Essential Thrombocythemia: Disease State Overview

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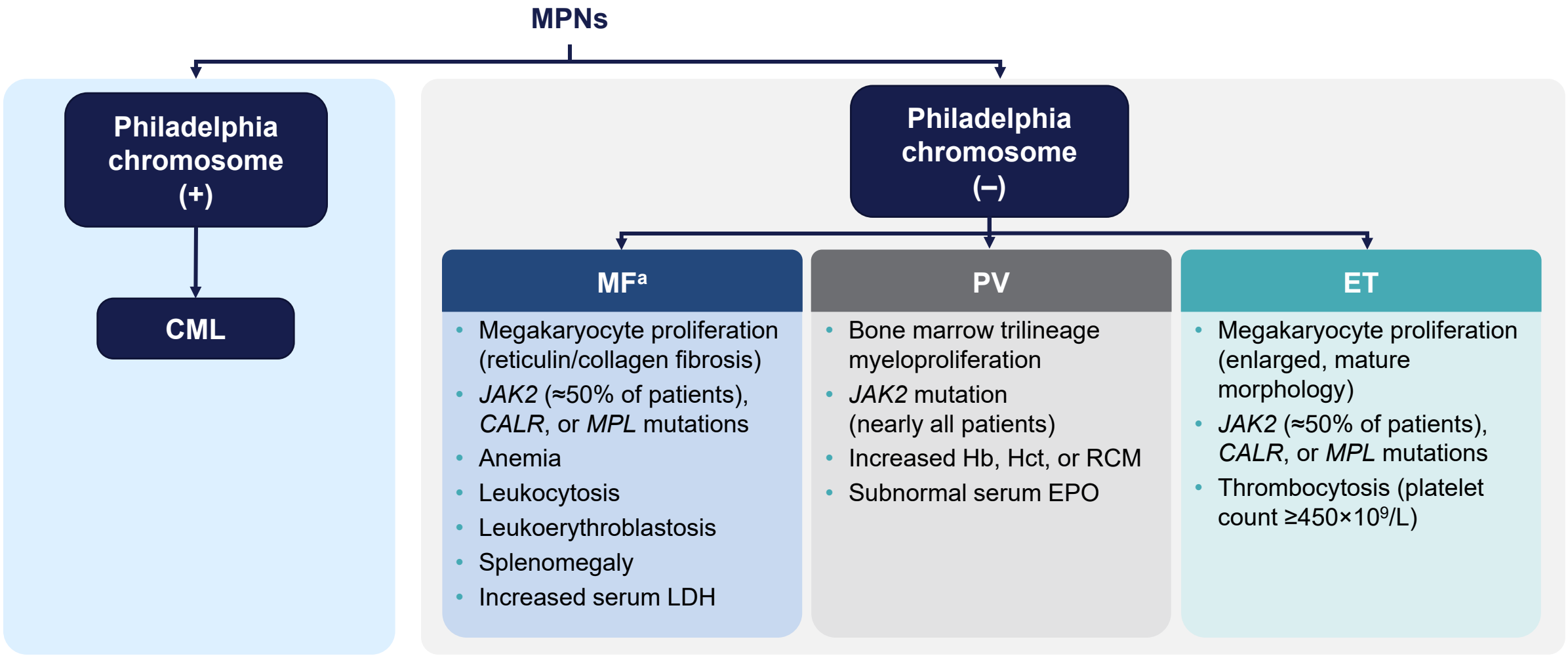
MPN Epidemiology and Overview

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.

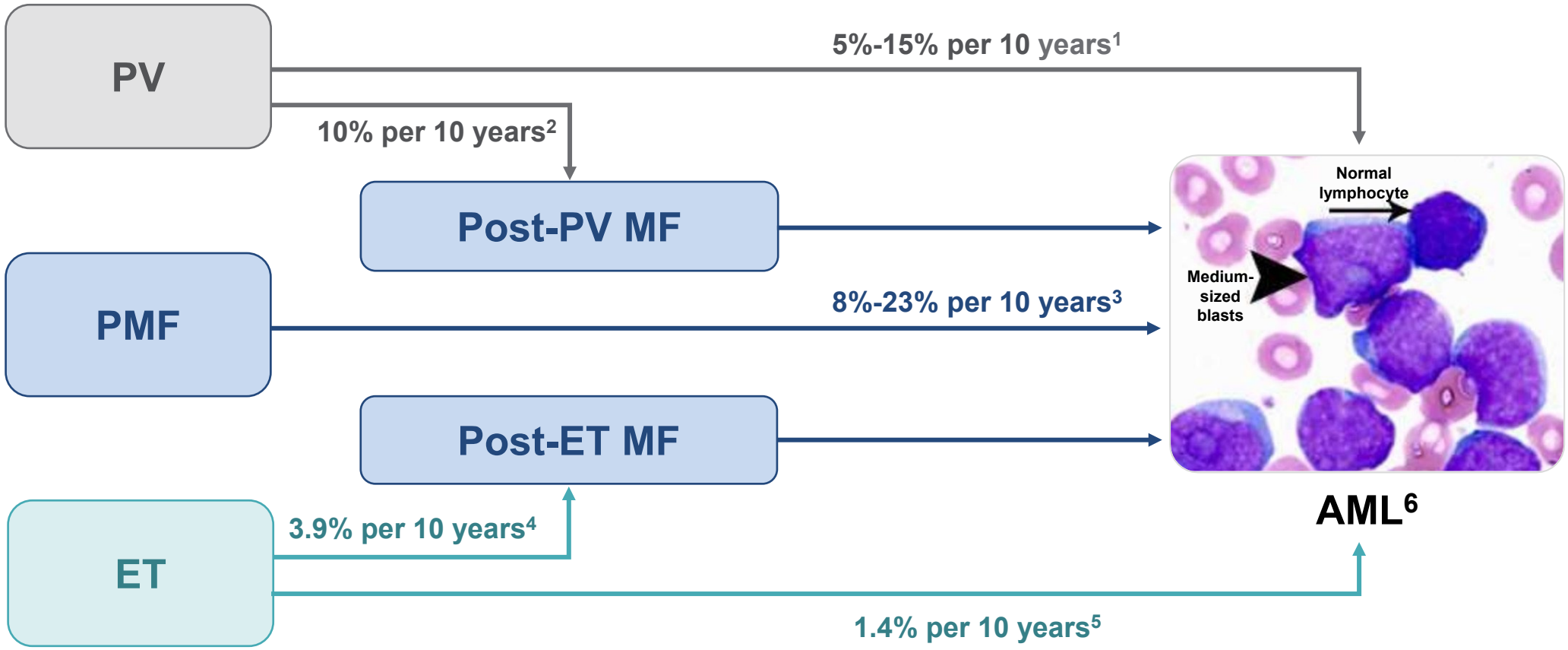
MPNs Are Rare and Usually Develop Later in Life

	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 *JAK2* 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 Aug 2022. 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.

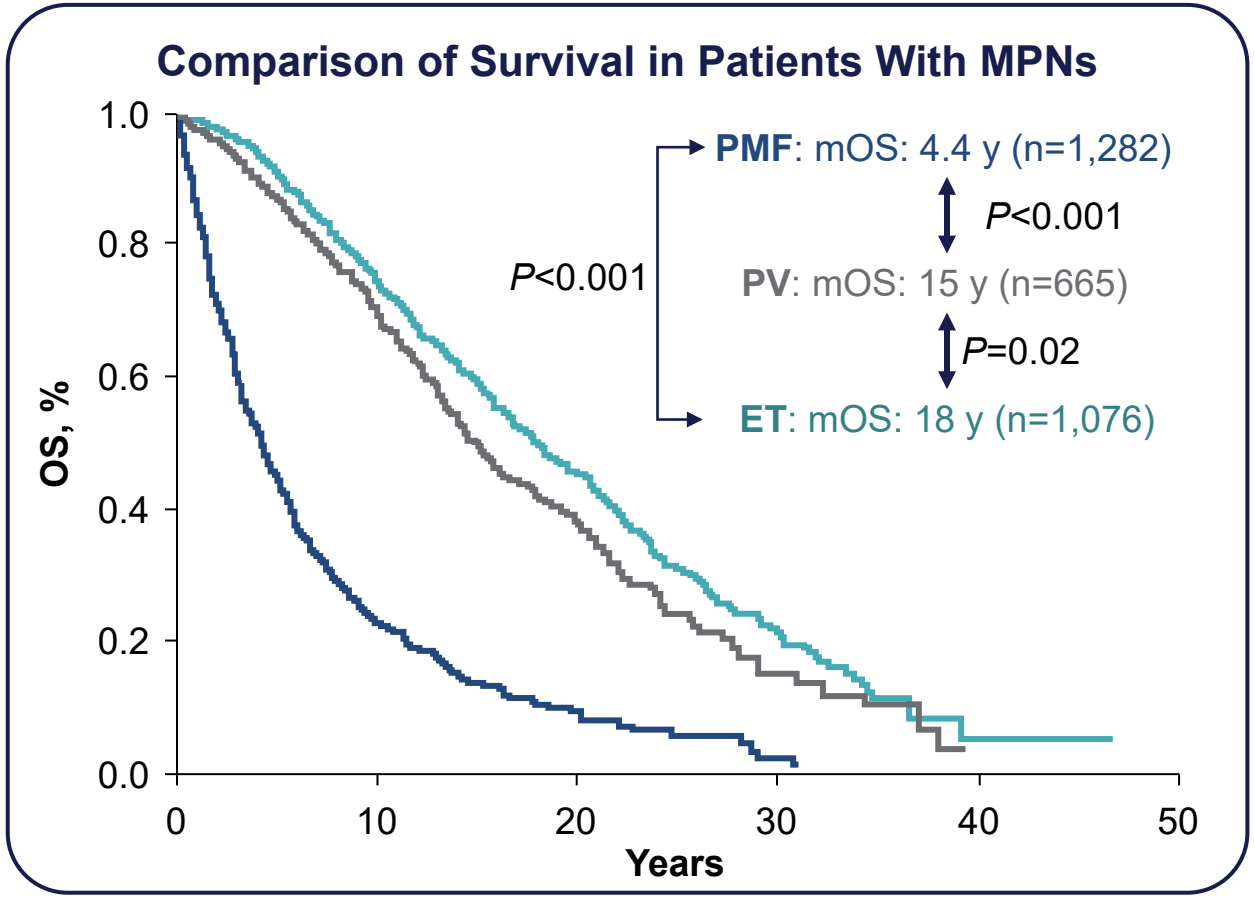
MPN Disease Progression and Transformation



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 Aug 2022. 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

Essential Thrombocythemia

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

BACK

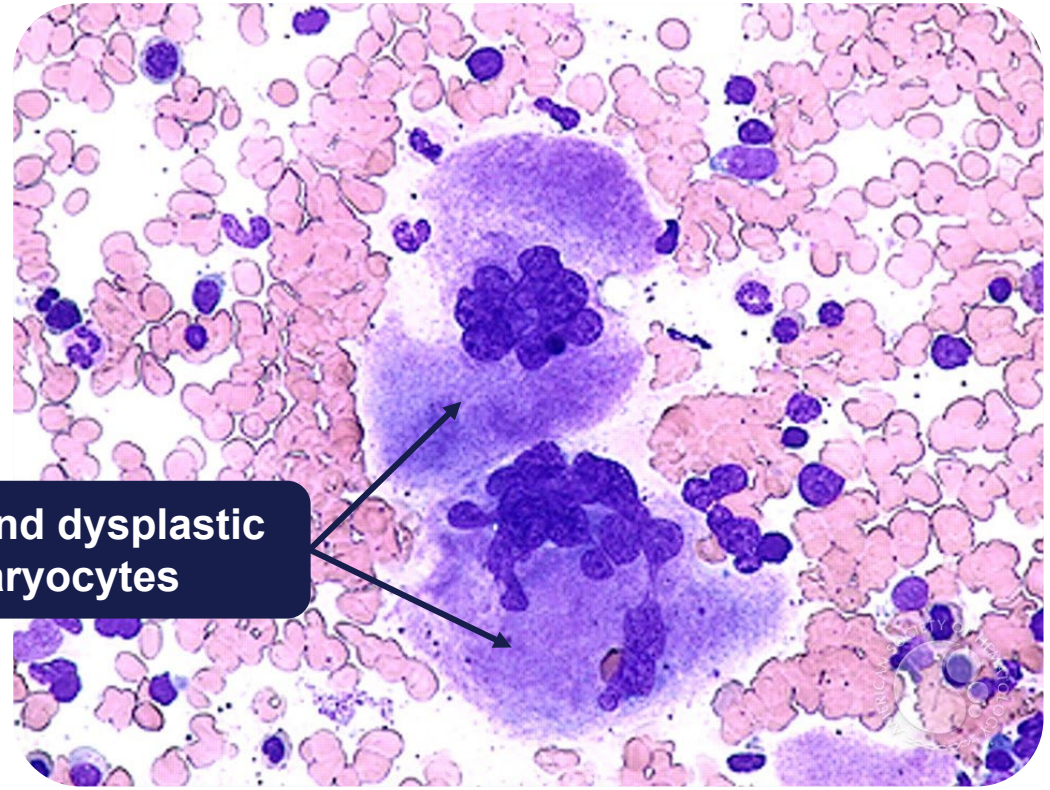
Disease Characteristics

Essential Thrombocythemia

ET Hematologic Features and Epidemiology

- ET is characterized predominantly by thrombocytosis and abnormal megakaryocyte proliferation[1]
- Patients with ET have an increased risk of arterial and venous thrombosis[2]
- Within 10 years, ≈4% of patients will progress to MF, and ≈1.4% will progress to AML[3,4]

Image Showing Megakaryocyte Dysplasia in a Patient Diagnosed With ET[5]

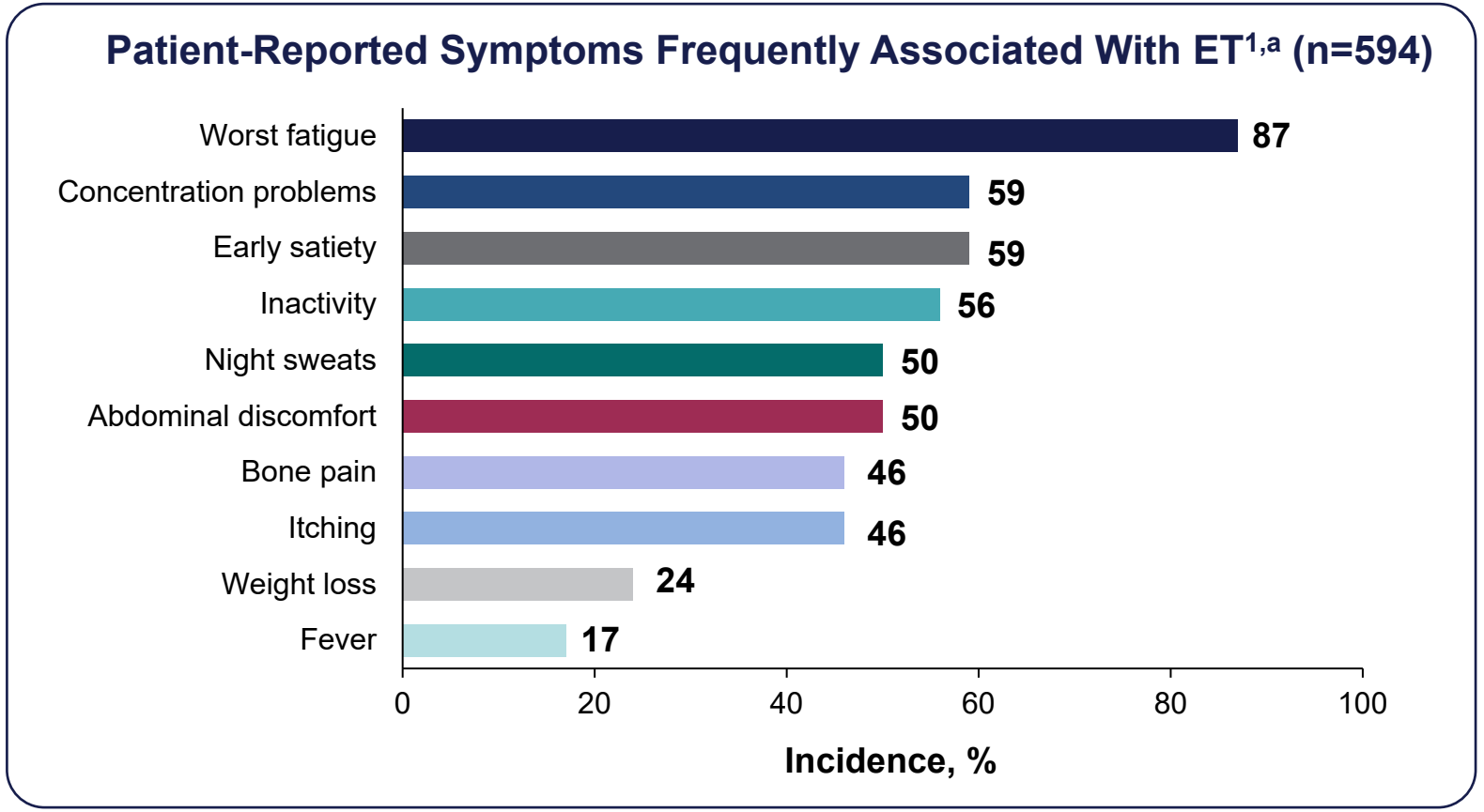


AML, acute myeloid leukemia; ET, essential thrombocythemia; MF, myelofibrosis.

1. Sanchez S, Ewton A. *Arch Pathol Lab Med*. 2006;130:1144-1150. 2. Kaifie A, et al. *J Hematol Oncol*. 2016;9:18. 3. Abdel-Wahab OI, Levine RL. *Annu Rev Med*. 2009;60:233-245. 4. Finazzi G, et al. *Blood*. 2005;105:2664-2670. 5. American Society of Hematology Image Bank. Accessed Jan 2018. http://imagebank.hematology.org/image/2736/essential-thrombocythemia--2?type=upload.

While Often Indolent, the Disease Can Be Associated With Substantial Symptom Burden[1,2]

- In a survey of 226 patients with ET, 37% reported that ET interfered with daily activities[3]
- The most common symptoms are fatigue, concentration problems, and early satiety[1]



[a] Symptoms were assessed using the BFI, MPN-SAF, and EORTC QLQ-C30, which was administered to a prospective cohort of 1,408 patients. The MPN-SAF TSS was then constructed using the 10 items that were deemed most clinically relevant.

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. Emanuel RM, et al. *J Clin Oncol*. 2012;30:4098-4103. 2. Chuzi S, Stein BL. *Leuk Lymphoma*. 2017;58:2786-2798. 3. Mesa R, et al. *BMC Cancer*. 2016;16:167.

BACK

Clinical Work-Up, Diagnosis, and Stratification

Essential Thrombocythemia

ET: 2016 WHO Diagnostic Criteria

2016 WHO Criteria: ☑ Must meet all 4 major OR the first 3 major and the minor

Major

- ☐ Platelet count ≥450×10^9/L
- ☐ Bone marrow biopsy showing proliferation mainly of the megakaryocyte lineage with increased numbers of enlarged, mature megakaryocytes with hyperlobulated nuclei. No significant increase or left-shift in neutrophil granulopoiesis or erythropoiesis and very rarely minor (grade 1) increase in reticulin fibers
- ☐ Not meeting WHO criteria for *BCR-ABL1*+ CML, PV, PMF, myelodysplastic syndromes, or other myeloid neoplasms
- ☐ Presence of *JAK2*, *CALR*, or *MPL* mutation

Minor

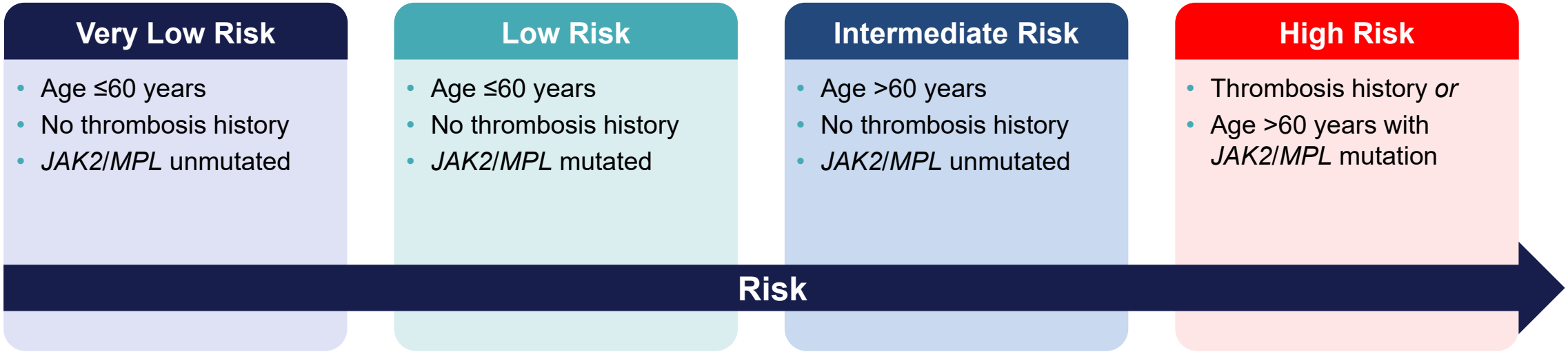
- ☐ Presence of a clonal marker or absence of evidence for reactive thrombocytosis

BCR-ABL, breakpoint cluster region–Abelson murine leukemia viral oncogene homologue; CALR, calreticulin; CML, chronic myeloid leukemia; JAK2, Janus kinase 2; MPL, MPL proto-oncogene thrombopoietin receptor; PMF, primary myelofibrosis; PV, polycythemia vera; WHO, World Health Organization.

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

Risk Stratification

Risk Stratification for ET Is Currently Divided Into 4 Major Categories



Because current therapy is aimed at lowering the risk of thrombosis, the most commonly used risk classification system is shaped according to thrombotic risk

Tefferi A, Barbui T. *Am J Hematol*. 2017;92:94-108.

Summary

- ET is characterized predominantly by thrombocytosis and abnormal megakaryocyte proliferation
- Disease transformation into MF and AML are potentially fatal disease complications
- At presentation, ET is asymptomatic in many patients; symptomatic patients typically present with vasomotor, constitutional, and spleen-associated symptoms
- Clinically, the presence of thrombocytosis and 1 of 3 mutations—*JAK2* V617F, *CALR*, and *MPL*—is a factor that can contribute to a diagnosis of ET
- Risk stratification is designed to estimate the likelihood of recurrent thromboembolic events