Myeloproliferative Neoplasms: Diagnosis, Treatment, and Side Effect Management

LEUKEMIA & LYMPHOMA SOCIETY®

LEARNING OBJECTIVES

- Describe the types of myeloproliferative neoplasms (MPNs), including myelofibrosis, polycythemia vera, and essential thrombocythemia
- Identify tests used to diagnose disease and monitor treatment of MPNs
- Explain the overarching goals of treatment for the various types of MPNs
- Explain approved and emerging treatment options for all MPNs, including stem cell transplantation, and the role of clinical trials
- Describe strategies to manage treatment side effects as well as potential long-term and late effects of treatments for MPNs
- Describe the healthcare professional's role in managing patients with MPNs

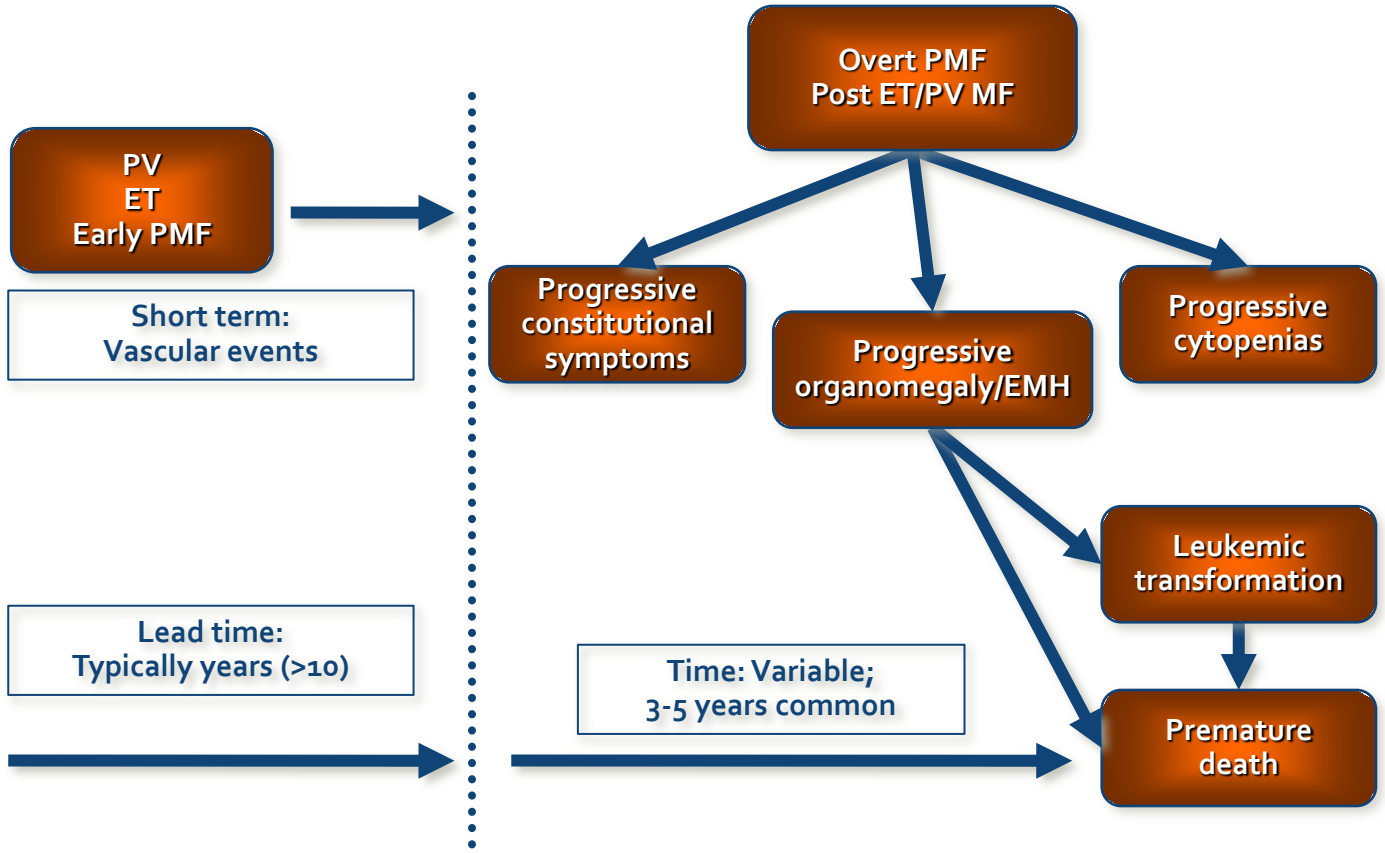
FACULTY

Michael Mauro, MD
Professor of Medicine
Director, Chronic Myeloid Leukemia Program
Leukemia Service
Memorial Sloan Kettering Cancer Center
New York, NY

Jacqueline Dela Pena, PharmD, BCOP
Clinical Pharmacy Specialist
Leukemia Service, Department of Pharmacy
Memorial Sloan Kettering Cancer Center
New York, NY

Carolanne Carini, MS, BSN, RN, BMTCN
Senior Nurse Coordinator, PAS
Memorial Sloan Kettering Cancer Center
New York, NY

MPN Overview: Timeframes

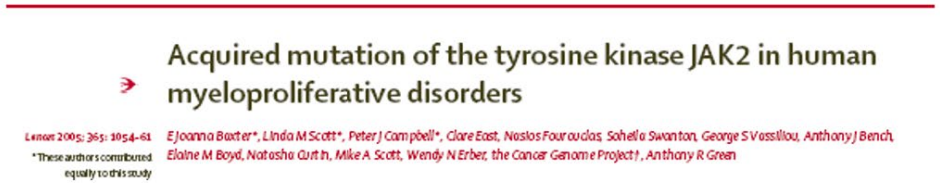


EMH, extramedullary hematopoiesis; ET, essential thrombocythemia; MF, myelofibrosis; PMF, primary myelofibrosis; PV, polycythemia vera.

Pinilla-Ibarz J, et al. *Onco Targets Ther*. 2016;9:4937-4957; Lichtman M et al. *Williams Manual of Hematology*. 8th ed. New York, NY: McGraw Hill Medical; 2011.

JAK2 V617F Mutation Discovery in MPNs: "The Other BCR-ABL"

March 18, 2005



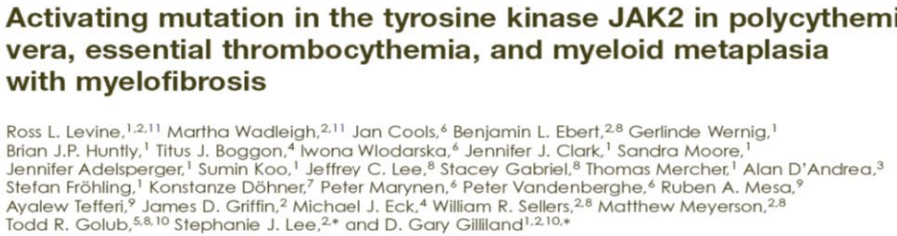
Acquired mutation of the tyrosine kinase JAK2 in human myeloproliferative disorders

Lancet 2005; 365: 1054–61

*These authors contributed equally to this study

E Joanna Baxter*, Linda M Scott*, Peter J Campbell*, Clare East, Nasios Fourouclas, Sahella Swanton, George S Vassiliou, Anthony J Bench, Elaine M Boyd, Natasha Curtin, Mike A Scott, Wendy N Erber, the Cancer Genome Project†, Anthony R Green

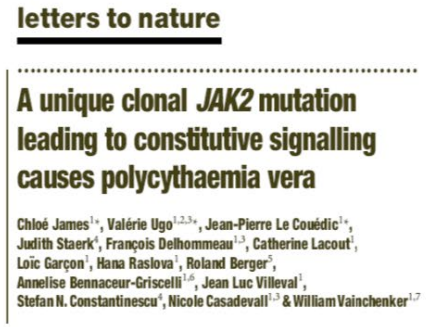
March 24, 2005



Activating mutation in the tyrosine kinase JAK2 in polycythemia vera, essential thrombocythemia, and myeloid metaplasia with myelofibrosis

Ross L. Levine,[1,2,11] Martha Wadleigh,[2,11] Jan Cools,[6] Benjamin L. Ebert,[2,8] Gerlinde Wernig,[1] Brian J.P. Huntly,[1] Titus J. Boggon,[4] Iwona Wlodarska,[6] Jennifer J. Clark,[1] Sandra Moore,[1] Jennifer Adelsperger,[1] Sumin Koo,[1] Jeffrey C. Lee,[8] Stacey Gabriel,[8] Thomas Mercher,[1] Alan D'Andrea,[3] Stefan Fröhling,[1] Konstanze Döhner,[7] Peter Marynen,[6] Peter Vandenberghe,[6] Ruben A. Mesa,[9] Ayalew Tefferi,[9] James D. Griffin,[2] Michael J. Eck,[4] William R. Sellers,[2,8] Matthew Meyerson,[2,8] Todd R. Golub,[5,8,10] Stephanie J. Lee,[2,*] and D. Gary Gilliland[1,2,10,*]

April 28, 2005



letters to nature

A unique clonal *JAK2* mutation leading to constitutive signalling causes polycythaemia vera

Chloé James[1*], Valérie Ugo[1,2,3*], Jean-Pierre Le Couédic[1*], Judith Staerk[4], François Delhommeau[1,3], Catherine Lacout[1], Loïc Garçon[1], Hana Raslova[1], Roland Berger[5], Annelise Bennaceur-Griscelli[1,6], Jean Luc Villeval[1], Stefan N. Constantinescu[4], Nicole Casadevall[1,3] & William Vainchenker[1,7]

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

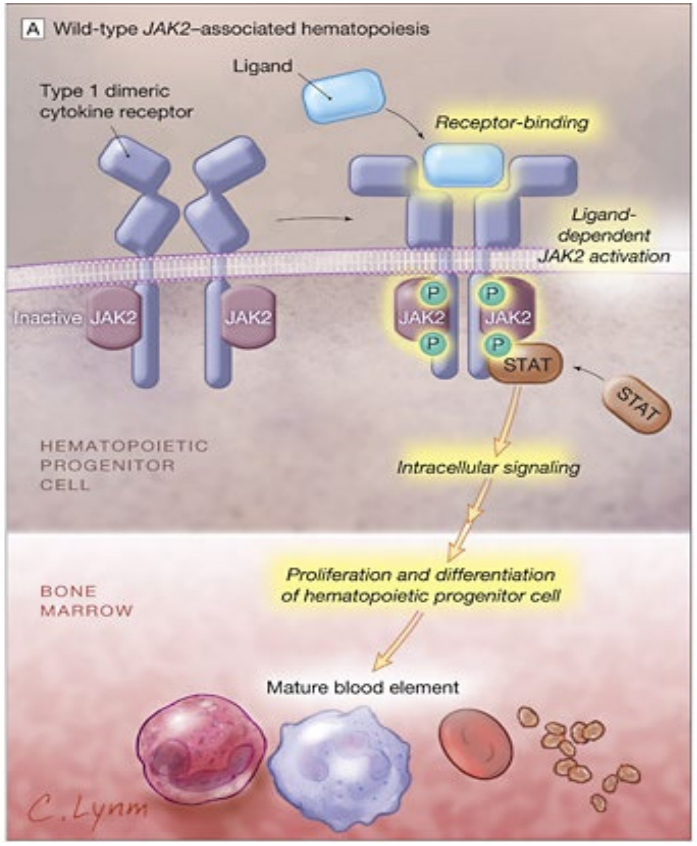
A Gain-of-Function Mutation of *JAK2* in Myeloproliferative Disorders

Robert Kralovics, Ph.D., Francesco Passamonti, M.D., Andreas S. Buser, M.D., Soon-Siong Teo, B.S., Ralph Tiedt, Ph.D., Jakob R. Passweg, M.D., Andre Tichelli, M.D., Mario Cazzola, M.D., and Radek C. Skoda, M.D.

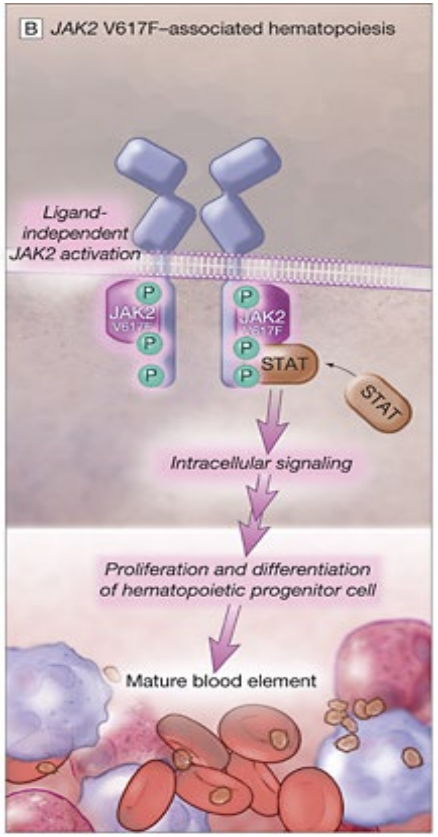
Baxter EJ, et al. *Lancet*. 2005;365(9464):1054-1061. Levine RL, et al. *Cancer Cell.* 2005;7(4):387-397; James C, et al. *Nature*. 2005;434(7037):1144-1148; Kralovics R, et al. *N Engl J Med*. 2005;352(17):1779-1790.

JAK2 Signaling in MPNs: Finding the "Driver"

Wild-type JAK2: Normal signaling



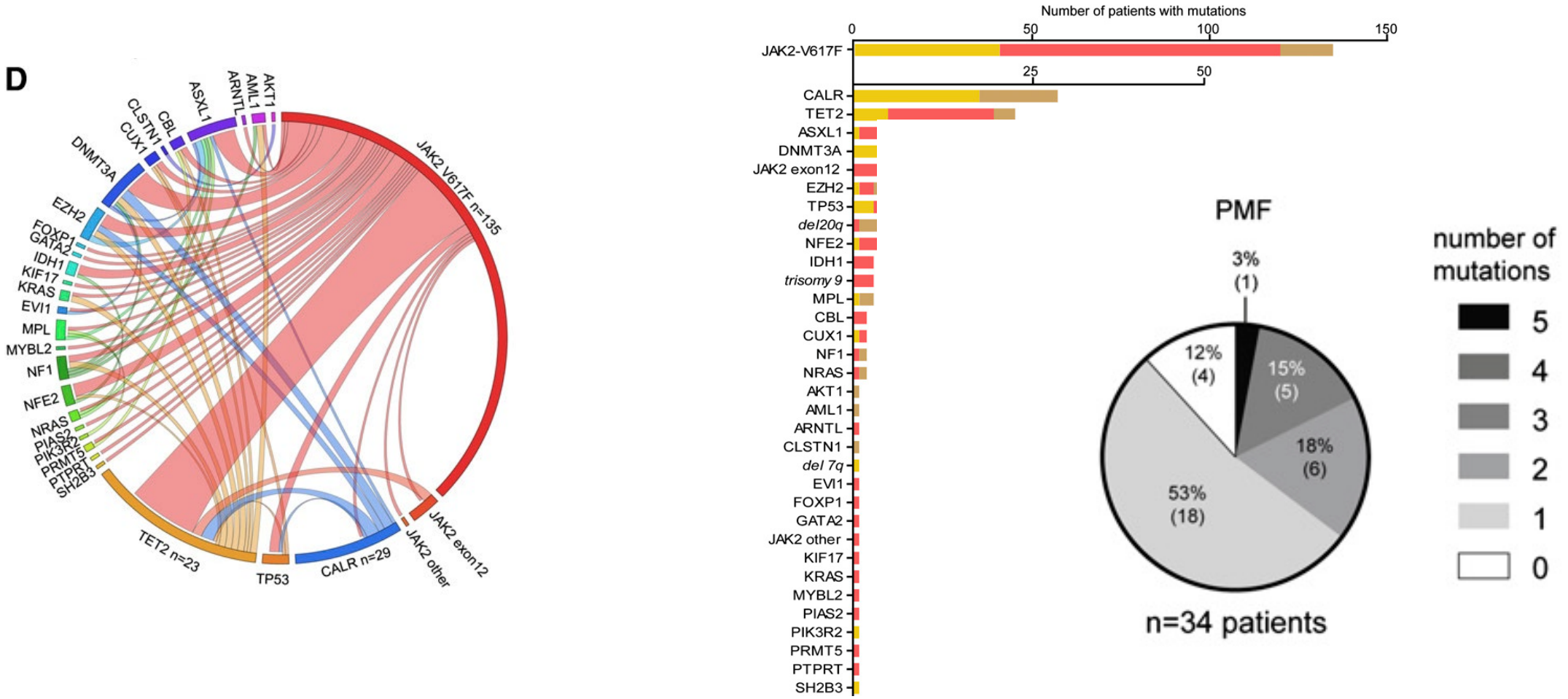
JAK2 V617F: Enthusiastic signaling



Disease	Frequency
PV	~95%
ET	~50-60%
PMF	~50-60%

Stein BL, Moliterno AR. *JAMA*. 2010;303(24):2513-2518.

Frequency and Distribution of "Driver" and Other Mutations in Patients With MPNs



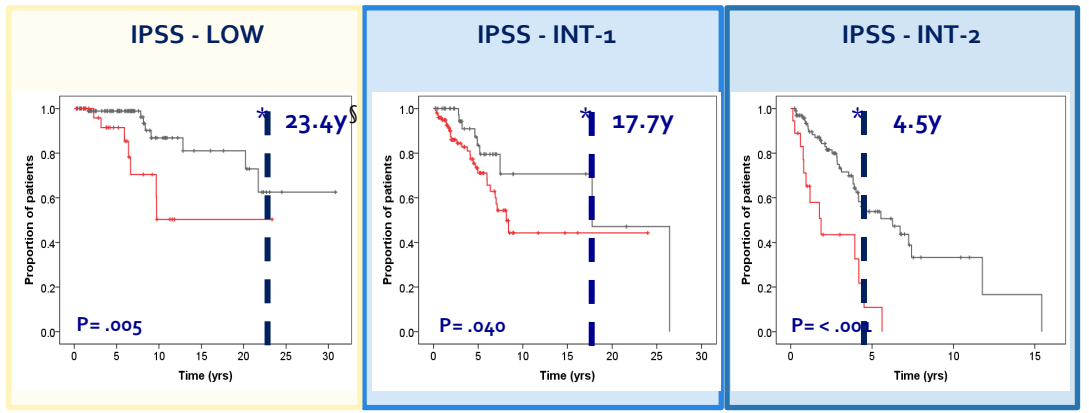
Courtesy of J. Mascarenhas; modified from Lundbertg P, et al. *Blood*. 2014;123(14):2220-2228.

Molecular International Prognostic Scoring System[1] in MF

MULTIVARIATE ANALYSIS			Weighted value
Variables	HR (95% CI)	P	
Age >60 yrs	3.8 (2.60-5.51)	<0.0001	1.5
Hgb <100 g/L	1.4 (1.01-1.99)	0.04	0.5
Constitutional Symptoms	1.5 (1.13-2.16)	0.007	0.5
PLT <200x10^9/L	2.5 (1.77-3.42)	<0.0001	1.0
Triple Negativity	3.9 (2.20-6.80)	<0.0001	1.5
JAK2/MPL mutation	1.8 (1.11-2.90)	0.016	0.5
ASXL1 mutation	1.4 (1.06-1.99)	0.02	0.5
SRSF2 mutation	1.7 (1.08-2.58)	0.02	0.5

Refines prognostic stratification within the IPSS categories→

*, IPSS Median Survival



MIPSS
§Estimated

Low 24.9y§	≤ Int-1 17.7y	< Int-2 6.2y
> Low 15.3y§	> Int-1 8.1y	> Int-2 1.9y

[1] Mutation-Enhanced International Prognostic Scoring System

HR, hazard ratio; IPSS, international Prognostic Scoring System

Vannucchi A, et al. *Blood.* 2014;124:405.

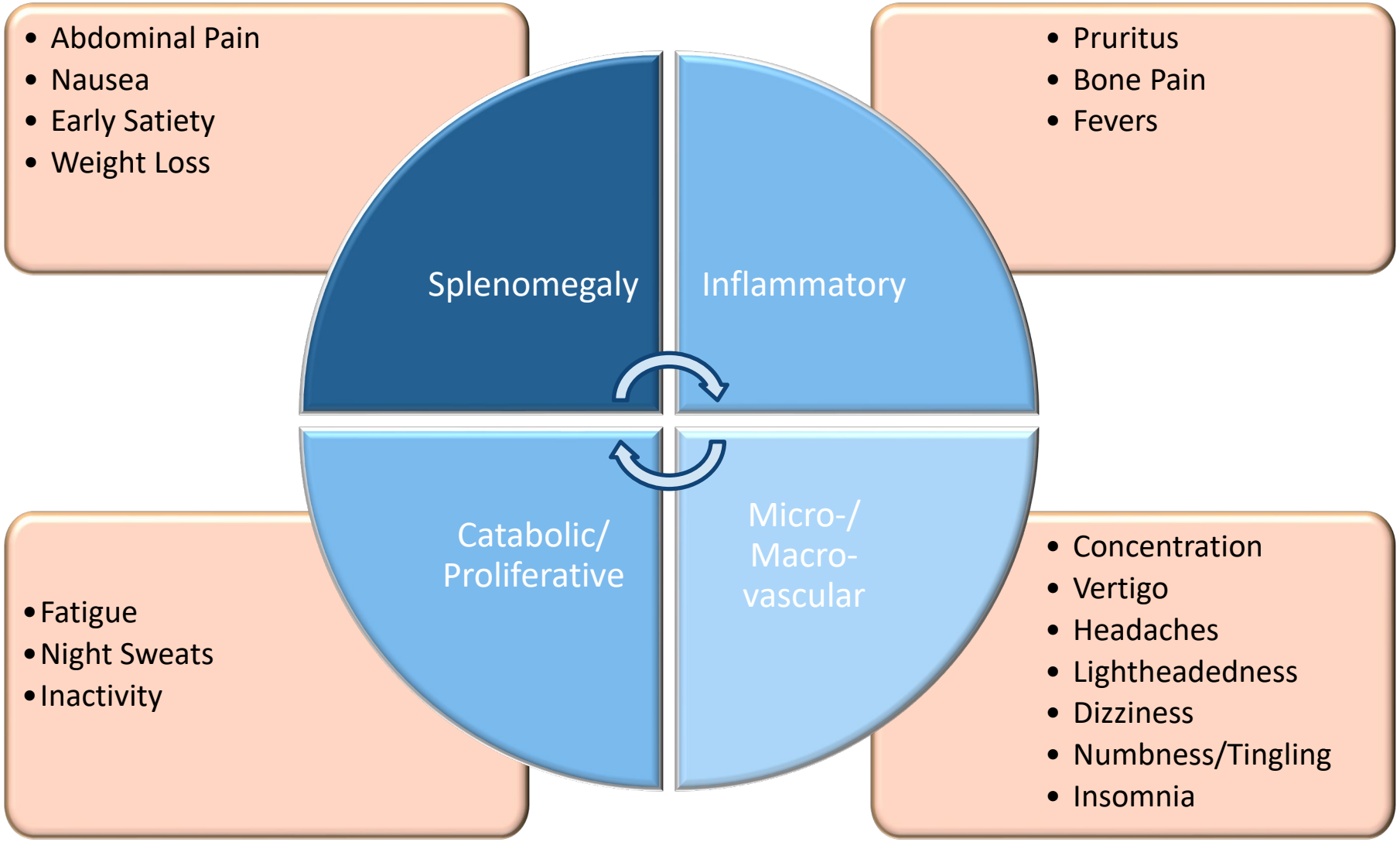
Assessing MPN Patient Risk: Prognostic Models

	IPSET (ET—3 groups) *Survival thrombosis risk*	PV Risk (4 groups) *Survival leukemia rates*	DIPSS (PMF—4 groups) *Survival*
Age, years	≥ 60 (2 points) *vs* < 60	≥ 67 (5 points) 57-66 (2 points), < 60 (0)	≥ 65 (1 point) *vs* < 65
Leukocytes	≥ 11 (1 point) *vs* < 11 × 10^9/L	≥ 15 (1 point) *vs* < 15 × 10^9/L	> 25 (1 point) vs ≤ 25 × 10^9/L
Hemoglobin (Hgb)			< 10 (2 points) *vs* ≥ 10 g/dL
Constitutional symptoms			Present (1 point) *vs* absent
Blasts			≥ 1% (1 point) *vs* < 1%
Prior thrombosis	Yes (1 point) *vs* No	Yes (1 Point) *vs* No	
Risk group point cutoffs	0; 1-2; 3-4 points	0; 1-2; 3; 4 points	0; 1-2; 3-4; ≥ 4 points

IPSET, International Prognostic Score of Thrombosis for Essential Thrombocythemia; DIPSS, Dynamic International Prognostic Scoring System

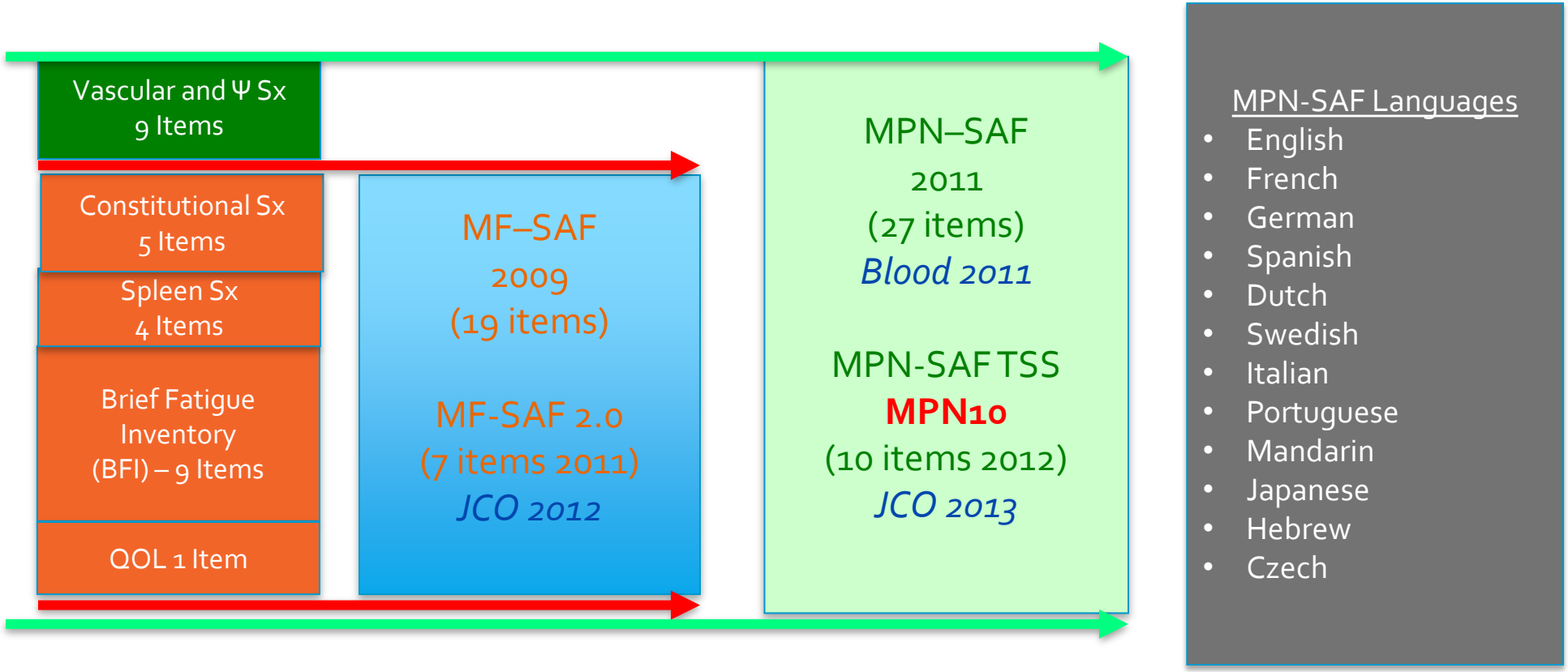
Bose & Verstovsek. *Cancer*. 2016;122(5):681-692.

Symptom Burden in MPNs



Courtesy of R Mesa, Mayo Clinic.

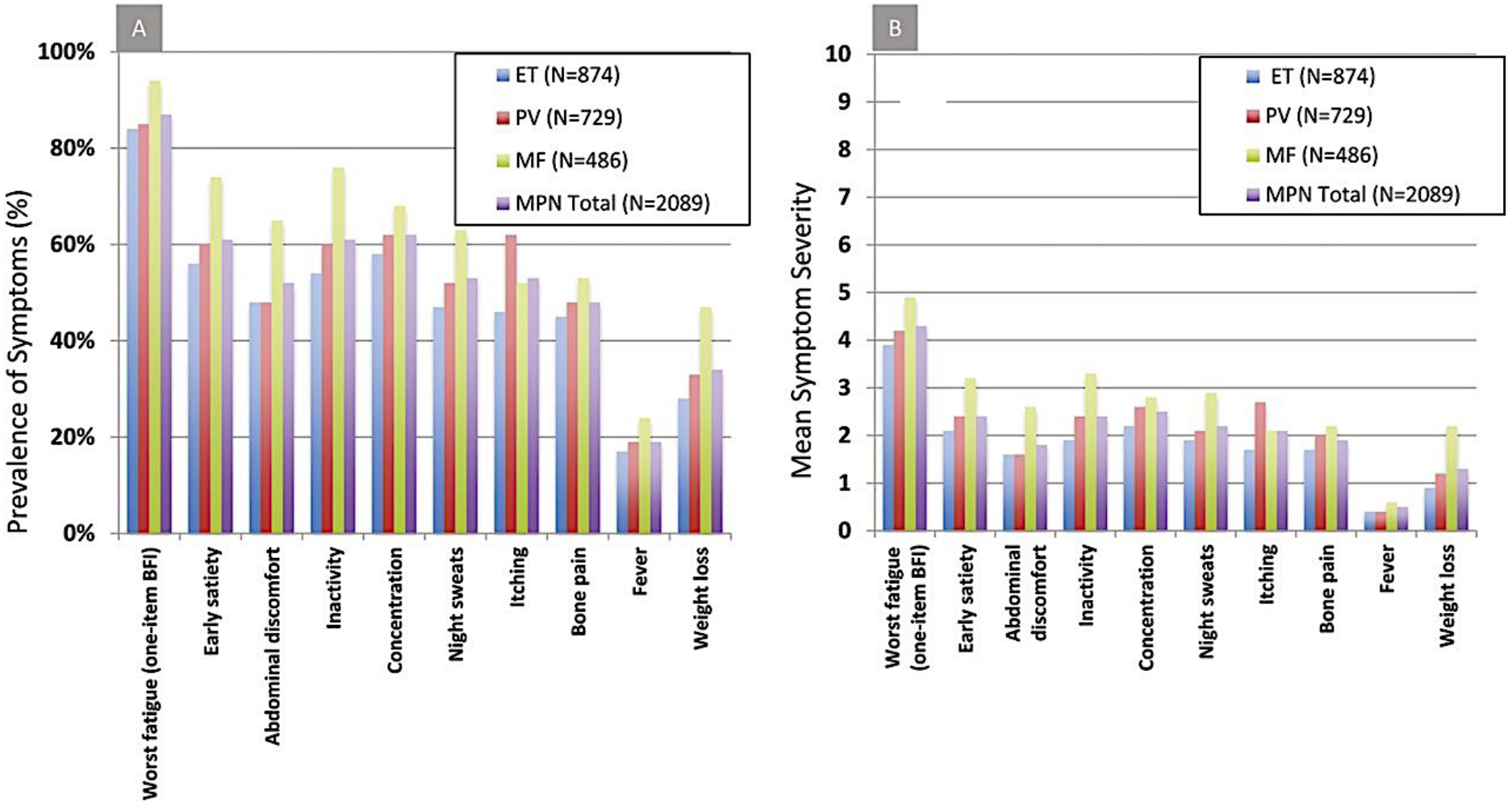
Formally Assessing MPN Symptom Burden: Symptom Assessment Form



JCO, Journal of Clinical Oncology; QOL, quality of life; SAF, Symptoms Assessment Form; Sx, symptoms; TSS, total symptom score.

Courtesy of R Mesa, Mayo Clinic.

Signs and Symptoms of MPNs: Often Under-Queried…

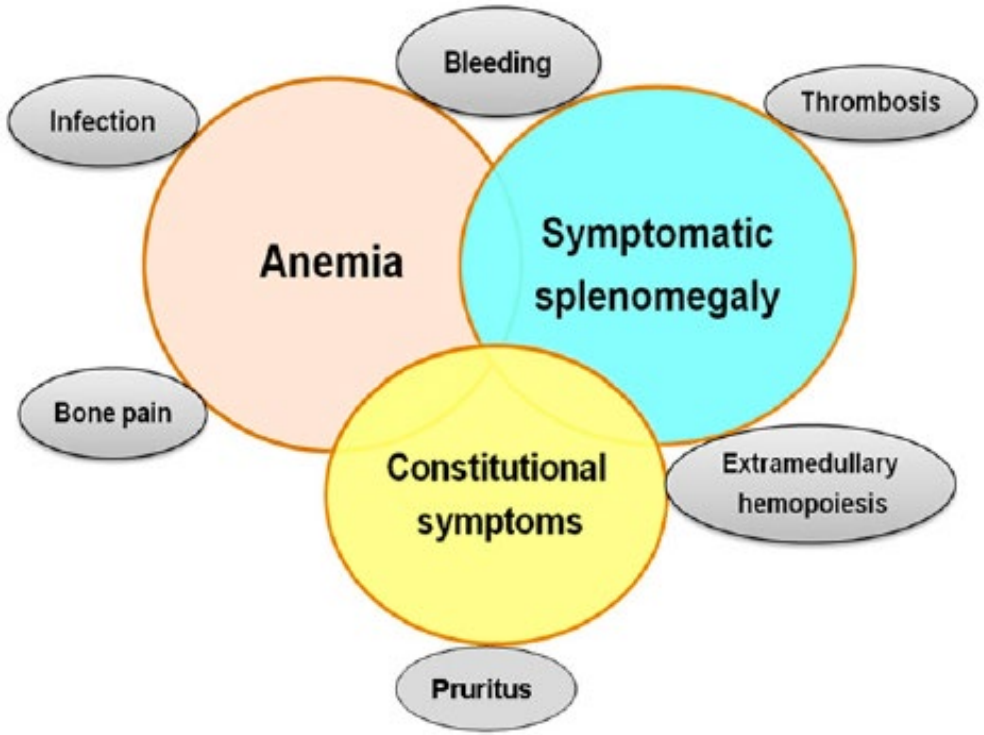


Geyer HL, et al. *Blood.* 2014;124:3529-3537.

Myelofibrosis

Clinical Features of Myelofibrosis (MF)

- **Bone marrow fibrosis**
- **Splenomegaly**
  - Splenomegaly-associated symptoms include abdominal pain/discomfort, early satiety
- **Cytopenias**
  - Anemia, thrombocytopenia
- **Constitutional symptoms**
  - Include fatigue, night sweats, pruritus (itching), bone aches, weight loss



Cervantes F. *Blood.* 2014;124(17):2635-2642.

WHO Criteria for Diagnosis of Overt Primary MF

ALL 3 major criteria plus at least 1 minor criterion

Major Criteria

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

Minor Criteria

At least 1 of the following, confirmed in 2 consecutive determinations:

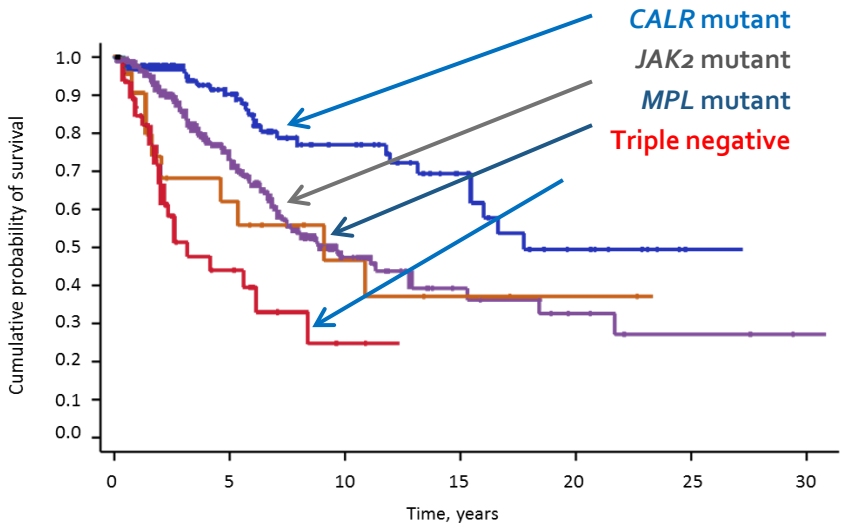
1. Anemia not attributed to a comorbid condition
2. Leukocytosis ≥ 11×10^9/L
3. Palpable splenomegaly
4. LDH increased to above upper normal limit of institutional reference range
5. Leukoerythroblastosis

CML, chronic myeloid leukemia; LDH, lactose dehydrogenase; MDS, myelodysplastic syndrome; MF, myelofibrosis; WHO, World Health Organization.

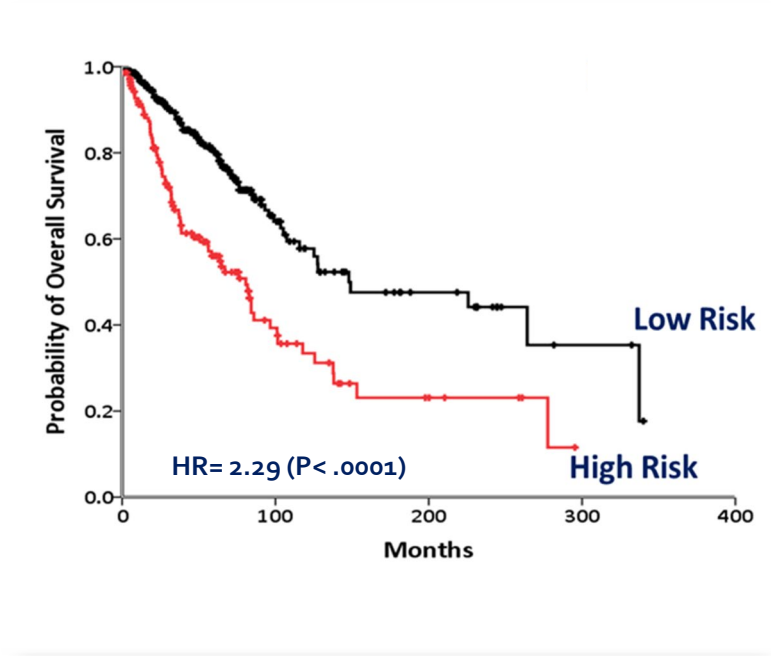
Arber D, et al. *Blood*. 2016;127:2391-2405.

The "Driver" Mutation and Other Alterations Affect Outcome in MF

The mutational status of *JAK2*, *MPL*, and *CALR* and the presence and number of other relevant mutations (*ASXL1*, *SRSF2*, *EZH2*, *IDH1/2*) provide IPSS/DIPSS-plus independent prognostic information.



Hazard Ratio:
2.3 for *JAK2*V617F (P<.001)
2.6 for *MPL* (*P=.009*)
6.2 for Triple Negative (*P<.001*)



High Risk:
Any mutation in *ASXL1*, *EZH2*, *SRSF2*, *IDH1/2*

Rumi E, et al. *Blood.* 2014;124(7):1062-1069; Vannucchi AM, et al. *Leukemia.* 2013;27(9):1861-1869.

Risk Stratification in MF

			Prognostic scoring system					
			Lille (1996)	IPSS (2009)	DIPSS (2010)	DIPSS+ (2011)	MIPSS (2014)	GPSS (2014)
Patient Specific Variable		Age		○	○	○	○	
Disease specific variables	Clinic	Constitutional symptoms		○	○	○	○	
	laboratory	WBC	○	○	○	○		
		Hemoglobin <10 g/dL	○	○	○	○	○	
		Peripheral blood blasts >1%		○	○	○		
		Platelet count				○	○	
		RBC Transfusional support				○		
	genetic	Karyotype (-8, -7, -5, i17q, 12p-, inv3, 11q23 or complex)				○		○
		Mutational status					○	○

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

Mascarenhas J. *Hematology Am Soc Hematol Educ Program*. 2015. 2015:2015:329-339

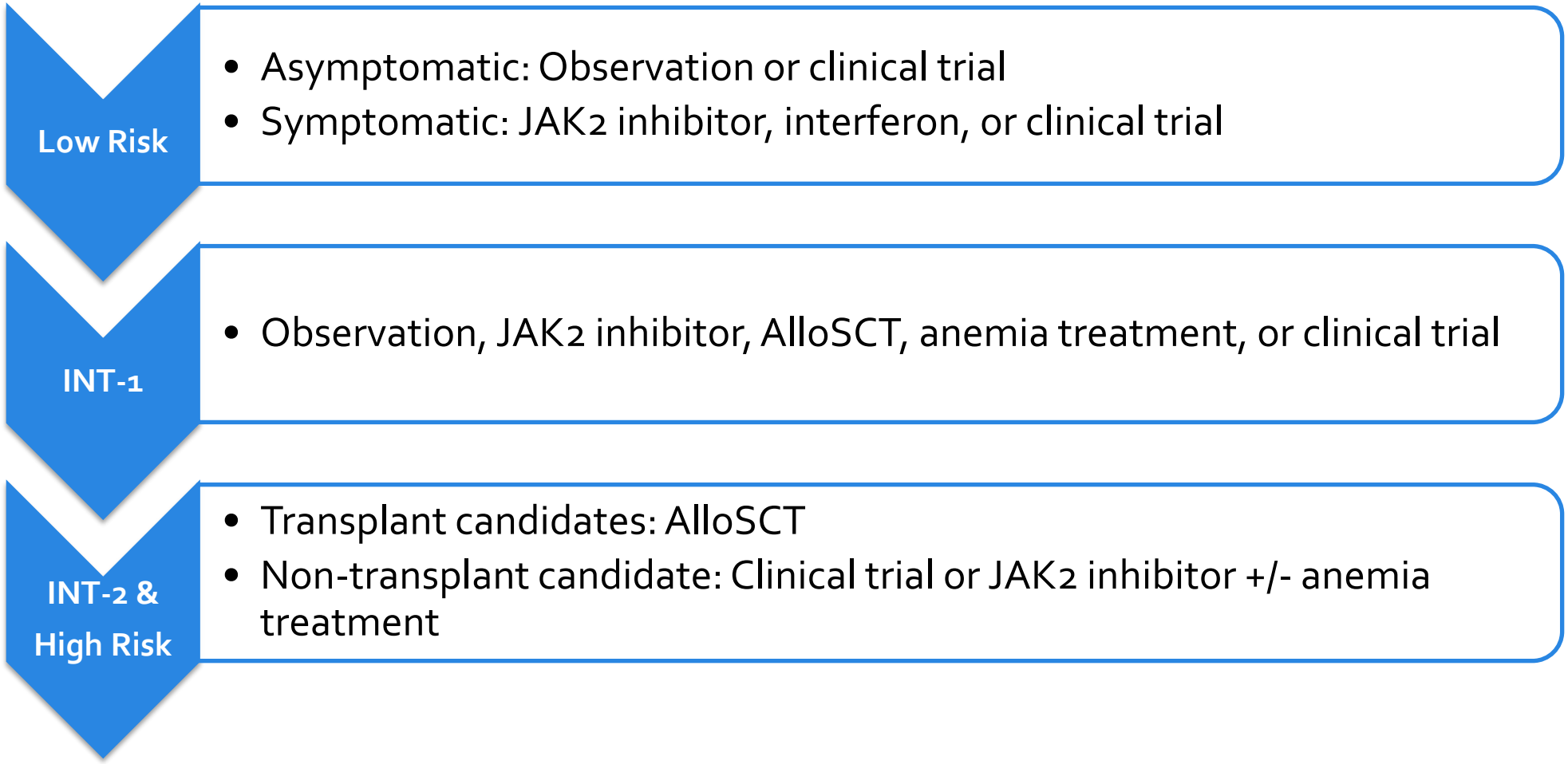
2008 IWG-MRT Diagnostic Criteria for Post-PV MF and Post-ET MF

Diagnostic criteria for post-PV MF	Diagnostic criteria for post-ET MF
REQUIRED CRITERIA	
1. Documentation of a previous diagnosis of ET or PV as defined by the WHO criteria	
2. Bone marrow fibrosis grade 2/3 (on a 0-3 scale) or grade 3/4 (on a 0-4 scale)	
ADDITIONAL CRITERIA (2 are required)	**ADDITIONAL CRITERIA (2 are required)**
1. Anemia or sustained loss of requirement for either phlebotomy (in the absence of cytoreductive therapy) or for cytoreductive treatment for erythrocytosis	1. Anemia and a ≥ 2 mg/mL decrease from baseline hemoglobin level
	2. A leukoerythroblastic peripheral blood picture
2. A leukoerythroblastic peripheral blood picture	3. Increasing splenomegaly of ≥ 5 cm (distance of the tip of the spleen from the left costal margin) or the appearance of newly palpable splenomegaly
3. Increasing splenomegaly of ≥ 5 cm (distance of the tip of the spleen from the left costal margin) or the appearance of a newly palpable splenomegaly	4. Increased LDH (above reference level)
4. Development of ≥ 1 of 3 constitutional symptoms: > 10% weight loss in 6 months, night sweats, unexplained fever (> 37.5°C)	5. Development of ≥ 1 of 3 constitutional symptoms: > 10% weight loss in 6 months, night sweats, unexplained fever (> 37.5°C)

IWG-MRT, International Working Group-Myeloproliferative Neoplasms Research and Treatment

Barosi G, et al. *Leukemia*. 2008;22(2):437-438.

Risk-Adapted Treatment of MF



Anemia treatment may include: Immunomodulatory imide drugs (IMID), androgens, erythropoiesis stimulating agents, clinical trial, splenectomy
AlloSCT, allogeneic stem cell transplant.

Mesa RA. *Leuk Lymphoma.* 2013;54(2):242-251; Geyer HL, Mesa RA. *Hematol.*2014;277-286;
National Comprehensive Cancer Network (NCCN). Myeloproliferative Neoplasms v3.2019. Accessed November 6, 2019.

Interferon for the Treatment of MF

Author, Year, Study Design	N	Intervention	CR/PR/ORR	Grade 3 – 4 ADRs
Jabbour E, et al., 2007, Prospective	11	PEG-INF-α-2b (Peg-Intron®) 2 - 3 mcg/kg SC weekly (median dose: 1.5 mcg/kg weekly)	9%/0%/NR	Fatigue, myalgias, weakness, thrombocytopenia
Silver RT, et al., 2013, Prospective single-arm trial	32	rIFN-α-2b (Intron A®) 500,000 - 1 million units SC thrice weekly PEG-INF-α-2a (Pegasys®) 45 mcg SC weekly	9.4%/37.5%/78%	Thrombocytopenia
Ianotto JC, et al., 2013, Retrospective	62	PEG-INF-α-2a (Pegasys®) 45 mcg SC weekly	ORR: 69 - 83% Spleen reduction: 46.5%	Anemia, thrombocytopenia, leukopenia

ADR, adverse drug reaction; CR, complete response; NR, nonresponsive; PEG-INF-α-2b (Peg-Intron®), Pegylated Interferon-alpha-2b (Peg-Intron®); rIFN-α-2b (Intron A®), Interferon-alpha 2b; PEG-INF-α-2a (Pegasys®), Pegylated Interferon-alpha-2b (Peg-Intron®); PR, partial response; SC, subcutaneous.

Jabbour E, et al. *Cancer*. 2007;110(9):2012-2018; Silver RT, et al. *Blood*. 2013;12(21): 4053;
Ianotto JC, et al. *Br J Haematol.* 2013;162(6):783-791.

Interferon From a Pharmacist's Perspective

- Data supporting the use of 3 different formulations
  - PEG-INF-α-2b (Peg-Intron®), rIFN-α-2b (Intron A®), PEG-INF-α-2a (Pegasys®)
- Initial dosing
  - Dependent on formulation
- Dose adjustments
  - Renal impairment
  - Hematologic toxicity
- Drug interactions
  - No major interactions
- Warnings and precautions
  - Cytopenias, cognitive impairment, cutaneous reactions, gastrointestinal (GI) hemorrhage, hepatotoxicity, hypersensitivity reactions, new or worsening depression, ophthalmic effects, pancreatitis, and pulmonary effects
- Administration
  - SC injection
- Dosage forms
  - Pre-filled syringes and solution for injection
- Storage
  - Store in the refrigerator
- Cost
  - $3,600 to $4,500/month
- Drug acquisition
  - Will likely require prior authorization
- Disposal
  - Sharps container
  - Adhere to state laws

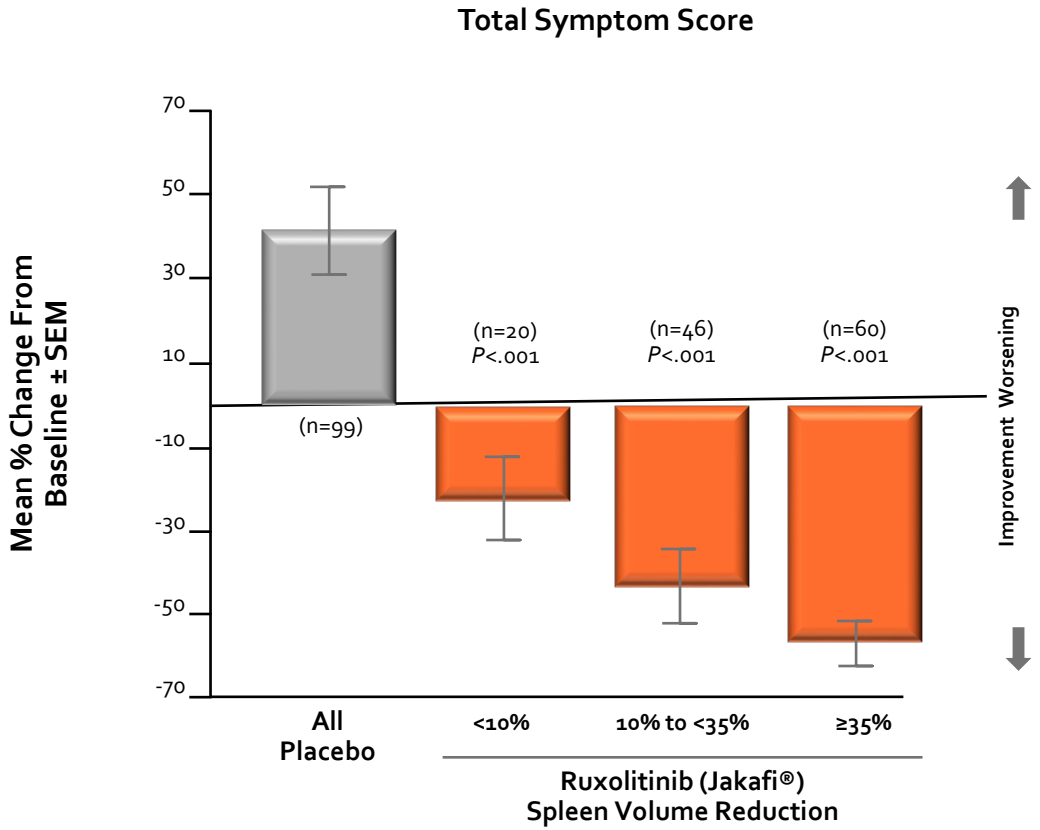
Vachhani P, et al. *Ther Adv Hematol*. 2024;15:20406207241229588;
NCCN. Myeloproliferative Neoplasms Version 2.2024. August 8, 2024. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf.

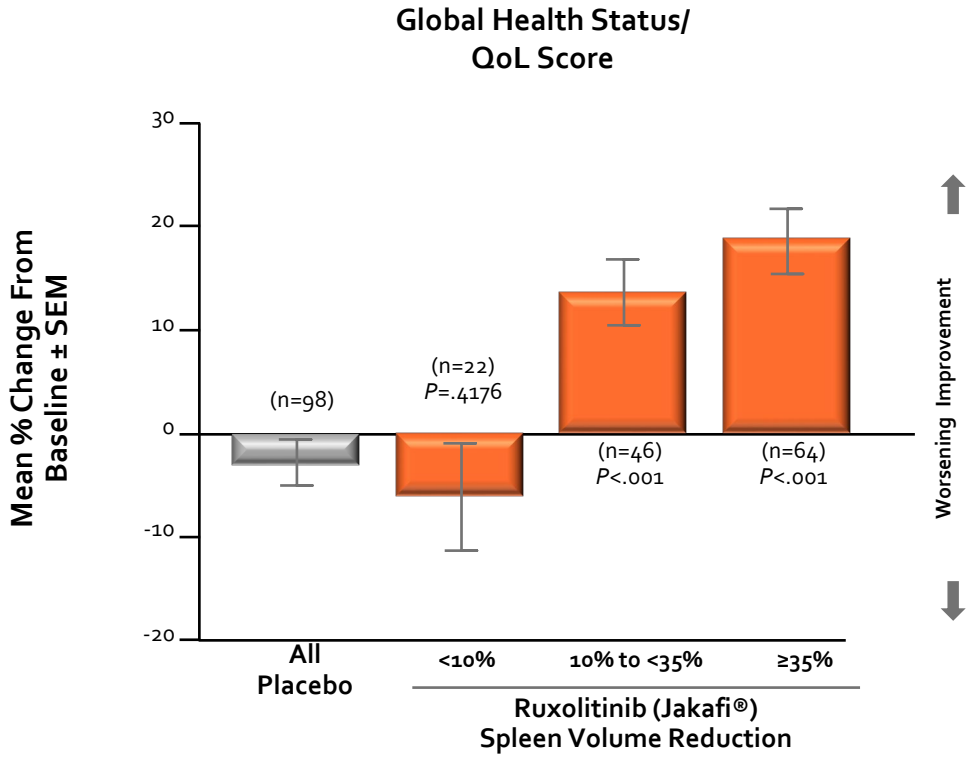
Ruxolitinib (Jakafi®) in MF

COMFORT-I (N = 309) **Ruxolitinib (Jakafi®) vs. placebo in patients with intermediate- or high-risk MF**	• 41.9% (ruxolitinib [Jakafi®]) vs 0.7% (placebo) had ≥35% reduction in spleen volume at week 24 (P < 0.001)
COMFORT-II (N = 219) **Ruxolitinib (Jakafi®) vs. best available therapy (BAT) in patients with intermediate- or high-risk MF**	• 32% (ruxolitinib [Jakafi®]) vs 0% BAT) had ≥ 35% reduction in spleen volume at week 24 (P < 0.001)

Verstovsek S, et al. *N Engl J Med.* 2012;366(9):799-807; Harrison C, et al. *N Engl J Med.* 2012;366(9):787-798.

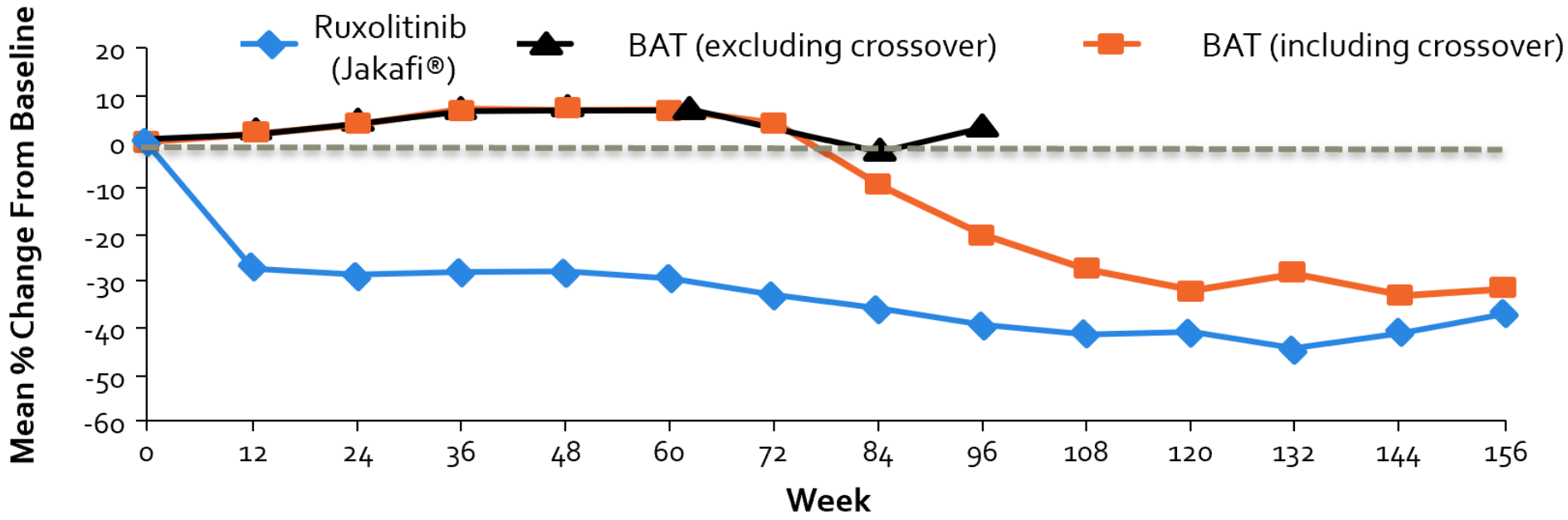
Effect of Spleen Volume Reduction on MF-Related Symptoms, QoL





Mesa RA, et al. *J Clin Oncol.* 2013;31(10):1285-1292.

COMFORT-II: Mean Percentage Change in Spleen Volume Over Time



Cervantes F, et al. *Blood*. 2013;122(25):4047-4053. Published correction appears in: *Blood*. 2016;128(25):3013.

COMFORT-I: Non-Hematologic Adverse Events in ≥ 10%

Adverse Event (AE)	Ruxolitinib (Jakafi®), n = 155 % With AE		Placebo, n = 151 % With AE	
	All Grades	Grade 3/4	All Grades	Grade 3/4
Fatigue	25	5	34	7
Diarrhea	23	2	21	0
Peripheral edema	19	0	23	1
Ecchymosis	**19**	**0**	**9**	**0**
Dyspnea	17	1	17	4
Dizziness	**15**	**1**	**7**	**0**
Nausea	15	0	19	1
Headache	**15**	**0**	**5**	**0**
Constipation	13	0	12	0
Vomiting	12	1	10	1
Pain in extremity	12	1	10	0
Insomnia	12	0	10	0
Arthralgia	11	2	9	1
Pyrexia	11	1	7	1
Abdominal pain	**10**	**3**	**41**	**11**

Verstovsek S, et al. *N Engl J Med.* 2012;366(9):799-807.

Ruxolitinib (Jakafi®): Survival Data

COMFORT-I			COMFORT-II		
RUX (n=155) vs Placebo (n=154)			RUX (n=146) vs Best available therapy (n=73)		
Median follow-up	HR (95% CI)	*P* value*	Median follow-up	HR (95% CI)	*P* value*
OS at 1 year	0.50 (0.25-0.98)	0.04	OS at 1 year	0.70 (0.20-2.49)	
OS at 2 years	0.58 (0.36-0.95)	0.03	OS at 2 years	0.51 (0.27-0.99)	0.041
OS at 3 years	0.69 (0.46-1.03)	0.067	OS at 3 years	0.48 (0.28-0.85)	0.009

Combined Survival Data for COMFORT-I and COMFORT-II		
Median follow-up	HR (95% CI)	*P* value*
OS at 5 years	0.70 (0.54-0.91)	0.0065

OS, overall survival.

Harrison C, et al. *N Engl J Med*. 2012;366(9):787–798; Cervantes F, et al. *Haematologica*. 2013;98(2):160–162; Cervantes F, et al. *Blood*. 2013;122(25):4047-4053 Published correction appears in: *Blood*. 2016;128(25):3013. Verstovsek S, et al. *N Engl J Med*. 2012;366(9):799–807; Verstovsek S, et al. *Haematologica*. 2013;98(12):1865–1871; Verstovsek S, et al. *Haematologica*. 2015;100(4):479-488; Verstovsek S, et al. *J Hematol Oncol*. 2017;10:156.

Summary: Ruxolitinib (Jakafi®) in Patients With MF

- COMFORT-I and COMFORT-II phase III trials:
  - Efficacy
    - Spleen size reduction, significant improvement in symptoms, QoL, performance status
    - Not selective for JAK2V617F (i.e., benefits patients with and without JAK2 mutation)
    - Possible prolongation of life in patients with advanced disease
  - Safety
    - Myelosuppression
    - Infection risk

Verstovsek S, et al. *N Engl J Med*. 2012;366(9):799-807;
Cervantes F, et al. *Blood*. 2013;122(25):4047-4053. Published correction appears in: *Blood*. 2016;128(25):3013.

Ruxolitinib (Jakafi®) From a Pharmacist's Perspective

- Initial dosing
  - Dependent on platelet count and renal/hepatic function
- Dose adjustments
  - Renal impairment
  - Hepatic impairment
  - Hematologic toxicity
- Drug interactions
  - CYP3A4 and CYP2C9
- Warnings and precautions
  - Cytopenias, infection, discontinuation syndrome, non-melanoma skin cancers, & lipid elevations
  - Following discontinuation of Jakafi®, symptoms from myeloproliferative neoplasms may return to pretreatment levels over a period of approximately one week. Some patients with MF have experienced one or more of the following AEs after discontinuing ruxolitinib (Jakafi®) :
    - Fever
    - Respiratory distress
    - Hypotension
    - Disseminated intravascular coagulation (DIC)
    - Multi-organ failure
- Administration
  - Regardless of food
  - Via nasogastric tube
- Dosage forms
  - 5, 10, 15, 20, and 25 mg tablets
- Cost
  - $12,703.20/month
- Drug acquisition
  - Specialty pharmacies only

Jakafi® (Ruxolitinib). Package insert. Incyte; 2016.

Fedratinib (Inrebic®): The Second Approved JAK Inhibitor for MF

- Phase II study of primary and secondary MF previously exposed to ruxolitinib (Jakafi®; n=97)
  - DIPSS INT-1 with constitutional symptoms
  - INT/High Risk
  - Splenomegaly ≥5cm below left CM
  - Platelets >50,000
- Primary endpoint: ≥35% reduction in spleen volume at 24 weeks
- Secondary endpoint: ≥50% reduction in total symptom score at 24 weeks
- Fedratinib (Inrebic®) 400 mg QD

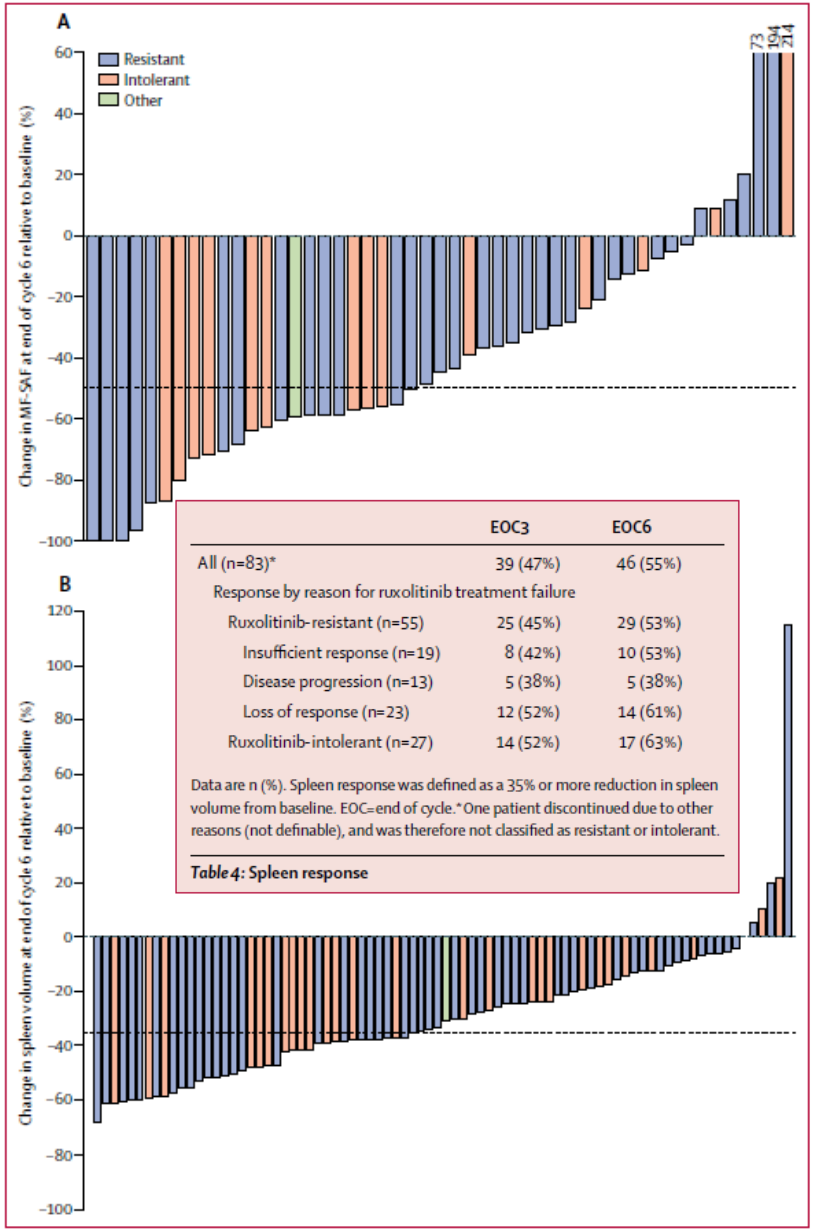
	Patients (n=97)
Initial daily ruxolitinib dose (mg)	
≤25	26 (27%)
30	39 (40%)
40	30 (31%)
50	2 (2%)
Cumulative dose administered (mg)	9040 (5075-13 005)
Duration of exposure (months)	10·25 (5·75–14·75)
Reduction in palpable spleen size at best response	
Ruxolitinib-resistant (n=53)	
≥50%	23/53 (43%)
<50%	30/53 (57%)
Ruxolitinib-intolerant (n=23)	
≥50%	10/23 (43%)
<50%	13/23 (57%)

Data are median (IQR), n (%), or n/N (%). Data are from the per-protocol population.

Table 3: Summary of previous ruxolitinib treatment

Prior RUX (Jakafi®) Response:

Fedratinib (Inrebic®) Response:



	EOC3	EOC6
All (n=83)*	39 (47%)	46 (55%)
Response by reason for ruxolitinib treatment failure		
Ruxolitinib-resistant (n=55)	25 (45%)	29 (53%)
Insufficient response (n=19)	8 (42%)	10 (53%)
Disease progression (n=13)	5 (38%)	5 (38%)
Loss of response (n=23)	12 (52%)	14 (61%)
Ruxolitinib-intolerant (n=27)	14 (52%)	17 (63%)

Data are n (%). Spleen response was defined as a 35% or more reduction in spleen volume from baseline. EOC=end of cycle.*One patient discontinued due to other reasons (not definable), and was therefore not classified as resistant or intolerant.

Table 4: Spleen response

QD, daily.

Harrison CN, et al. *Lancet Haematol.* 2017;4(7):e317-324.

Fedratinib (Inrebic®): The Second Approved JAK Inhibitor for MF

- Toxicity raised distinct novel AEs
  - 39% ≥ 1 dose reduction; most common for GI
  - 19% discontinuation for AEs
  - Most common AEs: anemia, thrombocytopenia
- During study concern over risk of **Wernicke encephalopathy** (WE): acute neurological condition characterized by a clinical triad of ophthalmoparesis with nystagmus, ataxia, and confusion, generally caused by thiamine deficiency
- Grade 3 encephalopathy in one patient, adjudicated to be hepatic not Wernicke

FDA Label:

WARNING: ENCEPHALOPATHY INCLUDING WERNICKE'S
See full prescribing information for complete boxed warning.

Serious and fatal encephalopathy, including Wernicke's, has occurred in patients treated with INREBIC. Wernicke's encephalopathy is a neurologic emergency. Assess thiamine levels in all patients prior to starting INREBIC, periodically during treatment, and as clinically indicated. Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue INREBIC and initiate parenteral thiamine. Monitor until symptoms resolve or improve and thiamine levels normalize. (2.6, 5.1, 6.1).

	Grade 1–2	Grade 3–4	Grade 5
Haematological adverse events* (n=97)			
Anaemia	10 (10%)	37 (38%)	0
Thrombocytopenia	5 (5%)	21 (22%)	0
Lymphopenia	1 (1%)	3 (3%)	0
Non-haematological adverse events (n=97)			
Diarrhoea	56 (58%)	4 (4%)	0
Nausea	54 (56%)	0	0
Vomiting	40 (41%)	0	0
Constipation	19 (20%)	1 (1%)	0
Pruritus	16 (16%)	0	0
Fatigue	13 (13%)	2 (2%)	0
Headache	12 (12%)	1 (1%)	0
Cough	13 (13%)	0	0
Urinary tract infection	12 (12%)	0	0
Dyspnoea	11 (11%)	1 (1%)	0
Dizziness	11 (11%)	0	0
Abdominal pain	7 (7%)	2 (2%)	0
Alanine aminotransferase increased	3 (3%)	3 (3%)	0
Pneumonia	3 (3%)	2 (2%)	1 (1%)
Hyperlipasaemia	1 (1%)	3 (3%)	0
Hyperuricaemia	2 (2%)	2 (2%)	0
Dehydration	1 (1%)	2 (2%)	0
Tumour lysis syndrome	0	2 (2%)	0
Cardiac failure	1 (1%)	2 (2%)	0
Amylase increased	1 (1%)	2 (2%)	0
Blood bilirubin increased	0	2 (2%)	0
Cardiac failure	1 (1%)	2 (2%)	0
Respiratory failure	0	0	1 (1%)
Splenic rupture	0	0	1 (1%)

Data are n (%). Shown are any grade event occurring in more than 10% of patients, grade 3–4 events occurring in more than one patient, and all deaths (excluding four deaths due to disease progression).*Laboratory measurements.

Table 5: **Adverse events**

Harrison CN, et al. *Lancet Haematol.* 2017;4(7):e317-324.

Fedratinib (Inrebic®) From a Pharmacist's Perspective

- Initial dosing
  - 400 mg PO daily
  - Baseline platelets >50
- Dose adjustments
  - Renal impairment
  - Hematologic toxicity
  - Non-hematologic toxicity
- Drug interactions
  - CYP3A4 and CYP2C19
- Warnings and precautions
  - Encephalopathy (Wernicke's), GI toxicity (N/V/D), cytopenias, hepatotoxicity
- Administration
  - Regardless of food
  - Take with high fatty meal to reduce N/V
- Dosage forms
  - 100 mg tablets
- Cost
  - $25,200/month
- Drug acquisition
  - Specialty pharmacies only

Check thiamine level prior to initiating treatment. Replete thiamine BEFORE starting fedratinib (Inrebic®)

N/V/D, nausea/vomiting/diarrhea; PO, orally.

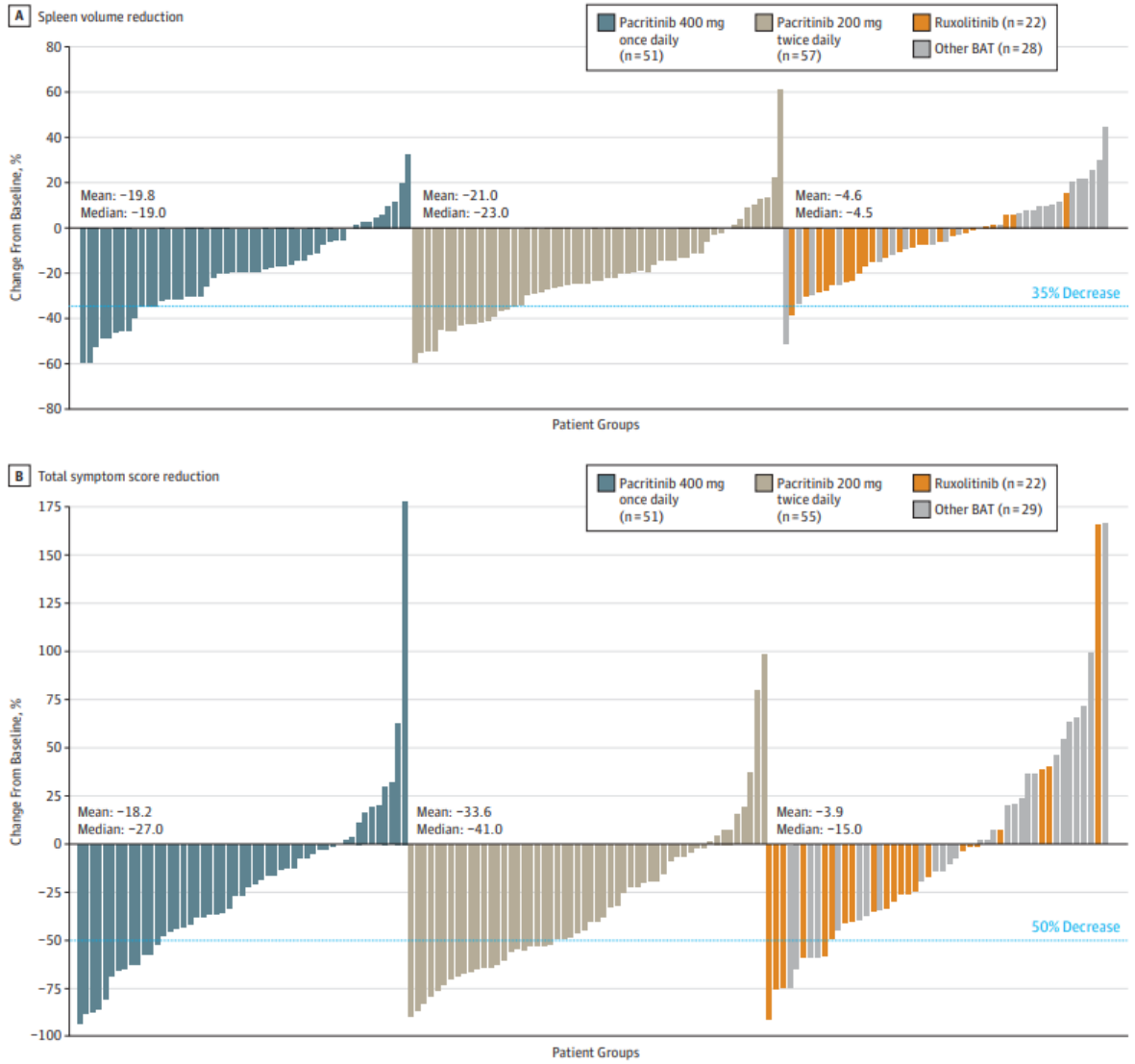
Inrebic® (fedratinib). Package insert. Bristol Myers Squibb; 2019.

Pacritinib (Vonjo®): The Third Approved JAK Inhibitor for MF

PERSIST-1 (N = 327) **Pacritinib (Vonjo®) vs. BAT, excluding ruxolitinib (Jakafi ®) in patients with intermediate- or high-risk MF;** **JAK inhibitor naïve**	• 19% (pacritinib [Vonjo®]) vs 5% BAT had ≥35% reduction in spleen volume at week 24 (P = 0.0003)
PERSIST-2 (N = 221) **Pacritinib (Vonjo®) 400 mg daily vs. pacritinib (Vonjo®) 200 mg twice daily vs. BAT, including ruxolitinib (Jakafi®), in pts with intermediate-risk or high-risk MF; Prior JAK inhibitor allowed; platelets ≤ 100**	• 22% (pacritinib [Vonjo®] 200 mg twice daily) vs 3% BAT had ≥35% reduction in spleen volume at week 24 (P = 0.001) • 32% (pacritinib [Vonjo®] 200 mg twice daily) vs 14% BAT had ≥50% reduction in TSS at week 24 (P=0.01)

Mesa RA, et al. *Lancet Haematol.* 2017;4(5):e225-e236; Mascarenhas J, et al. *JAMA Oncol.* 2018;4(5):652-659.

PERSIST-2: Change in TSS and Spleen Volume



TSS, total symptom score.

Mascarenhas J, et al. *JAMA Oncol.* 2018;4(5):652-659.

PERSIST-2: Change in TSS and Spleen Volume in Patients with Prior Ruxolitinib (Jakafi®) and in Patients with Baseline Platelets ≤ 50

Reductions From Baseline to Week 24	Pacritinib 200 mg Twice Daily	BAT
Patients With Prior Ruxolitinib		
Patients with ≥35% SVR		
Overall population, No.	31	33
Achieved end point, No. (%)	4 (13)	1 (3)
95% CI for the %[a]	3.6-29.8	0.1-15.8
Patients with ≥50% reduction in TSS		
Overall population, No.	31	33
Achieved end point, No. (%)	10 (32)	5 (15)
95% CI for the %[a]	16.7-51.4	5.1-31.9
Patients With Baseline Platelets <50 × 10^9/L		
Patients with ≥35% SVR from baseline to week 24		
Overall population, No.	31	32
Achieved end point, No. (%)	9 (29)	1 (3)
95% CI for the %[a]	14.2-48.0	0.1-16.2
Patients with ≥50% reduction in TSS		
Overall population, No.	31	32
Achieved end point, No. (%)	7 (23)	4 (13)
95% CI for the %[a]	9.6-41.1	3.5-29.0

AEs

- Diarrhea (48%), thrombocytopenia (34%), nausea (32%), anemia (24%), peripheral edema (20%)
- Discontinuation due to AEs: 15%

Mascarenhas J, et al. *JAMA Oncol.* 2018;4(5):652-659.

Pacritinib (Vonjo®) From a Pharmacist's Perspective

- Initial dosing
  - 200 mg PO twice daily
- Dose adjustments
  - Hematologic toxicity
  - Non-hematologic toxicity
- Drug interactions
  - CYP3A4, CYP1A2
  - P-gp, BCRP, OCT1
- Warnings and precautions
  - Hemorrhage, diarrhea, thrombocytopenia, Prolonged QT interval
- Administration
  - Regardless of food
- Dosage forms
  - 100 mg capsules
- Cost
  - $31,200/month
- Drug acquisition
  - Specialty pharmacies only

Vonjo® (pacritinib). Package insert. Sobi; 2022.

Momelotinib (Ojjaara®): The Fourth Approved JAK Inhibitor for MF

SIMPLIFY-1 (N = 432) **Momelotinib (Ojjaara®) vs. ruxolitinib (Jakafi®) in patients with intermediate- or high-risk MF; JAK inhibitor naïve**	• 27% (momelotinib [Ojjaara®]) vs 29% (ruxolitinib [Jakafi®]) had ≥35% reduction in spleen volume at week 24 (P = 0.011) (*met noninferiority)* • 28% (momelotinib [Ojjaara®]) vs 42% (ruxolitinib [Jakafi®]) had ≥50% reduction in TSS at week 24 (P = 0.98)
SIMPLIFY-2 (N = 156) **Momelotinib (Ojjaara®) vs. BAT in patients with intermediate-risk or higher MF; Prior JAK inhibitor**	• 7% (momelotinib [Ojjaara®]) vs 6% BAT had ≥35% reduction in spleen volume at week 24 (P = 0.9) • 26% (momelotinib [Ojjaara®]) vs 6% BAT had ≥50% reduction in TSS at week 24 (P = 0.0006)

Mesa RA, et al. *J Clin Onol.* 2017;35(34):3844-3850; Harrison CN, et al. *Lancet Haematol.* 2018;5(2):e73-e81.

SIMPLIFY-I: Treatment-Emergent AEs in ≥ 10%

Treatment-Emergent AE	Momelotinib (Ojjaara®), n=214 % With AE	Ruxolitinib (Jakafi®), n=216 % With AE
Thrombocytopenia	**19**	**29**
Diarrhea	18	20
Headache	17	20
Dizziness	16	12
Nausea	**16**	**4**
Fatigue	15	12
Anemia	**14**	**38**
Abdominal Pain	10	11

Mesa RA, et al. *J Clin Onol.* 2017;35(34):3844-3850.

Momelotinib (Ojjaara®) in MF – MOMENTUM Trial

Double-blind, randomized, controlled phase III study

Inclusion Criteria

- DIPPS INT-1 or higher risk
- Prior approved JAK inhibitor for 90+ days, OR 28+ days if transfusion criteria met per protocol, OR G3+ heme AE
- Hgb < 10
- Platelets > 25,000
- Splenomegaly ≥ be5cm below left CM
- ECOG ≤ 2

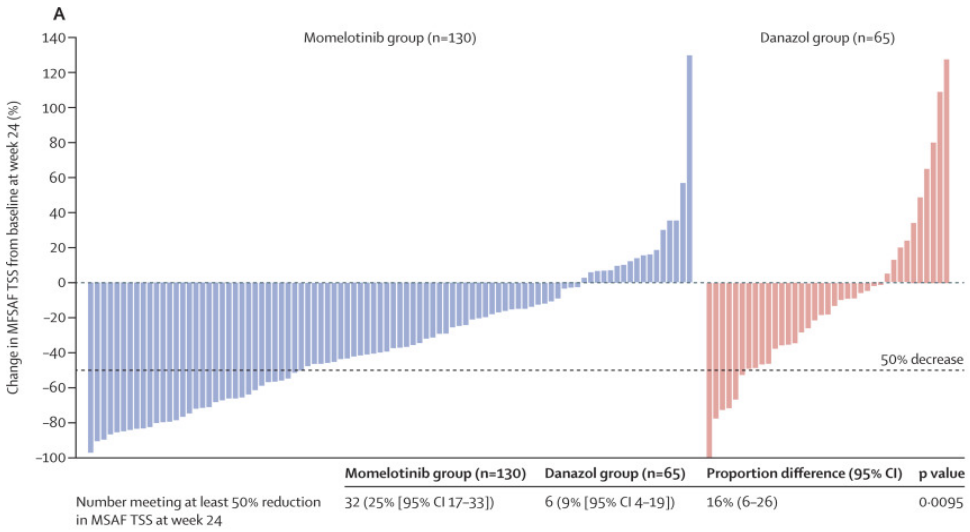
N = 130 → **Momelotinib (Ojjaara®) 200 mg daily + placebo**

N = 65 → **Danazol 300 mg twice daily + placebo**

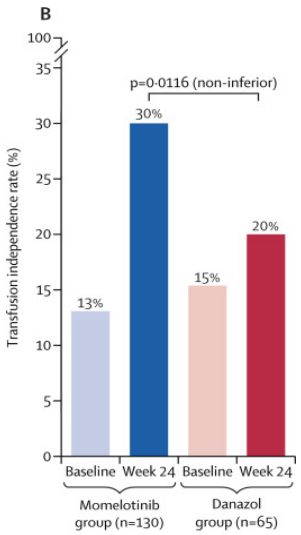
CM, costal margin; ECOG, Eastern Cooperative Oncology Group.

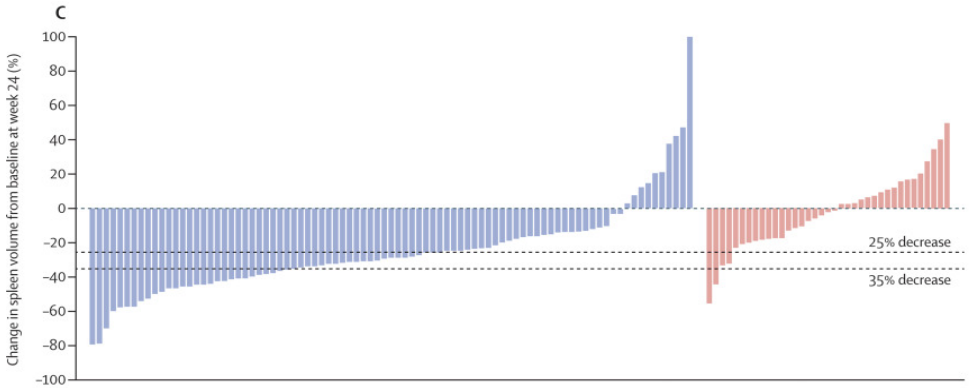
Verstovsek S, et al. *Lancet.* 2023;401(10373):269-280.

MOMENTUM Trial Results:
Change in TSS, Transfusion Independence, and Spleen Volume



	Momelotinib group (n=130)	Danazol group (n=65)	Proportion difference (95% CI)	p value
Number meeting at least 50% reduction in MSAF TSS at week 24	32 (25% [95% CI 17–33])	6 (9% [95% CI 4–19])	16% (6–26)	0·0095





	Momelotinib group (n=130)	Danazol group (n=65)	Proportion difference (95% CI)	p value
Number meeting at least 25% reduction in spleen volume	51 (39% [95% CI 31–48])	4 (6% [95% CI 2–15])	33% (23–44)	<0·0001
Number meeting at least 35% reduction in spleen volume	29 (22% [95% CI 15–30])	2 (3% [95% CI 0–11])	18 (10–27)	0·0011

Verstovsek S, et al. *Lancet.* 2023;401(10373):269-280.

MOMENTUM Trial Results: Treatment-Emergent AEs Observed in at Least 10% of Patients in Either Treatment Group During the 24-Week Randomized Treatment Period

AE	Momelotinib (Ojjaara®), n = 130 % With AE		Danazol, n = 65 % With AE	
	All Grades	Grade 3+	All Grades	Grade 3+
Diarrhea	**22**	**0**	**9**	**2**
Nausea	**16**	**2**	**9**	**3**
Asthenia	13	1	9	2
Pruritis	11	2	11	0
Weight decreased	11	0	6	0
Blood creatinine increased	8	1	15	3
Dyspnea	8	2	14	2
Peripheral edema	8	2	14	0
Fatigue	6	1	11	3
Acute kidney injury	5	3	12	9
Hematological Abnormalities				
Anemia	**99**	**61**	**100**	**75**
Thrombocytopenia	**76**	**28**	**62**	**26**
Neutropenia	29	12	26	9

Verstovsek S, et al. *Lancet.* 2023;401(10373):269-280.

Momelotinib (Ojjaara®) From a Pharmacist's Perspective

- Initial dosing
  - 200 mg PO daily
- Dose adjustments
  - Hepatic impairment
  - Hematologic toxicity
  - Non-hematologic toxicity
- Drug interactions
  - OATP 1B1/B3
  - BCRP substrates
- Warnings and precautions
  - Risk of infections, thrombocytopenia and neutropenia, hepatoxicity
- Administration
  - Regardless of food
- Dosage forms
  - 100 mg, 150 mg, and 200 mg tablets
- Cost
  - $32,200/month
- Drug acquisition
  - Specialty pharmacies only

Ojjaara® (momelotinib). Package insert. GlaxoSmithKline; 2023.

Patient Case: BP

- 60-year-old male with no major past medical history
- Presentation: Fatigue, pruritus, abdominal discomfort, 15-lb weight loss
- Physical exam: Splenomegaly by palpation (extends 8 cm below the left CM)

Diagnostics	
WBC	55 × 10^9/L (reference range: 4.3 to 10.5 × 10^9/L)
Peripheral blasts	3%
Hgb	8.1 g/dL (reference range: Male, 13.8 to 17.2 g/dL)
Platelets	130 × 10^9/L (reference range: 150 to 400 x 10^9/L)
LDH	1000 IU/L (reference range: 105 to 333 IU/L)
Bone marrow	Atypical megakaryocytes and proliferation; grade 3 reticulin fibrosis
Cytogenetics	Normal karyotype
Diagnostic molecular pathology	BCR-ABL negative, JAK2V617F mutation

Patient Case: BP

Based on the patient's presentation, laboratory, and bone marrow biopsy findings, does the patient meet the criteria for PMF?

- Yes
- No

ALL 3 major criteria plus at least 1 minor criteria

Major Criteria

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

Minor Criteria

At least 1 of the following, confirmed in 2 consecutive determinations:

1. Anemia not attributed to a comorbid condition
2. Leukocytosis ≥ 11×10^9/L
3. Palpable splenomegaly
4. LDH increased to above upper normal limit of institutional reference range
5. Leukoerythroblastosis

BP's Risk Status

Patient Review: This 60-year-old man presented with constitutional symptoms and splenomegaly, WBC 55 × 10^9/L, peripheral blasts 3%, Hgb 8.1 g/dL, platelets 130 × 10^9/L, megakaryocyte atypia, and grade 3 reticulin fibrosis, and *JAK2* V617F mutation.

What is the IPSS risk status of this newly-diagnosed PMF patient?

A. Low
B. Intermediate-1
C. Intermediate-2
D. High

IPSS Risk Assessment for PMF

Risk Factors	No. of Risk Factors	Risk Level	Median OS, months
❑ Age > 65 yrs	0	Low	135
★ Constitutional symptoms	1	Intermediate-1	95
★ Hgb < 10 g/dL	2	Intermediate-2	48
★ WBC count > 25 × 10^9/L	≥ 3	High	27
★ Blood blasts ≥ 1%			

Cervantes F, et al. *Blood.* 2009;113(13):2895-2901.

Treatment Options for BP

Patient Review: 60-year-old man presented with constitutional symptoms and splenomegaly, WBC 55 × 10^9/L, peripheral blasts 3%, Hgb 8.1 g/dL, platelets 130 × 10^9/L, megakaryocyte atypia, and grade 3 reticulin fibrosis, a *JAK2* V617F mutation, and an IPSS score of 4.

What is/are the best treatment options for BP?

A. Momelotinib (Ojjaara®)

B. AlloSCT

C. Ruxolitinib (Jakafi®)

D. Interferon

E. A, B, and C

F. Both B and C

Treatment for BP

While allogeneic SCT would be a potentially curative option, BP opted against proceeding with transplant. As such, his hematologist would like to prescribe ruxolitinib (Jakafi®) and comes to you, as the pharmacist, to assist with dosing and acquisition of the drug.

Dosing Considerations

- Platelet count: 130 × 10^9/L
- CrCL = 120 mL/hr
- Hepatic function: Normal
- Based on FDA labeling, the patient's dose would be 15 mg PO BID

Drug Acquisition

- Insurance information
- Specialty pharmacy
- Consider starting with 5-mg tablets
- Follow up with specialty pharmacy
- Assess financial feasibility
  - Identify co-pay assistance programs
- Follow up with patient

BID, twice a day.

Polycythemia Vera

WHO Criteria for Diagnosis of PV

Diagnosis of PV requires meeting either all 3 major criteria, or the first 2 major criteria and the minor criterion.

Major Criteria	Minor Criterion
1. Hgb > 16.5 g/dL or hematocrit (HCT) > 49% in men or Hgb > 16.0 or HCT > 48% in women or increased red cell mass 2. Bone marrow (BM) biopsy showing hypercellularity for age with trilineage growth (panmyelosis), including prominent erythroid, granulocytic, and megakaryocytic proliferation with pleomorphic, mature megakaryocytes (differences in size) 3. Presence of *JAK2* V617F or *JAK2* exon 12 mutation	1. Subnormal serum erythropoietin level

Arber D, et al. *Blood* 2016;127(20):2391-2405.

Risk-Adapted Management of Patients With PV

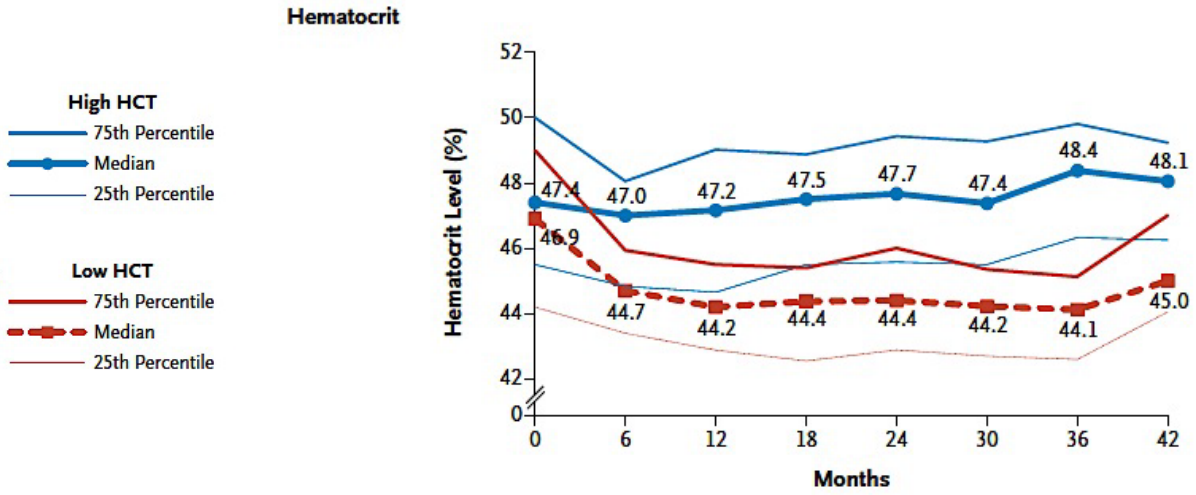
- HCT control is a key therapeutic goal
  - Maintaining HCT < 45% significantly decreases the risk of cardiovascular (CV) death and major thrombotic events

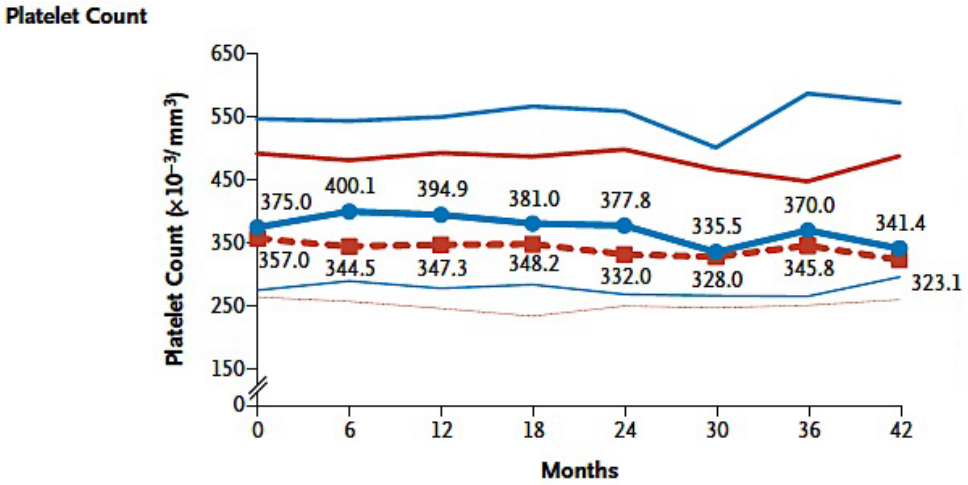
Conventional Risk Category	Risk Variables	Therapy
Low	• Age < 60 years • No thrombosis history	• Phlebotomy, and • Correction of CV risk factors, and • Aspirin
High	• Age ≥ 60 years and/or • Thrombosis history	• Cytoreduction*, and • Correction of CV risk factors, and • Aspirin, and • Phlebotomy

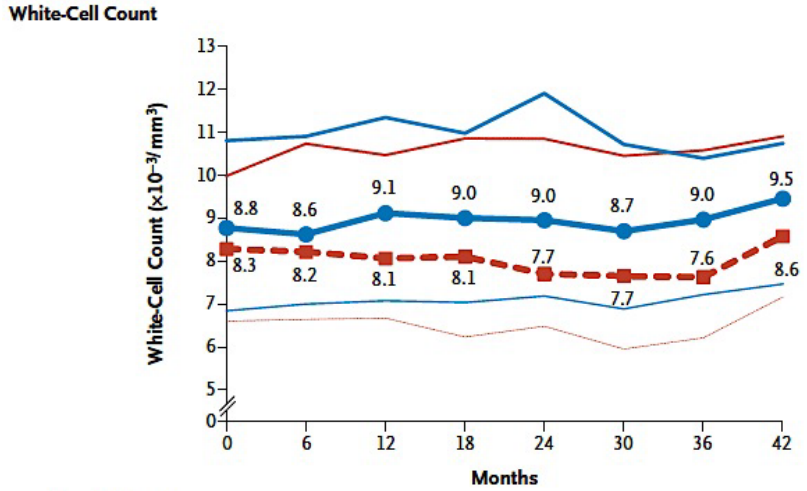
*Cytoreductive therapy includes hydroxyurea, interferon alfa, or busulfan for patients age > 75 years

Barbui T, et al. *J Clin Oncol*. 2011;29(6):761-770; Marchioli R, et al. *N Engl J Med*. 2013;368(1):22-33; Vannucchi AM. *Blood*. 2014;124(22):3212-3220.

Cyto-PV Study:
The Benefit of "Tight" HCT Control and WBC Reduction







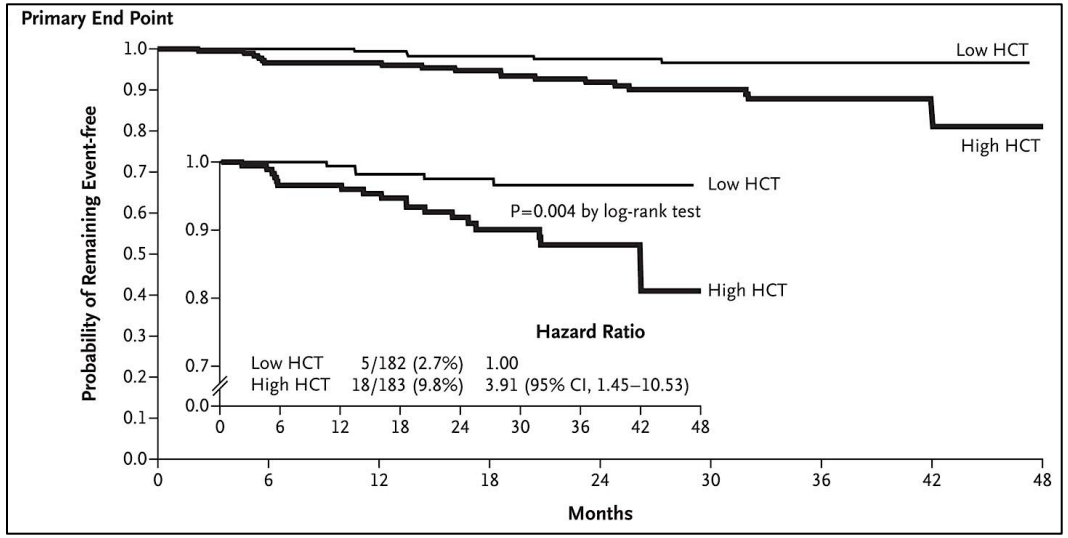
Marchioli R, et al. *N Engl J Med.* 2013;368(1):22-33.

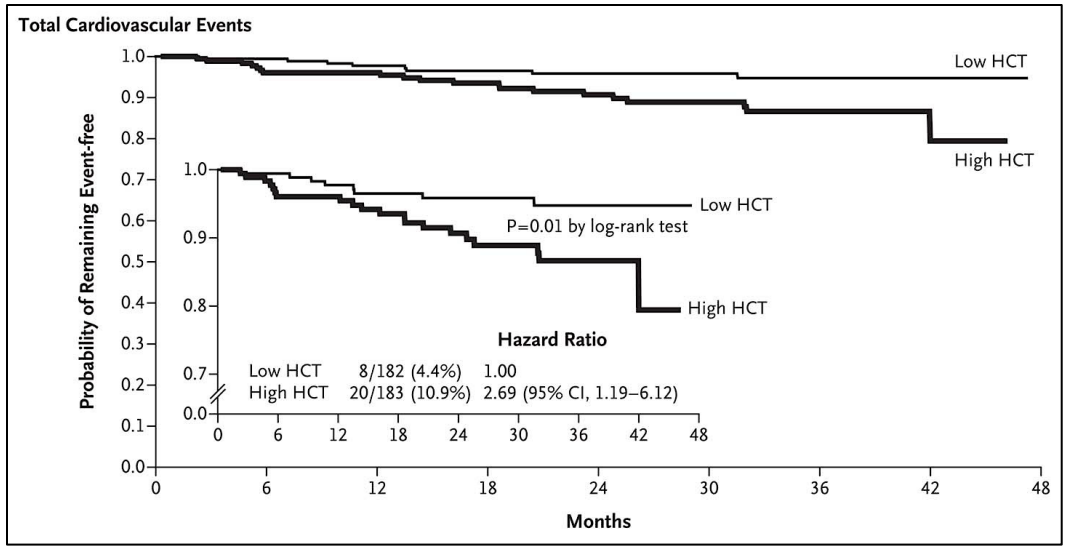
Cyto-PV Study: Events

Table 2. Primary and Secondary End Points.*

End Point	Low Hematocrit (N=182)	High Hematocrit (N=183)	All Patients (N=365)	Hazard Ratio (95% CI)	P Value
	number (percent)				
Primary end point†	5 (2.7)	18 (9.8)	23 (6.3)	3.91 (1.45–10.53)	0.007
Total cardiovascular events‡	8 (4.4)	20 (10.9)	28 (7.7)	2.69 (1.19–6.12)	0.02
Death					
All patients	3 (1.6)	6 (3.3)	9 (2.5)	2.15 (0.54–8.62)	0.28
Cardiovascular causes	0	4 (2.2)	4 (1.1)	NA	
Myocardial infarction	0	1 (0.5)	1 (0.3)	NA	
Stroke	0	2 (1.1)	2 (0.5)	NA	
Pulmonary embolism	0	1 (0.5)	1 (0.3)	NA	
Cancer	2 (1.1)	1 (0.5)	3 (0.8)	0.55 (0.05–6.02)	0.62
Nonfatal events					
Myocardial infarction	3 (1.6)	0	3 (0.8)	NA	
Stroke	0	4 (2.2)	4 (1.1)	NA	
Peripheral arterial thrombosis	0	3 (1.6)	3 (0.8)	NA	
Deep-vein thrombosis	1 (0.5)	4 (2.2)	5 (1.4)	4.11 (0.46–36.74)	0.21
Pulmonary embolism	0	1 (0.5)	1 (0.3)	NA	
Transient ischemic attack	1 (0.5)	4 (2.2)	5 (1.4)	4.24 (0.47–37.97)	0.20
Superficial thrombophlebitis	4 (2.2)	2 (1.1)	6 (1.6)	0.51 (0.09–2.79)	0.44
Bleeding	2 (1.1)	5 (2.7)	7 (1.9)	2.53 (0.49–13.06)	0.27
Hematologic progression or cancer					
Myelofibrosis	6 (3.3)	2 (1.1)	8 (2.2)	0.34 (0.07–1.67)	0.18
Myelodysplasia or acute leukemia	2 (1.1)	1 (0.5)	3 (0.8)	0.52 (0.05–5.71)	0.59
Other hematologic cancer	1 (0.5)	1 (0.5)	2 (0.5)	1.02 (0.06–16.23)	0.99
Solid cancer	7 (3.8)	5 (2.7)	12 (3.3)	0.74 (0.23–2.33)	0.60

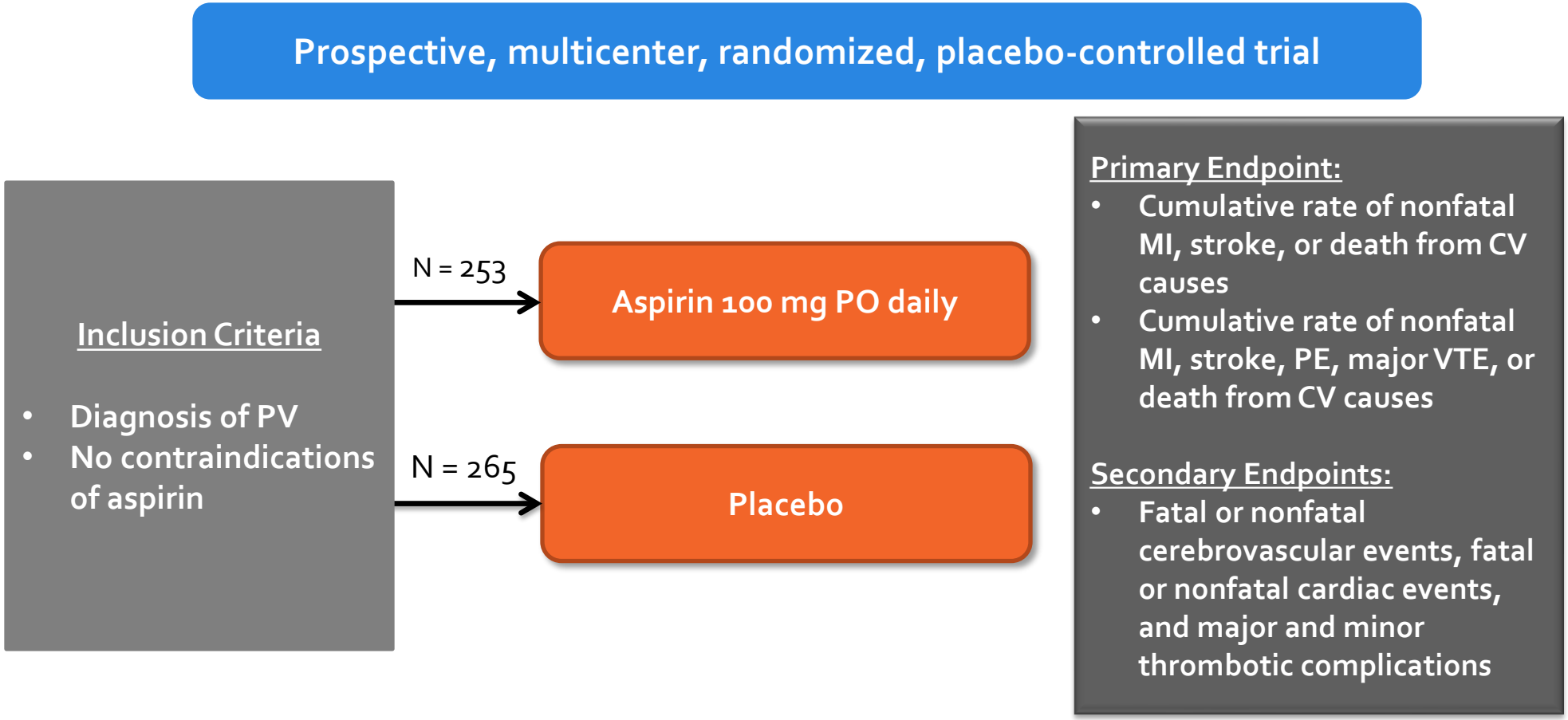
* NA denotes not applicable.
† The primary end point was death from cardiovascular causes or thrombotic events (stroke, acute coronary syndrome, transient ischemic attack, pulmonary embolism, abdominal thrombosis, deep-vein thrombosis, or peripheral arterial thrombosis). The incidence of the primary end point was 1.1 per 100 person-years in the low-hematocrit group, as compared with 4.4 per 100 person-years in the high-hematocrit group.
‡ Total cardiovascular events consisted of the primary end point plus superficial-vein thrombosis. The incidence of total cardiovascular events was 1.9 per 100 person-years in the low-hematocrit group, as compared with 5.0 per 100 person-years in the high-hematocrit group.





Marchioli R, et al. *N Engl J Med.* 2013;368(1):22-33.

ECLAP Trial – Study Design



MI, myocardial infarction; PE, pulmonary embolism; VTE, venous thromboembolism.

Landolfi R et al. *N Engl J Med*. 2004;350:114-24.

ECLAP Trial – Results

End Point	Aspirin (N=253)	Placebo (N=265)	Relative Risk (95% CI)	P value
Nonfatal MI, nonfatal stroke, PE, major VTE, or death from CV causes	8 (3.2)	21 (7.9)	0.4 (0.18-0.91)	0.03
Nonfatal MI, nonfatal stroke, PE, DVT, or death from any cause	13 (5.1)	29 (10.9)	0.47 (0.25-0.91)	0.02
Major or minor thrombosis	17 (6.7)	41 (15.5)	0.42 (0.24-0.74)	0.003
Any Bleeding	23 (9.1)	14 (5.3)	1.82 (0.94-3.53)	0.08
Major Bleeding	3 (1.2)	2 (0.8)	1.62 (0.27-9.71)	0.60
Minor Bleeding	20 (7.9)	12 (4.5)	1.83 (0.90-3.75)	0.10

Landolfi R et al. *N Engl J Med*. 2004;35(2):114-124.

Summary

- Low-dose aspirin can safely prevent thrombotic complications in patients with PV who have no contraindications to aspirin therapy
- If patients encounter GI discomfort with aspirin, consider adding H_2-antagonist
- Patients with extreme thrombocytosis (i.e., platelets > 1,000 × 10^9/L) should be screened for acquired Von Willebrand syndrome

Hydroxyurea (Hydrea®, Droxia™, Mylocel™) in PV Management

- Usually used as a first-line cytoreductive treatment
  - Controls myeloproliferation
  - Reduces splenomegaly
  - May reduce risk of major thrombosis

- Side effects
  - Myelosuppression
  - Leg ulcers
  - Hyperpigmentation
  - Fever
  - Alopecia
  - Increased risk of squamous cell carcinoma
  - Longstanding controversy re: leukemogenic risk

Sever M, et al. *Leuk Lymphoma*. 2014;55(12):2685-2690; Mascarenhas J, et al. *Haematologica.* 2014;99(6):945-949; Fruchtman SM, et al. *Semin Hematol.* 1997;34(1):17-23.

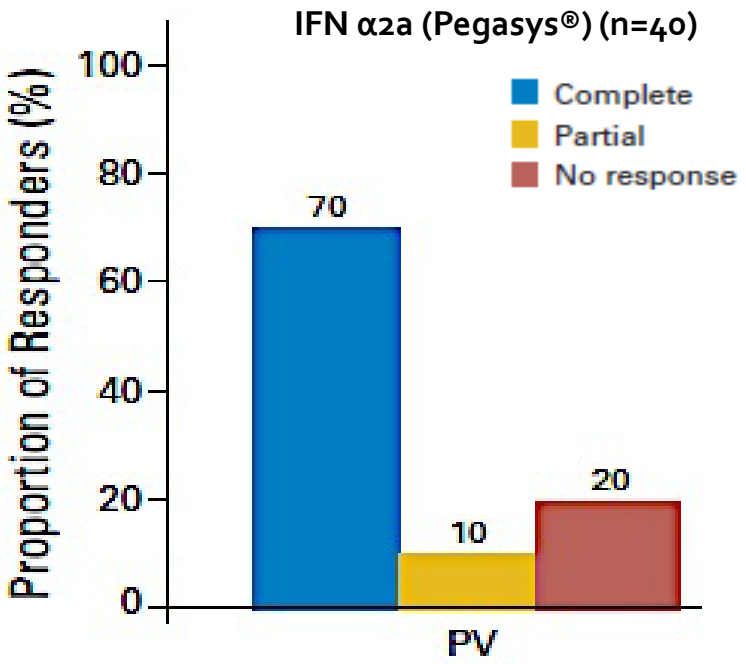
Definition of Hydroxyurea Resistance/Intolerance

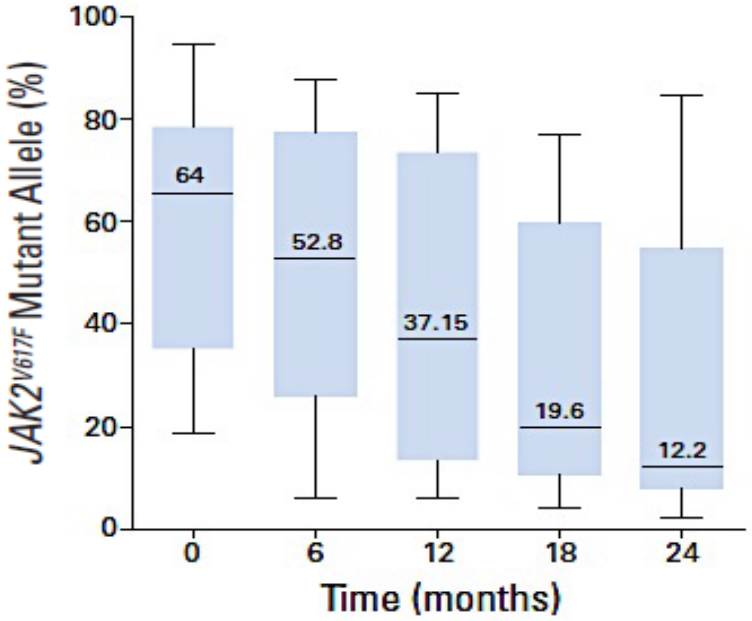
1. Need for phlebotomy to keep HCT < 45% after 3 months of at least 2 g/day of hydroxyurea (HU)
2. Uncontrolled myeloproliferation:
   - Platelet count > 400 × 10^9/L AND WBC > 10 × 10^9/L after 3 months of at least 2 g/day HU
3. Failure to reduce massive splenomegaly by more than 50% as measured by palpation, OR failure to completely relieve symptoms related to splenomegaly, after 3 months of at least 2 g/day of HU
4. Absolute neutrophil count (ANC) < 1.0 × 10^9/L OR platelet count < 100 × 10^9/L OR Hgb <10.0 g/dL at the lowest dose of HU required to achieve a CR or PR
5. Presence unacceptable HU non-hematological toxicities:
   - Leg ulcers
   - Mucocutaneous manifestations
   - GI symptoms
   - Pneumonitis
   - Fever at any dose of HU

Barosi G, et al. *Br J Haematol*. 2010;148(6):961-963.

Interferon in the Treatment of PV

<u>Phase II studies</u>: Treatment with PEG-IFN-α2a (Pegasys®) or α2b (Peg-Intron®) resulted in high rates of complete hematologic and molecular response, and low rates of thrombosis.





Quintas-Cardama A, et al. *J Clin Oncol*. 2009;27(32):5418-5424.

Interferon Tolerability in PV

All patients

Toxicity	Grade 3		Grade 4	
	No.	%	No.	%
Neutropenia	3	8	0	0
Elevated LFTs	2	5	0	0
Fatigue	1	3	0	0
Pain	1	3	0	0
Infection	1	3	0	0
Depression	1	3	0	0
Diarrhea	1	3	0	0
Mucositis	0	0	0	0
Blurred vision	1	3	0	0
Dizziness	1	3	0	0
Anemia	0	0	0	0

Patients treated at 90 mcg/week

Toxicity	Grade 3		Grade 4	
	No.	%	No.	%
Neutropenia	0	0	0	0
Diarrhea	0	0	0	0
Elevated LFTs	0	0	0	0

Quintas-Cardama A, et al. *J Clin Oncol*. 2009;27(32):5418-5424.

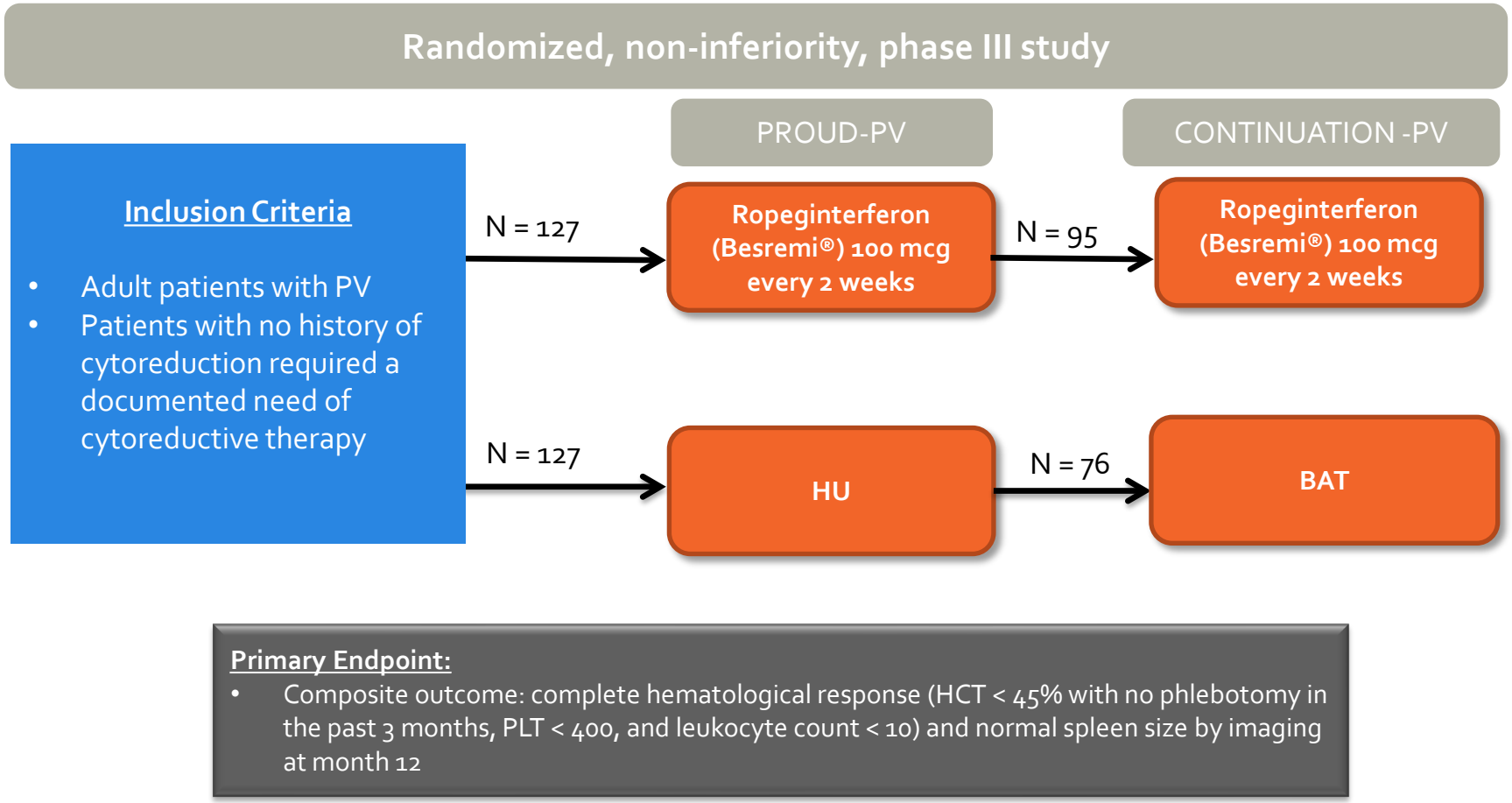
Ropeginterferon (Besremi®) in the Treatment of PV

Author, Year, Study Design	N	Intervention	Response	ADRs
Gisslinger H et al., 2015, PEGINVERA Phase I/II	Phase I = 25 Phase II = 26	Phase I = rIFN-α-2b (Intron A®) 50-540 µg SC every 2 weeks (no MTD) Phase II = Response-driven dosing up to 540 µg SC every 2 weeks (median dose: 250 µg SC every 2 weeks	Dose <300 µg (n=37): 43% (CR)/ 43% (PR) Dose ≥300 µg (n=14): 57% (CR)/43% (PR)	Common: Pruritus, arthralgia, fatigue, headache, diarrhea, influenza-like illness, vertigo Serious: Psychiatric ADR (31%), autoimmune thyroiditis (2 pts)
Gisslinger H et al., 2016, ASH Abstract PROUD-PV Phase III	254	rIFN-α-2b (Intron A®) with response-driven dosing up to 540 µg SC every 2 weeks (median dose: 450 µg SC every 2 weeks HU with CBC-driven dosing (median dose: 1250 mg) *Treatment for 12 months	*Met non-inferiority analysis CHR: 43.1% (rIFN-α-2b [Intron A®]) vs. 45.6% (HU), p = 00.28	No difference in endocrine disorders, psychiatric disorders, cardiac/vascular disorders, and tissue disorders. 5 secondary malignancies in HU group vs. 0 in rIFN-α-2b (Intron A®) group
Gisslinger H et al., 2017, Mature results from PROUD-PV called CONTINUATION-PV	171	rIFN-α-2b (Intron A®) with response-driven dosing up to 540 µg SC every 2 weeks (median dose: 450 µg SC every 2 weeks BAT)	CHR: 70.5% vs. 49.3%, p = 0.0101 Partial molecular response: 49.5% vs. 36.6%, p = 0.1183	Thrombocytopenia (19.7% vs. 26.8%), leukopenia (18.9% vs. 22%), anemia (9.4% vs. 22%), increased GGT (11% vs. 0%), endocrine (3.9% vs. 0.8%), and psychiatric (2.4% vs. 0.8%)

MTD, maximum treatment dosage.

Gisslinger H, et al. *Blood*. 2015;126 (15):1762-1769; Gisslinger H, et al. *Blood*. 2016;128(suppl 22):75; Gisslinger H, et al. *Blood*. 2017;130(suppl 1):320.

Ropeginterferon (Besremi®) in the Treatment of PV PROUD-PV and CONTINUATION-PV



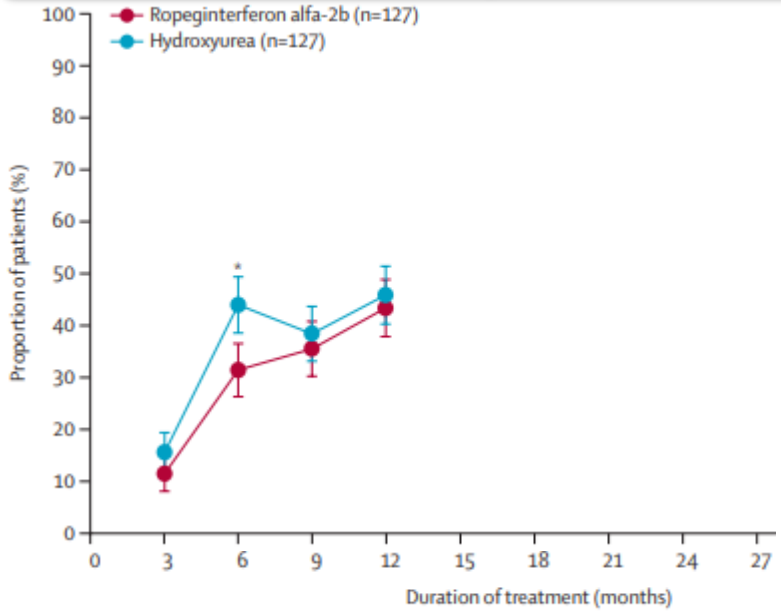
Primary Endpoint:

- Composite outcome: complete hematological response (HCT < 45% with no phlebotomy in the past 3 months, PLT < 400, and leukocyte count < 10) and normal spleen size by imaging at month 12

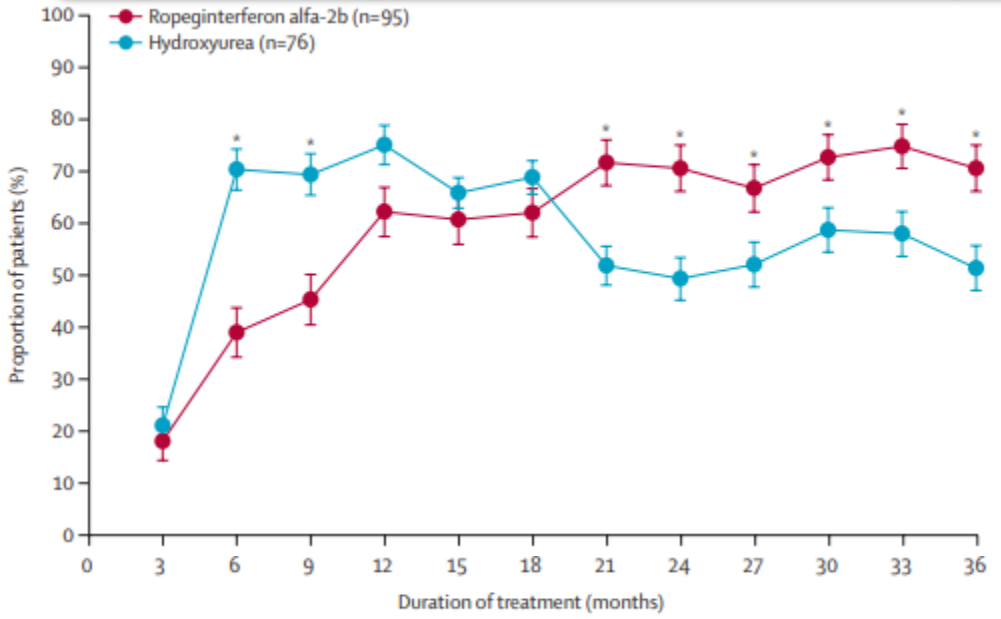
Gisslinger H et al. *Lancet Haematol.* 2020;7(3)e196-e208.

PROUD-PV and CONTINUATION-PV – Results

Proportion of patients with complete hematological response over 12 months during the PROUD-PV study



Proportion of patients with complete hematological response over 36 months among patients in the CONTINUATION-PV study



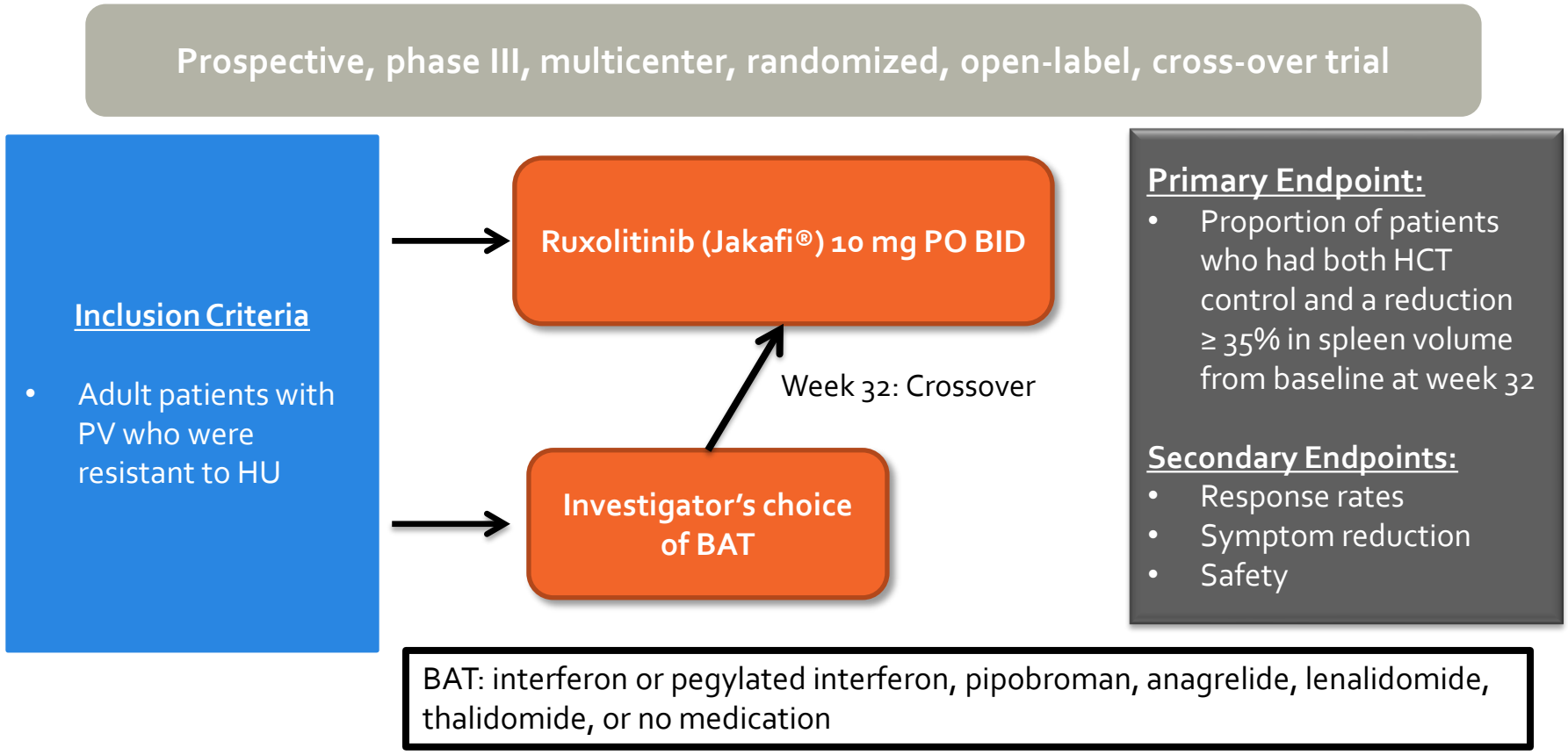
Gisslinger H, et al. *Lancet Haematol.* 2020;7(3)e196-e208.

Ropeginterferon (Besremi®) From a Pharmacist's Perspective

- Initial dosing
  - 100 mcg SC every 2 weeks
  - If on HU, 50 mcg SQ every 2 weeks
- Dose adjustments
  - Hematologic toxicity
  - Non-hematologic toxicity
- Drug interactions
  - None known
- Warnings and precautions
  - Depression and suicide, endocrine toxicity, CV toxicity, decreased blood counts, pancreatitis, pulmonary toxicity, eye toxicity, hyperlipidemia, hepatoxicity, renal toxicity, dental toxicity, cutaneous toxicity
- Administration
  - SC injection
- Dosage forms
  - 500 mcg/mL solution in a single-dose prefilled syringe
- Storage
  - Store in refrigerator in original package
- Cost
  - $20,000/month
- Drug acquisition
  - Specialty pharmacies only
- Disposal
  - Sharps container
  - Adhere to state laws

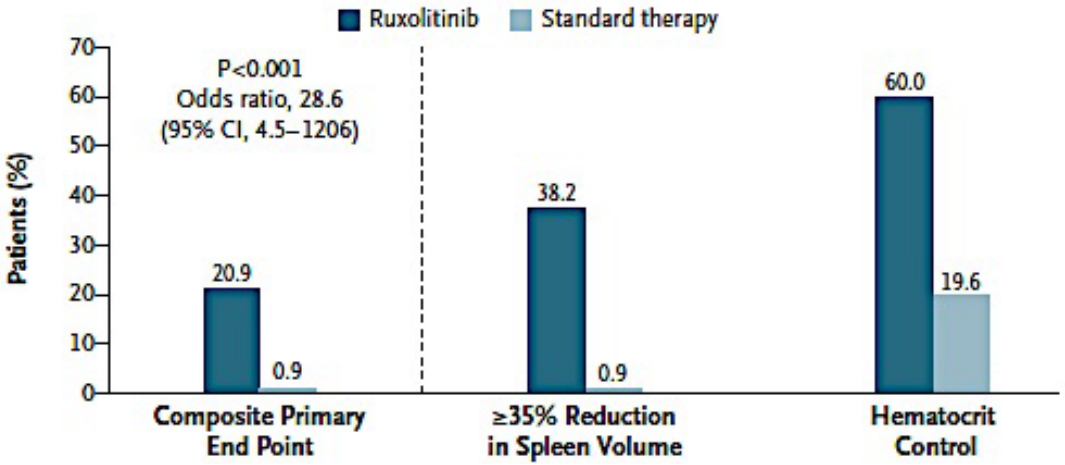
Ojjaara® (momelotinib). Package insert. GlaxoSmithKline; 2023.

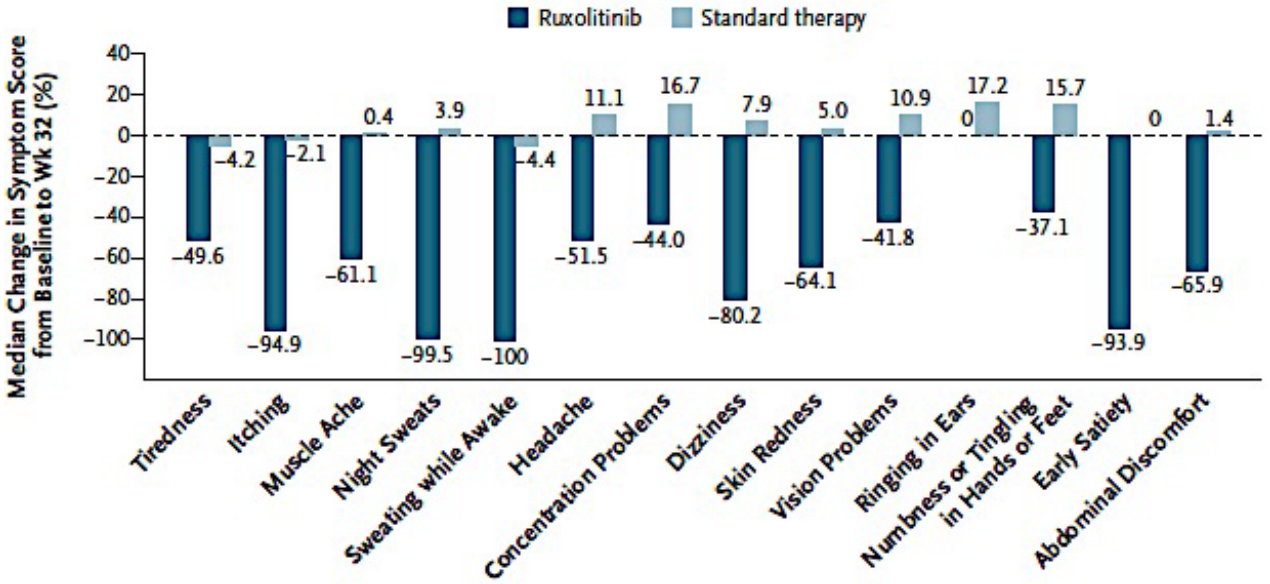
Ruxolitinib (Jakafi®) in PV – RESPONSE Trial



Marchioli R, et al. *N Engl J Med*. 2013;368(1):22-33.

RESPONSE Trial – Results





Ruxolitinib (Jakafi®) is indicated for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of HU.

Marchioli R, et al. *N Engl J Med*. 2013;368(1):22-33; Jakafi® (Ruxolitinib). Package insert. Incyte; 2016.

RESPONSE Trial – Safety Results

Patients, %	Ruxolitinib (Jakafi®) (n = 110)		BAT (n = 111)	
	All Grades	Grade 3/4	All Grades	Grade 3/4
Anemia	43.6	1.8	30.6	0.0
Thrombocytopenia	24.5	5.5	18.9	3.6
Neutropenia	1.8	0.9	8.1	0.9

- Most common grade 3/4 non-hematologic AEs in the ruxolitinib (Jakafi®) arm: dyspnea (2.7%) and asthenia (1.8%)
- Rate of herpes zoster infection was higher in the ruxolitinib (Jakafi®) group (6.4% vs 0; all grade 1-2)
- Thromboembolic events occurred in 1 patient receiving ruxolitinib (Jakafi®) and in 6 patients receiving standard therapy

Marchioli R, et al. *N Engl J Med*. 2013;368(1):22-33.

Treatment Summary

- Treatment for patients with PV combines:
  - Modification of CV risk factors
  - Phlebotomy (HCT target < 45%)
  - Antiplatelet therapy
  - First-line cytoreductive therapy: HU or PEG-IFN
  - Second-line: Ruxolitinib (Jakafi®) for patients resistant to or intolerant of HU
    - Other options may include busulfan

PV-Associated Pruritus

Feature	PV-associated pruritus	Idiopathic AP	AP of the elderly
Mean age (years)	59 (range 21-89)	29.4 (females), 34.5(males)	> 60
Gender distribution (F:M)	~1:1	~1:1	3:1
Family history	None	33%	None
Relationship of pruritus to water	Usually follows contact with water at any temperature, but less frequently after contact with cold water	Hot water causes symptoms in 30% and cold water in 35% of patients	Itching is invariably absent during bathing, but starts soon after (during drying)
Clinical features	Distributed over torso and extensor surface of limbs, lower rate of arterial thrombosis, negative impact on QoL	Onset of itching is upon contact with water, duration averages 40 min, condition is usually unremitting, psychiatric symptoms may be present	Fair color, dry scaly skin, females have more severe symptoms, itching begins in lower extremities and spreads upwards, but spares head, symptoms are worse in winter, and are progressive
Histopathological features	Increased skin mast cells, mononuclear cells and eosinophils, itching correlates with homozygosity for the *JAK2* V617F mutation	Normal number of skin mast cells, acetylcholine mediated, increased cutaneous fibrinolytic activity	Non-specific lymphocytic perivenular infiltrate

Saini KS et al. *Eur J Clin Invest*. 2010 Sep;40(9):828-34.

Management of PV-Associated Pruritus

Typically Effective	Mixed Results	Typically Ineffective
• Interferon-α • Ruxolitinib (Jakafi®) • SSRIs • Phototherapy	• Anti-histamines	• Cytoreductive therapy • Phlebotomy

SSRIs, selective serotonin reuptake inhibitors.

Tefferi A, et al. *Blood.* 2002;99(7):2627; Sharon R, et al. *Cancer*. 1986;57(4):718–720; Mesa R, et al. *Eur J Haematol*. 2016;97(2):192-200; Diehn F et al. *Br J Haematol.* 2001;115(3):619-621; Jackson N et al. *Br J Dermatol*. 1987;116(1):21-29; de Wolf JT, et al. *Lancet*. 1991;8735:241; Baldo A, et al. *Br J Dermatol*. 2002;147:979–81.

Patient Case: BP

- 66-year-old male with a history of a right lower extremity DVT
- Presentation: fatigue, persistent pruritus, and headaches
- Physical exam: No evidence of splenomegaly by palpation

Diagnostics 4/15/2008	
WBC	6.7 × 10^9/L (reference range: 4.3 to 10.5 × 10^9/L)
Peripheral blasts	0%
Hgb	18.1 g/dL (reference range: Male, 13.8 to 17.2 g/dL)
HCT	54% (reference range: Male, 38.8 to 52%)
Platelets	223 × 10^9/L (reference range: 150 to 400 x 10^9/L)
BM biopsy	Hypercellular, trilineage hematopoiesis with pleomorphic, mature megakaryocytes
Cytogenetics	Normal karyotype
Diagnostic molecular pathology	BCR-ABL negative, *JAK2* V617F mutation
Erythropoietin level	<1.0 mIU/mL (reference range: 2.6 to 18.5 mIU/mL)

Patient Case: BP

Based on the patient's presentation, laboratory, and molecular findings does the patient meet the criteria for PV?

- Yes
- No

All 3 major criteria, or the first 2 major criteria and the minor criterion

Major Criteria	Minor Criteria
★ Hgb >16.5 g/dL or HCT > 49% in men or Hgb > 16.0 or HCT > 48% in women or increased red cell mass ★ BM biopsy showing hypercellularity for age with trilineage growth (panmyelosis) including prominent erythroid, granulocytic, and megakaryocytic proliferation with pleomorphic, mature megakaryocytes (differences in size) ★ Presence of *JAK2* V617F or *JAK2* exon 12 mutation	★ Subnormal serum erythropoietin level

BP's Risk Status

Patient Review: This 66-year-old man presented with fatigue, persistent pruritus, and headaches, WBC 6.7 × 10^9/L, Hgb 18.1 g/dL, HCT 54%, platelets 223 × 10^9/L, a *JAK2* V617F mutation, and a previous history of a deep vein thrombosis (DVT).

What is the risk status of this patient with newly-diagnosed PV?

A. Low

B. High

Patient Case: BP

Patient Review: This 66-year-old man presented with fatigue, persistent pruritus, and headaches, WBC 6.7 x 10^9/L, Hgb 18.1 g/dL, HCT 54%, platelets 223 x 10^9/L, a *JAK2V617F* mutation, and a previous history of a DVT.

What is/are the best treatment options for BP?

A. Hydroxyurea
B. Aspirin
C. Ruxolitinib (Jakafi®)
D. Interferon
E. Both A and B
F. None of the above

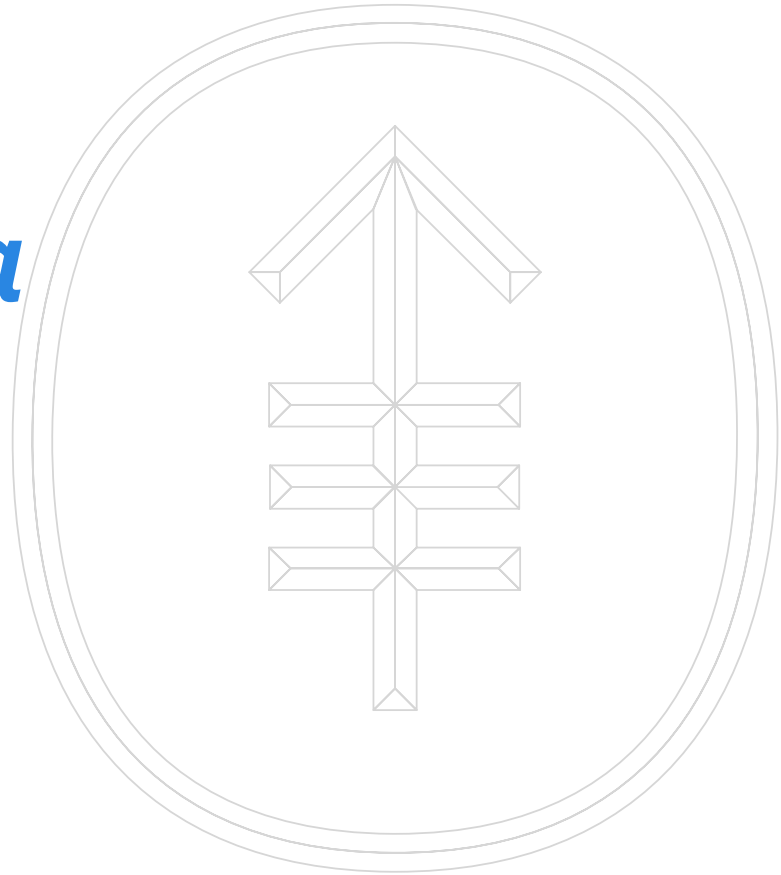
Patient Case: BP

Patient Review: This 66-year-old man presented with fatigue, persistent pruritus, and headaches, WBC 6.7 × 10^9/L, Hgb 18.1 g/dL, HCT 54%, platelets 223 × 10^9/L, a *JAK2* V617F mutation, and a previous history of a DVT. He was placed on hydroxyurea (Hydrea®, Droxia™, Mylocel™) and tolerated it well until today, when he presented to clinic with leg ulcers, increasing Hgb and HCT, and a return of his constitutional symptoms.

What should we do now?

a. Continue hydroxyurea, but increase the dose
b. Consider starting ruxolitinib (Jakafi®)
c. Admit the patient to start 7+3 chemotherapy

Essential Thrombocythemia



Diagnosis of Essential Thrombocythemia (ET)

WHO Diagnosis of ET requires ALL 4 major criteria or the first 3 major criteria and the minor criterion

Major Criteria	Minor Criteria
1. Platelet count ≥ 450 × 10^9/L 2. BM 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 3. Not meeting WHO criteria for BCR-ABL1+ CML, PV, PMF, MDS, or other MPNs 4. Presence of *JAK2*, *CALR*, or *MPL* mutation	1. Presence of a clonal marker or absence of evidence for reactive thrombocytosis

Arber D, et al. *Blood* 2016;127(20):2391-2405.

ET Risk Assessment

- IPSET Prognostic Features
  - Age > 60 years (2 points)
  - Prior history of thrombosis (1 point)
  - Leukocytes >11 × 10^9/L (1 point)

IPSET Risk Group:
0 points: Low
1-2 points: Intermediate
3-4 points: High

IPSET-thrombosis			
Low	**Intermediate**	**High**	**Total**
n = 281	n = 277	n = 32	N = 590
48%	47%	5%	100%
0.59%pts/y	1.55%pts/y	1.77%pts/y	0.95%pts/y
n = 193	n = 194	n = 243	N = 630
31%	31%	39%	100%
1.27%pts/y	2.67%pts/y	3.71%pts/y	2.86%pts/y
n = 474	n = 471	n = 275	N = 1220
39%	39%	23%	100%
1.03%pts/y	2.35%pts/y	3.56%pts/y	1.77%pts/y

IPSET, International Prognosis Score of thrombosis in ET.

Barbui T, et al. *J Clin Oncol.* 2011;29(6):761-770.

ET Risk Assessment

- IPSET Prognostic Features
  - Age > 60 years (2 points)
  - Prior history of thrombosis (1 point)
  - Leukocytes >11 × 10^9/L (1 point)

IPSET Risk Group:
0 points: Low
1-2 points: Intermediate
3-4 points: High

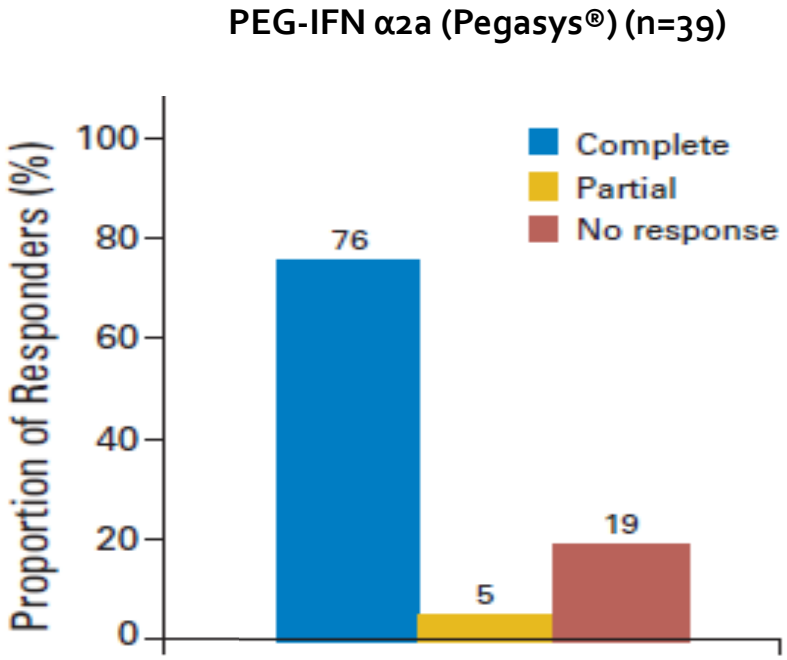
Conventional Risk Category	Risk Variables	Therapy
Low	• None	• Observation • Correction of CV risk factors
High	• Age ≥ 60 years **OR** • Thrombosis history **OR** • Platelet count ≥ 1 500 × 10^9/L	• Cytoreduction*, and • Correction of CV risk factors, and • Aspirin**

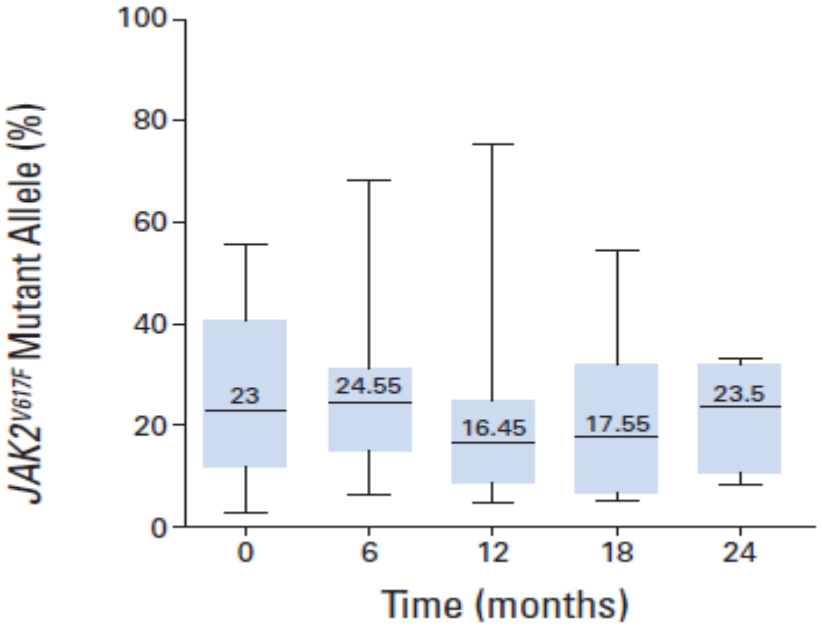
*HU (Hydrea®, Droxia™, Mylocel™) is the first-line treatment of choice. Anagrelide (Agrylin®) is generally 2nd-line therapy if resistant or intolerant to HU. IFN-α is used for young patients, pregnant women, or patients who are refractory/intolerant to HU
**Acquired Von Willebrand syndrome should be assessed if platelet count is ≥ 1000 × 10^9/L

Rumi E, et al. *Blood*. 2016;128(20):2403-2414; Beer PA et al. *Blood*. 2011;117(5):1472-1482.

Interferon in the Treatment of ET

Treatment with PEG-IFN- α2a (Pegasys®) resulted in high rates of complete hematologic and molecular response, and low rates of thrombosis.





Quintas-Cardama A, et al. *J Clin Oncol*. 2009;27(32):5418-5424.

Interferon Tolerability in ET

All patients

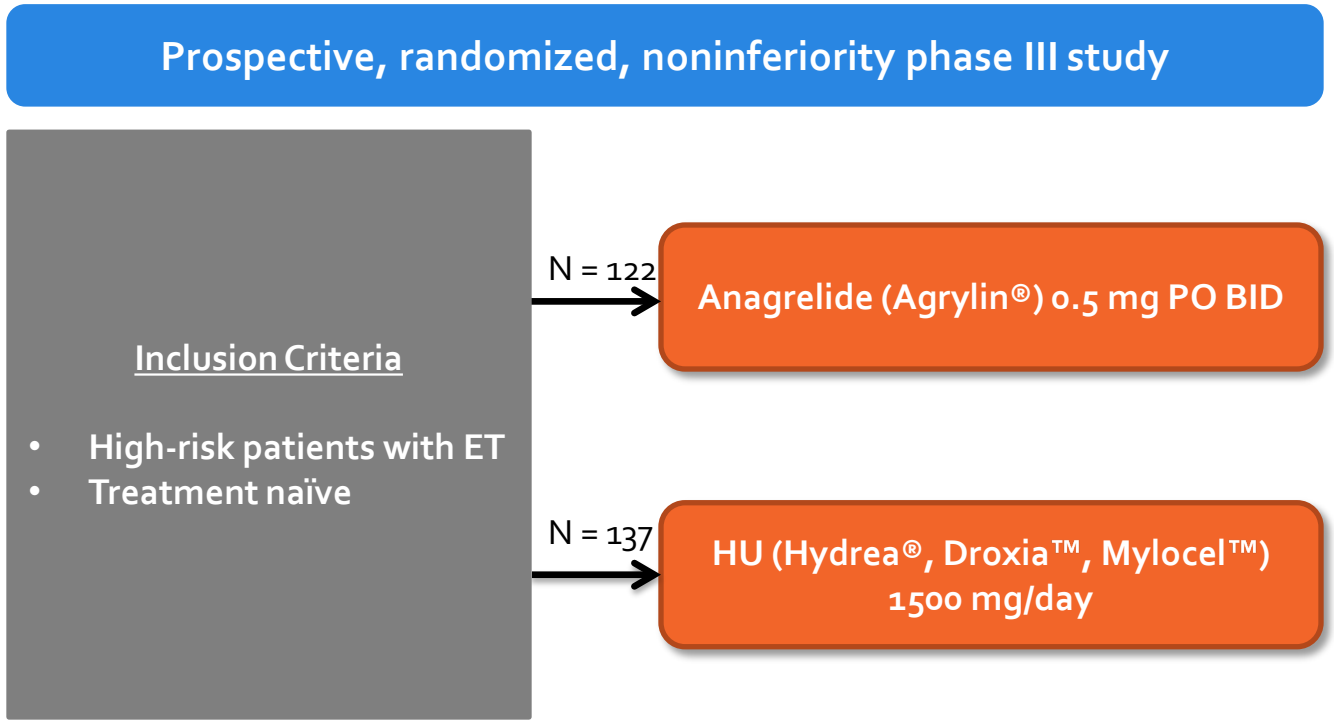
Toxicity	Grade 3		Grade 4	
	No.	%	No.	%
Neutropenia	12	31	1	3
Elevated LFTs	3	8	0	0
Fatigue	2	5	0	0
Pain	1	3	0	0
Infection	1	3	0	0
Depression	1	3	0	0
Diarrhea	0	0	0	0
Mucositis	1	3	0	0
Blurred vision	0	0	0	0
Dizziness	0	0	0	0
Anemia	1	3	0	0

Patients treated at 90 mcg/week

Toxicity	Grade 3		Grade 4	
	No.	%	No.	%
Neutropenia	2	13	0	0
Diarrhea	1	6	0	0
Elevated LFTs	1	6	0	0

Quintas-Cardama A, et al. *J Clin Oncol*. 2009;27(32):5418-5424.

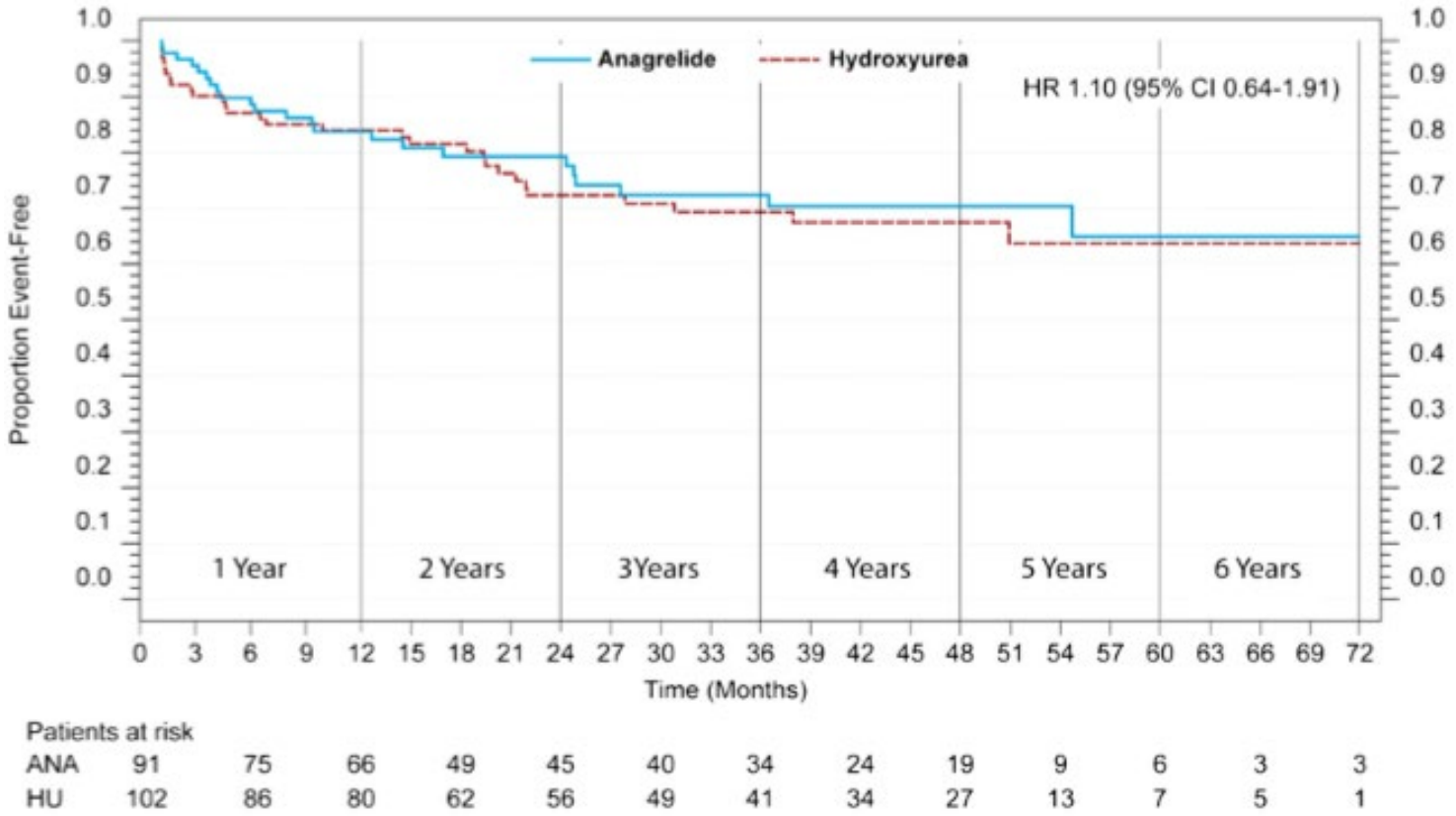
Anagrelide (Agrylin®) for Treatment of ET: ANAHYDRET Study



Gisslinger H et al. *Blood*. 2013;121(10):1720-1728.

Anagrelide (Agrylin®) for Treatment of ET: ANAHYDRET Study

Figure 3. Event-free survival for ET-related events for patients who were rediagnosed as having WHO-ET ("true-ET"). The HR (95% CI) is presented after an observation time of 6 years.



Anagrelide Agrylin®; Hydroxyurea (Hydrea®, Droxia™, Mylocel™)

Gisslinger H et al. *Blood*. 2013;121(10):1720-1728.

Safety of Anagrelide (Agrylin®) in ANAHYRDET Study

Table 5. Safety profile according to organ classes

Organ manifestations	Symptoms	No. of patients		*P* value
		Anagrelide group	Hydroxyurea group	
Infections and infestations	Herpes (simplex, labialis, zoster)	1	4	.37
	Infections (viral, influenza-like symptoms)	12	28	.01
★ Blood and lymphatic system disorders	Anemia	11	24	.04
	Epistaxis	6	15	.07
	Leukopenia	1	37	< .01
Nervous system disorders	Headache	29	22	.21
	Vertigo	6	14	.10
Ear and labyrinth disorders	Dizziness	7	2	.09
★ Cardiac disorders	Hypertension	14	4	.01
	Palpitations	30	3	< .01
	Tachycardia	13	3	.01
Respiratory, thoracic, and mediastinal disorders	Bronchitis	3	8	.22
Gastrointestinal disorders	Abdominal pain	11	11	1.00
	Diarrhea	17	10	.15
	Other gastrointestinal events	11	14	.83
★ Skin and subcutaneous tissue disorders	Alopecia	0	5	.06
	Skin disorders	7	16	.12

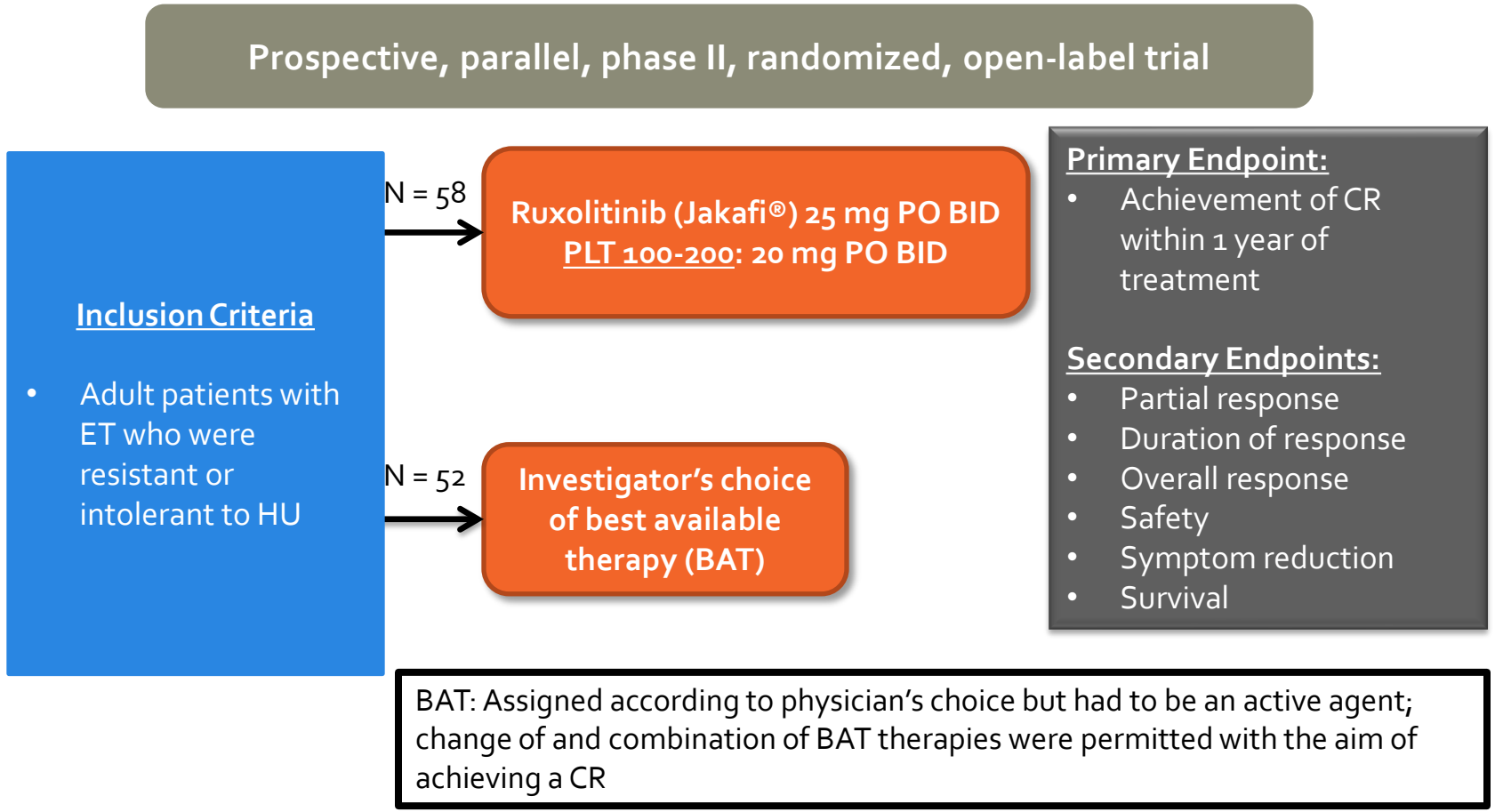
Gisslinger H et al. *Blood*. 2013;121(10):1720-1728.

Anagrelide (Agrylin®) From a Pharmacist's Perspective

- Initial dosing
  - 0.5 mg PO BID
  - Dose adjust to platelet count to < 600, ideally between 150 and 400
- Dose adjustments
  - Hepatic impairment
  - Hematologic toxicity
- Drug interactions
  - Antiplatelet and anticoagulation
- Warnings and precautions
  - Bleeding risk, CV, pulmonary hypertension, pulmonary toxicity, renal abnormalities
- Administration
  - Regardless of food
- Dosage forms
  - 0.5 and 1 mg capsules
- Cost
  - $669.60/month
- Drug acquisition
  - Retail pharmacy

Anagrelide (Agrylin®). Package insert. Shire US Inc.; 2016.

Ruxolitinib (Jakafi®) in ET: MAJIC-ET Trial



Harrison CN, et al. *Blood*. 2017;130(17):1889-1897.

Ruxolitinib (Jakafi®) in ET: MAJIC-ET Trial

	Ruxolitinib (Jakafi®)	BAT	P Value
CR	46.5%	44.2%	0.40
PR	46.5%	51.9%	*Not reported
OS	0.98	0.98	0.99
PFS	0.93	0.96	0.97
Thrombotic event	17.2%	5.8%	0.09
Hemorrhagic event	1.7%	8.9%	0.14
Maximum % TSS reduction at any point during first 12 months	32%	0%	**0.03**
Symptom response at 2 months	19%	3%	**0.04**

PFS, progression-free survival.

Harrison CN, et al. *Blood*. 2017;130(17):1889-1897.

Ruxolitinib (Jakafi®) in ET: MAJIC-ET Trial

Grade 3/4	Ruxolitinib (Jakafi®)	BAT	P value
Anemia	21%	0%	< 0.005
Thrombocytopenia	3.4%	0%	0.32
Infection	15.5%	3.5%	0.03

Overview of assigned therapy switches and discontinuations per treatment arm

	Ruxolitinib	BAT	Total
Assigned therapy switches			
Patients that switched BAT therapy at least once	N/A	30	30
Total number of times BAT therapy was switched	N/A	86	86
Discontinuations			
Transformation	9	3	12
Loss of response	11	0	11
Lack of efficacy	5	1	6
Toxicity			
Anemia	2	0	2
Other	3	1	4
Other	3	3	6
Death	1	2	3
Withdrawal of consent	1	0	1
Total	35	10	45

Harrison CN, et al. *Blood*. 2017;130(17):1889-1897.

Patient Case: MT

- 62-year-old man had elevated platelet count (780 × 10^9/L) was recently admitted for a DVT
- History, examination, and laboratory tests (iron status, inflammatory markers, rheumatoid disease, and malignancy screening) did not reveal underlying cause

Diagnostics	
WBC	9.6 × 10^9/L (reference range: 4.3 to 10.5 × 10^9/L)
Hgb	14.3 g/dL (reference range: Male, 13.8 to 17.2 g/dL)
Platelets	775 × 10^9/L (reference range: 150 to 400 x 10^9/L)
BM biopsy	Increased megakaryocytes with prominent large hyperlobulated forms; reticulin is not increased
Cytogenetics	Normal karyotype
Diagnostic molecular pathology	BCR-ABL negative, *JAK2* V617F mutation present

Patient Case: MT

Does MT meet the diagnostic criteria for ET?

A. Yes

B. No

Major Criteria

1. Platelet count ≥ 450 × 10^9/L
2. BM 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
3. Not meeting WHO criteria for BCR-ABL1+ CML, PV, PMF, MDS, or other MPNs
4. Presence of *JAK2*, *CALR*, or *MPL* mutation

Minor Criteria

1. Presence of a clonal marker or absence of evidence for reactive thrombocytosis

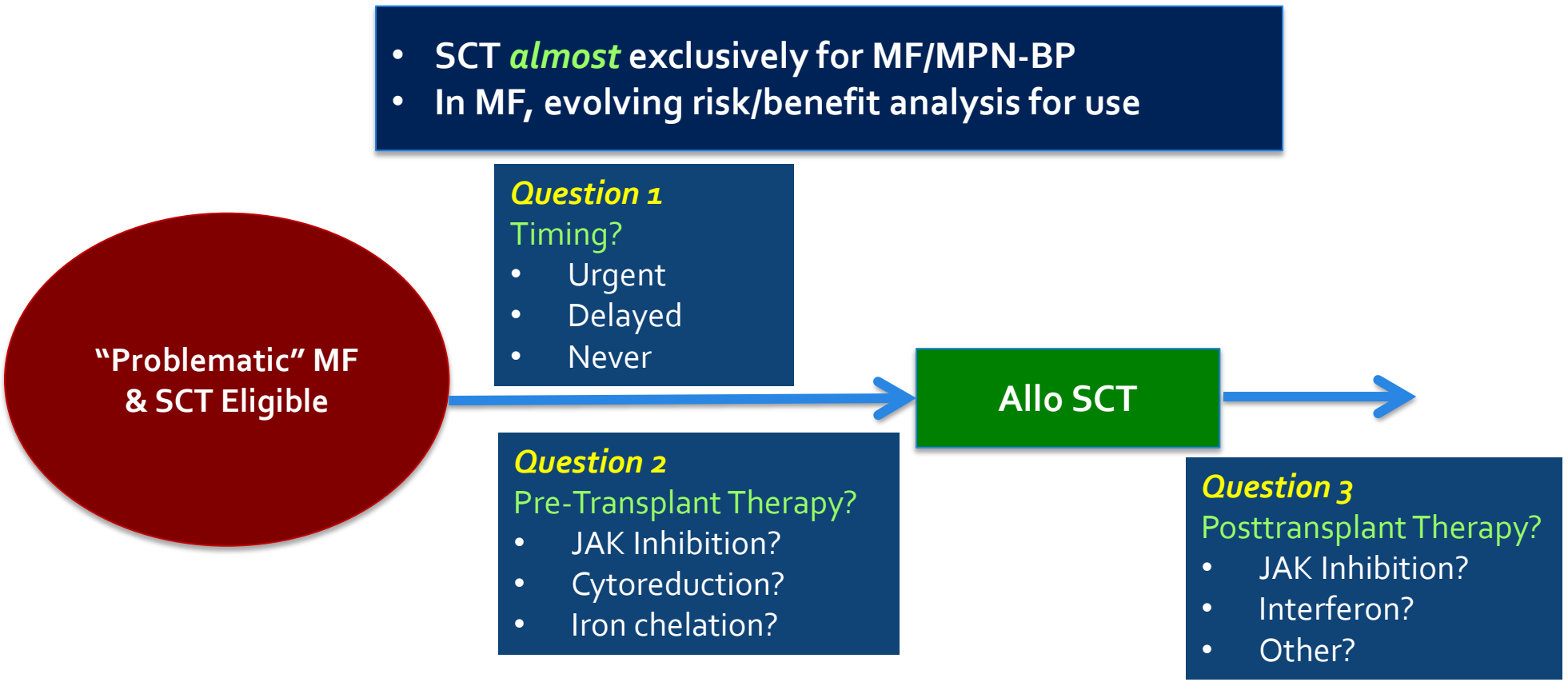
Patient Case: MT

Patient Review: 62-year-old man had elevated platelet count (780 × 10^9/L), was found to have a DVT and subsequently diagnosed with ET.

What initial treatment should MT start to reduce the risk of thrombosis?

A. Rituximab (Rituxan®)
B. Hydroxyurea (Hydrea®, Droxia™, Mylocel™).
C. Aspirin
D. Busulfan (Busulfex® and Myleran®)
E. Both B and C

SCT Use in MPNs



MPN-BP, myeloproliferative neoplasms in blast phase; SCT, stem cell transplant.

Courtesy of R Mesa, Mayo Clinic.

MPN Conclusions

- MPNs are chronic and variably progressive hematopoietic diseases with shared biology, clinical features, and molecular basis
- Proper diagnosis is essential, given overlaps
- Patient-reported symptom burden is crucial and quantifiable through treatment
- Treatment strategies can vary depending on the individual's risk status and management needs
- Thrombosis is a shared risk, and antiplatelet therapy a mainstay for a majority of patients
- Ruxolitinib (Jakafi®) represented a major paradigm shift and can significantly improve the outlook for many patients with MF or HU-resistant/intolerant PV, but it does not cure these diseases
- Interferon may offer significant benefit, but toxicity warrants careful patient selection and monitoring
- Novel therapies for MPNs are needed, and a number of strategies are in development:
  - Novel JAK pathway inhibitors: approval of fedratinib (Inrebic®), pacritinib(Vonjo®), and momelotinib (Ojjaara®) have broadened treatment options significantly, specifically addressing cytopenias
  - Antifibrotics
  - Telomerase inhibitors
  - Combination approaches (hypomethylating agents + JAK inhibitors in BP, numerous in early disease)

Vachhani P, et al. *Ther Adv Hematol*. 2024;15:20406207241229588; Mesa R, et al. *BMC Cancer*. 2016;16:167;
NCCN. Myeloproliferative Neoplasms Version 2.2024. August 8, 2024. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf.

Resources

- The Leukemia & Lymphoma Society
- MPN Advocacy Network
- NCCN
- Patient Access Network
- Needymeds.org

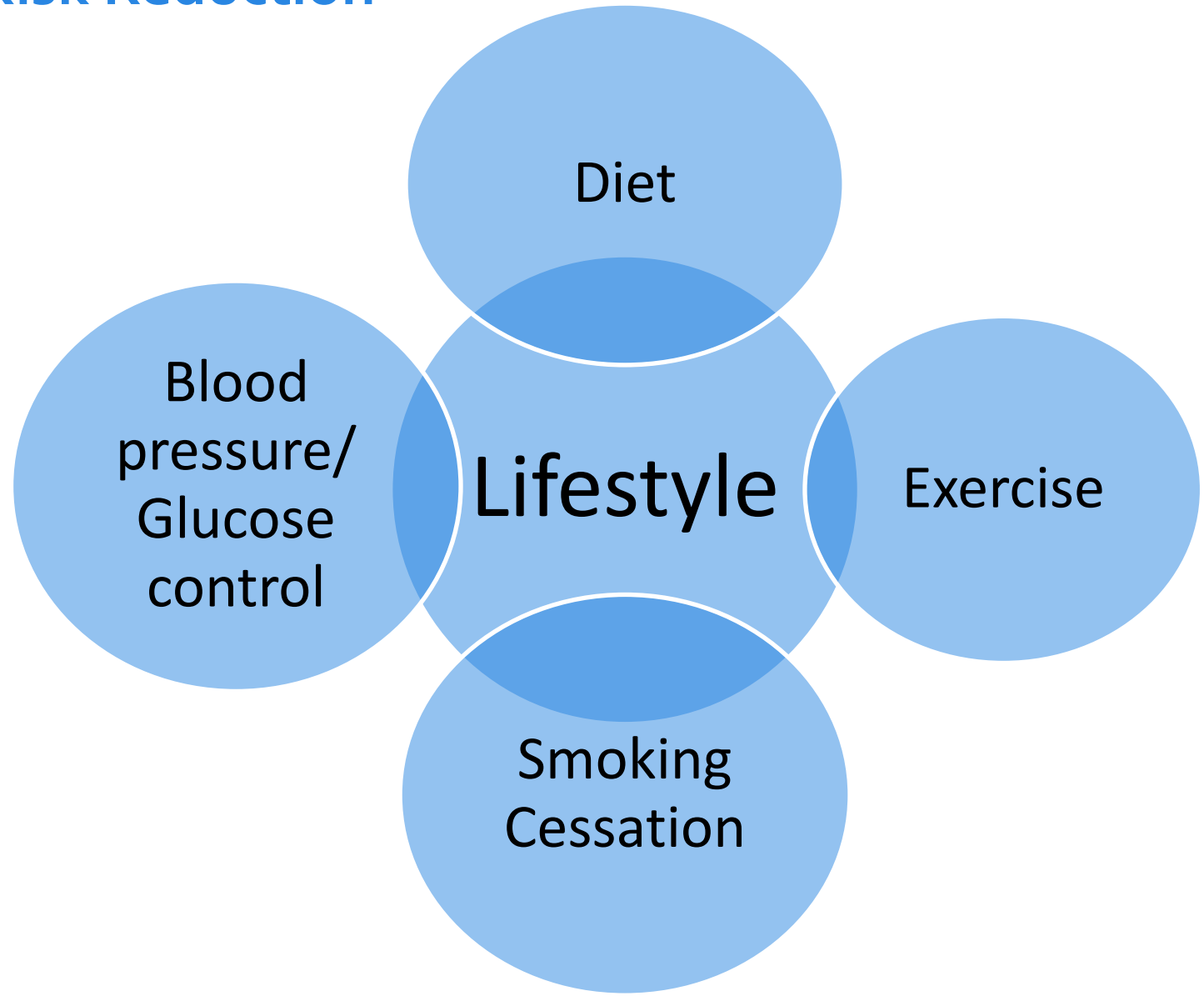
Treatment Goals

- Reduction in life-threatening disease sequelae
- Slow/reduce disease progression
- Improve QoL

Common Symptoms

- Vascular
  - Micro- and macro-vascular
    - Neurologic, cognitive, cardiac, pulmonary
- Inflammation
- Proliferation
- Gastrointestinal

Cardiovascular Risk Reduction



Symptom: Splenomegaly

- Prevalent in MF, also common in PV and ET
- Symptoms:
  - Early satiety
  - Abdominal fullness
  - Nausea
  - Increased abdominal girth
- Nursing interventions

Symptom: Pruritus

- Most common in PV
- Related to increased number of mast cells
- Worse after showering
- Treatment

Constitutional Symptoms

- Associated with inflammation in bone marrow and throughout the body
- Common symptoms:
  - Fatigue
  - Night sweats
  - Bone pain
  - Low-grade fevers
  - Weight loss

Treatment: Therapeutic Phlebotomy

- Used in PV patients
- Remove approximately 450cc of blood
- Target HCT< 45%
- Nursing implications:
  - Monitor patient labs
  - Hydration
  - What to avoid
  - What to expect

Treatment: Aspirin (ASA)

- Low dose aspirin to prevent thrombotic complications

- Nursing implications:
  - Review patient history
  - Monitor for sign of bleeding
  - Very high platelets and Von Willebrand disease

Treatment: HU

- Cytoreductive agent, reduce risk of thrombotic events by managing blood levels

- Nursing Implications:
  - Monitor blood counts
  - Immune suppression
  - Dermatologic changes

Treatment: Interferon

- Used to control erythrocytosis and thrombocytosis

- Nursing Implications:
  - Monitor labs
  - Administered subcutaneously
  - Local reactions
  - Side effects

Conclusions

- Focus on symptom recognition and assessment
- Educate on lifestyle changes and strategies for cardiovascular risk reduction
- Collaborate with interdisciplinary team

THANK YOU

We have one goal: A world without blood cancers

LEUKEMIA & LYMPHOMA SOCIETY®