Meet The Professor
Current and Future Management of Myelofibrosis

Srdan Verstovsek, MD, PhD
Professor of Medicine
Director, Hanns A Pielenz Clinical Research Center
for Myeloproliferative Neoplasms
Department of Leukemia
The University of Texas MD Anderson Cancer Center
Houston, Texas

Commercial Support

This activity is supported by educational grants from CTI BioPharma Corp and Incyte Corporation.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Mersana Therapeutics Inc, Natera Inc, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

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Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Verstovsek — Disclosures

No relevant conflicts of interest to disclose

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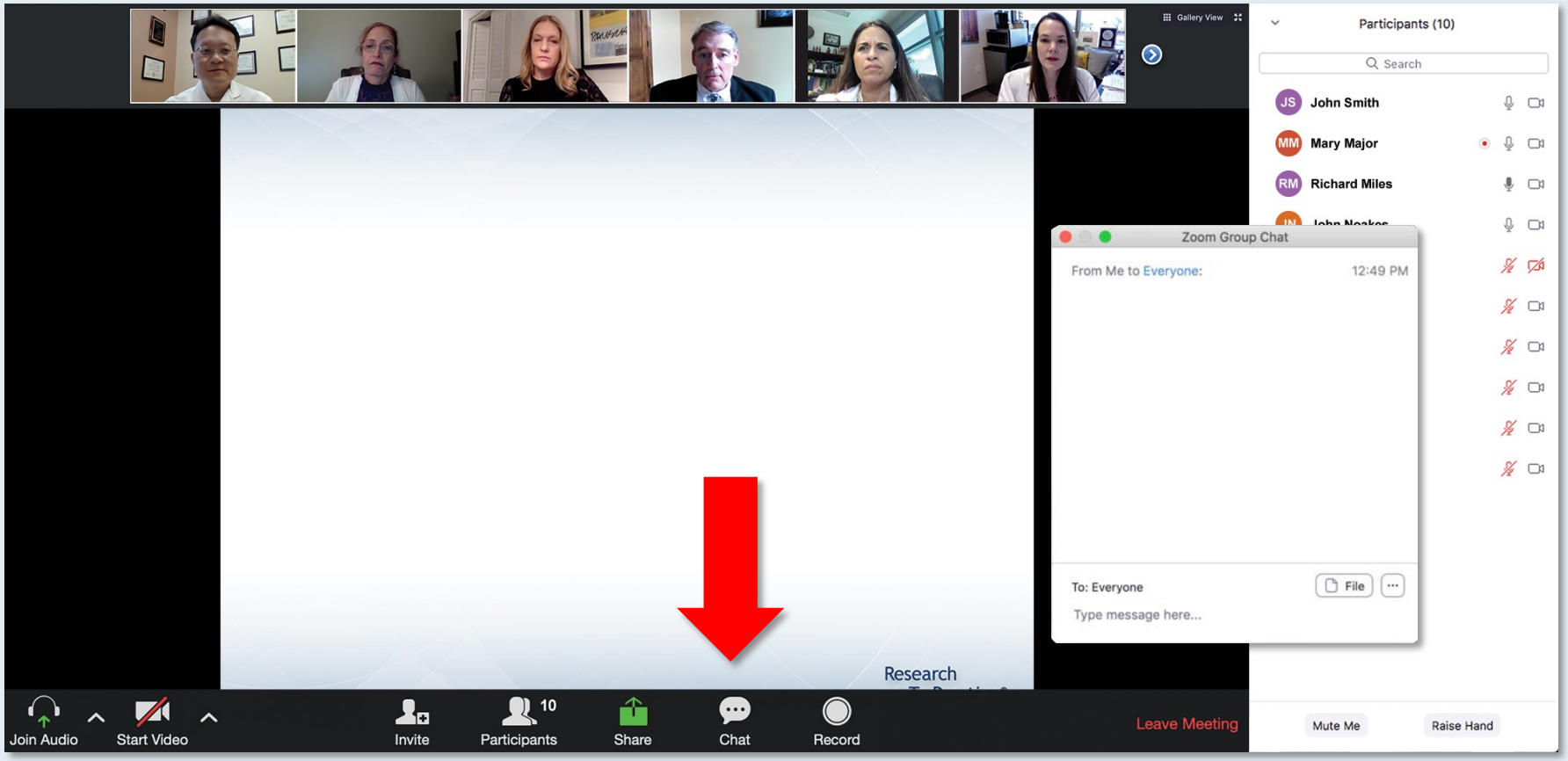
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

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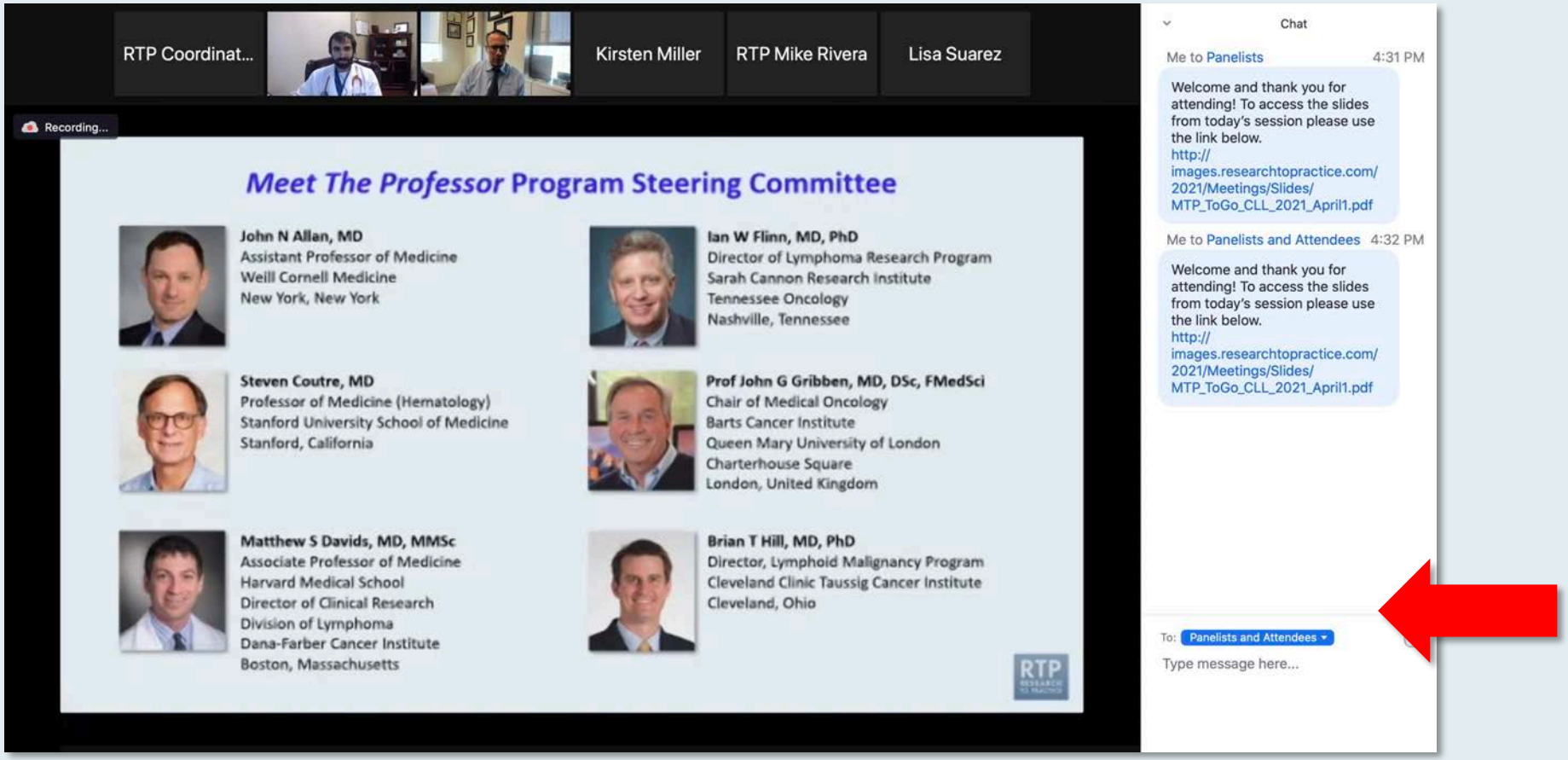
Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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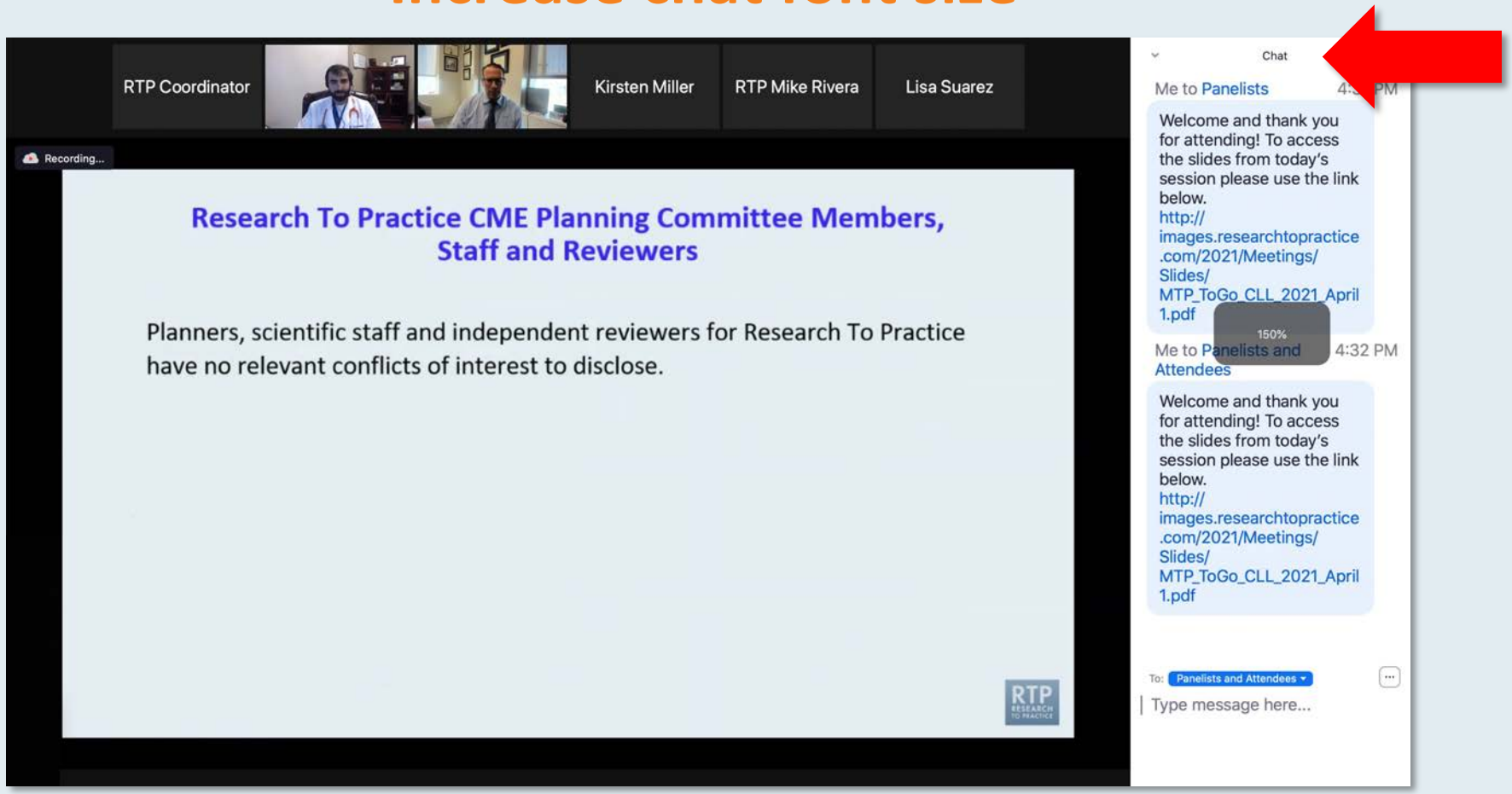

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Key Presentations on Advances in Myeloproliferative Neoplasms from ASH 2021

DR PRITHVIRAJ BOSE

THE UNIVERSITY OF TEXAS
MD ANDERSON CANCER CENTER

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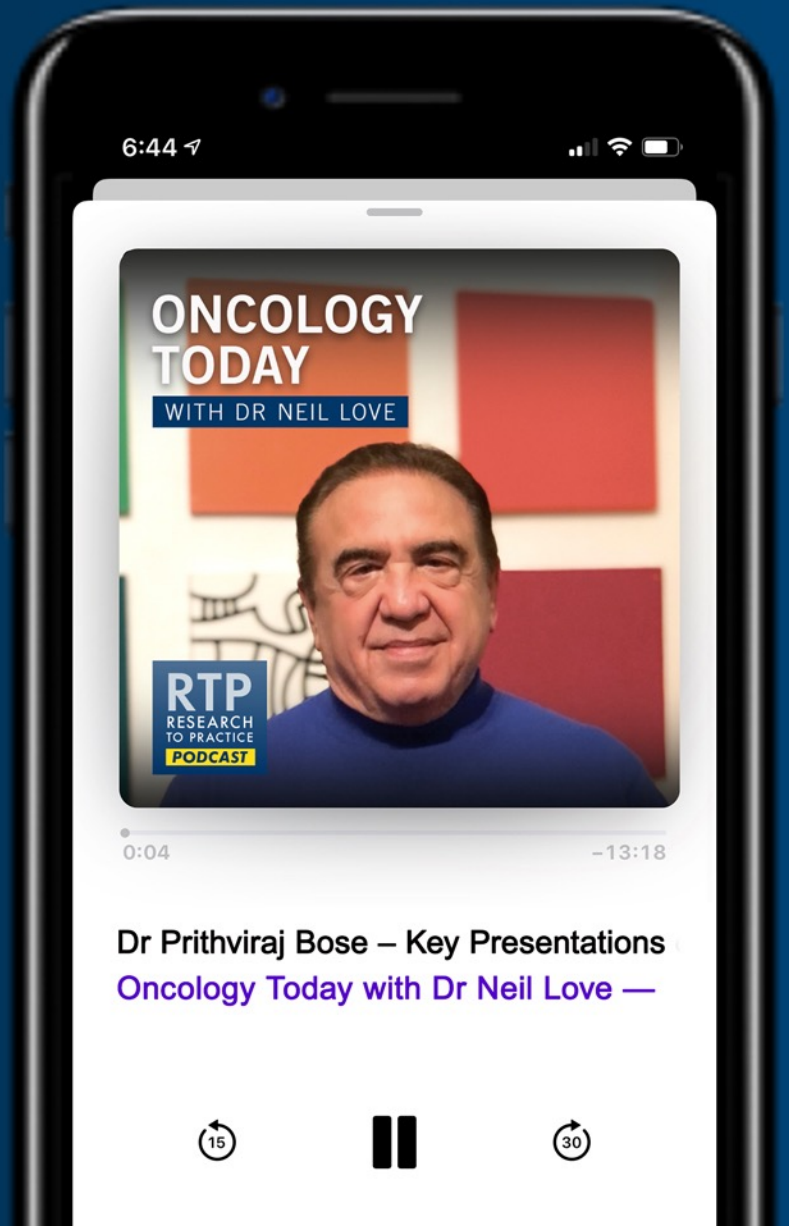
Spotify

Listen on Google Podcasts



Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Tuesday, March 15, 2022
5:00 PM – 6:00 PM ET

Faculty

Sonali M Smith, MD

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 17, 2022
5:00 PM – 6:00 PM ET

Faculty

Peter Hillmen, MB ChB, PhD

Moderator

Neil Love, MD

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Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Ovarian Cancer

Saturday, March 19, 2022

2:30 PM – 4:00 PM ET

Faculty

Mansoor Raza Mirza, MD
Kathleen N Moore, MD, MS
David M O'Malley, MD

Moderator

Robert L Coleman, MD

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TO PRACTICE

Meet The Professor

Current and Future Role of Immunotherapy in the Management of Lung Cancer

Wednesday, March 30, 2022
5:00 PM – 6:00 PM ET

Faculty

Sarah B Goldberg, MD, MPH

Moderator

Neil Love, MD

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RESEARCH
TO PRACTICE

Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 31, 2022
5:00 PM – 6:00 PM ET

Faculty

Kerry Rogers, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Myelodysplastic Syndromes

Tuesday, April 5, 2022
5:00 PM – 6:00 PM ET

Faculty

Rami Komrokji, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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Current and Future Management of Myelofibrosis

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Department of Leukemia
The University of Texas MD Anderson Cancer Center
Houston, Texas

Meet The Professor Program Participating Faculty

Professor Claire Harrison
Professor of Myeloproliferative Neoplasms
and Clinical Director
Guy's and St Thomas' NHS Foundation Trust
London, United Kingdom

Srdan Verstovsek, MD, PhD
Professor of Medicine
Director, Hanns A Pielenz Clinical Research
Center for Myeloproliferative Neoplasms
Department of Leukemia
The University of Texas
MD Anderson Cancer Center
Houston, Texas

John Mascarenhas, MD
Director, Adult Leukemia Program
Professor of Medicine
Tisch Cancer Institute
Icahn School of Medicine at Mount Sinai
New York, New York

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

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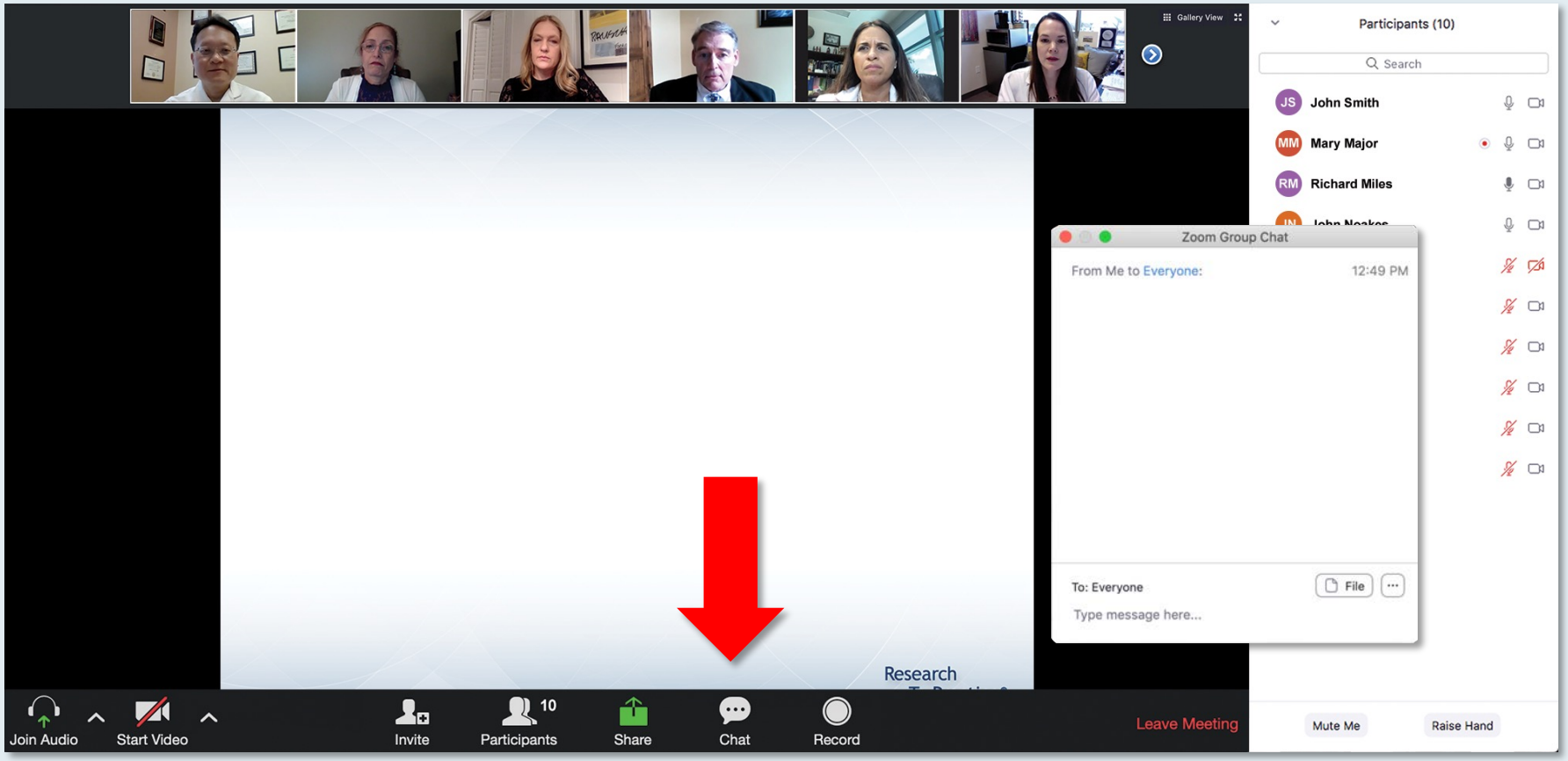
We Encourage Clinicians in Practice to Submit Questions



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THE UNIVERSITY OF TEXAS
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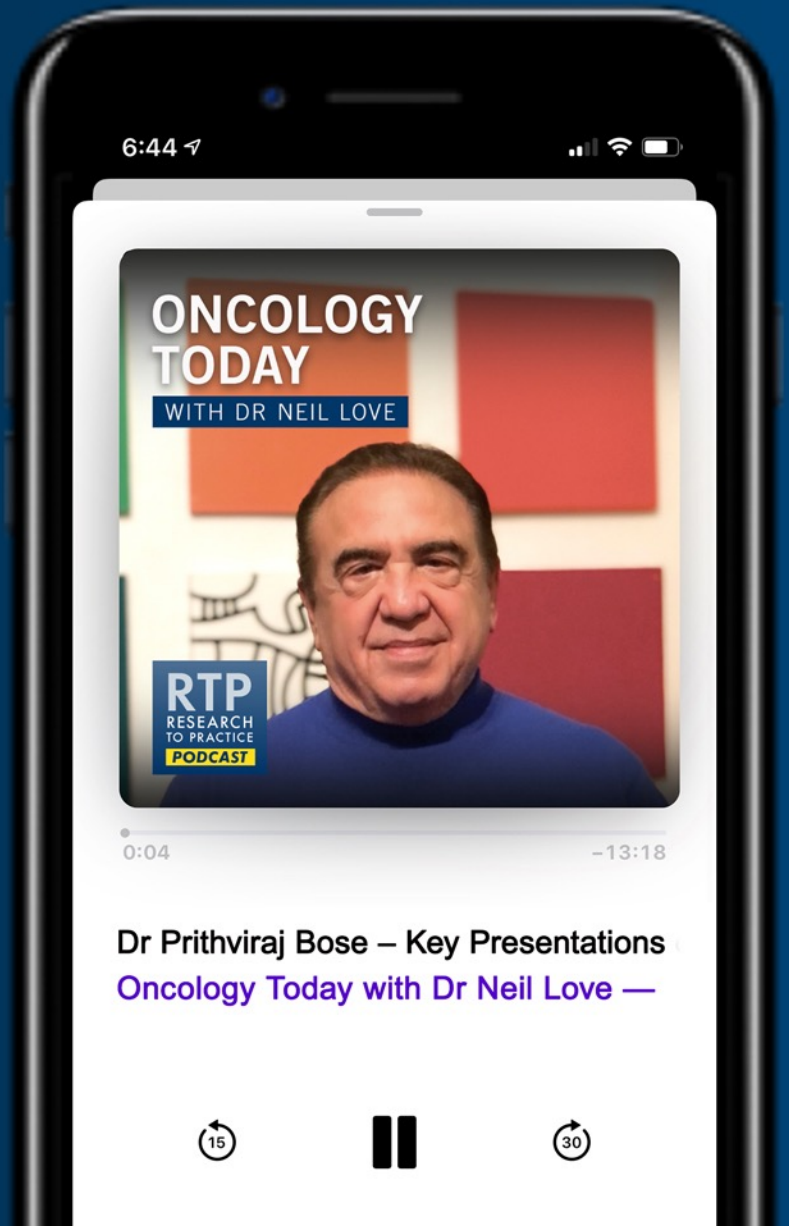

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Dr Verstovsek — Disclosures

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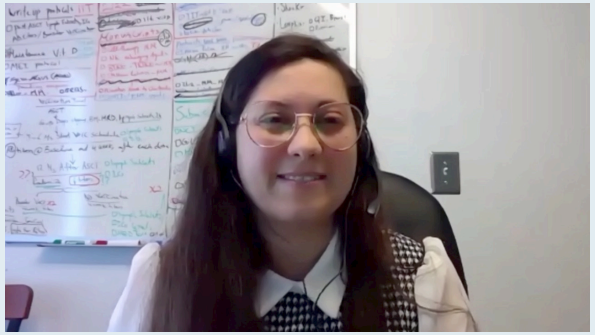
Bhavana (Tina) Bhatnagar, DO
West Virginia University Cancer Institute
Wheeling, West Virginia

Niyati A Nathwani, MD
Carolina Blood and Cancer Care Associates
Charlotte, North Carolina



Amany R Keruakous, MD, MS
Georgia Cancer Center
Augusta University
Augusta, Georgia

Jeanne Palmer, MD
Mayo Clinic, Arizona
Phoenix, Arizona

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Meet The Professor with Dr Verstovsek

Introduction

Module 1: Case Presentations

- Dr Keruakous: A 72-year-old man with JAK2-positive Intermediate-risk MF, a CALR mutation and multiple comorbidities
- Dr Bhatnagar: A 76-year-old woman with JAK2 V617F-positive primary myelofibrosis (MF) treated with ruxolitinib
- Dr Palmer: An 80-year-old woman with primary MF and pancytopenia (Hb 7.2 g/dL, platelets 38,000/uL)
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Module 2: Journal Club with Dr Verstovsek

Module 3: Faculty Survey

Module 4: Appendix of Key Publications

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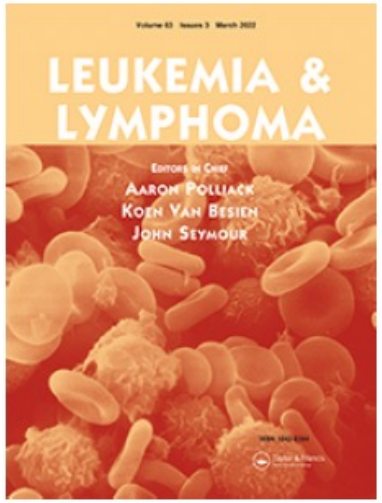
Blood Adv 2021;5(8):2156-64.
REGULAR ARTICLE
blood advances

Single-center experience with venetoclax combinations in patients with newly diagnosed and relapsed AML evolving from MPNs

Lucia Masarova, Courtney D. DiNardo, Prithviraj Bose, Naveen Pemmaraju, Naval G. Daver, Tapan M. Kadia, Helen T. Chifotides, Lingsha Zhou, Gautam Borthakur, Zeev Estrov, Marina Konopleva, and Srdan Verstovsek



Leukemia & Lymphoma

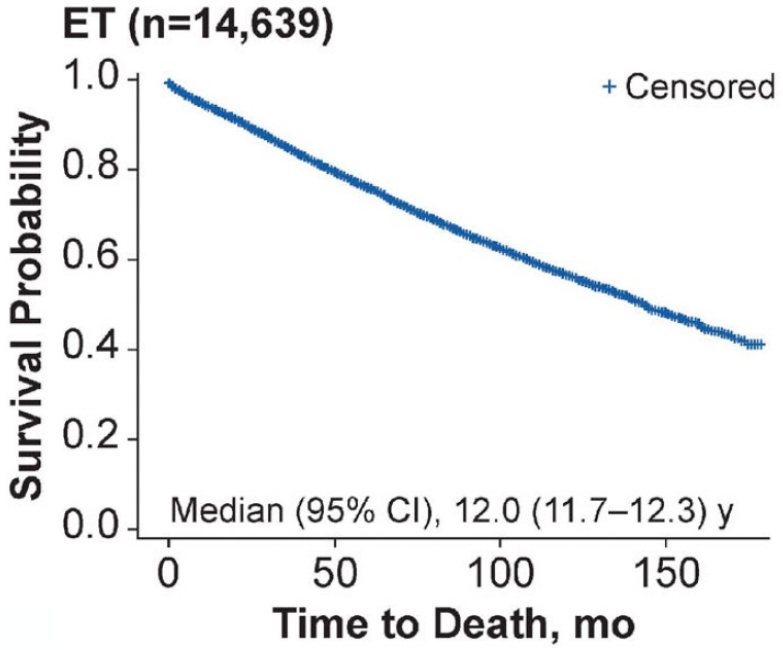
Leuk Lymphoma 2021:1-9

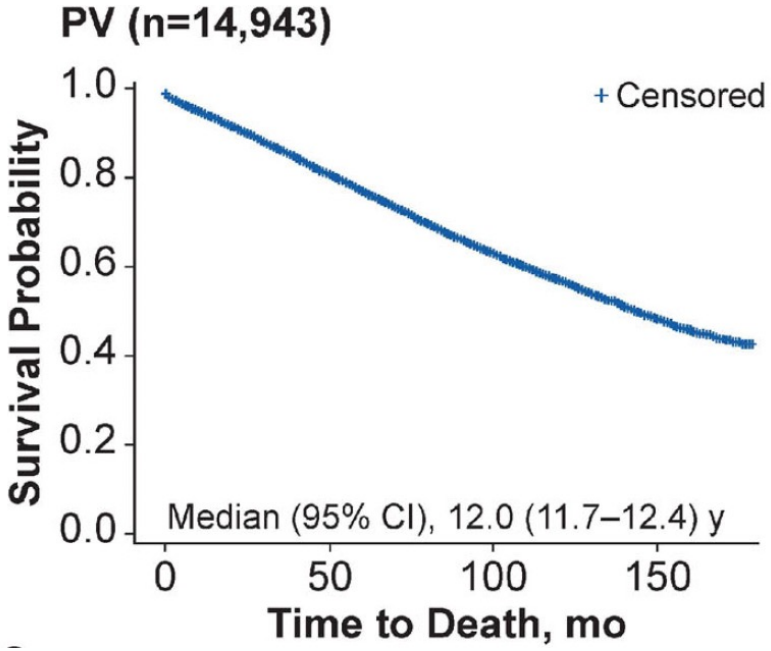
ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ilal20

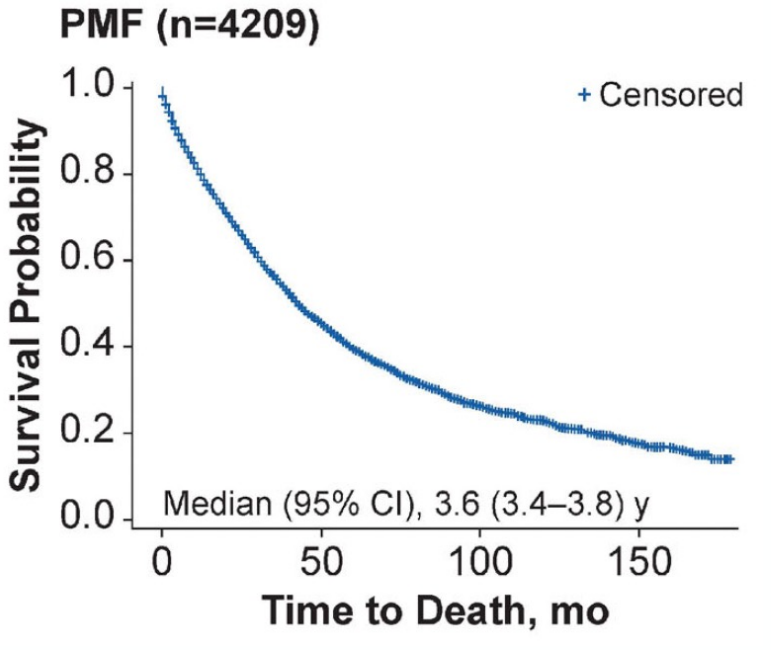
Changes in the incidence and overall survival of patients with myeloproliferative neoplasms between 2002 and 2016 in the United States

Srdan Verstovsek, Jingbo Yu, Robyn M. Scherber, Sumit Verma, Christopher Dieyi, Chien-Cheng Chen & Shreekant Parasuraman

Overall Survival for Essential Thrombocytothemia (ET), Polycythemia Vera (PV) and Primary MF (PMF) in the United States Between 2002 and 2016







Verstovsek S et al. *Leuk Lymphoma* 2021:1-9.

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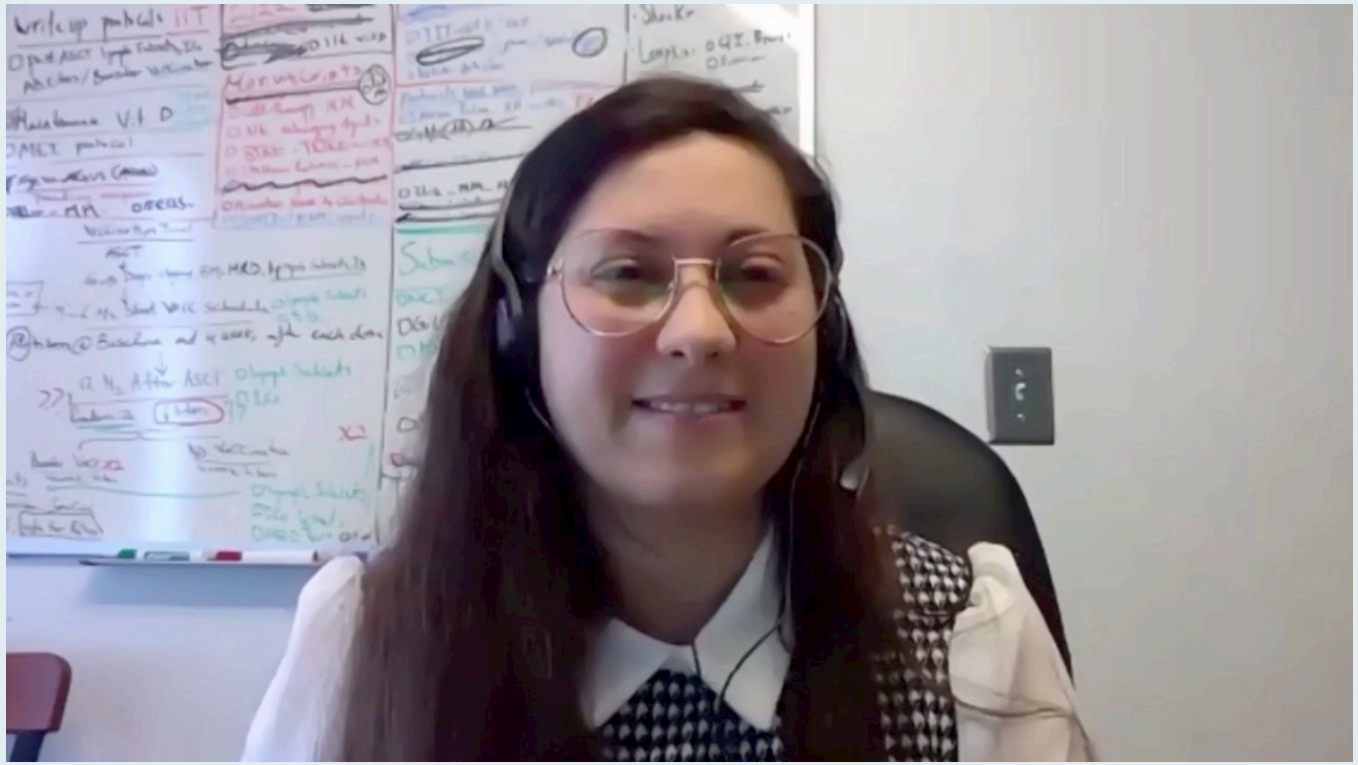

Dr Amany Keruakous (Augusta, Georgia)

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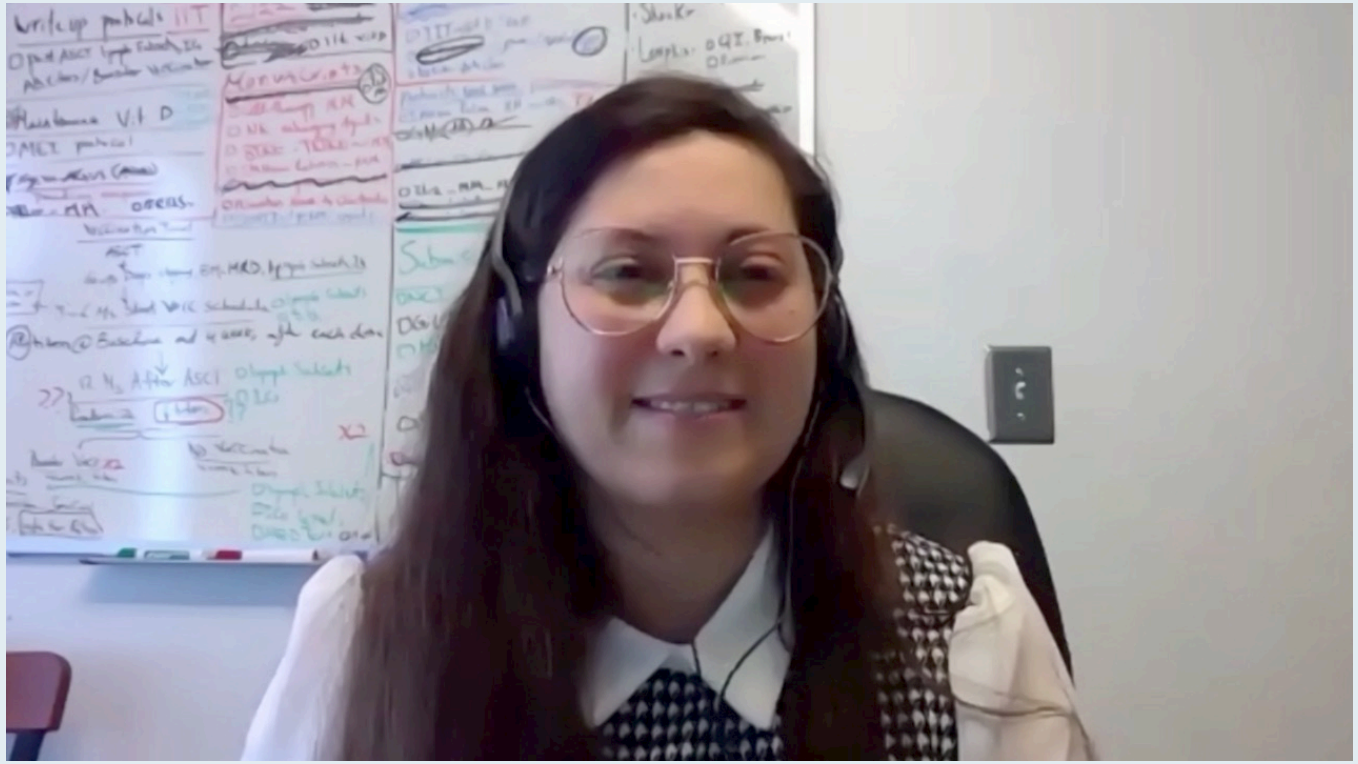
Case Presentation: A 72-year-old man with JAK2-positive Intermediate-risk MF, a CALR mutation and multiple comorbidities (continued)



Dr Amany Keruakous (Augusta, Georgia)

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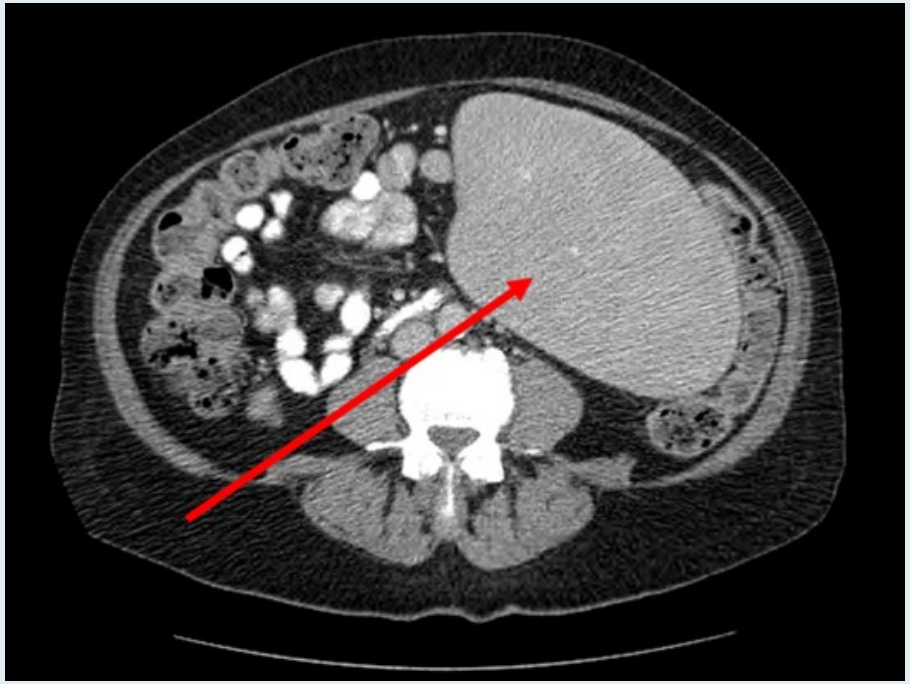
Case Presentation: A 76-year-old woman with JAK2 V617F-positive primary MF treated with ruxolitinib

Dr Tina Bhatnagar (Wheeling, West Virginia)



CT showing splenomegaly

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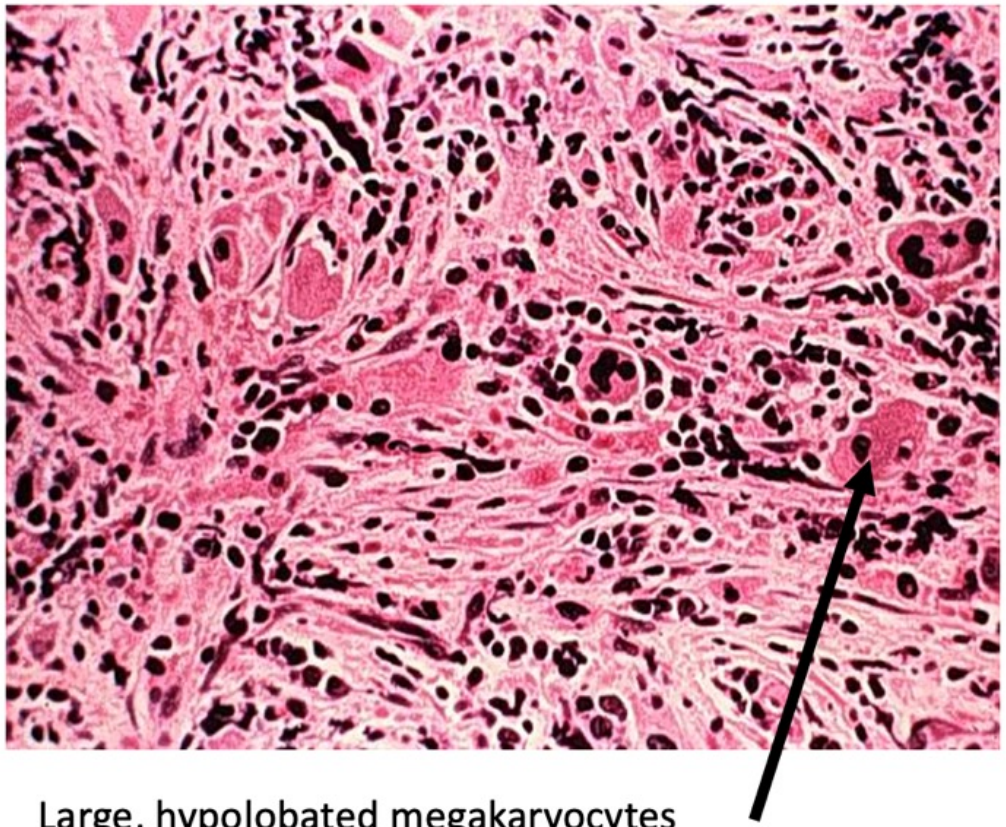
Case Presentation: An 80-year-old woman with primary MF and pancytopenia (Hb 7.2 g/dL, platelets 38,000/uL)

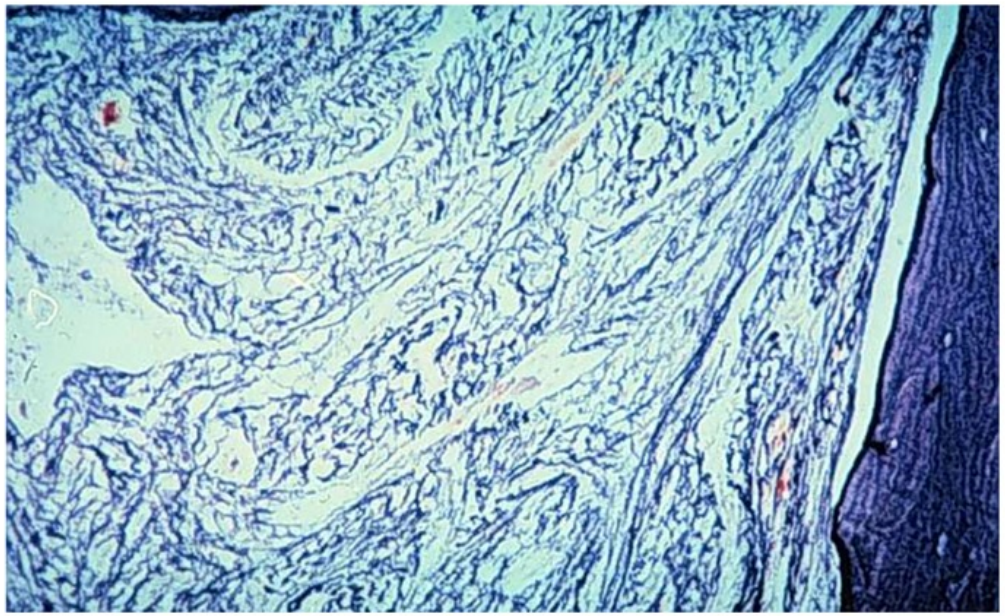
Dr Jeanne Palmer (Phoenix, Arizona)

Case Presentation: An 80-year-old woman with primary MF and pancytopenia (Hb 7.2, platelets 38,000/uL), cont

Dr Jeanne Palmer



Large, hypolobated megakaryocytes



Bone marrow reticulin screen

Case Presentation: A 66-year-old man with JAK2-positive primary MF and pancytopenia who develops recurrent herpes zoster on ruxolitinib

Dr Niyati Nathwani (Charlotte, North Carolina)

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Case Presentation: A 64-year-old man with an unspecified myeloproliferative neoplasm, pancytopenia and a JAK2 mutation

Dr Tina Bhatnagar (Wheeling, West Virginia)

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Selection of patients appropriate for treatment with ruxolitinib

Dr Jeanne Palmer (Phoenix, Arizona)

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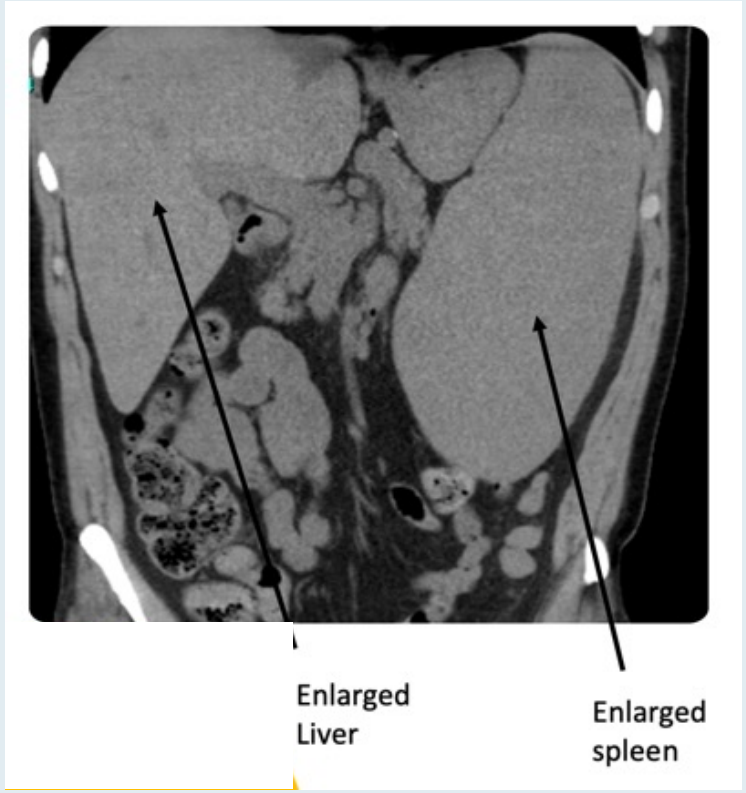
Case Presentation: A 65-year-old man with post-PV MF and ASXL1, SRSF2 mutations



Dr Jeanne Palmer (Phoenix, Arizona)

Case Presentation: A 65-year-old man with post-PCV MF and ASXL1, SRSF2 mutations (continued)

Dr Jeanne Palmer (Phoenix, Arizona)

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Disease Modification in Myelofibrosis: An Elusive Goal?

Pankit Vachhani, MD[1]; Srdan Verstovsek, MD, PhD[2]; and Prithviraj Bose, MD[2]

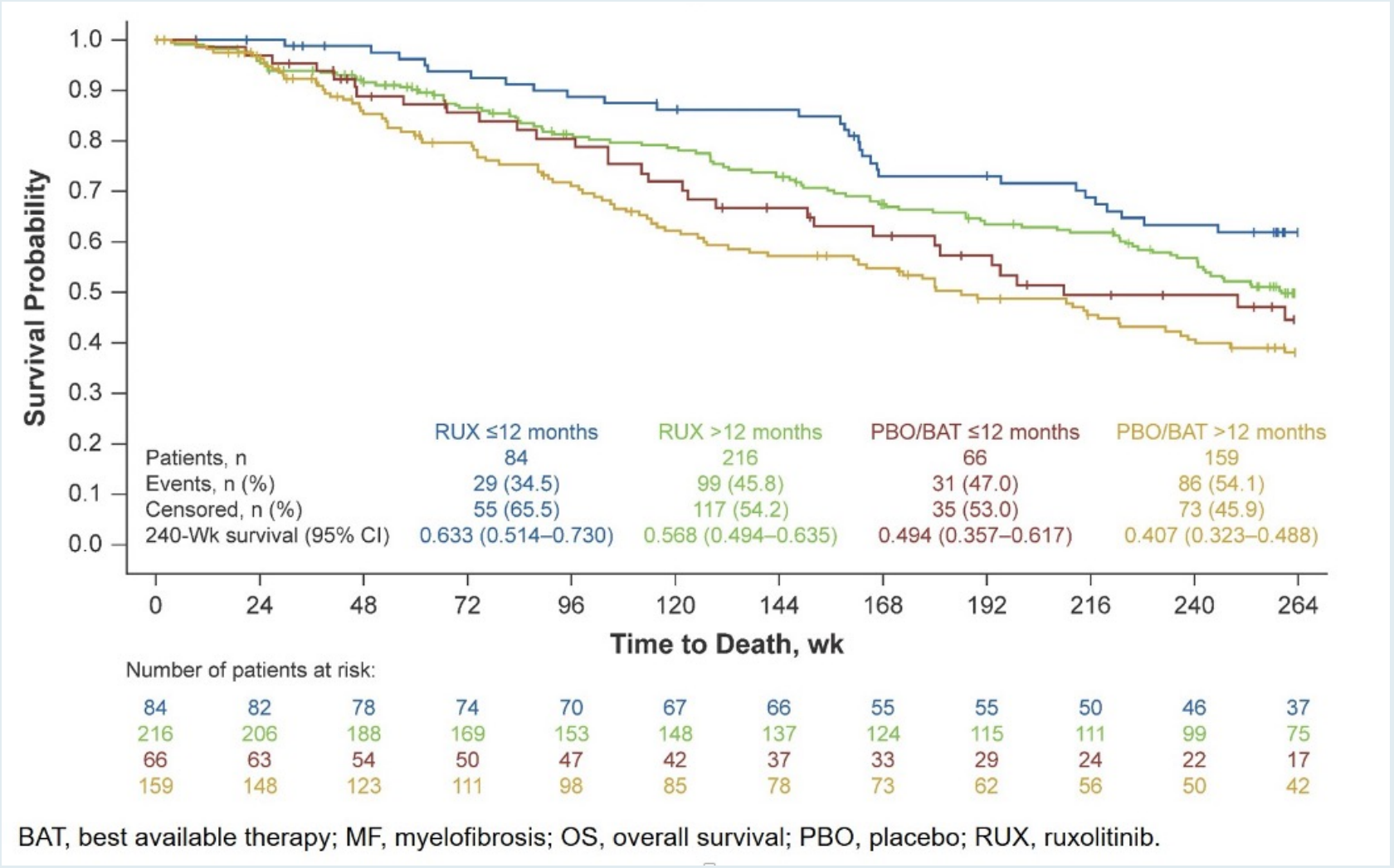
J Clin Oncol 2022;[Online ahead of print].

Does Early Intervention in Myelofibrosis Impact Outcomes? A Pooled Analysis of the Comfort I and II Studies

Verstovsek S et al.

ASH 2021;Abstract 1505.

Overall Survival for Patients with MF, Stratified by Disease Duration Before Ruxolitinib Initiation



BAT, best available therapy; MF, myelofibrosis; OS, overall survival; PBO, placebo; RUX, ruxolitinib.

Verstovsek S et al. ASH 2021;Abstract 1505.

Annals of Hematology (2022) 101:131–137
https://doi.org/10.1007/s00277-021-04682-x

ORIGINAL ARTICLE

Real-world survival of US patients with intermediate- to high-risk myelofibrosis: impact of ruxolitinib approval

Srdan Verstovsek[1] · Shreekant Parasuraman[2] · Jingbo Yu[2] · Anne Shah[3] · Shambhavi Kumar[3] · Ann Xi[3] · Claire Harrison[4]

Acta Haematologica

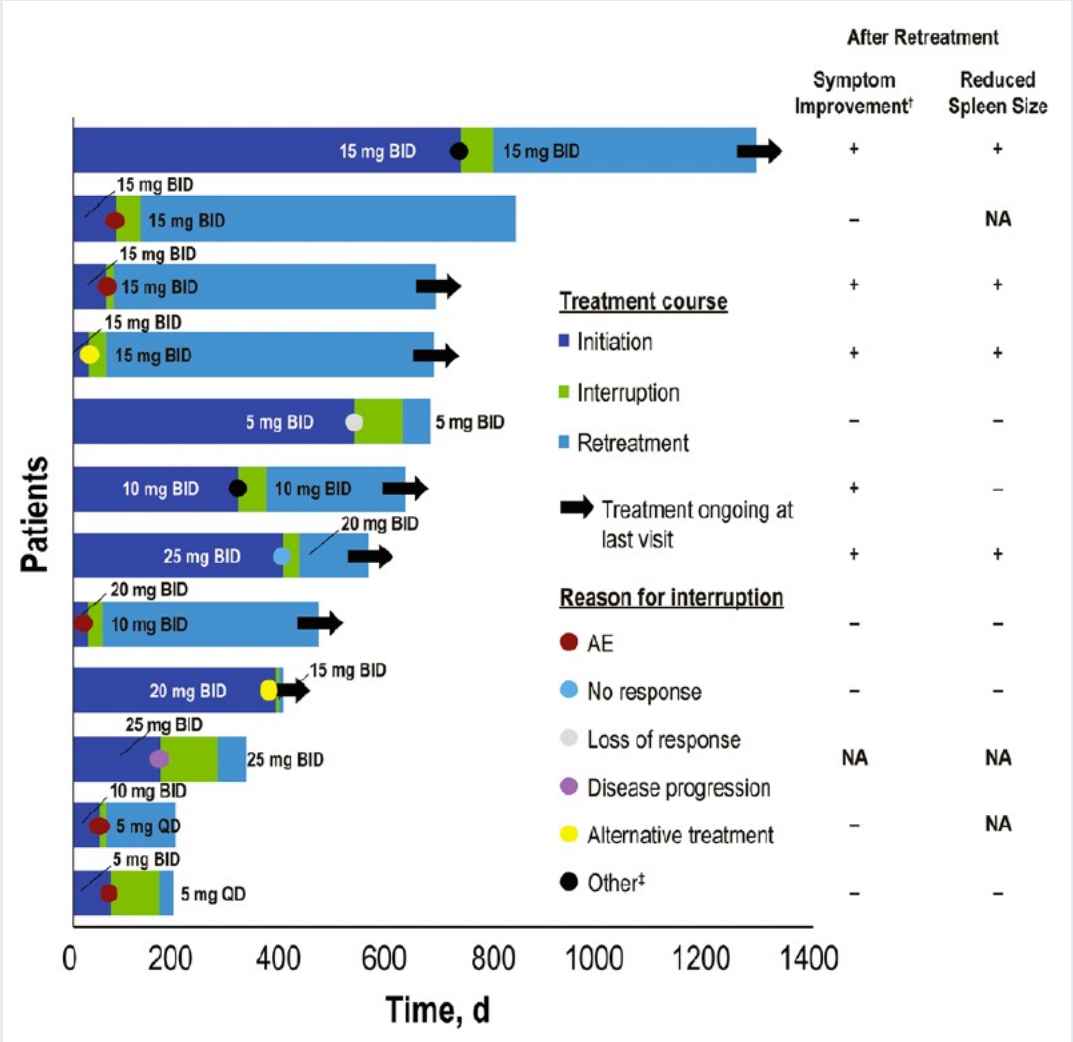
Brief Report

Acta Haematol 2022;10:1-5

Ruxolitinib Re-Treatment in Patients with Myelofibrosis: Real-World Evidence on Patient Characteristics and Outcomes

Aaron T. Gerds[a] Jingbo Yu[b] Robyn M. Scherber[b] Dilan Paranagama[b]
Jonathan K. Kish[c] Jay Visaria[d] Mukul Singhal[d] Srdan Verstovsek[e]
Naveen Pemmaraju[e]

Ruxolitinib Treatment Course Among Individual Patients from the OPEN Analysis Set



Gerds AT et al. *Acta Haematol* 2022;10:1-5.

Verstovsek S et al. Leukemia Research 110 (2021) 106711

Contents lists available at ScienceDirect

Leukemia Research

journal homepage: www.elsevier.com/locate/leukres

Letter to the Editor

Real-world patient characteristics and treatment patterns of ruxolitinib among patients with advanced essential thrombocythemia at community clinical practice

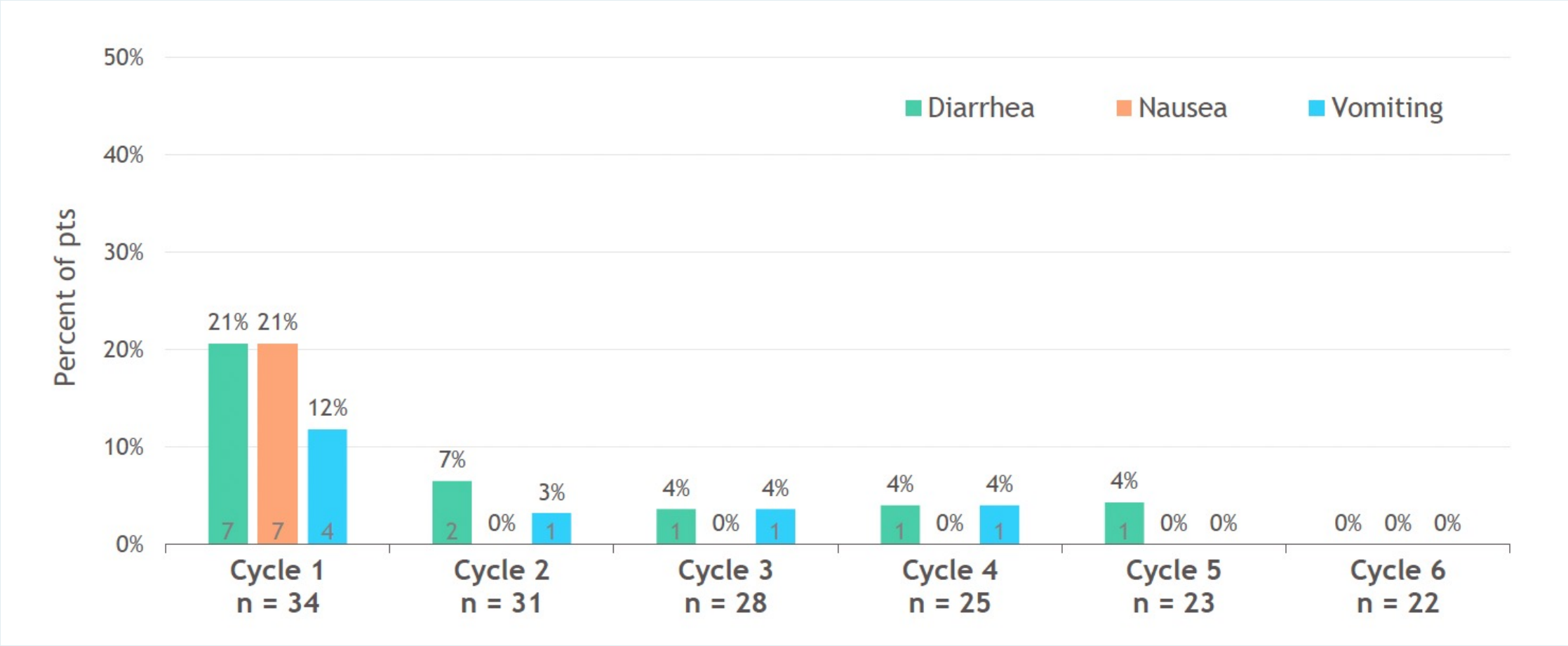
ASH 2021;Abstract 389

Safety and tolerability of fedratinib, an oral inhibitor of Janus kinase 2, in patients with intermediate- or high-risk myelofibrosis previously treated with ruxolitinib: results from the phase 3b FREEDOM trial

Vikas Gupta[1]; Abdulraheem Yacoub[2]; Srdan Verstovsek[3]; Ruben Mesa[4]; Claire Harrison[5]; Giovanni Barosi[6]; Jean-Jacques Kiladjian[7]; H. Joachim Deeg[8]; Salman Fazal[9]; Lynda Foltz[10]; Ryan Mattison[11]; Carole Miller[12]; Vinod Parameswaran[13]; Vishwanath Gharpure[14]; Christopher Hernandez[14]; Jun Zhang[14]; and Moshe Talpaz[15]

[1]Princess Margaret Cancer Centre, Toronto, Canada; [2]University of Kansas Medical Center, Kansas City, KS; [3]The University of Texas MD Anderson Cancer Center, Houston, TX; [4]Mays Cancer Center at UT Health San Antonio MD Anderson, San Antonio, TX; [5]Guy's and St Thomas' Hospital, London, United Kingdom; [6]Fondazione I.R.C.C.S. Policlinico San Matteo, Pavia, Italy; [7]Hôpital Saint-Louis; Université de Paris, Inserm, Paris, France; [8]Fred Hutchinson Cancer Center, Seattle, WA; [9]Allegheny Health Network Cancer Institute, Pittsburgh, PA; [10]St. Paul's Hospital, University of British Columbia, Vancouver, Canada; [11]University of Wisconsin Carbone Comprehensive Cancer Center, Madison, WI; [12]Ascension Saint Agnes Hospital, Baltimore, MD; [13]Avera Cancer Institute, Sioux Falls, SD; [14]Bristol Myers Squibb, Princeton, NJ; [15]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI

Frequency of Nausea, Vomiting and Diarrhea by Treatment Cycle



Gupta V et a. ASH 2021;Abstract 389.

Pacritinib Granted Accelerated Approval for MF with Severe Thrombocytopenia

Press Release: February 28, 2022

"Pacritinib received accelerated approval from the FDA at a twice daily, 200-mg dose for patients with intermediate- or high-risk primary or secondary myelofibrosis who are experiencing severe thrombocytopenia with a platelet count below 50 × 10^9/L. The agency's decision comes from results of the phase 3 PERSIST-2 study (NCT02055781).

Treatment with pacritinib at 200 mg resulted in a reduction in spleen volume of at least 35% for 29% of patients, vs 3% of patients who received the best available therapy, including ruxolitinib (Jakafi). As part of the post-approval plans for pacritinib, the phase 3 PACIFICA trial (NCT03165734) will be completed with results estimated in 2025.

The PERSIST-2 study, which assessed the use of pacritinib compared with best available therapy in patients with myelofibrosis and thrombocytopenia, enrolled 311 patients. Those who enrolled were randomized into 1 of 3 treatment regimens, including pacritinib once daily (n = 104), pacritinib twice daily (n = 107), or a best alternative treatment (n = 100). Best alternative treatments included ruxolitinib (45%), hydroxyurea (19%), and prednisone and/or prednisolone (13%)."

https://www.cancernetwork.com/view/pacritinib-granted-accelerated-approval-for-use-in-myelofibrosis-with-severe-thrombocytopenia?utm_source=sfmc&utm_medium=email&utm_campaign=3.01.22_CN_Breaking_B&eKey=cmthZGVybWFuQHJlc2VhcmNodG9wcmFjdGljZS5jb20=

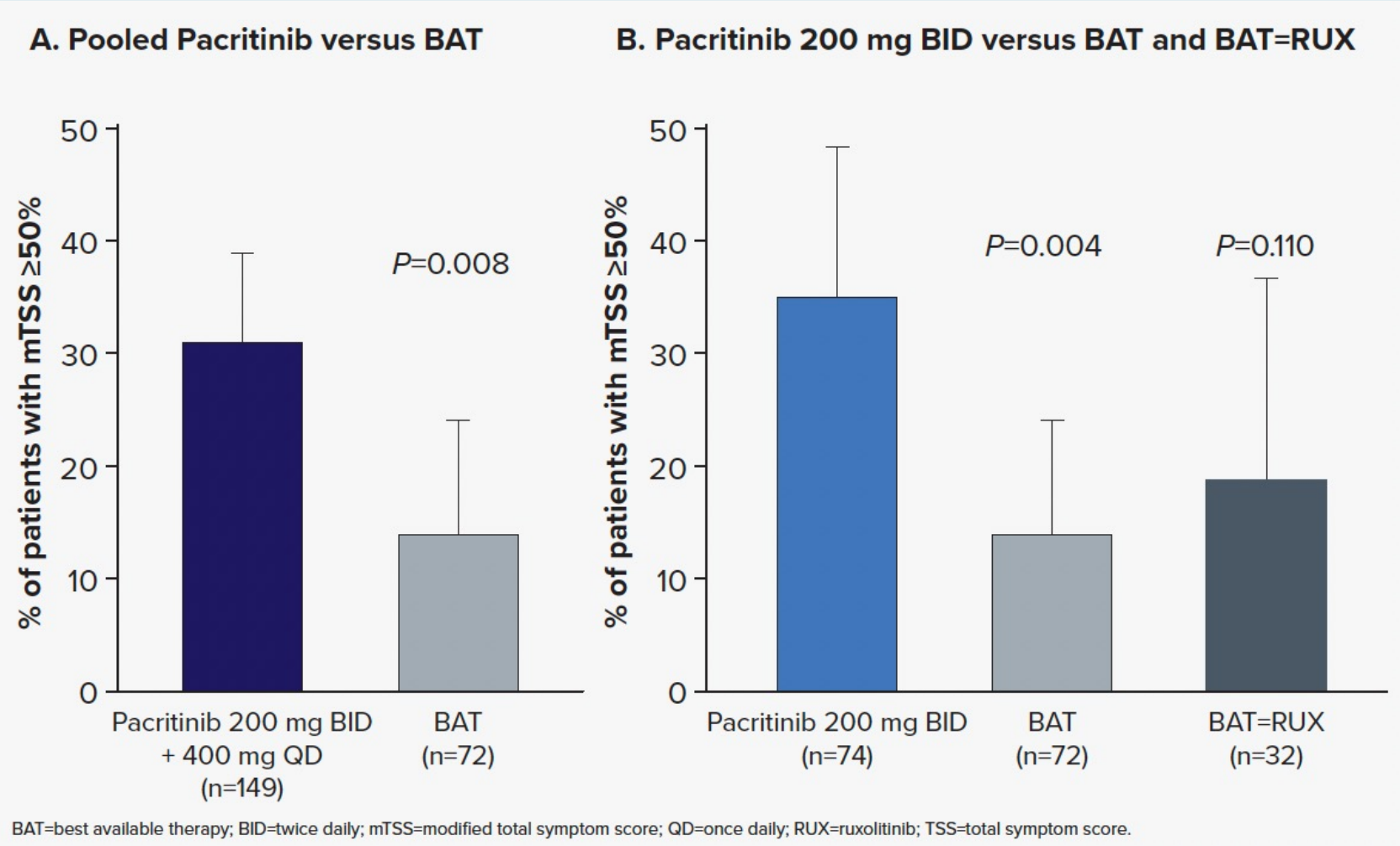
RTP RESEARCH TO PRACTICE

The Impact of Pacritinib on Myelofibrosis Symptoms

Palmer J et al.

ASH 2021;Abstract 3628.

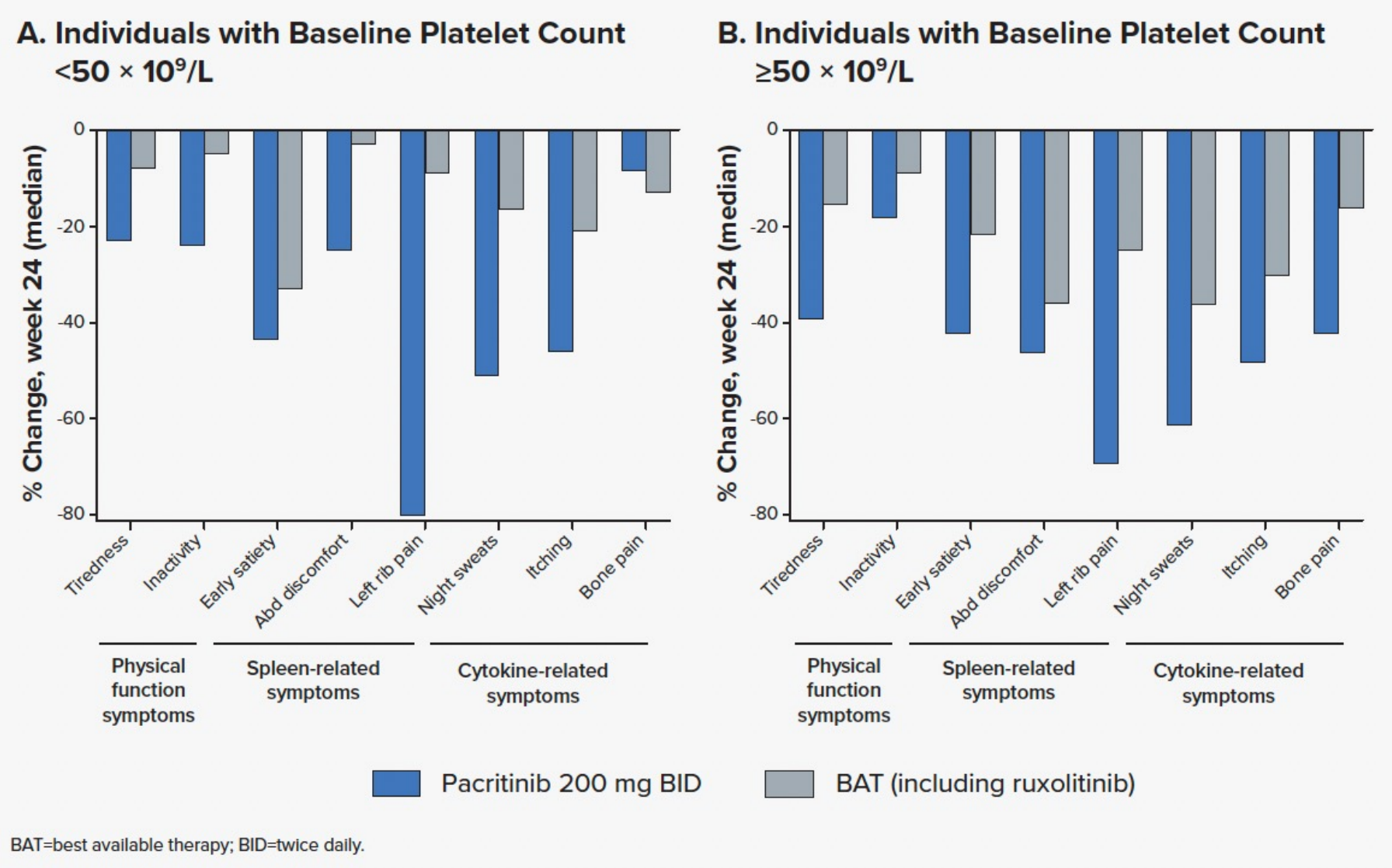
Modified TSS Response Rates (Week 24) in PERSIST-2



BAT=best available therapy; BID=twice daily; mTSS=modified total symptom score; QD=once daily; RUX=ruxolitinib; TSS=total symptom score.

Palmer J et al. ASH 2021;Abstract 3628.

Percent Change in Individual Symptom Scores in PERSIST-2



BAT=best available therapy; BID=twice daily.

Palmer J et al. ASH 2021;Abstract 3628.

haematologica
Journal of The Ferrata Storti Foundation

Haematologica 2021;[Online ahead of print].

Retrospective analysis of pacritinib in patients with myelofibrosis and severe thrombocytopenia

by Srdan Verstovsek, Ruben Mesa, Moshe Talpaz, Jean-Jacques Kiladjian, Claire N. Harrison, Stephen T. Oh, Alessandro M. Vannucchi, Raajit Rampal, Bart L. Scott, Sarah A. Buckley, Adam R. Craig, Karisse Roman-Torres, and John O. Mascarenhas

Baseline Patient and Disease Characteristics in Patients Receiving Pacritinib or Best Available Therapy (BAT)

	Pacritinib (n = 132)	BAT (n = 57)	P-value**
Age, median (range)	69 (50–91)	69 (50–84)	0.95
Male sex, n (%)	80 (61)	28 (49)	0.14
ECOG PS, n* (%)			0.93
0-1	100/132 (76)	42/55 (76)	
2-3	32/132 (24)	13/55 (24)	
Prior JAK2 inhibitor, n (%)	43 (33)	21 (37)	0.57
MF diagnosis, n (%)			0.27
Primary MF	98 (74)	38 (67)	
PPV-MF	20 (15)	8 (14)	
PET-MF	14 (11)	11 (19)	
Time since MF diagnosis (years), median (IQR)	2.0 (0–27)	2.6 (0–14)	0.72
DIPSS risk category, n (%)			0.17
Intermediate-1	26 (20)	5 (9)	
Intermediate-2	63 (48)	30 (53)	
High	43 (33)	22 (39)	
Reticulin and collagen fibrosis staging, n* (%)			0.58
MF 0-1	18/122 (15)	11/52 (21)	
MF 2	38/122 (31)	15/52 (29)	
MF 3	66/122 (54)	26/52 (50)	
Bone marrow cellularity, n* (%)			0.26
<20%	27/110 (25)	18/49 (37)	
20-40%	18/110 (16)	8/49 (16)	
41-100%	65/110 (59)	23/49 (47)	

	Pacritinib (n = 132)	BAT (n = 57)	P-value**
Bone marrow blast category, n* (%)			0.82
≥1%	96/115 (84)	41/50 (82)	
<1%	19/115 (17)	11/50 (18)	
Peripheral blood blasts category, n* (%)			0.18
≥1%	60/118 (51)	31/50 (62)	
<1%	58/118 (49)	19/50 (38)	
Platelet count (10^9/L), median (range)	29 (6–49)	25 (5–49)	0.27
Hemoglobin <10 g/dL, n* (%)	85/132 (64)	35/56 (63)	0.80
RBC transfusion dependence†, n (%)			0.66
Dependent	38 (29)	20 (35)	
Independent	61 (46)	23 (40)	
Indeterminate	33 (25)	14 (25)	
Spleen volume at baseline (cm^3)‡, median (IQR)	2566 (1633–3680)	2466 (1786–3727)	0.87
Modified TSS score at baseline‡, median (IQR)	17 (12–29)	17 (12–27)	0.94
Study enrollment, n (%)			0.98
PERSIST-1	35 (27)	15 (26)	
PERSIST-2	97 (73)	42 (74)	

Verstovsek S et al. *Haematologica* 2021;[Online ahead of print].

SVR and Modified TSS Response Rates by Subgroup of Patients Randomly Assigned to Pacritinib versus BAT

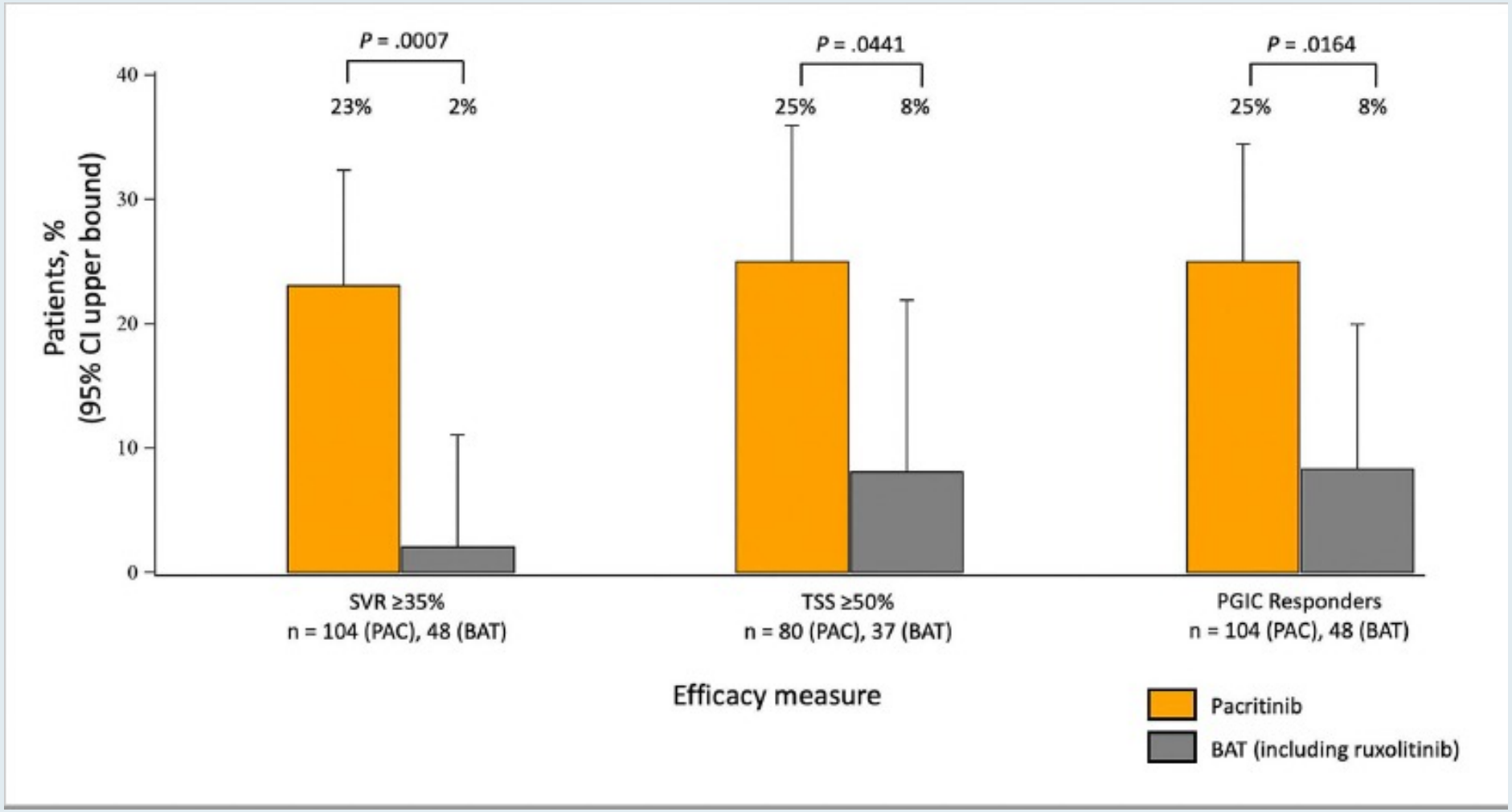
Response rate at week 24	Pacritinib	BAT	P-value*
Patients with ≥35% spleen volume reduction, % (n/N)			
Prior JAK2 inhibitor exposure			0.07
Yes	17.9 (5/28)	7.7 (1/13)	
No	25.0 (19/76)	0 (0/35)	
MF diagnosis			0.52
Primary	24.0 (18/75)	3.1 (1/32)	
Secondary	20.7 (6/29)	0 (0/16)	
Patients with ≥50% reduction in modified TSS, % (n/N)			
Prior JAK2 inhibitors			0.14
Yes	17.9 (5/28)	15.4 (2/13)	
No	28.8 (15/52)	4.2 (1/24)	
MF diagnosis			0.43
Primary	30.4 (17/56)	12.0 (3/25)	
Secondary	12.5 (3/24)	0 (0/12)	
Patients with "much" or "very much" improved PGIC scores, % (n/N)			
Prior JAK2 inhibitors			0.08
Yes	14.3 (4/28)	15.4 (2/13)	
No	28.9 (22/76)	5.7 (2/35)	
MF diagnosis			0.45
Primary	30.7 (23/75)	12.5 (4/32)	
Secondary	10.3 (3/29)	0 (0/16)	

BAT, best available therapy; JAK2, Janus kinase 2; MF, myelofibrosis; PGIC, Patient Global Impression of Change; SVR, spleen volume reduction; TSS, Total Symptom Score.

* Breslow and Day homogeneity test

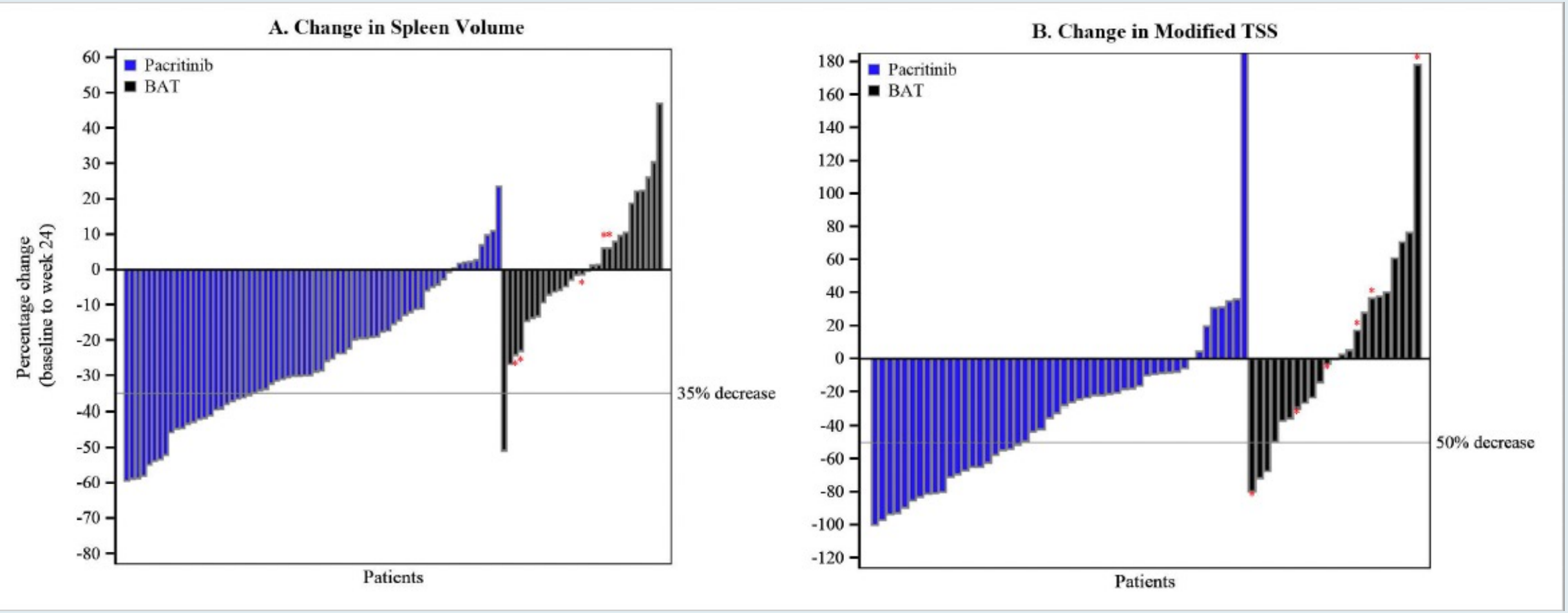
Verstovsek S et al. *Haematologica* 2021;[Online ahead of print].

Efficacy of Pacritinib versus BAT Based on 24-Week Response Rates for Patients with Severe Thrombocytopenia



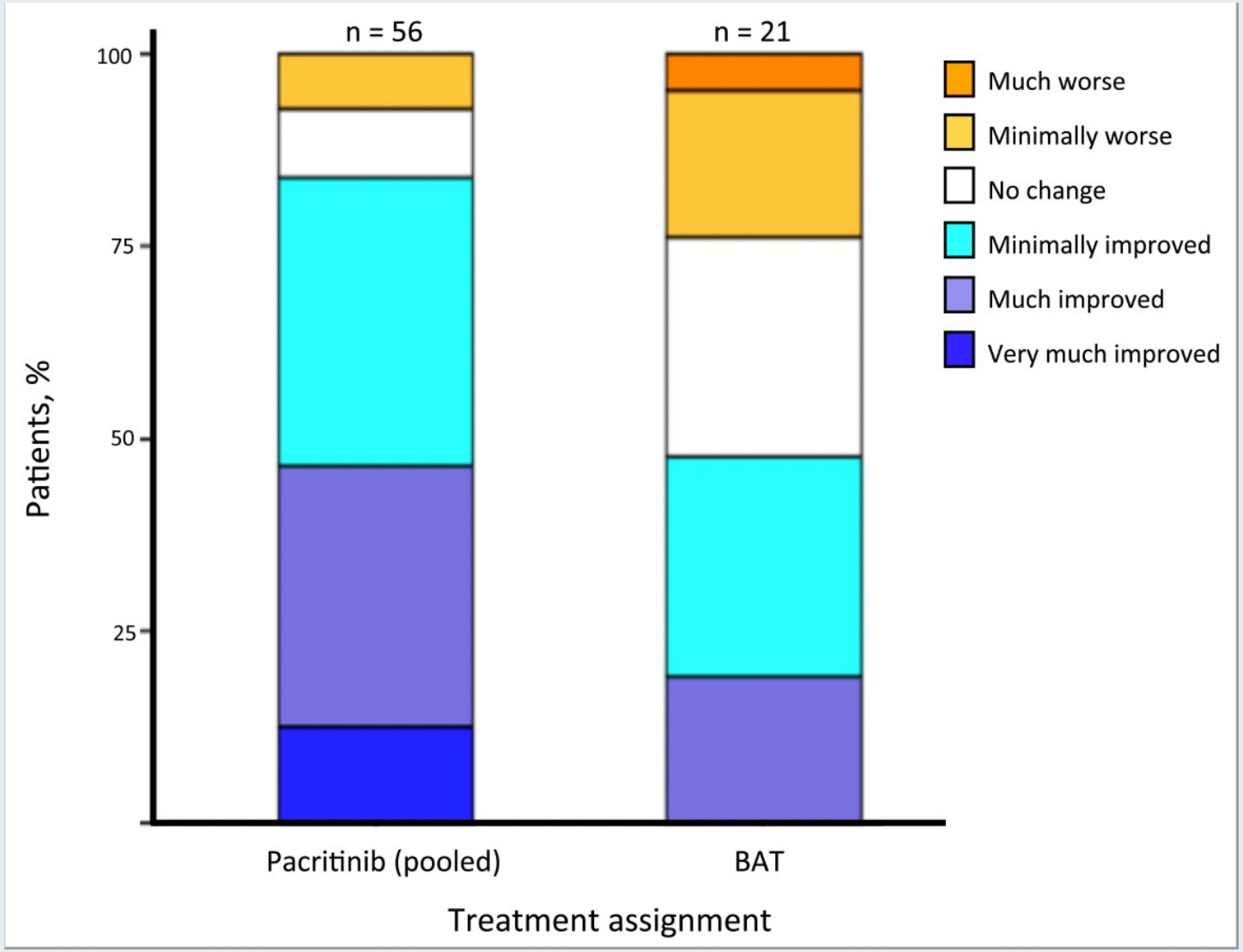
Verstovsek S et al. *Haematologica* 2021;[Online ahead of print].

Waterfall Plots of Percent Change from Baseline



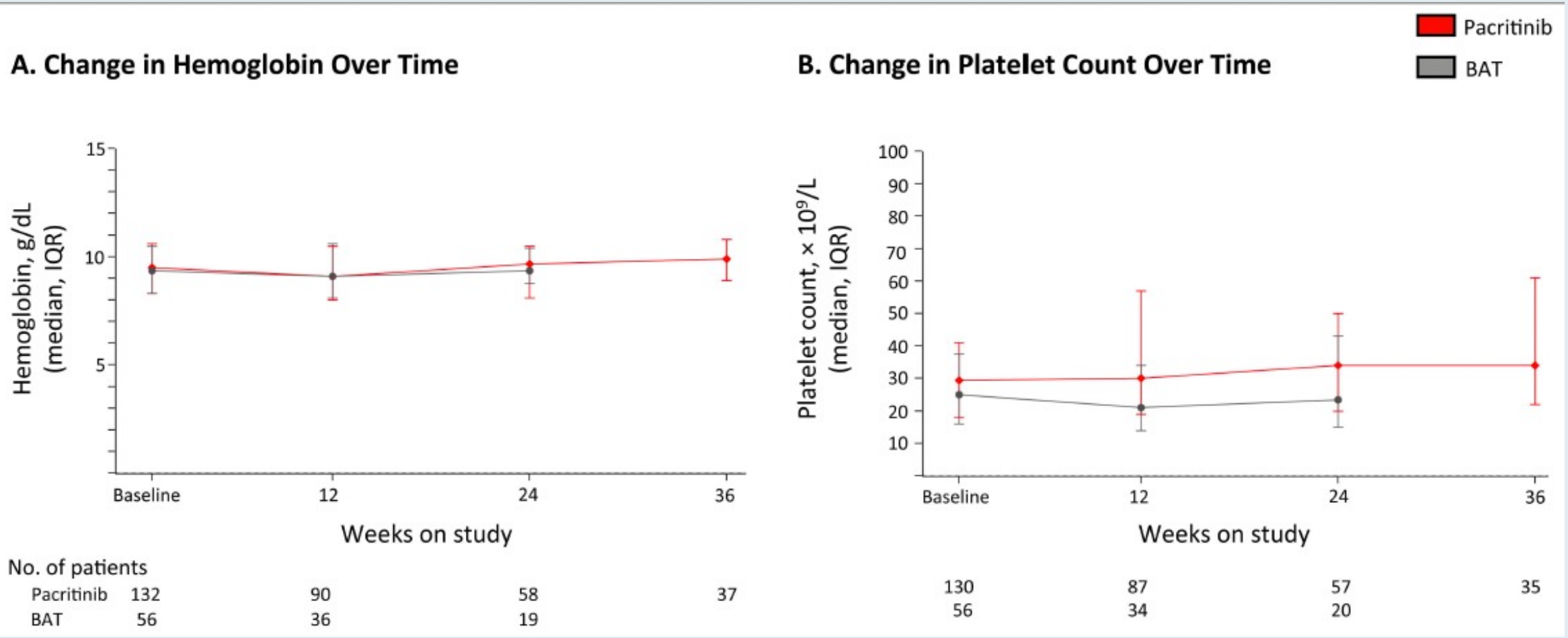
Verstovsek S et al. *Haematologica* 2021;[Online ahead of print].

Self-Reported Symptoms by Treatment Group of Patients Who Completed the Patient Global Impression of Change at Week 24



Verstovsek S et al. *Haematologica* 2021;[Online ahead of print].

Median Hemoglobin and Platelet Count Over Time Through Week 24



Verstovsek S et al. *Haematologica* 2021;[Online ahead of print].

Review Article

Clin Lymphoma Myeloma Leuk 2021;[Online ahead of print].

SOHO State of the Art Updates and Next Questions: Novel Therapies in Development for Myelofibrosis

Helen T. Chifotides, Prithviraj Bose, Lucia Masarova, Naveen Pemmaraju, Srdan Verstovsek

Clin Lymphoma Myeloma Leuk 2021;21(10):641-9.

Review Article

SOHO State of the Art Updates and Next Questions: Identifying and Treating "Progression" in Myelofibrosis

Prithviraj Bose, Srdan Verstovsek

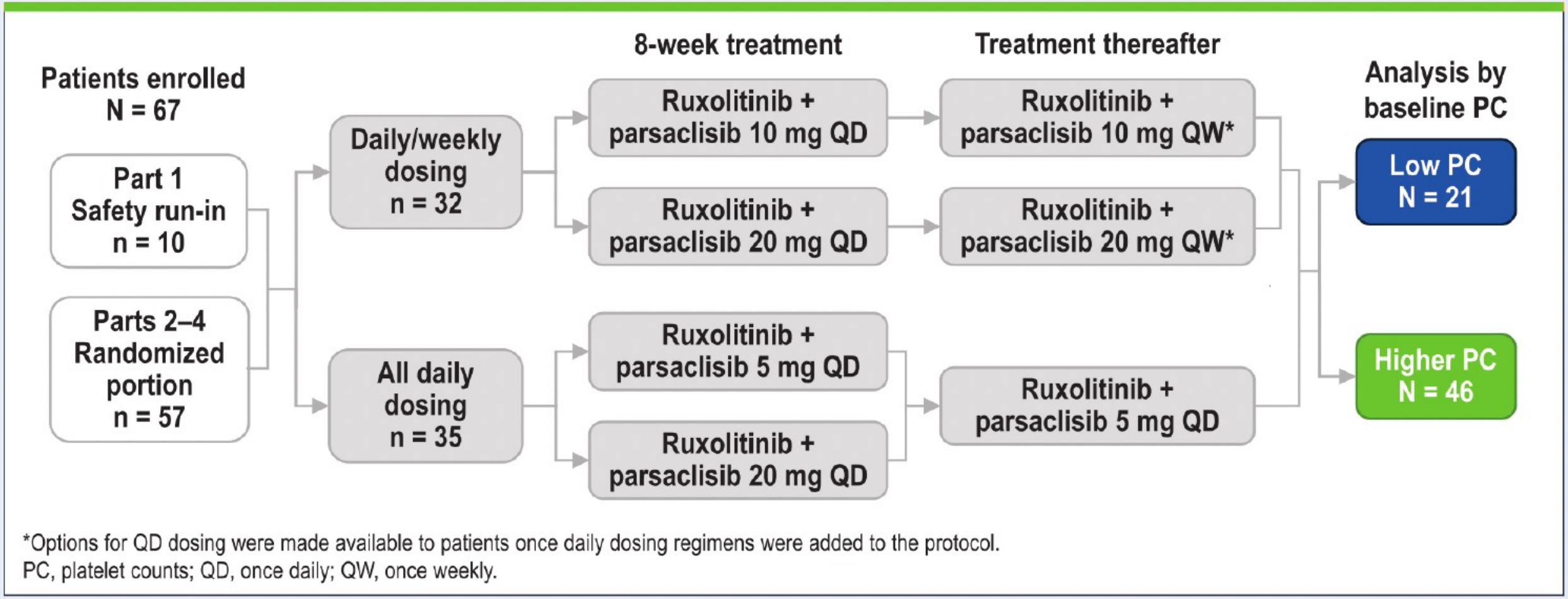
Subgroup Analysis From a Phase 2 Study of the Efficacy and Safety of Parsaclisib, a Selective PI3Kδ Inhibitor, in Combination With Ruxolitinib in Patients With Myelofibrosis

Abdulraheem Yacoub,[1] Uma Borate,[2] Raajit Rampal,[3] Haris Ali,[4] Eunice Wang,[5] Aaron Gerds,[6] Gabriela Hobbs,[7] Marina Kremyanskaya,[8] Elliott Winton,[9] Casey O'Connell,[10] Swati Goel,[11] Stephen Oh,[12] Gary Schiller,[13] Albert Assad,[14] Sue Erickson-Viitanen,[14] Feng Zhou,[14] Naval Daver[15]

[1]University of Kansas Cancer Center, Westwood, KS, USA; [2]Oregon Health & Science University, Portland, OR, USA; [3]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]City of Hope National Medical Center, Duarte, CA, USA; [5]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [6]Cleveland Clinic, Cleveland, OH, USA; [7]Massachusetts General Hospital, Boston, MA, USA; [8]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [9]Emory University, Atlanta, GA, USA; [10]University of Southern California, Los Angeles, CA, USA; [11]Montefiore Medical Center, Bronx, NY, USA; [12]Washington University School of Medicine, St. Louis, MO, USA; [13]David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA; [14]Incyte Corporation, Wilmington, DE, USA; [15]University of Texas MD Anderson Cancer Center, Houston, TX, USA

ASH 2021;Abstract 3647.

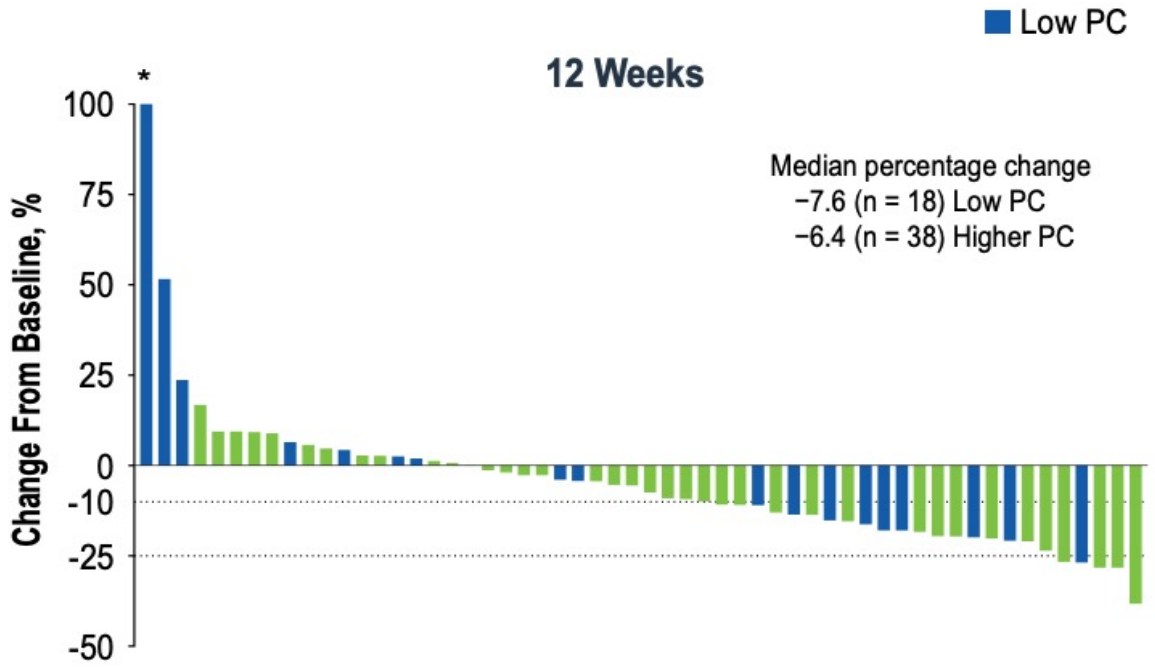
Phase II INCB 50465-201 Study of Adding Parsaclisib to Ruxolitinib

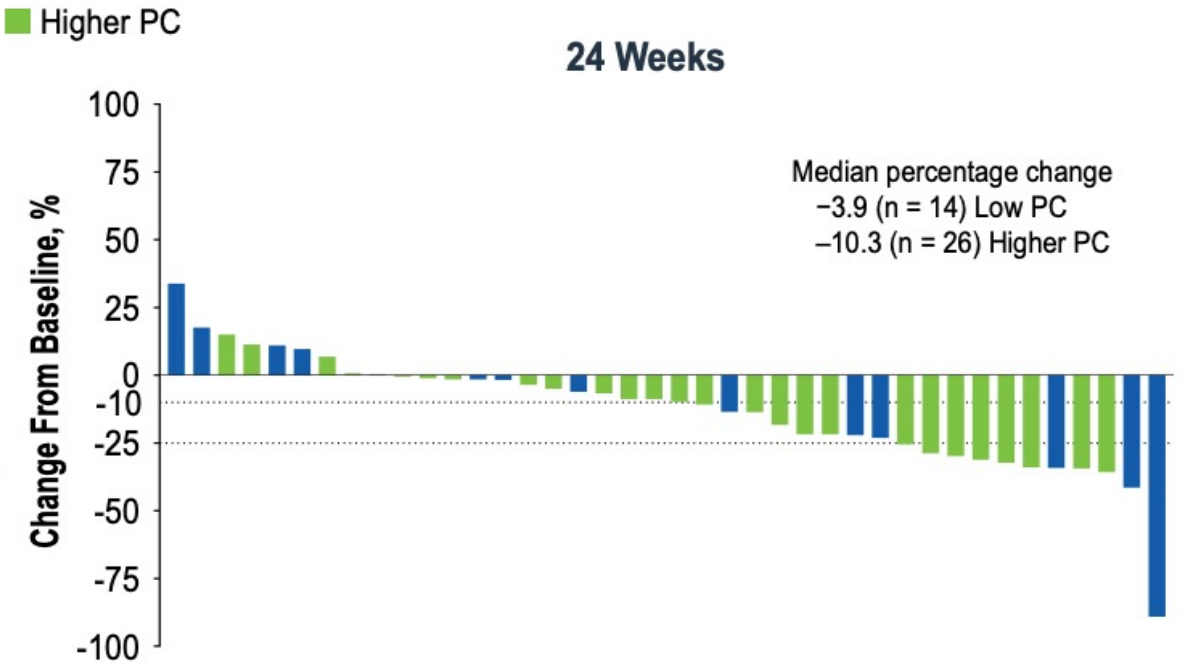


*Options for QD dosing were made available to patients once daily dosing regimens were added to the protocol.
PC, platelet counts; QD, once daily; QW, once weekly.

Yacoub A et al. ASH 2021;Abstract 3647.

Phase II INCB 50465-201: Percent Change in Spleen Volume



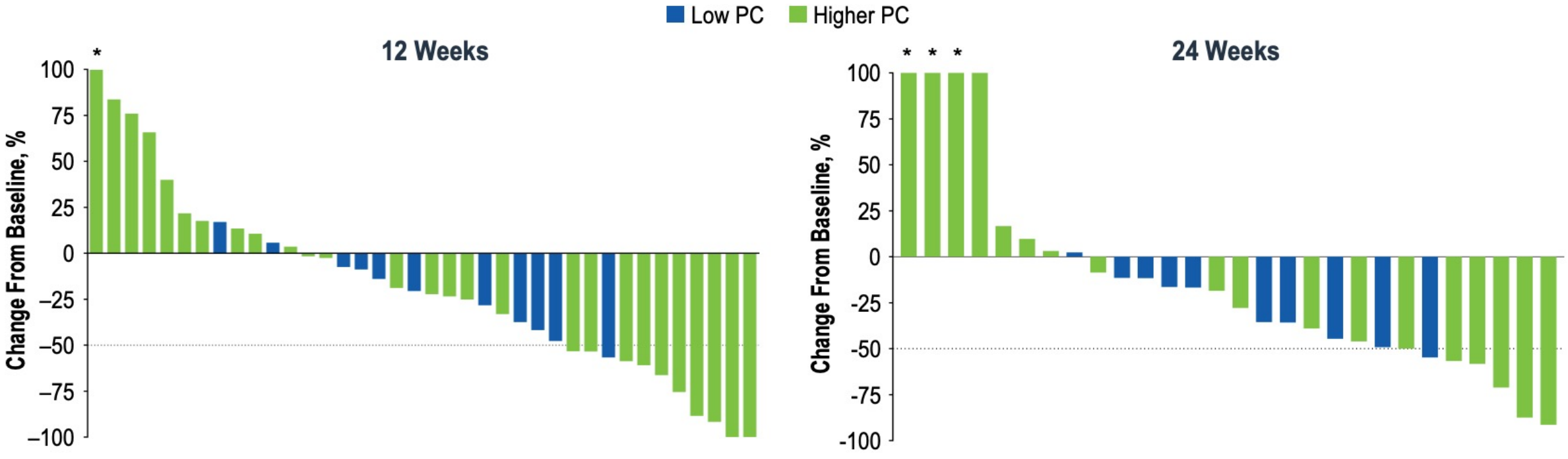


Response Category, n (%)	Low PC	Higher PC
Week 12	n = 18	n = 38
≥10% reduction	9 (50)	15 (39)
≥25% reduction	1 (6)	4 (11)
≥35% reduction	0	1 (3)

Response Category, n (%)	Low PC	Higher PC
Week 24	n = 17	n = 35
≥10% reduction	6 (35)	13 (37)
≥25% reduction	3 (18)	8 (23)
≥35% reduction	2 (12)	1 (3)

Yacoub A et al. ASH 2021;Abstract 3647.

Phase II INCB 50465-201: Percent Change in MFSAF-TSS

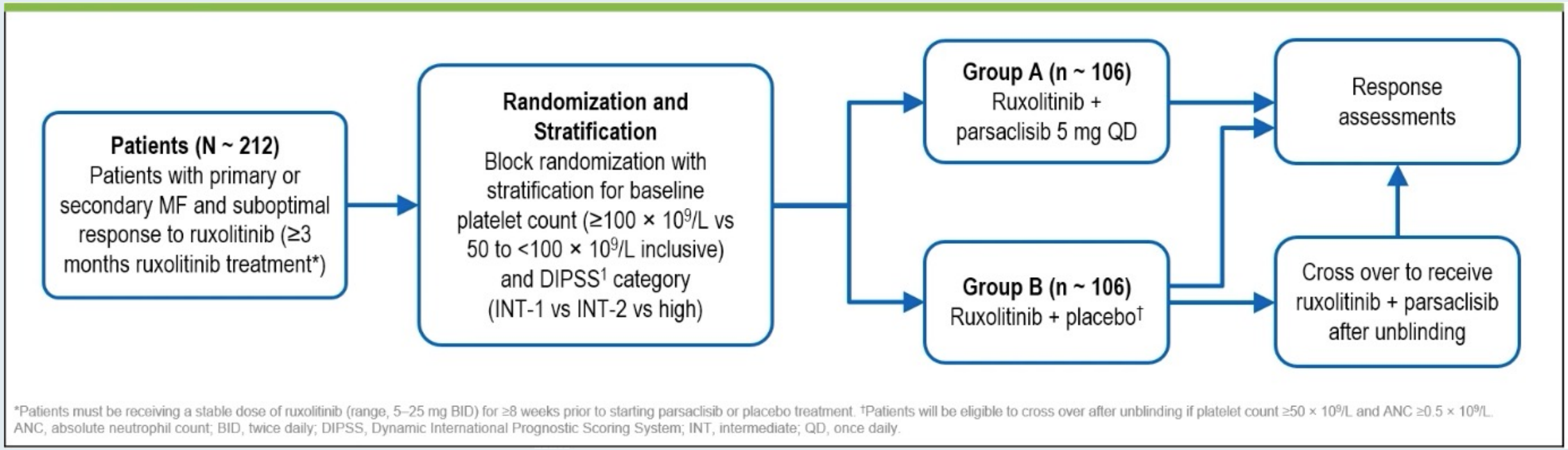


Median change in MFSAF-TSS at 12 Weeks	n	% Change (Range)
Low PC	11	−20.5 (−56.6 to 17.1)
Higher PC	27	−22.2 (−100.0 to 500.0)

Median change in MFSAF-TSS at 24 Weeks	n	% Change (Range)
Low PC	10	−26.1 (−54.7 to 2.4)
Higher PC	18	−23.1 (−91.3 to 222.5)

Yacoub A et al. ASH 2021;Abstract 3647.

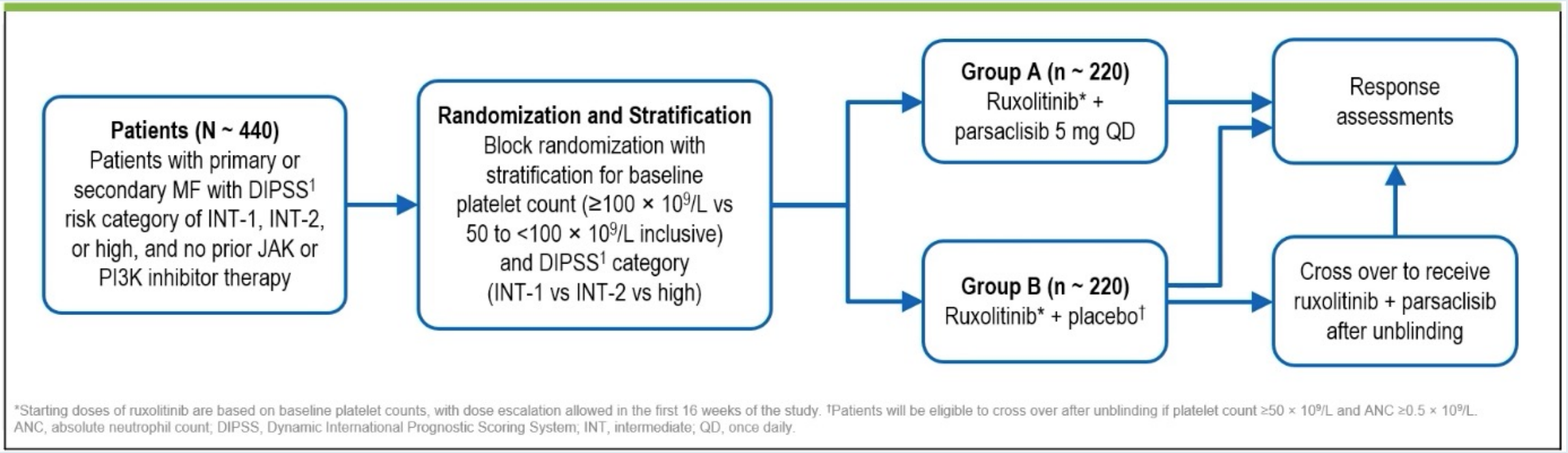
LIMBER-304 Phase III Study Design



*Patients must be receiving a stable dose of ruxolitinib (range, 5–25 mg BID) for ≥8 weeks prior to starting parsaclisib or placebo treatment. †Patients will be eligible to cross over after unblinding if platelet count ≥50 × 10^9/L and ANC ≥0.5 × 10^9/L.
ANC, absolute neutrophil count; BID, twice daily; DIPSS, Dynamic International Prognostic Scoring System; INT, intermediate; QD, once daily.

Yacoub A et al. ASH 2021;Abstract 1502.

LIMBER-313 Phase III First-Line Study Design



*Starting doses of ruxolitinib are based on baseline platelet counts, with dose escalation allowed in the first 16 weeks of the study. †Patients will be eligible to cross over after unblinding if platelet count ≥50 × 10⁹/L and ANC ≥0.5 × 10⁹/L.
ANC, absolute neutrophil count; DIPSS, Dynamic International Prognostic Scoring System; INT, intermediate; QD, once daily.

Yacoub A et al. ASH 2021;Abstract 2579.

Leukemia

www.nature.com/leu

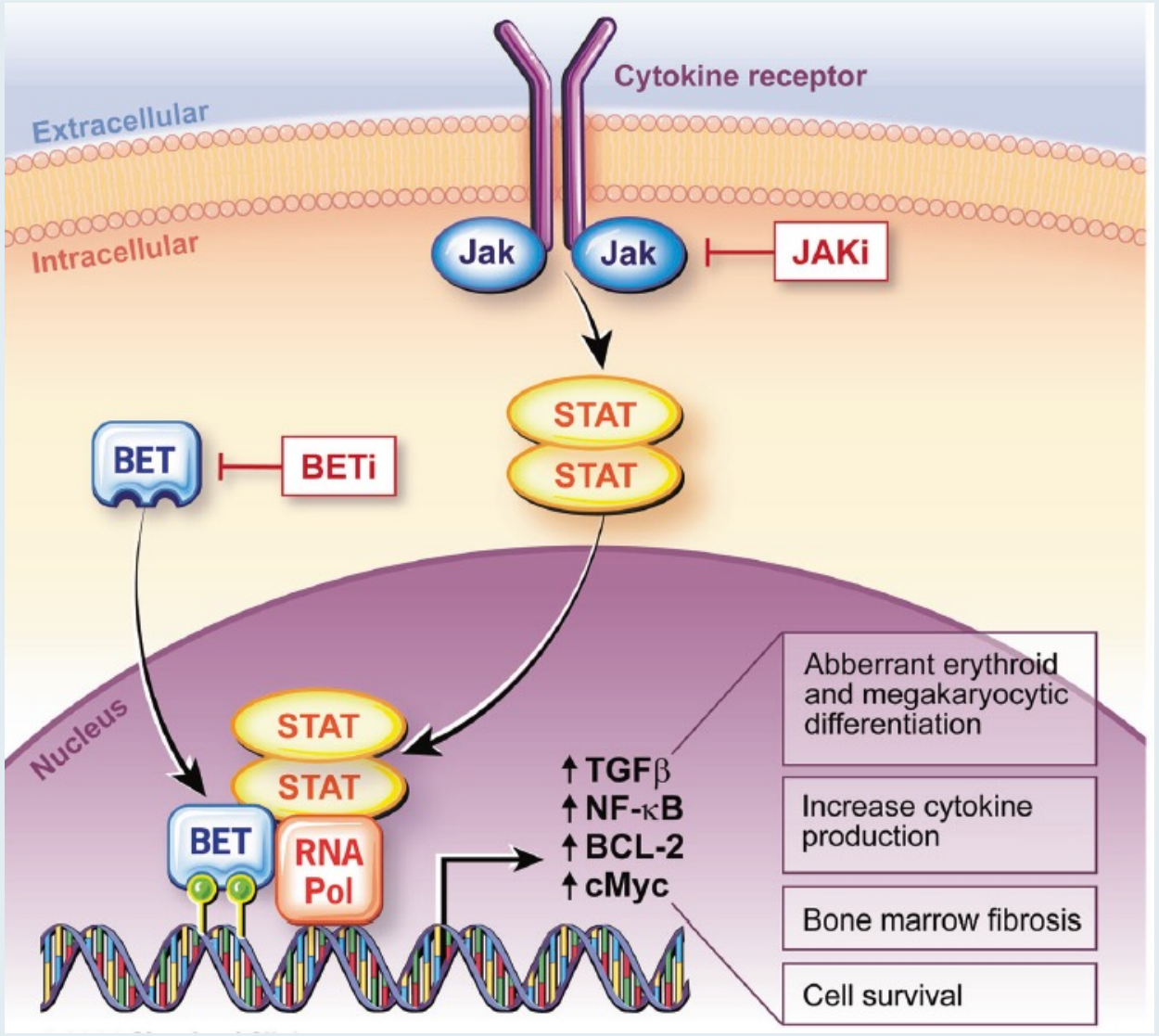
PERSPECTIVE OPEN

Paradigm shift: combination BET and JAK inhibition in myelofibrosis

John Mascarenhas[1]✉, Aaron Gerds[2] and Srdan Verstovsek[3]

Leukemia (2021) 35:3361–3363; https://doi.org/10.1038/s41375-021-01405-z

Mechanism of Action of BET Inhibitor Pelabresib



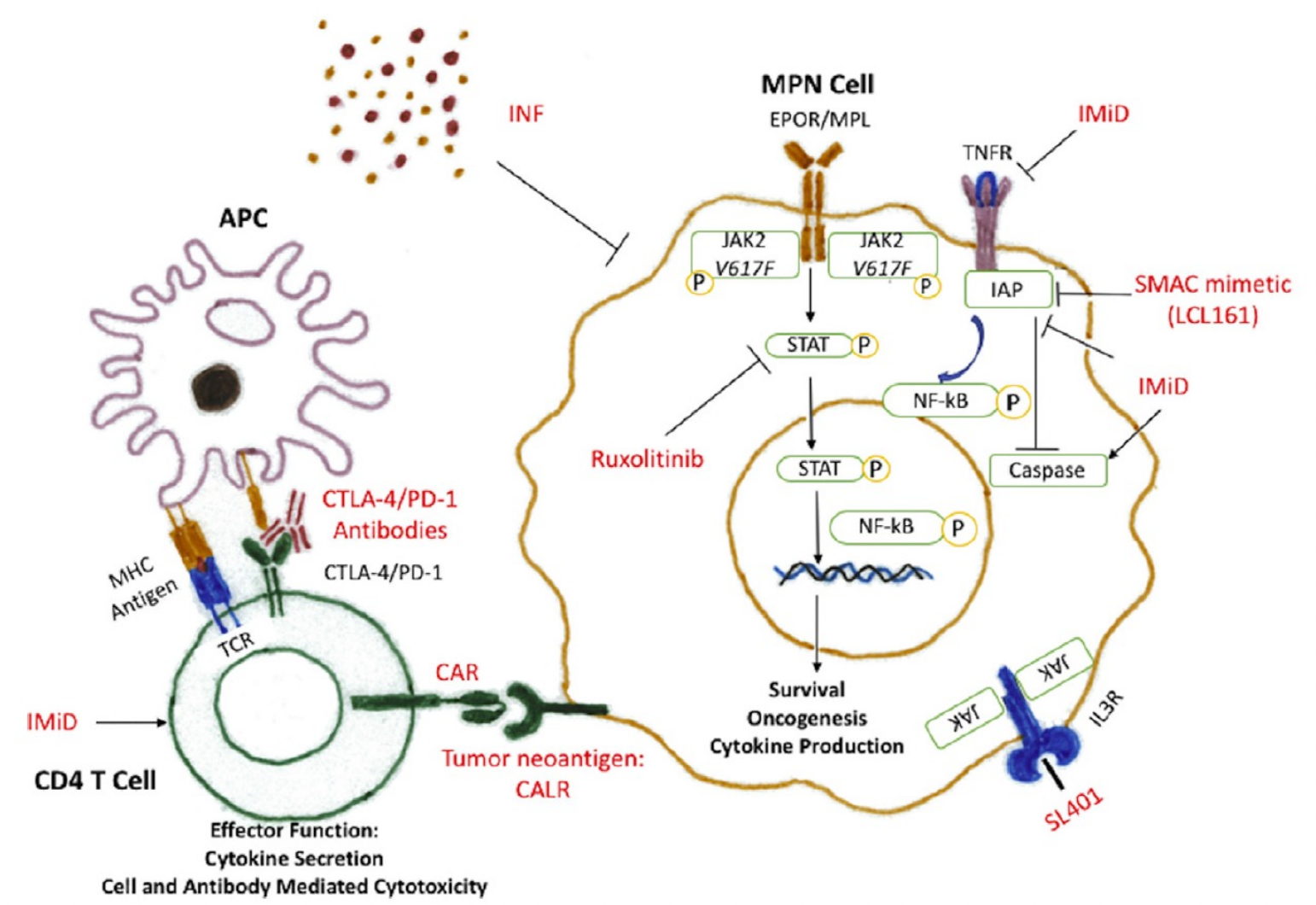
Mascarenhas J et al. *Leukemia* 2021;35(12):3361-3.

Hematol Oncol Clin North Am 2021;35(2):409-29.

Immunotherapy and Immunomodulation in Myeloproliferative Neoplasms

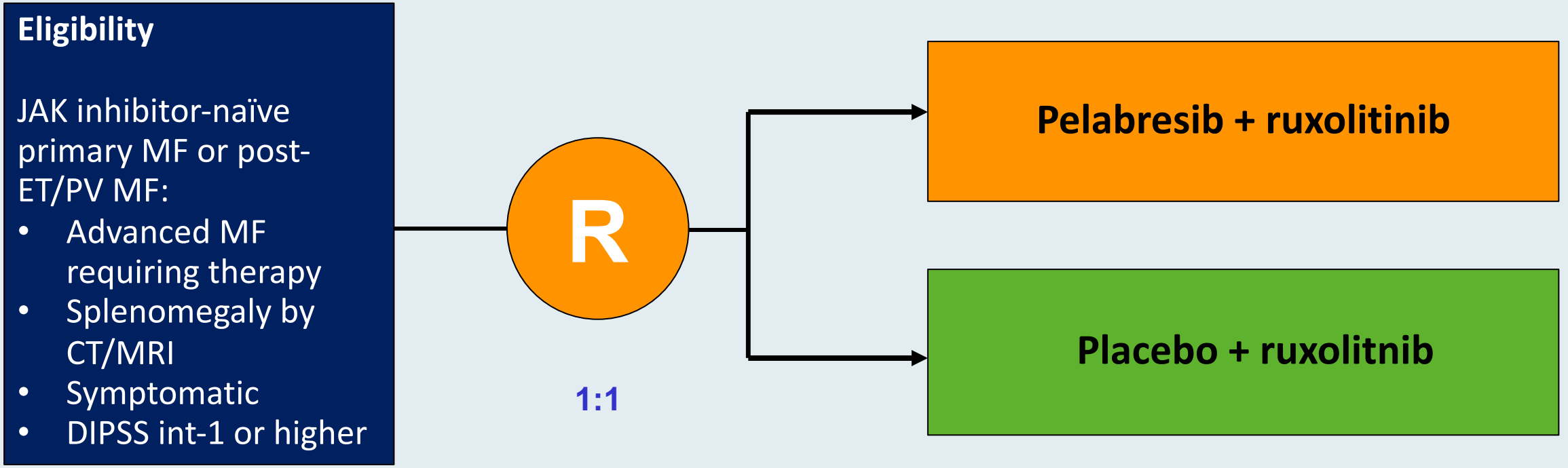
Naveen Pemmaraju, MD[a,*], Natalie C. Chen, MD, PhD[b], Srdan Verstovsek, MD, PhD[c]

Immunomodulating Agents in MPN Treatment



Pemmaraju N et al. *Hematol Oncol Clin North Am* 2021;35(2):409-29.

MANIFEST-2: Phase III Trial Design



Primary Endpoint: SVR35 at 24 weeks
Key Secondary Endpoint: TSS50 by at 24 weeks

Kremyanskaya M et al. ASH 2021;Abstract 141.

Momelotinib Yields Statistically Significant Improvement in Symptoms for Myelofibrosis

Press Release: January 27, 2022

"Topline findings from the phase 3 MOMENTUM study indicated that patients with myelofibrosis experienced a statistically significant reduction in symptoms following treatment with momelotinib.

Treatment with momelotinib resulted in a statistically significant reduction in symptoms for patients with myelofibrosis, according to a press release of the topline findings from the pivotal phase 3 MOMENTUM trial (NCT04173494).

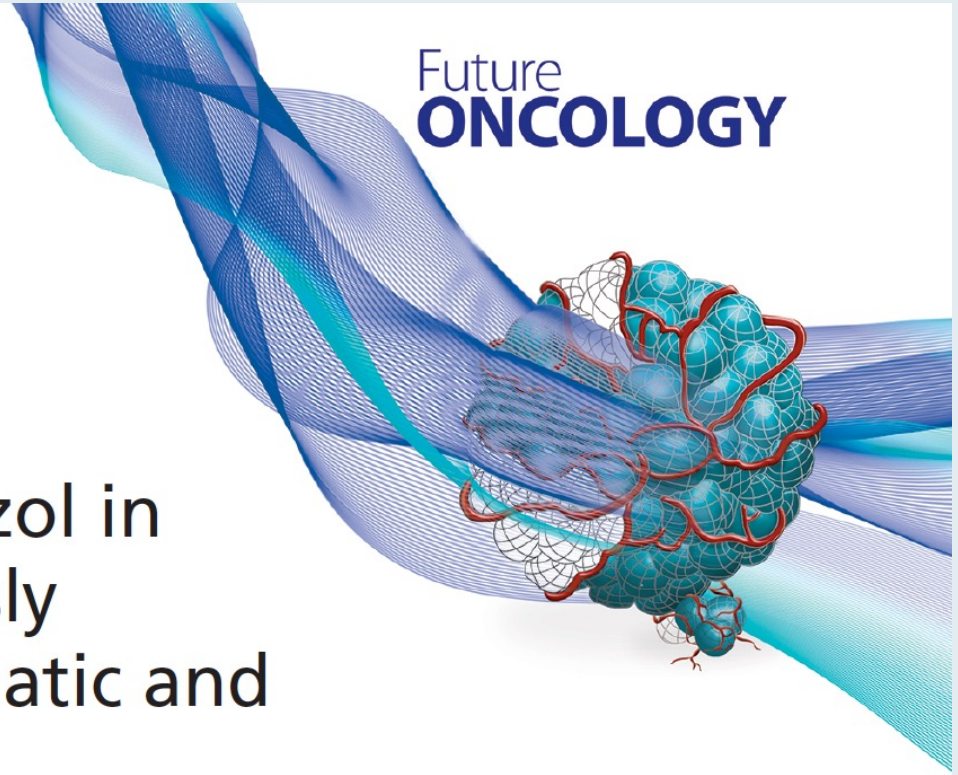
In a population of 195 patients, specifically 130 who received momelotinib and 65 who received danazol, 25% and 9% of patients, respectively, had a total symptom score of more than 50% (*P* = .0095). Additionally, 31% of patients in the momelotinib arm and 20% in the control arm were transfusion independent following treatment (one-sided *P* = .0064), indicating non-inferiority. Investigators also reported a splenic response rate of over 35% in 23% of patients in the experimental arm compared with 3% of patients in the control arm (*P* = .0006).

The full data are set to be presented at an upcoming medical meeting and plans have been put in place to submit a new drug application for the agent in the second quarter of 2022."

https://www.cancernetwork.com/view/momelotinib-yields-statistically-significant-improvement-in-symptoms-for-myelofibrosis

Future Oncol 2021;17(12):1449-58.

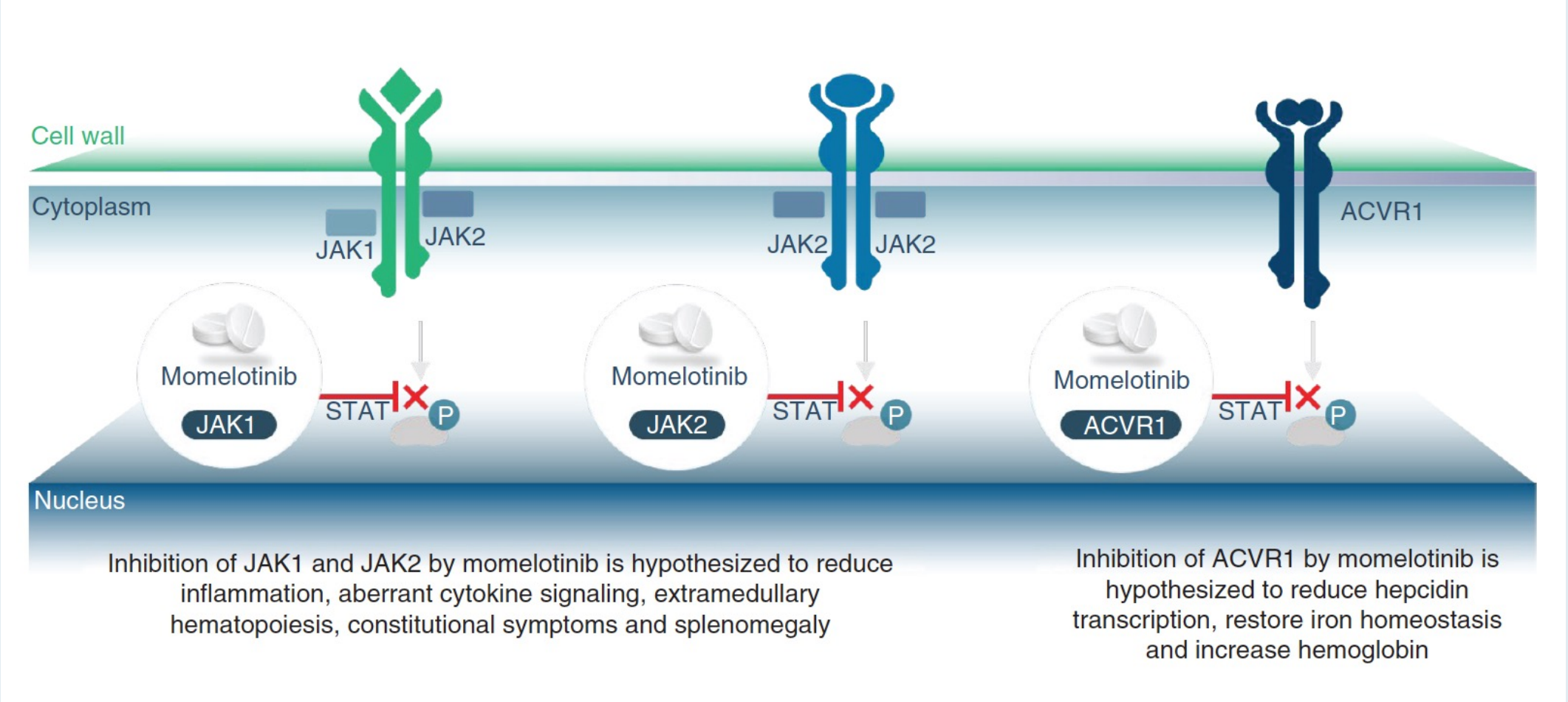
Clinical Trial Protocol



MOMENTUM: momelotinib vs danazol in patients with myelofibrosis previously treated with JAKi who are symptomatic and anemic

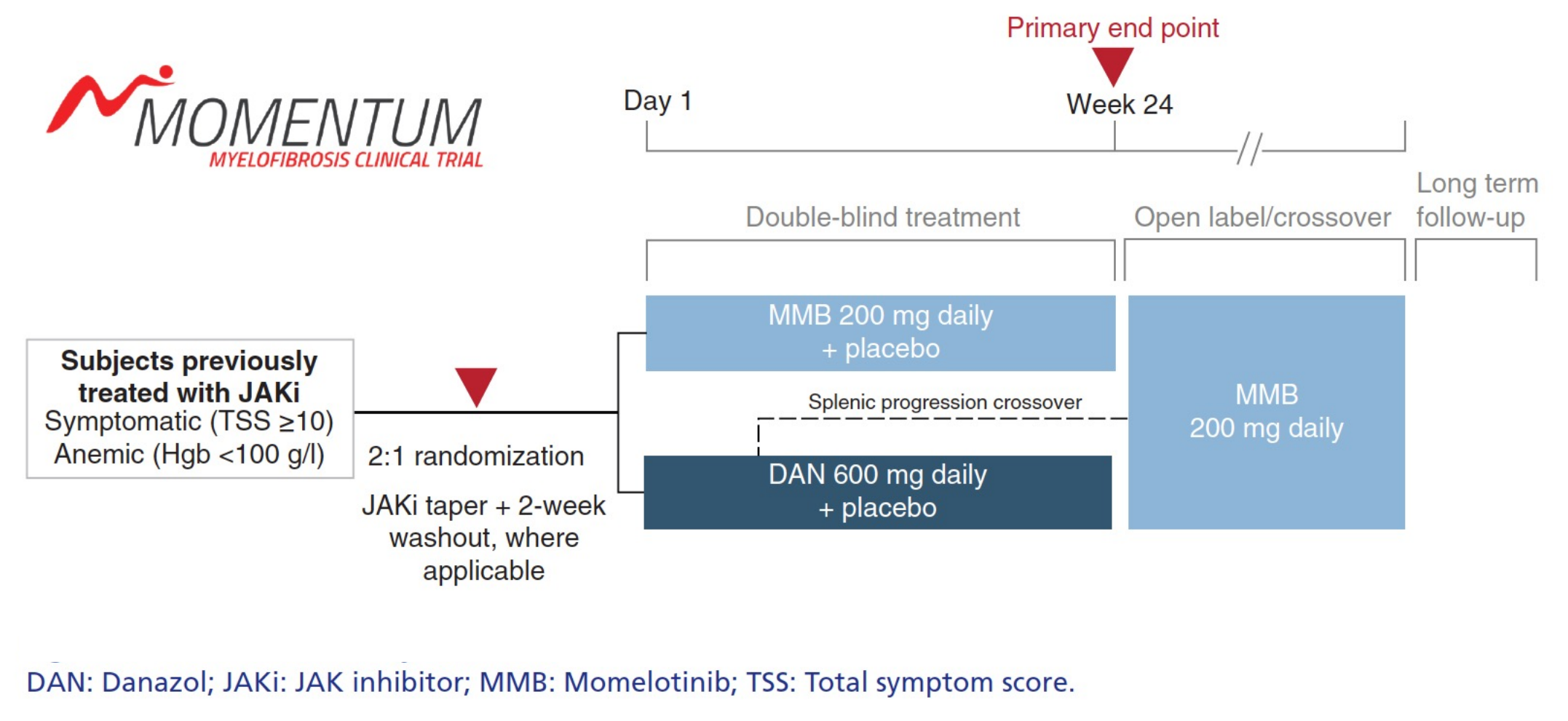
Srdan Verstovsek[1], Chih-Cheng Chen[2], Miklós Egyed[3], Martin Ellis[4], Laura Fox[5], Yeow T Goh[6], Vikas Gupta[7], Claire Harrison[8], Jean-Jacques Kiladjian[9], Mihaela C Lazaroiu[10], Adam Mead[11], Donal McLornan[12], Mary F McMullin[13], Stephen T Oh[14], Andrew Perkins[15], Uwe Platzbecker[16], Christof Scheid[17], Alessandro Vannucchi[18], Sung-Soo Yoon[19], Mark M Kowalski*,[20] & Ruben A Mesa[21]

Momelotinib Therapy May Decrease Inflammation, Improve Splenomegaly and Normalize Hemoglobin



Verstovsek S et al. *Future Oncol* 2021;17(12):1449-58.

MOMENTUM Study Schematic



DAN: Danazol; JAKi: JAK inhibitor; MMB: Momelotinib; TSS: Total symptom score.

Verstovsek S et al. *Future Oncol* 2021;17(12):1449-58.

Chifotides *et al.*
Journal of Hematology & Oncology (2022) 15:7
https://doi.org/10.1186/s13045-021-01157-4

Journal of Hematology & Oncology

REVIEW

Open Access

Momelotinib: an emerging treatment for myelofibrosis patients with anemia

Helen T. Chifotides, Prithviraj Bose and Srdan Verstovsek*

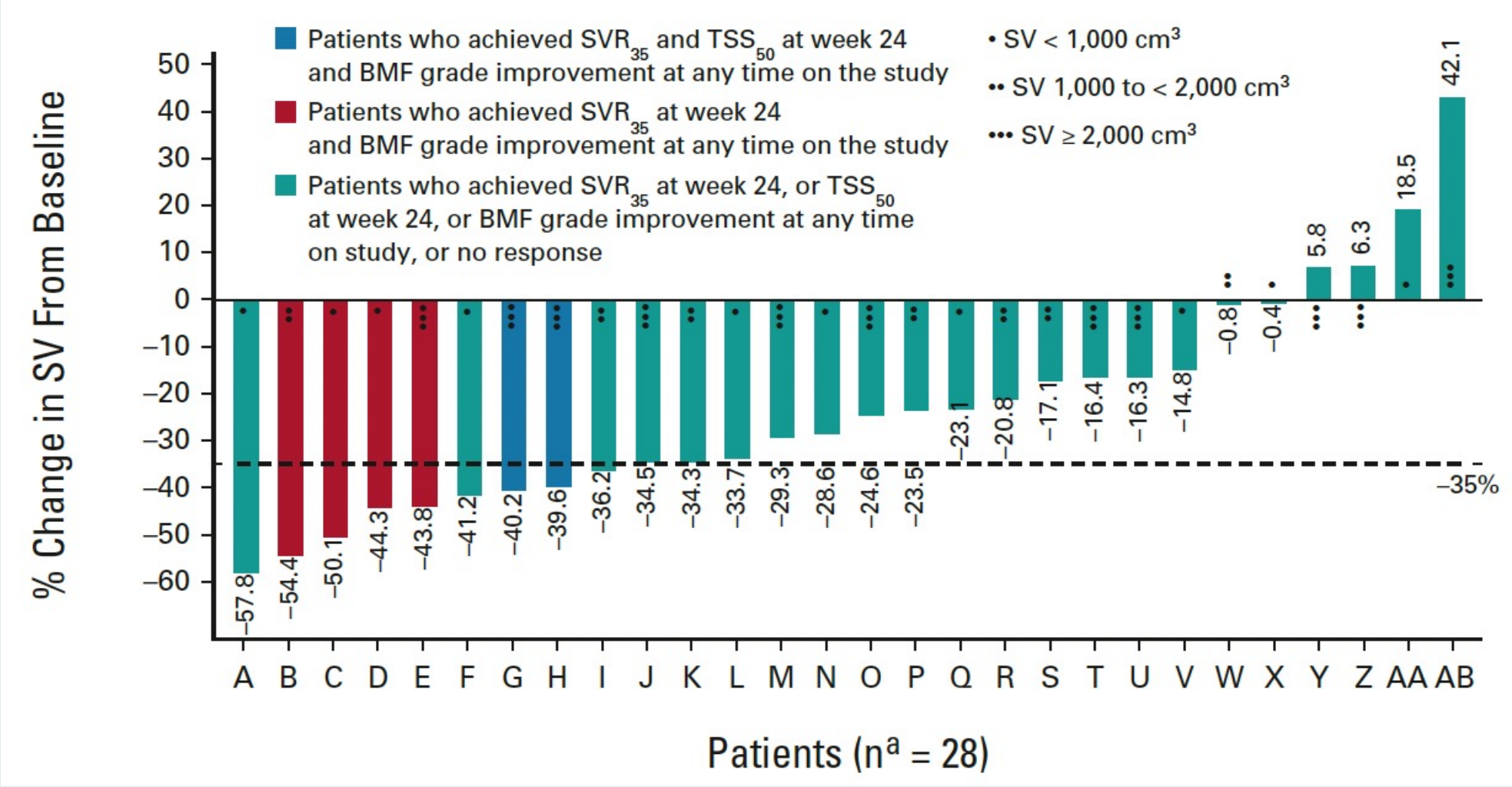
original reports

Addition of Navitoclax to Ongoing Ruxolitinib Therapy for Patients With Myelofibrosis With Progression or Suboptimal Response: Phase II Safety and Efficacy

Claire N. Harrison, MD[1]; Jacqueline S. Garcia, MD[2]; Tim C. P. Somervaille, MBBS, PhD[3,4]; James M. Foran, MD[5]; Srdan Verstovsek, MD, PhD[6]; Catriona Jamieson, MD, PhD[7]; Ruben Mesa, MD[8]; Ellen K. Ritchie, MD[9]; Srinivas K. Tantravahi, MBBS[10]; Pankit Vachhani, MD[11]; Casey L. O'Connell, MD[12]; Rami S. Komrokji, MD[13]; Jason Harb, PhD[14]; Jessica E. Hutti, PhD[14]; Leanne Holes, MBA[14]; Abdullah A. Masud, MS, PhD[14]; Silpa Nuthalapati, PhD[14]; Jalaja Potluri, MD[14]; and Naveen Pemmaraju, MD[6]

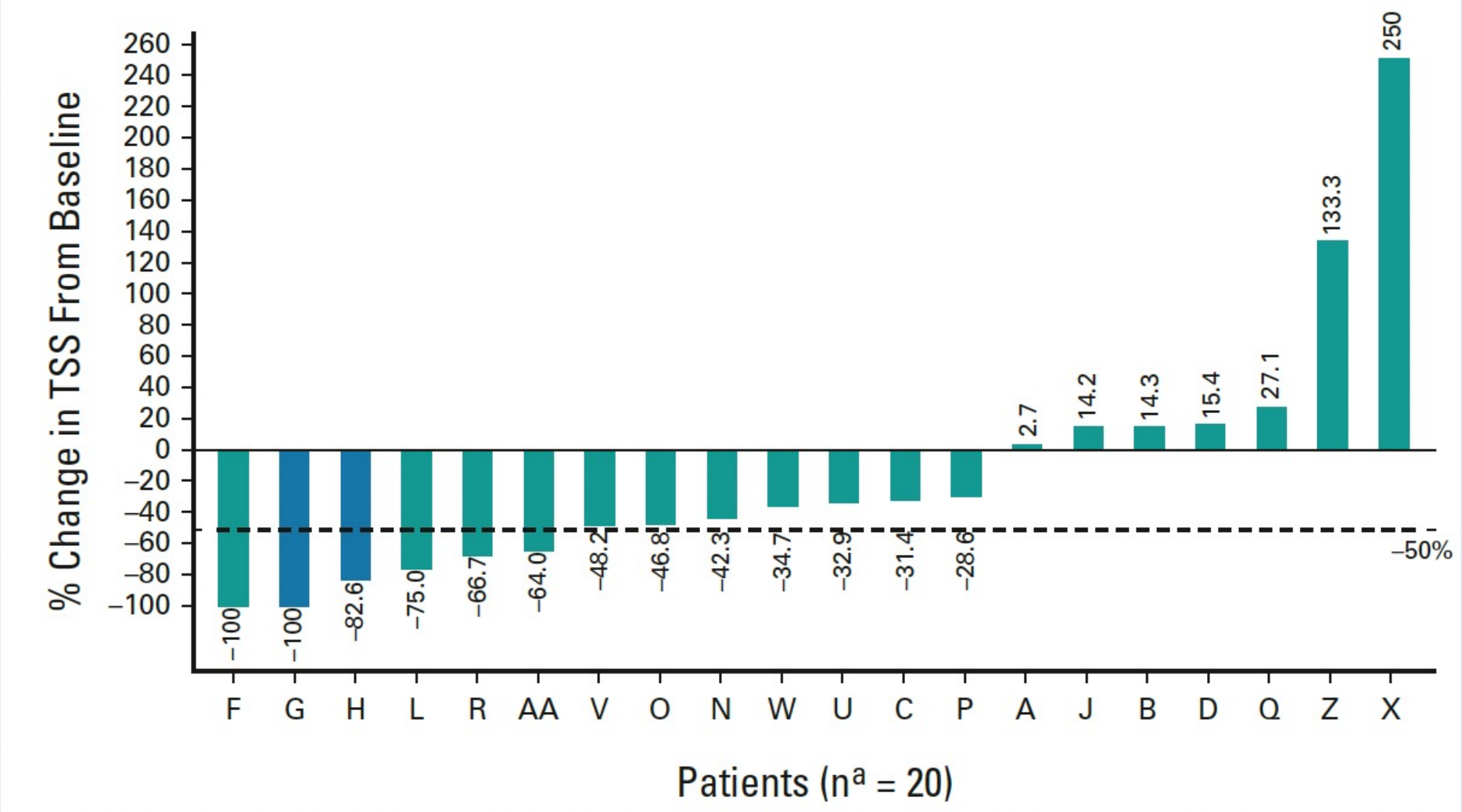
J Clin Oncol 2022;[Online ahead of print].

Percent Change in Spleen Volume from Baseline



Harrison CN et al. *J Clin Oncol* 2022;[Online ahead of print].

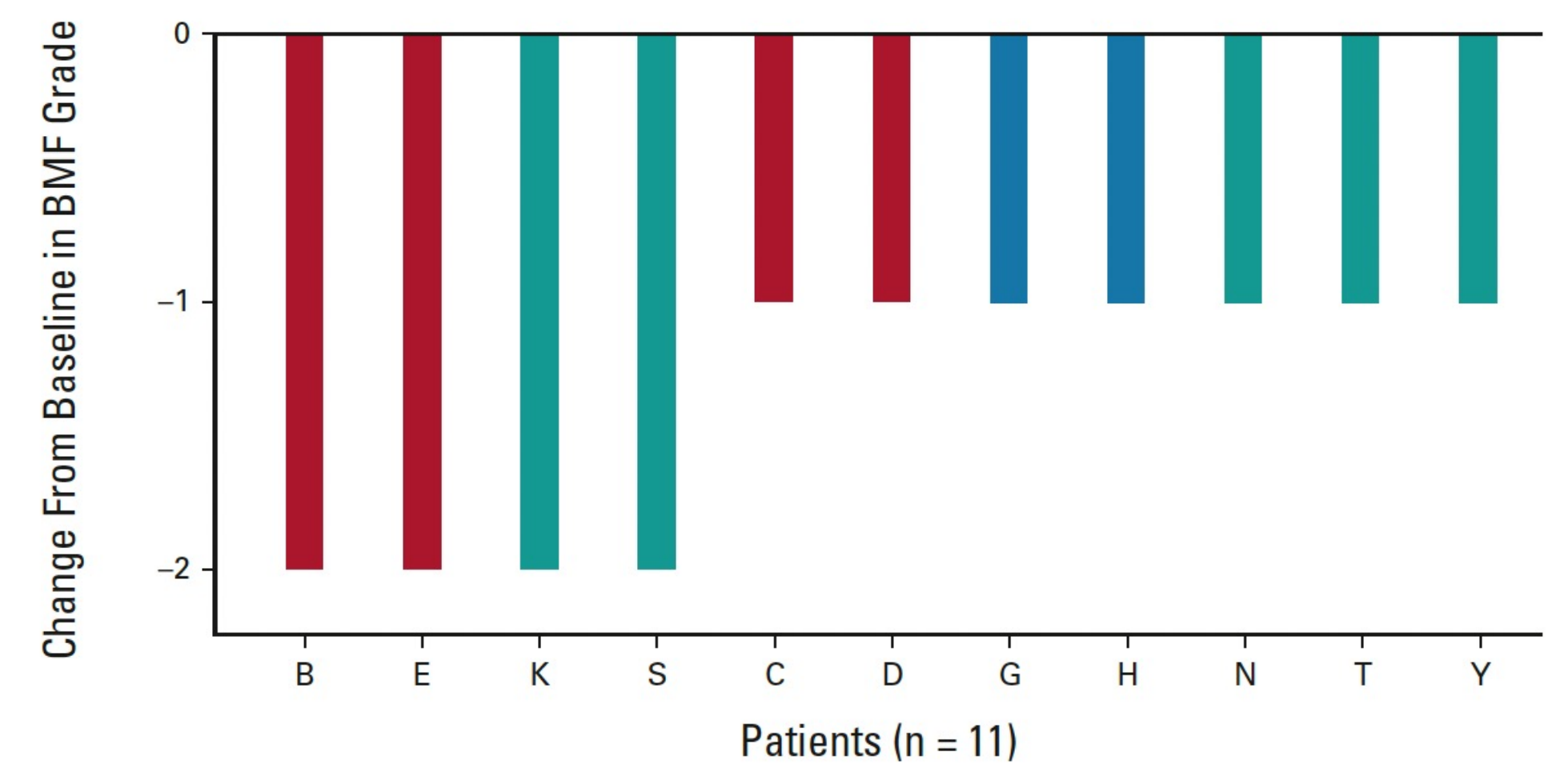
Percent Change in TSS from Baseline at Week 24



TSS = total symptom score

Harrison CN et al. *J Clin Oncol* 2022;[Online ahead of print].

Percent Change in Bone Marrow Fibrosis (BMF) from Baseline



Harrison CN et al. *J Clin Oncol* 2022;[Online ahead of print].

A Randomized Open-Label, Phase 3 Study to Evaluate Imetelstat versus Best Available Therapy (BAT) in Patients with Intermediate-2 (Int-2) or High-Risk Myelofibrosis (MF) Refractory to Janus Kinase Inhibitor (JAKi)

Mascarenhas J et al.

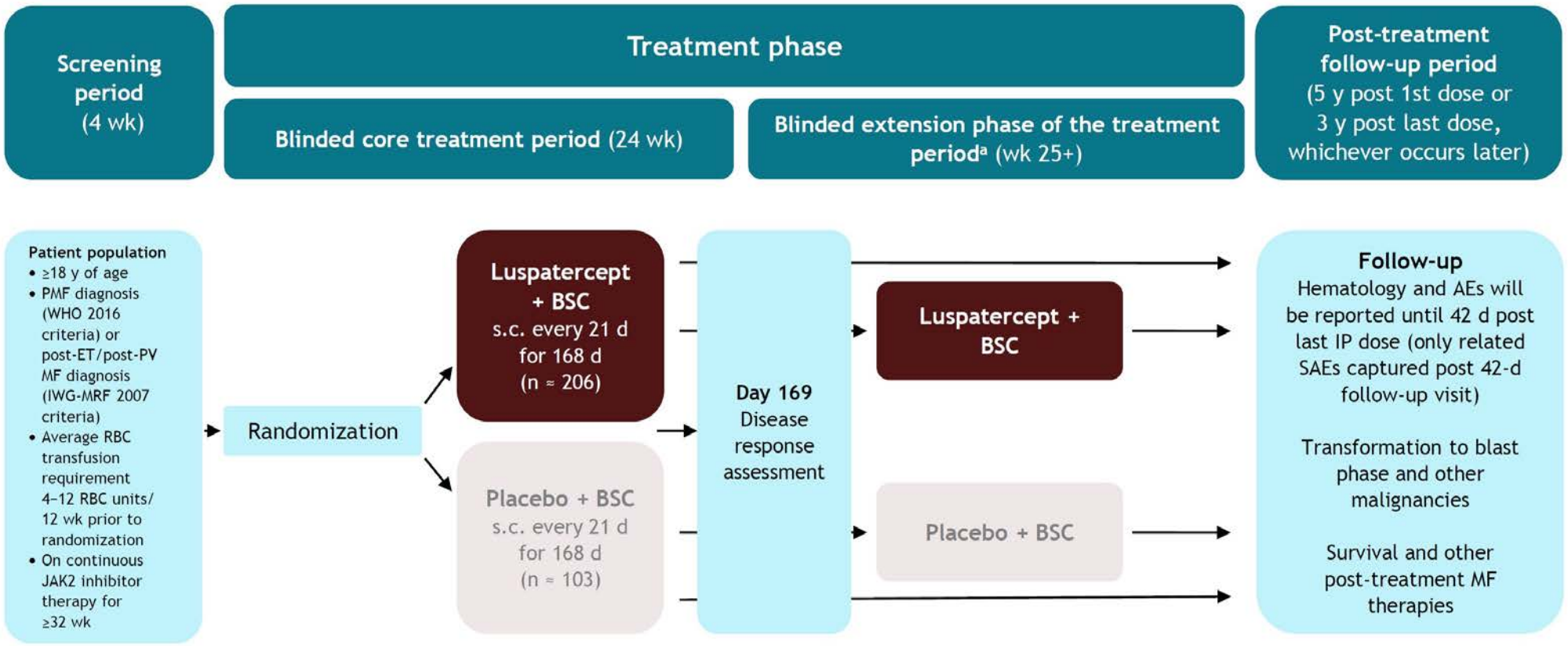
ASH 2021;Abstract 1503.

INDEPENDENCE: A Phase 3 Study of Efficacy and Safety of Luspatercept versus Placebo in Patients with Myeloproliferative Neoplasm-Associated Myelofibrosis on JAK2 Inhibitor Therapy and Requiring Red Blood Cell Transfusions

Mesa RA et al.

ASH 2021;Abstract 1490.

Figure. The INDEPENDENCE trial design



[a]Patients on study can be unblinded after analysis of the primary endpoint and with data monitoring committee consultation. Patients receiving placebo have the opportunity to receive luspatercept treatment and be treated for ≥ 24 wk in the open-label extension treatment period as long as they continue to demonstrate benefit from treatment, or they experience transformation to blast phase, unacceptable toxicities, or meet any other criteria for treatment discontinuation.

AE, adverse event; BSC, best supportive care; d, day; ET, essential thrombocythemia; IP, investigational product; IWG-MRF, International Working Group for Myelofibrosis Research and Treatment; MF, myelofibrosis; PMF, primary myelofibrosis; PV, polycythemia vera; RBC, red blood cell; SAE, serious adverse event; s.c., subcutaneously; WHO, World Health Organization; wk, week; y, year.

Mesa RA et al. ASH 2021;Abstract 1490.

Meet The Professor with Dr Verstovsek

Introduction

Module 1: Case Presentations

- Dr Keruakous: A 72-year-old man with JAK2-positive Intermediate-risk MF, a CALR mutation and multiple comorbidities
- Dr Bhatnagar: A 76-year-old woman with JAK2 V617F-positive primary myelofibrosis (MF) treated with ruxolitinib
- Dr Palmer: An 80-year-old woman with primary MF and pancytopenia (Hb 7.2 g/dL, platelets 38,000/uL)
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Module 2: Journal Club with Dr Verstovsek

Module 3: Faculty Survey

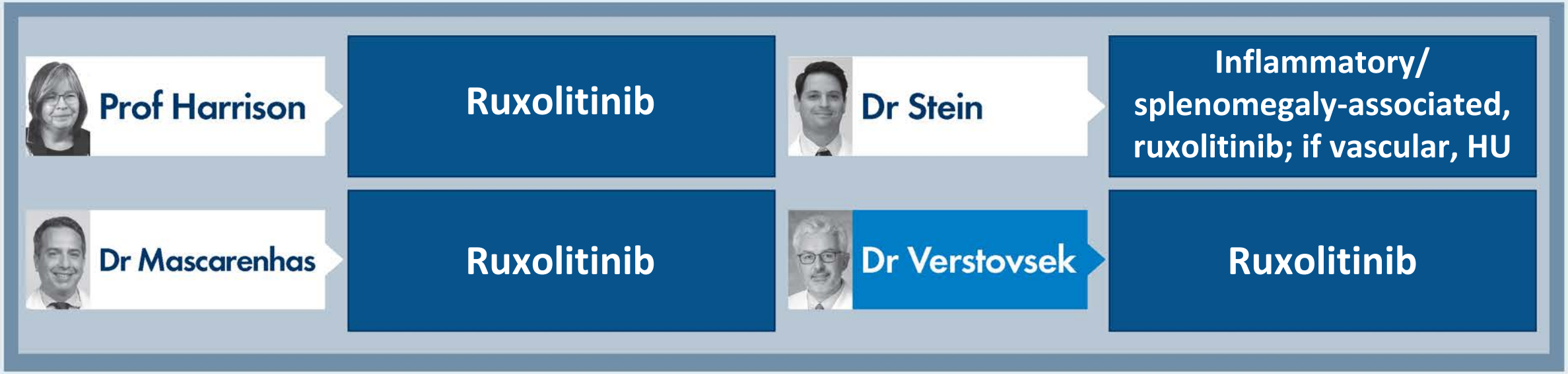
Module 4: Appendix of Key Publications

RTP
RESEARCH
TO PRACTICE

Which prognostic tool do you typically use for your patients with myelofibrosis (MF)?

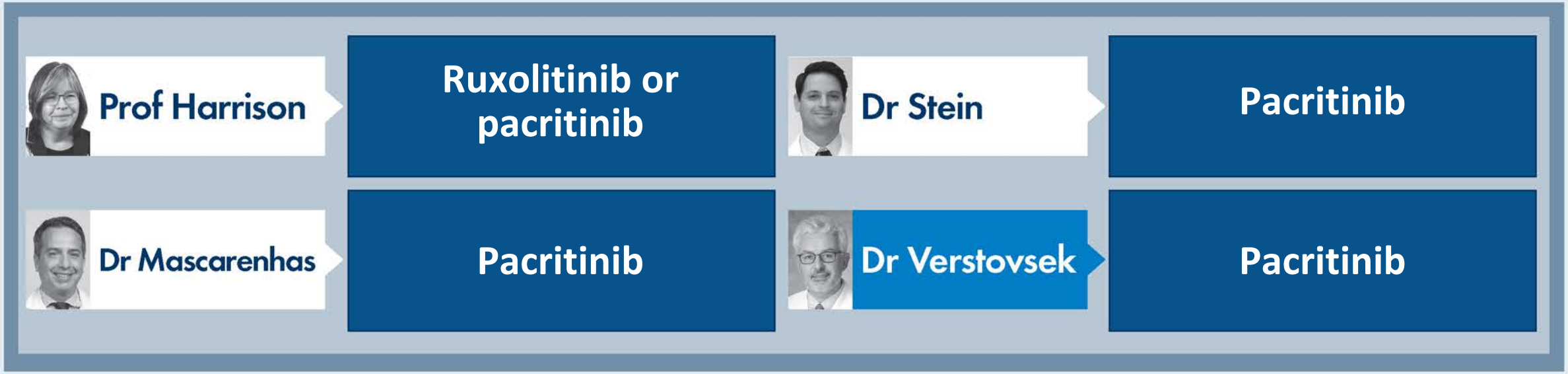
 Prof Harrison	Multiple tools, but don't tend to use GIPSS	 Dr Stein	MIPSS70 plus version 2.0
 Dr Mascarenhas	DIPSS	 Dr Verstovsek	DIPSS

For a 65-year-old patient with lower-risk, symptomatic MF, which treatment would you generally recommend?



HU = hydroxyurea

Regulatory and reimbursement issues aside and assuming you could access all these agents, for a 65-year-old patient with higher-risk, symptomatic MF, splenomegaly and a platelet count of 40,000/µL, which treatment would you generally recommend (assuming the patient is not a transplant candidate)?

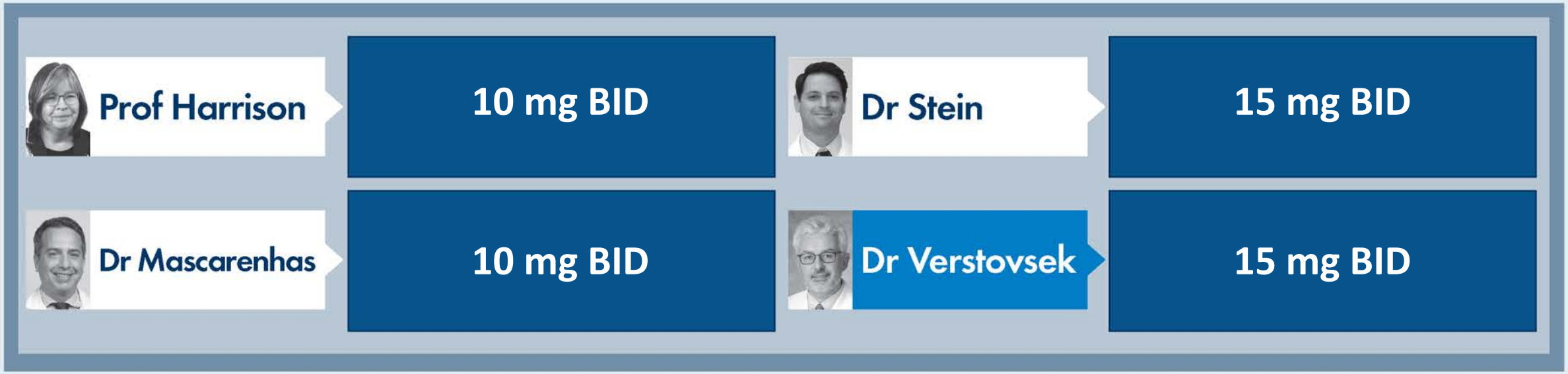


Regulatory and reimbursement issues aside and assuming you could access all these agents, for a 65-year-old patient with higher-risk, symptomatic MF, splenomegaly and transfusion-dependent anemia (Hgb 8.0 g/dL), which treatment would you generally recommend (assuming the patient is not a transplant candidate)?

 Prof Harrison	Ruxolitinib	 Dr Stein	Momelotinib
 Dr Mascarenhas	Momelotinib	 Dr Verstovsek	Momelotinib

RTP RESEARCH TO PRACTICE

If treating a patient with higher-risk, symptomatic MF, splenomegaly and a platelet count of 150,000/µL with ruxolitinib, what starting dose would you generally use?



RTP
RESEARCH
TO PRACTICE

What is the maximum dose of ruxolitinib that you would use for a patient with MF?

 Prof Harrison	25 mg BID	 Dr Stein	20 mg BID
 Dr Mascarenhas	25 mg BID	 Dr Verstovsek	25 mg BID

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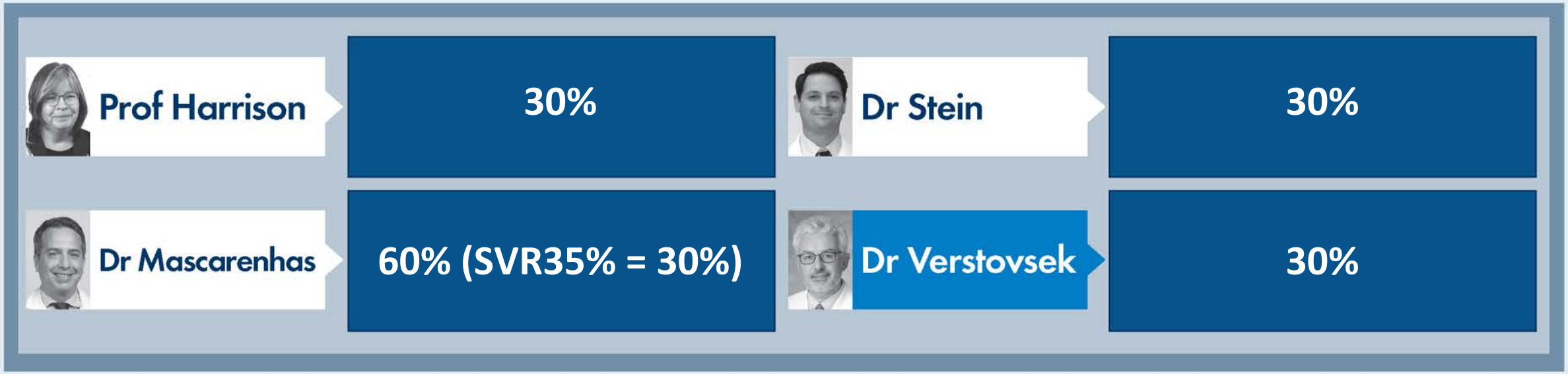
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside and assuming you could access all these agents, if a 65-year-old patient with higher-risk, symptomatic MF did not experience reduction in spleen size or improvement in symptoms after 3 months of standard-dose ruxolitinib, which of the following would you most likely attempt (assuming normal renal and hepatic function and a platelet count >200,000/µL)?

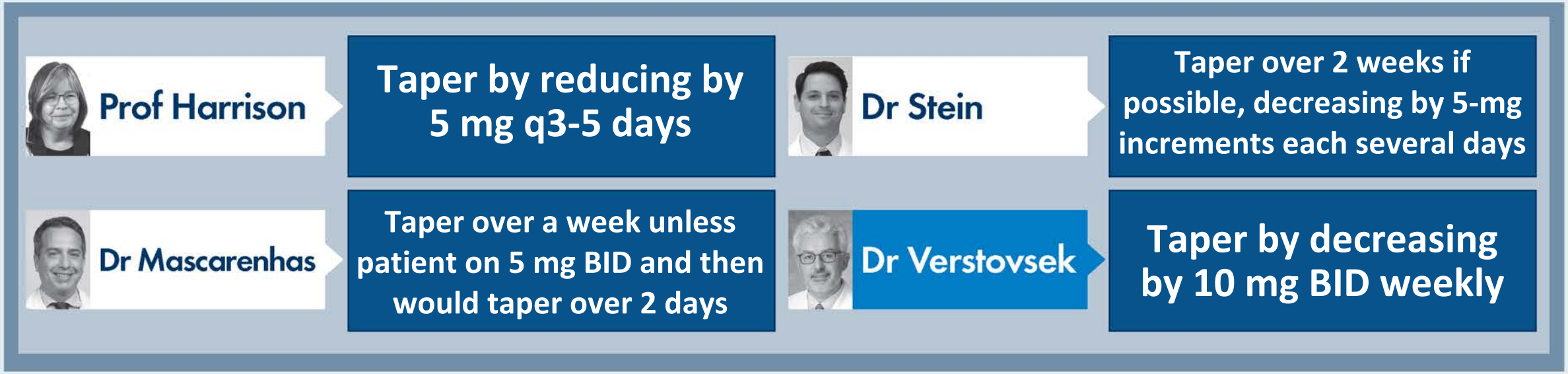
 Prof Harrison	Escalate dose of ruxolitinib, consider BMT	 Dr Stein	Switch to fedratinib
 Dr Mascarenhas	Switch to fedratinib	 Dr Verstovsek	Escalate dose of ruxolitinib

BMT = bone marrow transplant

If you decided to switch to fedratinib for the patient in the previous scenario, what would you estimate is the likelihood that he or she would respond?



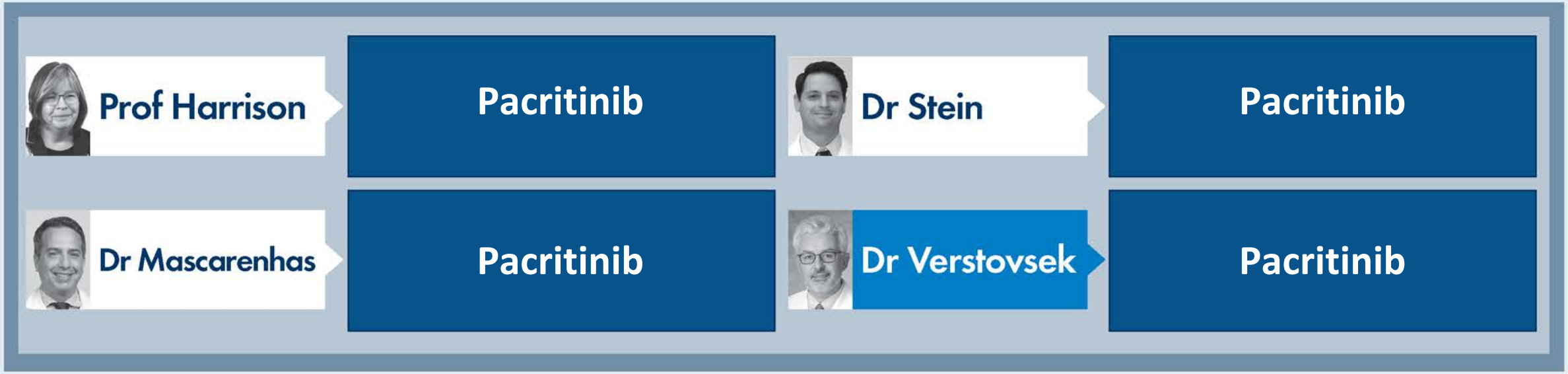
When discontinuing ruxolitinib due to insufficient response, intolerance or progressive disease, do you generally taper off or discontinue immediately?



Based on current clinical trial data and your personal experience, how would you compare patient-reported symptom relief with ruxolitinib to that with fedratinib?

 Prof Harrison	Ruxolitinib provides greater improvement in symptoms	 Dr Stein	Ruxolitinib provides greater improvement in symptoms
 Dr Mascarenhas	Ruxolitinib provides greater improvement in symptoms	 Dr Verstovsek	About the same

A 65-year-old man with symptomatic, higher-risk MF and splenomegaly (baseline platelet count 110,000/µL) receives ruxolitinib 15 mg BID and responds with significant clinical improvement. Approximately 3 years later, he presents with drenching night sweats, fatigue, abdominal discomfort and an increase in spleen size. Platelet count = 44,000/µL, Hgb = 11.2 g/dL. Regulatory and reimbursement issues aside, what treatment would you most likely recommend next if the patient is transplant ineligible?



RTP
RESEARCH
TO PRACTICE

Do you believe pacritinib has real pharmacologic advantages over other available JAK inhibitors that make it a preferable treatment option for patients with MF and low platelet counts?

Do you believe that the risk of bleeding and/or cardiovascular toxicities is a significant concern for patients with MF receiving pacritinib?

RTP
RESEARCH
TO PRACTICE

A 70-year-old woman presents with lower-risk MF and anemia, for which she has been transfusion dependent for 4 months. Nutritional deficiency and hemolysis are ruled out, and she does not have any other symptoms and no splenomegaly on physical exam. Her serum EPO is 750 mU/mL. What would you recommend?

 Prof Harrison	Lenalidomide	 Dr Stein	Danazol or thalidomide
 Dr Mascarenhas	Danazol	 Dr Verstovsek	Danazol

A 55-year-old man with higher-risk MF is receiving ruxolitinib while awaiting allogeneic stem cell transplantation, with significant improvement of splenomegaly. When would you stop ruxolitinib?

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RESEARCH
TO PRACTICE

N Engl J Med 2012;366:799-807

The NEW ENGLAND JOURNAL of MEDICINE

COMFORT-I

ORIGINAL ARTICLE

A Double-Blind, Placebo-Controlled Trial of Ruxolitinib for Myelofibrosis

Srdan Verstovsek, M.D., Ph.D., Ruben A. Mesa, M.D., Jason Gotlib, M.D.,
., Vikas Gupta, M.D., John F. DiPersio, M.D., Ph.D.,
., Michael Deininger, M.D., Ph.D., Carole Miller, M.D.,
M.D., Moshe Talpaz, M.D., Elliott F. Winton, M.D.,
M.D., Murat O. Arcasoy, M.D., Elizabeth Hexner, M.D.,
, M.D., Ronald Paquette, M.D., Azra Raza, M.D.,
n Erickson-Viitanen, Ph.D., Iphigenia L. Koumenis, M.S.,
Victor Sandor, M.D., and Hagop M. Kantarjian, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 1, 2012 VOL. 366 NO. 9

COMFORT-II

JAK Inhibition with Ruxolitinib versus Best Available Therapy for Myelofibrosis

Claire Harrison, D.M., Jean-Jacques Kiladjian, M.D., Ph.D., Haifa Kathrin Al-Ali, M.D., Heinz Gisslinger, M.D., Roger Waltzman, M.D., M.B.A., Viktoriya Stalbovskaya, Ph.D., Mari McQuitty, R.N., M.P.H., Deborah S. Hunter, Ph.D., Richard Levy, M.D., Laurent Knoops, M.D., Ph.D., Francisco Cervantes, M.D., Ph.D., Alessandro M. Vannucchi, M.D., Tiziano Barbui, M.D., and Giovanni Barosi, M.D.

RTP RESEARCH TO PRACTICE

COMFORT-I and COMFORT-II: Ruxolitinib for Intermediate-2- or High-Risk MF

- **Randomized Phase III studies in which patients with intermediate 2- or high-risk MF received ruxolitinib (15 or 20 mg BID) versus placebo (COMFORT-I, N = 309) or best available therapy (COMFORT-II, N = 149)**

Efficacy outcomes	COMFORT-I, Wk 24[1]			COMFORT-II, Wk 48[2]		
	Ruxolitinib (n = 155)	Placebo (n = 154)	*p*-value	Ruxolitinib (n = 144)	BAT (n = 72)	*p*-value
Spleen volume reduction ≥35%	41.9%	0.7%	< 0.001	28%	0	< 0.001
≥50% reduction in MF-SAF TSS	45.9%	5.3%	< 0.001	NR	NR	NR
Safety outcomes						
Discontinued due to AEs	11.0%	10.6%	NR	8%	5%	NR
Grade 3/4 anemia	45%	19%		NR	NR	
Grade 3/4 thrombocytopenia	13%	1%		NR	NR	
Grade 3/4 neutropenia	7%	2%		NR	NR	

1. Verstovsek. *NEJM* 2012;366:799. 2. Harrison. *NEJM* 2012;366:787.

Verstovsek *et al. Journal of Hematology & Oncology* (2017) 10:156
DOI 10.1186/s13045-017-0527-7

Journal of Hematology & Oncology

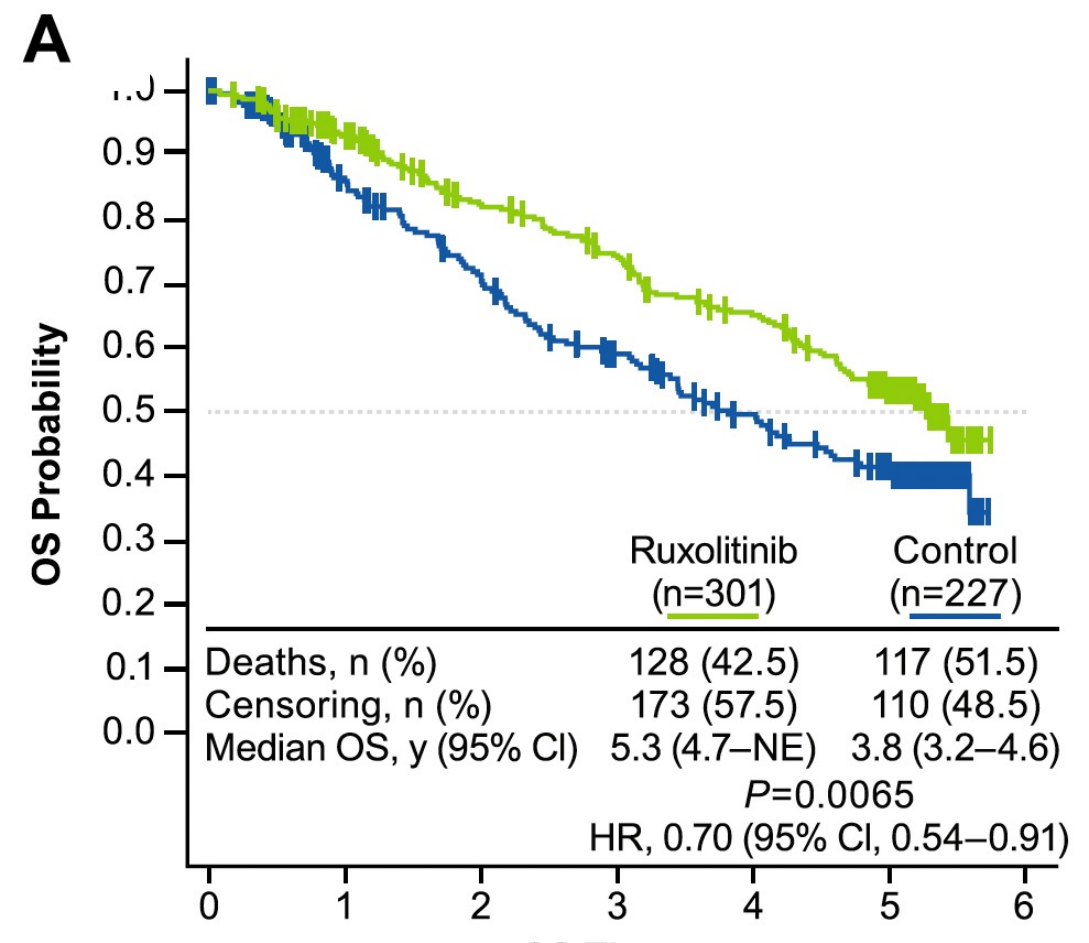
RESEARCH Open Access

Long-term survival in patients treated with ruxolitinib for myelofibrosis: COMFORT-I and -II pooled analyses

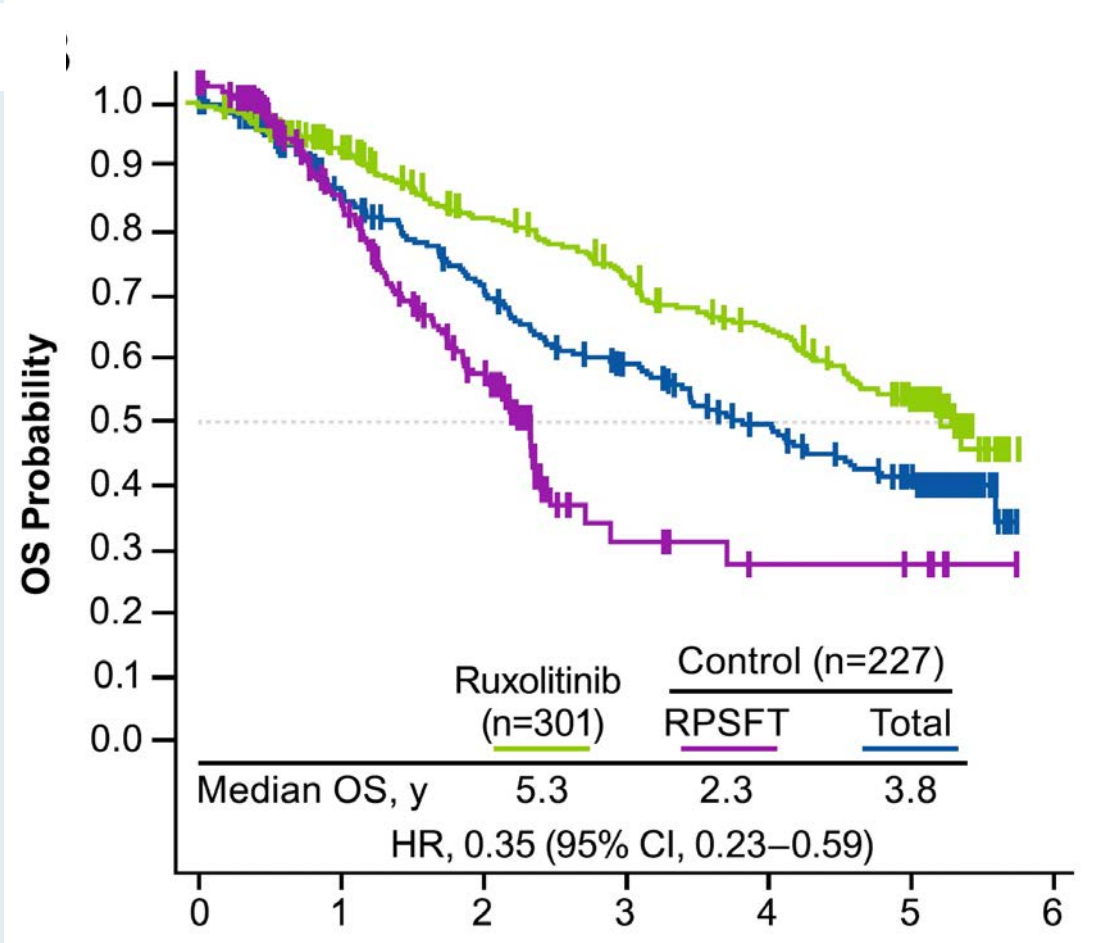
Srdan Verstovsek[1*], Jason Gotlib[2], Ruben A. Mesa[3], Alessandro M. Vannucchi[4], Jean-Jacques Kiladjian[5], Francisco Cervantes[6], Claire N. Harrison[7], Ronald Paquette[8], William Sun[9], Ahmad Naim[9], Peter Langmuir[9], Tuochuan Dong[10], Prashanth Gopalakrishna[11] and Vikas Gupta[12]

COMFORT-I and COMFORT-II Pooled Analyses: Long-Term Survival with Ruxolitinib

OS (5-Year ITT Population)



OS (Corrected for Crossover)



Verstovsek S et al. *J Hem Onc* 2017;10:156.

RTP RESEARCH TO PRACTICE

OPEN

Leukemia (2016) **30**, 1701–1707

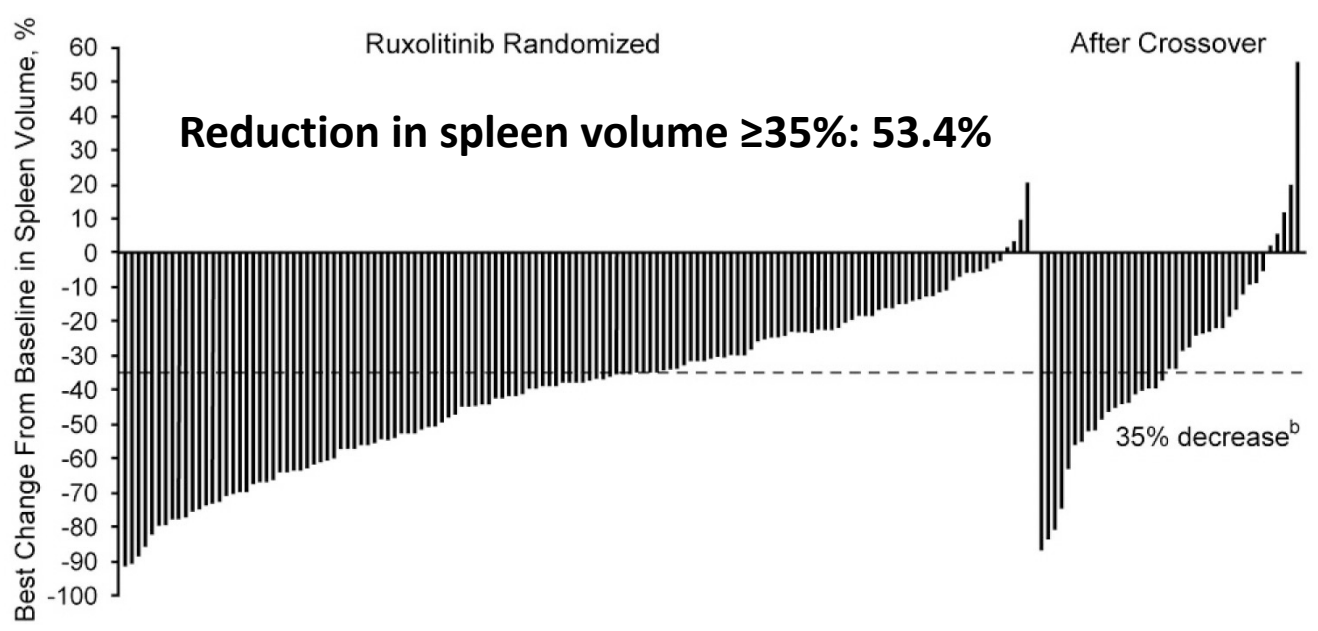
www.nature.com/leu

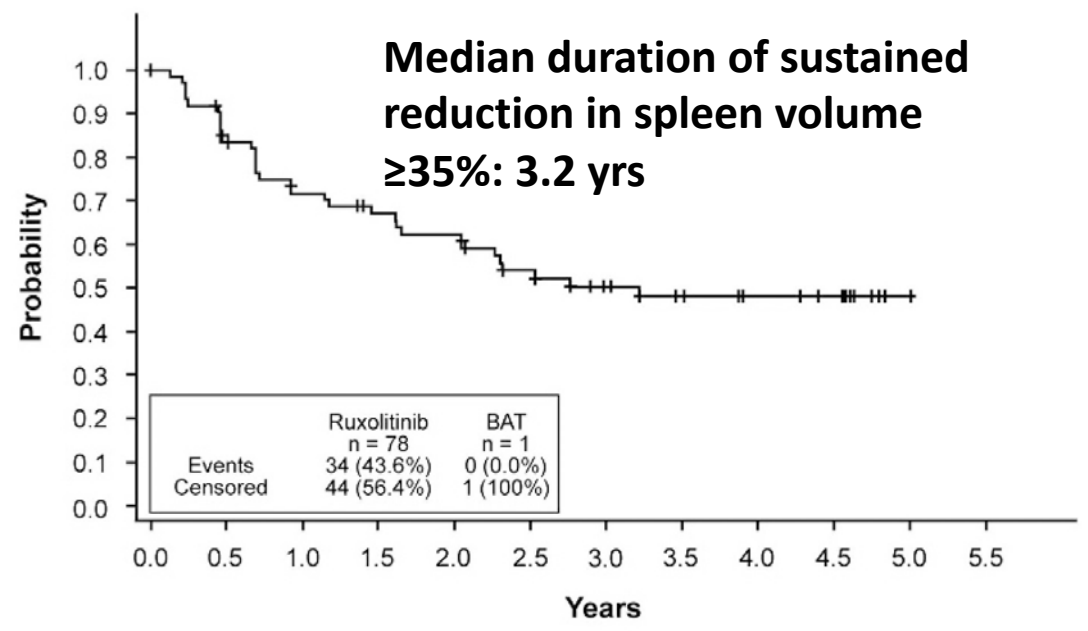
ORIGINAL ARTICLE

Long-term findings from COMFORT-II, a phase 3 study of ruxolitinib vs best available therapy for myelofibrosis

CN Harrison[1], AM Vannucchi[2], J-J Kiladjian[3], HK Al-Ali[4], H Gisslinger[5], L Knoops[6], F Cervantes[7], MM Jones[8], K Sun[8], M McQuitty[9], V Stalbovskaya[9], P Gopalakrishna[9] and T Barbui[10] on behalf of the COMFORT-II Investigators[11]

COMFORT-II Final 5-Year Analysis: Rates and Duration of Splenic Reduction





Harrison CN et al. *Leukemia* 2016;30:1701-7.

RTP RESEARCH TO PRACTICE

COMFORT-II Final 5-Year Analysis: Exposure-Adjusted Rates of Grade 3/4 Adverse Events

	BAT (n = 73)	Ruxolitinib (n = 191)
Any AE	36%	275
Anemia	8%	9%
Thrombocytopenia	6%	6%
Pneumonia	6%	2%
General physical health deterioration	5%	2%
Acute renal failure	0	1%

Harrison CN et al. *Leukemia* 2016;30:1701-7.

bjh research paper

Primary analysis of JUMP, a phase 3b, expanded-access study evaluating the safety and efficacy of ruxolitinib in patients with myelofibrosis, including those with low platelet counts

Haifa Kathrin Al-Ali,[1,†] Martin Griesshammer,[2,†] Lynda Foltz,[3] Giuseppe A. Palumbo,[4] Bruno Martino,[5] Francesca Palandri,[6] Anna Marina Liberati,[7] Philipp le Coutre,[8] Carmen García-Hernández,[9] Andrey Zaritskey,[10] Renato Tavares,[11] Vikas Gupta,[12] Pia Raanani,[13] Pilar Giraldo,[14] Mathias Hänel,[15] Daniela Damiani,[16] Tomasz Sacha,[17] Catherine Bouard,[18] Carole Paley,[19] Ranjan Tiwari,[20] Francesco Mannelli[21] and Alessandro M. Vannucchi[21]

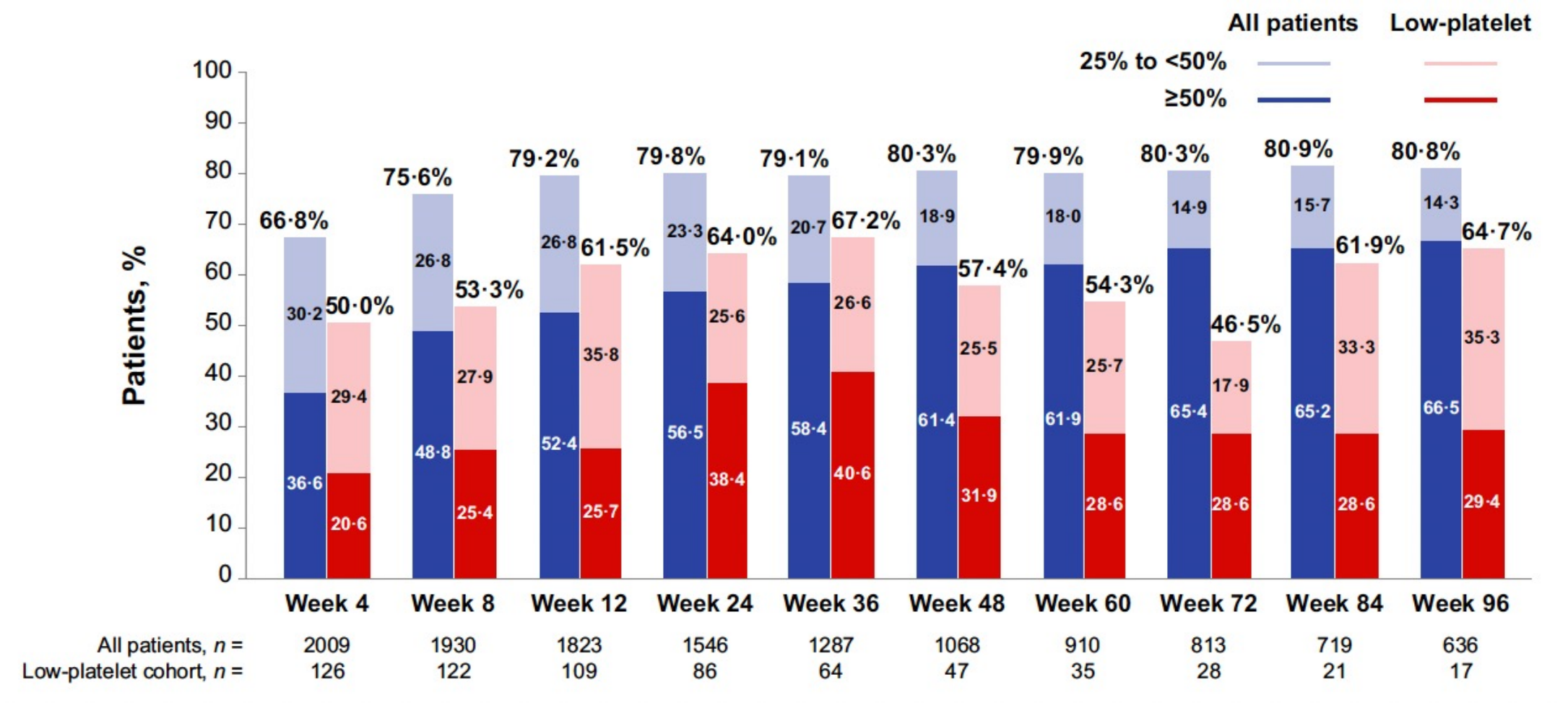
Br J Haematol 2020;189(5):888-903

JUMP: Baseline Characteristics

Parameter	All patients (N = 2,233)	Plt count (<100 x 10^9/l) (n = 138)	Plt count (≥100 x 10^9/l) (n = 2,087)
Median age	67.0	67.5	67.0
Time since initial diagnosis	25.8 mo	36.1 mo	25.1 mo
DIPSS risk status			
Low	2.7%	0	2.9%
Intermediate-1	37.4%	23.9%	38.4%
Intermediate-2	33.8%	43.5%	33.3%
High	8.7%	8.7%	8.7%
Platelet count, x 10^9/l			
<50	<0.1%	0.7%	0
≥50 to <75	1.3%	20.3%	0
≥100 to <200	4.9%	79.0%	0
≥200	62.6%	0	67.0%

Al-Ali HK et al. *Br J Haematol* 2020;189(5):888-903.

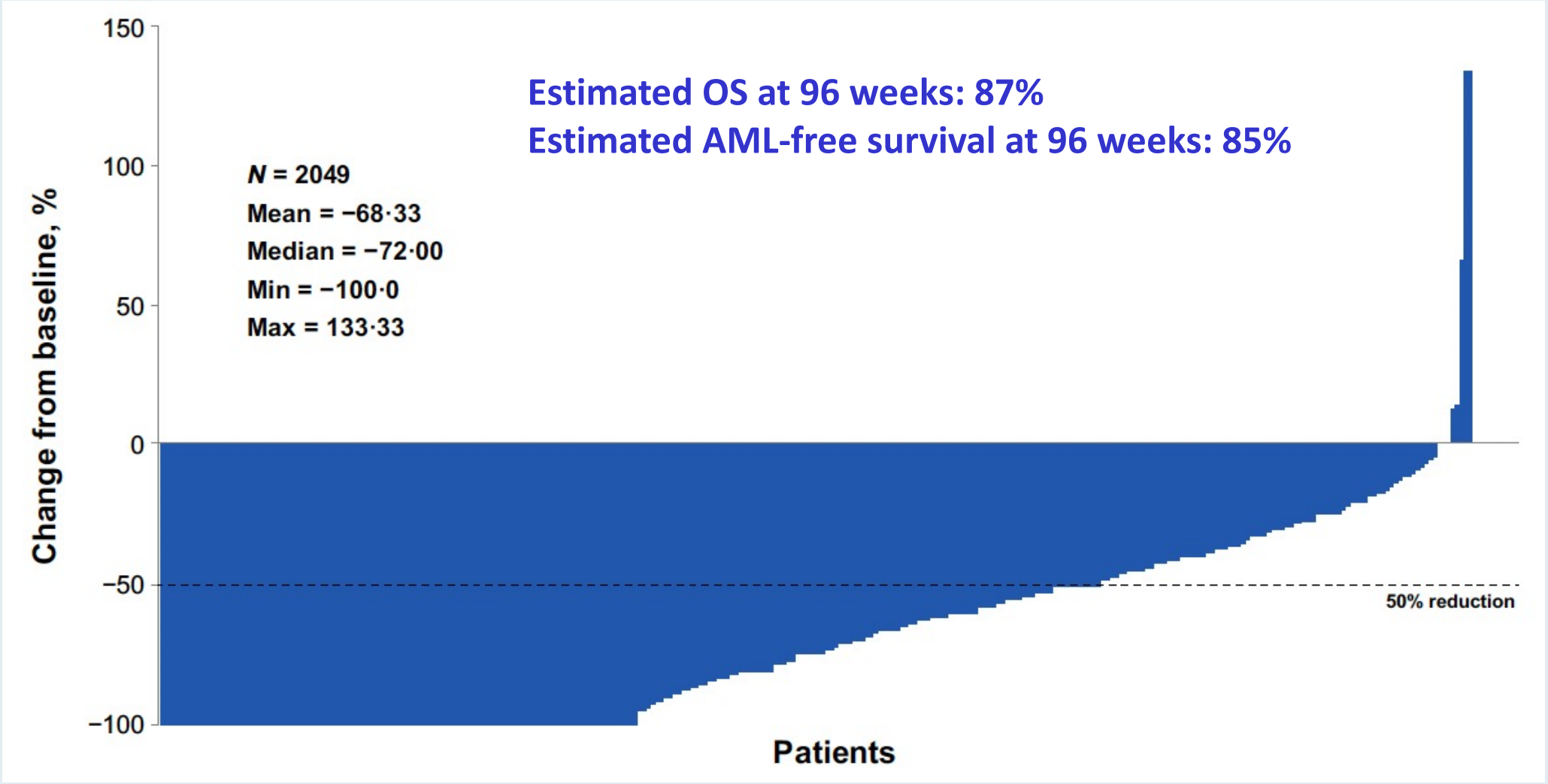
JUMP: Patients with a ≥25% and a ≥50% Decrease from Baseline in Spleen Length



Al-Ali HK et al. *Br J Haematol* 2020;189(5):888-903.

RTP RESEARCH TO PRACTICE

JUMP: Best Percent Change from Baseline in Palpable Spleen Length at Any Time in the Overall Patient Population



Al-Ali HK et al. *Br J Haematol* 2020;189(5):888-903.

RTP RESEARCH TO PRACTICE

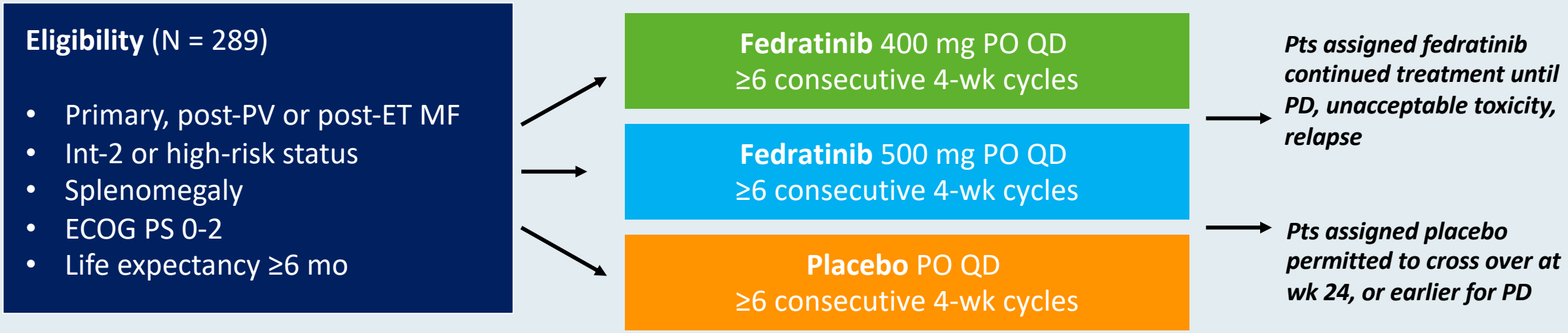
bjh short report

Updated results of the placebo-controlled, phase III JAKARTA trial of fedratinib in patients with intermediate-2 or high-risk myelofibrosis

Animesh Pardanani,[1] Ayalew Tefferi,[1] Tamás Masszi,[2] Elena Mishchenko,[3] Mark Drummond,[4] Eric Jourdan,[5] Alessandro Vannucchi,[6] Mindaugas Jurgutis,[7] Vincent Ribrag,[8] Alessandro Rambaldi,[9,10] Liang Piu Koh,[11] Shelonitda Rose,[12] Jun Zhang[12] and Claire Harrison[13]

Br J Haematol 2021;195:244-8.

JAKARTA Phase III Study Design

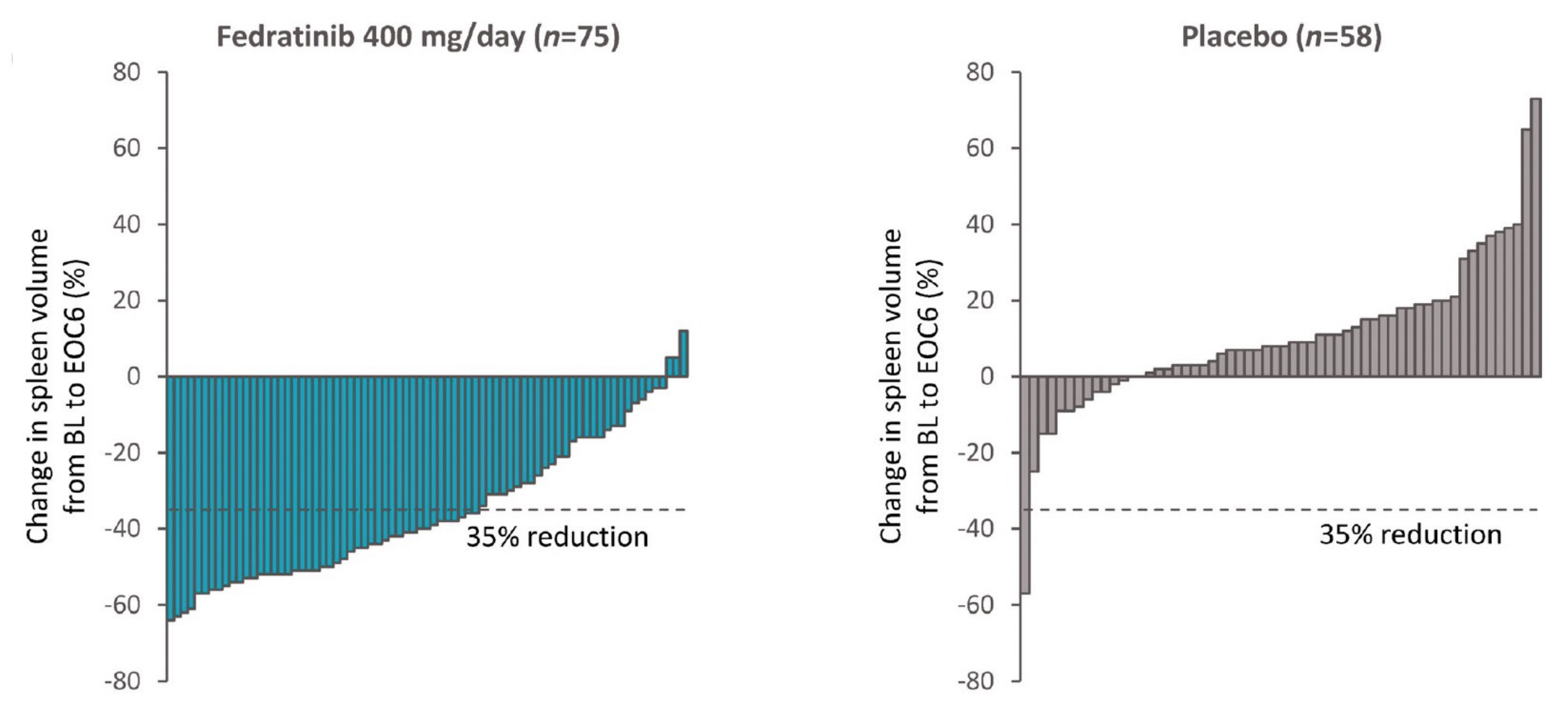


Primary endpoint: Spleen response (≥35% reduction in spleen volume vs BL) at Wk 24, and confirmed 4 wks later

Secondary endpoints: Symptom response (≥50% reduction in TSS), safety

Pardanani A et al. *JAMA Oncol* 2015;1:643-51.

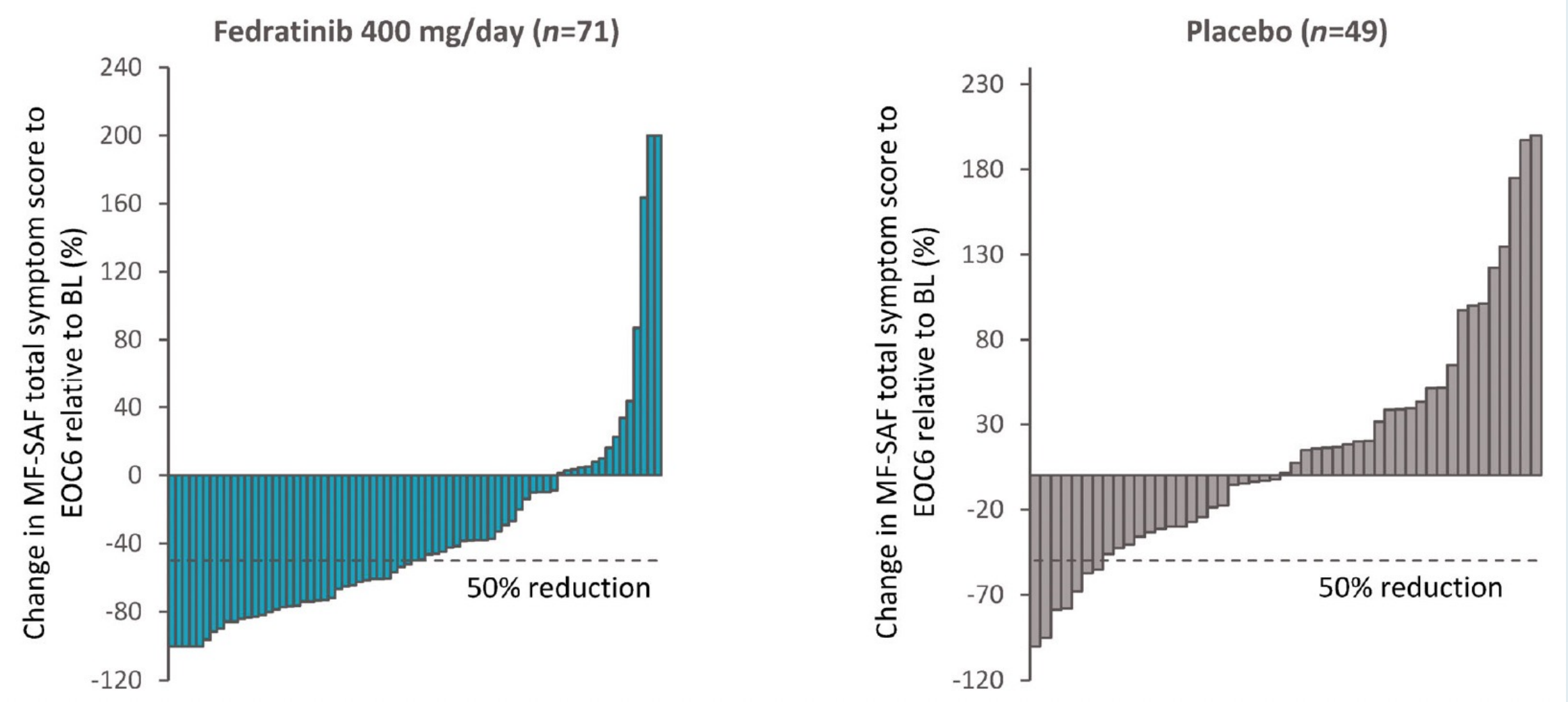
JAKARTA: Change in Spleen Volume from Baseline to End of Cycle 6



Pardanani A et al. *Br J Haematol* 2021;195:244-8.

RTP RESEARCH TO PRACTICE

JAKARTA: Change in Total Symptom Scores from Baseline to End of Cycle 6



Pardanani A et al. *Br J Haematol* 2021;195:244-8.

JAKARTA: Selected Adverse Events

Adverse events	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	19%	5%	16%	1.1%
Laboratory parameters				
Anemia	74%	34%	32%	10%
Thrombocytopenia	47%	12%	26%	10%
Neutropenia	23%	5%	13%	3.3%
Biochemistry				
Lipase increased	35%	10%	7%	2.2%

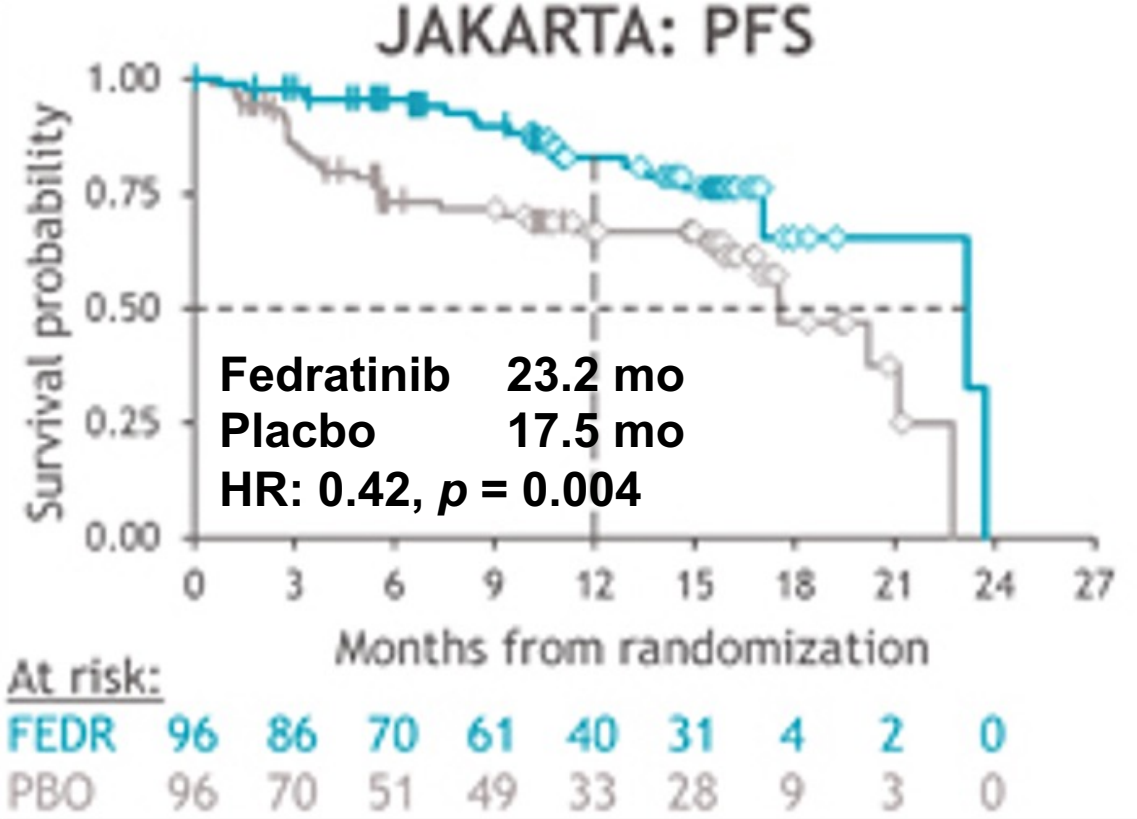
Pardanani A et al. *Br J Haematol* 2021;195:244-8.

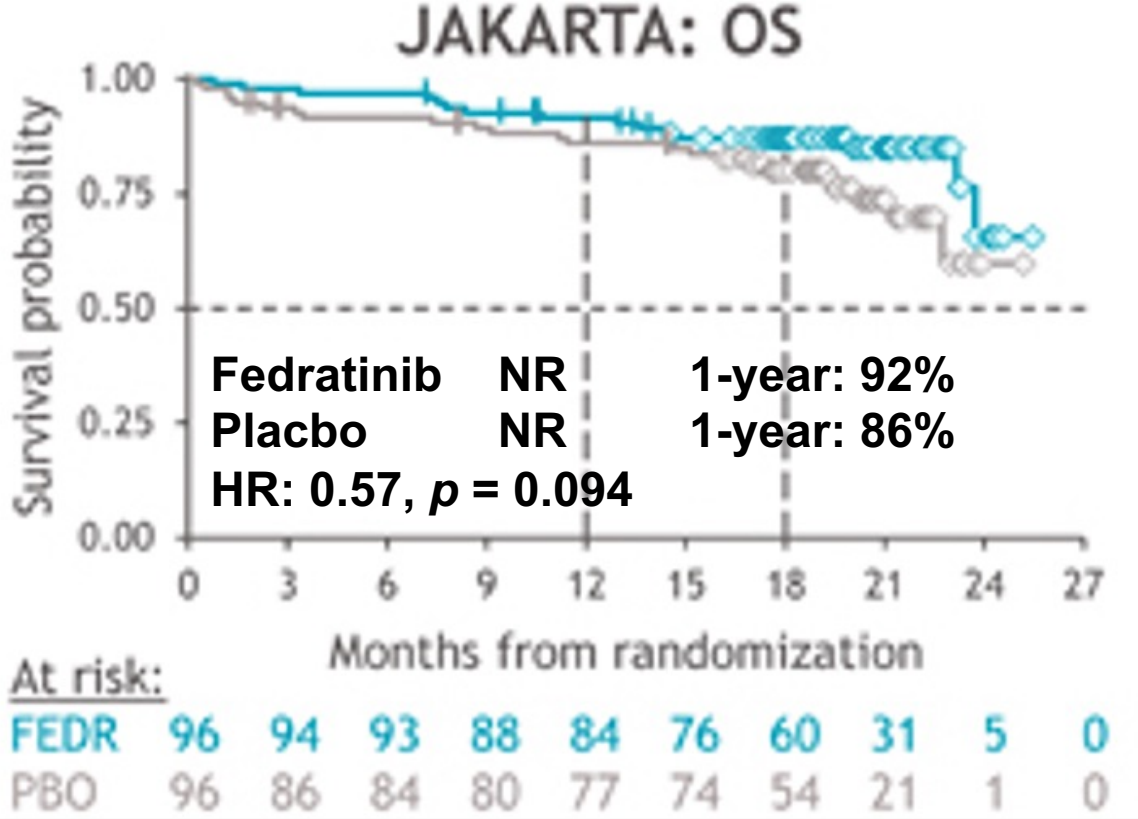
Overall and Progression-Free Survival in Patients Treated with Fedratinib as First-Line Myelofibrosis (MF) Therapy and After Prior Ruxoltinib (RUX): Results from the JAKARTA and JAKARTA2 Trials

Harrison C et al.

EHA 2021;Abstract S203.

JAKARTA: Survival Analysis



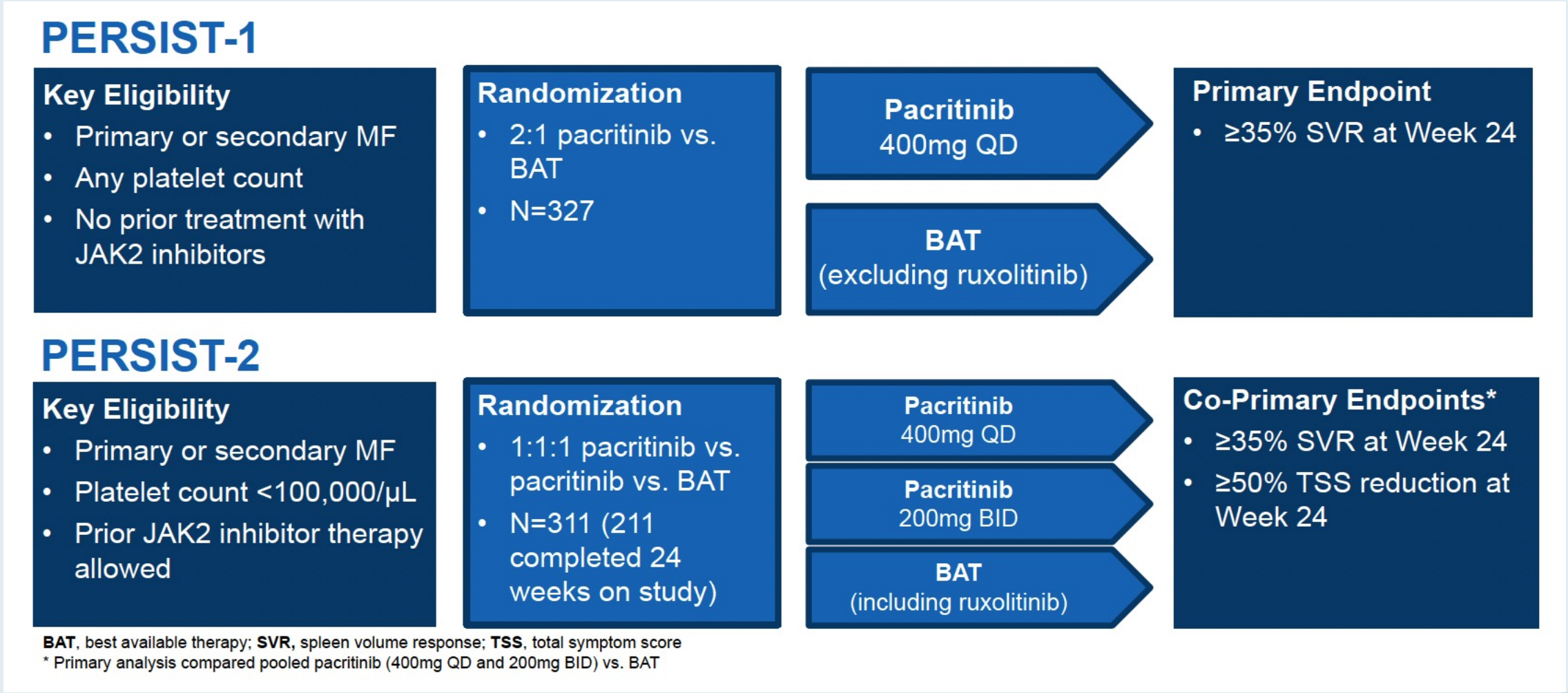


Harrison C et al. EHA 2021;Abstract S203.

RTP RESEARCH TO PRACTICE

New Option for the Management of MF in Patients with Thrombocytopenia: Pacritinib

Phase III PERSIST-1 and PERSIST-2 Study Designs



BAT, best available therapy; **SVR**, spleen volume response; **TSS**, total symptom score
* Primary analysis compared pooled pacritinib (400mg QD and 200mg BID) vs. BAT

Mesa RA et al. ASH 2019;Ab 4195.

Research

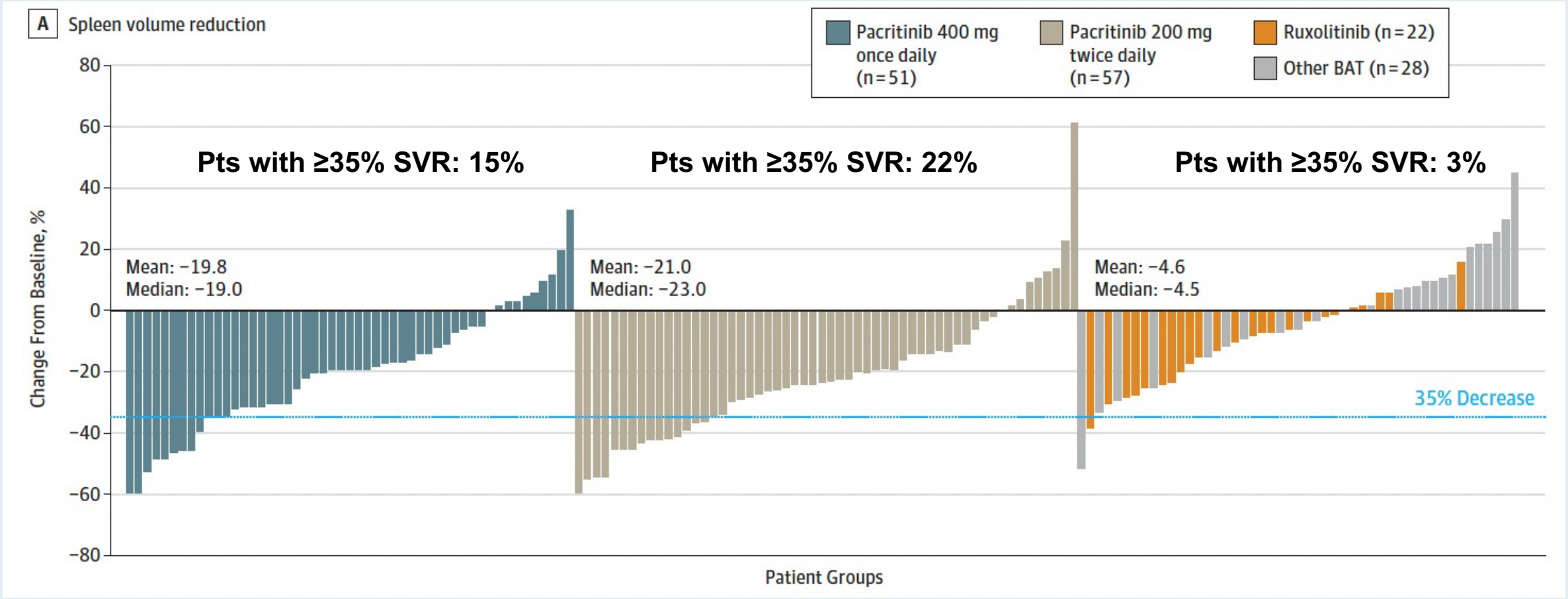
JAMA Oncol 2018;4(5):652-9.

JAMA Oncology | Original Investigation

Pacritinib vs Best Available Therapy, Including Ruxolitinib, in Patients With Myelofibrosis
A Randomized Clinical Trial

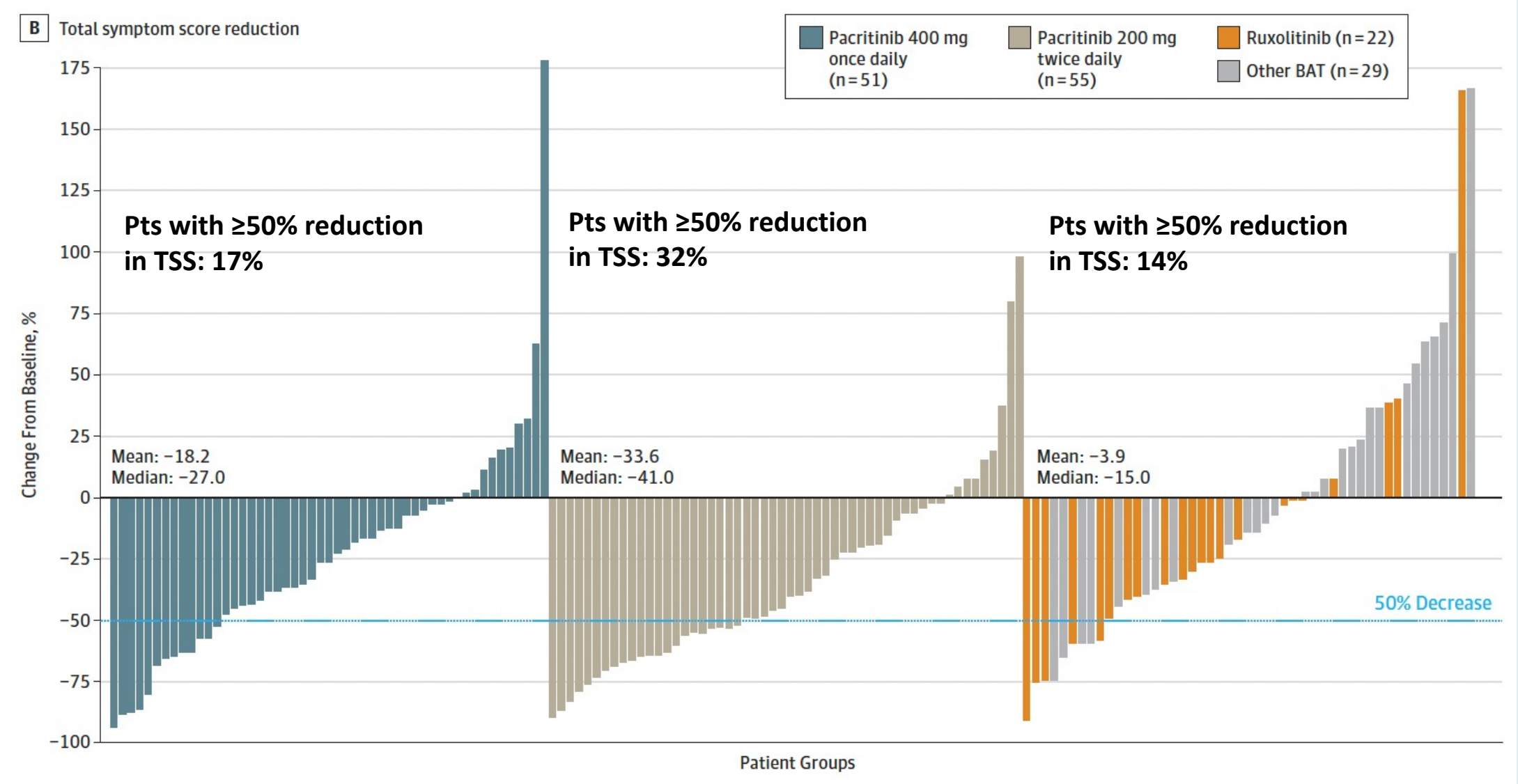
John Mascarenhas, MD; Ronald Hoffman, MD; Moshe Talpaz, MD; Aaron T. Gerds, MD; Brady Stein, MD; Vikas Gupta, MD, FRCP, FRCPath; Anita Szoke, MD; Mark Drummond, MBChB, PhD, FRCPath; Alexander Pristupa, MD; Tanya Granston, PhD; Robert Daly, PhD; Suliman Al-Fayoumi, PhD; Jennifer A. Callahan, MS; Jack W. Singer, MD; Jason Gotlib, MD; Catriona Jamieson, MD, PhD; Claire Harrison, MD, DM, FRCP, PRCPath; Ruben Mesa, MD, FACP; Srdan Verstovsek, MD, PhD

PERSIST-2: Spleen Volume Reduction



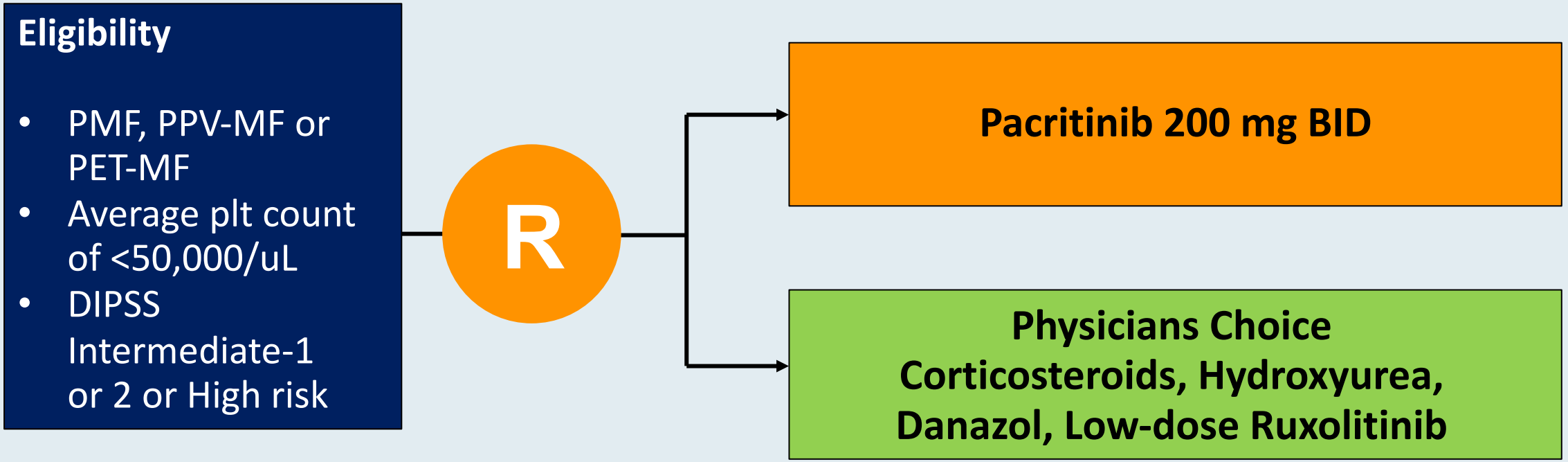
Mascarenhas J et al. *JAMA Oncol* 2018;4(5):652-9.

PERSIST-2: Reduction in Total Symptom Score



Mascarenhas J et al. *JAMA Oncol* 2018;4(5):652-9.

PACIFICA (PAC303) Study Design



Primary Endpoint: Spleen volume
Secondary Endpoints: Total Symptom Score, OS, Patient Global Impression of Change

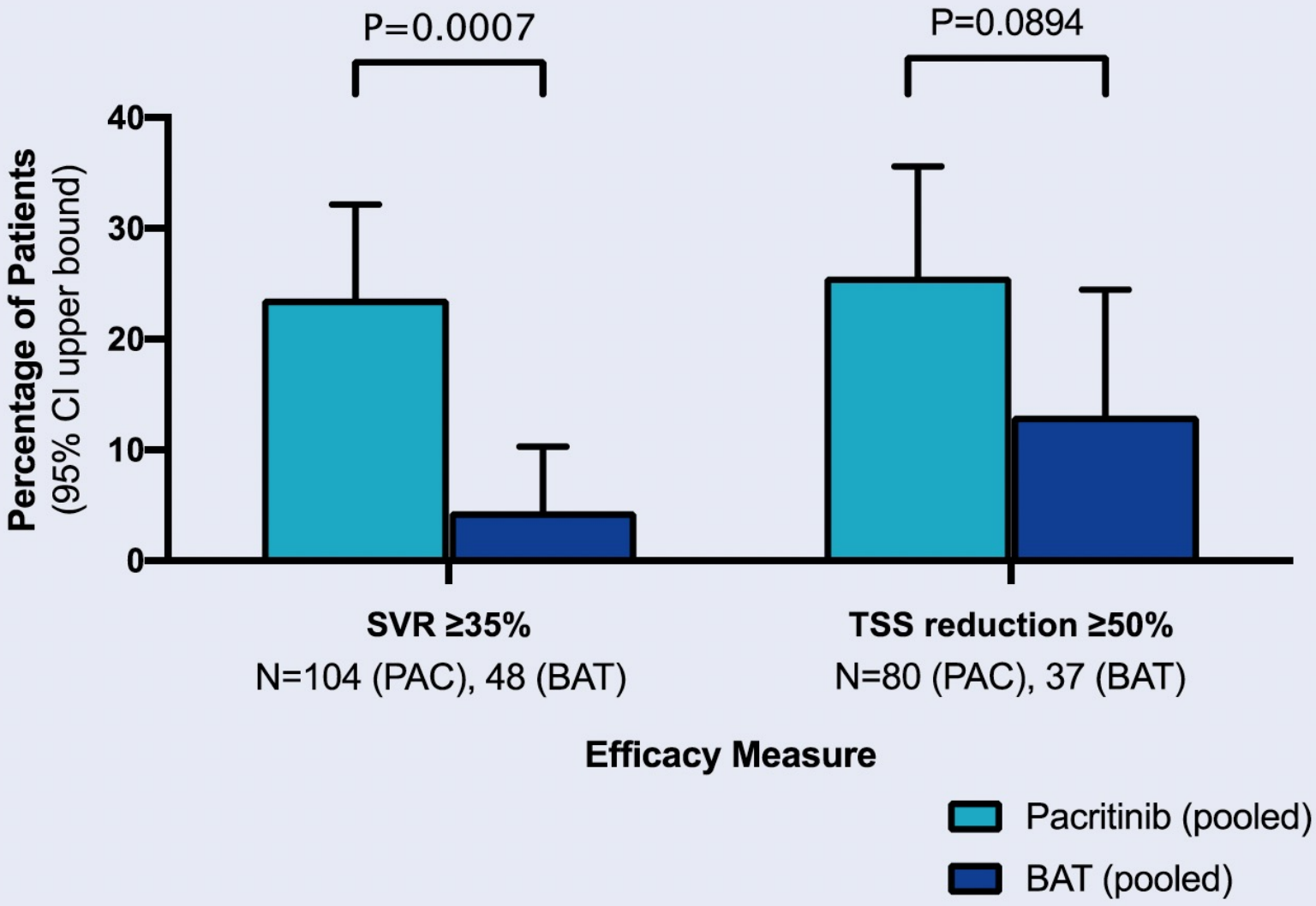
https://clinicaltrials.gov/ct2/show/NCT03165734

Pacritinib Demonstrates Efficacy Versus Best Available Therapy in Myelofibrosis Patients with Severe Thrombocytopenia in Two Phase 3 Studies

Mesa RA et al.

ASH 2019;Abstract 4195.

PERSIST-1 and PERSIST-2: Pacritinib versus BAT Efficacy Outcomes (Week 24) in Patients with Baseline Platelet Counts <50,000/µL



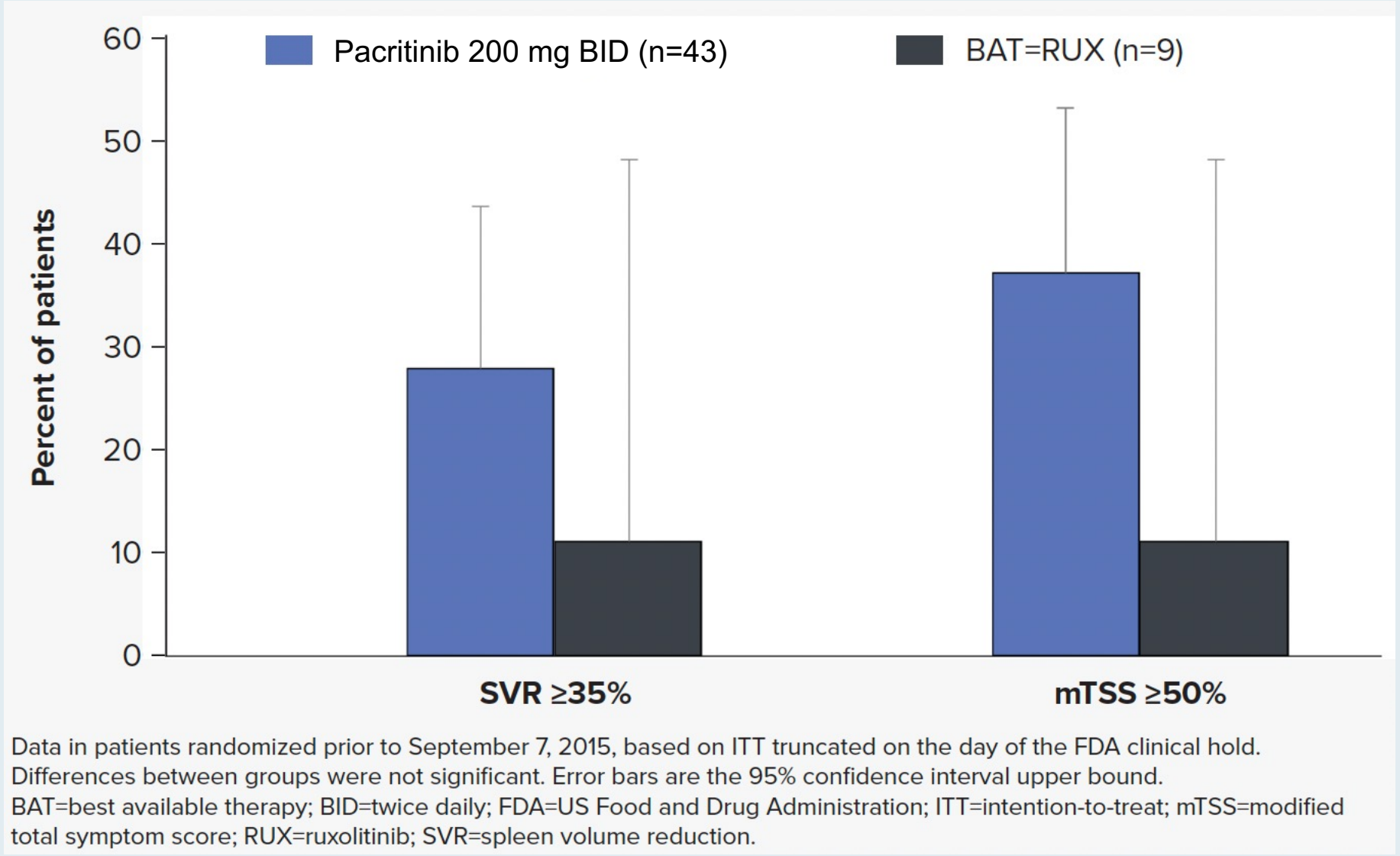
Mesa RA et al. ASH 2019;Abstract 4195.

A Retrospective Head-to-Head Comparison Between Pacritinib and Ruxolitinib in Patients with Myelofibrosis and Moderate-to-Severe Thrombocytopenia

Mascarenhas J et al.

ASH 2021;Abstract 3639.

Proportion of Patients Meeting SVR and Modified TSS Thresholds in a Retrospective Analysis of PERSIST-2



Data in patients randomized prior to September 7, 2015, based on ITT truncated on the day of the FDA clinical hold. Differences between groups were not significant. Error bars are the 95% confidence interval upper bound.
BAT=best available therapy; BID=twice daily; FDA=US Food and Drug Administration; ITT=intention-to-treat; mTSS=modified total symptom score; RUX=ruxolitinib; SVR=spleen volume reduction.

Mascarenhas J et al. ASH 2021;Abstract 3639.

Safety Analysis of Pacritinib in Patients with Myelofibrosis and Severe Thrombocytopenia

Mascarenhas J et al.

ASH 2021;Abstract 3640.

Overview of Adverse Events in the Target Population in PERSIST-2 and PAC203

AE, n (%)	PERSIST-2		PAC203	Total (pooled)
	Pacritinib 200 mg BID (n=47)	BAT[a] (n=42)	pacritinib 200 mg BID (n=24)	pacritinib 200 mg BID (N=71)
TEAE (all grades)	46 (98)	38 (91)	24 (100)	70 (99)
Grade ≥3 TEAE	39 (83)	26 (62)	23 (96)	62 (87)
Treatment-emergent serious AE	28 (60)	16 (38)	16 (67)	44 (62)
Grade ≥3 treatment-emergent serious AE	25 (53)	15 (36)	14 (58)	39 (55)
TEAE leading to study drug discontinuation	10 (21)	7 (17)	4 (17)	14 (20)
TEAE with an outcome of death	6 (13)	8 (19)	3 (13)	9 (13)

[a]The most common BAT was ruxolitinib (40%) and watch and wait (31%).
AE=adverse event; BAT=best available therapy; BID=twice daily; TEAE=treatment-emergent adverse event.

Mascarenhas J et al. ASH 2021;Abstract 3640.

Summary of Hemorrhage AEs, Cardiac AEs and MACE in the Target Population in PERSIST-2 and PAC203

AE, n (%)	PERSIST-2 Pacritinib 200 mg BID (n=47)	PERSIST-2 BAT[a] (n=42)	PAC203 pacritinib 200 mg BID (n=24)	Total (pooled) pacritinib 200 mg BID (N=71)
Treatment-emergent hemorrhage AEs (SMQ)[b]				
Any-grade bleeding AEs	23 (49)	26 (62)	18 (75)	41 (58)
Serious bleeding AEs	6 (13)	4 (10)	2 (8)	8 (11)
Grade ≥3 bleeding AEs	8 (17)	5 (12)	3 (13)	11 (16)
Treatment-emergent cardiac AEs (SMQ)[b]				
Any-grade cardiac AEs	16 (34)	19 (45)	13 (54)	29 (41)
Serious cardiac AEs	4 (9)	9 (21)	3 (13)	7 (10)
Grade ≥3 cardiac AEs	4 (9)	8 (19)	2 (8)	6 (9)
MACE category[c]				
MACE	0 (0)	2 (5)	0 (0)	0 (0)
MACE death (Grade 5)	0 (0)	1 (2)	0 (0)	0 (0)

[a]The most common BAT agents were ruxolitinib and watch and wait. [b]Bleeding and cardiac events defined by SMQ include the preferred terms in hemorrhage and cardiac arrhythmias, cardiac failure, ischemic heart disease, and embolic and thrombotic events, respectively.

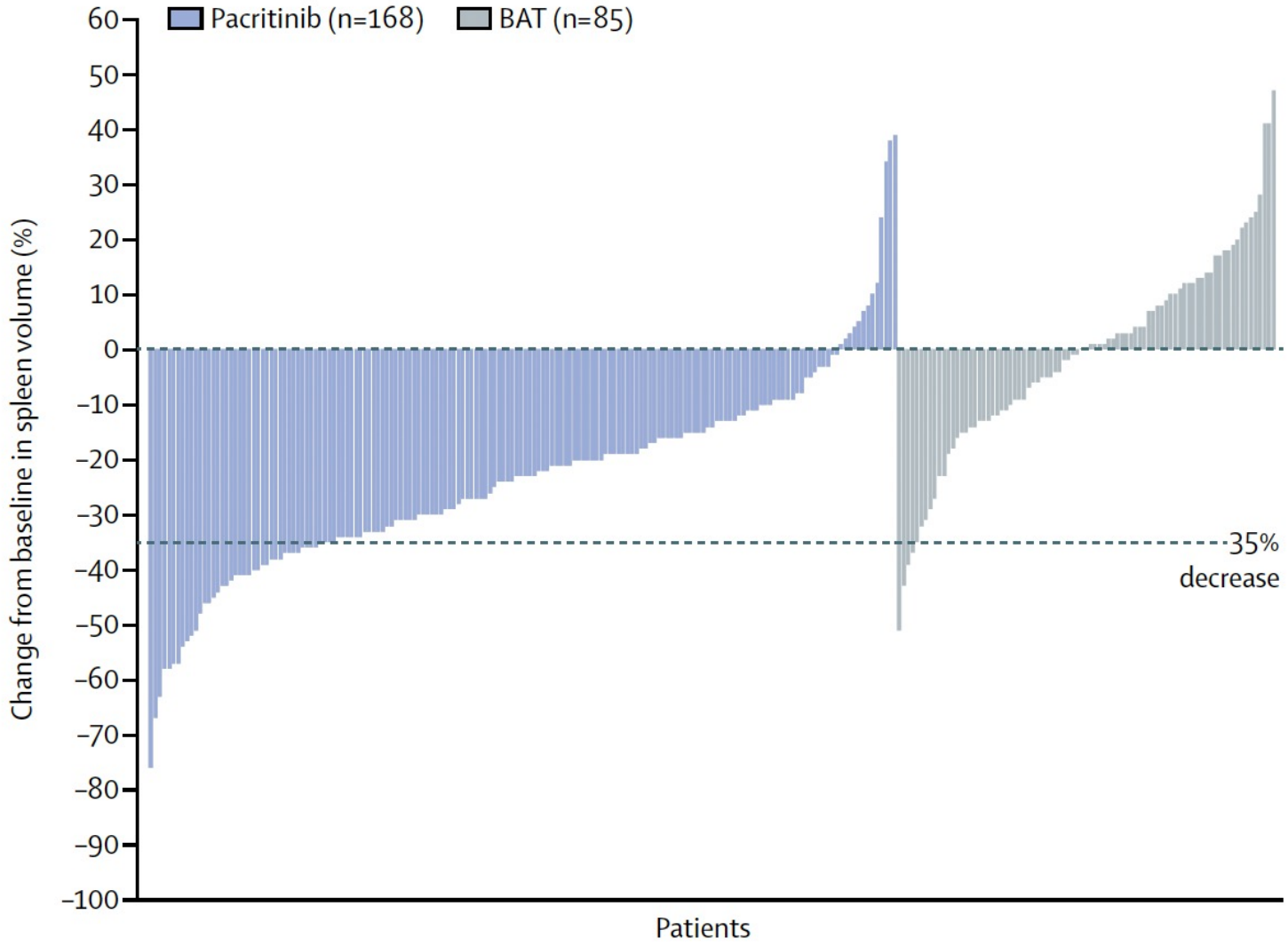
Mascarenhas J et al. ASH 2021;Abstract 3640.

Lancet Haematol 2017;4:e225-36

Pacritinib versus best available therapy for the treatment of myelofibrosis irrespective of baseline cytopenias (PERSIST-1): an international, randomised, phase 3 trial

Ruben A Mesa, Alessandro M Vannucchi, Adam Mead, Miklos Egyed, Anita Szoke, Aleksandr Suvorov, Janos Jakucs, Andrew Perkins, Ritam Prasad, Jiri Mayer, Judit Demeter, Peter Ganly, Jack W Singer, Huafeng Zhou, James P Dean, Peter A te Boekhorst, Jyoti Nangalia, Jean-Jacques Kiladjian, Claire N Harrison

PERSIST-1: Reduction in Spleen Volume at Week 24



≥35% reduction in spleen volume at week 24 in evaluable patients			
	Pacritinib (N = 168)	**BAT (n = 85)**	***p*-value**
Overall	25%	6%	0.0001
Plts <100,000/uL	24%	0	0.0072
Plts <50,000/uL	33%	0	0.037

Mesa RA et al. *Lancet Haematol* 2017;4:e225-36.

PERSIST-1: Patients Achieving ≥50% Reduction in Total Symptom Score 2.0 at weeks 24 and 48

	Week 24			Week 48		
	Pacritinib	BAT	p value	Pacritinib	BAT	p value
Overall	19/100 (19%)	5/48 (10%)	0·24	15/100 (15%)	0/48	0·0027
Platelets						
<100 000/μL	7/28 (25%)	1/13 (8%)	0·40	3/28 (11%)	0/13	0·54
<50 000/μL	3/11 (27%)	0/5	0·51	2/11 (18%)	0/5	1·0

Data are n/N (%).

Mesa RA et al. *Lancet Haematol* 2017;4:e225-36.

PERSIST-1: Select Adverse Events

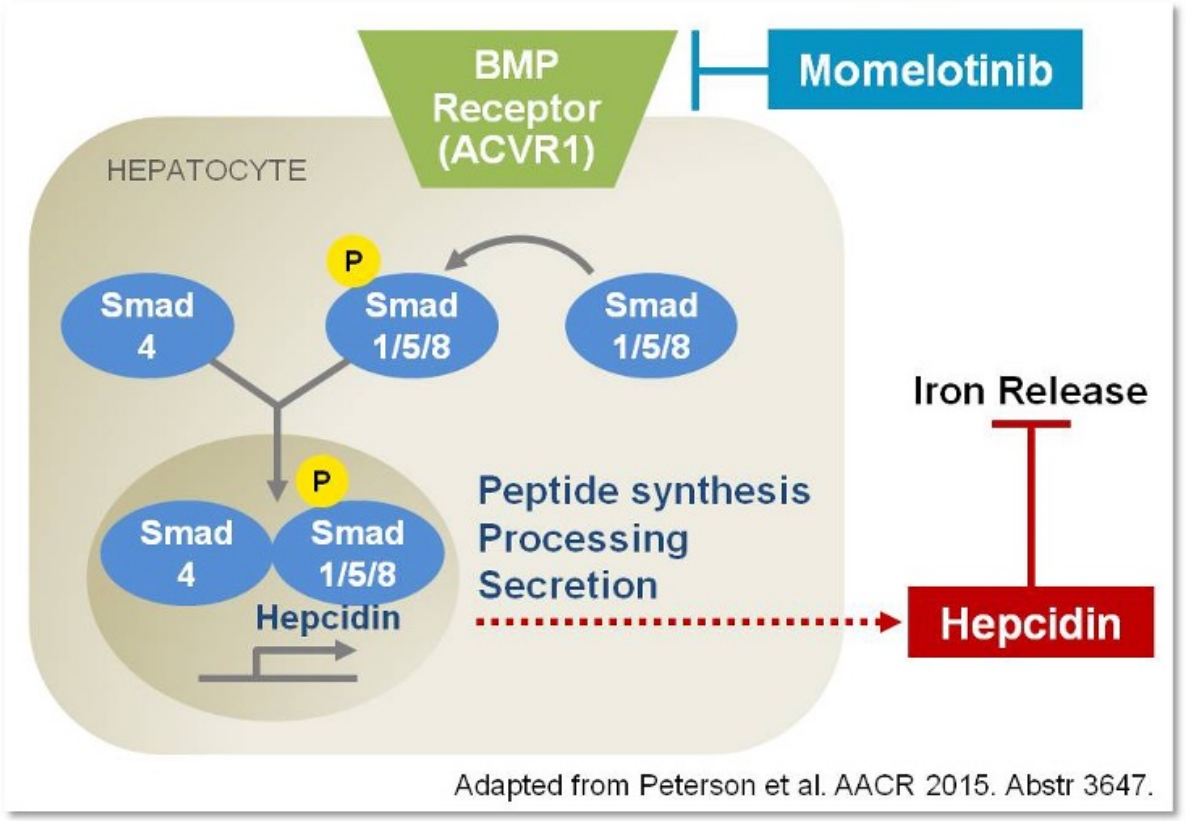
	Pacritinib (N = 220)		BAT (N = 106)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Diarrhea	55%	5%	10%	0
Nausea	27%	1%	7%	0
Anemia	24%	17%	20%	15%
Thrombocytopenia	17%	11%	14%	11%
Vomiting	16%	1%	6%	0
Fatigue	10%	2%	9%	1%

Mesa RA et al. *Lancet Haematol* 2017;4:e225-36.

Potential Front-Line Option for Patients with MF and Significant Anemia and/or Transfusion Dependence: Momelotinib

Momelotinib Mechanism of Action

- MMB also inhibits activin A receptor, Type 1 (ACVR1)
- ACVR1 activation leads to increased hepcidin gene expression[1]
- Hepcidin decreases plasma iron and hepcidin is elevated in MF[2]
- MMB ameliorates anemia in a rodent ACD model[1]



Adapted from Peterson et al. AACR 2015. Abstr 3647.

1. Asshoff M, et al. Blood 2017;129:1823-30; 2. Pardanani A, et al. Am J Hematology 2013;88:312-6.
ACVR1: Activin A Receptor, Type 1; BMP, bone morphogenic protein.

Harrison CN et al. ASCO 2017;Abstract 7001.

VOLUME 35 · NUMBER 34 · DECEMBER 1, 2017

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

SIMPLIFY-1: A Phase III Randomized Trial of Momelotinib Versus Ruxolitinib in Janus Kinase Inhibitor–Naïve Patients With Myelofibrosis

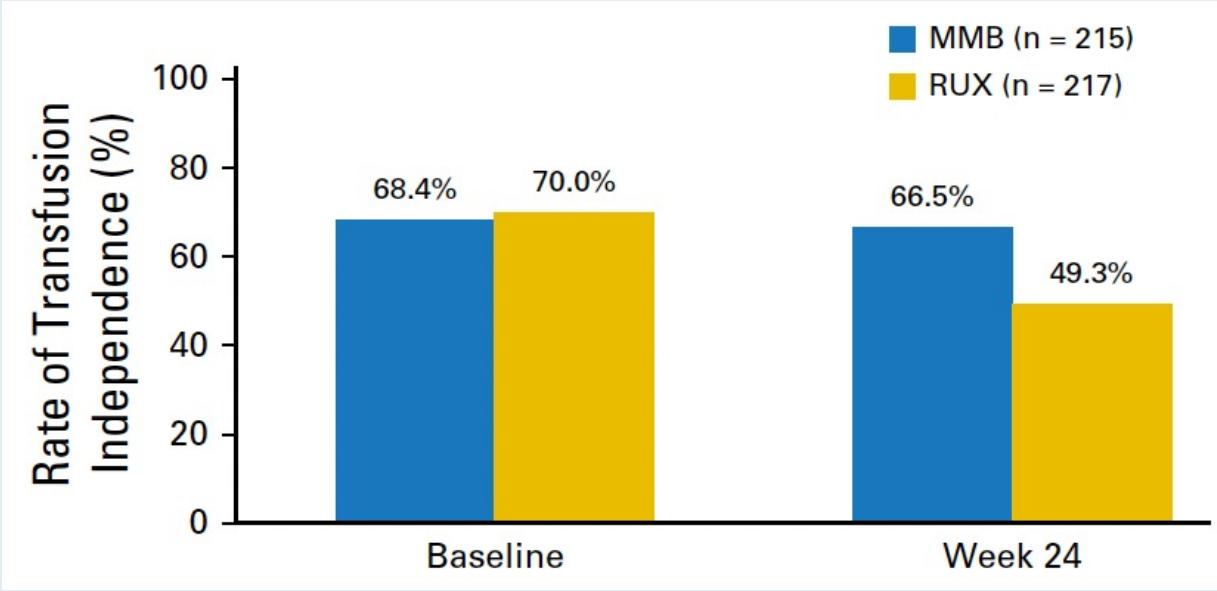
Ruben A. Mesa, Jean-Jacques Kiladjian, John V. Catalano, Timothy Devos, Miklos Egyed, Andrzei Hellmann, Donal McLornan, Kazuya Shimoda, Elliott F. Winton, Wei Deng, Ronald L. Dubowy, Julia D. Maltzman, Francisco Cervantes, and Jason Gotlib

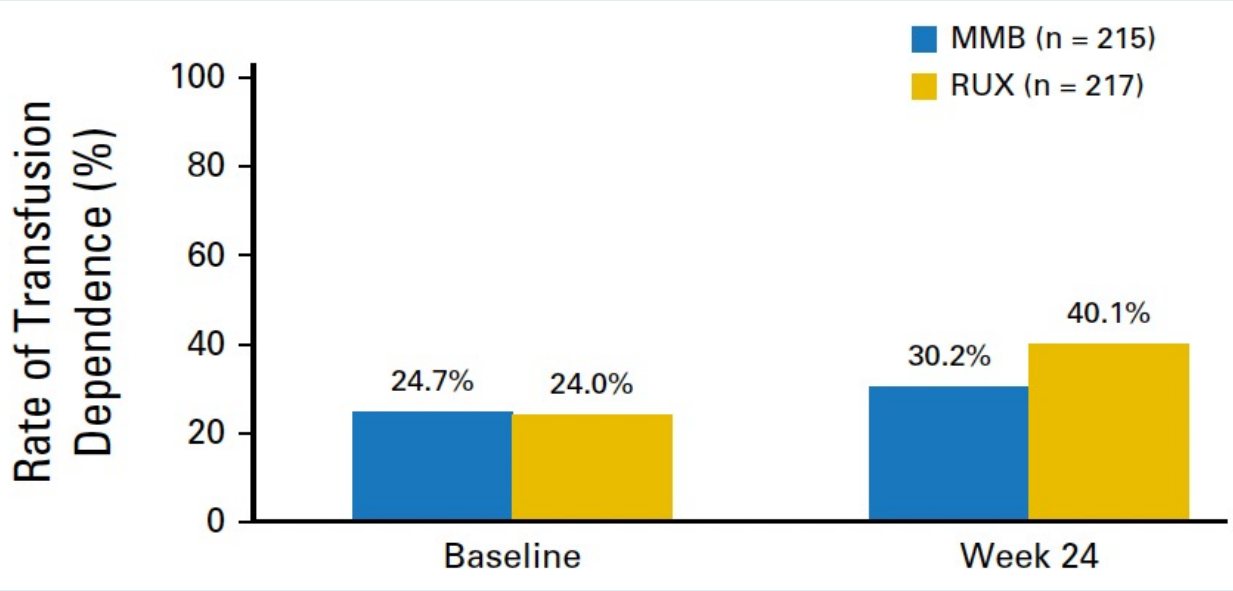
SIMPLIFY-1 Trial of Momelotinib (MMB) in Patients with Treatment-Naïve MF

Efficacy outcomes	SIMPLIFY-1, Wk 24[1]		
	MMB (n = 215)	RUX (n = 217)	*p*-value
Spleen volume reduction ≥ 35%	26.5%	29.0%	0.011
≥50% reduction in MF-SAF TSS	28.4%	42.2%	0.98
Transfusion independence at week 24	66.5%	49.3%	<0.001
Safety outcomes			
Discontinued due to AEs	13.1%	5.6%	NR
Grade 3/4 anemia	5.6%	23.1%	
Grade 3/4 thrombocytopenia	7.0%	4.6%	
Grade 3/4 neutropenia	2.8%	4.6%	

Mesa RA et al. *J Clin Oncol* 2017;35(34):3844-50.

SIMPLIFY-1: Momelotinib versus Ruxolitinib Effects on Transfusion Requirements at Week 24





Mesa RA et al. *J Clin Oncol* 2017;35(34):3844-50.

RTP RESEARCH TO PRACTICE

Evolving Therapeutic Landscape for Individuals with MF Progressing on or Intolerant to Initial JAK Inhibitor Therapy

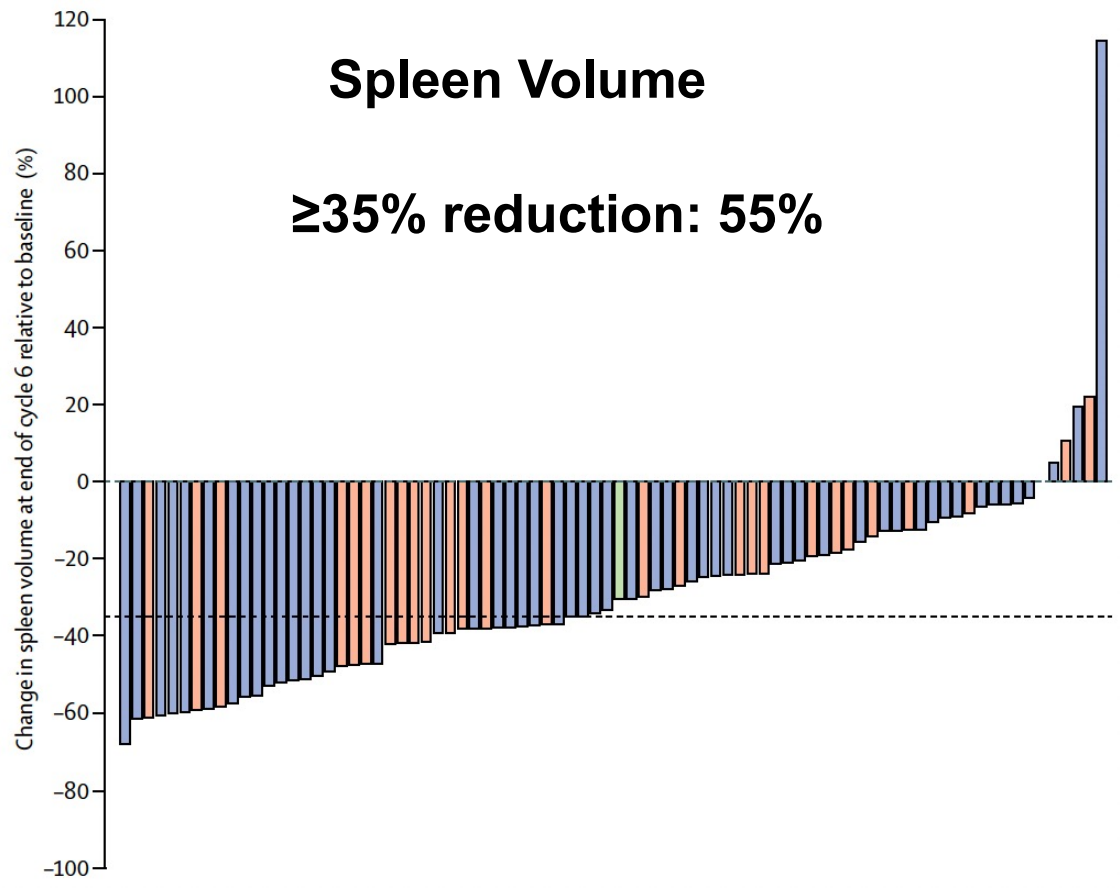
- JAKARTA-2: Fedratinib in patients with intermediate- or high-risk MF resistant or intolerant to ruxolitinib
- Ongoing FREEDOM and FREEDOM2 trials of fedratinib after ruxolitinib
- SIMPLIFY-2: Momelotinib

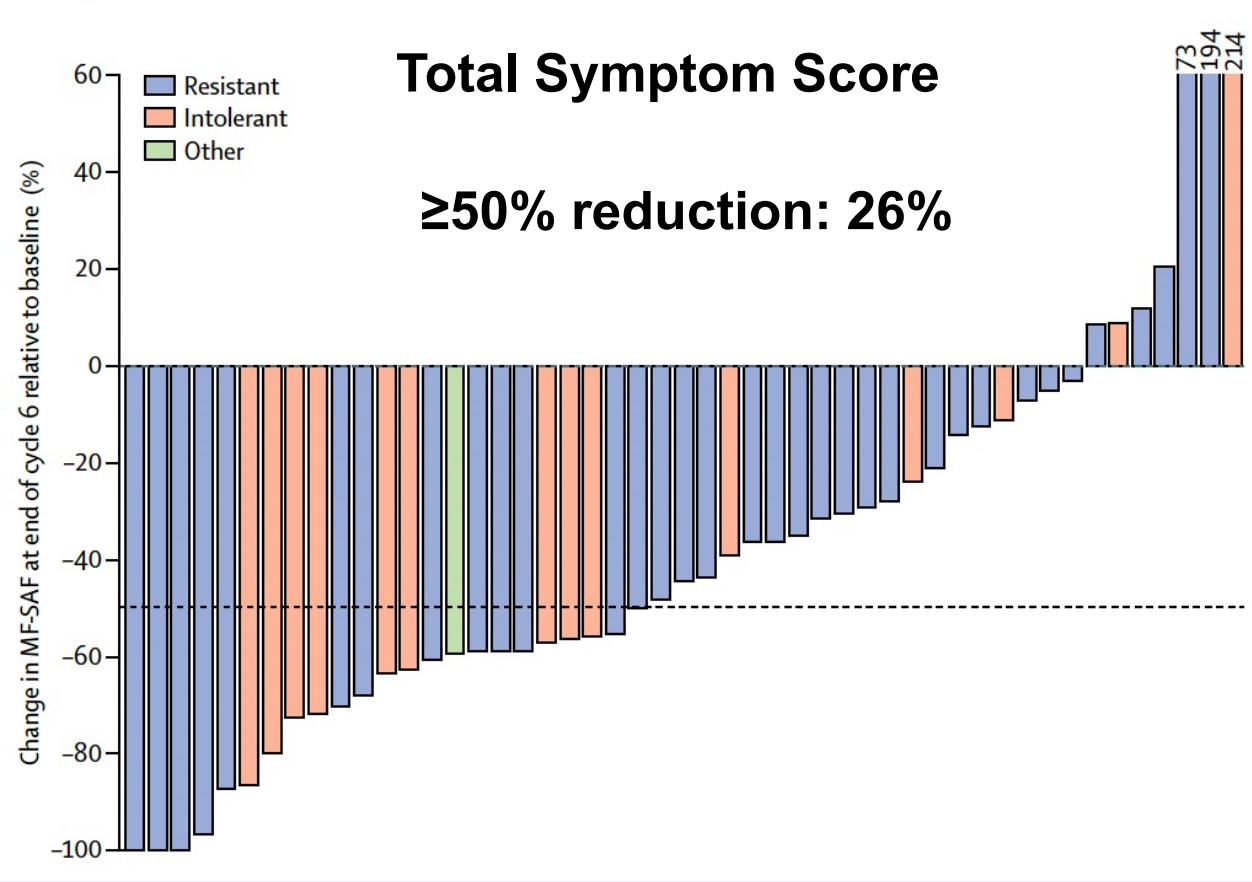
Lancet Haematol 2017;4:e317-24.

Janus kinase-2 inhibitor fedratinib in patients with myelofibrosis previously treated with ruxolitinib (JAKARTA-2): a single-arm, open-label, non-randomised, phase 2, multicentre study

Claire N Harrison, Nicolaas Schaap, Alessandro M Vannucchi, Jean-Jacques Kiladjian, Ramon V Tiu, Pierre Zachee, Eric Jourdan, Elliott Winton, Richard T Silver, Harry C Schouten, Francesco Passamonti, Sonja Zweegman, Moshe Talpaz, Joanne Lager, Zhenming Shun, Ruben A Mesa

JAKARTA-2: Change in Total Symptom Score and Spleen Volume from Baseline to End of Cycle 6





Harrison CN et al. *Lancet Haematol* 2017;4:e317-24.

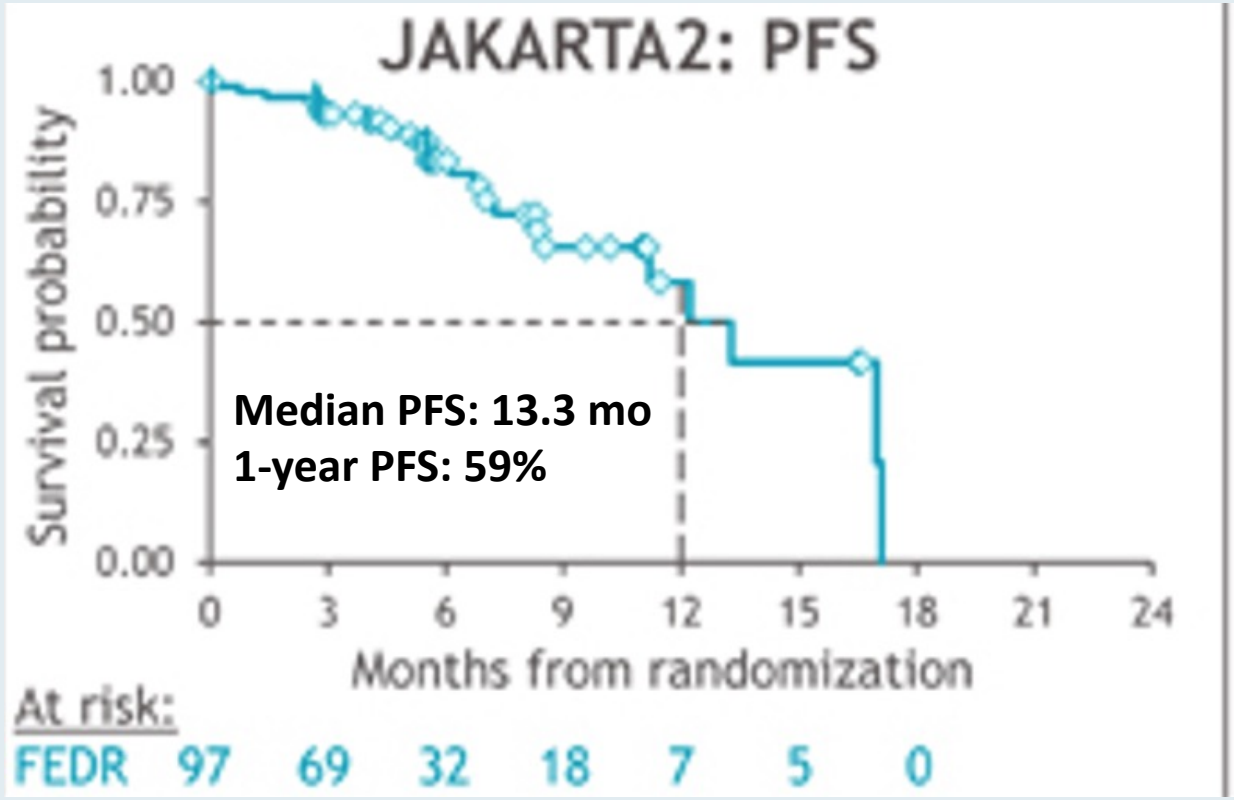
RTP RESEARCH TO PRACTICE

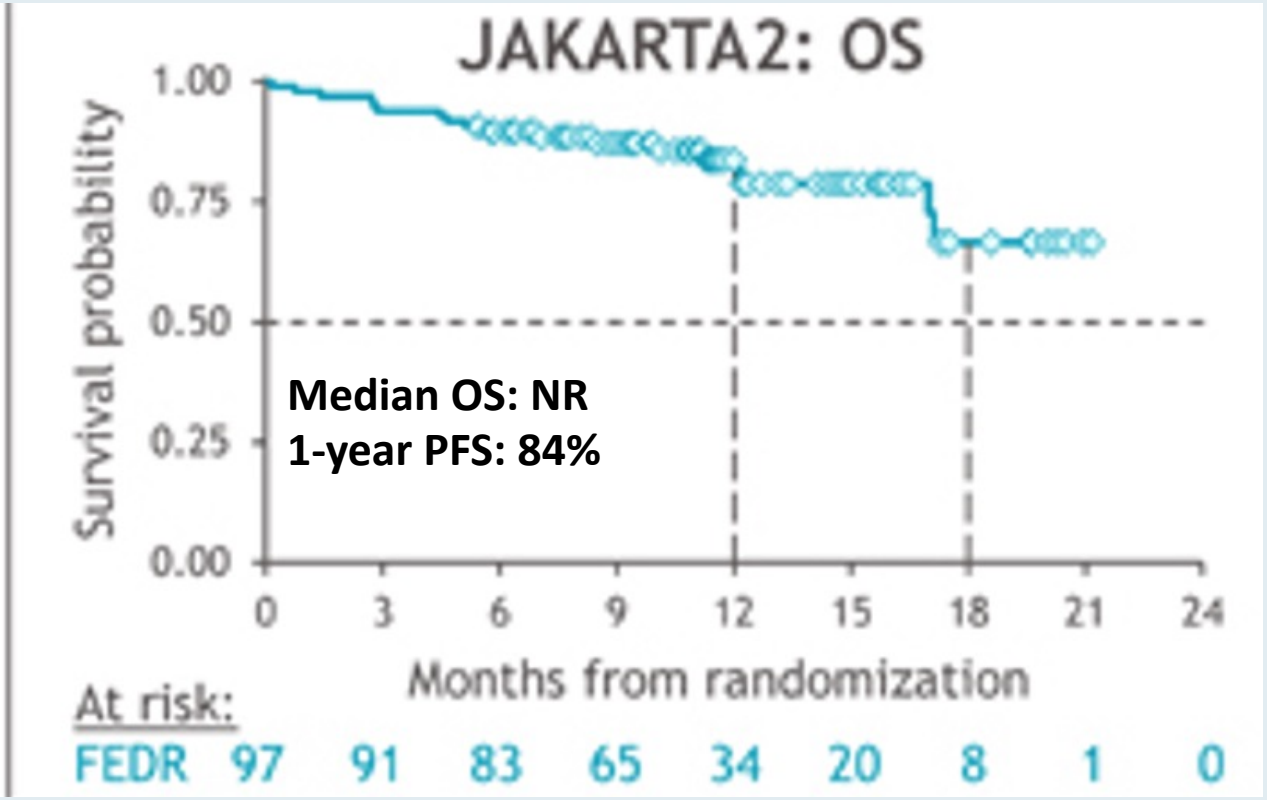
Overall and Progression-Free Survival in Patients Treated with Fedratinib as First-Line Myelofibrosis (MF) Therapy and After Prior Ruxoltinib (RUX): Results from the JAKARTA and JAKARTA2 Trials

Harrison C et al.

EHA 2021;Abstract S203.

JAKARTA2: Survival Analysis





Harrison C et al. EHA 2021;Abstract S203.

RTP RESEARCH TO PRACTICE

FREEDOM: Trial Design and Key Eligibility Criteria

International, single-arm, open-label, phase 3b trial (NCT03755518)

Key eligibility criteria

- Age ≥ 18 years
- Primary, post-PV, or post-ET MF
- Prior Tx with RUX[a]
- DIPSS Int/High risk
- ECOG PS score ≤ 2
- Platelets ≥ 50 × 10^9/L
- ANC ≥ 1 × 10^9/L
- Spleen volume ≥ 450 cm^3 *or* palpable spleen ≥ 5 cm below LCM
- PB blasts ≤ 5%

Treatment phase

Fedratinib 400 mg/d
(Continuous 28d Tx cycles)

Total enrollment: N = 38

Continue fedratinib until lack of efficacy, intolerance, disease progression or withdrawal of consent

Follow-up

Follow-up for 12 months after end of Tx

Primary endpoint:

- **SVRR at EOC6: Proportion of pts with ≥ 35% spleen volume reduction from baseline (BL)**

Key secondary endpoints:

- Symptom RR at EOC6: Proportion of pts with ≥ 50% improvement in MFSAF TSS from BL
- Safety; assess risk mitigation for GI AEs and potential WE
- Spleen response by palpation
- Durability of spleen and symptom responses

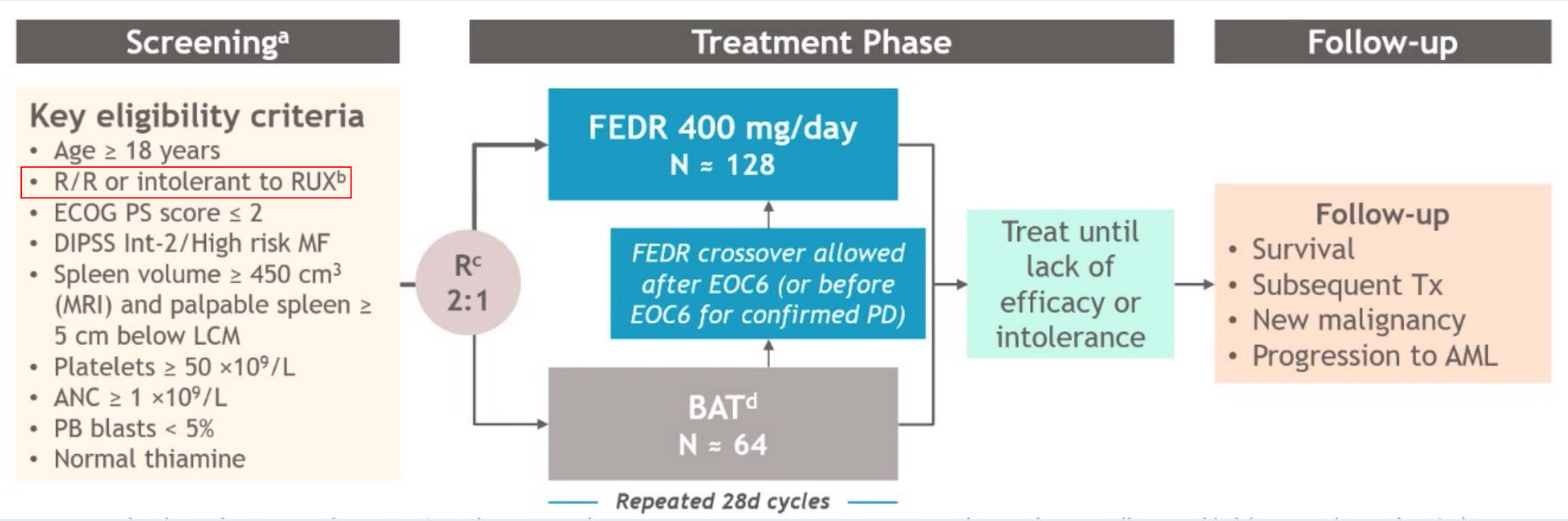
AE mitigation strategies:

- Prophylactic/symptomatic use of anti-emetic/vomiting and anti-diarrheal Tx
- Administration of fedratinib with food
- Fedratinib dosing modifications
- Thiamine supplementation

[a]Pts must have received RUX for ≥3 mo, or for ≥28 d with development of RBC transfusion requirement (≥2 units/mo for 2 mo) or Grade ≥3 thrombocytopenia, anemia, hematoma or hemorrhage.

Gupta V et al. ASH 2021;Abstract 389.

FREEDOM2 Phase III Study Design



Vianelli N et al. ASH 2021;Abstract 3643.

Articles

Momelotinib versus best available therapy in patients with myelofibrosis previously treated with ruxolitinib (SIMPLIFY 2): a randomised, open-label, phase 3 trial

Claire N Harrison, Alessandro M Vannucchi, Uwe Platzbecker, Francisco Cervantes, Vikas Gupta, David Lavie, Francesco Passamonti, Elliott F Winton, Hua Dong, Jun Kawashima, Julia D Maltzman, Jean-Jacques Kiladjian, Srdan Verstovsek

Lancet Haematol 2018;5(2):e73-81.

SIMPLIFY-2 Trial of Momelotinib (MMB) in Patients with MF Previously Treated with Ruxolitinib

Efficacy outcomes	SIMPLIFY-2, Wk 24		*p*-value
	MMB (n = 104)	BAT (n = 52)	
Spleen volume reduction ≥35%	7%	6%	0.90
≥50% reduction in MF-SAF TSS	26%	6%	0.0006
Transfusion independence	43%	26%	0.0012
Safety outcomes			
Discontinued due to AEs	21%	16%	NR
Grade 3/4 anemia	14%	14%	
Grade 3/4 thrombocytopenia	7%	6%	
Grade 3/4 neutropenia	NR	NR	

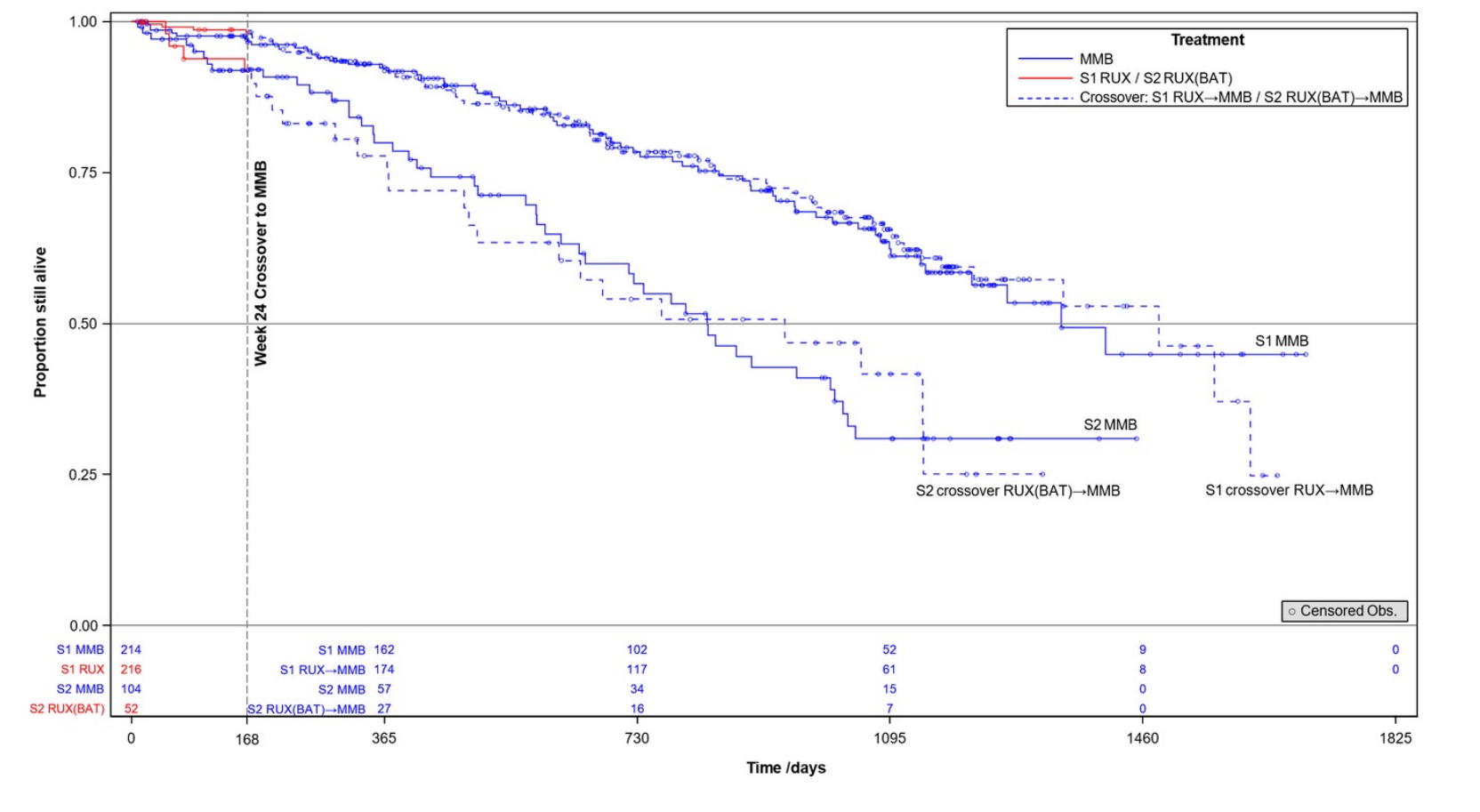
Harrison CN et al. *Lancet Haematol* 2018;5(2):e73-81.

Robust Overall Survival and Sustained Efficacy Outcomes during Long Term Exposure to Momelotinib in JAK Inhibitor Naïve and Previously JAK Inhibitor Treated Intermediate/High Risk Myelofibrosis Patients

Verstovsek S et al.

ASH 2020;Abstract 54.

SIMPLIFY-1 (S1) and SIMPLIFY-2 (S2): Long-Term Outcomes with MMB



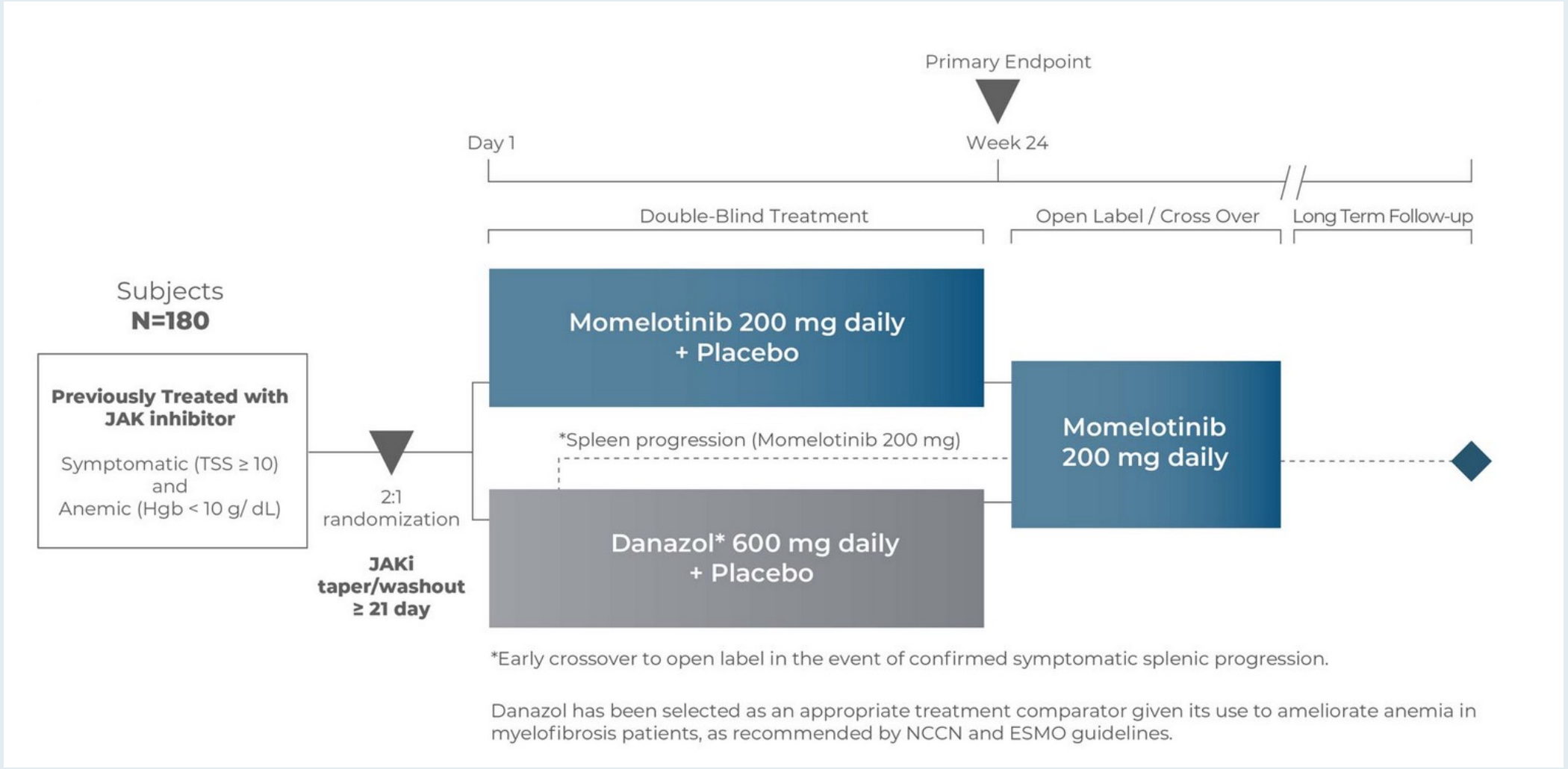
- S1 reduction in spleen volume of ≥35% from baseline at week 24 (MMB vs RUX): 26.5% vs 29.5%
- S1 transfusion independence at week 24 (MMB vs RUX): 70% vs 54%
- S2 transfusion independence at week 24 (MMB vs BAT/RUX): 44% vs 27%

Verstovsek S et al. ASH 2020;Abstract 54.

RTP RESEARCH TO PRACTICE

MOMENTUM: Phase III Trial Schema of Momelotinib in MF

Trial Identifier: NCT04173494 (Closed)



Verstovsek S et al. *Future Oncology* 2021;17(12):1449-58.

RTP RESEARCH TO PRACTICE

Novel Agents and Strategies Beyond JAK Inhibitors Under Investigation in MF

A Phase 2 Study of the LSD1 Inhibitor Img-7289 (Bomedemstat) for the Treatment of Advanced Myelofibrosis

Gill H et al.

ASH 2021;Abstract 139.

Phase I/II Trial of Bomedemstat for Advanced MF

Primary Endpoints

- Safety and tolerability
- Pharmacokinetics in first 15 patients
- Spleen volume reduction

Secondary Endpoints

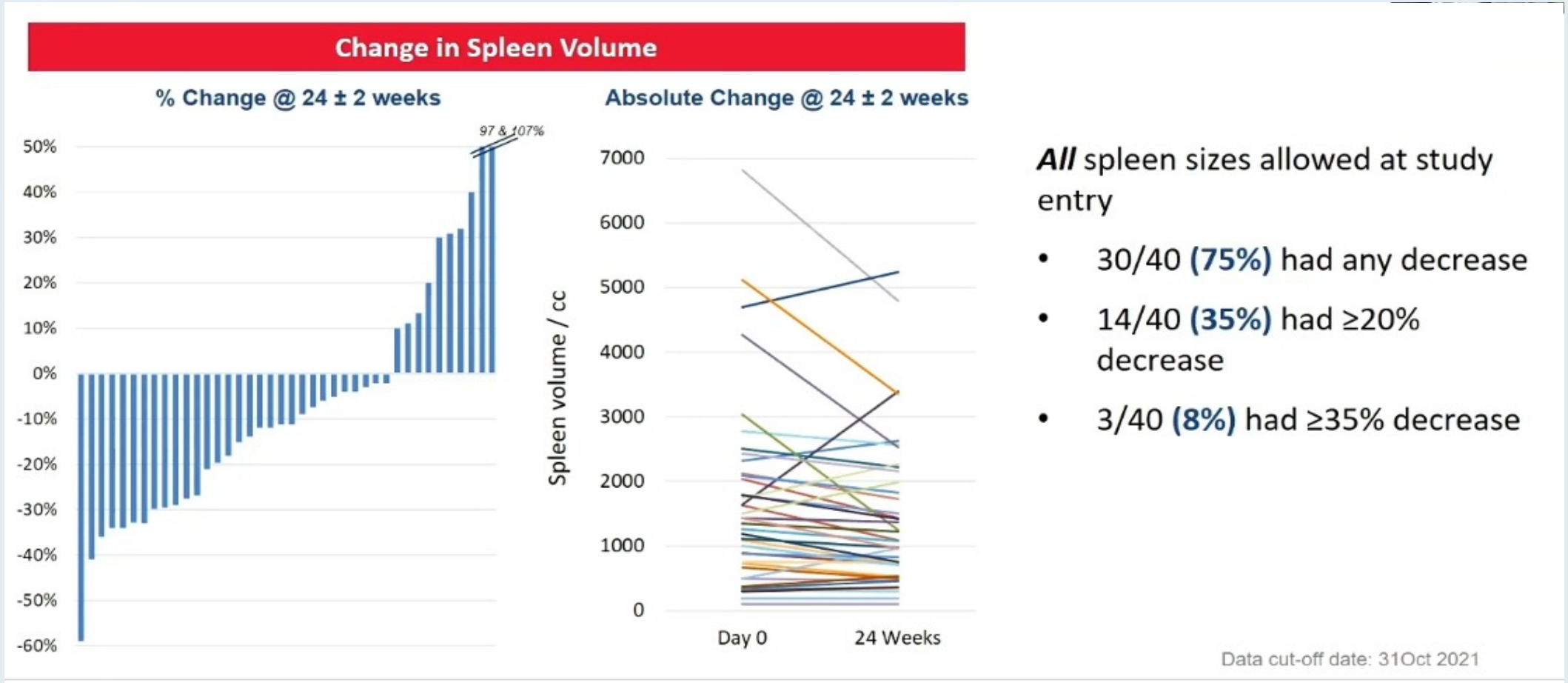
- Symptom reduction (MPN-SAF TSS)
- Changes in cytokine profiles
- Changes in mutant allele frequencies (MAF)
- Changes in bone marrow (BM) fibrosis

Key Eligibility Criteria

- Dx of PMF, PET-MF, or PPV-MF
- Refractory or resistant to, intolerant of, inadequate control by, or ineligible for, available approved therapies
- IPSS Intermediate-1, -2 or High-risk disease
- **Platelets ≥100 x10^9/L**
- Peripheral blasts ≤10%
- Spleen of ***any size***
- ECOG PS ≤2

Gill H et al. ASH 2021;Abstract 139.

Spleen Volume Reduction and Total Symptom Score at 24 Weeks with Bomedemstat



- 17/23 patients (74%) had a decrease in TSS and 6/23 patients (26%) had a decrease of ≥50%.

Gill H et al. ASH 2021;Abstract 139.

RTP RESEARCH TO PRACTICE

Safety and Tolerability of Bomedemstat

Preferred Term (N=90)	Any Grade AEs	Grade 3/4 AEs
Thrombocytopenia	42 (47%)	35 (39%)
Dysgeusia	29 (32%)	0
Anaemia	29 (32%)	20 (22%)
Diarrhoea	27 (30%)	0
Nausea	25 (28%)	2 (2%)
Fatigue	22 (24%)	4 (4%)
Constipation	21 (23%)	1 (1%)
Oedema peripheral	18 (20%)	1 (1%)
Arthralgia	16 (18%)	0
Abdominal pain	15 (17%)	1 (1%)
Decreased appetite	14 (16%)	2 (2%)
Pruritus	14 (16%)	2 (2%)

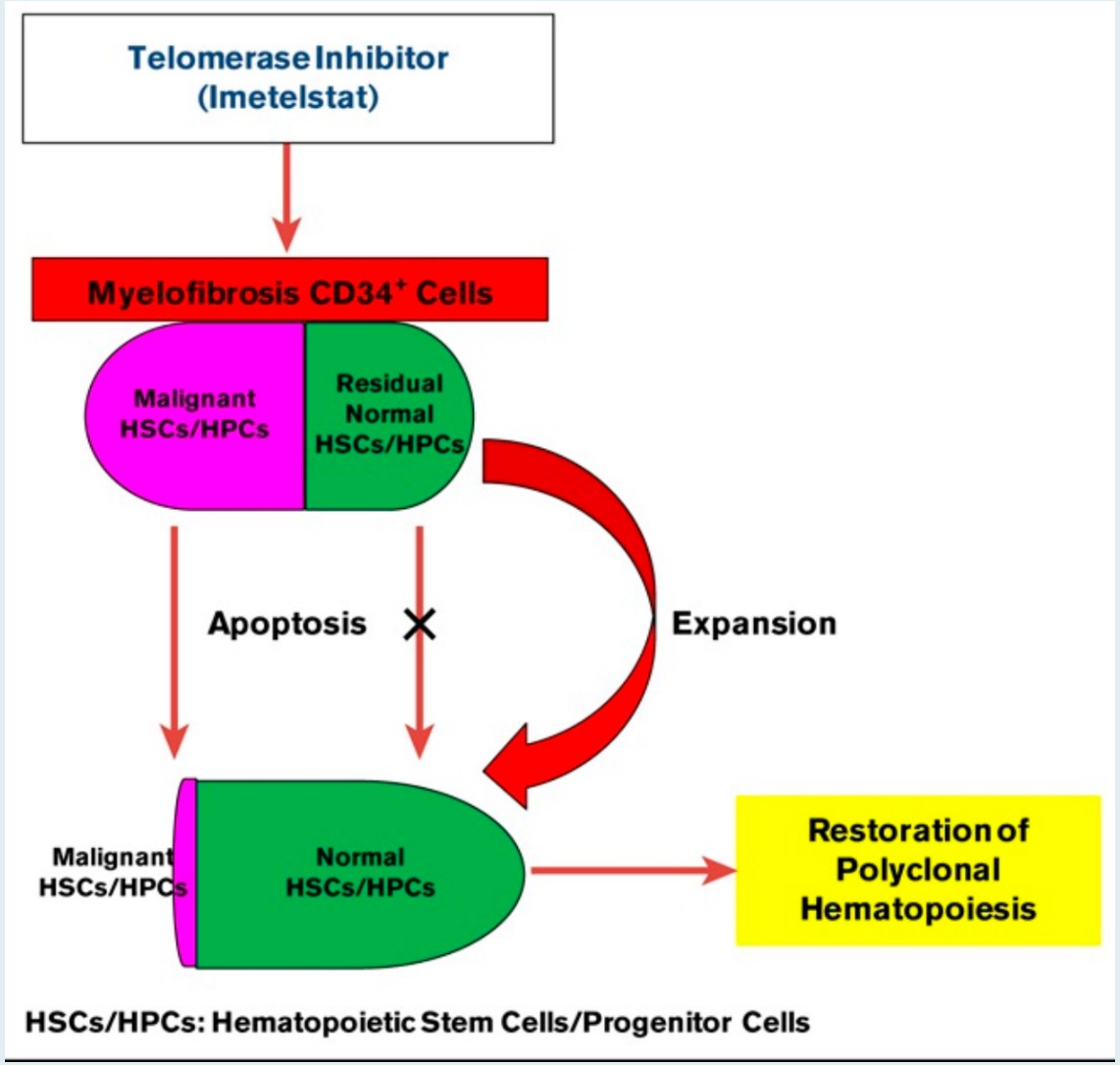
Any grade of AE occurring at a frequency of >15% included regardless of relatedness; total number of events = 1443

- Bomedemstat is generally well tolerated
- Most common hematologic AE, thrombocytopenia, is anticipated because dose titration rules target Grade 2 (50-75 x 10^9/L)
- The most common non-hematologic AE **related** to bomedemstat was dysgeusia (n=27, 30% of patients) with 1 patient who discontinued

Gill H et al. ASH 2021;Abstract 139.

RTP RESEARCH TO PRACTICE

Telomerase Inhibitor Imetelstat: Mechanism of Action



Wang X et al. *Blood Advances* 2018;2(18):2378-88.

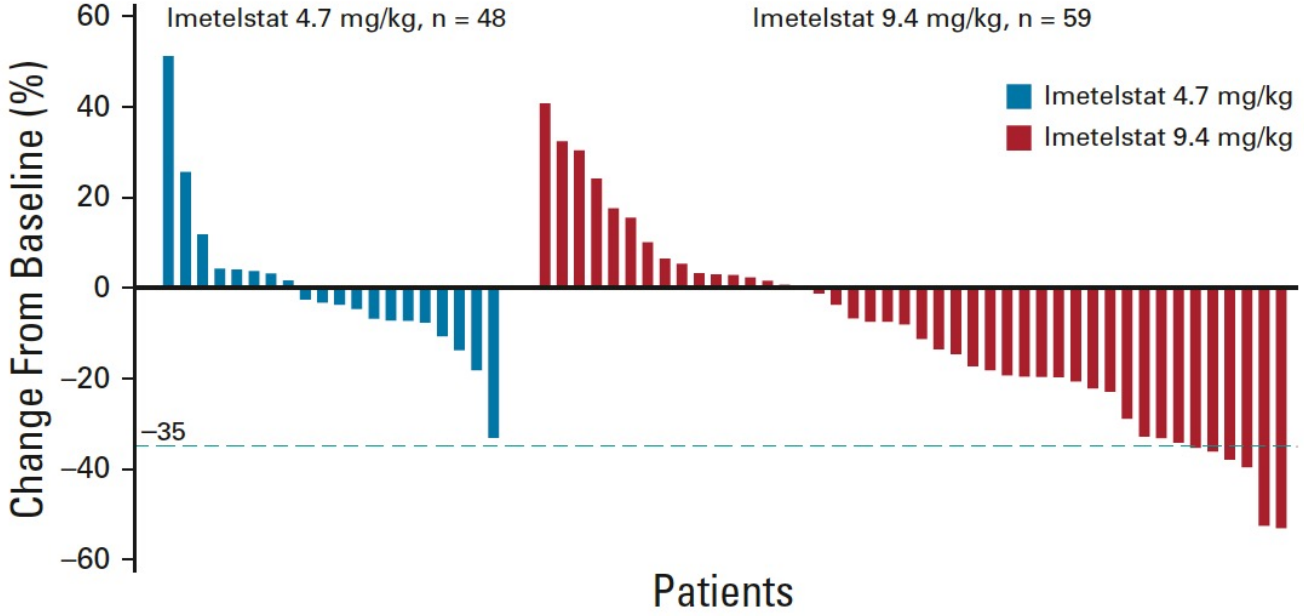
original reports

Randomized, Single-Blind, Multicenter Phase II Study of Two Doses of Imetelstat in Relapsed or Refractory Myelofibrosis

John Mascarenhas, MD[1]; Rami S. Komrokji, MD[2]; Francesca Palandri, MD[3]; Bruno Martino, MD[4]; Dietger Niederwieser, MD, PhD[5]; Andreas Reiter, MD[6]; Bart L. Scott, MD[7]; Maria R. Baer, MD[8]; Ronald Hoffman, MD[1]; Olatoyosi Odenike, MD[9]; Alessandro M. Vannucchi, MD[10]; Jacqueline Bussolari, PhD[11]; Eugene Zhu, PhD[11]; Esther Rose, MD[11]; Laurie Sherman, BSN[12]; Souria Dougherty, BS, MBA[12]; Libo Sun, PhD[12]; Fei Huang, PhD[12]; Ying Wan, PhD[12]; Faye M. Feller, MD[12]; Aleksandra Rizo, MD, PhD[12]; and Jean-Jacques Kiladjian, MD, PhD[13]

J Clin Oncol 2021;39:2881-92.

Phase II Trial of Imetelstat in Relapsed/Refractory Myelofibrosis



Spleen Response	4.7 mg/kg (n = 48)	9.4 mg/kg (n = 59)
≥ 10% SVR at week 24, No. (%)	4 (8.3)	22 (37.3)
≥ 20% SVR at week 24, No. (%)	1 (2.1)	13 (22)
≥ 35% SVR at week 24, No. (%)	0	6 (10.2)

- At week 24, symptom response rates were 32.2% in the 9.4-mg/kg arm and 6.3% in the 4.7-mg/kg arm.
- Most common adverse events on both arms were grade 3 or 4 reversible cytopenias.

Mascarenhas J et al. *J Clin Oncol* 2021;39:2881-92.

RTP RESEARCH TO PRACTICE

original reports

Addition of Navitoclax to Ongoing Ruxolitinib Therapy for Patients With Myelofibrosis With Progression or Suboptimal Response: Phase II Safety and Efficacy

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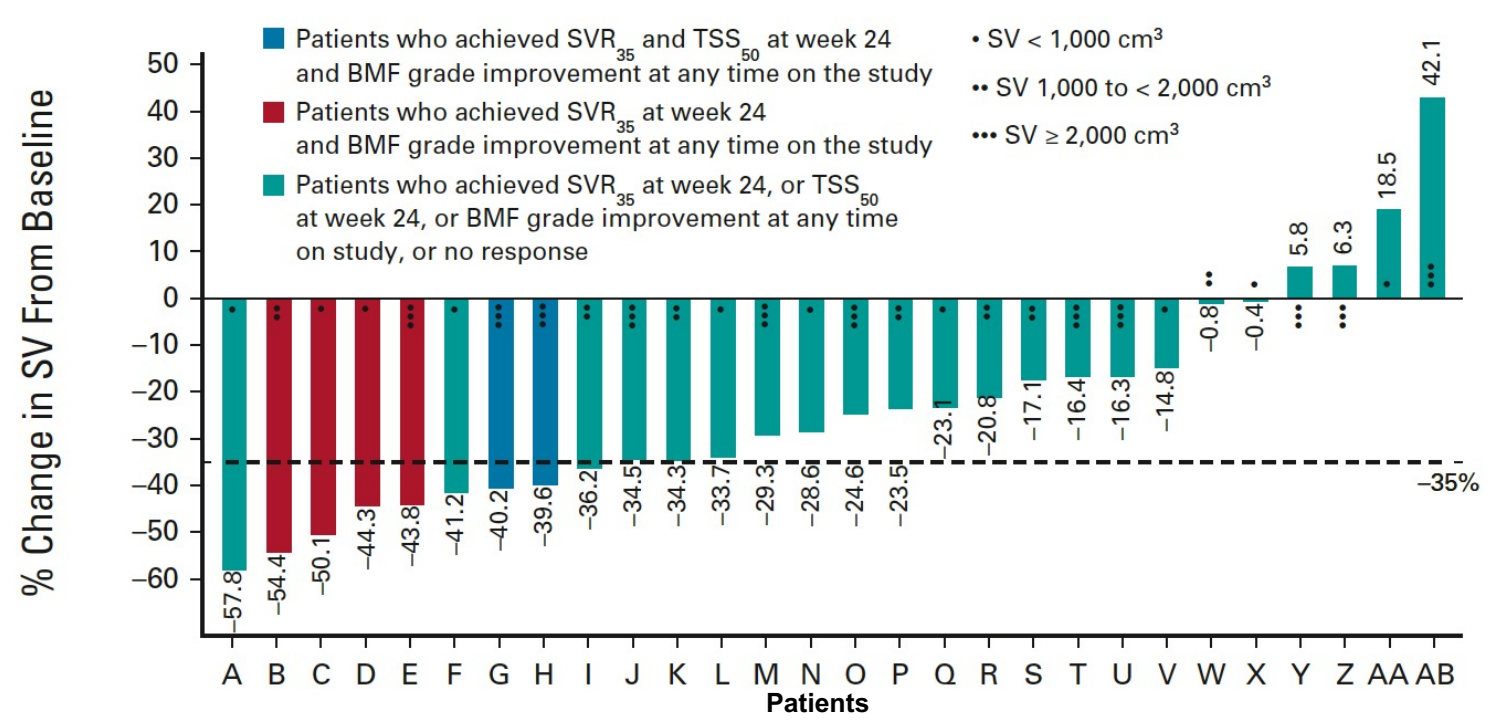
J Clin Oncol 2022;[Online ahead of print].

Phase II Trial of Adding the Bcl-XL/Bcl-2 Inhibitor Navitoclax to Ruxolitinib for Patients with MF and Disease Progression or a Suboptimal Response



- ≥50% reduction in total symptom score (TSS50) was achieved by 30% (6 of 20) of patients at week 24, and bone marrow fibrosis improved by 1-2 grades.
- Reversible thrombocytopenia without clinically significant bleeding was the most common adverse event (88%) but was manageable with dose reductions and interruptions.

Harrison CN et al. *J Clin Oncol* 2022;[Online ahead of print].

Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Tuesday, March 15, 2022
5:00 PM – 6:00 PM ET

Faculty

Sonali M Smith, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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