

TREATING MYELOPROLIFERATIVE NEOPLASMS: SPOTLIGHT ON MYELOFIBROSIS

May 15, 2024

Jointly provided by The Leukemia & Lymphoma Society and Postgraduate Institute for Medicine



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Professional Education & Engagement

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LEARNING OBJECTIVES

- Provide an overview of MPNs
- Apply diagnostic criteria for a correct diagnosis and grade
- Explain low-risk symptomatic myelofibrosis, intermediate, and high-risk primary or secondary, including genetic mutations, and risk stratification
- Apply data on approved treatments and clinical trials into clinical practice
- Implement strategies across the care team to educate and support patients



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CE DESIGNATION



Physician Continuing Medical Education

In support of improving patient care, this activity has been planned and implemented by the Postgraduate Institute for Medicine and The Leukemia & Lymphoma Society. Postgraduate Institute for Medicine is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

The Postgraduate Institute for Medicine designates this CME activity for a maximum of 1 AMA PRA Category 1 Credit(s)[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.



Registered Nursing Credit Designation

Approval for nurses has been obtained by the National Office of The Leukemia & Lymphoma Society under Provider Number CEP 5832 to award 1.0 continuing education contact hour through the California Board of Registered Nursing.



Interprofessional Continuing Education

This activity was planned by and for the healthcare team, and learners will receive 1 Interprofessional Continuing Education (IPCE) credit for learning and change.



Continuing Physician Assistant Education

Postgraduate Institute for Medicine has been authorized by the American Academy of PAs (AAPA) to award AAPA Category 1 CME credit for activities planned in accordance with AAPA CME Criteria. This activity is designated for 1 AAPA Category 1 CME credits. PAs should only claim credit commensurate with the extent of their participation.



Social Worker Continuing Education

The Leukemia & Lymphoma Society (LLS) Provider Number 1105, is approved as an ACE provider to offer social work continuing education by the Association of Social Work Boards (ASWB) Approved Continuing Education (ACE) program. Regulatory boards are the final authority on courses accepted for continuing education credit. ACE provider approval period: 12/10/2023-12/10/2026. Social workers completing this course receive 1.0 clinical continuing education credit.

The Leukemia & Lymphoma Society (LLS) is recognized by the New York State Education Departments State Board for Social Work as an approved provider of continuing education for licensed social workers #SW-0117. LLS maintains responsibility for the program. Social workers will receive 1.0 clinical CE contact hour for this activity.



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SPEAKERS



John Mascarenhas, MD
*Director, Center of Excellence in Blood Cancers
 and Myeloid Disorders*
Director, Adult Leukemia Program
Leader, Myeloproliferative Disorders Clinical Research Program
 Tisch Cancer Institute, Division of Hematology/Oncology
Professor of Medicine
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 New York, NY



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Clinical Program Manager
 Tisch Cancer Institute
 Icahn School of Medicine at Mount Sinai
 New York, NY



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DISCLOSURES

- **John Mascarenhas, MD**
 - **Research Funding:** Incyte, Novartis, BMS, CTI/SOBI, AbbVie, Geron, PharmaEssentia
 - **Consulting:** Incyte, Novartis, BMS, Geron, Kartos, Karyopharm, AbbVie, GSK, Galecto, PharmaEssentia, MorphoSys, Merck, Pfizer, and CTI/SOBI
- **Kathryn Johnson, DNP, MSc, FNP-BC**
 - **Speakers:** CTI Biopharma/SOBI

The PIM planners and others have nothing to disclose. The Leukemia & Lymphoma Society planners and others have nothing to disclose.



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Case RH: Initial Presentation



RH is a 77-year-old woman who was referred to you by her primary care clinician for progressive fatigue and noted anemia.

– Medical history

- Hypertension, well controlled on beta blocker
- High cholesterol, on statin

– Symptoms

- Mild fatigue, no systemic symptoms, and no spleen-related concerns

– Physical exam findings

- Spleen 4 cm below LCM and nontender
- No edema

– Laboratory findings

- As shown on the right

Current labs:

- Hgb = 9.2 g/dL
- PLT = $162 \times 10^9/L$
- Differential = 1% blasts

BM biopsy:

- Mutation = *CALR*
- *Hypercellular with atypical MK in tight clusters*
- Fibrosis = grade 2
- Karyotype = 46,XX

NGS:

Mutations = *CALR*, *TET2*

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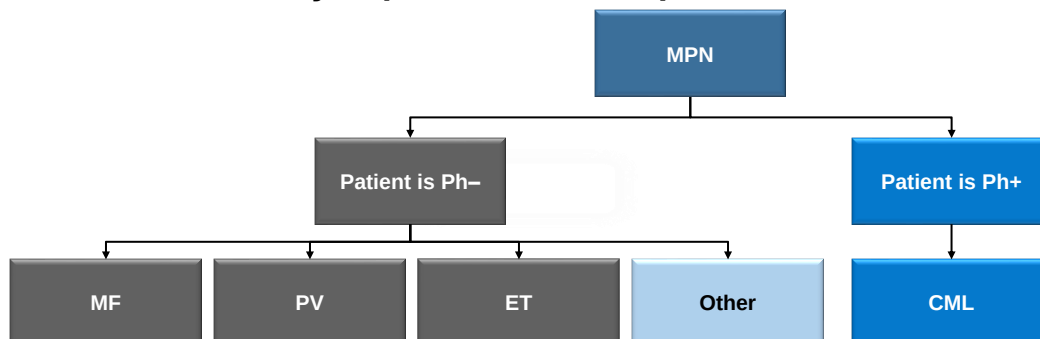
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Myelofibrosis Diagnosis and Risk Stratification

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Myeloproliferative Neoplasms



- MF, PV, and ET are 3 Ph-negative MPNs characterized by increased myeloid/erythroid cell proliferation¹⁻⁴
- Chronic, unregulated proliferation may occur in ≥ 1 myeloid cell line, including erythrocytes, platelets, and sometimes granulocytes⁵⁻⁷

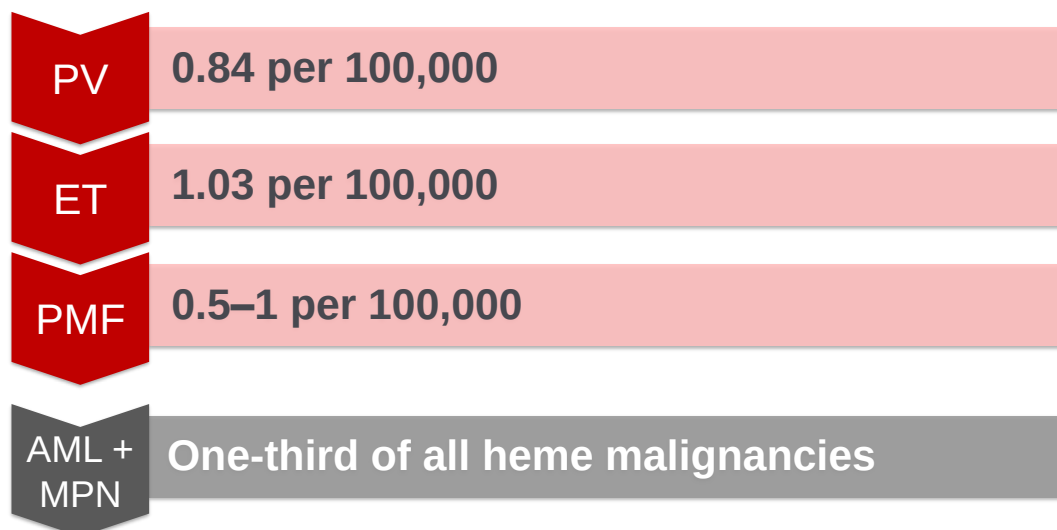
CML, chronic myelogenous leukemia; ET, essential thrombocytopoenia; MF, myelofibrosis; MPN, myeloproliferative neoplasm; PV, polycythemia vera.

1. Vannucchi AM, et al. *Haematologica*. 2008;93:972-976; 2. Vannucchi AM, et al. *CA Cancer J Clin*. 2009;59:171-191; 3. Verstovsek S. *Clin Cancer Res*. 2010;16:1988-1996; 4. Tefferi A, et al. *Leukemia*. 2008;22:14-22; 5. Thiele J, Kvasnicka HM. *Curr Hematol Malig Rep*. 2009;4:3340; 6. Delhommeau F, et al. *Int J Hematol*. 2010;91:165-173; 7. Verstovsek S. *Hematology Am Soc Hematol Educ Program*. 2009;1:636-642.

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Incidence of MPNs



Titmarsh GJ, et al. *Am J Hematol*. 2014;89:581-587; Aetiology of Myeloproliferative Neoplasms. *Cancers* (Basel). 2020 Jul 6;12(7):1810. doi: 10.3390/cancers12071810. PMID: 32640679; PMCID: PMC7408762.

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Which of the following constitutional symptoms is common in MF?

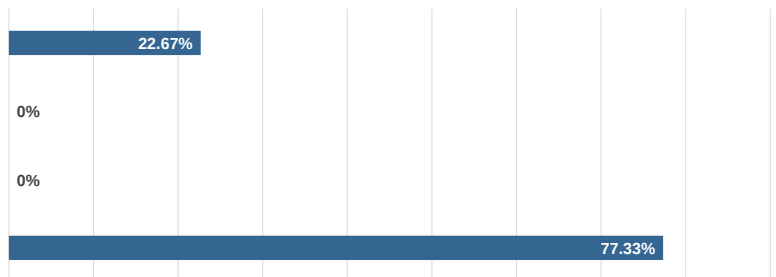
- A. Fatigue
- B. Weight loss
- C. Night sweats
- D. All of the above

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Which of the following constitutional symptoms is common in MF?

- A. Fatigue
- B. Weight loss
- C. Night sweats
- D. All of the above

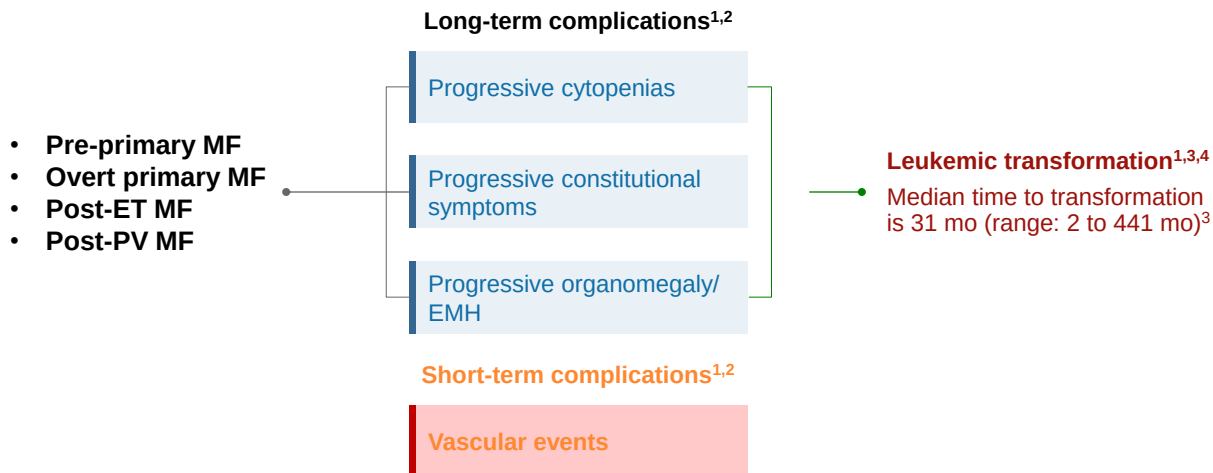


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MF Is a Progressive Disease

Time to progression is variable; most patients progress within first 10 years¹



1. Abdel-Wahab, Levine RL. *Annu Rev Med.* 2009;60:233-245; 2. Tefferi A. *Am J Hematol.* 2016;91:50-80; 3. Mesa RA, et al. *Blood.* 2005;105:973-977; 4. Cervantes F, et al. *J Clin Oncol.* 2012;30:2981-2987.

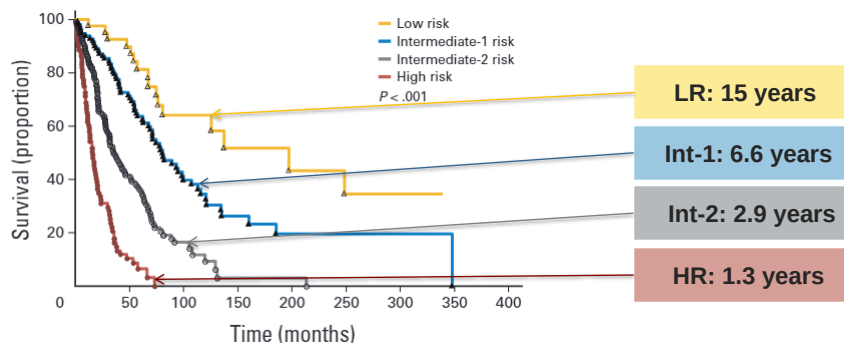
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DIPSS Plus Integrates Other Clinical and Cytogenetic Data

Risk Factors	Points
DIPSS int-1	1
DIPSS int-2	2
DIPSS HR	3
Unfav. cytogenetics	1
PLT <100 × 10 ⁹ /L	1
Transfusion dep.	1

Risk Categories/Score	Score
LR	0
Int-1	1
Int-2	2-3
HR	4-6



Gangat N, et al. *J Clin Oncol.* 2011;29:392-397.

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Preferred Risk Stratification Tool for Primary MF Below Age 70 MIPSS-70

Mutation-Enhanced IPSS for Patients With PMF
Age ≤ 70 Years (MIPSS-70)

Prognostic Variable	Points
Hgb < 10 g/dL	1
Leukocytes > 25 × 10 ⁹ /L	2
PLT < 100 × 10 ⁹ /L	2
Circulating blasts ≥ 2%	1
BM fibrosis grade ≥ 2	1
Constitutional symptoms	1
CALR type 1 unmutated genotype	1
HMR mutations	1
≥ 2 HMR mutations	2

Risk Group	Points
Low	0 to 1
Intermediate	2 to 4
High	≥ 5

Online calculator for MIPSS-70
can be found at
<http://www.mipss70score.it/>

BM, bone marrow; PLT, platelets.

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

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Preferred Risk Stratification Tool for Primary MF in Ages 70+ MIPSS-70+ Version 2.0

Mutation and Karyotype-Enhanced IPSS for Patients With
Primary MF (MIPSS-70+)

Prognostic Variable	Points
Severe anemia (Hgb < 8 g/dL women, < 9 g/dL men)	2
Moderate anemia (Hgb 8–9.9 g/dL women, 9–10.9 g/dL men)	1
Circulating blasts ≥ 2%	1
Constitutional symptoms	2
Absence of CALR type 1 mutation	2
High molecular risk (HMR) mutations	2
≥ 2 HMR mutations	3
Unfavorable karyotype	3
Very high-risk (VHR) karyotype	4

Risk Group	Points
Very low	0
Low	1 to 2
Intermediate	3 to 4
High	5 to 8
Very high	9

Online calculator for MIPSS-70+ Version 2.0 can be found at
<http://www.mipss70score.it/>

Hgb, hemoglobin; IPSS, International Prognostic Scoring System.

1. Tefferi A, et al. *J Clin Oncol*. 2018;36:1769-1770; 2. Tefferi A, et al. *Leukemia*. 2018;32:1189-1199.

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Preferred Risk Stratification Tool for Secondary MF *MYSEC-PM*

MF Secondary to PV and ET Prognostic Model
(MYSEC-PM)

Prognostic Variable	Points
Age at diagnosis	0.15 per patient year of age (71 × 0.15 = 10.65)
Hgb < 11 g/dL	2
Circulating blasts ≥ 3%	2
Absence of <i>CALR</i> type 1 mutation	2
PLT < 150 × 10 ⁹ /L	1
Constitutional symptoms	1

Risk Group	Points
Low	< 11
INT-1	≥ 11
INT-2	≥ 14 and < 16
High	≥ 16

Online calculator for MYSEC can be found at <http://mysec-pm.eu>

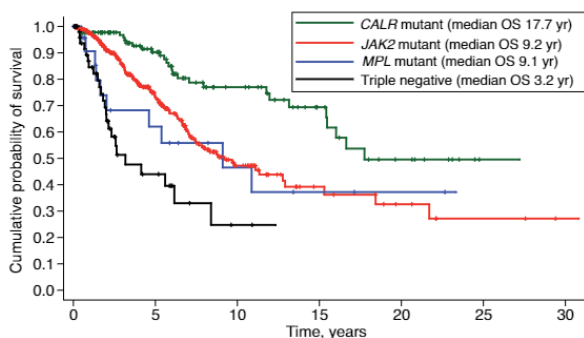
Passamonti F, et al. *Leukemia*. 2017;31:2726-2731.

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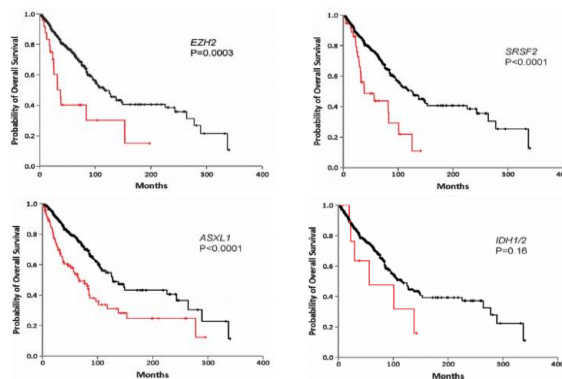
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Prognostic Impact of Mutations in PMF

JAK2 V617F vs *CALR* vs triple negative¹



HMR mutations impact outcome²

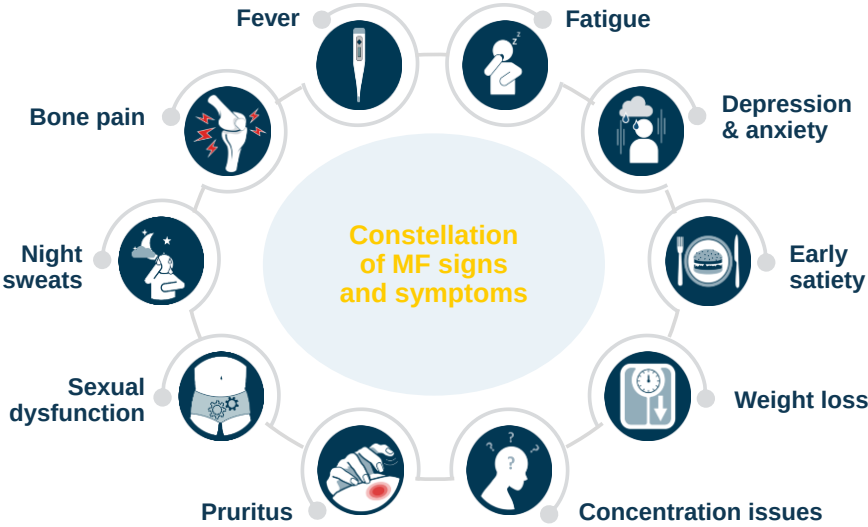


1. Rumi E, et al. *Blood*. 2014;124:1062-1069; 2. Vannucchi AM, et al. *Leukemia*. 2013;27:1861-1869.

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Symptom Burden in MF Wide Range of Constitutional Symptoms



Yoon J, et al. *Expert Rev Hematol.* 2021;14:607-619; Verstovsek S, et al. *Leukemia.* 2016;30:1413-1415; Cervantes F, et al. *Expert Rev Hematol.* 2016;9:489-496.

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Assessing Symptoms in MF MPN-SAF TSS (MPN-10)

- Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS)**

- 10-symptom assessment scale for MPNs
- Each symptom is rated on a 0 to 10 scale from absent (0) to worst imaginable (10)
- Total possible score: 100

Symptom	1 to 10 (0 if absent) ranking 1 is most favorable and 10 least favorable
Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during past 24 hours	(No Fatigue) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)

Circle the one number that describes, during the past week, how much difficulty you have had with each of the following symptoms

Filling up quickly when you eat (early satiety)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Abdominal discomfort	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Inactivity	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Problems with concentration-compared to prior to my MPD	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Night sweats	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Itching (pruritus)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Bone pain (diffuse not joint pain or arthritis)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Fever (>100 F)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Daily)
Unintentional weight loss last 6 months	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)

Emanuel RM, et al. *J Clin Oncol.* 2012;30:4098-4103.

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Case RH: TSS and Risk Stratification

MPN-SAF TSS and Clinical Parameters	Baseline	MIPSS-70+ V 2.0	
Fatigue (24 h)	4	Prognostic Variable	Points
Early satiety	0	Severe anemia (Hgb < 8 g/dL women, < 9 g/dL men)	0
Abdominal discomfort	0	Moderate anemia (Hgb 8–9.9 g/dL women, 9–10.9 g/dL men)	1
Inactivity	1	Circulating blasts ≥ 2%	0
Concentration	0	Constitutional symptoms	0
Night sweats	0	Absence of CALR type 1 mutation	0
Pruritus	0	High molecular risk (HMR) mutations	0
Bone pain	0	≥ 2 HMR mutations	0
Fever	0	Unfavorable karyotype	0
Unintentional weight loss	0	Very high-risk (VHR) karyotype	0
TSS	5	Total Score	1
		MIPSS70+ V 2.0 Risk Category	Low (10-y OS = 56%)

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NCCN Guidelines Recommended Treatments for Lower Risk MF

www.NCCN.org

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Case: RH

Initial Management and Follow-Up



- **Diagnosis and baseline status**
 - Primary MF with *CALR* mutation
 - Baseline TSS = 5
 - MIPSS-70+ risk category = Low

- **Initial management**

- RH chooses watchful waiting with a follow-up visit in 6 months

- **Changes at follow-up visit**

- Anemia has progressed
 - Now reporting some symptoms (mild night sweats and bone pain)

Current labs:

- Hgb = 7.9 g/dL
- PLT = $168 \times 10^9/L$
- Differential = 1% blasts
- EPO = 550 mU/mL

BM biopsy:

- Mutation = *CALR*
- Hypercellular and atypical MK
- Blasts <5% by IHC
- Fibrosis = grade 2
- Karyotype = 46,XX

NGS:

Mutation = *CALR*, *TET2*

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What would RH's MIPSS-70+ risk group be now?

- A. Low
- B. Intermediate
- C. High
- D. Very high

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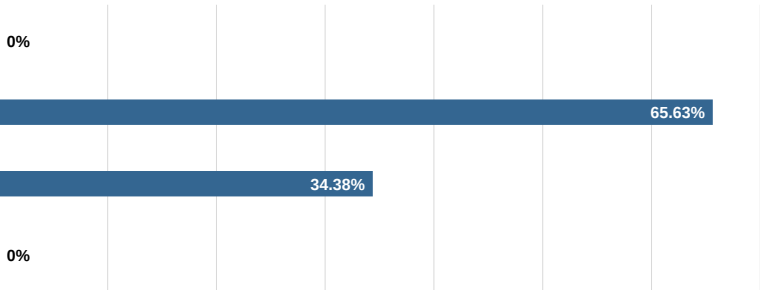
What would RH's MIPSS-70+ risk group be now?

A. Low

B. Intermediate

C. High

D. Very high



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Case RH: TSS and Risk Stratification

MPN-SAF TSS and Clinical Parameters	BL	6-Mo f/u	MIPSS-70+ V 2.0	
			Prognostic Variable	Points
Fatigue (24 h)	4	6	Severe anemia (Hgb < 8 g/dL women, < 9 g/dL men)	2
Early satiety	0	0	Moderate anemia (Hgb 8–9.9 g/dL women, 9–10.9 g/dL men)	0
Abdominal discomfort	0	0	Circulating blasts ≥ 2%	0
Inactivity	1	3	Constitutional symptoms	2
Concentration	0	0	Absence of CALR type 1 mutation	0
Night sweats	0	3	High molecular risk (HMR) mutations	0
Pruritus	0	0	≥ 2 HMR mutations	0
Bone pain	0	3	Unfavorable karyotype	0
Fever	0	0	Very high-risk (VHR) karyotype	0
Unintentional weight loss	0	0	Total Score	4
TSS	5	15	MIPSS70+ V 2.0 Risk Category	INT (10-y OS = 37%)

BL, baseline.

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Impact and Management of Anemia in Myelofibrosis

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Anemia in Myelofibrosis: Pathogenesis

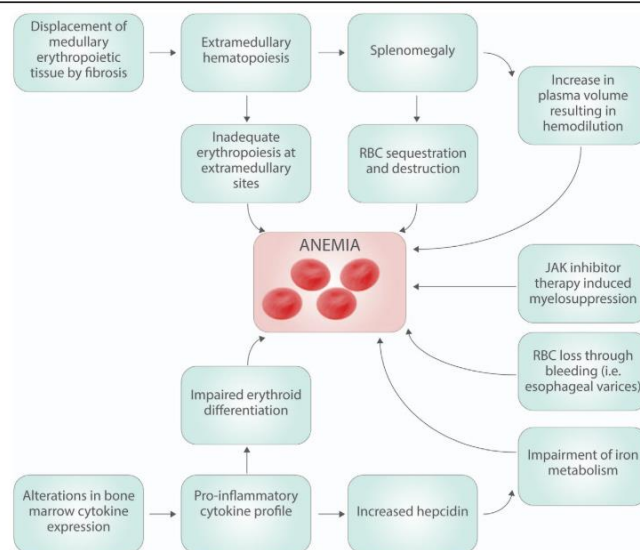


Figure 1. The pathogenesis of anemia in myelofibrosis is the result of a multifactorial process, which is only partially understood. The relative contributions of each of the above etiologies vary from patient to patient, and this variability in pathogenesis may explain the variability in responses to different therapeutic modalities. RBC = red blood cell.

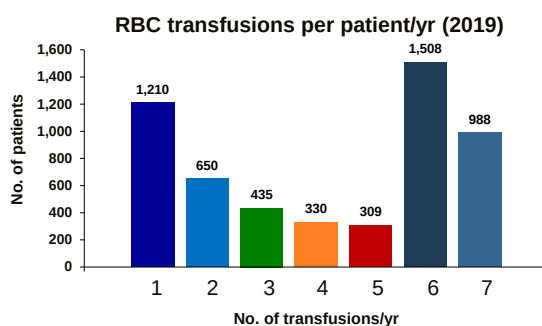
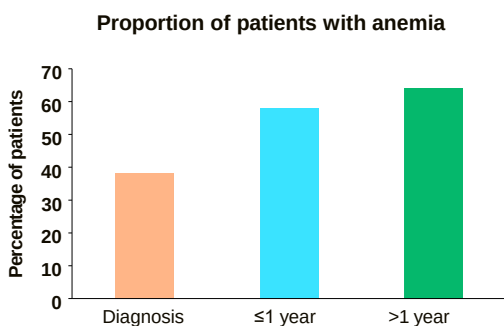
Naymagon L, Mascarenhas J. *HemaSphere*. 2017;1:e1.

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Anemia in MF

- Anemia presents in 35% to 54% of patients at diagnosis¹
- ~50% of patients with MF require ≥ 6 RBC transfusions/year
- Independent prognostic risk factor for leukemic transformation^{2,3}
- Up to 46% of patients become dependent on RBC transfusions within 1 year of diagnosis^{4,5}



JAKi, JAK inhibitor; MF, myelofibrosis; RBC, red blood cell; yr, year.

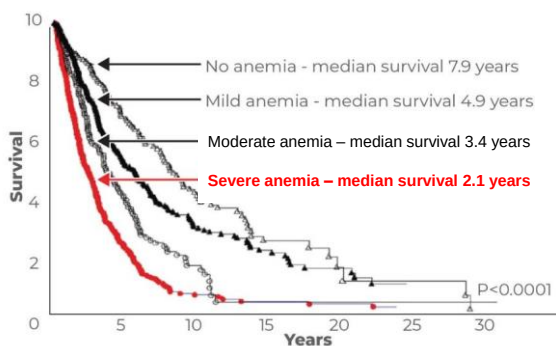
1. Tefferi A, et al. *Blood*. 2013;122:1395-1398; 2. Rago A, et al. *Leuk Res*. 2015;3:314-317; 3. Curto-Garcia N, et al. *Future Oncol*. 2018;14:137-150; 4. Harrison CN, et al. *Leukemia*. 2016;30:1701-1707; 5. Tefferi A, et al. *Mayo Clin Proc*. 2012;87:25-33.

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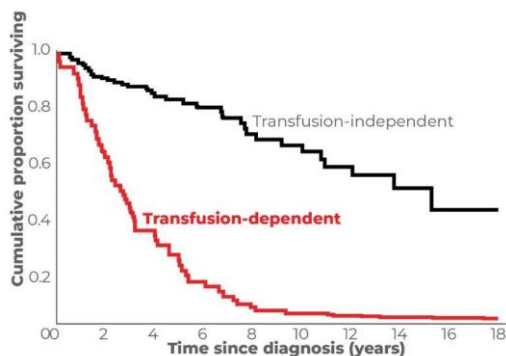
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Anemia Is Associated With Worsened Overall Survival in MF

OS stratified by degree of anemia¹



OS according to RBC transfusion dependency²



1. Adapted from Nicolosi M, et al. *Leukemia*. 2018;32:1254-1258; 2. Adapted from Elena C, et al. *Haematologica*. 2011;96:167-170.

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NCCN Guidelines: Management of MF-Associated Anemia

www.NCCN.org

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JAK Inhibitor Options Higher Risk MF

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NCCN Guidelines: Treatment for Higher Risk MF

www.NCCN.org

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JAK Inhibitors: Kinome Mapping

	IC ₅₀ (nanomolar)						
	JAK1	JAK2	JAK3	TYK2	ACVR1	IRAK1	FLT3
Ruxolitinib ^{1,2}	2.8	4.5	322	30	>1000	---	---
Fedratinib ¹⁻³	105	3	>1000	405	273	---	15
Pacritinib ^{1,2,4}	1280	6.0	18.3	27	16.7	13.6	14.8
Momelotinib ^{1,2,5}	11	18	155	17	52.5	---	401

ACVR1, activin A receptor type 1; FLT3, FMS-like tyrosine kinase 3; IC₅₀, half-maximal inhibitory concentration; IRAK1, interleukin-1 receptor-associated kinase; TYK2, tyrosine kinase 2.

1. Duenas-Perez AB, Mead AJ. *Ther Adv Hematol*. 2015;6:186-201; 2. Oh S, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22(suppl 2):S327. Poster MPN-145; 3. Talpaz M, et al. *Leukemia*. 2021;35:1-17; 4. Singer JW, et al. *J Exp Pharmacol*. 2016;8:11-19; 5. Azhar M, et al. *Blood Adv*. 2022;6:1186-1192.

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Ruxolitinib

	IC ₅₀ (nanomolar)						
	JAK1	JAK2	JAK3	TYK2	ACVR1	IRAK1	FLT3
Ruxolitinib ^{1,2}	2.8	4.5	322	30	>1000	---	---
Fedratinib ^{1,3}	105	3	>1000	405	273	---	15
Pacritinib ^{1,2,4}	1280	6.0	18.3	27	16.7	13.6	14.8
Momelotinib ^{1,2,5}	11	18	155	17	52.5	---	401

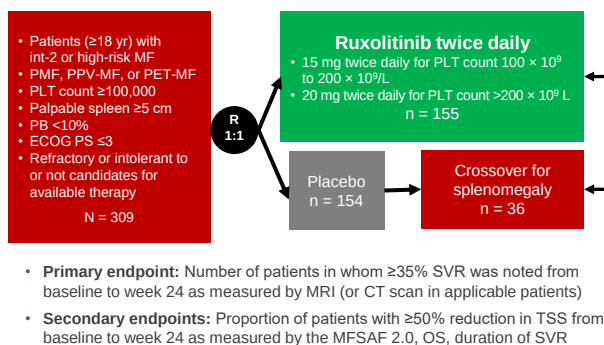
1. Duenas-Perez AB, Mead AJ. *Ther Adv Hematol*. 2015;6:186-201; 2. Oh S, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22(suppl 2):S327. Poster MPN-145; 3. Talpaz M, et al. *Leukemia*. 2021;35:1-17; 4. Singer JW, et al. *J Exp Pharmacol*. 2016;8:11-19; 5. Azhar M, et al. *Blood Adv*. 2022;6:1186-1192.

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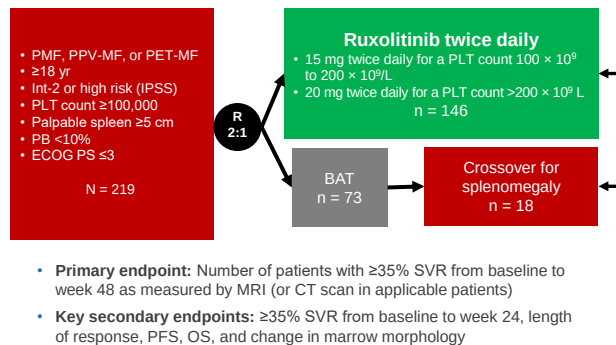
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Ruxolitinib Phase III Trials: COMFORT-I and COMFORT-II

COMFORT-I: Randomized, double-blind, placebo-controlled, multicenter, phase III trial¹



COMFORT-II: Randomized, open-label, phase III trial²



BAT, best available therapy; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; Int, intermediate; MFSAF, Myelofibrosis Symptom Assessment Form; MRI, magnetic resonance imaging; PET-MF, postessential thrombocythemia MF; PLT, platelet; PFS, progression-free survival; PMF, primary MF; PPV-MF, postpolycythemia vera MF; SVR, spleen volume reduction; TSS, Total Symptom Score.

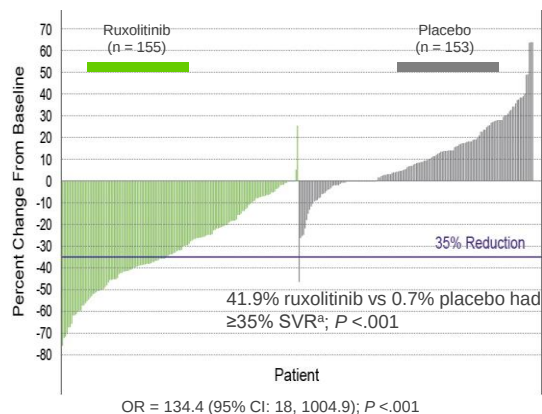
1. Verstovsek S, et al. *N Engl J Med*. 2012;366:799-807; 2. Harrison CN, et al. *N Engl J Med*. 2012;366:787-798.

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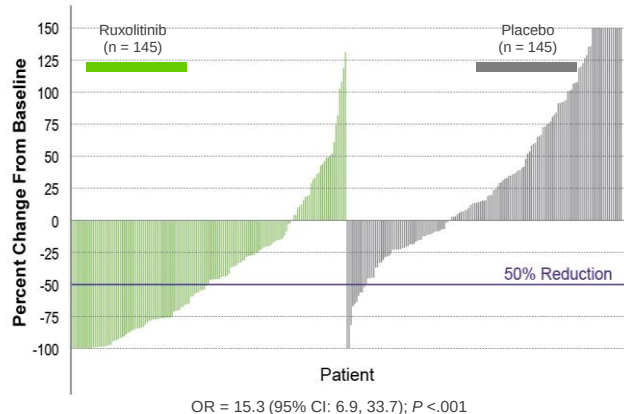
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COMFORT-I: Key Efficacy Endpoints

Primary endpoint: $\geq 35\%$ SVR at 24 weeks



TSS at 24 weeks



SVR responses were seen with ruxolitinib in $JAK2^{V617F}$ -positive and $JAK2^{V617F}$ -negative patients, relative to placebo

^aChanges in palpable spleen length in the ruxolitinib and placebo groups mirrored the changes in spleen volume.

OR, odds ratio.

Verstovsek S, et al. *N Engl J Med*. 2012;366:799-807.

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COMFORT-I: Worst Hematologic Laboratory Test Abnormalities

Hematologic Adverse Reactions ¹	Ruxolitinib n = 155		Placebo n = 151	
	All Grades, %	Grade 3/4, %	All Grades, %	Grade 3/4, %
Thrombocytopenia	69.7	12.9	30.5	1.3
Anemia	96.1	45.2	86.8	19.2
Neutropenia	18.7	7.1	4.0	2.0

Hematologic adverse reactions rarely led to treatment discontinuation. The following percentages are from both phase III studies: anemia (0.3%), thrombocytopenia (0.7%), neutropenia (1.0%)

• Management of hematologic abnormalities²

- **Thrombocytopenia:** Generally reversible; usually managed by reducing the dose or temporarily withholding ruxolitinib; if clinically indicated, platelet transfusions may be administered
- **Anemia:** Some patients may require blood transfusions; dose modifications may also be considered
- **Neutropenia (ANC $<0.5 \times 10^9/L$):** Generally reversible; managed by temporarily withholding ruxolitinib

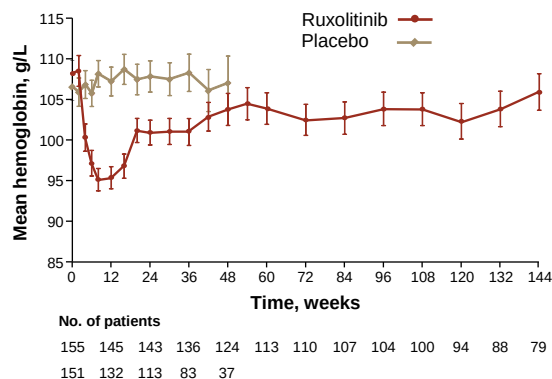
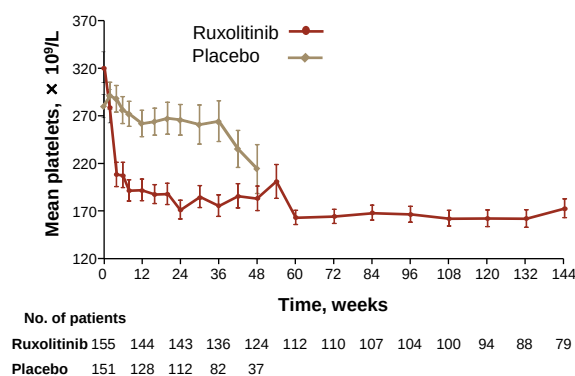
ANC, absolute neutrophil count.

1. Verstovsek S, et al. *N Engl J Med*. 2012;366:799-807; 2. Talpaz M, et al. *J Hematol Oncol*. 2013;6:81-91.

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COMFORT-I: Mean Platelet Count and Hemoglobin Over Time



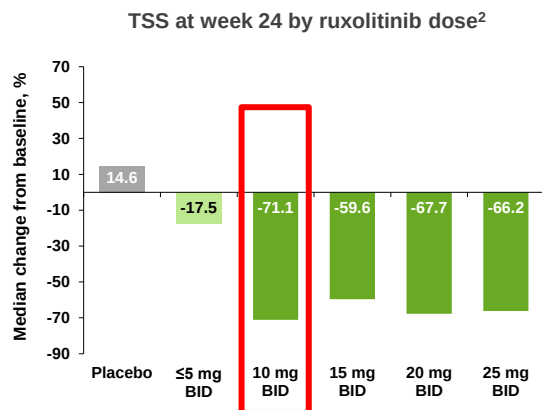
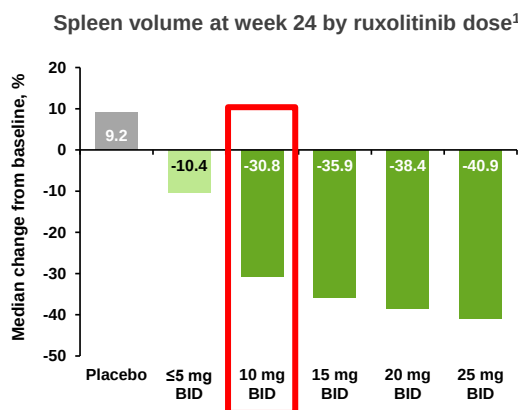
Verstovsek S, et al. *Haematologica*. 2015;100:479-488.

39

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COMFORT-I: Spleen Volume and Symptom Scores

- Limited change from baseline in spleen volume and TSS with low-dose ruxolitinib^{1,a}
- Long-term maintenance with low-dose ruxolitinib has not shown responses in patients with myelofibrosis²



^a≤5 mg twice daily.

BID, twice daily.

1. Verstovsek S, et al. *OncoTargets Ther*. 2014;7:13-21; 2. Jakafi® (ruxolitinib) [prescribing information]. Incyte Corporation; 2023.

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40

Case RH

New Management Approach



– Shared decision-making process

- The options we discussed with RH were JAK inhibitors
- First choice for her was ruxolitinib to address symptoms
- RH's treatment priority was improvement in symptoms and functionality
- We chose ruxolitinib to balance symptom control and potential for worsening anemia

Current labs:

- Hgb = 7.9 g/dL
- PLT = $168 \times 10^9/L$
- Differential = 1% blasts
- EPO = 550 mU/mL

BM biopsy:

- Mutation = *CALR*
- Fibrosis = grade 2
- Karyotype = 46,XX

NGS:

Mutation = *CALR*, *TET2*

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Based on ruxolitinib labelling instructions, what would optimal/target dose of ruxolitinib be for RH with plt 168?

- A. 5mg twice daily
- B. 10mg twice daily
- C. 15mg twice daily
- D. 20mg twice daily

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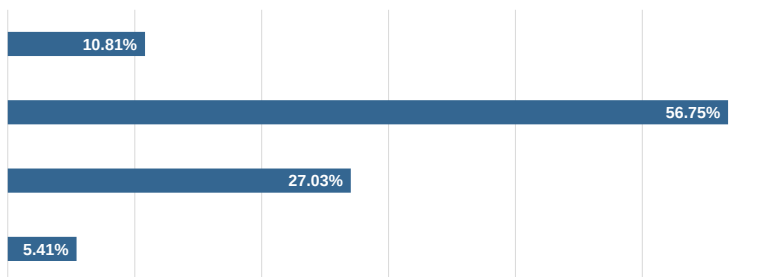
Based on ruxolitinib labelling instructions, what would optimal/target dose of ruxolitinib be for RH with plt 168?

A. 5mg twice daily

B. 10mg twice daily

C. 15mg twice daily

D. 20mg twice daily



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Case RH
Response to Treatment



– Initial response at 3-month follow-up

- RH is now feeling much better, with resolution of nights sweats and bone pain, and improvement in energy and activity level
- Her Hgb has stabilized at 7.2 g/dL after initially requiring RBC transfusions
- Her symptom burden is reduced (TSS = 2)
- The plan is to continue ruxolitinib and follow up every 2 weeks

Current labs:

- Hgb = 7.9 g/dL
- PLT = $168 \times 10^9/L$
- Differential = 1% blasts
- EPO = 550 mU/mL

BM biopsy:

- Mutation = *CALR*
- Fibrosis = grade 1
- Karyotype = 46,XX

NGS:

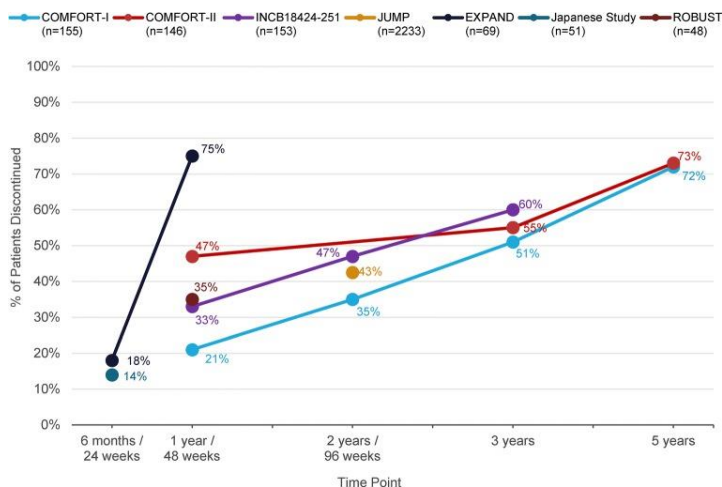
Mutation = *CALR*, *TET2*

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Ruxolitinib Discontinuation Over Time

Approximately 50% of patients originally randomized to ruxolitinib remain on therapy at 3 years



COMFORT-I ruxolitinib discontinuation rates

- Year 1: 21%
- Year 2: 35%
- Year 3: 51%
- Year 5: 72%

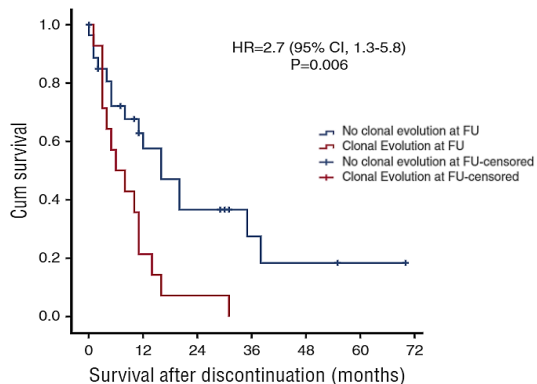
Harrison CN, et al. *Ann Hematol.* 2020;99:1177-1191.

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Outcomes After Ruxolitinib Discontinuation

- Retrospective analysis of clonal evolution and outcomes after ruxolitinib discontinuation in an open-label phase I/II study (N = 56)



- Median OS = 14 mo
- Survival improved if baseline platelets ≥ 260 vs $< 260 \times 10^9/L$ (HR = 2.7; $P = .006$)
- Survival improved if follow-up platelets ≥ 100 vs $< 100 \times 10^9/L$ (HR = 4.1; $P = .001$)
- 35% of patients acquired a new mutation while on ruxolitinib, most commonly ASXL1

Hashed lines = censored.

ASXL1, additional sex combs like 1; HR, hazard ratio; OS, overall survival.
Newberry KJ, et al. *Blood.* 2017;130:1125-1131.

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RUXOREL-MF (NCT03959371): An Ambispective Observational Study of Ruxolitinib-Treated Patients With MF

N = 209
Inclusion criteria

- ≥6 months of follow-up after RUX initiation
- Platelet count >50 × 10⁹/L
- Spleen enlargement of at least 5 cm below the left costal margin
- IPSS intermediate-1 risk

- Clinical and laboratory data collected at initiation of RUX and 3, 6, 12, 18, 24, 36, and 48 months post-RUX start
- Risk category assessed at 6 months using DIPSS for patients with primary MF and MYSEC-PM for patients with secondary MF

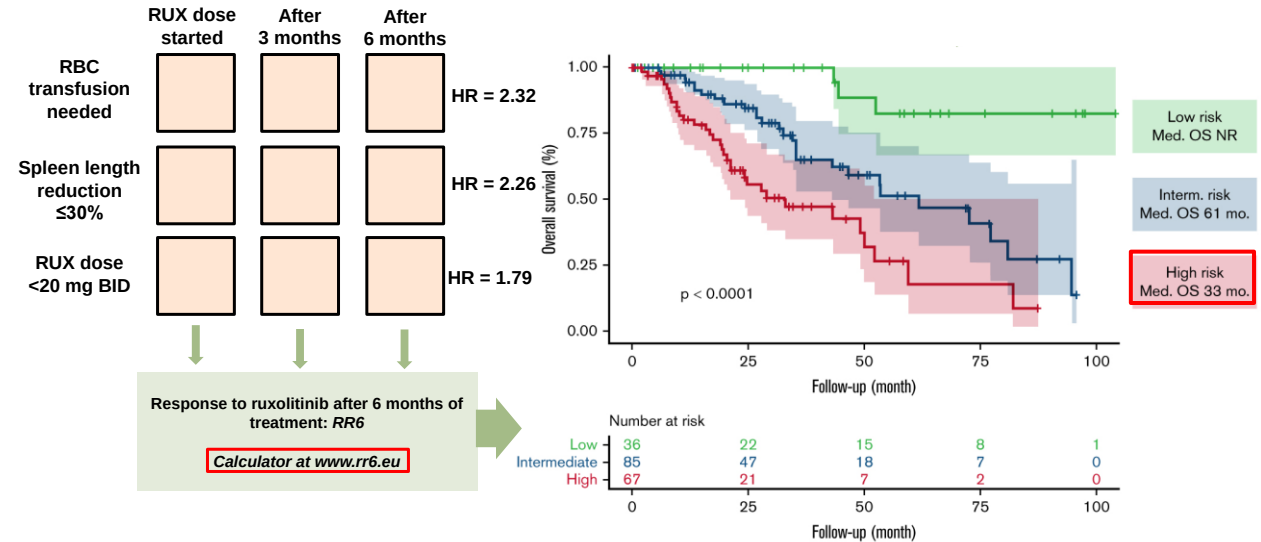
RUX Dose at Treatment Initiation	
5 mg BID n (%)	31 (14.8)
10 mg BID n (%)	45 (21.5)
15 mg BID n (%)	55 (26.3)
20 mg BID n (%)	78 (37.3)

MYSEC-PM, Myelofibrosis Secondary to Polycythemia Vera and Essential Thrombocythemia – Prognostic Model; RR6, response to ruxolitinib after 6 months. Maffioli M, et al. *Blood Adv.* 2022;6:1855-1864.

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3 Factors Predict Survival Benefit



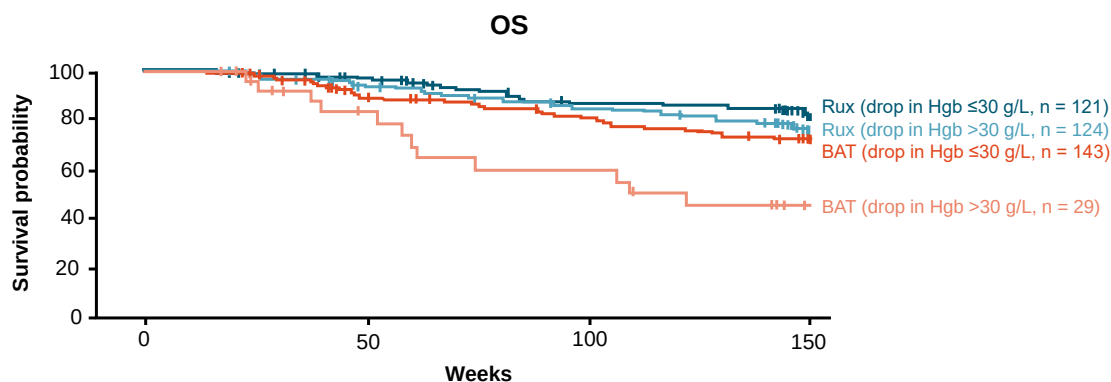
NR, not reached. Maffioli M, et al. *Blood Adv.* 2022;6:1855-1864.

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The RR6 model was validated in another cohort of patients (n = 40; P = .0276) treated with ruxolitinib at Moffitt Cancer Center.

COMFORT Studies: Ruxolitinib Overcomes Adverse Prognostic Effect of Anemia in MF



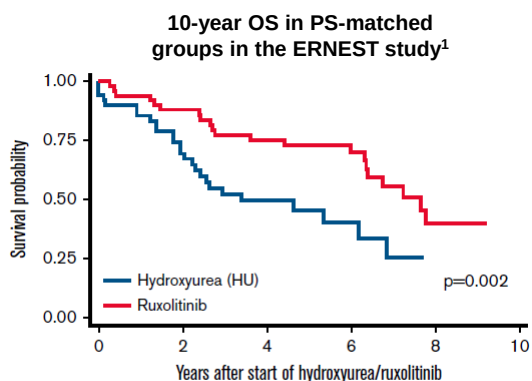
- Anemia is not a contraindication for ruxolitinib use; Hgb changes on ruxolitinib treatment do not bear the same prognostic implications as Hgb changes that occur as a consequence of MF pathology

Al-Ali HK, et al. *Leuk Lymphoma*. 2016;57:2464-2467; Gupta V, et al. *Haematologica*. 2016;101:e482-e484.

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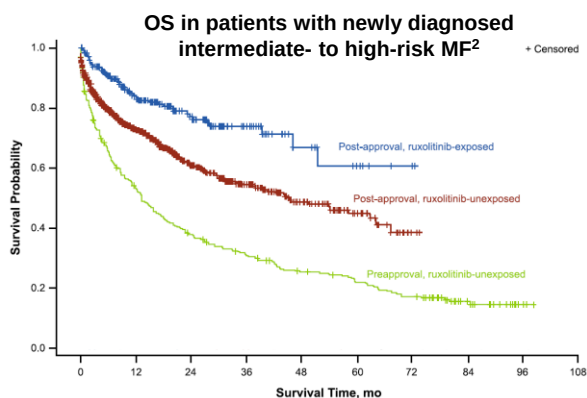
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Impact of Ruxolitinib on Survival in Real-Life Settings



N at risk	0	2	4	6	8	10
HU	50	30	16	6	1	1
Ruxo	50	42	33	25	6	1

Median OS with ruxolitinib vs HU: 6.7 vs 5.1 years; $P = .001$



HR (95% CI); P Value	Postapproval Ruxolitinib Exposed	Postapproval Ruxolitinib Unexposed
Preapproval Ruxolitinib unexposed	0.36 (0.26–0.50); $<.001$	0.67 (0.56–0.80); $<.001$

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Case RH: no longer responding to ruxolitinib



RH had been taking ruxolitinib for 15 months with good response. She presents for a follow-up visit.

– Changes since previous visit

- Previous spleen volume response is no longer being maintained; splenomegaly now at 9 below LCM
- Anemia has worsened
- PLT count has dropped below 100
- Symptom burden has increased (night sweats, bone pains, spleen pressure)

Current labs:

- Hgb = 6.7 g/dL
- PLT = $40 \times 10^9/L$
- Differential = 3% blasts

BM biopsy:

- Mutation = *CALR*
- Fibrosis = grade 2
- Karyotype = 46,XX

NGS:

Mutation = *CALR*, *TET2*

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Based on NCCN guideline recommendations for patients with higher risk MF, which of the following could be considered for RH?

- A. Fedratinib
- B. Momelotinib
- C. Pacritinib
- D. Clinical trial
- E. All of the above

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Based on NCCN guideline recommendations for patients with higher risk MF, which of the following could be considered for RH?

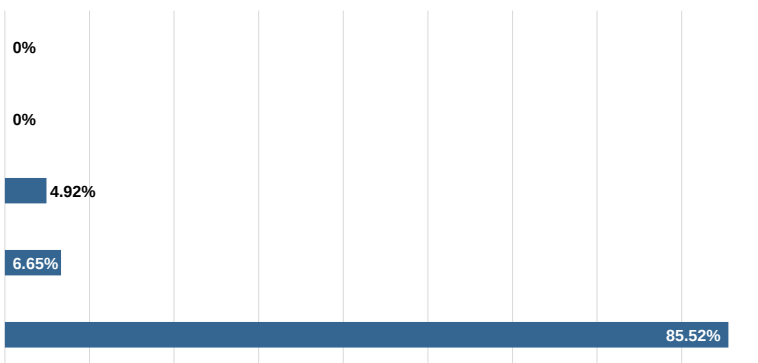
A. Fedratinib

B. Momelotinib

C. Pacritinib

D. Clinical trial

E. All of the above



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Fedratinib

	IC ₅₀ (nanomolar)						
	JAK1	JAK2	JAK3	TYK2	ACVR1	IRAK1	FLT3
Ruxolitinib ^{1,2}	2.8	4.5	322	30	>1000	---	---
Fedratinib¹⁻³	105	3	>1000	405	273	---	15
Pacritinib ^{1,2,4}	1280	6.0	18.3	27	16.7	13.6	14.8
Momelotinib ^{1,2,5}	11	18	155	17	52.5	---	401

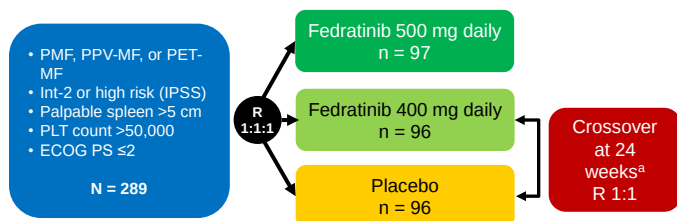
1. Duenas-Perez AB, Mead AJ. *Ther Adv Hematol*. 2015;6:186-201; 2. Oh S, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22(suppl 2):S327. Poster MPN-145; 3. Talpaz M, et al. *Leukemia*. 2021;35:1-17; 4. Singer JW, et al. *J Exp Pharmacol*. 2016;8:11-19; 5. Azhar M, et al. *Blood Adv*. 2022;6:1186-1192.

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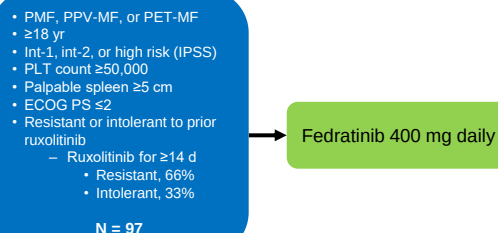
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Fedratinib Clinical Trials: JAKARTA (phase III) and JAKARTA-2 (phase II)

JAKARTA: Phase III, randomized, double-blind, placebo-controlled trial¹



JAKARTA-2: Phase II, single-arm, open-label, nonrandomized, multicenter study²



- **Primary endpoint:** number of patients with ≥35% SVR from baseline to week 24 as measured by MRI (or CT scan in applicable patients)
- **Key secondary endpoint:** proportion of patients with ≥50% reduction in TSS from baseline to week 24 as measured by the MFSAF 2.0

^aCrossover prior to 24 weeks was permitted if patients experienced progressive disease as defined in the study protocol.

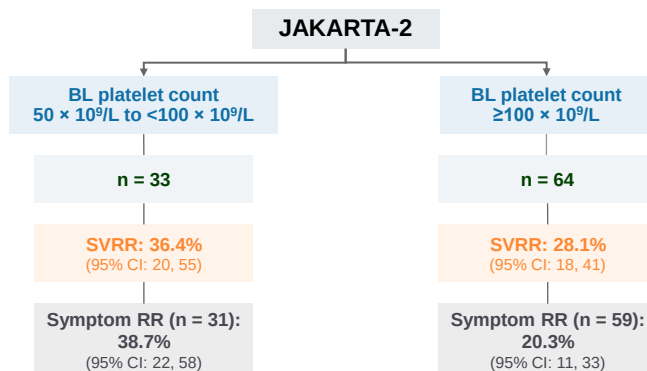
1. Pardanani A, et al. *JAMA Oncol.* 2015;1:643-651; 2. Harrison CN, et al. *Lancet Haematol.* 2017;4:e317-e324.

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Second-Line Fedratinib: Spleen Volume and Symptom Responses

- Overall SVRR was 31% (95% CI: 22, 41) and symptom RR was 27% (95% CI: 18, 37)
- There was no statistically significant difference in SVRR or symptom RR between BL platelet count subgroups



Statistical comparisons between BL platelet count subgroups should be interpreted with caution due to small sample sizes.

RR, response rate; SVRR, spleen volume response rate.

Harrison CN, et al. *Am J Hematol.* 2020;95:594-603

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JAKARTA and JAKARTA-2: Safety

Black Box Warning: Wernicke's Encephalopathy

Adverse events occurring in JAKARTA^a

Adverse Event, % ^{a,1}	Fedratinib 400 mg (n = 96)		Placebo (n = 95)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Diarrhea	66	5	16	0
Nausea	62	0	15	0
Anemia	40	30	14	7
Vomiting	39	3.1	5	0
Fatigue or asthenia	19	5	16	1.1
Muscle spasms	12	0	1.1	0
Blood creatinine increased	10	1	1.1	0
Pain in extremity	10	0	4.2	0

Adverse events occurring in JAKARTA-2

TEAEs Reported in >10% of Patients	ITT Population (N = 97) ^a	
	Any Grade, n (%)	Grade 3–4, n (%)
Diarrhea	60 (62)	4 (4)
Nausea	54 (56)	0
Anemia	47 (49)	37 (38)
Thrombocytopenia	26 (27)	21 (22)
Vomiting	40 (41)	0
Constipation	20 (21)	1 (1)
Pruritus	17 (18)	0
Fatigue	15 (16)	2 (2)
Cough	13 (13)	0
Headache	13 (13)	1 (1)
Urinary tract infection	12 (12)	0
Abdominal pain	12 (12)	2 (2)
Dyspnea	12 (12)	1 (1)
Asthenia	11 (11)	1 (1)
Dizziness	11 (11)	0
Pyrexia	11 (11)	1 (1)

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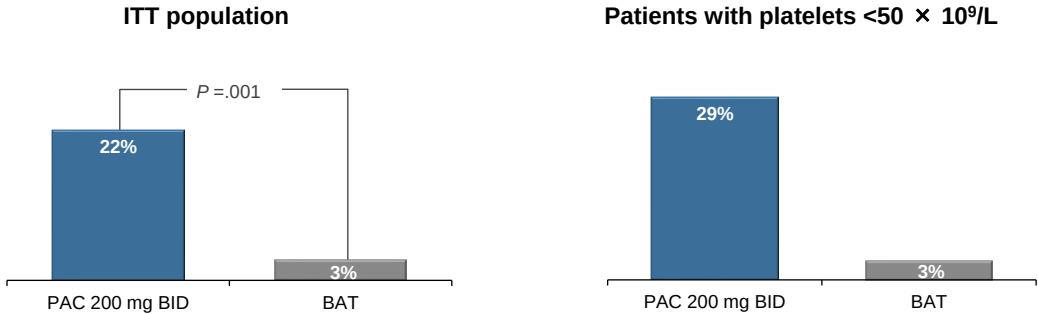
Pacritinib

	IC ₅₀ (nanomolar)						
	JAK1	JAK2	JAK3	TYK2	ACVR1	IRAK1	FLT3
Ruxolitinib ^{1,2}	2.8	4.5	322	30	>1000	---	---
Fedratinib ¹⁻³	105	3	>1000	405	273	---	15
Pacritinib ^{1,2,4}	1280	6.0	18.3	27	16.7	13.6	14.8
Momelotinib ^{1,2,5}	11	18	155	17	52.5	---	401

1. Duenas-Perez AB, Mead AJ. *Ther Adv Hematol.* 2015;6:186-201; 2. Oh S, et al. *Clin Lymphoma Myeloma Leuk.* 2022;22(suppl 2):S327. Poster MPN-145; 3. Talpaz M, et al. *Leukemia.* 2021;35:1-17; 4. Singer JW, et al. *J Exp Pharmacol.* 2016;8:11-19; 5. Azhar M, et al. *Blood Adv.* 2022;6:1186-1192.

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PERSIST-2: Spleen Volume Responses ≥35% at Week 24



Additional subgroup analyses demonstrated patients receiving pacritinib had SVR ≥35% regardless of subgroup (eg, sex, age, JAK2 V617F mutation status, prior treatment with JAK2 inhibitors, and baseline cytopenias)

ITT, intention-to-treat; PAC, pacritinib.
Mascarenhas J, et al. *JAMA Oncol.* 2018;4:652-659.

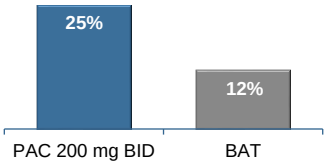
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PERSIST-2: Hematologic Stability

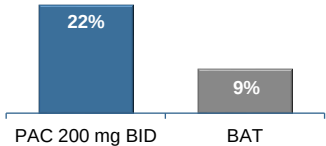
Clinical improvement in hemoglobin levels in patients with baseline anemia^a

Baseline to week 24



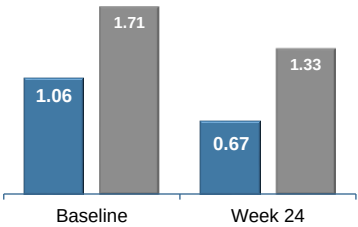
Pacritinib reduced transfusion burden in patients not TI at baseline

Baseline to week 24



Transfusion burden in patients who received ≥1 RBC transfusion on study

Units per month



TI defined according to Gale criteria (0 units over the course of 12 weeks).
^aInternational Working Group response criteria: increase of ≥2.0 g/dL or RBC transfusion independence for ≥8 weeks prior; anemia defined as hemoglobin <10 g/dL.
TI, transfusion independent.
Mascarenhas J, et al. *JAMA Oncol.* 2018;4:652-659.

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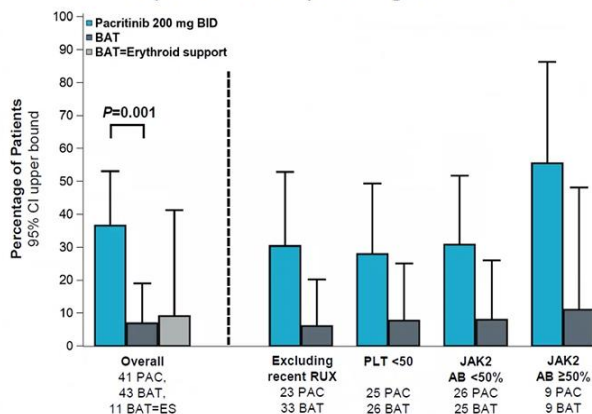
More Pacritinib Patients Had TI (Gale criteria)

TI Conversion Rate

Pacritinib n = 41	BAT n = 43	P Value
37%	7%	.001

- TI conversion better on pacritinib than BAT, including patients receiving erythroid support agents as BAT
- Erythroid support agents were prohibited on the pacritinib arm

Rate of TI (Gale criteria) through Week 24

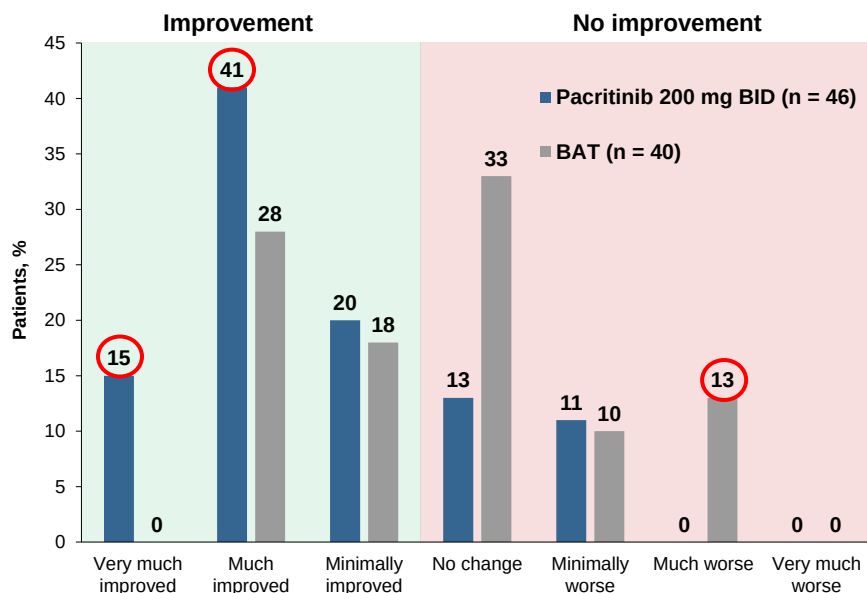


Oh S, et al. *Blood*. 2022;140(suppl 1):1518-1521.

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Improved Quality of Life Associated With 200 mg BID Pacritinib



- 56% reported “much improved” or “very much improved” in the 200-mg BID pacritinib arm
- 13% reported “much worse” in the BAT arm

Mascarenhas J, et al. *JAMA Oncol*. 2018;4:652-659.

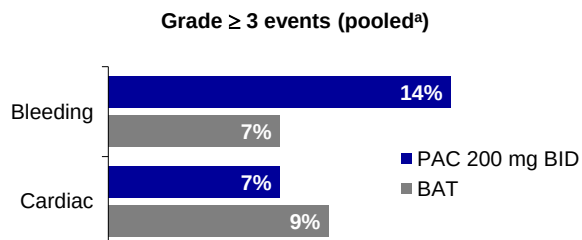
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PERSIST-2: Adverse Events

Adverse Reactions	PAC 200 mg BID (n = 106)	BAT (n = 98)
Any-grade AEs in >15% of patients in either arm, %		
Diarrhea	48	15
Thrombocytopenia	34	24
Nausea	32	11
Anemia	24	15
Peripheral edema	20	15
Vomiting	19	5
Fatigue	17	16
Grade ≥3 AEs in >5% of patients in either arm, %		
Thrombocytopenia	32	18
Anemia	22	14
Neutropenia	7	5
Pneumonia	7	3
Serious AEs in >3% of patients in either arm, %		
Anemia	8	3
Thrombocytopenia	6	2
Pneumonia	6	4
Congestive heart failure	4	2

- Diarrhea with pacritinib most often occurred during weeks 1 through 8, was manageable, and resolved within 1 to 2 weeks
- Neurologic AEs and opportunistic infections rarely reported with pacritinib
- Safety outcomes with pacritinib were similar for those with $<50 \times 10^9/L$ vs 50 to $100 \times 10^9/L$ platelets at baseline**



^aPooled, per standardized MedDRA queries.
MedDRA, Medical Dictionary for Regulatory Activities.
Mascarenhas J, et al. *JAMA Oncol.* 2018;4:652-659..

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Risk-Adjusted AEs of Interest

Patients With Events per 100 Patient-Years at Risk (number of patients/total patient-years)	PAC203 PAC	PERSIST-2			Pooled PAC
		PAC	BAT	BAT = RUX	
Cancers					
Malignancy – excluding leukemic transformation ^a	0 (0/29.6)	8 (5/63.7)	7 (3/40.8)	11 (2/17.8)	5 (5/93.3)
Nonmelanoma skin cancer ^b	0 (0/29.6)	5 (3/64.2)	7 (3/40.8)	11 (2/17.8)	3 (3/93.8)
Viral infections					
Viral infection ^c	7 (2/29.2)	5 (3/65.1)	12 (5/41.1)	11 (2/18.3)	5 (5/94.3)
Zoster ^d	0 (0/29.6)	0 (0/65.7)	2 (1/41.5)	6 (1/18.3)	0 (0/95.3)
Fungal infection	10 (3/29.1)	5 (3/64.1)	12 (5/40.8)	6 (1/18.3)	6 (6/93.1)

^aIncludes all events within the Systems Order Class (SOC) "Neoplasms benign, malignant, and unspecified," excluding acute leukemia, myelofibrosis, and benign tumors; ^bIncludes basal cell and squamous cell carcinoma of the skin, as determined by medical review; ^cIncludes any infection event attributed to a specific virus (eg, cytomegalovirus reactivation, herpes keratitis), or described as being "viral" (eg, viral gastroenteritis, viral upper respiratory tract infection), as determined by medical review; ^dIncludes any infection event relating to "zoster" or "shingles," as determined by medical review.
Pemmaraju N, et al. *ASCO* 2022. Poster 7058.

Risk-adjusted incidence rate calculated on the basis of exposure-adjusted incidence per 100 patient-years:

$100 \times (\text{number of patients with an event} / \text{total patient-years at risk of the event})$

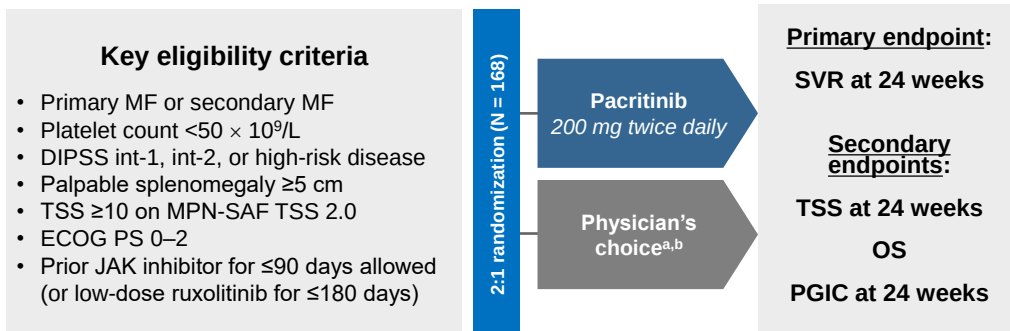
Total patient-years at risk of the event calculated as

- For patients with no event: (date last dose – date first dose) + 1/365.25
- For patients with an event: (date event – date first dose) + 1/365.25

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PACIFICA: Phase III Pacritinib Trial – Enrollment Completed in United States (ongoing outside United States)



^aPhysician's choice includes any 1 of the following: low-dose ruxolitinib, corticosteroids, hydroxyurea, danazol. Investigators may select individual physician's choice agents but cannot combine agents or give them sequentially; ^bCrossover not permitted.

PGIC, Patient Global Impression of Change.

ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT03165734>.

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Momelotinib

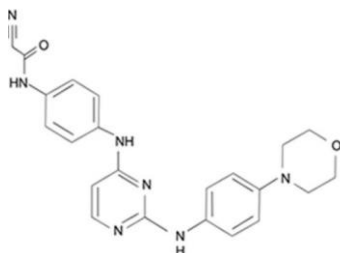
	IC ₅₀ (nanomolar)						
	JAK1	JAK2	JAK3	TYK2	ACVR1	IRAK1	FLT3
Ruxolitinib ^{1,2}	2.8	4.5	322	30	>1000	---	---
Fedratinib ¹⁻³	105	3	>1000	405	273	---	15
Pacritinib ^{1,2,4}	1280	6.0	18.3	27	16.7	13.6	14.8
Momelotinib ^{1,2,5}	11	18	155	17	52.5	---	401

1. Duenas-Perez AB, Mead AJ. *Ther Adv Hematol*. 2015;6:186-201; 2. Oh S, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22(suppl 2):S327. Poster MPN-145; 3. Talpaz M, et al. *Leukemia*. 2021;35:1-17; 4. Singer JW, et al. *J Exp Pharmacol*. 2016;8:11-19; 5. Azhar M, et al. *Blood Adv*. 2022;6:1186-1192.

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Momelotinib: Emerging JAK1, JAK2, and ACVR1 Inhibitor



Momelotinib

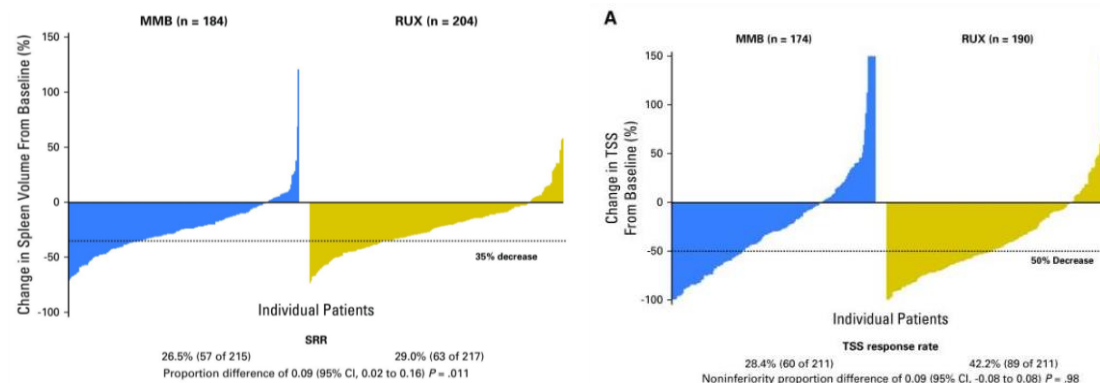
- Momelotinib is an inhibitor of JAK1, JAK2, and ACVR1 that recently received FDA approval^{1,2}
- SIMPLIFY-1 and SIMPLIFY-2: completed phase III trials of momelotinib in first-line and second-line settings^{1,2}
- MOMENTUM: ongoing phase III trial comparing momelotinib to danazol for MF with anemia³
- Most frequent nonhematologic AEs: diarrhea, nausea, and asthenia/fatigue³

FDA, US Food and Drug Administration.

1. Mesa RA, et al. *J Clin Oncol*. 2017;35:3844-3850; 2. Harrison CN, et al. *Lancet Haematol*. 2018;5:e73-e81; 3. Mesa RA, et al. *J Clin Oncol*. 2022;40(suppl 16): abstract 7002.⁶⁹

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Momelotinib Is a JAK1/JAK2 Inhibitor



Momelotinib noninferior for spleen reduction but NOT noninferior for symptom improvement

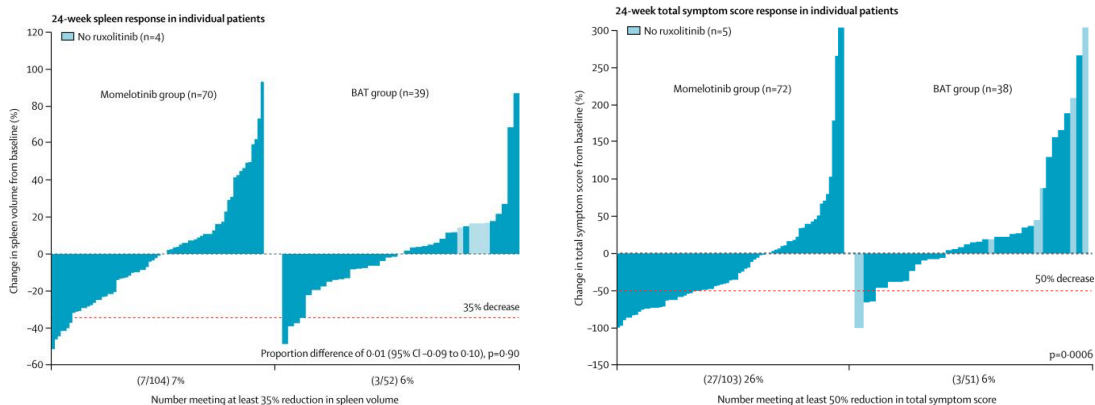
SRR, spleen response rate.

Mesa RA, et al. *J Clin Oncol*. 2017;35:3844-3850.

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Momelotinib Is a JAK1/JAK2 Inhibitor



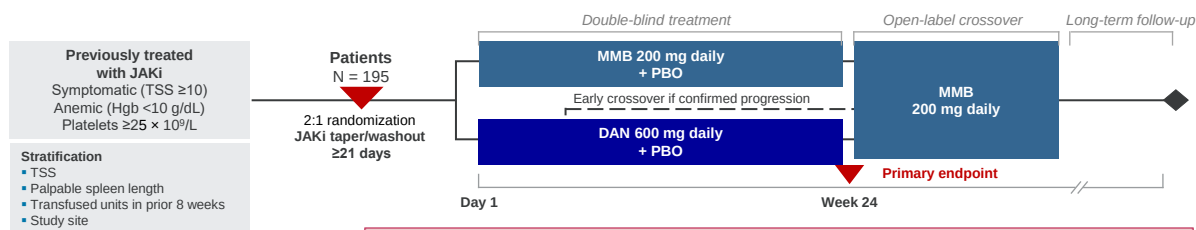
Momelotinib was superior in terms of symptom response but not superior in terms of spleen response

Harrison CN, et al. *Lancet Haematol*. 2018;5:e73-e81.

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Momelotinib vs Danazol in Symptomatic, Anemic, JAKi-Experienced Patients: MOMENTUM Study



	Test order	Criterion for significance	Momelotinib group (n=130)	Danazol group (n=65)	p value
TSS response rate*	1	Superiority (ps0.05)	32 (25%)	6 (9%)	Two-sided 0.0095 (superior)
Transfusion independence rate†	2	Non-inferiority	39 (30%)	13 (20%)	One-sided 0.0116 (non-inferior)‡
Spleen response rate (≥25% reduction)	3	Superiority (ps0.05)	51 (39%)	4 (6%)	Two-sided <0.0001 (superior)
Absolute TSS change from baseline§	4	Superiority (ps0.05)	-11.5	-3.9	Two-sided 0.0014 (superior)¶
Spleen response rate (≥35% reduction)	5	Superiority (ps0.05)	29 (22%)	2 (3%)	Two-sided 0.0011 (superior)
Rate of zero transfusions to week 24	6	Superiority (ps0.05)	46 (35%)	11 (17%)	Two-sided 0.0012 (superior)

Data are n (%), unless otherwise specified. TSS=total symptom score. *Primary endpoint was TSS response, defined as a 50% or more reduction in mean TSS over the 28 days immediately before the end of week 24 compared with baseline. †Proportion of patients with transfusion-independent status defined as not requiring red blood cell transfusion for the last 12 weeks of the 24-week randomised period, with all haemoglobin concentrations during the 12-week interval of 8 g/dL or more. ‡Non-inferior if p (momelotinib) - 0.8 × p (danazol) >0 with significance. Transfusion independence tested for superiority with a p value (two-sided) of 0.1265. §Mean change from baseline in TSS at week 24. ¶p value for the least squares mean difference between the two groups from the mixed effect repeated measures model.

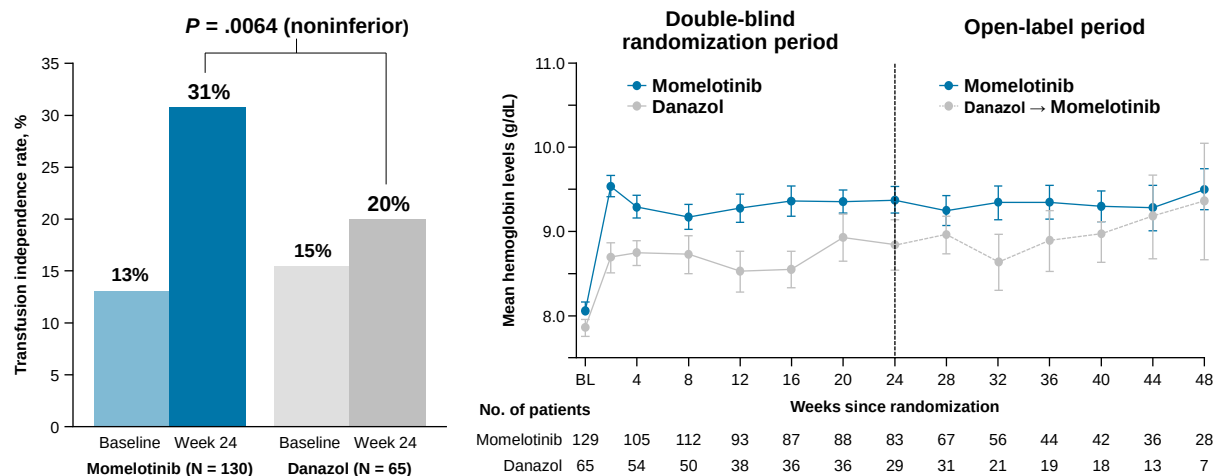
Table 2: Summary of primary and key secondary efficacy endpoint analyses at week 24

PBO, placebo.
Verstovsek S, et al. *Lancet*. 2023;401:269-280.

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MOMENTUM: Transfusion Independence at Week 24

Verstovsek S, et al. *Lancet*. 2023;401:269-280.

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Mometotinib Survival and Safety

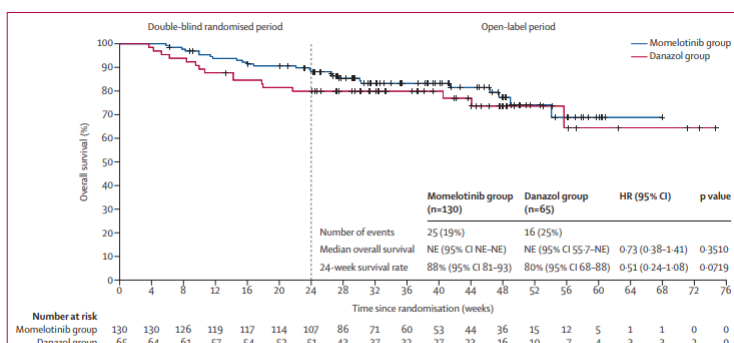


Figure 3: Overall survival in the intention-to-treat population

Kaplan-Meier estimates of overall survival in the intention-to-treat population from the time of randomisation to the data cutoff date (Dec 3, 2021). The vertical line at week 24 indicates the transition between the double-blind randomised period and the open-label period when patients ongoing in the study started receiving open-label mometotinib treatment. p value from a stratified log-rank test; HR (mometotinib group vs danazol group) from a stratified Cox proportional hazards model with a single factor of treatment group and stratified by baseline stratification factors. HR=hazard ratio. NE=not estimable.

	Mometotinib group (n=130)		Danazol group (n=65)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Non-haematological abnormalities (preferred term)				
Diarrhoea	29 (22%)	0	6 (9%)	1 (2%)
Nausea	21 (16%)	3 (2%)	6 (9%)	2 (3%)
Asthenia	17 (13%)	1 (1%)	6 (9%)	1 (2%)
Pruritus	14 (11%)	2 (2%)	7 (11%)	0
Weight decreased	14 (11%)	0	4 (6%)	0
Blood creatinine increased	10 (8%)	1 (1%)	10 (15%)	2 (3%)
Dyspnoea	10 (8%)	3 (2%)	9 (14%)	1 (2%)
Peripheral oedema	10 (8%)	2 (2%)	9 (14%)	0
Fatigue	8 (6%)	1 (1%)	7 (11%)	2 (3%)
Acute kidney injury	6 (5%)	4 (3%)	8 (12%)	6 (9%)
Haematological abnormalities*				
Anaemia	129 (99%)	79 (61%)	65 (100%)	49 (75%)
Thrombocytopenia	99 (76%)	36 (28%)	40 (62%)	17 (26%)
Neutropenia	38 (29%)	16 (12%)	17 (26%)	6 (9%)

Data are n (%). *Haematological abnormalities are based on laboratory values. The data shown are for events of the worst grade during the 24-week randomised treatment phase of the study, regardless of whether this grade was a change from baseline.

Table 3: Treatment-emergent adverse events observed in at least 10% of patients in either treatment group during the 24-week randomised treatment period

Verstovsek S, et al. *Lancet*. 2023;401:269-280.

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Case RH

Change in Management



– New approach to management

- We chose to switch her to pacritinib 200 mg BID to address worsening anemia and thrombocytopenia, symptoms, and spleen volume

■ Considerations in management approach

- **Approach to transition:** immediate switch; taper/ramp up is not needed due to poor disease control at current dosage
- **Dose modification considerations:** use full dose
- **Initial response at 3-month follow-up**
 - RH's symptoms have decreased significantly (TSS = 4)
 - Her spleen volume has decreased by 40%; Hgb is 8.1g/dL; PLT are 65K
 - The plan is to continue pacritinib and follow up in 1 month

Current labs:

- Hgb = 8.1 g/dL
- PLT = $65 \times 10^9/L$
- Differential = 3% blasts

BM biopsy:

- Mutation = JAK2V617F
- Hypercellular, atypical MK
- <5% blasts by IHC
- Fibrosis = grade 2
- Karyotype = 46,XX

NGS:

Mutation = CALR, TET2

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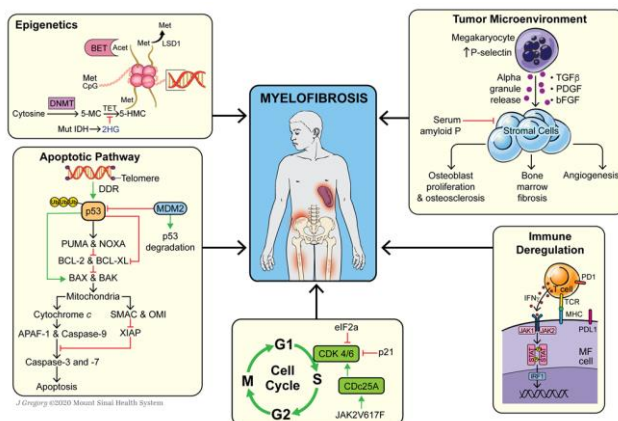
Novel Agents in Development for MF

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Preclinical Evidence Translates to the Clinic

- Aberrant trafficking of CD34+ MPN HSC¹
- Constitutive JAK-STAT signaling²
- Epigenetic deregulation³
- Elevated levels of IL-8⁴
- Increased NFκB activity⁵
- Increased BCL-2/X_L expression⁶
- Reduced TP53 activity (increased MDM2 expression)⁷
- Constitutive telomerase expression in CD34+ MPN cells⁸



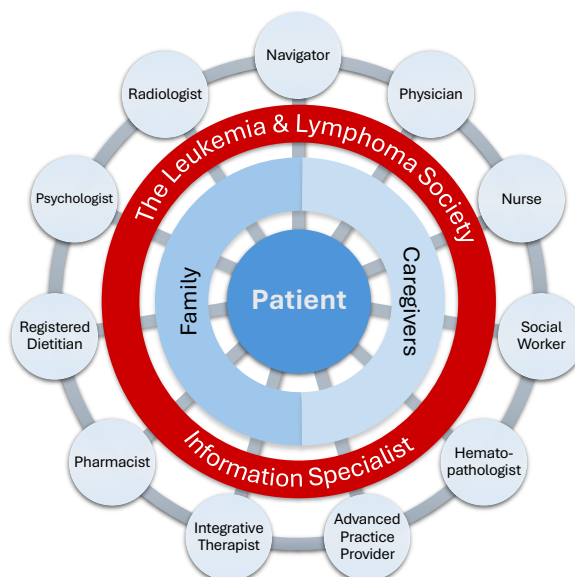
Venugopal S, Mascarenhas J. *Hematol Oncol Clin North Am.* 2021;35:353-373.

1. Xu M, et al. *Blood.* 2005;105:4508-4515; 2. Kralovics R, et al. *N Engl J Med.* 2005;352:1779-1790; 3. Mascarenhas J, et al. *Clin Epigenetics.* 2011;2:197-212; 4. Tefferi A, et al. *J Clin Oncol.* 2011;29:1356-1363; 5. Fischer DAC, et al. *Leukemia.* 2017;31:1962-1974; 6. Lu M, et al. *Blood.* 2010;116:4284-4287; 7. Lu M, et al. *Blood.* 2014;124:771-779; 8. Wang X, et al. *Blood Adv.* 2018;25:2378-2388.

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Patient-centric Care Team

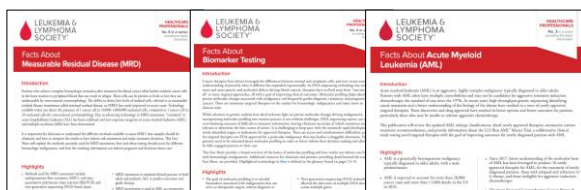
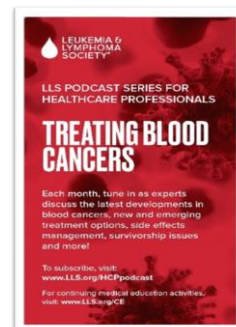


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FREE LLS RESOURCES FOR HEALTHCARE PROVIDERS

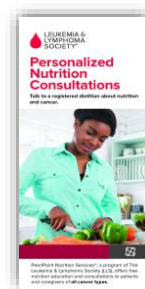
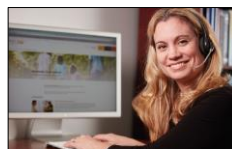
- ❑ CME & CE courses: www.LLS.org/CE
- ❑ Fact Sheets for HCPs: www.LLS.org/HCPbooklets
- ❑ Videos for HCPs: www.LLS.org/HCPvideos
- ❑ Podcast series for HCPs: www.LLS.org/HCPpodcast



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FREE LLS RESOURCES FOR PATIENTS

- ❑ **Information Specialists (IRC)** – Personalized assistance for managing treatment decisions, side effects, and dealing with financial and psychosocial challenges.
- ❑ **Clinical Trial Nurse Navigators (CTSC)** – provide personalized service for patients seeking treatment in a clinical trial, sift through and provide information to bring back to the HC team www.LLS.org/CTSC
- ❑ **Nutrition Education Services Center (NESC)** – one-on-one **free** nutrition education and consultations to patients of all cancer types with RDs who have expertise in oncology nutrition www.LLS.org/Nutrition
- ❑ **Reach out Monday–Friday, 9 am to 9 pm ET**
 - Phone: 800.955.4572
 - Live chat: www.LLS.org/IRC
 - Email: LLS.org/ContactUs
 - HCP Patient Referral Form: www.LLS.org/HCPreferral



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FREE LLS RESOURCES FOR PATIENTS AND CAREGIVERS

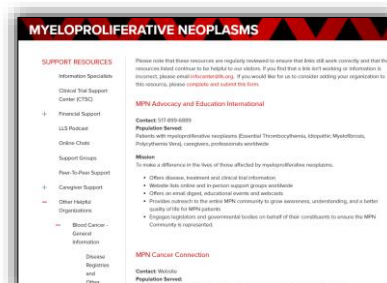
❑ Webcasts, Videos, Podcasts, booklets:

- www.LLS.org/Webcasts
- www.LLS.org/EducationVideos
- www.LLS.org/Podcast
- www.LLS.org/Booklets

❑ www.LLS.org/MPN

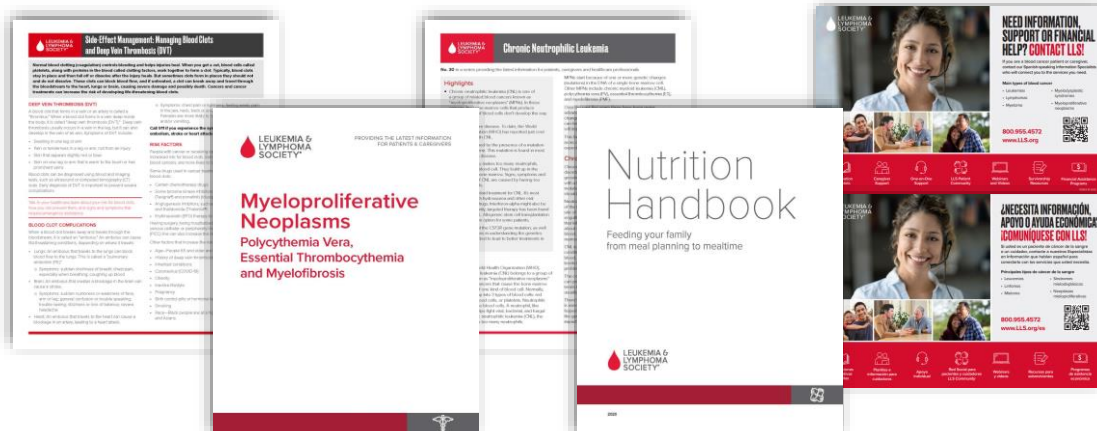
❑ Support Resources

- Financial Assistance: www.LLS.org/Finances
 - Urgent Need
 - Patient Aid
 - Travel Assistance
- Other Support: www.LLS.org/Support
 - LLS Regions
 - Online Weekly Chats Facilitated by Oncology SW
 - LLS Community Social Media Platform
 - First Connection Peer to Peer Program



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FREE LLS RESOURCES FOR YOUR PATIENTS



BOOKLETS AND FACT SHEETS

English – www.LLS.org/Booklets

Spanish – www.LLS.org/Materiales



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Q & A



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