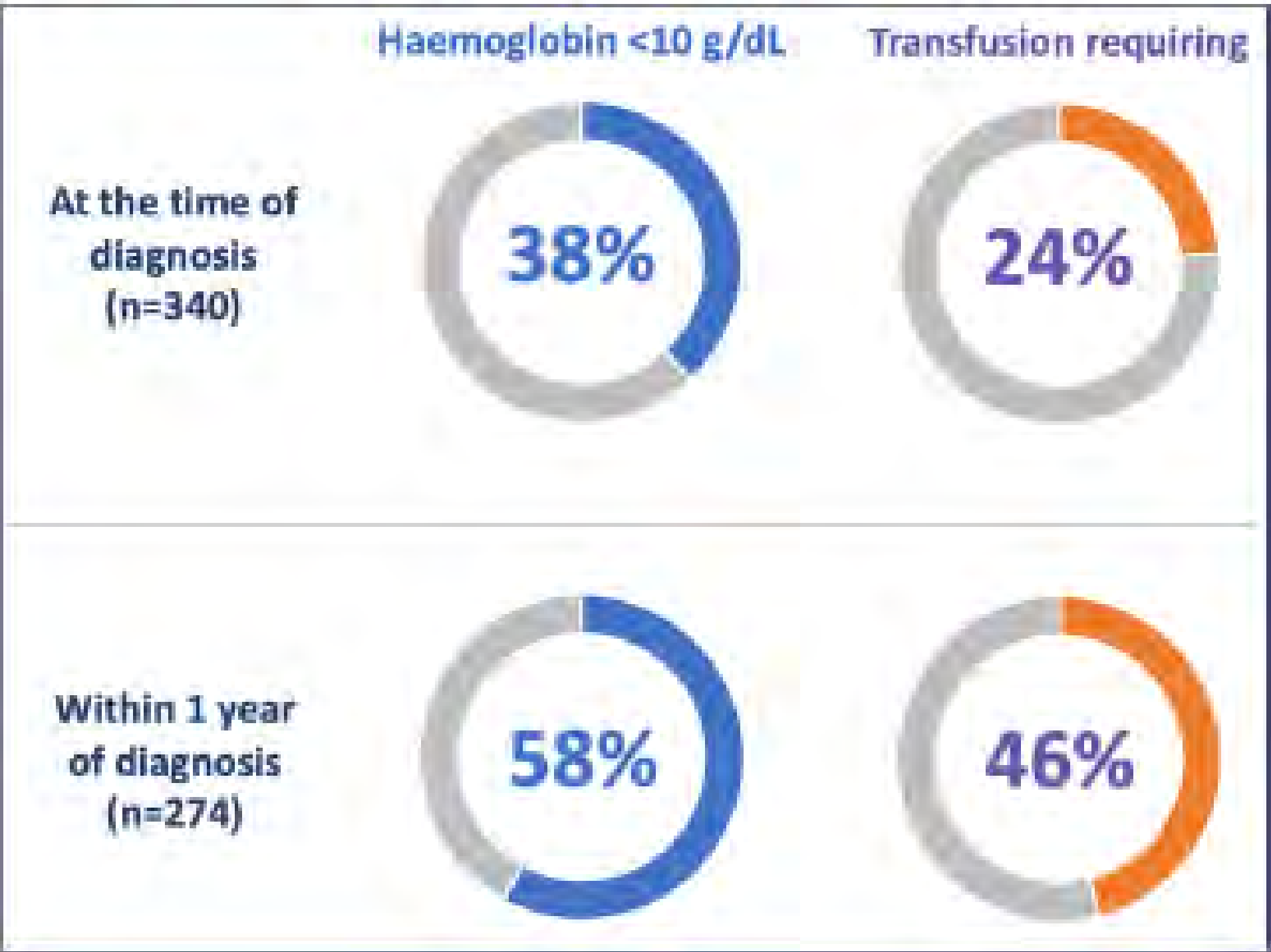
La mielofibrosi è una malattia progressiva



Anemia is among the cardinal features of MF

During their disease course, virtually all patients with MF will eventually develop anemia (hemoglobin < 10 g/dL)¹

PMF: the Mayo Clinic cohort



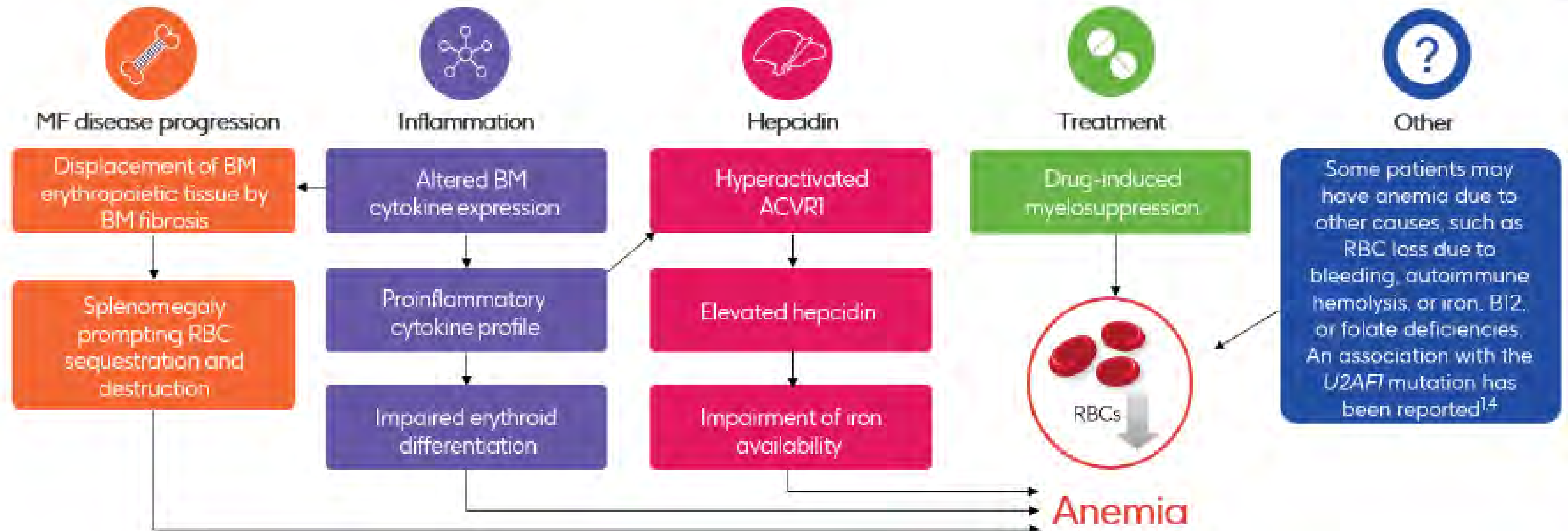
SMF: the MYSEC international cohort

	Hb (g/dl), median (range)	Hb <10 (g/dl), n (%)	Hb <8 (g/dl), n (%)
SMF (1258)	11.1 (4.2-16.0)	363 (30.3)	62 (5.2)
PPV-MF (615)	11.9 (6.3-16.0)	131 (22.4)	17 (2.9)
PET-MF (643)	10.6 (4.2-16.0)	232 (37.7)	45 (7.3)
p-value	<0.0001	<0.0001	0.001

1. Naymagon L & Mascarenhas J. Hemasphere. 2017;1:e1; 2. Tefferi A, et al. Mayo Clin Proc. 2012;87:25–33. ; Passamonti et al, Leukemia 2017; Mora et al, Leukemia 2022



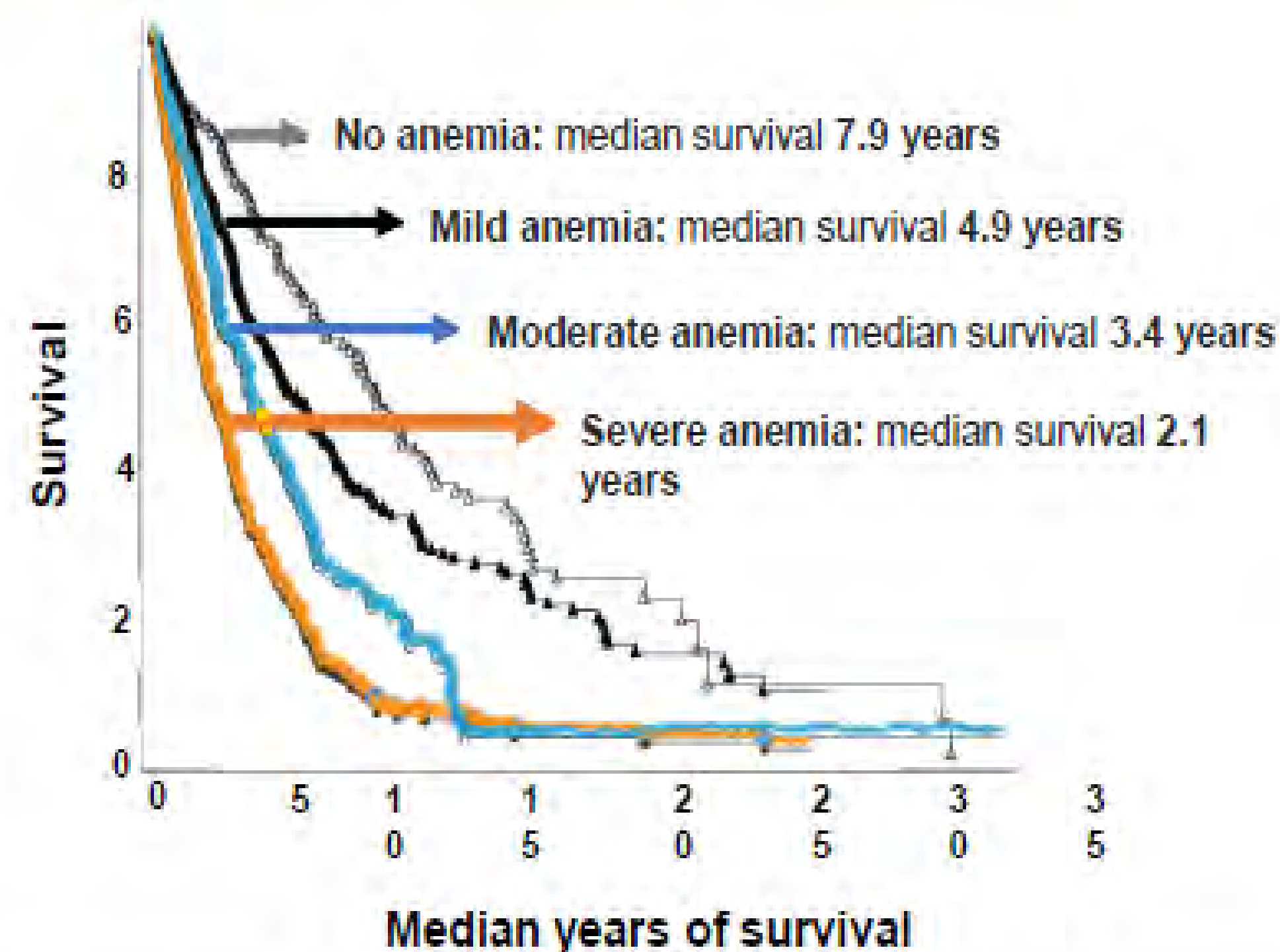
Pathophysiology of anemia in MF is multifactorial



Severity of anemia directly correlates with reduced survival in MF

Severity of anemia in MF is associated with median survival

Severity of anemia	Median survival, years
No anemia	7.9
Mild	4.9
Moderate	3.4
Severe	2.1

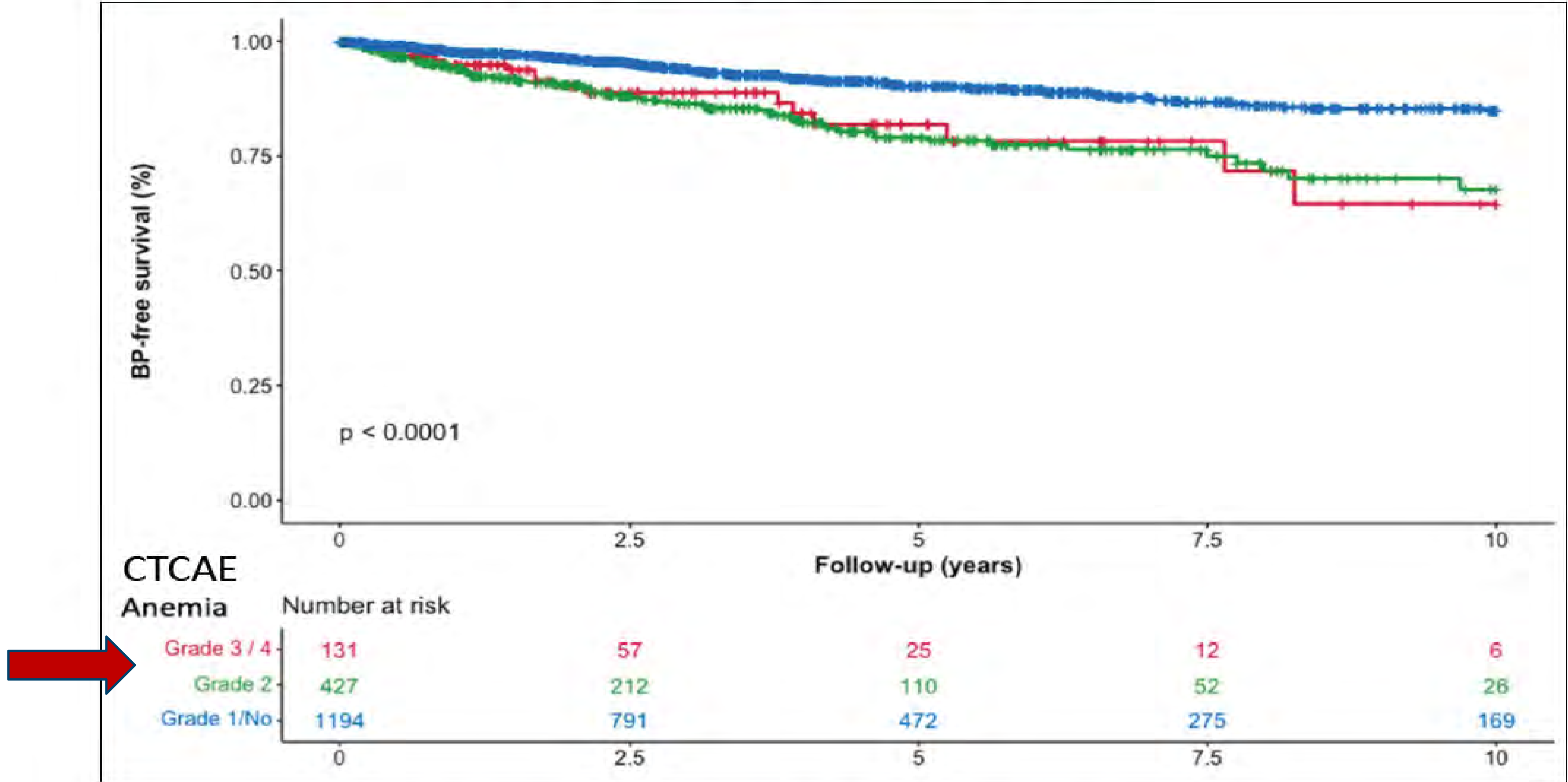


A study of 1109 patients with primary MF at the Mayo Clinic found that all grades of anemia adversely impact survival, with a nearly 4-fold shorter median survival for patients with severe anemia compared to patients with no anemia

Il grado di anemia alla diagnosi impatta sulla sopravvivenza libera da evoluzione leucemica

N= 136 pre-PMF, 638 overt-PMF and 978 SMF

1752 pts



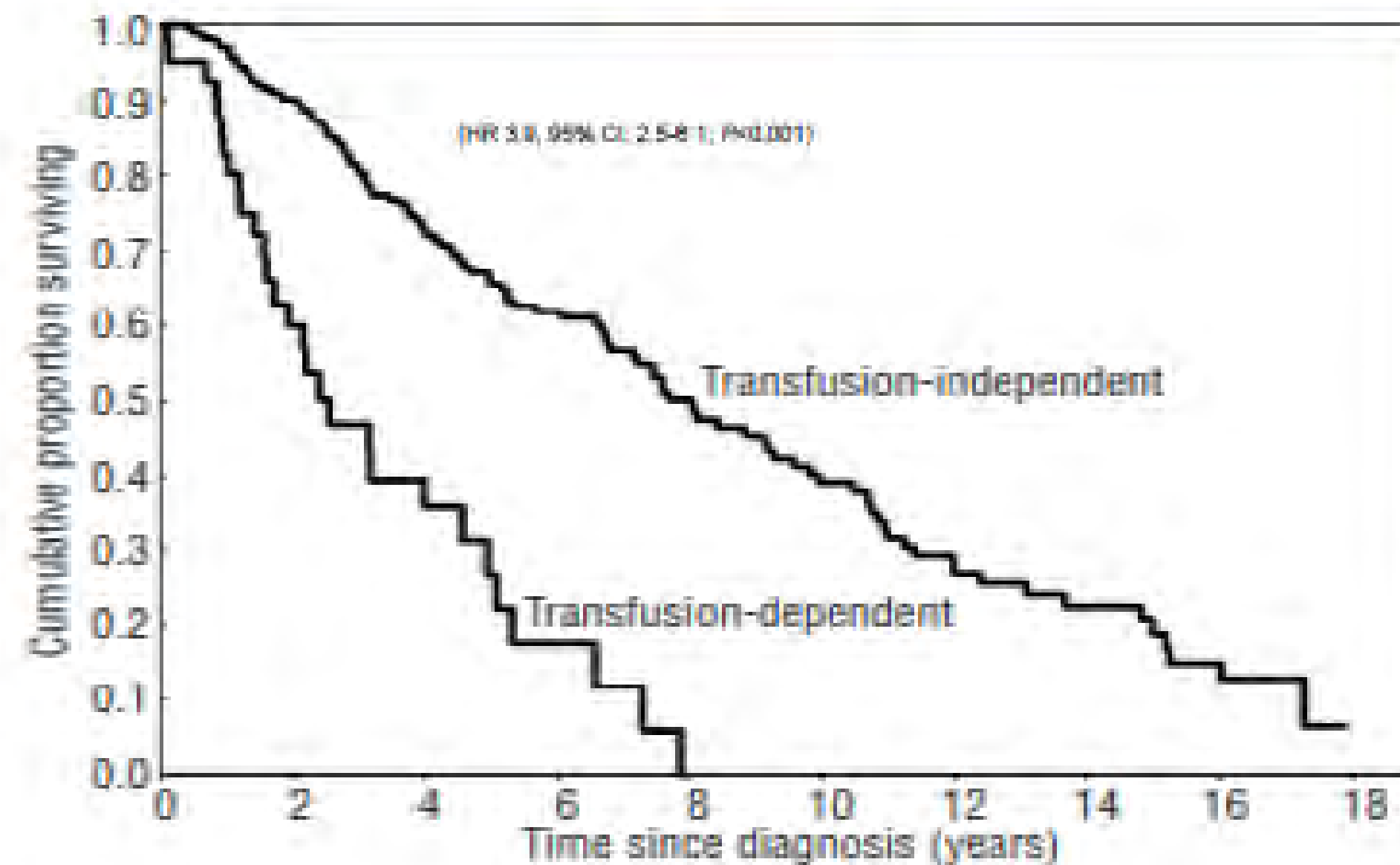
Legend: grade 3/4 anemia= Hb <8 g/dL; grade 2= Hb 8–10 g/dL; grade 1 (Hb >10 g/dL) anemia grouped together with normal Hb values.

Transfusion dependency is associated with reduced OS in MF

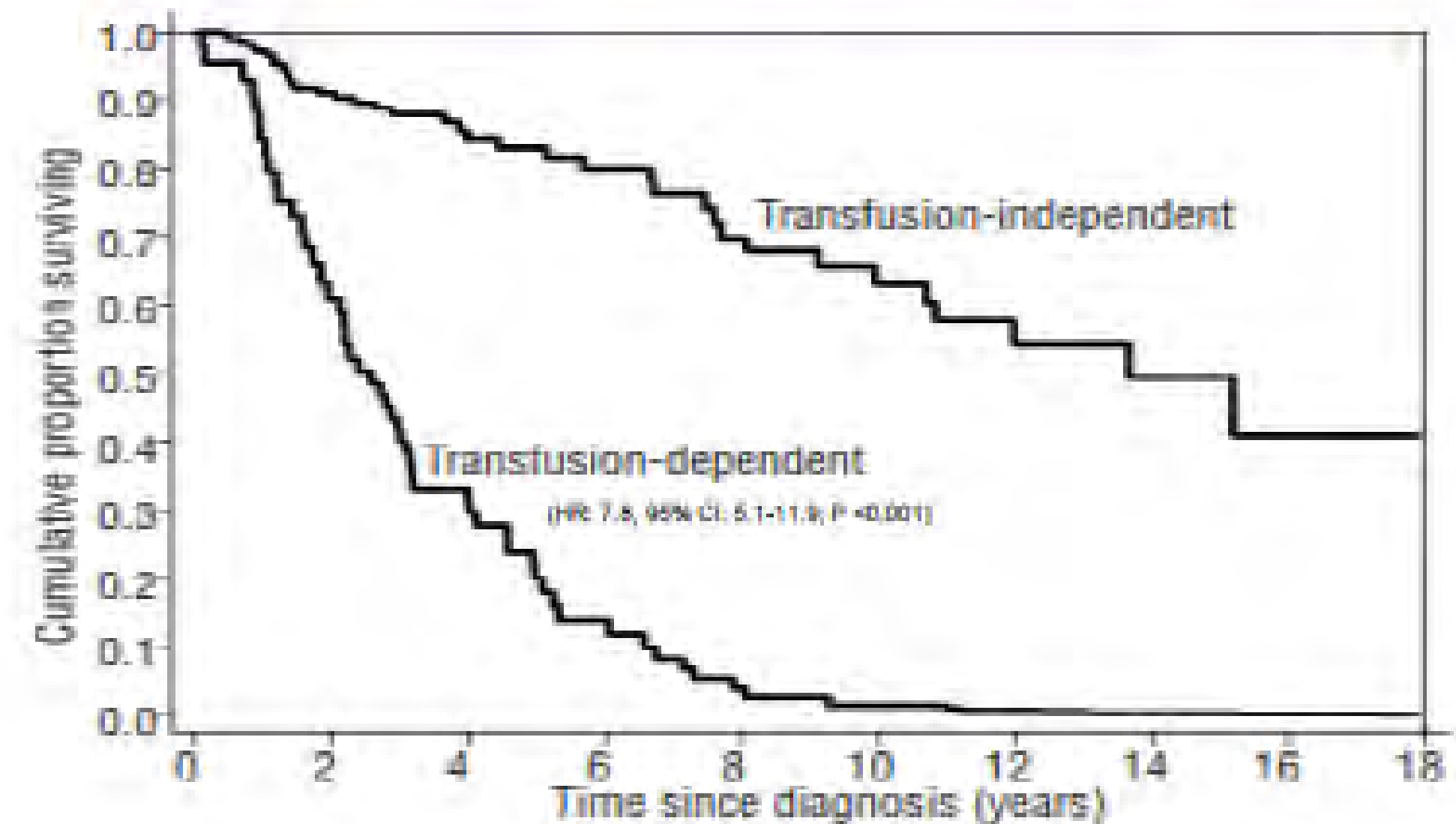
An analysis of 288 patients with primary MF demonstrated:

- TD of patients *at diagnosis* significantly affects survival (median survival 2.6 years), compared to patients who did not receive transfusions at diagnosis (median survival 8 years)
- TD of patients occurring *at any time* was also associated with worse survival, compared with patients who remained transfusion independent during follow-up

OS according to RBC-TD at time of diagnosis in 288 patients with primary MF



OS according to RBC-TD assessed as a time-dependent variable in 220 regularly followed patients with primary MF



Ruolo Prognostico negativo dell' anemia in MF alla diagnosi integrato negli score prognostici

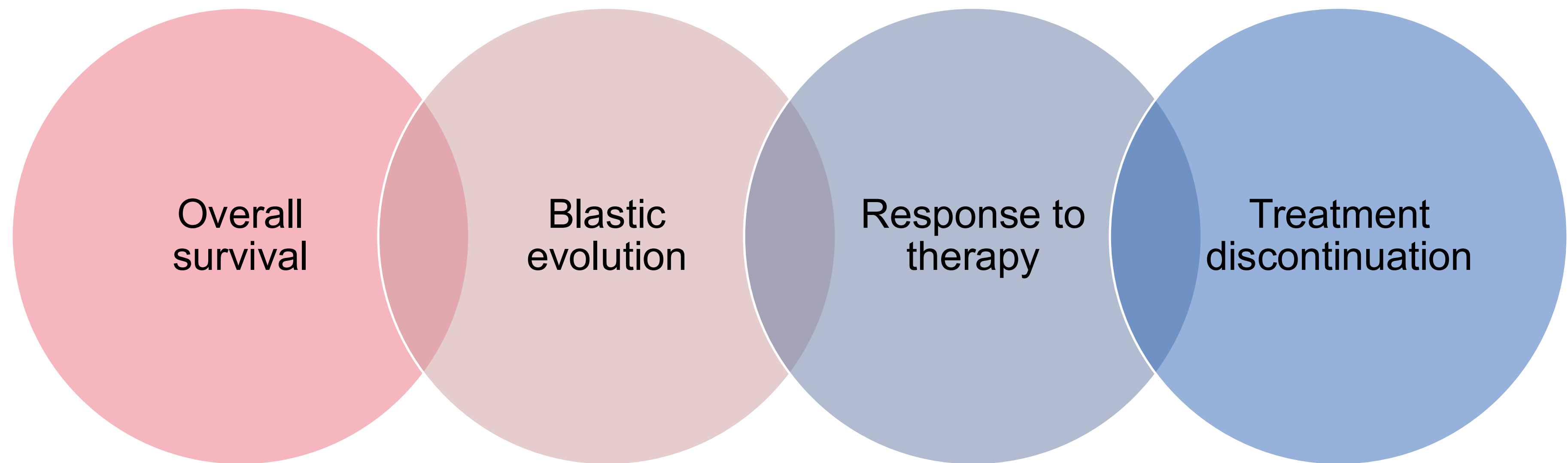
Scoring System	IPSS	DIPSS	DIPSS Plus	MIPSS ^{27,a}	GPSS ^{28,a}
Factors (points)	• Age >65 y (1) • Hb <100 g/L (1) • WCC >25 × 10⁹/L (1) • PB blasts ≥1% (1) • C Sx (1)	• Age >65 y (1) • Hb <100 g/L (2) • WCC >25 × 10⁹/L (1) • PB blasts ≥1% (1) • C Sx (1)	• Age >65 y (1) • Hb <100 g/L (1) • WCC >25 × 10⁹/L (1) • PB blasts ≥1% (1) • C Sx (1) • Unfavorable karyotype^b (1) • Transfusion dependency (1) • Plt <100 × 10⁹/L (1)	• Age >60 y (1.5) • Hb <100 g/L (0.5) • Plt <200 × 10⁹/L (1) • C Sx (0.5) • <i>JAK2</i> (0.5) • <i>MPL</i> (0.5) • <i>ASXL1/SRSF2</i> (0.5) • Triple negativity (1.5)	• Age >60 y (2) • Very high-risk karyotype (3) • High-risk karyotype (1) • <i>JAK2</i> (2) • <i>MPL</i> (2) • <i>CALR</i> type 2/2-like (2) • <i>ASXL1/SRSF2</i> (1) • Triple negativity (2)
Risk groups, scores (OS)					
• low	0 (11.3 y)	0 (not reached)	0 (185 mo)	0-0.5 (26.4 y)	0 (not reached)
• int-1	1 (7.9 y)	1-2 (14.2 y)	1 (78 mo)	1-1.5 (9.7 y)	1-2 (9 y)
• int-2	2 (4 y)	3-4 (4 y)	2-3 (35 mo)	2-3.5 (6.4 y)	2-3 (5 y)
• high	≥3 (2.3 y)	≥5 (1.5 y)	≥4 (16 mo)	≥4 (1.9 y)	≥5 (2.2 y)

C Sx, constitutional symptoms; DIPSS, Dynamic International Prognostic Scoring System; GPSS, Genetics-Based Prognostic Scoring System; Hb, hemoglobin; int, intermediate; IPSS, International Prognostic Scoring System; mo, months; MIPSS, Mutation-Enhanced International Prognostic Scoring System; OS, median overall survival; PB, peripheral blood; Plt, platelet count; WCC, white cell count; y, years.

^aProposed scoring system, not used in standard practice.

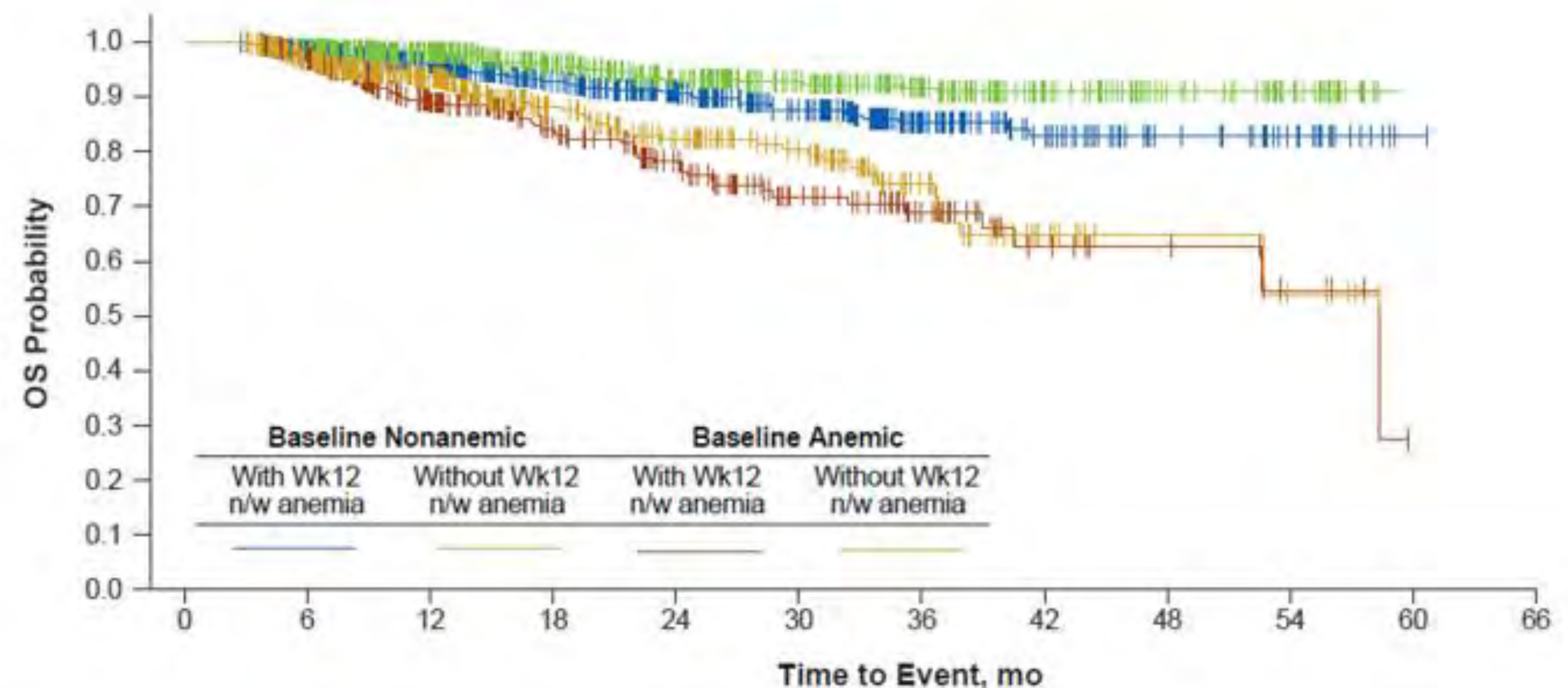
^bMonosomal karyotype, isochromosome of the long arm of chromosome 17 and inversion of chromosome 3.

Anemia during JAK inhibitors impacts on outcome and prognostic role



Ruxolitinib: Post Hoc Analysis of the JUMP Expanded-Access Phase 3b Trial in Patients With and Without New/Worsening Anemia at Week 12 of Treatment

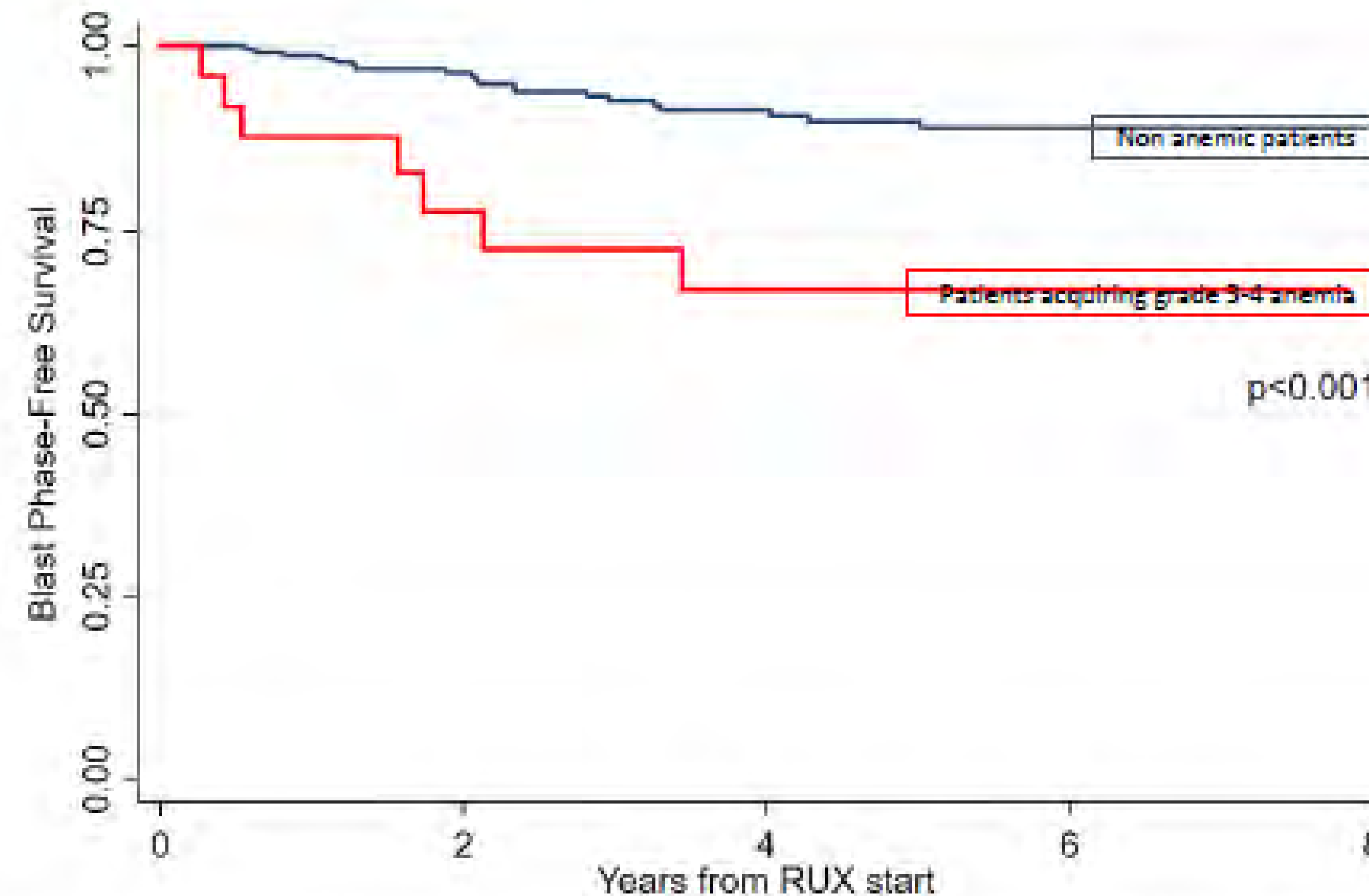
- ❖ Rates of SLR at Week 24 among patients with vs without new or worsening anemia were 31.5% vs 31.2%, respectively
- ❖ For non anemic patients at baseline a better OS was seen in those without vs with new/worsening anemia ($P=0.01$)
- ❖ For patients with baseline anemia (NTRA and TRA), no difference in OS was observed in those with or without new/worsening anemia ($P=0.24$)



Patients at Risk, n												
Baseline Nonanemic												
With Wk12 n/w anemia	702	632	437	322	254	185	109	63	31	18	1	0
Without Wk12 n/w anemia	577	538	404	303	243	191	132	74	43	23	0	0
Baseline Anemic												
With Wk12 n/w anemia	331	295	187	134	98	64	38	16	10	5	0	0
Without Wk12 n/w anemia	423	361	225	148	109	81	37	14	6	4	0	0

Occurrence of de-novo anemia after 6 months of RUX monotherapy predicts leukemic transformation

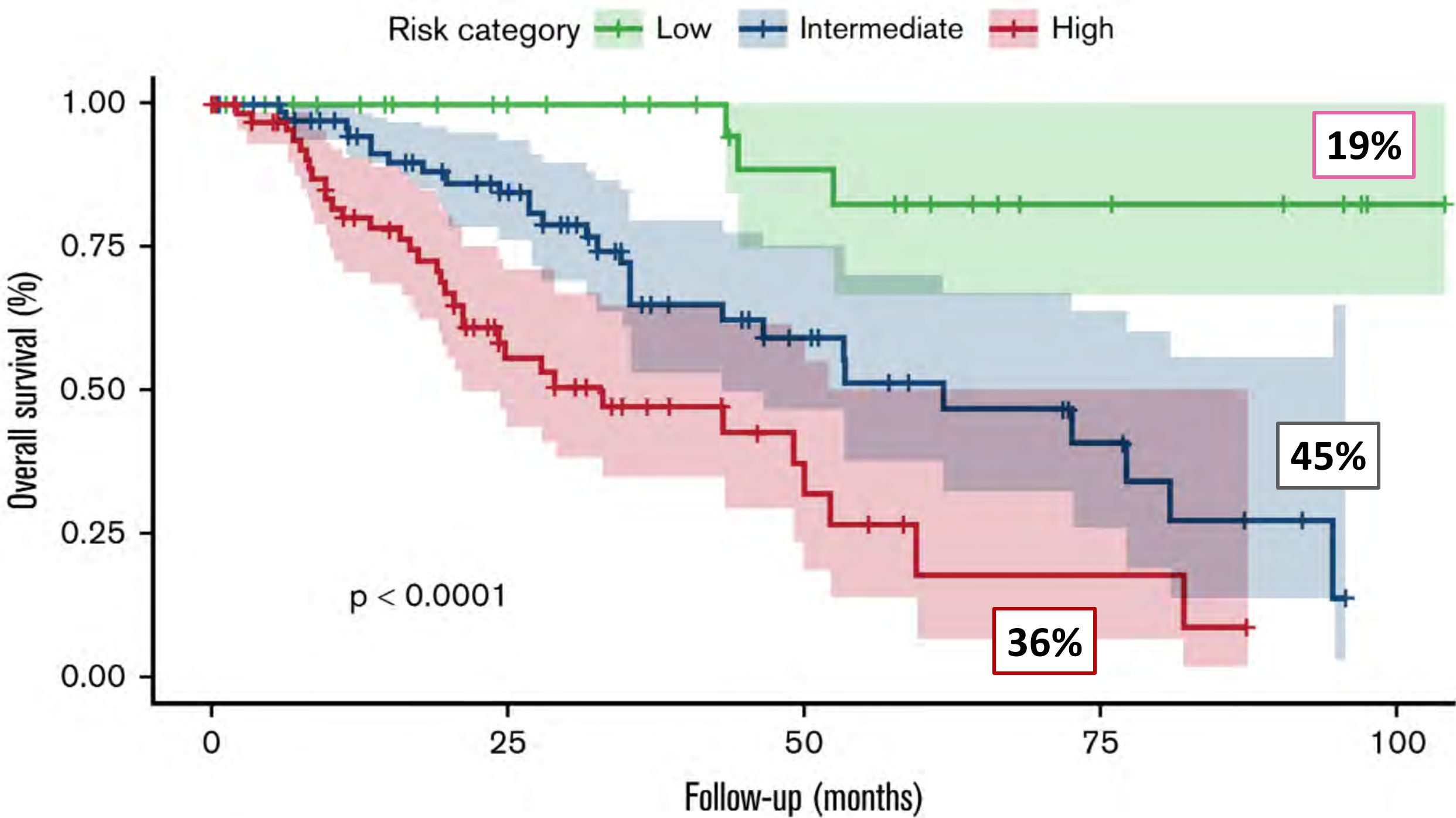
- Among the 289 patients who started ruxolitinib without anemia, 260 were still on therapy after 6 months.
- 24 (9.2%) of these 260 patients developed a CTCAE grade 3-4 anemia during ruxolitinib.



By landmark analysis considering only BP occurring after the 6-month timepoint, BP-FS was significantly worse in patients acquiring grade 3-4 anemia (69.3% vs 88.1% at 5 years, $p < 0.001$)

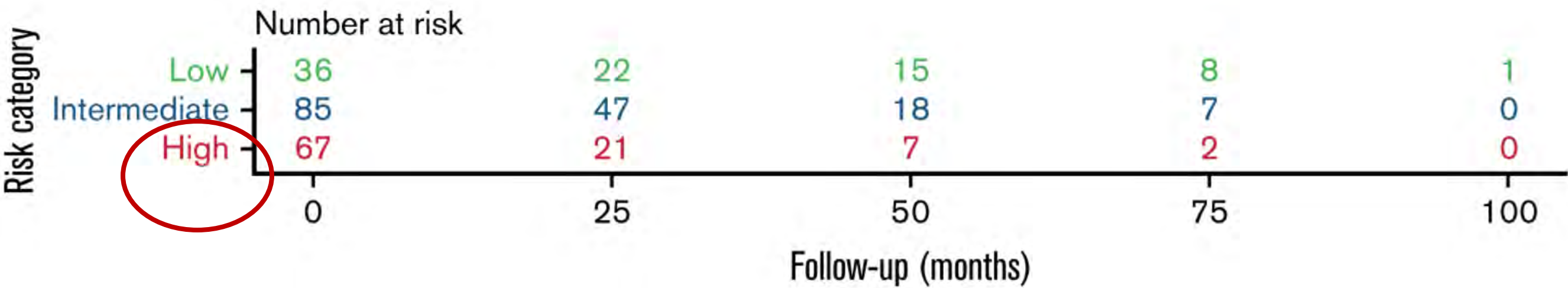
How to predict long-term outcome in patients receiving ruxolitinib

<http://www.rr6.eu/>



RR6 model: Response to ruxolitinib after 6 months

Risk category	% of pts	OS (months)	HR	Score
Low	19	NR		0
Intermediate	45	61	43-80	1-2
High	36	33	21-50	≥2.5



The 2024 Three-Strata Baseline Anemia Definition of the Revised IWG-ELN Criteria Dissects Survival in Ruxolitinib-Treated Myelofibrosis Patients

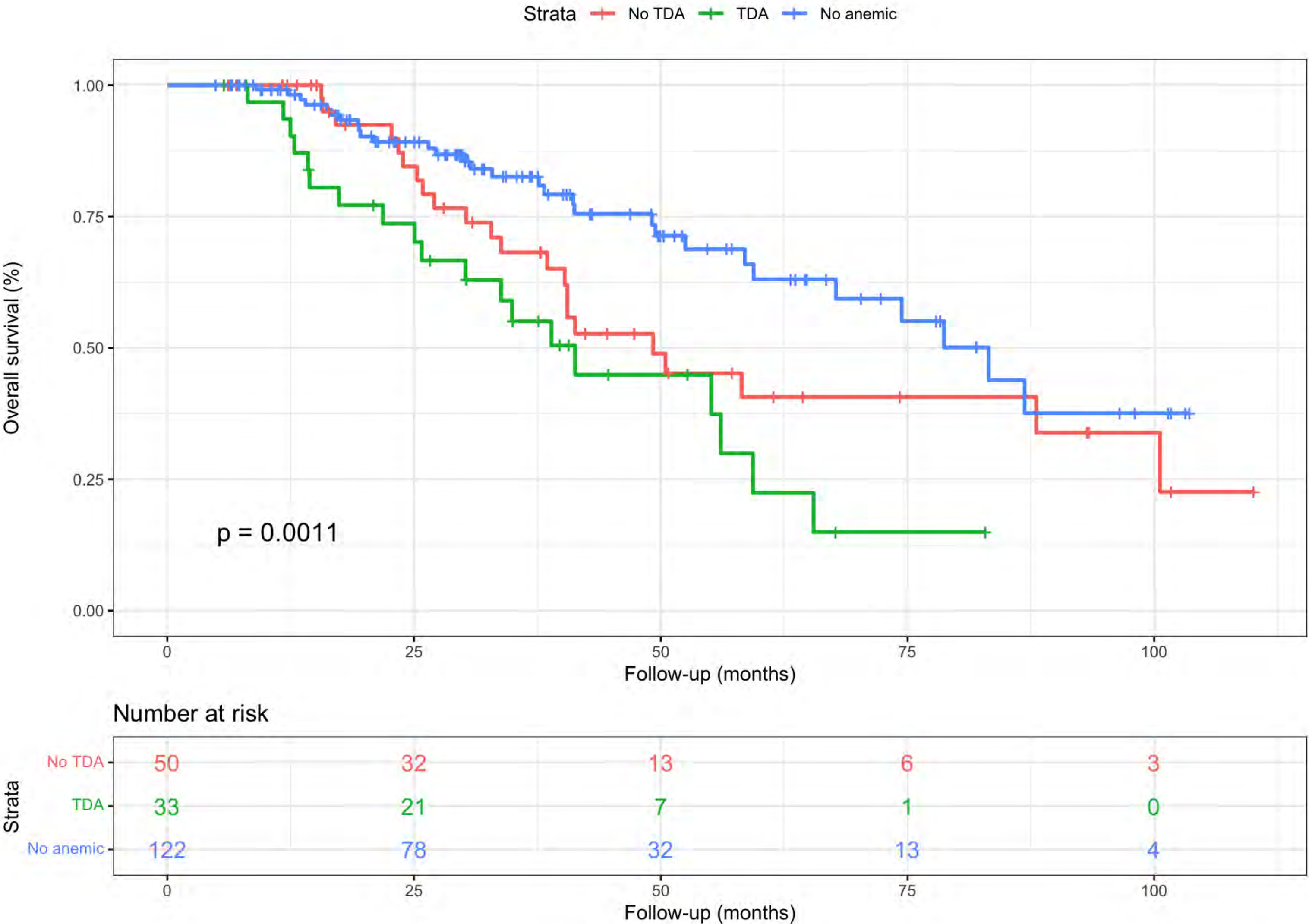
The revised IWG-ELN criteria proposed **3** strata for anemia definition, and we applied them to the RUXOREL-MF cohort.

Inclusion pts: Hb < 10 g/l, irrespective of gender

N = 205

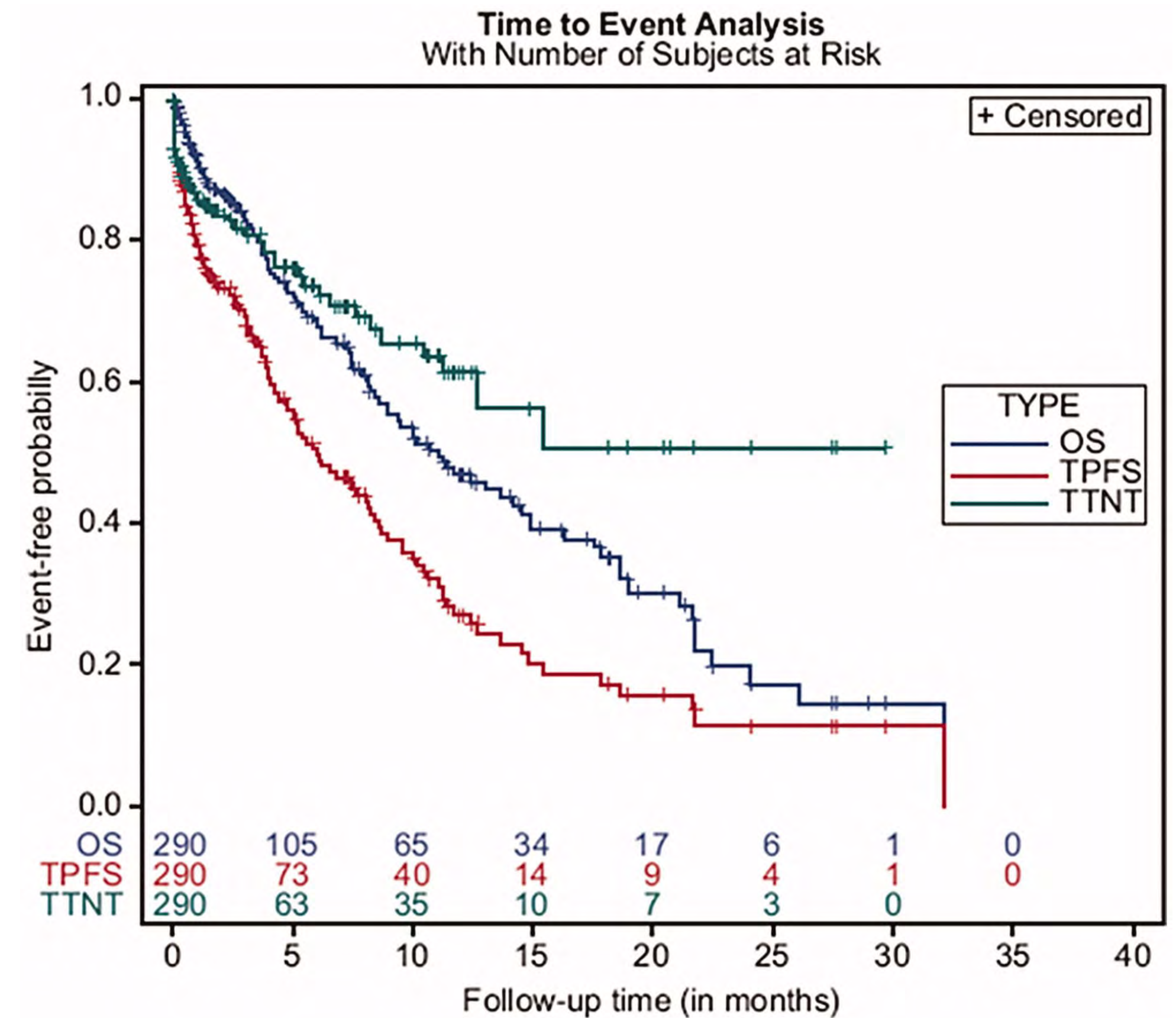
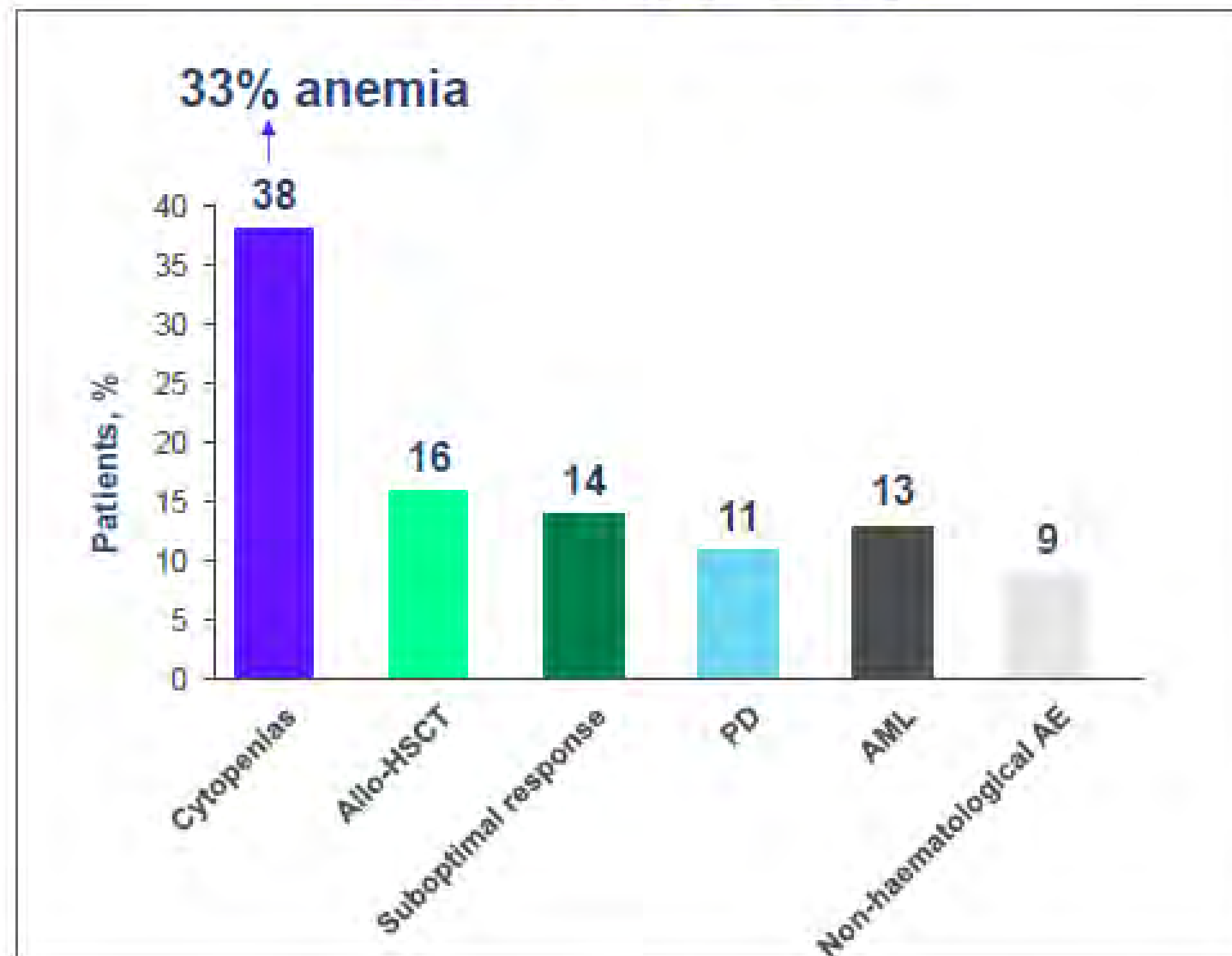
TDA 
for ≥ 3 units **GRC**/12 weeks.

Non-TDA
anemic subjects who do not qualify for TDA



Anemia is a main reason of RUX discontinuation in the real world and is associated with poor outcome

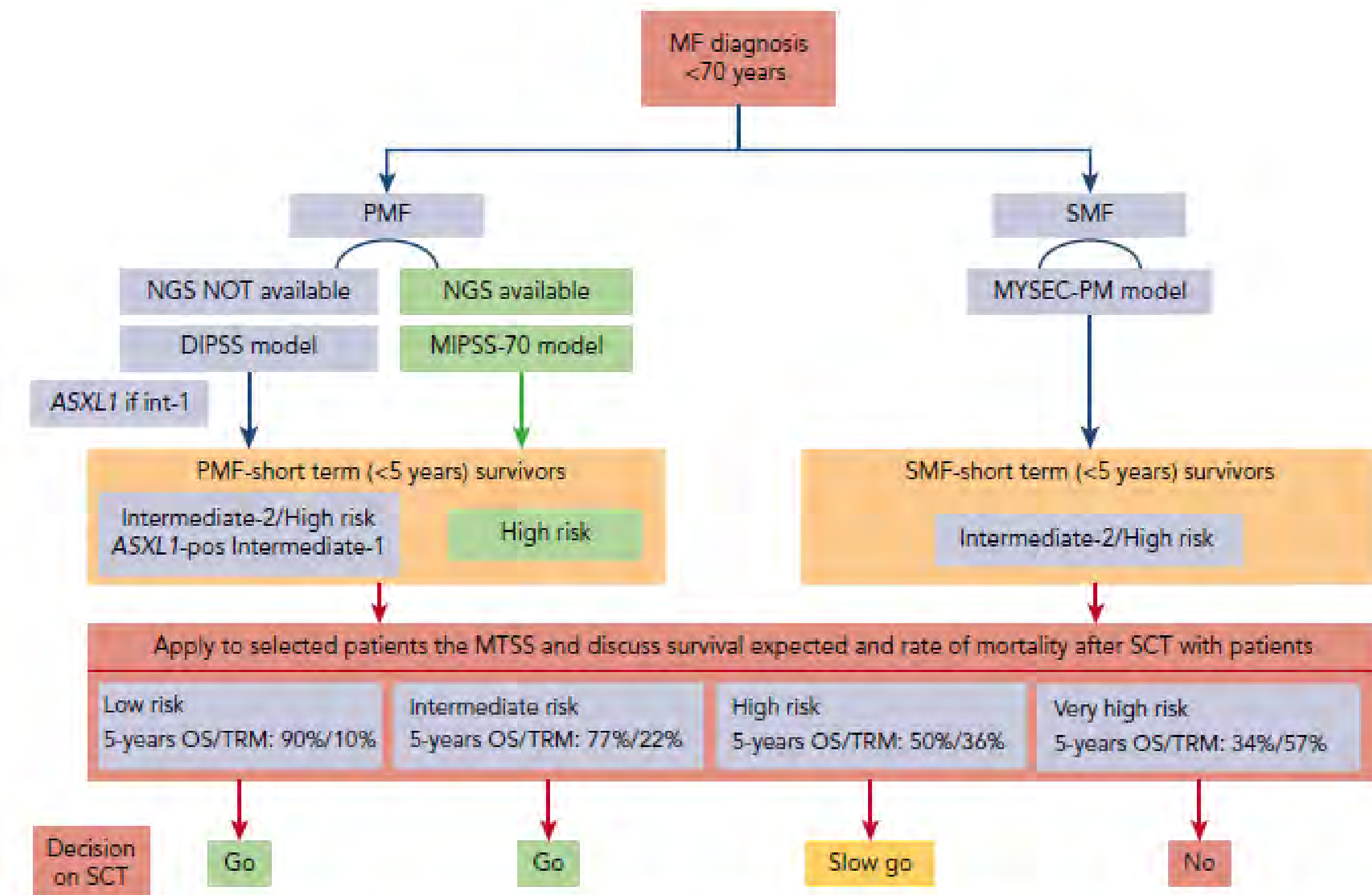
Moffitt study (Florida)



After rux discontinuation, median TPFS was 6.0 months, and median OS was 11.1 months

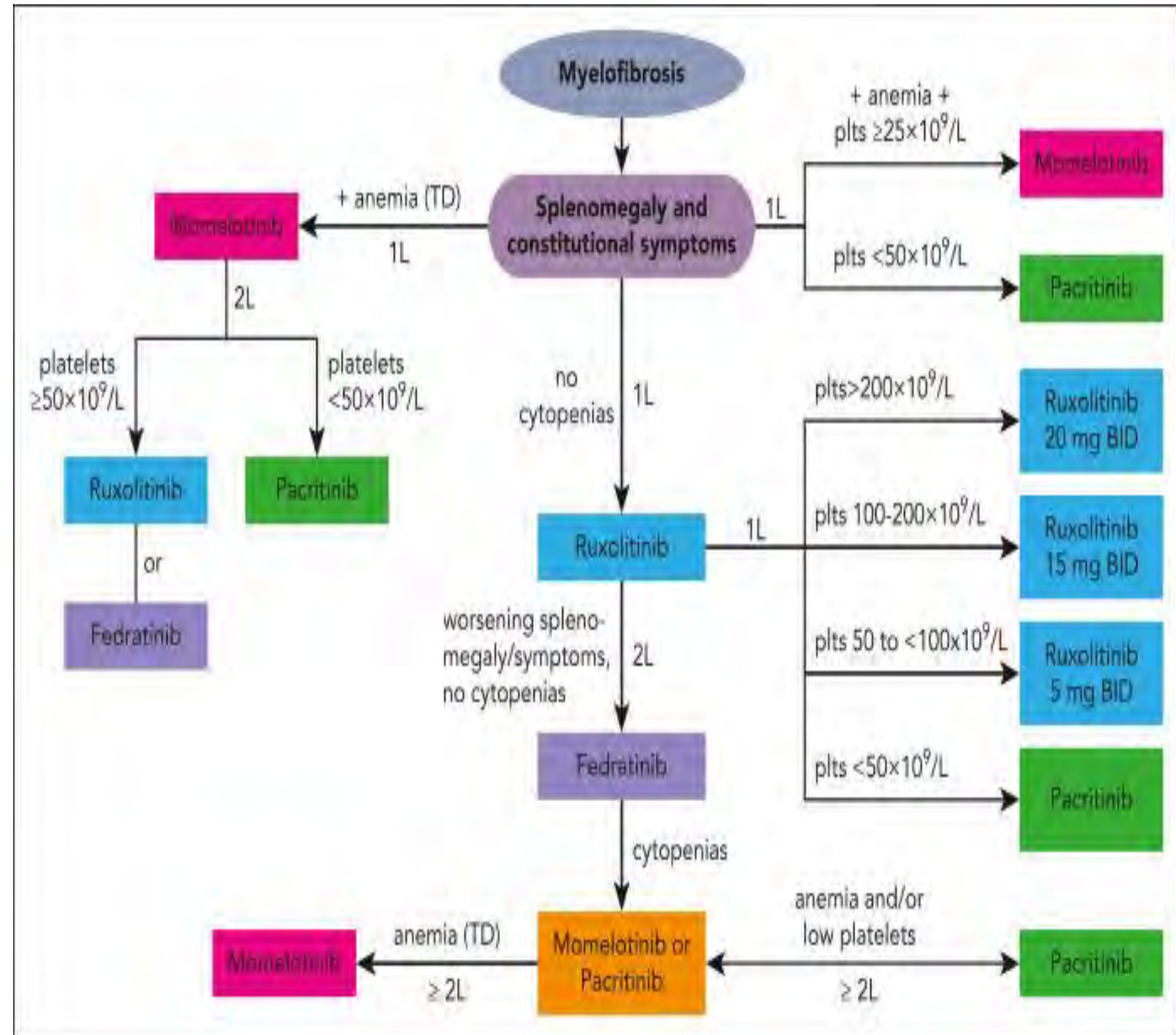
Take home messages

- ❑ La mielofibrosi è una malattia complessa che richiede un approccio diagnostico accurato multidisciplinare e una stratificazione prognostica puntuale
- ❑ Gli attuali strumenti diagnostici e prognostici consentono di individuare precocemente il paziente che può beneficiare di una procedura di trapianto di midollo vs candidabile a terapia medica



	Age	Hb, g/dL	PLT, x10 ⁹ /L	WBC, x10 ⁹ /L	Blast, %	P.S.	BMF	Driver mutation	Other mut.	Donor
DIPSS	>65 (1)	<10 (2)	-	>25 (1)	≥1% (1)	C.S. (1)		-	-	-
MIPSS-70	-	<10 (1)	<100 (2)	>25 (2)	≥2 (1)	C.S. (1)	≥2 (1)	Non CALR T1 (1)	HMR (1) />2 (2)	-
MYSEC-PM	Cont (0.15)	<11 (2)	<150 (1)	-	≥3 (2)	C.S. (1)		Non CALR (2)	-	-
MTSS	>57 (1)	-	<150 (1)	>25 (1)	-	K. < 90% (1)	-	Non-CALR/MPL (2)	ASXL1 (1)	MMU (2)

- ❑ I principali « clinical needs» del paziente devono guidare la scelta del trattamento
- ❑ La presenza di anemia alla diagnosi o durante il trattamento costituisce un fattore prognostico importante che impatta sull'outcome (OS e LFS), sulla risposta ai JAK inibitori (Ruxolitinib) e sulla probabilità di discontinuazione
- ❑ L'anemia pertanto costituisce uno dei elementi driver nella scelta del trattamento con JAK inibitori di I vs II generazione, oltre alla splenomegalia e ai sintomi costituzionali





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