Myelofibrosis: Disease State Overview

MI-DIS-US-0078 03/26

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BACK

MPN Epidemiology and Overview

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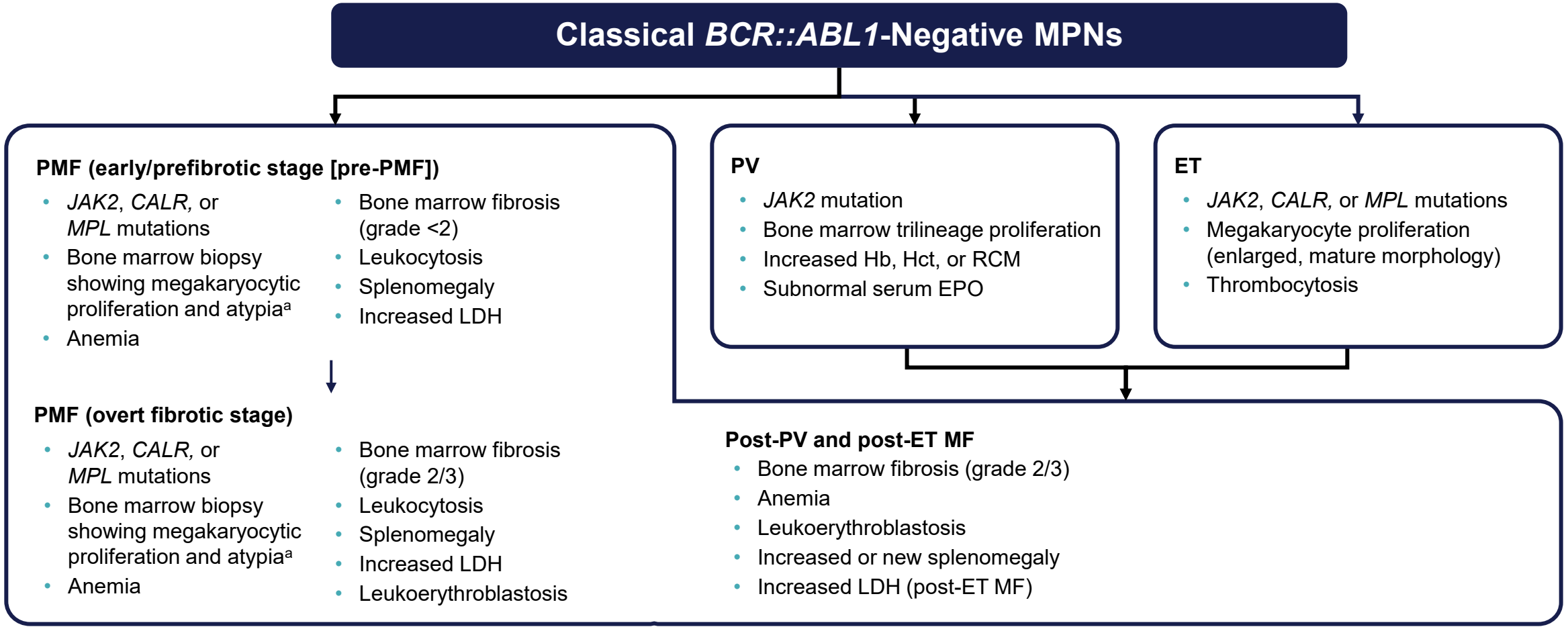
MF, PV, and ET Are *BCR::ABL1*-Negative MPNs



[a] Morphology of megakaryocytes in pre-PMF and overt PMF usually demonstrates a higher degree of megakaryocytic atypia than in any other MPN subtype.
ABL1, Abelson murine leukemia viral oncogene homolog 1; BCR, breakpoint cluster region; CALR, calreticulin; EPO, erythropoietin; ET, essential thrombocytopenia; Hb, hemoglobin; Hct, hematocrit; JAK, Janus kinase; LDH, lactate dehydrogenase; MF, myelofibrosis; MPL, myeloproliferative leukemia proto-oncogene, thrombopoietin receptor; MPN, myeloproliferative neoplasm; PMF, primary MF; PV, polycythemia vera; RCM, red blood cell mass.
Arber DA, et al. *Blood.* 2022;140:1200-1228.

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MPNs Are Rare and Usually Develop Later in Life

	MF	PV	ET
Prevalence	4-6 cases per 100,000[1]	44-57 cases per 100,000[1]	38-57 cases per 100,000[1]
Incidence	2-3 cases per 100,000 patient-years[1]	1.57 cases per 100,000 patient-years[2]	1.55 cases per 100,000 patient-years[2]
Median age at diagnosis	65 years; slightly more common in men than in women, with men making up ≈60% of patients[3]	61-62 years; similar frequency in men and women[4-6]	58 years[4]
Bone marrow abnormalities	Excess fibrous tissue, megakaryocytes proliferation and atypia[7]	Bone marrow trilineage proliferation and pleomorphic megakaryocytes[7]	Increased megakaryocytes[7]
Blood cell abnormalities	Reduced RBCs, increased WBCs[7]	Elevated Hb, evelated Hct, increased RCM[7]	Elevated platelets[7]
% with *JAK2* mutation	*JAK2*V617F mutation: ≈60% of patients[8]	*JAK2*V617F mutation: ≈96% of patients[9] *JAK2* exon 12 mutation: ≈3% of patients[9]	*JAK2*V617F mutation: ≈55% of patients[9]
% with *CALR* mutation[a]	≈35% of patients[10]	Not observed[10]	≈25% of patients[10]
Median survival	3.6-7.4 years[2,4,11,12]	11.9-14.1 years[2,4,5,11,12]	12.0-20.6 years[2,4,11-13]

[a] Based on an MPN cohort of 896 patients.[10]

RBC, red blood cell; WBC, white blood cell.

1. Mehta J, et al. *Leuk Lymphoma*. 2014;55:595-600. 2. Verstovsek S, et al. *Leuk Lymphoma.* 2022;63:694-702. 3. Gangat N, et al. *J Clin Oncol*. 2010;29:392-397. 4. Szuber N, et al. *Mayo Clin Proc*. 2019;94:599-610. 5. Tefferi A, et al. *Leukemia*. 2013;27:1874-1881. 6. Tefferi A, et al. *Am J Hematol.* 2023; 98(9):1465-1487. 7. Arber DA, et al. *Blood.* 2022;140:1200-1228. 8. Rafati M, et al. *Blood Adv.* 2023;7(24):7506-7515. 9. Tefferi A. *Am J Hematol*. 2021;96:145-162. 10. Klampfl T, et al. *N Engl J Med*. 2013;369:2379-2390. 11. Tefferi A, et al. *Blood*. 2014;124:2507-2513. 12. Smith CJ, et al. *Am J Hematol*. 2021;96:E464-E468. 13. Gangat N, et al. *Blood Cancer J*. 2024;14:11.

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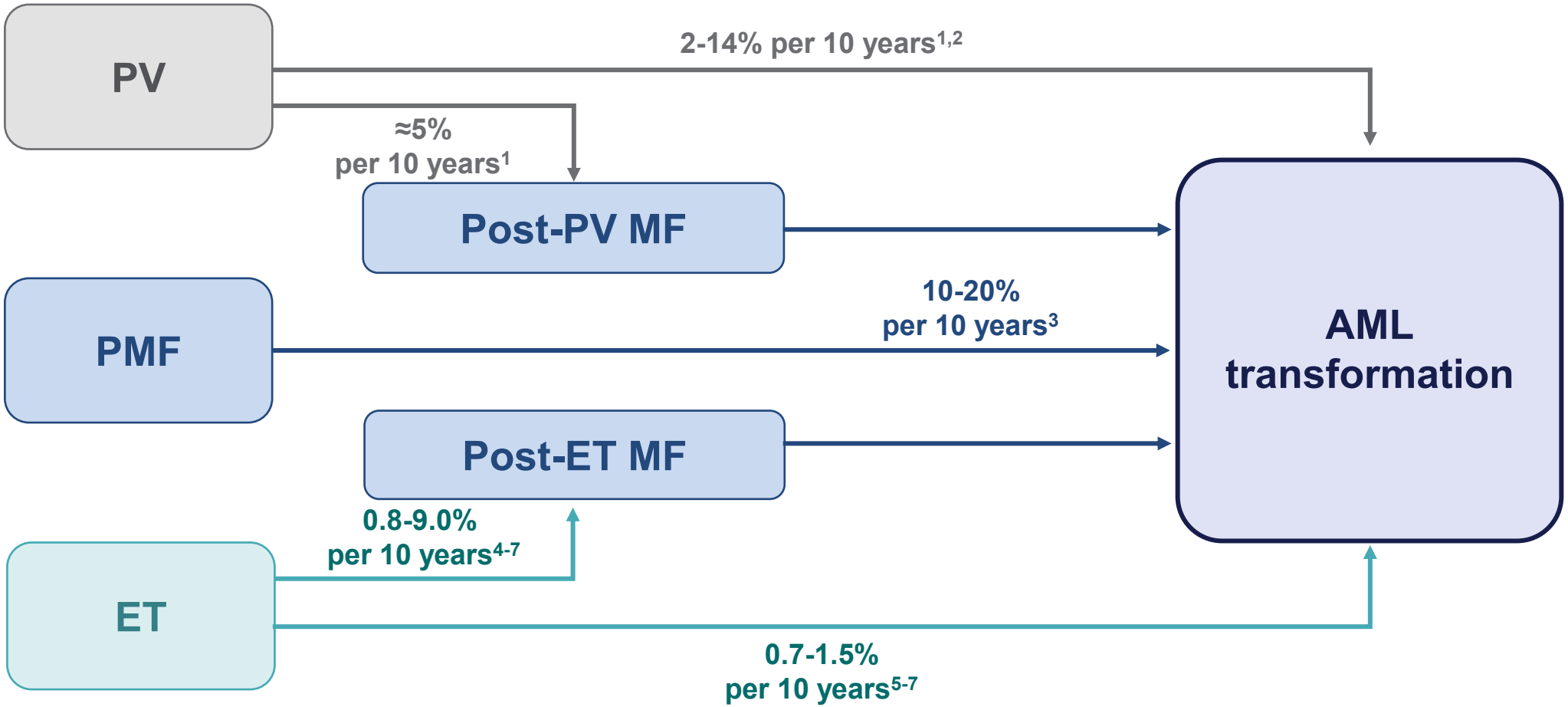
MPN Disease Progression and Transformation



AML, acute myeloid leukemia.

1. Cerquozzi S, Tefferi A. *Blood Cancer J*. 2015;5:e366. 2. Tefferi A, et al. *Leukemia.* 2013;27(9):1874-1881. 3. Yogarajah M, Tefferi A. *Mayo Clin Proc*. 2017;92(7):1118-1128. 4. Arber DA, et al. *Blood.* 2022;140:1200-1228. 5. Tefferi A, et al. *Am J Hematol.* 2024;99:697-718. 6. Gangat N, et al. *Blood Cancer J*. 2024;14:11. 7. Barbui T, et al. *J Clin Oncol*. 2011;29(23):3179-3184.

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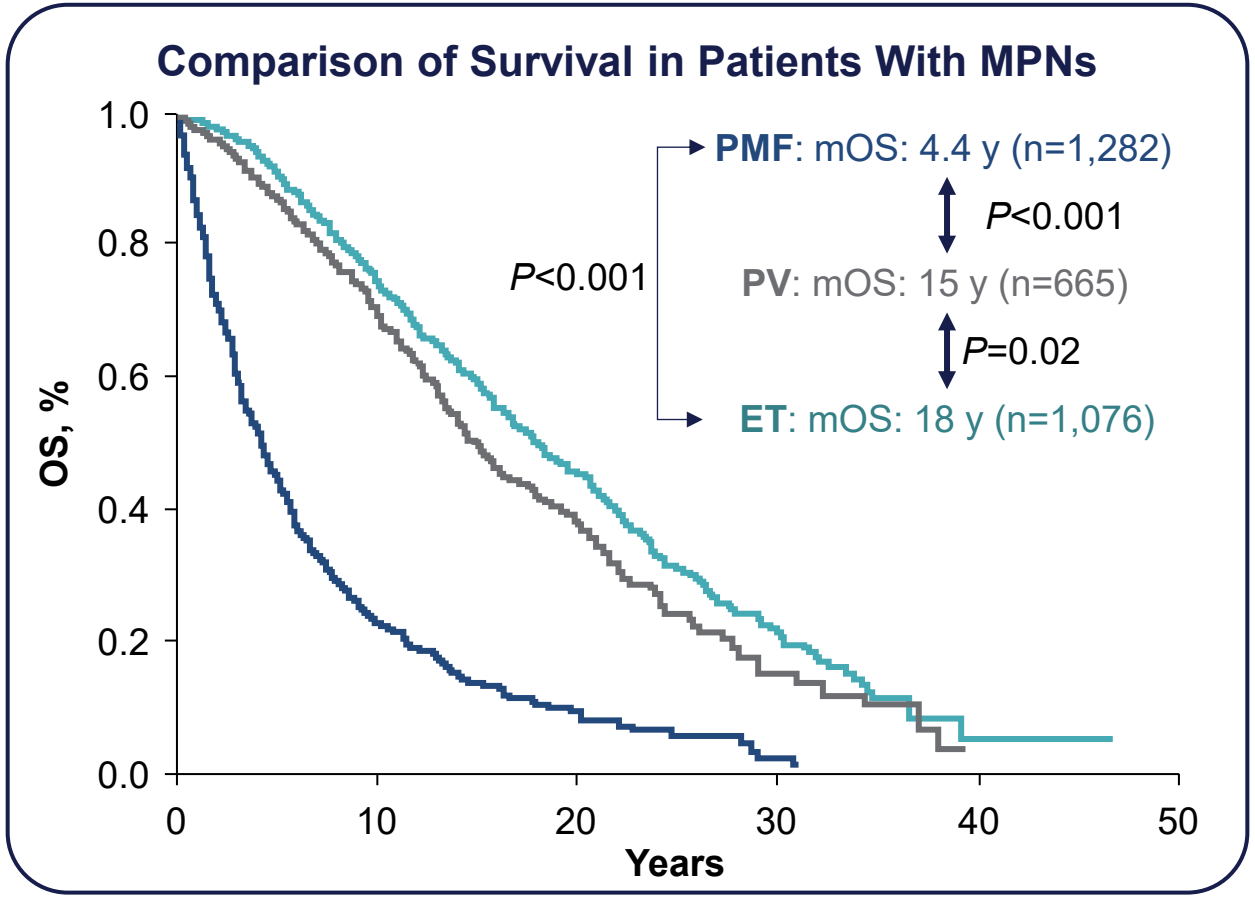
MPN Survival Outcomes



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 OS; OS, overall survival.

Szuber N, et al. *Mayo Clin Proc*. 2019;94:599-610.

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BACK

Myelofibrosis

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

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BACK

Mechanism of Disease

Myelofibrosis

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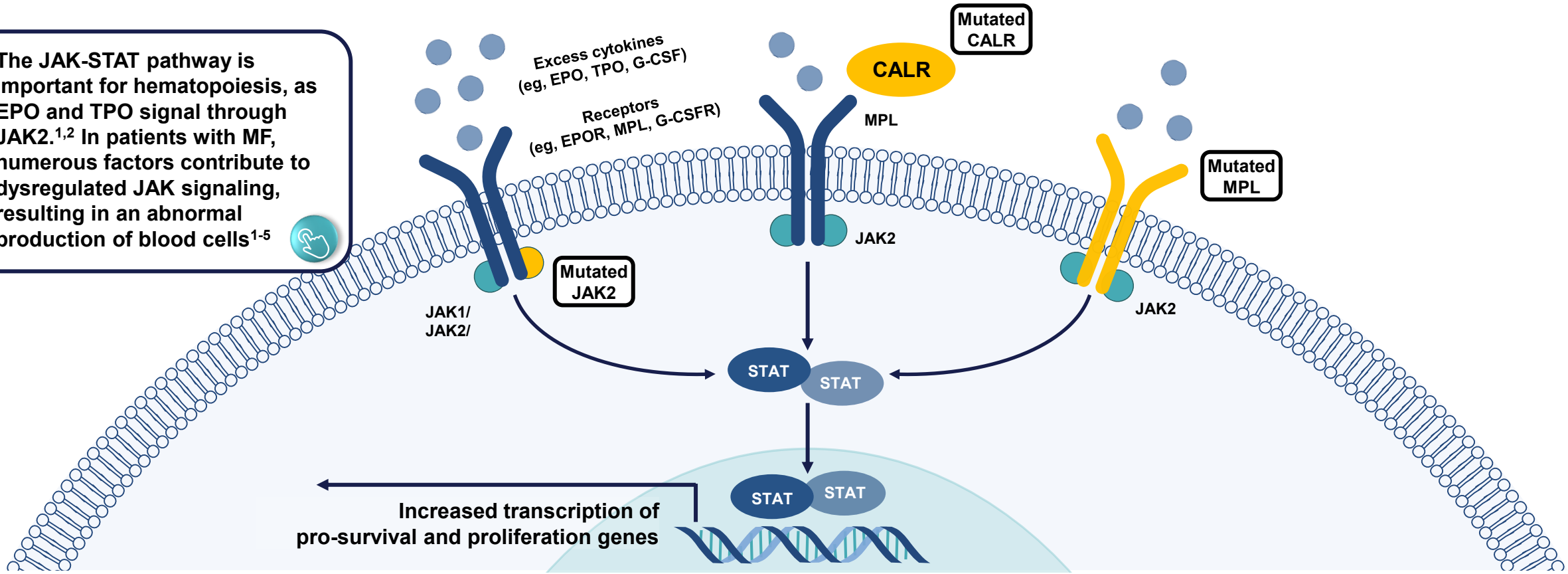
Overactive JAK Signaling Is Present in All Patients With MF, Leading to Abnormal Blood Cell Production

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 cells[1-5]



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.

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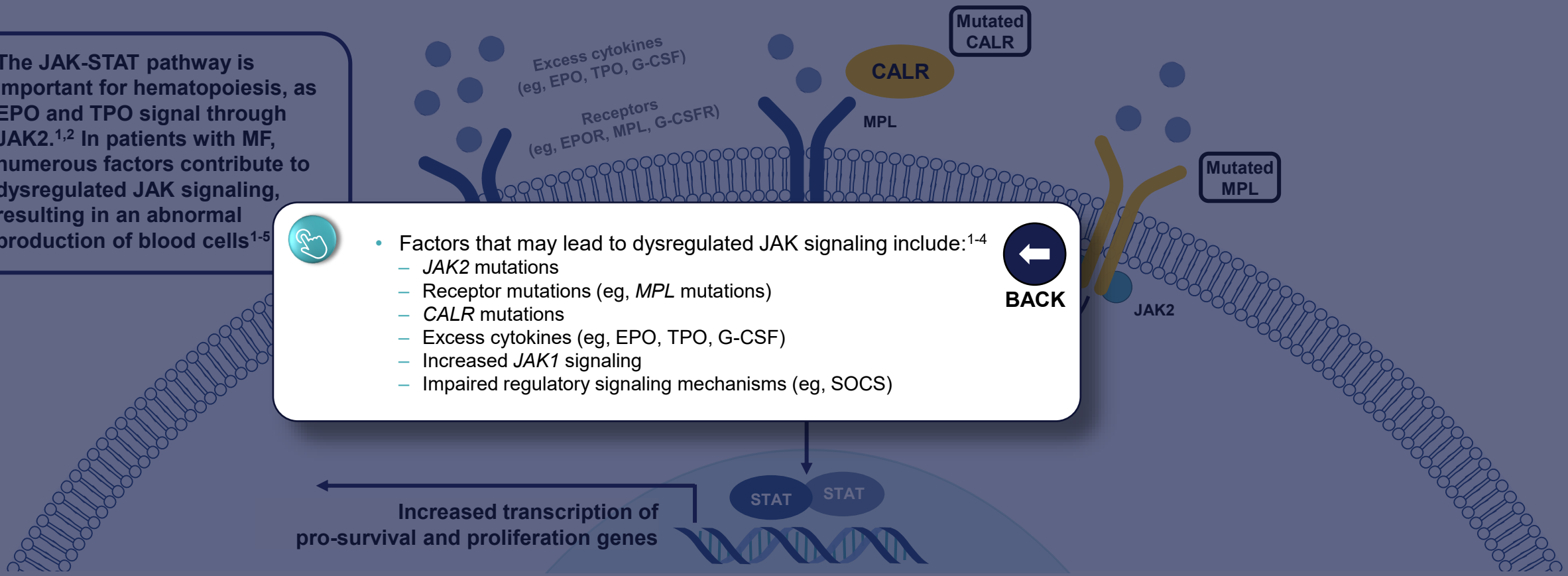
Overactive JAK Signaling Is Present in All Patients With MF, Leading to Abnormal Blood Cell Production

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 cells[1-5]



- 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)

BACK

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.

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BACK

Disease Characteristics

Myelofibrosis

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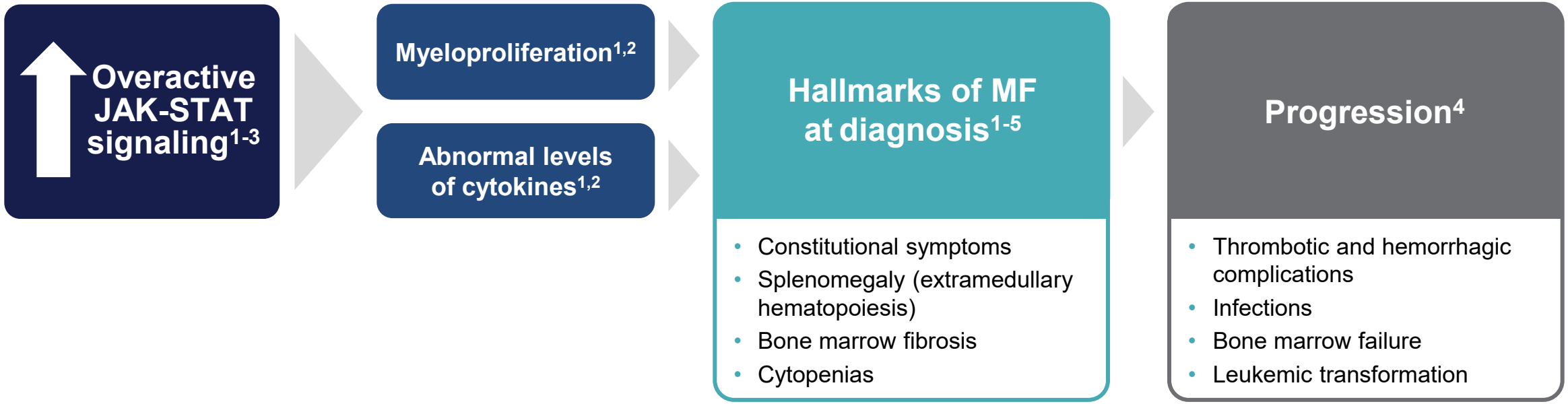
Downstream Effects of Overactive JAK-STAT Signaling Give Rise to Hallmark Clinical Manifestations of MF[1,2]



Median time from diagnosis to leukemic transformation is 31 months (range: 2-441 months)[6]

1. Spivak JL. *N Engl J Med.* 2017;376:2168-2181. 2. Tremblay D, Mascarenhas J. *Cells.* 2021;10:1034. 3. Al-Ali HK, Vannucchi AM. *Ann Hematol.* 2017;96:537-548.
4. Passamonti F, et al. *Crit Rev Oncol Hematol.* 2022;180:103862. 5. Quintás-Cardama A, et al. *Nat Rev Drug Discov.* 2011;10:127-140. 6. Mesa RA, et al. *Blood*. 2005;105:973-977.

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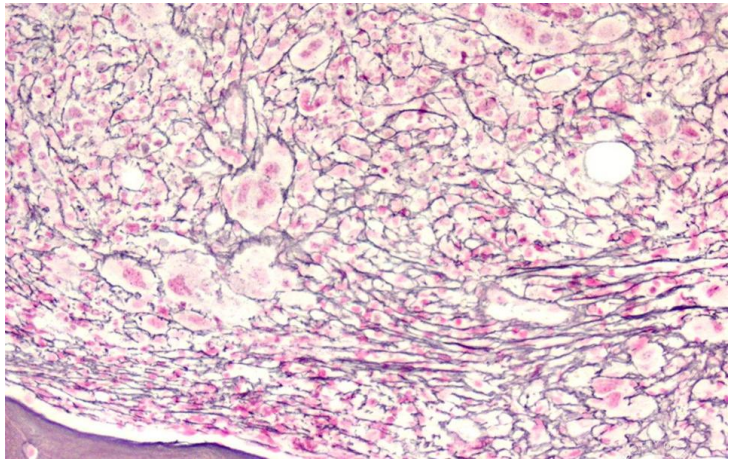
Hallmarks of MF: Bone Marrow Fibrosis Is a Central Pathologic Feature[1-4]

- Bone marrow fibrosis is a reactive phenomenon to megakaryocyte abnormalities, whereby increased levels of inflammatory and fibrogenic cytokines promote **abnormal deposition of reticulin and collagen fibers**[3-5]

Bone Marrow Fibrosis Grading by European Consensus[6]

Grading	Description[a]
MF - 0	Scattered linear reticulin with no intersections (crossovers) corresponding to normal bone marrow
MF - 1	Loose network of reticulin with many intersections, especially in perivascular areas
MF - 2	Diffuse and dense increase in reticulin with extensive intersections, occasionally with only focal bundles of collagen and/or focal osteosclerosis
MF - 3	Diffuse and dense increase in reticulin with extensive intersections with coarse bundles of collagen, often associated with significant osteosclerosis

Marrow Fibrosis in PMF[7]



Reticulin stain showing extensive fibrotic response (grade 3) and megakaryocytic hyperplasia[b]

[a] Fiber density should be assessed in hematopoietic (cellular) areas. [b] Image reproduced with permission from Lazarchick J. Marrow Fibrosis in Primary Myelofibrosis. ASH Image Bank. 2009; #00004100. © American Society of Hematology.
PMF, primary MF.

1. Arber DA, et al. *Blood.* 2022;140:1200-1228. 2. Kröger N, et al. *Biol Blood Marrow Transplant*. 2014;20:812-815. 3. Zahr AA, et al. *Haematologica*. 2016;101:660-671. 4. Guglielmelli P, et al. *Am J Hematol*. 2016;91:918-922. 5. Nazha A, et al. *Oncologist*. 2015;20:1154-1160. 6. Thiele J, et al. *Haematologica.* 2005;90:1128-1132. 7. Lazarchick J. Accessed Nov 2025. http://imagebank.hematology.org/image/4100/marrow-fibrosis-in-primary-myelofibrosis--2

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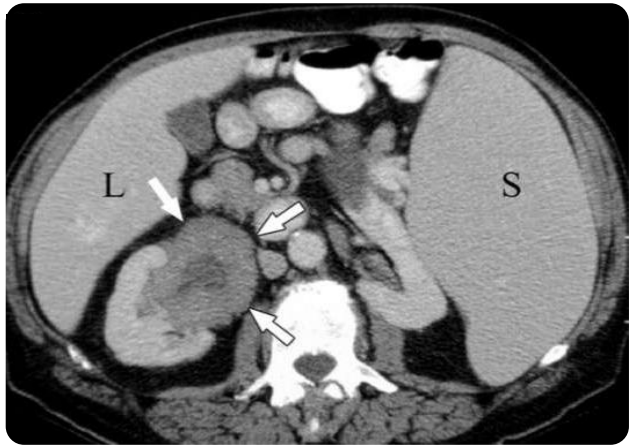
Hallmarks of MF: Splenomegaly Occurs Secondary to Extramedullary Hematopoiesis[1]

Extramedullary Hematopoiesis:
Abnormal trafficking of HSCs due to dysregulated marrow microenvironment leads to extramedullary engraftment[1,2]

Splenomegaly[b]
Palpable splenomegaly is common; in a study of 1,054 patients with PMF, 89% had palpable splenomegaly at diagnosis[4]

Consequences of Splenomegaly
Increased morbidity and decreased QOL[5,6]



Contrast-enhanced CT scan of the upper abdomen showing massive splenomegaly (S), the liver (L), and a renal pelvic mass (arrows) suggesting extramedullary hematopoiesis[3,a]

- Abdominal pain and discomfort
- Bloating, early satiety
- Portal hypertension
- Splenic infarction
- Exacerbation of cytopenias secondary to splenic sequestration

[a] Figure adapted from Choi H, et al. *Radiology*. 2004;231:52-56. Permission to use granted by Radiological Society of North America. [b] Photograph courtesy of Srdan Verstovsek, MD, PhD. MD Anderson Cancer Center. Houston, TX, US.
CT, computed tomography; HSC, hematopoietic stem cell; QOL, quality of life.
1. Tremblay D, et al. *Ann Hematol.* 2020;99:1141-1451. 2. Georgiades CS, et al. *AJR Am J Roentgenol.* 2002;179:1239-1243. 3. Choi H, et al. *Radiology*. 2004;231:52-56.
4. Langlais BT, et al. *Leuk Lymphoma.* 2019;60:402-408. 5. Randhawa J, et al. *J Hematol Oncol.* 2012;5:43. 6. Mesa RA, et al. *Cancer.* 2006;107:361-370.

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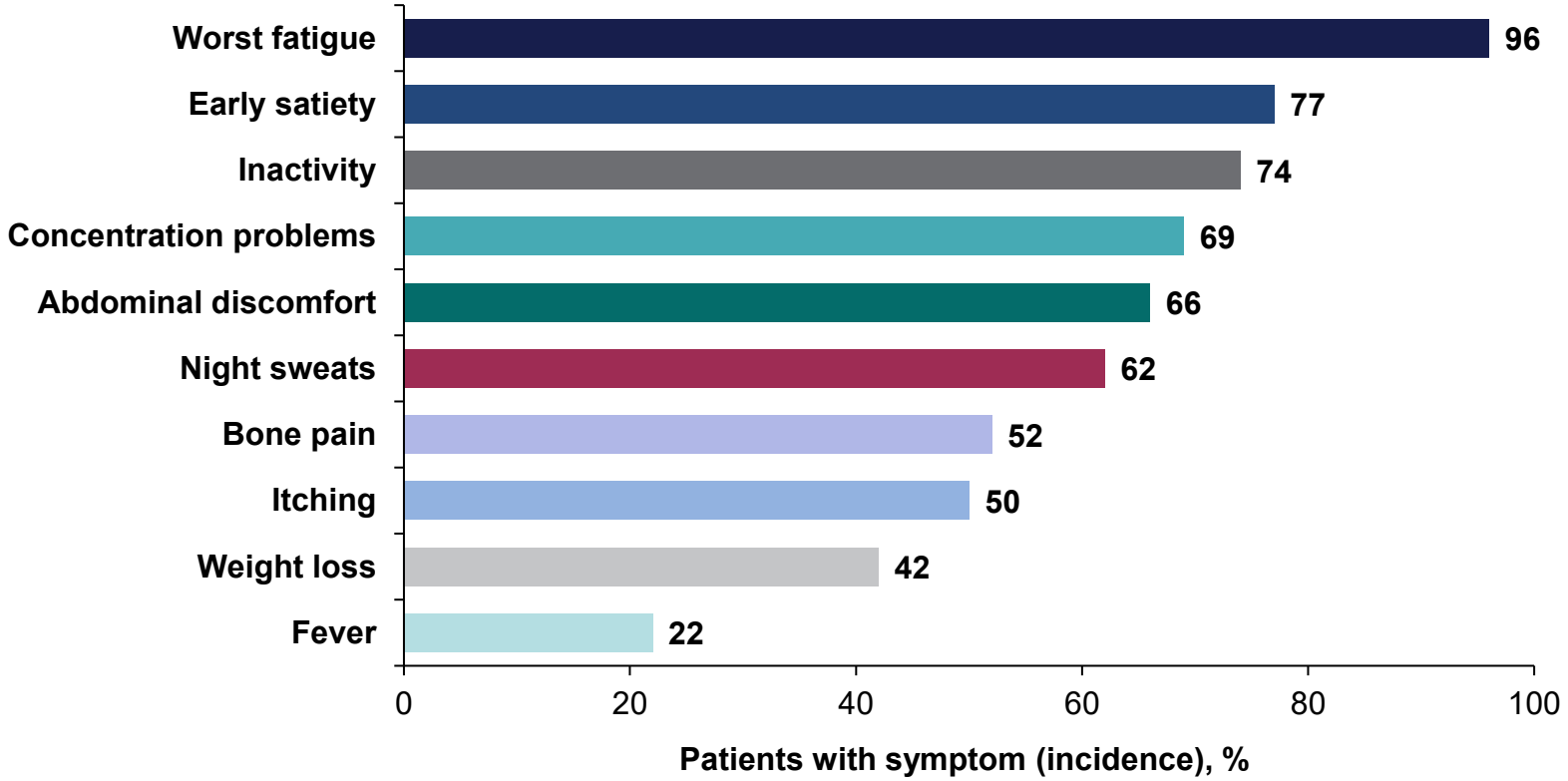
Hallmarks of MF: Debilitating Constitutional Symptoms That Impair QOL[1-3]

Patient-Reported Symptoms Frequently Associated With MF (N=293)[3,a,b]



42%
of patients with MF reported **clinically deficient QOL**[3,c]

[a] Symptom severity was rated on a linear analog self-assessment scale from 0 (absent/as good as it can be) to 10 (worst imaginable/as bad as it can be). [b] MPN-SAF TSS was constructed from the 9 most clinically relevant symptoms from the 17-item MPN-SAF in addition to "worst fatigue" from the BFI. MPN-SAF TSS has a possible range of 0 to 100, with 100 representing the highest level of symptom severity. [c] QOL scores were defined as "clinically deficient" if scores were rated as at least 4 of 10 on a 0-to-10 scoring system.
BFI, Brief Fatigue Inventory; MPN-SAF, Myeloproliferative Neoplasm Symptom Assessment Form; TSS, total symptom score.
1. Mesa R, et al. *Leuk Res*. 2009;33:1199-1203. 2. Langlais BT, et al. *Leuk Lymphoma.* 2019;60:402-408. 3. Emanuel RM, et al. *J Clin Oncol.* 2012;30:4098-4103.

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BACK

Clinical Work-Up, Diagnosis, and Stratification

Myelofibrosis

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The Integration of Molecular Findings With Bone Marrow Morphology and Blood Counts Remains the Cornerstone of MF Diagnosis[1]

History and Physical[2,3]

- 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[1,2]

- Peripheral blood smear showing leukoerythroblastosis or blasts
- Anemia[a]
- Thrombocytosis or thrombocythemia
- LDH levels
- Leukopenia or leukocytosis
- *BCR-ABL* negative and presence of *JAK2*V617F, *CALR*, *MPL, JAK2* exon 12 mutations, trisomy 9, or del(13q)

Bone Marrow Biopsy[1-4]

- Grade of fibrosis
- Megakaryocytic atypia
- Age-adjusted cellularity
- Changes in erythropoiesis
- Neutrophil granulopoiesis

Following a comprehensive work-up and evaluation, a differential diagnosis might include:[1]

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

[a] Below the reference range given age, sex, and altitude considerations; not attributed to a comorbid condition.

BCR-ABL, breakpoint cluster region–Abelson murine leukemia viral oncogene homolog; CML, chronic myeloid leukemia; del, deletion; LDH, lactate dehydrogenase; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasm.

1. Arber DA, et al. *Blood.* 2022;140:1200-1228. 2. Tefferi A. *Am J Hematol*. 2016;91:1261-1271. 3. Tefferi A. *Am J Hematol*. 2021;96:145-162.
4. Khoury J, *et al. Leukemia.* 2022;36:1703-1719.

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Diagnostic Criteria for PMF (Overt Fibrotic Stage)

International Consensus Classification of Myeloid Neoplasms and Acute Leukemias

☑ Must meet all 3 major AND at least 1 minor criteria[a]

Major

- ☐ Bone marrow biopsy showing megakaryocytic proliferation and atypia,[b] accompanied by reticulin and/or collagen fibrosis grades 2 or 3
- ☐ *JAK2*, *CALR*, or *MPL* mutation or presence of another clonal marker[c] or absence of reactive bone marrow reticulin fibrosis[d]
- ☐ Diagnostic criteria for ET, PV, *BCR::ABL1*−positive CMML, MDS, or other myeloid neoplasms are not met

Minor

- ☐ Anemia not attributed to a comorbid condition
- ☐ Leukocytosis ≥11×10^9/L
- ☐ Palpable splenomegaly
- ☐ LDH level above the reference range
- ☐ Leukoerythroblastosis

[a] Confirmed in 2 consecutive determinations. [b] Distinctive features of megakaryocytes include small to giant megakaryocytes with a prevalence of severe maturation defects (cloud-like, hypolobulated, and hyperchromatic nuclei) and presence of abnormal large dense clusters (>6 megakaryocytes lying strictly adjacent). [c] Mutations associated with myeloid neoplasms (eg, *ASXL1, EZH2, IDH1, IDH2, SF3B1, SRSF2*, and *TET2* mutations) assessed by cytogenetics or sensitive NGS techniques. [d] 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.
CMML, chronic myelomonocytic leukemia; ET, essential thrombocythemia; NGS, next generation sequencing; PV, polycythemia vera; SF3B1, splicing factor 3b subunit 1; SRSF2, serine and arginine rich splicing factor 2; TET2, tet methylcytosine dioxygenase 2.

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

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Diagnostic Criteria for Post-PV MF

International Consensus Classification of Myeloid Neoplasms and Acute Leukemias

Must meet ALL required AND at least 2 additional criteria

Required

- ☐ Previous established diagnosis of PV
- ☐ Bone marrow fibrosis of grade 2 or 3

Additional

- ☐ Anemia[a] or sustained loss of requirement of either phlebotomy (in the absence of cytoreductive therapy) or cytoreductive treatment for erythrocytosis
- ☐ Leukoerythroblastosis
- ☐ Increase in palpable splenomegaly of >5 cm from baseline or the development of a newly palpable splenomegaly
- ☐ Development of ≥2 of the following constitutional symptoms: >10% weight loss in 6 months, night sweats, unexplained fever (>37.5°C)

[a] Below the reference range given age, sex, and altitude considerations.

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

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Diagnostic Criteria for Post-ET MF

International Consensus Classification of Myeloid Neoplasms and Acute Leukemias

Must meet ALL required AND at least 2 additional criteria

Required

- ☐ Previous established diagnosis of ET
- ☐ Bone marrow fibrosis of grade 2 or 3

Additional

- ☐ Anemia[a] and a >2 g/dL decrease from baseline Hb concentration
- ☐ Leukoerythroblastosis
- ☐ Increase in palpable splenomegaly of >5 cm from baseline or the development of a newly palpable splenomegaly
- ☐ Elevated LDH level above the reference range
- ☐ Development of ≥2 of the following constitutional symptoms: >10% weight loss in 6 months, night sweats, unexplained fever (>37.5°C)

[a] Below the reference range given age, sex, and altitude considerations.

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

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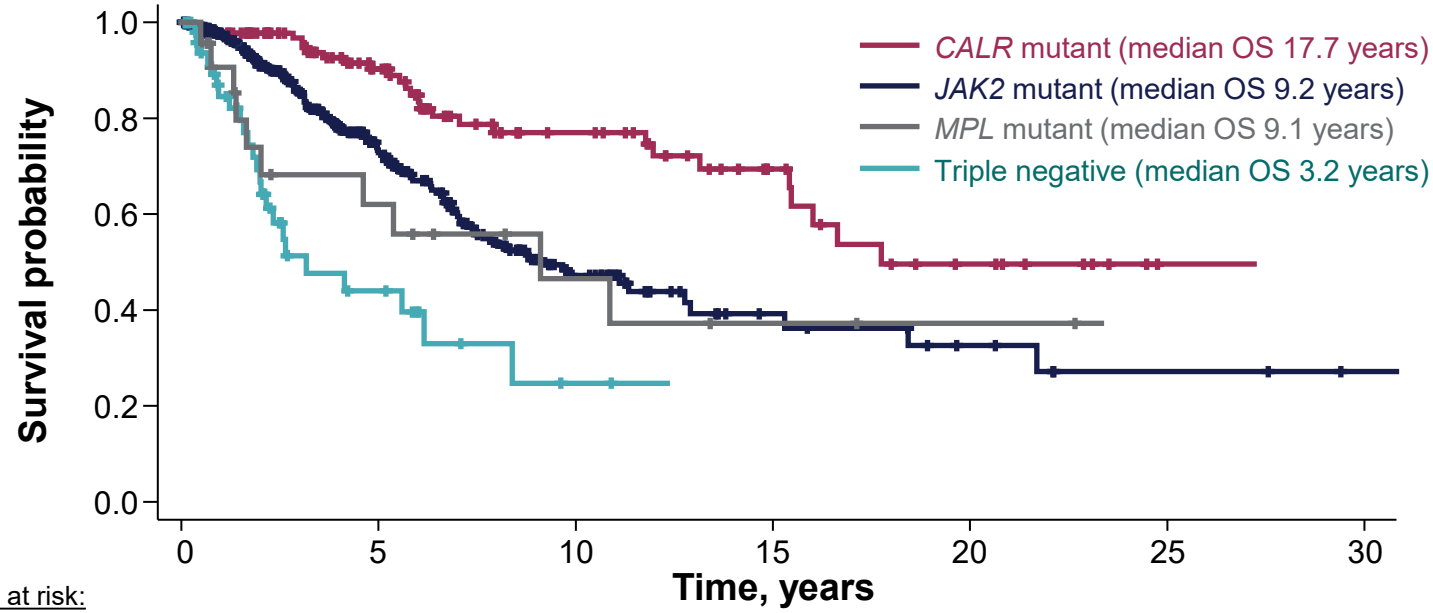
Certain Genomic Alterations in MPNs Are Driver Mutations That Exhibit Prognostic Significance[1-3]

- Driver mutations are essential for development of MPN phenotypes[1]
- The clinical course of MPNs is profoundly influenced by the founding driver mutations
- *JAK2*V617F is the most prevalent driver mutation in the *BCR::ABL1*-negative MPNs[1]

OS in Patients With PMF According to Presence of Driver Mutations[4,a]



Patients at risk:

CALR mutant	140	72	37	19	9	1
JAK2 mutant	396	135	39	13	7	3
MPL mutant	25	10	5	3	2	0
Triple negative	53	11	2	0	0	0

[a] Figure reproduced from Rumi E, et al. *Blood.* 2014;127:1062-1069, with permission. Copyright © 2014, Elsevier.

1. Tefferi A. *Am J Hematol*. 2021;96:145-162. 2. Szuber N, Tefferi A. *Curr Opin Hematol*. 2018;25:129-135. 3. Tefferi A. *Blood*. 2014;124:2507-2513.
4. Rumi E, et al. *Blood.* 2014;127:1062-1069.

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Risk Stratification Using a Prognostic Scoring System Can Optimize Management of 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[e]
Constitutional symptoms (weight loss, fever, night sweats)	1	1	1[e]
Anemia (Hb <10 g/dL)	1	2	2[e]
WBC count >25×10^9/L	1	1	1[e]
Circulating blasts ≥1%	1[f]	1	1[e]
Platelets <100×10^9/L	–	–	1
RBC transfusion need	–	–	1
Unfavorable karyotype (complex karyotype or with ≥1 abnormalities including complex karyotype or with ≥1 abnormalities including +8, -7/7q-, i(17q), -5/5q-, 12p-, inv(3), or 11q23 rearrangement)	–	–	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 is more recently designed but less widely used than the other scoring systems. [e] 0, 1, 2, and 3 points are assigned to DIPSS categories of low, intermediate-1, intermediate-2, and high risk, respectively; features are not weighted individually. [f] Circulating blasts >1%.

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

1. Vannucchi A. *ASH Education Book*. 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;115:1703-1708. 5. Gangat N, et al. *J Clin Oncol*. 2011;29:392-397.

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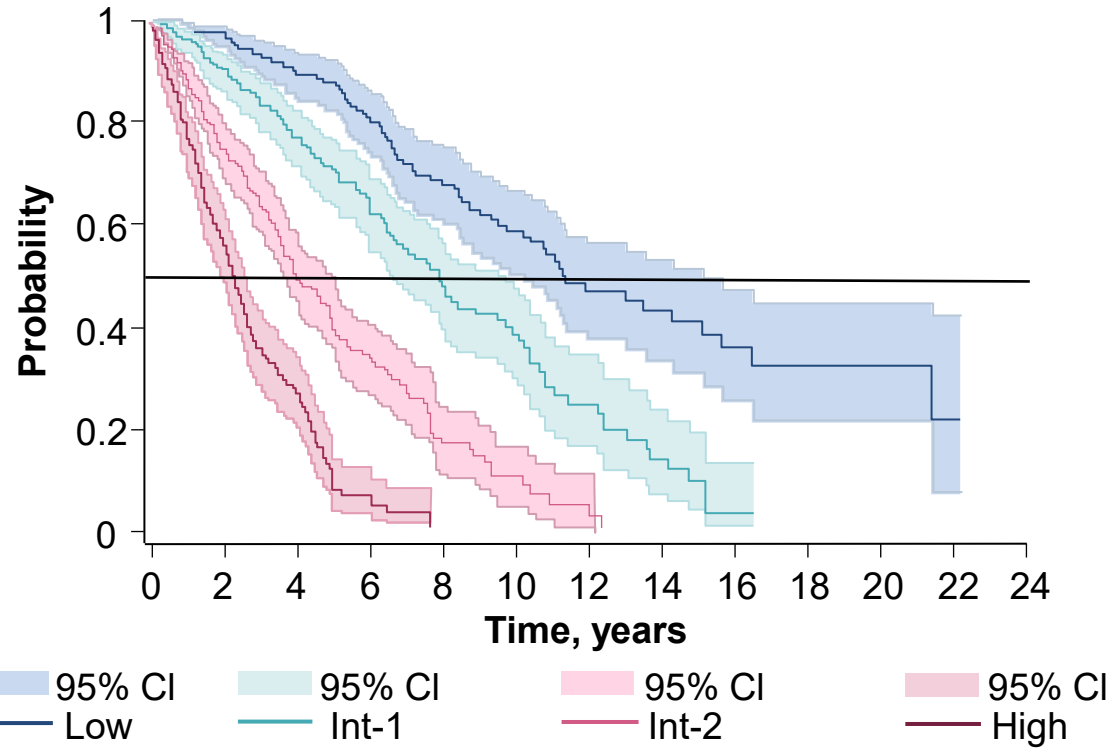
The Number of Risk Factors at Diagnosis Is Prognostic for Median Survival

IPSS Risk and Survival

Risk category	Number of risk factors	Median survival, years
High	≥3	2.3
Int-2	2	4.0
Int-1	1	7.9
Low	0	11.3

Survival Curves of Prognostic PMF Risk Groups[a]



[a] Permission to use granted by the American Society of Hematology.
Int-1, intermediate 1; Int-2, intermediate 2.
Cervantes F, et al. *Blood*. 2009;113:2895-2901.

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MF Remains a Debilitating, Chronic, Progressive Disease With a Need for Improved, Individualized Treatment Options[1-3]

Primary goals of treatment

- Reduce symptom burden and minimize the risk of leukemic transformation[4]
- Symptom status should be monitored for changes that could indicate disease progression and to prompt evaluation of treatment efficacy and/or disease status[4]

Personalization of treatment

- Considering individuals' clinical presentation (ie, age, spleen size, symptom burden, presence of driver mutations and high-molecular risk mutations, extent of bone marrow fibrosis, levels of circulating blasts, presence of cytopenias, etc) to determine prognosis and inform treatment choices[3-7]

Addressing unmet needs

- While currently approved therapies provide clinical benefits, they can lead to unwanted treatment-associated cytopenias or off-target effects[8]
- A subset of patients may experience suboptimal responses, resistance, or loss of response to JAK inhibitors, limiting the extent of attainable spleen size reductions and long-term control of symptoms[1,2,9,10]
- The only potentially curative treatment is allogeneic hematopoietic stem cell transplantation[11]—a procedure for which fewer than 10% of patients are eligible[12]

1. Petruk C, Mathias J. *Adv Ther.* 2020;37:2050-2070. 2. Gerds AT, et al. *Expert Rev Anticancer Ther.* 2022;22:835-843. 3. McLornan DP, et al. *Br J Haematol*. 2024;204:136-150. 4. Cervantes F, et al. *Blood*. 2009;113:2895-2901. 5. Passamonti F, et al. *Blood*. 2010;115:1703-1708. 6. Gangat N, et al. *J Clin Oncol*. 2011;29:392-397. 7. Guglielmelli J, et al. *J Clin Oncol*. 2018;36:310-318. 8. How J, et al. *Blood*. 2023;141:1922-1933. 9. Tremblay D, Mascarenhas J. *Cells.* 2021;10:1034. 10. Harrison CN, et al. *Ann Hematol.* 2020;99:1177-1191. 11. Tefferi A. *Am J Hematol*. 2023;98:801-821. 12. Barosi G, et al. *Lancet Haematol*. 2024;11:e383-e389.

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Summary

- MF is characterized by bone marrow fibrosis, splenomegaly, severe anemia, and constitutional symptoms[1]
- 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 International Consensus Classification of Myeloid Neoplasms and Acute Leukemias diagnostic criteria to be diagnosed with MF[3]
- Proper risk stratification is recommended for optimal treatment and disease management, as survival worsens as risk increases[4,5]
- The primary management goals for PMF are reducing splenomegaly, improving symptoms, and improving cytopenias[6]

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. Arber DA, et al. Blood. 2022;140:1200-1228. 4. Cervantes F, et al. *Blood*. 2009;113:2895-2901. 5. Passamonti F, et al. *Blood*. 2010;116:2857-2858. 6. Tefferi A, Vainchenker W. *J Clin Oncol*. 2011;29:573-582.

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