



Myelofibrosis: Disease State Overview

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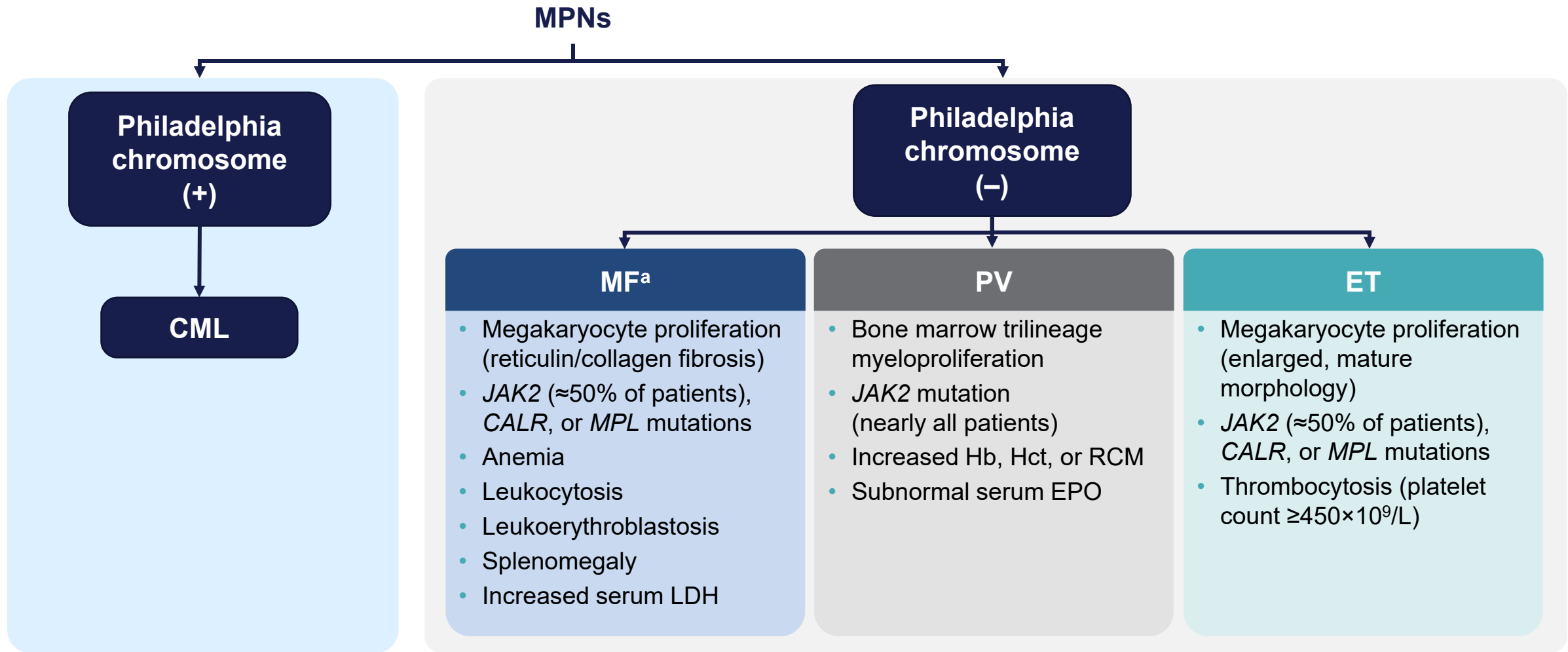
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BACK

MPN Epidemiology and Overview

MF, PV, and ET Are Philadelphia-Negative MPNs



^a MF includes primary MF, post-PV MF, and post-ET MF.

CALR, calreticulin; CML, chronic myeloid leukemia; EPO, erythropoietin; ET, essential thrombocythemia; Hb, hemoglobin; Hct, hematocrit; *JAK2*, Janus kinase 2; LDH, lactate dehydrogenase; MF, myelofibrosis; *MPL*, *MPL* proto-oncogene thrombopoietin receptor; MPNs, myeloproliferative neoplasms; PV, polycythemia vera; RCM, red cell mass.

Arber DA, et al. *Blood*. 2016;127:2391-2405.



MPNs Are Rare and Usually Develop Later in Life

	MF	PV	ET
Prevalence	4-6 cases per 100,000 ^{1,2}	44-57 cases per 100,000 ^{1,3}	38-57 cases per 100,000 ¹
Incidence	≈2-3 cases per 100,000 annually ^{1,2}	≈1-3 cases per 100,000 annually ⁴	2.0-2.4 cases per 100,000 ^{1,5}
Median age at diagnosis	>65 years and slightly more common in men than in women; ≈60% of affected patients are men ⁶	60 years; similar frequency in men and women ^{7,8}	60 years ⁵
Bone marrow abnormalities	Excess fibrous tissue and increase in megakaryocytes ⁹	Trilineage myeloproliferation and pleomorphic megakaryocytes ¹⁰	Increased megakaryocytes ⁹
Blood cell abnormalities	Reduced RBCs; ⁹ variable/increased WBCs ⁹	High Hct; ⁹ increased RCM ⁹	Elevated platelets; ⁹ no or few WBCs or RBCs ⁹
% with <i>JAK2</i> mutation	≈50% of patients ¹⁰	>99% ^{11,a}	≈50% of patients ¹⁰
Median survival	4.4-7.4 years ^{12,13}	14-15 years after diagnosis ^{8,13}	15-20 years ^{13,14}

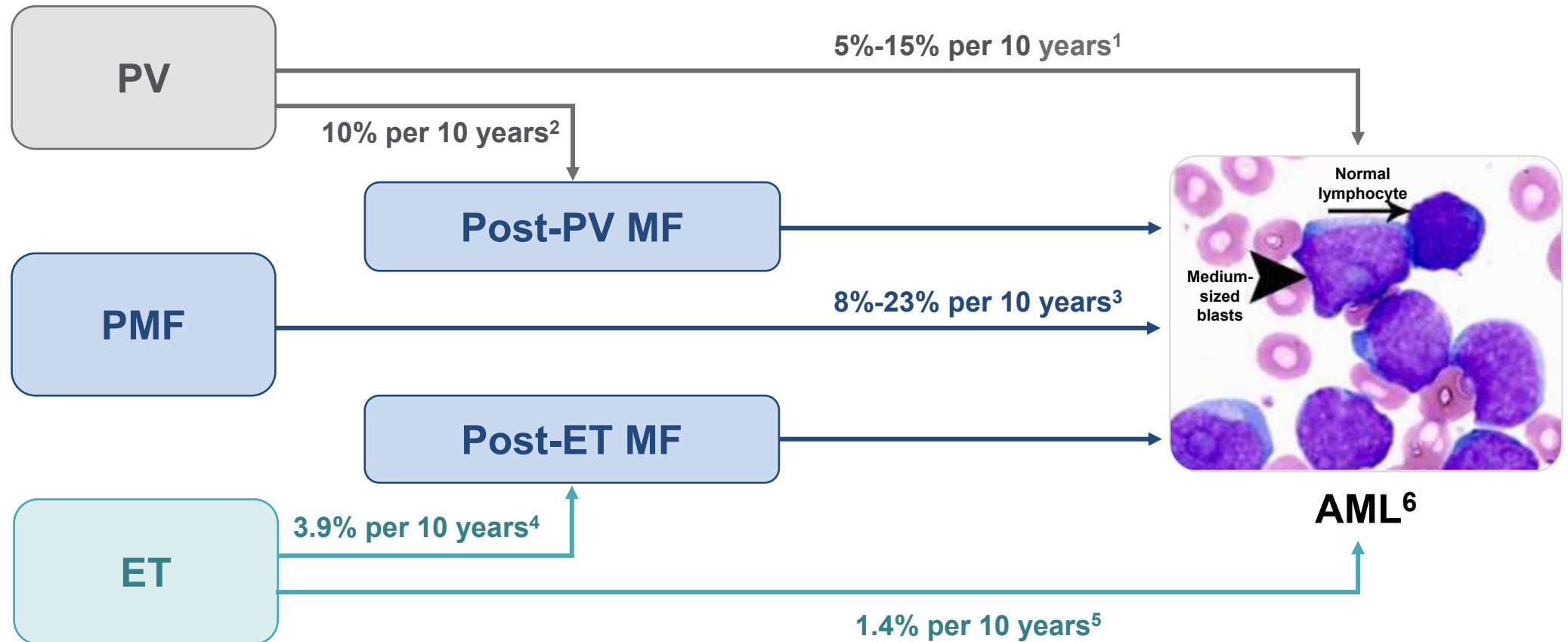
^a *JAK2* alterations include *JAK2* V617F mutations and *JAK2* exon 12 mutations.

RBCs, red blood cells; WBCs, white blood cells.

1. Mehta J, et al. *Leuk Lymphoma*. 2014;55:595-600. 2. Data on file, Incyte Corporation. 3. Stein B, et al. *J Clin Oncol*. 2015;33:3953-3960. 4. Johansson P. *Semin Thromb Hemost*. 2006;32:171-173. 5. Girodon F, et al. *Haematologica*. 2009;94:865-869. 6. Gangat N, et al. *J Clin Oncol*. 2010;29:392-397. 7. National Cancer Institute. Accessed Sep 2024. <http://seer.cancer.gov/seertools/hemelymph/51f6cf57e3e27c3994bd538d/>. 8. Tefferi A, et al. *Leukemia*. 2013;27:1874-1881. 9. Campbell PJ, Green AR. *N Engl J Med*. 2006;355:2452-2466. 10. Arber DA, et al. *Blood*. 2016;127:2391-2405. 11. Pardanani A, et al. *Leukemia*. 2007;21:1960-1963. 12. Cervantes F, et al. *J Clin Oncol*. 2012;30:2981-2987. 13. Szuber N, et al. *Mayo Clin Proc*. 2019;94:599-610. 14. Barbui T, et al. *J Clin Oncol*. 2011;29:761-770.



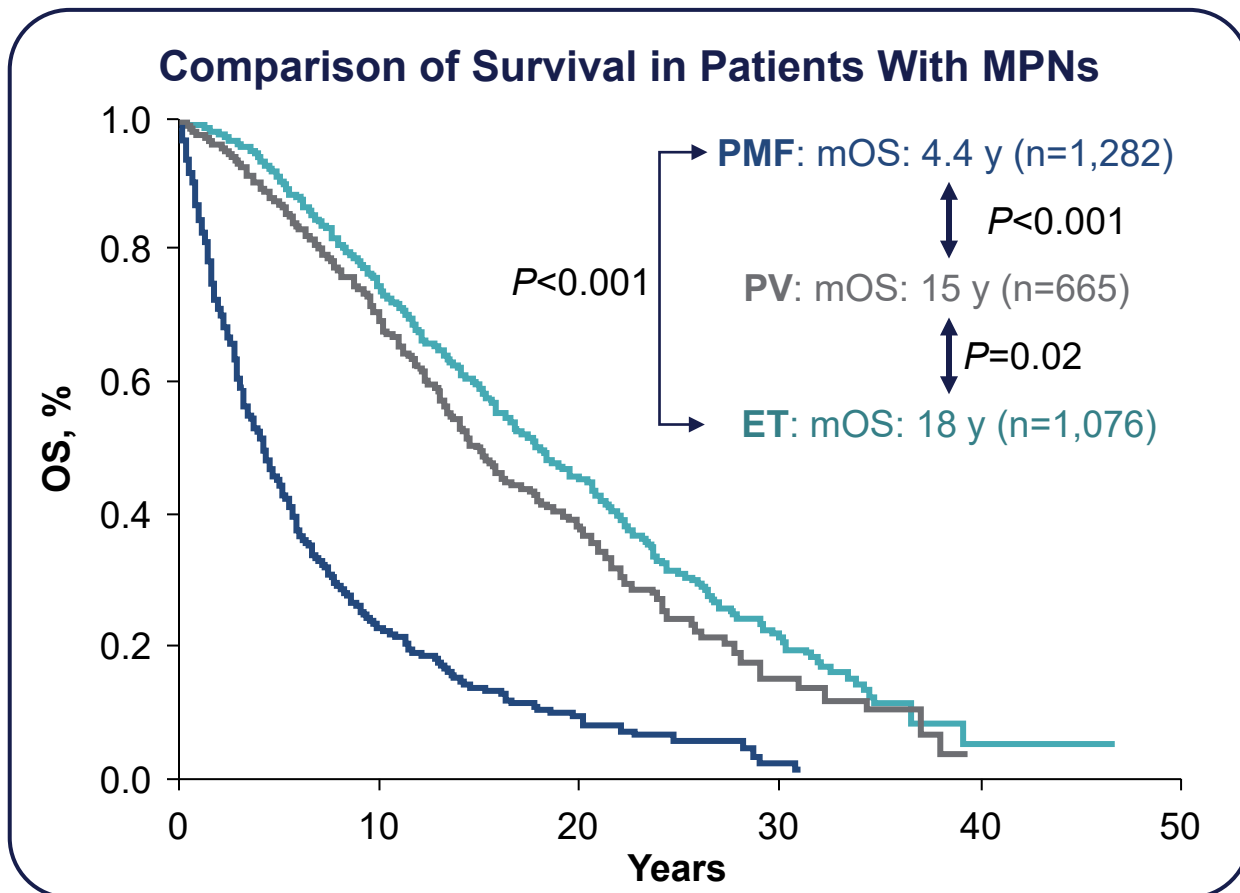
MPN Disease Progression and Transformation



AML, acute myeloid leukemia; PMF, primary myelofibrosis.

1. Finazzi G, et al. *Blood*. 2005;105:2664-2670. 2. Tefferi A. *Am J Hematol*. 2008;83:491-497. 3. Mesa RA, et al. *Blood*. 2005;105:973-977. 4. Cerquozzi S, Tefferi A. *Blood Cancer J*. 2015;5:e366. 5. Wolanskyj AP, et al. *Mayo Clin Proc*. 2006;81:159-166. 6. Reproduced with permission from Pathpedia. AML-M0, blood. Accessed Sep 2024. www.pathpedia.com/education/eatlas/histopathology/blood_cells/aml-m0_blood.aspx.

MPN Survival Outcomes



MPN	Median Survival (All Patients)
PMF	4.4 years
PV	15 years
ET	18 years

MPN	Median Survival (High-Risk Patients)
PMF	1.5 years
PV	9.6 years
ET	10.2 years

mOS, median overall survival; OS, overall survival.
 Szuber N, et al. *Mayo Clin Proc.* 2019;94:599-610.





BACK

Myelofibrosis

- Mechanism of Disease
- Disease Characteristics
- Clinical Work-Up, Diagnosis, and Stratification



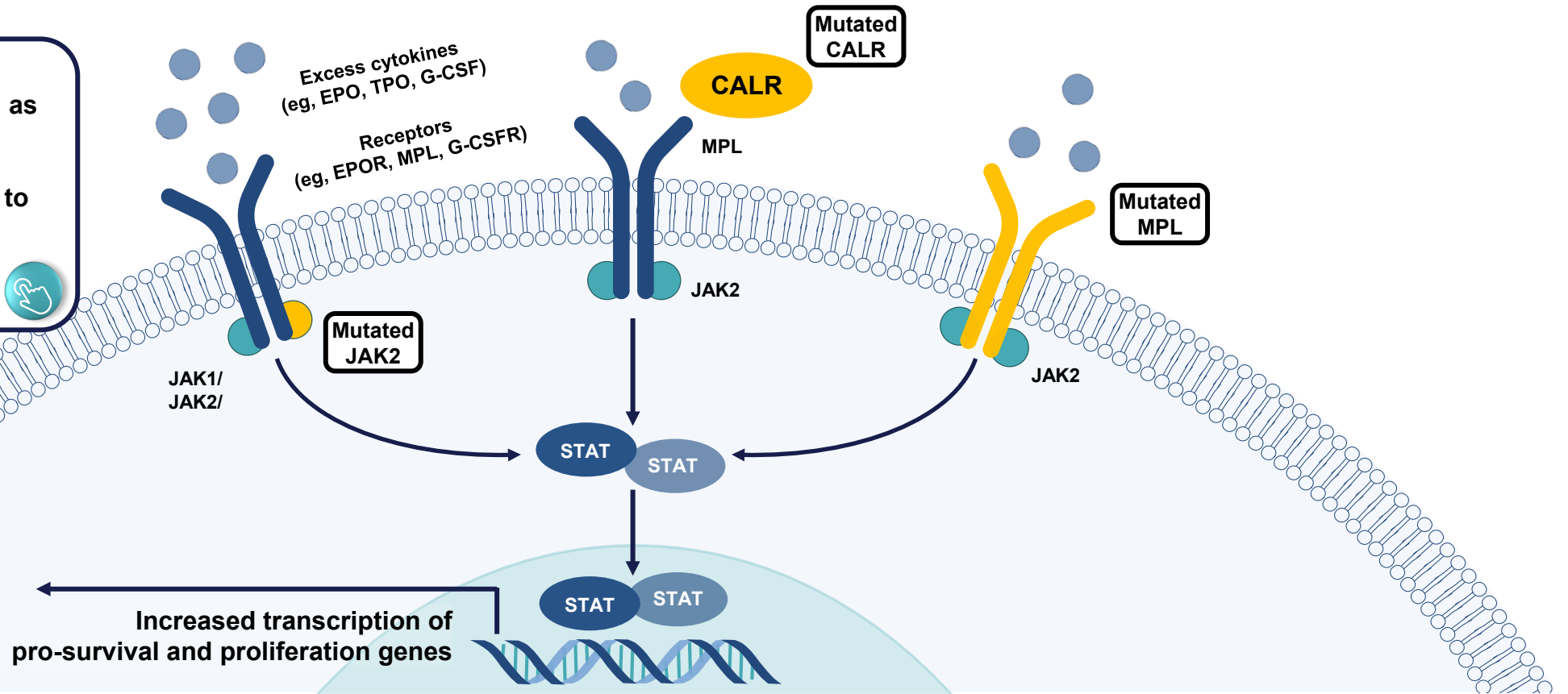
BACK

Mechanism of Disease

Myelofibrosis

Overactive JAK Signaling Is Present in All Patients With MF, Leading to Abnormal Blood Cell Production

The JAK-STAT pathway is important for hematopoiesis, as EPO and TPO signal through JAK2.^{1,2} In patients with MF, numerous factors contribute to dysregulated JAK signaling, resulting in an abnormal production of blood cells¹⁻⁵



CALR, calreticulin; EPO, erythropoietin; EPOR, erythropoietin receptor; G-CSF, granulocyte colony-stimulating factor; G-CSFR, granulocyte colony-stimulating factor receptor; JAK, Janus kinase; MF, myelofibrosis; MPL, thrombopoietin receptor; SOCS, suppressor of cytokine signaling; STAT, signal transducer and activator of transcription; TPO, thrombopoietin; TYK2, tyrosine protein kinase 2.

1. Quintás-Cardama A, et al. *Nat Rev Drug Discov*. 2011;10:127-140. 2. Klampfl T, et al. *N Engl J Med*. 2013;369:2379-2390. 3. Vainchenker W, et al. *Blood*. 2011;118:1723-1735. 4. Vainchenker W, Kralovics R. *Blood*. 2017;129:667-679. 5. Jang MA, Choi CW. *Korean J Intern Med*. 2020;35:1-11.

Overactive JAK Signaling Is Present in All Patients With MF, Leading to Abnormal Blood Cell Production

The JAK-STAT pathway is important for hematopoiesis, as EPO and TPO signal through JAK2.^{1,2} In patients with MF, numerous factors contribute to dysregulated JAK signaling, resulting in an abnormal production of blood cells¹⁻⁵



- Factors that may lead to dysregulated JAK signaling include:¹⁻⁴
 - JAK2 mutations
 - Receptor mutations (eg, *MPL* mutations)
 - *CALR* mutations
 - Excess cytokines (eg, EPO, TPO, G-CSF)
 - Increased *JAK1* signaling
 - Impaired regulatory signaling mechanisms (eg, SOCS)



Increased transcription of pro-survival and proliferation genes

CALR, calreticulin; EPO, erythropoietin; EPOR, erythropoietin receptor; G-CSF, granulocyte colony-stimulating factor; G-CSFR, granulocyte colony-stimulating factor receptor; JAK, Janus kinase; MF, myelofibrosis; MPL, thrombopoietin receptor; SOCS, suppressor of cytokine signaling; STAT, signal transducer and activator of transcription; TPO, thrombopoietin; TYK2, tyrosine protein kinase 2.

1. Quintás-Cardama A, et al. *Nat Rev Drug Discov*. 2011;10:127-140. 2. Klampfl T, et al. *N Engl J Med*. 2013;369:2379-2390. 3. Vainchenker W, et al. *Blood*. 2011;118:1723-1735. 4. Vainchenker W, Kralovics R. *Blood*. 2017;129:667-679. 5. Jang MA, Choi CW. *Korean J Intern Med*. 2020;35:1-11.



BACK

Disease Characteristics

Myelofibrosis

Abnormal Blood Counts

Anemia¹

- Anemia is the most common laboratory complication in PMF
 - 35% of patients with MF are anemic (Hb <10 g/dL) at diagnosis; by 3.5 years postdiagnosis, this increases to 47%
- Anemia is a negative prognostic factor and is difficult to treat
 - There is only a 10%-30% success rate, and efficacy is often temporary

Thrombocytosis/Thrombocytopenia²⁻⁴

- Thrombocytosis is the result of aberrant TPO signaling that causes megakaryocyte abnormalities
 - Mutations in *c-MPL*, *JAK2*, and *CALR* are associated with overactive TPO pathway activity, which leads to increased megakaryocyte proliferation and subsequent thrombocytosis
 - Abnormal megakaryocytes produce high levels of cytokines/growth factors, leading to progressive bone marrow fibrosis
- Thrombocytopenia occurs with regular frequency in patients with MF
 - ≈16%-26% of patients have platelet counts <100×10⁹/L, and ≈11%-16% of patients have platelet counts <50×10⁹/L
 - Thrombocytopenia in MF is attributed to ineffective megakaryocytopoiesis caused by excessive bone marrow fibrosis, splenomegaly, and autoimmune reactions against platelets

c-MPL, c-MPL proto-oncogene thrombopoietin receptor; Hb, hemoglobin; PMF, primary myelofibrosis.

1. Guglielmelli P, Vannucchi AM. *Leuk Res*. 2013;37:1429-1431. 2. Vainchenker W, Kralovics R. *Blood*. 2017;129:667-679. 3. Deutsch VR, Tomer A. *Br J Haematol*. 2006;134:453-466.

4. Al-Ali HK, Vannucchi AM. *Ann Hematol*. 2017;96:537-548.

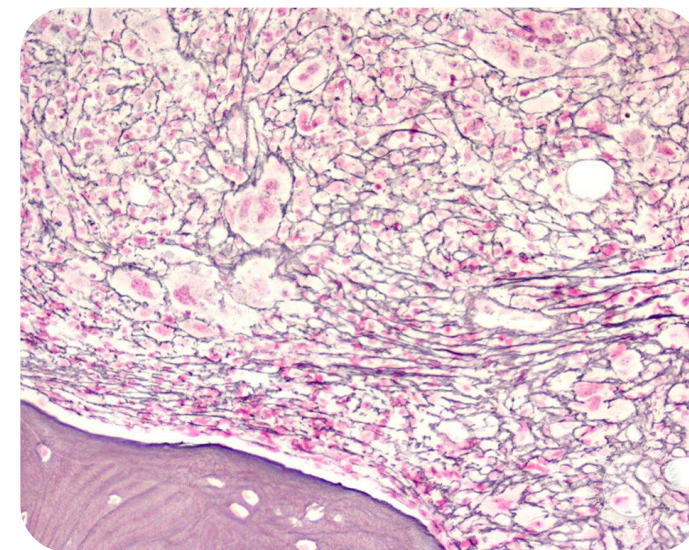
Bone Marrow Fibrosis Is a Central Pathologic Feature of PMF¹

- Characterized by an increase in reticulin and, potentially, collagen fibers in the bone marrow
- Studies suggest a link between fibrosis grade and other clinical manifestations of PMF (eg, symptoms, splenomegaly, cytopenias), as well as prognosis¹⁻³

Bone Marrow Fibrosis Grading by European Consensus⁴

Grading	Description
MF-0	<ul style="list-style-type: none">• Scattered linear reticulin with no intersections (crossovers) corresponding to normal bone marrow
MF-1	<ul style="list-style-type: none">• Loose network of reticulin with many intersections, especially in perivascular areas
MF-2	<ul style="list-style-type: none">• Diffuse and dense increase in reticulin with extensive intersections, occasionally with only focal bundles of collagen and/or focal osteosclerosis
MF-3	<ul style="list-style-type: none">• Diffuse and dense increase in reticulin with extensive intersections with coarse bundles of collagen, often associated with significant osteosclerosis

Bone Marrow Reticulin Fibrosis⁵

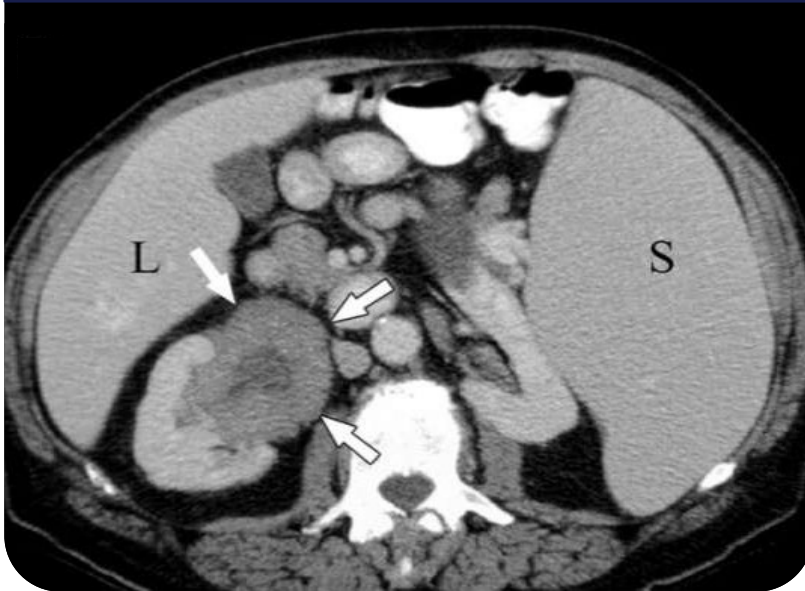


Bone marrow fibrotic response and megakaryocytic hyperplasia in PMF

1. Zahr AA, et al. *Haematologica*. 2016;101:660-671. 2. Kröger N, et al. *Biol Blood Marrow Transplant*. 2014;20:812-815. 3. Guglielmelli P, et al. *Am J Hematol*. 2016;91:918-922. 4. Thiele J, et al. *Haematologica*. 2005;90:1128-1132. 5. Lazarchick J. Accessed Sep 2024. <http://imagebank.hematology.org/image/4100/marrow-fibrosis-in-primary-myelofibrosis--2>.

Splenomegaly

Extramedullary Hematopoiesis:
a reactive process that occurs because of
MF and commonly involves the spleen^{1,2,a}



Contrast-enhanced CT scan of the upper abdomen showing massive splenomegaly (S), the liver (L), and a renal pelvic mass (arrows) suggesting extramedullary hematopoiesis

Splenomegaly^b



**Increased Morbidity and
Decreased QOL^{3,4}**

Consequences of
splenomegaly include:

- Abdominal pain and discomfort
- Bloating, early satiety, and cachexia
- Portal hypertension
- Splenic infarct
- Splenic sequestration and exacerbation of cytopenias
- Engraftment delay in transplant candidates

^a Figure adapted from Choi H, et al. *Radiology*. 2004;231:52-56. Permission to use granted by RSNA. ^b Photograph courtesy of Srdan Verstovsek, MD, PhD. MD Anderson Cancer Center. Houston, TX.

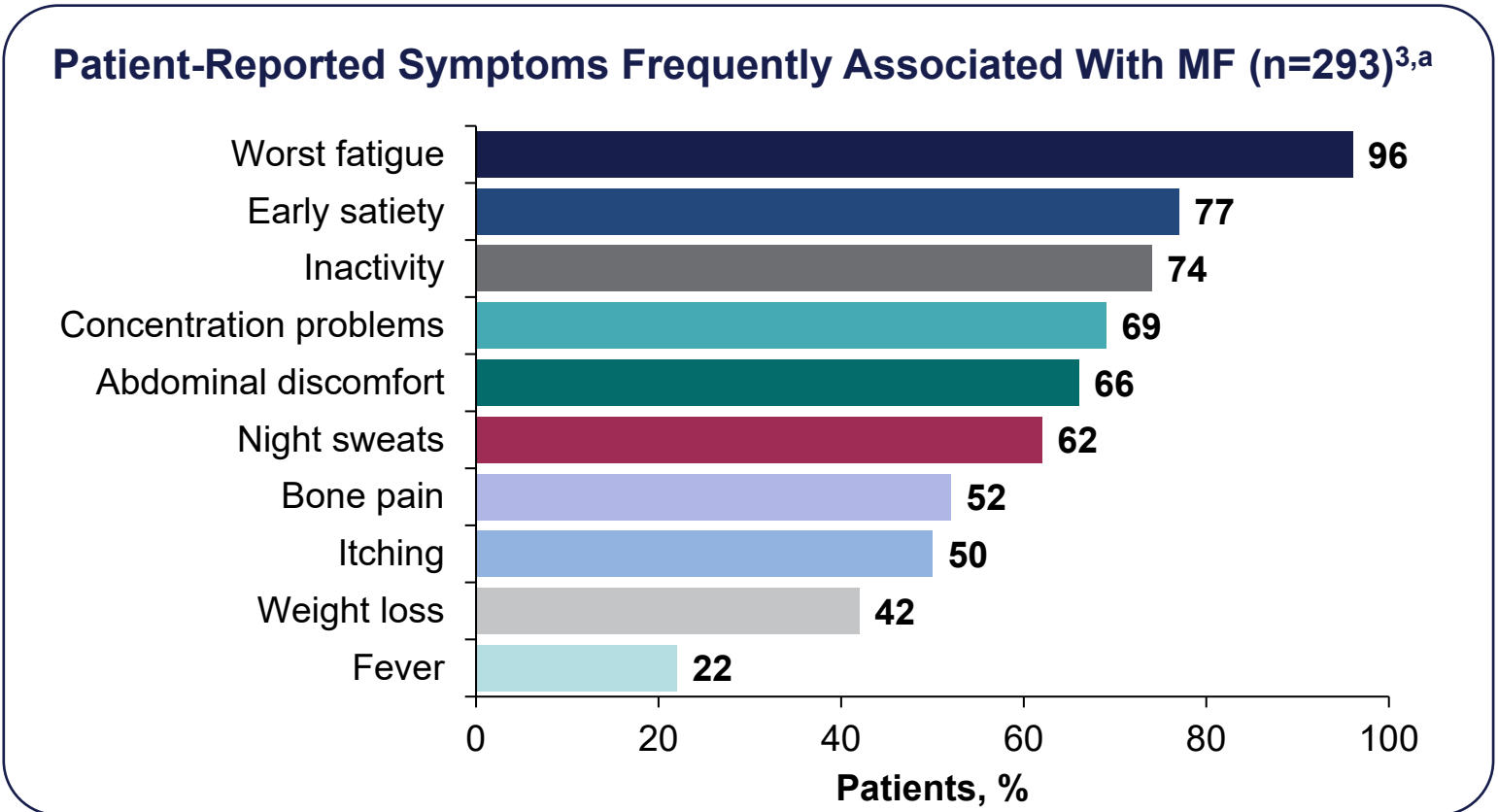
CT, computed tomography; QOL, quality of life.

1. Georgiades CS, et al. *AJR Am J Roentgenol*. 2002;179:1239-1243. 2. Choi H, et al. *Radiology*. 2004;231:52-56. 3. Randhawa J, et al. *J Hematol Oncol*. 2012;5:43.

4. Mesa RA, et al. *Cancer*. 2006;107:361-370.

Patients Often Report Symptoms Related to Splenomegaly and Chronic Inflammation^{1,2}

- MF-related symptoms have been shown to reduce QOL in up to 42% of patients³
- The most common symptoms reported are fatigue, early satiety, and inactivity^{3,a}



^a Symptom assessment was conducted using the BFI, MPN-SAF, and the EORTC QLQ-C30. The MPN-SAF TSS was then constructed using the 10 items that were deemed most clinically relevant. Symptom severity was rated on a scale of 0 (absent/as good as it can be) to 10 (worst imaginable/as bad as it can be). The MPN-SAF TSS has a possible range of 0 to 100, with 100 representing the highest level of symptom severity.

BFI, Brief Fatigue Inventory; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30; MPN-SAF, Myeloproliferative Neoplasm Symptom Assessment Form; TSS, Total Symptom Score.

1. Harrison CN, et al. *Ann Hematol.* 2017;96:1653-1665. 2. Scherber R, et al. *Blood.* 2011;118:401-408. 3. Emanuel RM, et al. *J Clin Oncol.* 2012;30:4098-4103.





BACK

Clinical Work-Up, Diagnosis, and Stratification

Myelofibrosis

MF Diagnosis Requires a Comprehensive Evaluation



History and Physical^{1,2}

- Constitutional symptoms: weight loss, fever, and night sweats
 - Other symptoms, including fatigue, cachexia, bone pain, and pruritus
- History of thrombosis or bleeding
- Presence of marked hepatosplenomegaly



Blood Tests^{1,3}

- Peripheral blood smear showing leukoerythroblastosis or blasts
- Anemia (Hb <10 g/dL)
- Thrombocytosis or thrombocythemia
- Leukopenia or leukocytosis
- *BCR-ABL* negative and presence of *JAK2* V617F, *CALR*, *MPL*, *JAK2* exon 12 mutations, trisomy 9, or del(13q)



Bone Marrow Biopsy³

- Bone marrow biopsy showing fibrosis and abnormal cytogenetics
- Careful analysis of biopsy sample is essential for distinguishing MF from other closely related MPNs

Following a comprehensive work-up and evaluation, a differential diagnosis might include:³

Secondary lymphoma • CML • Metastatic cancer • MDS • Hairy cell leukemia • Other MPNs

BCR-ABL, breakpoint cluster region–Abelson murine leukemia viral oncogene homologue; CML, chronic myeloid leukemia; del, deletion; MDS, myelodysplastic syndrome; MPNs, myeloproliferative neoplasms.

1. Tefferi A. *Am J Hematol*. 2016;91:1261-1271. 2. Gangat N, et al. *J Clin Oncol*. 2011;29:392-397. 3. Arber DA, et al. *Blood*. 2016;127:2391-2405.

2016 WHO Diagnostic Criteria: Pre-PMF

Pre-PMF WHO Criteria: Must meet all 3 major AND at least 1 minor^a

Major

- Megakaryocytic proliferation and atypia, without reticulin fibrosis grade >1, accompanied by increased age-adjusted bone marrow cellularity, granulocytic proliferation, and often decreased erythropoiesis
- Not meeting WHO criteria for ET, PV, *BCR-ABL1*+ CML, myelodysplastic syndromes, or other myeloid neoplasms
- Presence of *JAK2*, *CALR*, or *MPL* mutation or, in the absence of these mutations, presence of another clonal marker,^b or absence of minor reactive bone marrow reticulin fibrosis^c

Minor

- Anemia not attributed to a comorbid condition
- Palpable splenomegaly
- LDH increased to above upper normal limit of institutional reference range
- Leukocytosis $\geq 11 \times 10^9/L$

^a Confirmed in 2 consecutive determinations. ^b In the absence of any of the 3 major clonal mutations, the search for the most frequent accompanying mutations is of help in determining the clonal nature of the disease. ^c Minor (grade 1) reticulin fibrosis secondary to infection, autoimmune disorder, or other chronic inflammatory conditions, hairy cell leukemia or other lymphoid neoplasm, metastatic malignancy, or toxic (chronic) myelopathies.

ET, essential thrombocythemia; LDH, lactate dehydrogenase; PV, polycythemia vera; WHO, World Health Organization. Arber DA, et al. *Blood*. 2016;127:2391-2405.

2016 WHO Diagnostic Criteria: Overt Primary MF

MF WHO Criteria: Must meet all 3 major AND at least 1 minor^a

Major

- Presence of megakaryocytic proliferation and atypia, accompanied by either reticulin and/or collagen fibrosis grades 2 or 3
- Not meeting WHO criteria for ET, PV, *BCR-ABL1*+ CML, myelodysplastic syndromes, or other myeloid neoplasms
- Presence of *JAK2*, *CALR*, or *MPL* mutation or, in the absence of these mutations, presence of another clonal marker,^b or absence of reactive MF^c

Minor

- Anemia not attributed to a comorbid condition
- Palpable splenomegaly
- LDH increased to above upper normal limit of institutional reference range
- Leukoerythroblastosis
- Leukocytosis $\geq 11 \times 10^9/L$

^a Confirmed in 2 consecutive determinations. ^b In the absence of any of the 3 major clonal mutations, the search for the most frequent accompanying mutations is of help in determining the clonal nature of the disease. ^c Bone marrow fibrosis secondary to infection, autoimmune disorder, or other chronic inflammatory conditions, hairy cell leukemia or other lymphoid neoplasm, metastatic malignancy, or toxic (chronic) myelopathies. Arber DA, et al. *Blood*. 2016;127:2391-2405.

IWG-MRT Diagnostic Criteria: Post-PV MF

MF IWG-MRT Criteria: Must meet all major AND at least 2 minor

Major

- Documentation of a previous diagnosis of PV as defined by the WHO criteria
- Bone marrow fibrosis grade 2/3 (on a scale of 0-3)^a or grade 3/4 (on a scale of 0-4)^{b,c}

Minor

- Anemia^d or sustained loss of requirement of either phlebotomy (in the absence of cytoreductive therapy) or cytoreductive treatment for erythrocytosis
- A leukoerythroblastic peripheral blood picture
- Increasing splenomegaly, defined as either an increase in palpable splenomegaly of ≥ 5 cm (distance to the tip of the spleen from the left costal margin) or the appearance of a newly palpable splenomegaly
- Development of ≥ 1 of 3 constitutional symptoms: $>10\%$ weight loss in 6 months, night sweats, unexplained fever (>37.5 °C)

^a Diffuse, often coarse fiber network with no evidence of collagenization (negative trichrome stain) or diffuse, coarse fiber network with areas of collagenization (positive trichrome stain). Grade 3/4 according to the standard classification. ^b Diffuse and dense increase in reticulin with extensive intersections, occasionally with only focal bundles of collagen and/or focal osteosclerosis or diffuse and dense increase in reticulin with extensive intersections with coarse bundles of collagen, often associated with significant osteosclerosis. ^c Grade 2/3 according to the European classification. ^d Below the reference range for appropriate age, sex, gender, and altitude considerations.
IWG-MRT, International Working Group–Myelofibrosis Research and Treatment.
Barosi G, et al. *Leukemia*. 2008;22:437-438.

IWG-MRT Diagnostic Criteria: Post-ET MF

MF IWG-MRT Criteria: Must meet all major AND at least 2 minor

Major

- Documentation of a previous diagnosis of ET as defined by the WHO criteria
- Bone marrow fibrosis grade 2/3 (on a scale of 0-3)^a or grade 3/4 (on a scale of 0-4)^{b,c}

Minor

- Anemia^d and a ≥ 2 mg/mL decrease from baseline Hb level
- A leukoerythroblastic peripheral blood picture
- Increasing splenomegaly, defined as either an increase in palpable splenomegaly of ≥ 5 cm (distance to the tip of the spleen from the left costal margin) or the appearance of a newly palpable splenomegaly
- Increased LDH (above reference level)
- Development of ≥ 1 of 3 constitutional symptoms: $>10\%$ weight loss in 6 months, night sweats, unexplained fever ($>37.5^{\circ}\text{C}$)

^a Diffuse, often coarse fiber network with no evidence of collagenization (negative trichrome stain) or diffuse, coarse fiber network with areas of collagenization (positive trichrome stain). Grade 3/4 according to the standard classification. ^b Diffuse and dense increase in reticulin with extensive intersections, occasionally with only focal bundles of collagen and/or focal osteosclerosis or diffuse and dense increase in reticulin with extensive intersections with coarse bundles of collagen, often associated with significant osteosclerosis. ^c Grade 2/3 according to the European classification. ^d Below the reference range for appropriate age, sex, gender, and altitude considerations. Barosi G, et al. *Leukemia*. 2008;22:437-438.

Various MF Prognostic Scales Are Available to Assess Risk and Median Survival

- Proper risk stratification of patients with MF is recommended for optimal disease treatment and management^{1,2}
- Several prognostic scoring systems have been developed to appropriately stratify patients with MF^{1,2}

Risk Factor ^{1,2,a}	Prognostic Scale and Points per Risk Factor		
	IPSS (2009) ^{3,b}	DIPSS (2010) ^{4,c}	DIPSS-Plus (2011) ^{5,c,d}
Age >65 years	1	1	1
Constitutional symptoms (weight loss, fever, night sweats)	1	1	1
Anemia (Hb <10 g/dL)	1	2	1
WBC count >25×10 ⁹ /L	1	1	1
Circulating blast ≥1%	1	1	1
Platelets <100×10 ⁹ /L	–	–	1
RBC transfusion need	–	–	1
Unfavorable karyotype (complex karyotype or a single or 2 abnormalities including +8, -7/7q-, i(17q), -5/5q-, 12p-, inv(3), or 11q23)	–	–	1

^a Risk factors are related to underlying disease and not pharmacotherapy. ^b For use at diagnosis. ^c For use at follow-up. ^d Scoring system differs for DIPSS and DIPSS-Plus.

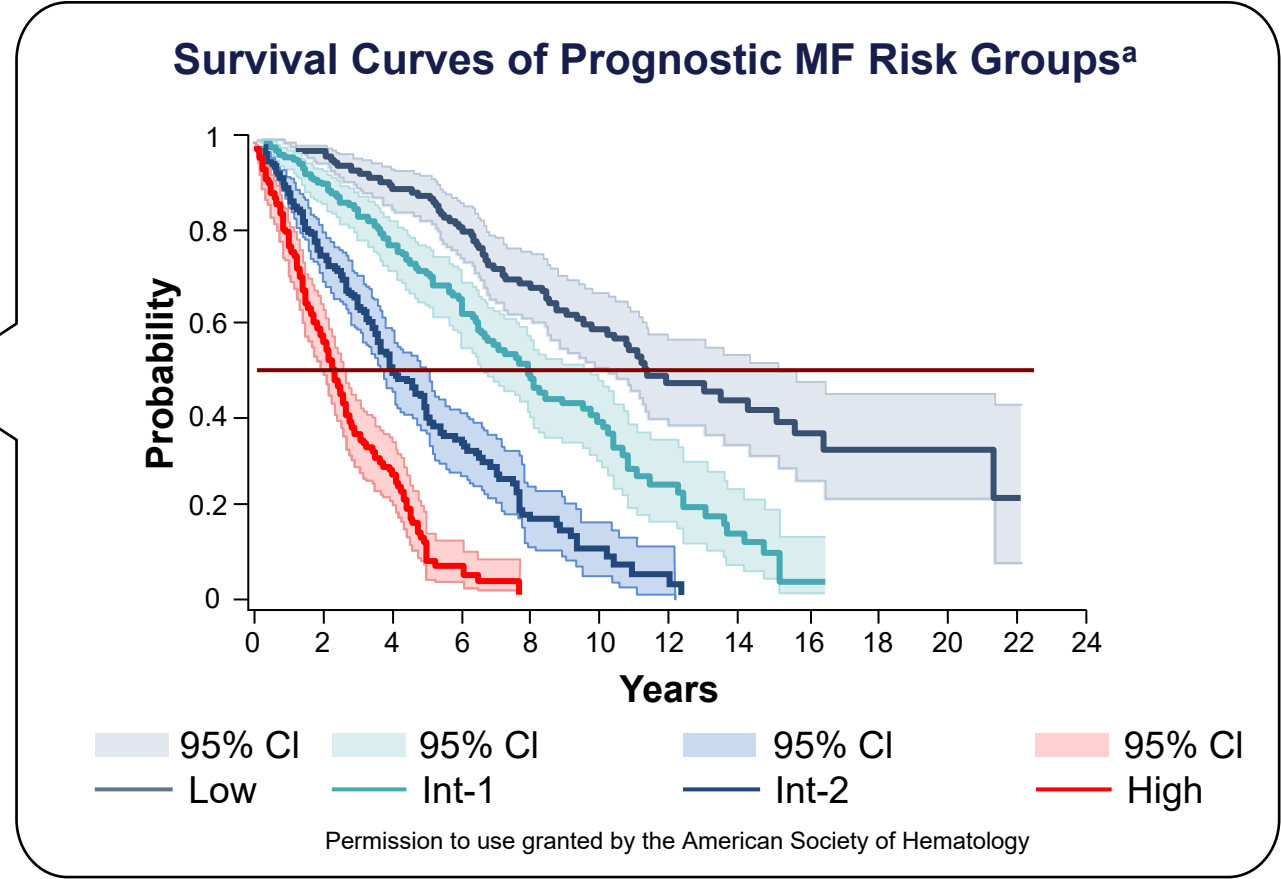
DIPSS-Plus was more recently designed but less widely used than the other scoring systems.

DIPSS, Dynamic International Prognostic Scoring System; IPSS, International Prognostic Scoring System; RBC, red blood cell; WBC, white blood cell.

1. Vannucchi AM, et al. *Hematology Am Soc Hematol Educ Program*. 2011;2011:222-230. 2. Bose P, Verstovsek S. *Cancer*. 2016;122:681-692. 3. Cervantes F, et al. *Blood*. 2009;113:2895-2901. 4. Passamonti F, et al. *Blood*. 2010;116:2857-2858. 5. Gangat N, et al. *J Clin Oncol*. 2011;29:392-397.

MF Risk at Diagnosis Is Assigned Based on the Number of IPSS Risk Factors

IPSS Risk and Survival		
Risk Category	Number of Risk Factors	Median Survival, y
High	≥3	2.3
Int-2	2	4.0
Int-1	1	7.9
Low	0	11.3



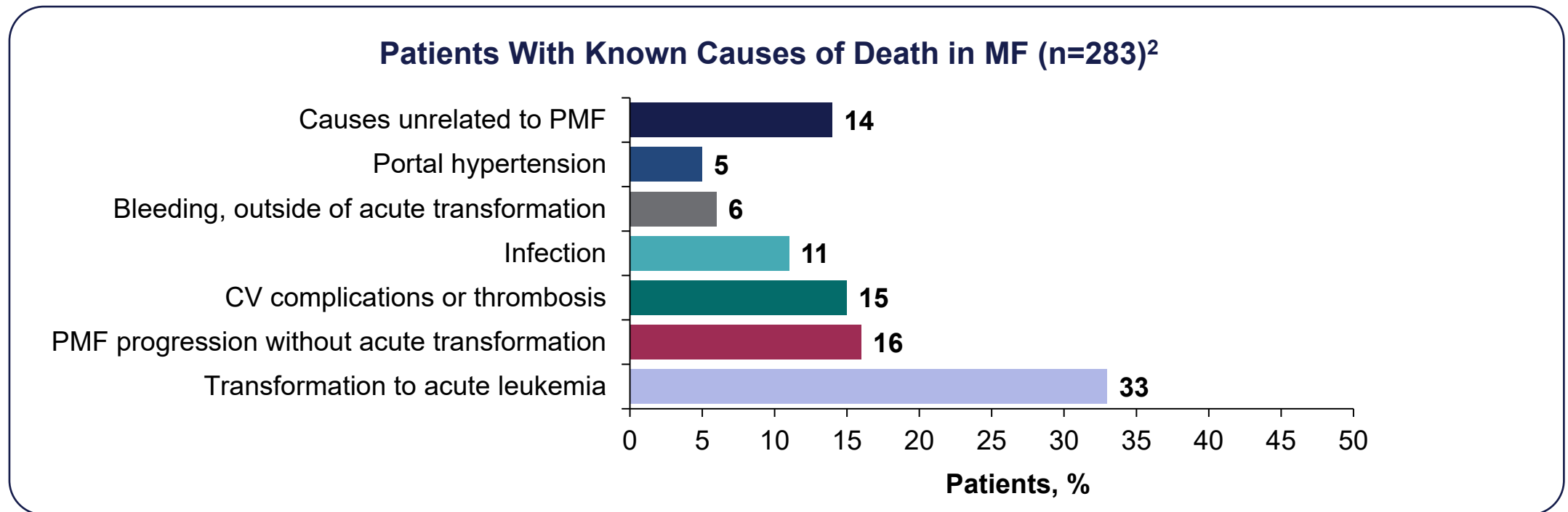
The number of risk factors present at diagnosis is prognostic for median survival

^a Includes PMF, post-ET MF, and post-PV MF data points.
 CI, confidence interval; Int-1, Intermediate 1; Int-2, Intermediate 2.
 Cervantes F, et al. *Blood*. 2009;113:2895-2901.



Survival Trends and Known Causes of Mortality in PMF

- Patients with MPNs have a higher overall mortality than matched controls¹
- In a study of 802 patients with primary MF:^{2,a}
 - 541 patients (67%) had died at the time of analysis, with a median survival of 5.2 years (95% CI, 4.9-5.9 years)
 - Based on the known causes of death (n=283), 86% were caused by complications related to MF²



^a In 4 European countries, PMF was diagnosed in 802 patients who were compared for the presentation of features and survival according to the diagnostic periods 1980-1995 and 1996-2007. CV, cardiovascular.

1. Hultcrantz M, et al. *J Clin Oncol*. 2015;33:2288-2295. 2. Cervantes F, et al. *J Clin Oncol*. 2012;30:2981-2987.

Management Goals^{1,2}



Reduce Splenomegaly

Reducing splenomegaly may decrease associated morbidities and improve QOL^{3,4}



Improve Symptoms

In a survey of 207 patients with MF, 81% of patients reported that their MF-related symptoms reduced their QOL^{5,a}



Alleviate Anemia

Anemia is the most common laboratory abnormality and is a negative prognostic factor⁶

Management goals may evolve over time and may vary based on risk¹

^a Based on an analysis of the MPN Landmark survey, a web-based survey that included 65 multiple-choice questions with an estimated completion time of 20-25 minutes. Questions evaluating emotional impact and burden of disease were evaluated on a scale that ranged from 1 (not at all) to 5 (a great deal).

1. Tefferi A, Vainchenker W. *J Clin Oncol*. 2011;29:573-582. 2. Tefferi A. *Am J Hematol*. 2016;91:1262-1271. 3. Randhawa J, et al. *J Hematol Oncol*. 2012;5:43. 4. Mesa RA, et al. *Cancer*. 2006;107:361-370. 5. Mesa R, et al. *BMC Cancer*. 2016;16:167. 6. Guglielmelli P, Vannucchi AM. *Leuk Res*. 2013;37:1429-1431.

Summary

- MF is characterized by bone marrow fibrosis, splenomegaly, severe anemia, and constitutional symptoms¹
- Overactive JAK-STAT signaling is a significant contributor to MF pathogenesis, with 95% of patients possessing a mutation in 1 of 3 genes: *JAK2*, *CALR*, or *MPL*^{1,2}
- Following a comprehensive evaluation involving patient history and physical examination, blood tests, and bone marrow biopsy, patients must meet the 2016 WHO diagnostic criteria to be diagnosed with MF^{1,3,4}
- Proper risk stratification is recommended for optimal treatment and disease management, as survival worsens as risk increases^{5,6}
- The primary management goals for PMF are reducing splenomegaly, improving symptoms, and improving cytopenias⁷

1. Tefferi A. *Am J Hematol*. 2016;91:1262-1271. 2. Quintás-Cardama A, et al. *Nat Rev Drug Discov*. 2011;10:127-140. 3. Gangat N, et al. *J Clin Oncol*. 2011;29:392-397. 4. Arber DA, et al. *Blood*. 2016;127:2391-2405. 5. Cervantes F, et al. *Blood*. 2009;113:2895-2901. 6. Passamonti F, et al. *Blood*. 2010;116:2857-2858. 7. Tefferi A, Vainchenker W. *J Clin Oncol*. 2011;29:573-582.



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