Meet The Professor

Optimizing the Management of Myelofibrosis

Thursday, February 1, 2024
5:00 PM – 6:00 PM ET

Faculty

Stephen T Oh, MD, PhD

Moderator

Neil Love, MD

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Commercial Support

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Dr Love — Disclosures

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Dr Oh — Disclosures
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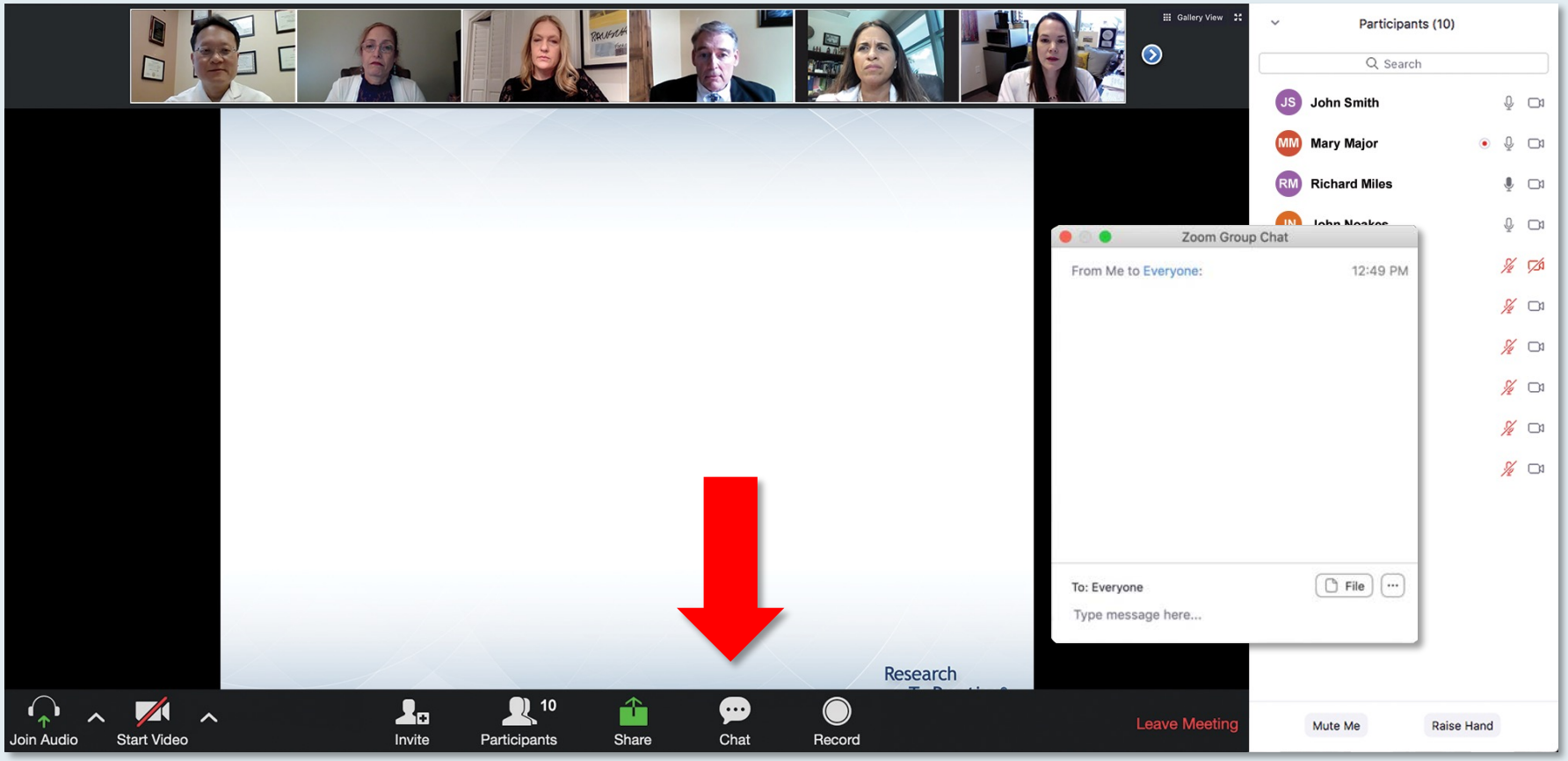

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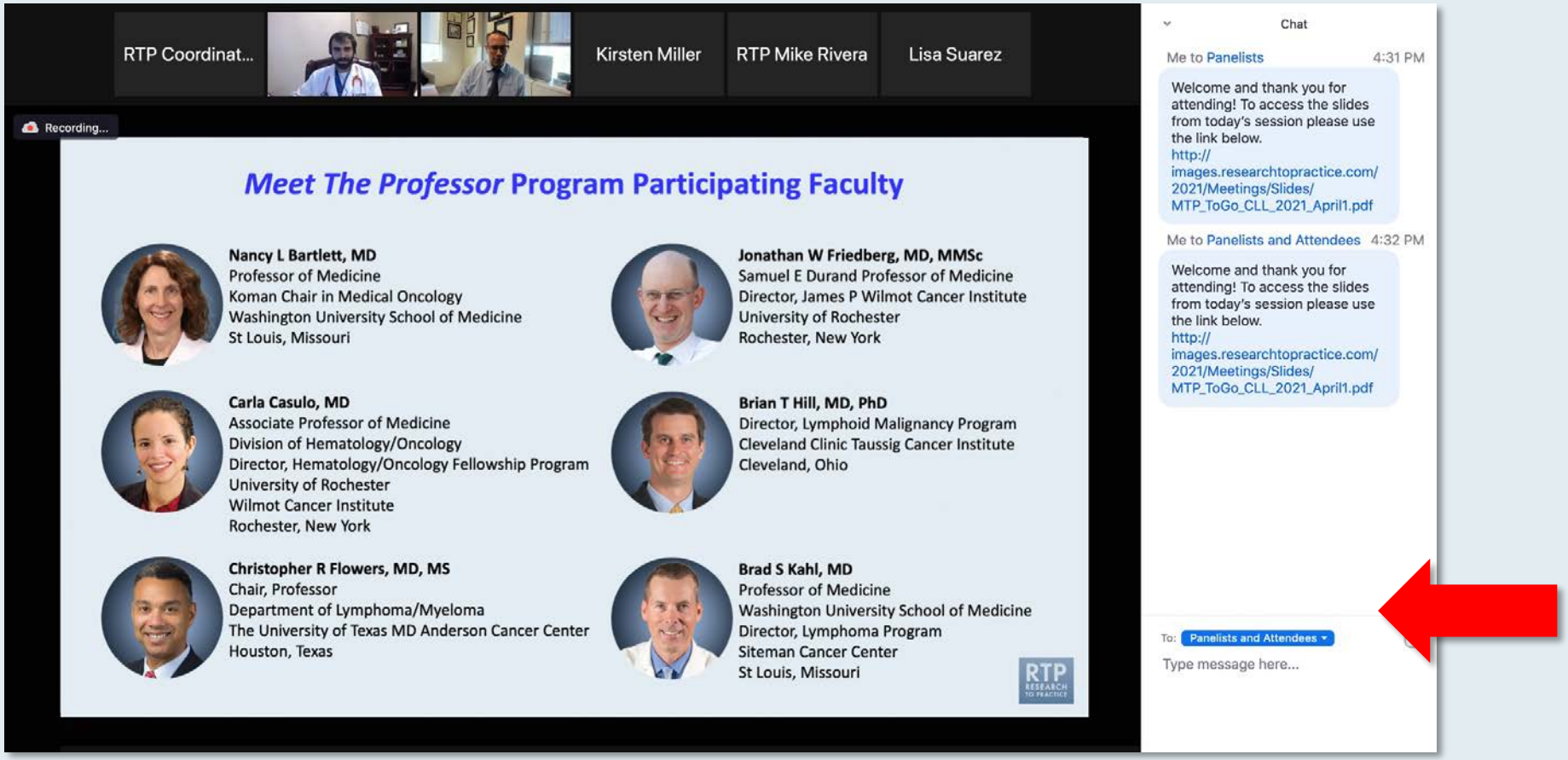

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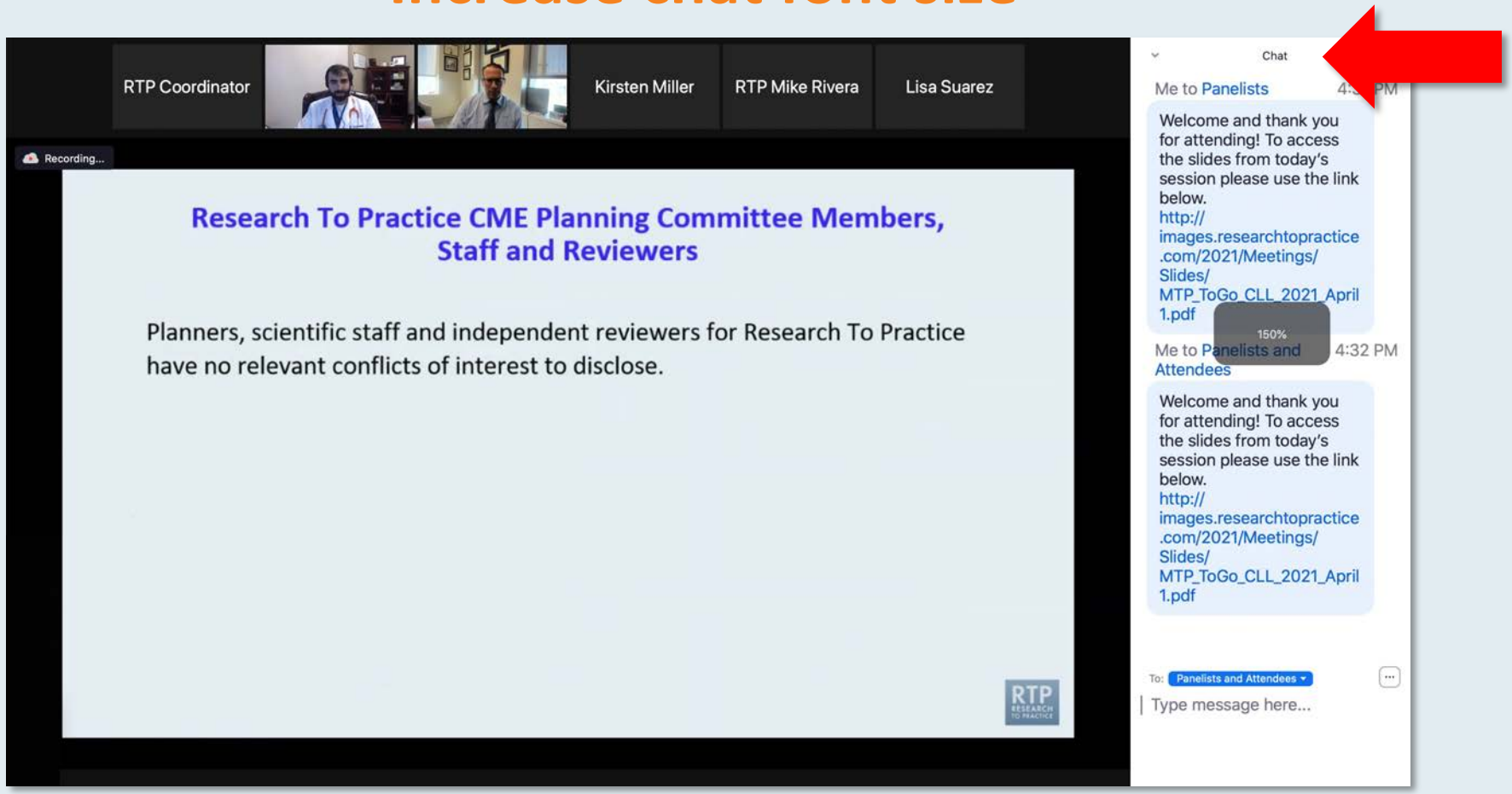

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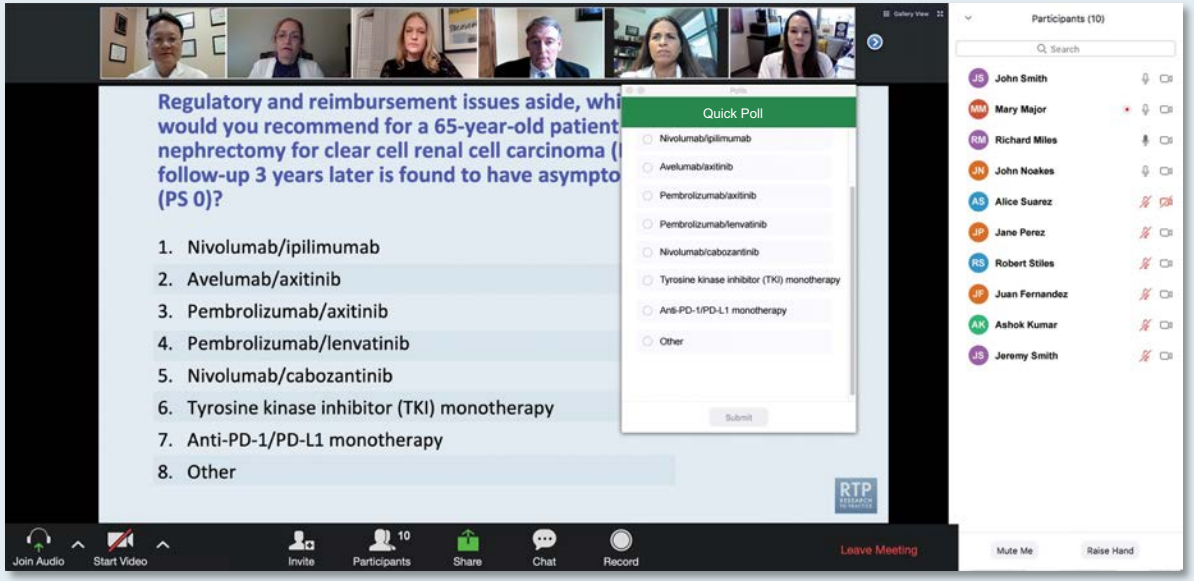

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Novel Agents and Strategies in Myelofibrosis

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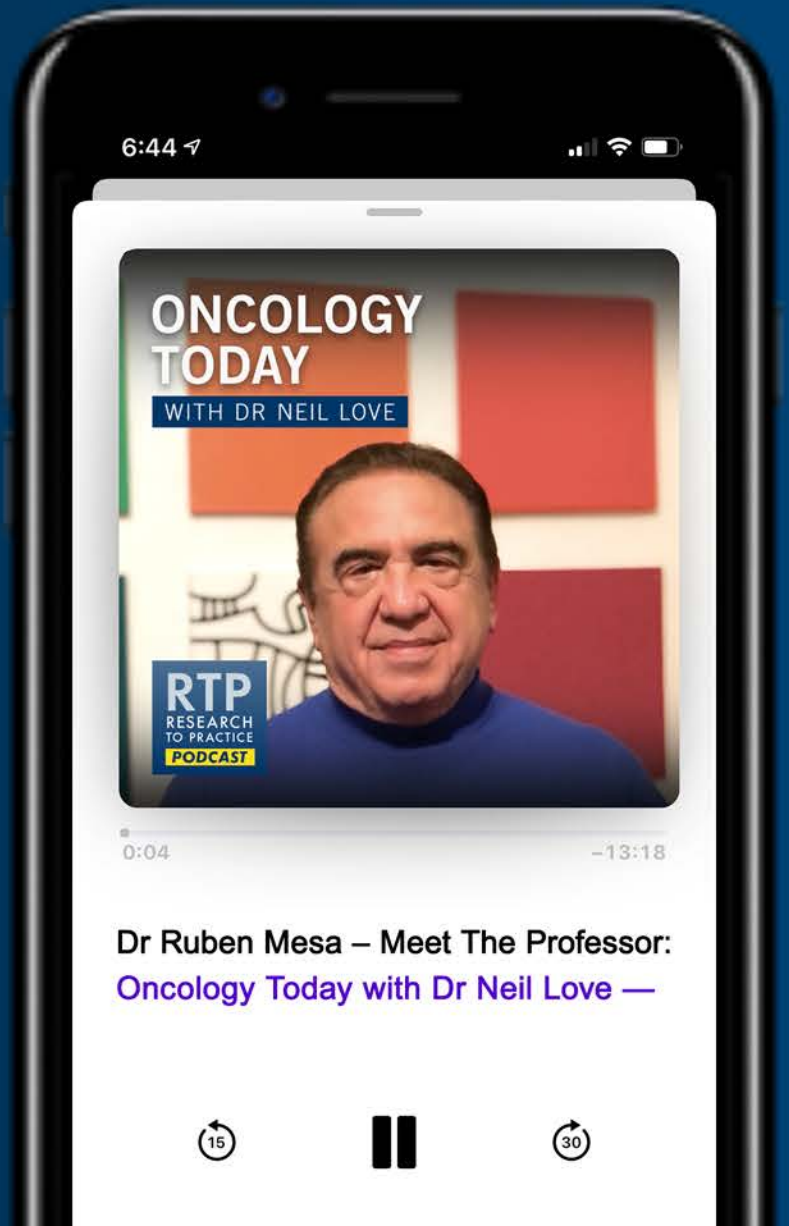

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Chronic Lymphocytic Leukemia

Tuesday, February 6, 2024
5:00 PM – 6:00 PM ET

Faculty

Lindsey Roeker, MD

Jeff Sharman, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

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Gastroesophageal Cancers

Thursday, February 8, 2024
5:00 PM – 6:00 PM ET

Faculty

Yelena Y Janjigian, MD

Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Lymphoma

Tuesday, February 13, 2024
5:00 PM – 6:00 PM ET

Faculty

Andrew M Evens, DO, MBA, MSc
Sonali M Smith, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Consensus or Controversy? Investigator Perspectives on the Current and Future Role of Immune Checkpoint Inhibitors in the Management of Hepatobiliary Cancers — A 2024 Post-ASCO Gastrointestinal Cancers Symposium Review

A CME-Accredited Virtual Event

Thursday, February 15, 2024
5:00 PM – 6:00 PM ET

Faculty

Robin (Katie) Kelley, MD
Mark Yarchoan, MD

Moderator

Neil Love, MD

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Urothelial Bladder Cancer

Thursday, February 22, 2024
5:00 PM – 6:00 PM ET

Faculty

Shilpa Gupta, MD

Thomas Powles, MBBS, MRCP, 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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Stephen T Oh, MD, PhD
Associate Professor of Medicine
Co-Chief, Division of Hematology
Washington University School of Medicine
St Louis, Missouri

Meet The Professor Program Participating Faculty

Aaron T Gerds, MD, MS
Associate Professor of Medicine
Hematology and Medical Oncology
Deputy Director for Clinical Research
Cleveland Clinic Taussig Cancer Institute
Medical Director
Case Comprehensive Cancer Center Clinical Research Office
Cleveland Clinic
Cleveland, Ohio

Stephen Oh, MD, PhD
Associate Professor of Medicine
Co-Chief, Division of Hematology
Washington University School of Medicine
St Louis, Missouri

Ruben A Mesa, MD
President, Enterprise Cancer Service Line
Executive Director, Atrium Health Wake Forest Baptist Comprehensive Cancer Center
Enterprise Senior Vice President, Atrium Health
Vice Dean for Cancer Programs
Professor of Medicine
Wake Forest University School of Medicine
Winston-Salem, North Carolina

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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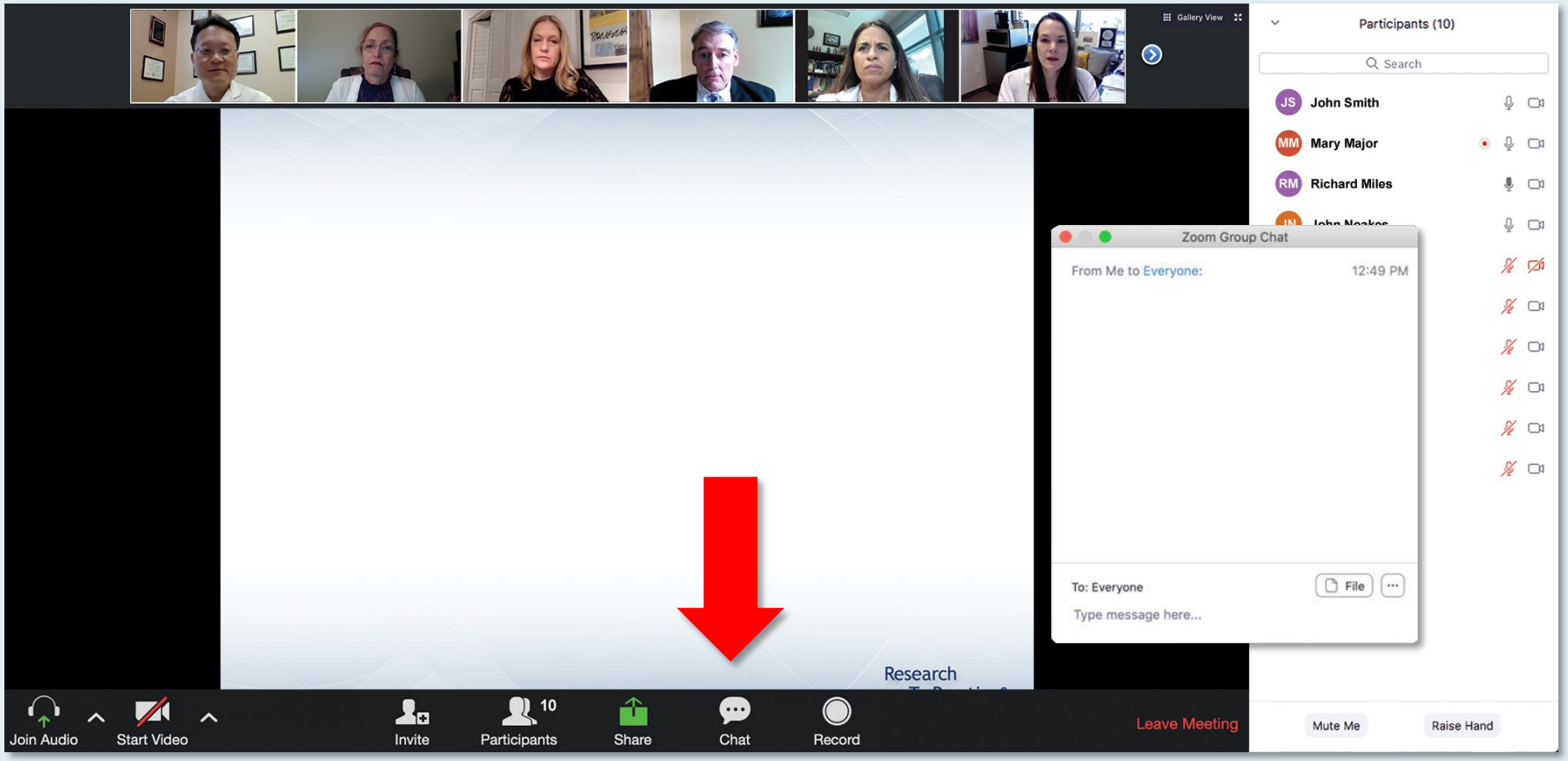

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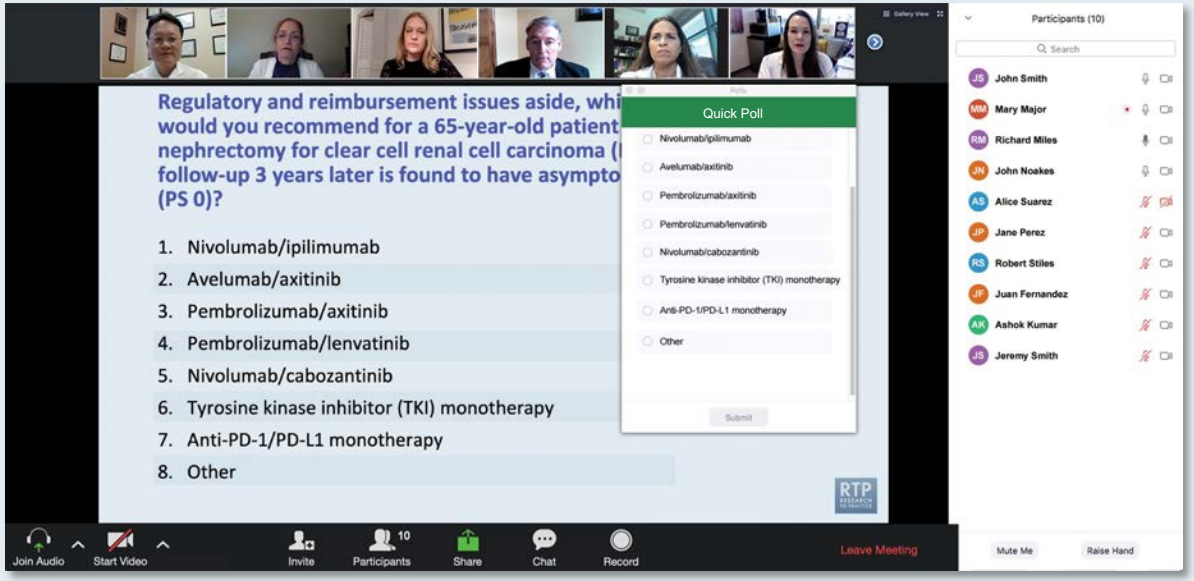

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Third Annual **National General Medical Oncology Summit**

Friday, March 22, 2024

6:30 PM – 7:00 PM

Welcome Reception

7:00 PM – 9:00 PM

Keynote Session: ER-Positive Metastatic Breast Cancer

Erika Hamilton, MD
Kevin Kalinsky, MD, MS
Joyce O'Shaughnessy, MD
Hope S Rugo, MD

Special Feature: Clinicians with Breast Cancer

Third Annual **National General Medical Oncology Summit**

Saturday, March 23, 2024

7:30 AM – 9:10 AM

Hodgkin and Non-Hodgkin Lymphoma

Ann S LaCasce, MD, MMSc
Matthew Lunning, DO
Kami Maddocks, MD
Andrew D Zelenetz, MD, PhD

9:30 AM – 10:20 AM

Gynecologic Cancers

Bradley J Monk, MD
David M O'Malley, MD

10:20 AM – 11:10 AM

Localized Breast Cancer; SABCS 2023 Review

Virginia Kaklamani, MD, DSc
Kevin Kalinsky, MD, MS
Joyce O'Shaughnessy, MD

11:10 AM – 12:00 PM

Metastatic Breast Cancer, Triple-Negative Breast Cancer, HER2-Positive Breast Cancer; SABCS 2023 Review

Erika Hamilton, MD
Virginia Kaklamani, MD, DSc
Hope S Rugo, MD

Third Annual **National General Medical Oncology Summit**

Saturday, March 23, 2024

12:30 PM – 1:20 PM

Prostate Cancer

Emmanuel S Antonarakis, MD
Rana R McKay, MD

1:20 PM – 2:10 PM

Urothelial Bladder Cancer

Matthew D Galsky, MD
Jonathan E Rosenberg, MD

2:10 PM – 3:00 PM

Renal Cell Carcinoma

Eric Jonasch, MD
Brian Rini, MD

3:20 PM – 4:10 PM

Targeted Therapy for Non-Small Cell Lung Cancer

Ibiayi Dagogo-Jack, MD
Helena Yu, MD

4:10 PM – 5:00 PM

Nontargeted Treatments for Lung Cancer

Edward B Garon, MD, MS
Corey J Langer, MD

Third Annual **National General Medical Oncology Summit**

Sunday, March 24, 2024

7:30 AM – 8:20 AM

Multiple Myeloma

Natalie S Callander, MD
Paul G Richardson, MD

8:20 AM – 9:10 AM

Gastroesophageal Cancers

Yelena Y Janjigian, MD
Samuel J Klempner, MD

9:30 AM – 10:20 AM

Hepatobiliary Cancers

Ghassan Abou-Alfa, MD, MBA
Richard S Finn, MD

10:20 AM – 11:10 AM

Colorectal Cancer

Kristen K Ciombor, MD, MSCI
John Strickler, MD

11:10 AM – 12:00 PM

Topic and faculty to be announced

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Novel Agents and Strategies in Myelofibrosis

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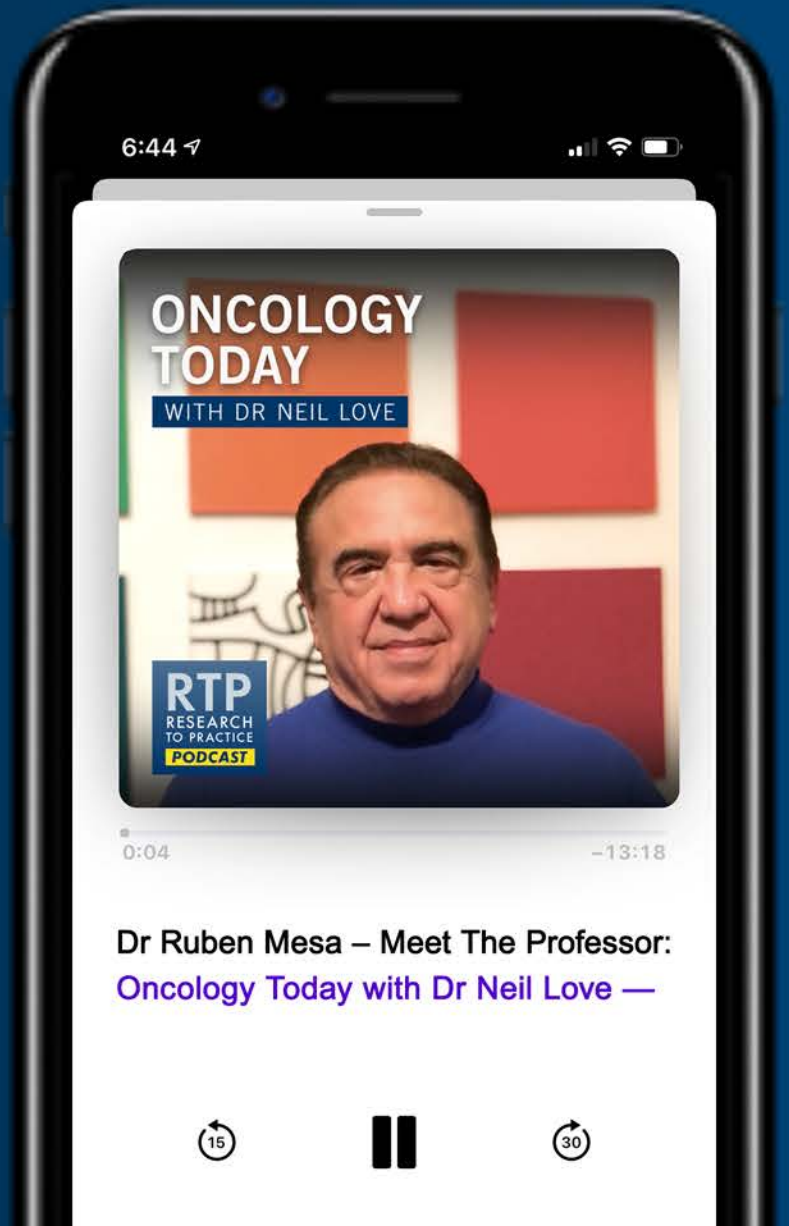

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Washington University School of Medicine
St Louis, Missouri

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

Rao Mushtaq, MD
National Jewish Health
Thornton, Colorado

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

Jeanne Palmer, MD
Mayo Clinic in Arizona
Phoenix, Arizona

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Meet The Professor with Dr Oh

INTRODUCTION: ASH 2023 Update

MODULE 1: Case Presentations

MODULE 2: Faculty Survey

MODULE 3: Appendix

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Meet The Professor with Dr Oh

INTRODUCTION: ASH 2023 Update

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Pelabresib in combination with ruxolitinib for Janus kinase inhibitor treatment-naïve patients with myelofibrosis: results of the MANIFEST-2 randomized, double-blind, Phase 3 study

Raajit Rampal,[1] Sebastian Grosicki, Dominik Chraniuk, Elisabetta Abruzzese, Prithviraj Bose, Aaron T Gerds, Alessandro M Vannucchi, Francesca Palandri, Sung-Eun Lee, Vikas Gupta, Alessandro Lucchesi, Stephen Oh, Andrew T Kuykendall, Andrea Patriarca, Alberto Álvarez-Larrán, Ruben Mesa, Jean-Jacques Kiladjian, Moshe Talpaz, Morgan Harris, Sarah-Katharina Kays, Anna Maria Jegg, Qing Li, Barbara Brown, Claire Harrison*, John Mascarenhas*

*Both authors contributed equally

[1]Leukemia Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Oral 628

Pelabresib Clinical Development in Myelofibrosis (MF)

- Myelofibrosis (MF) is a debilitating and progressive disease, characterized by four hallmarks: bone marrow fibrosis, cytopenias (e.g., anemia), MF-associated symptoms, and splenomegaly[1]
  - Reduction of spleen size is associated with improved overall survival[2]
- MF results from the dysregulation of the JAK/STAT pathway and BET-mediated gene modulation[3]
- JAK inhibition is the standard of care in intermediate- and high-risk MF[4]
- Unmet medical need persists due to the limited depth and durability of response and treatment-emergent adverse events[1,5]
- Pelabresib (CPI-0610) is an investigational, oral, small-molecule drug designed to inhibit BET proteins and decrease BET-mediated gene expression involved in MF pathogenesis[6,7]

The objective of the MANIFEST-2 study is to assess the efficacy and safety of the combination of pelabresib + ruxolitinib in JAKi-naïve patients with MF

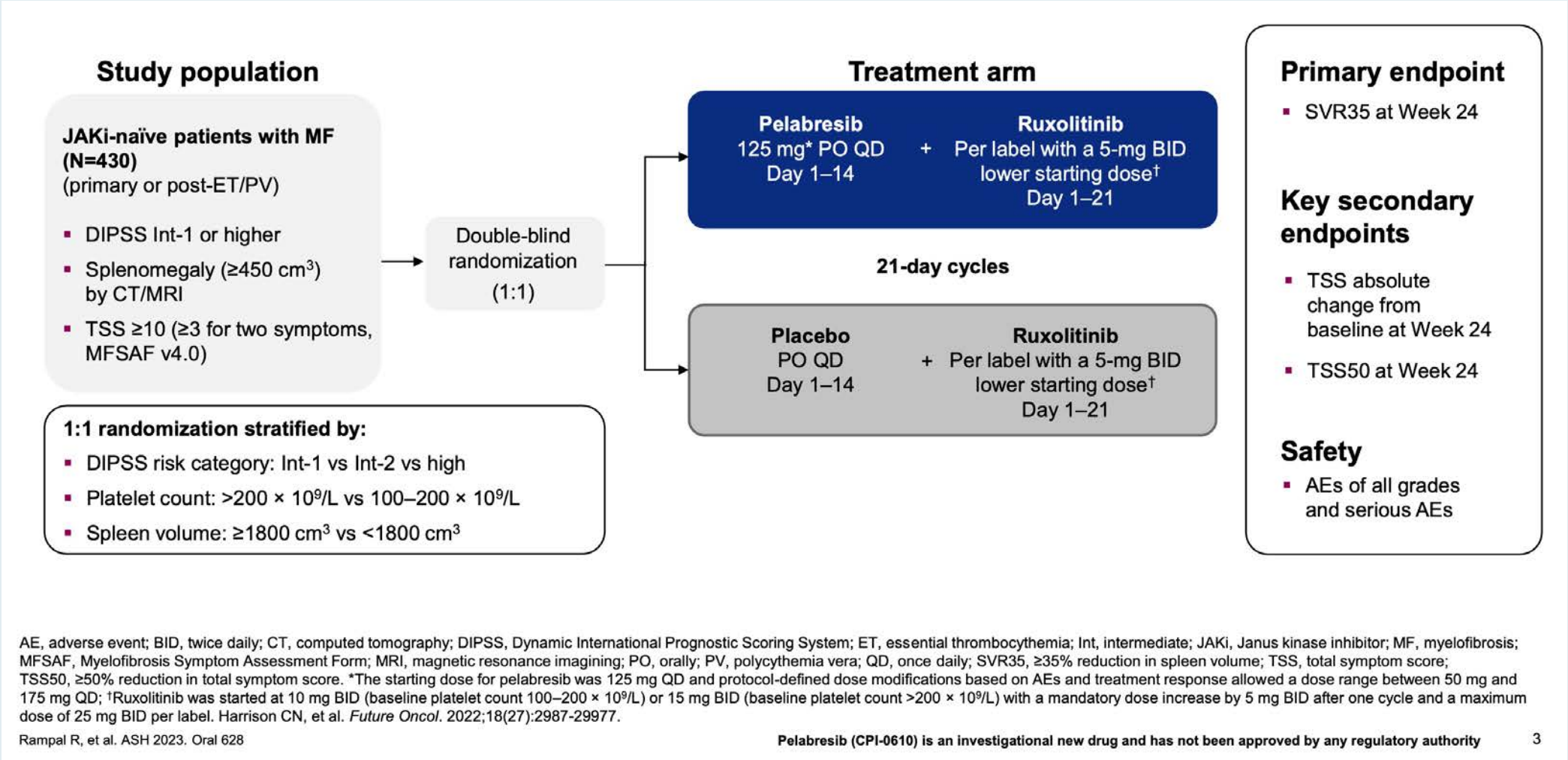
BET, bromodomain and extraterminal domain; JAK, Janus kinase; JAKi, Janus kinase inhibitor; MF, myelofibrosis; STAT, signal transducer and activator of transcription. 1. Tefferi A. *Am J Hematol*. 2021;96(1):145-162; 2. Bewersdorf J, et al. *Hemasphere*. 2023;7(S3):1965-66; 3. Kleppe M, et al. *Cancer Cell*. 2018;33(1):29-43.e7; 4. Bose P, Verstovsek S. *Hemasphere*. 2020;4(4):e424; 5. Harrison CN, et al. *Future Oncol*. 2022;18(27):2987-29977; 6. Albrecht BK, et al. *J Med Chem*. 2016;59(4):1330-1339; 7. Mascarenhas J, et al. *J Clin Oncol*. 2023;41(32):4993-5004.

Rampal R, et al. ASH 2023. Oral 628

Pelabresib (CPI-0610) is an investigational new drug and has not been approved by any regulatory authority

Rampal R et al. ASH 2023;Abstract 628.

MANIFEST-2: A Phase III Trial of Pelabresib with Ruxolitinib for JAK Inhibitor-Naïve Myelofibrosis



AE, adverse event; BID, twice daily; CT, computed tomography; DIPSS, Dynamic International Prognostic Scoring System; ET, essential thrombocythemia; Int, intermediate; JAKi, Janus kinase inhibitor; MF, myelofibrosis; MFSAF, Myelofibrosis Symptom Assessment Form; MRI, magnetic resonance imagining; PO, orally; PV, polycythemia vera; QD, once daily; SVR35, ≥35% reduction in spleen volume; TSS, total symptom score; TSS50, ≥50% reduction in total symptom score. *The starting dose for pelabresib was 125 mg QD and protocol-defined dose modifications based on AEs and treatment response allowed a dose range between 50 mg and 175 mg QD; †Ruxolitinib was started at 10 mg BID (baseline platelet count 100–200 × 10^9/L) or 15 mg BID (baseline platelet count >200 × 10^9/L) with a mandatory dose increase by 5 mg BID after one cycle and a maximum dose of 25 mg BID per label. Harrison CN, et al. *Future Oncol*. 2022;18(27):2987-29977.

Rampal R, et al. ASH 2023. Oral 628

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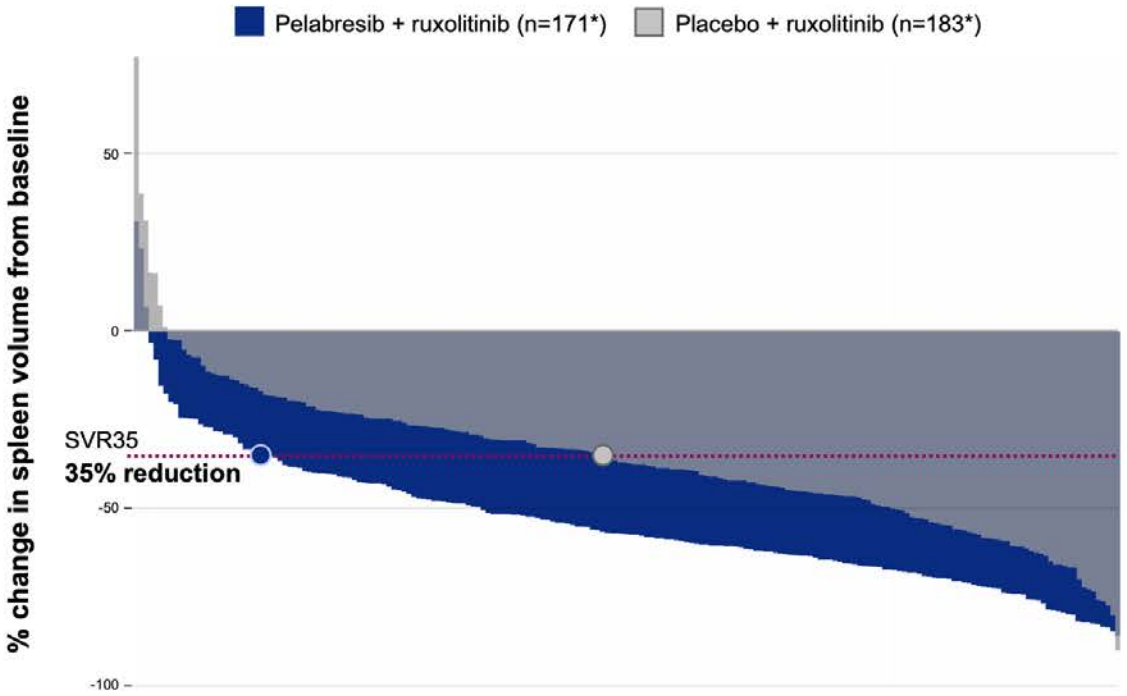
Rampal R et al. ASH 2023;Abstract 628.

MANIFEST-2: Spleen Volume Reduction with Pelabresib and Ruxolitinib for Treatment-Naïve Myelofibrosis

Significantly greater response in patients treated with pelabresib + ruxolitinib vs placebo + ruxolitinib



ITT population

	Pelabresib + ruxolitinib (N=214)	Placebo + ruxolitinib (N=216)	p-value
SVR35 at Week 24	65.9%	35.2%	
Difference† (95% CI)	30.4 (21.6, 39.3)		<0.001
Mean % change in spleen volume at Week 24‡	-50.6 (n=171)	-30.6 (n=183)	
95% CI	-53.2, -48	-33.7, -27.5	

Data cut off: August 31, 2023. CI, confidence interval; ITT, intent-to-treat; SVR35, ≥35% reduction in spleen volume. Spleen volume assessed by central read. *Waterfall plots represent patients who have baseline and Week 24 data. †Calculated by stratified Cochran–Mantel–Haenszel test; ‡Patients without Week 24 assessment are considered non-responders.

Rampal R, et al. ASH 2023. Oral 628

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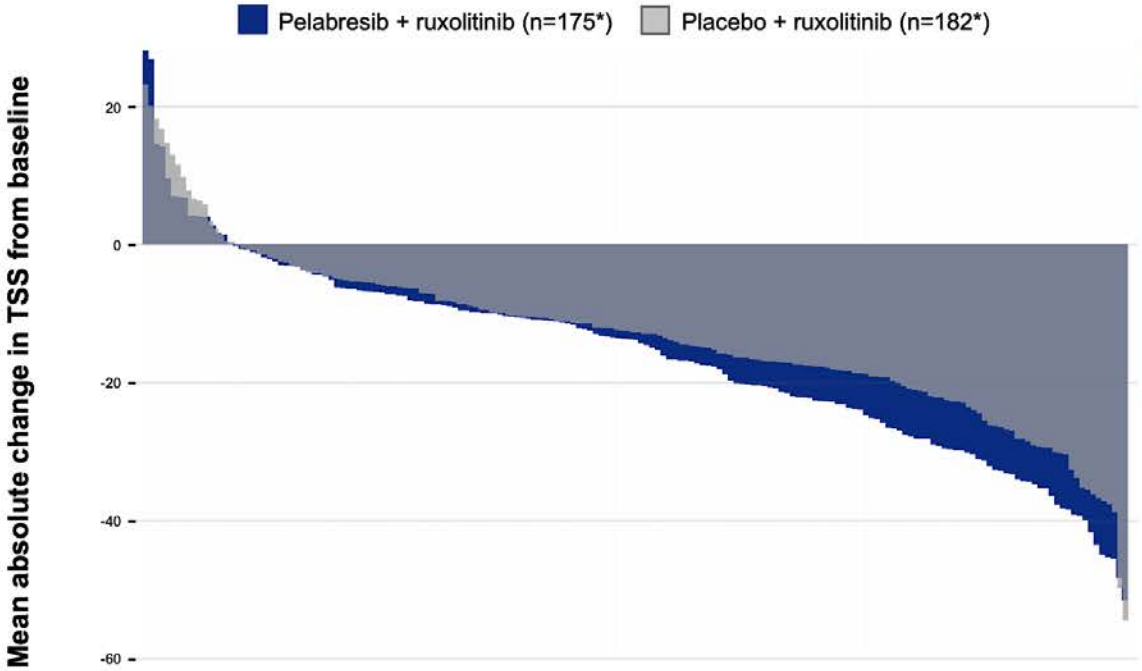
MANIFEST-2: TSS Outcomes with Pelabresib and Ruxolitinib for Treatment-Naïve Myelofibrosis

Strong numerical improvements for patients treated with pelabresib + ruxolitinib vs placebo + ruxolitinib



ITT population

	Pelabresib + ruxolitinib (N=214)	Placebo + ruxolitinib (N=216)	p-value
TSS change† from baseline at Week 24	-15.99	-14.05	
Mean difference‡ (95% CI)	-1.94 (-3.92, 0.04)		0.0545

- **Absolute change in TSS is a continuous endpoint** that estimates magnitude of symptom burden reduction with enhanced precision

Data cut off: August 31, 2023. ANCOVA, analysis of covariance; CI, confidence interval; ITT, intent-to-treat; TSS, total symptom score. *Waterfall plots represent patients who have baseline and Week 24 data. †Change from baseline determined by ANCOVA model using Multiple Imputation. ‡Least square mean difference from ANCOVA model using baseline DIPSS, baseline platelet count and baseline spleen volume as factors, and baseline TSS as covariate.

Rampal R, et al. ASH 2023. Oral 628

Pelabresib (CPI-0610) is an investigational new drug and has not been approved by any regulatory authority

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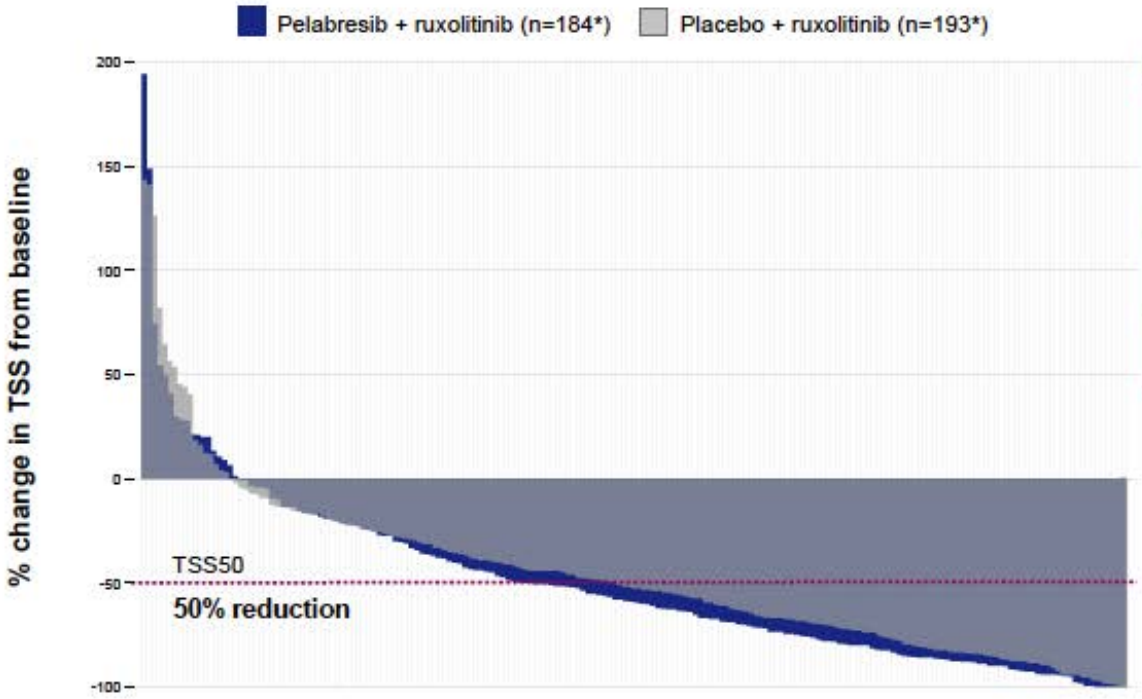
Rampal R et al. ASH 2023;Abstract 628.

MANIFEST-2: TSS50 Response at Week 24 with Pelabresib and Ruxolitinib for Treatment-Naïve Myelofibrosis

Numerically greater in patients treated with pelabresib + ruxolitinib vs placebo + ruxolitinib



ITT population

	Pelabresib + ruxolitinib (N=214)	Placebo + ruxolitinib (N=216)	p-value
TSS50 at Week 24	52.3%	46.3%	
Difference† (95% CI)	6.0 (-3.5, 15.5)		0.216

Data cut off: August 31, 2023. CI, confidence interval; ITT, intent-to-treat; TSS, total symptom score; TSS50, ≥50% reduction in total symptom score. Patients are evaluable for TSS50 at Week 24 if they have had Week 24 TSS assessment by the data cutoff date or discontinued without Week 24 assessment at any time. *Waterfall plots represent patients who have baseline and Week 24 data. †Difference in treatment groups analyzed by stratified Cochran–Mantel–Haenszel test (weighted 95% CI adjusted across strata).

Rampal R, et al. ASH 2023. Oral 628

Pelabresib (CPI-0610) is an investigational new drug and has not been approved by any regulatory authority

Rampal R et al. ASH 2023;Abstract 628.

MANIFEST-2: Conclusions

- **Pelabresib in combination with ruxolitinib compared with placebo in combination with ruxolitinib in JAK inhibitor treatment-naïve patients at Week 24:**
  - Significantly reduced splenomegaly (SVR35: 66% vs 35%; p<0.001)
  - Demonstrated strong trends in reducing the mean absolute TSS (p=0.0545) and improving TSS50 response
  - Doubled the percentage of patients with dual SVR35 / TSS50 response
- **Fewer anemia adverse events, higher rates of hemoglobin responses and fewer patients with transfusion requirement**
- **The safety profile appeared generally comparable to the established safety profile of ruxolitinib with fewer grade ≥ 3 events**
- **Pelabresib in combination with ruxolitinib showed reduction of pro-inflammatory cytokines, and improvement in bone marrow fibrosis and anemia response, addressing the four hallmarks of myelofibrosis**

These results support a potential paradigm shift in the treatment of patients with myelofibrosis

JAK, Janus kinase; SVR35, ≥35% reduction in spleen volume; TSS50, ≥50% reduction in total symptom score.

Rampal R, et al. ASH 2023. Oral 628

Pelabresib (CPI-0610) is an investigational new drug and has not been approved by any regulatory authority

Rampal R et al. ASH 2023;Abstract 628.

TRANSFORM-1: A Randomized, Double-Blind, Placebo-Controlled, Multicenter, International Phase 3 Study of Navitoclax in Combination With Ruxolitinib Versus Ruxolitinib Plus Placebo in Patients With Untreated Myelofibrosis

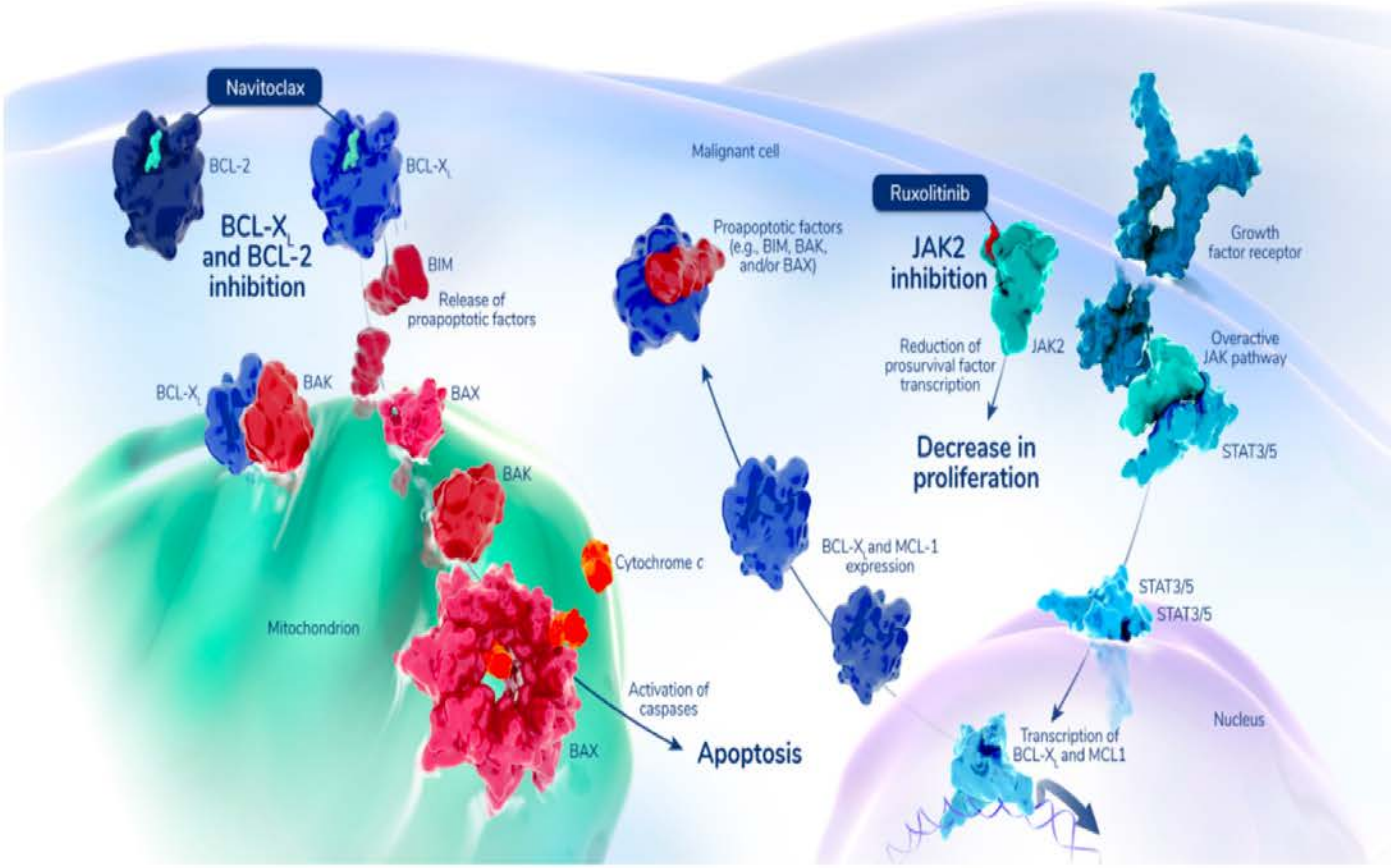
Naveen Pemmaraju[1], Adam J. Mead[2], Tim CP Somervaille[3], James McCloskey[4], Francesca Palandri[5], Steffen Koschmieder[6], David Lavie[7], Brian Leber[8], Su-Peng Yeh[9], Maria Teresa Gomez Casares[10], Emanuele Ammatuna[11], Ho-Jin Shin[12], Keita Kirito[13], Eric Jourdan[14], Timothy Devos[15], Hun S. Chuah[16], Atanas Radinoff[17], Andrija Bogdanovic[18], Rastislav Moskal[19], Qi Jiang[19], Avijeet S Chopra[19], Elektra J Papadopoulos[19], Jalaja Potluri[19], Francesco Passamonti[20]

ASH 2023;Abstract 620

Navitoclax Mechanism of Action in Myelofibrosis

- **Navitoclax is a novel, oral inhibitor of BCL-X_L and BCL-2, anti-apoptotic members of the BCL-2 family[1]**

- Preclinical studies suggest that JAK2 + BCL-2/BCL-X_L inhibition could overcome acquired resistance to single-agent JAKi treatment[2]
- Navitoclax, in combination with ruxolitinib, demonstrated pronounced antitumor activity, including clinical responses in patients with MF who no longer benefited from ruxolitinib in the phase 2 REFINE trial (NCT03222609)[3]

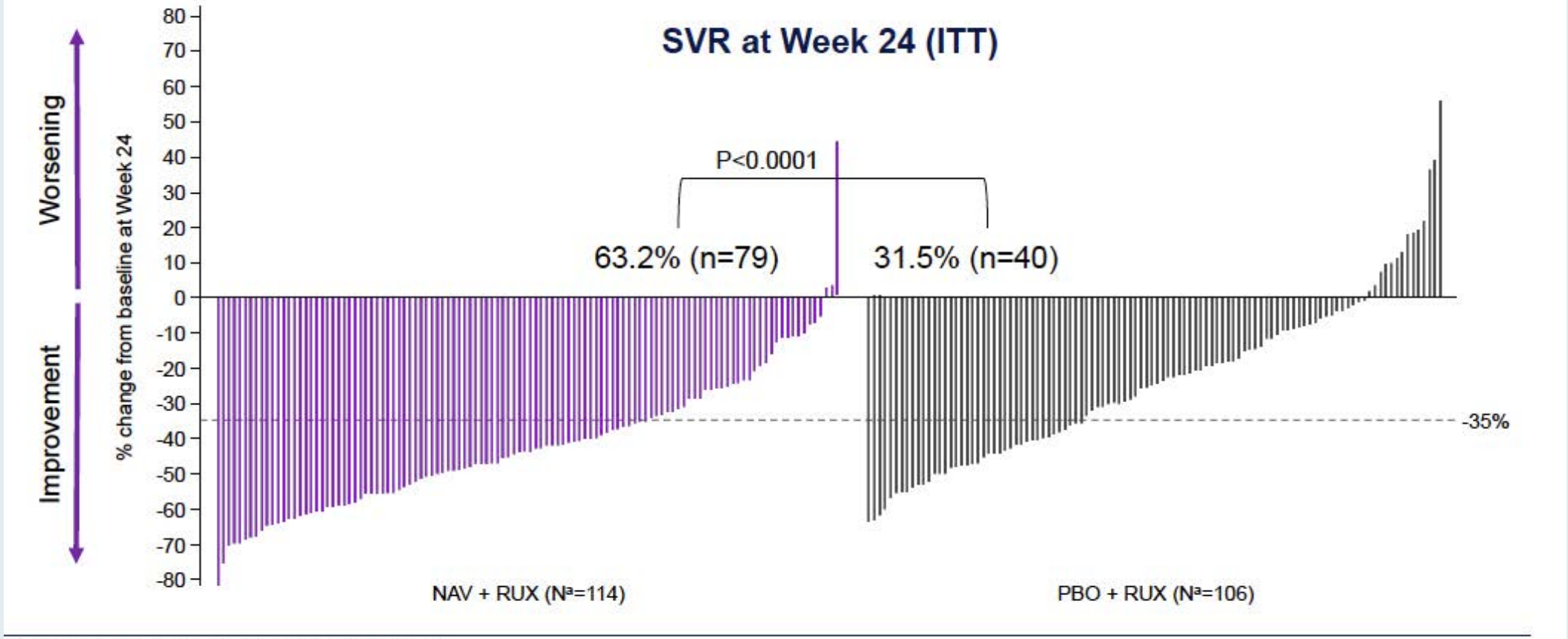


1. Tse C, et al. *Cancer Res*. 2008;68(9):3421–3428; 2. Waibel M, et al. *Cell Rep*. 2013;5:1047–1059; 3. Harrison et al. *J Clin Oncol*. 2022;40:1671–1680.
BCL-X_L, B-cell lymphoma-extra large; BCL-2, B-cell lymphoma 2; JAK2, Janus kinase 2; JAKi, Janus kinase inhibitor; MF, myelofibrosis.

Pemmaraju N et al. ASH 2023;Abstract 620.

TRANSFORM-1: SVR_{35} at Week 24 with Navitoclax and Ruxolitinib

- A significantly higher number of patients achieved SVR_{35W24} in NAV + RUX arm compared with PBO + RUX [79 (63.2%) vs 40 (31.5%); P<0.0001]



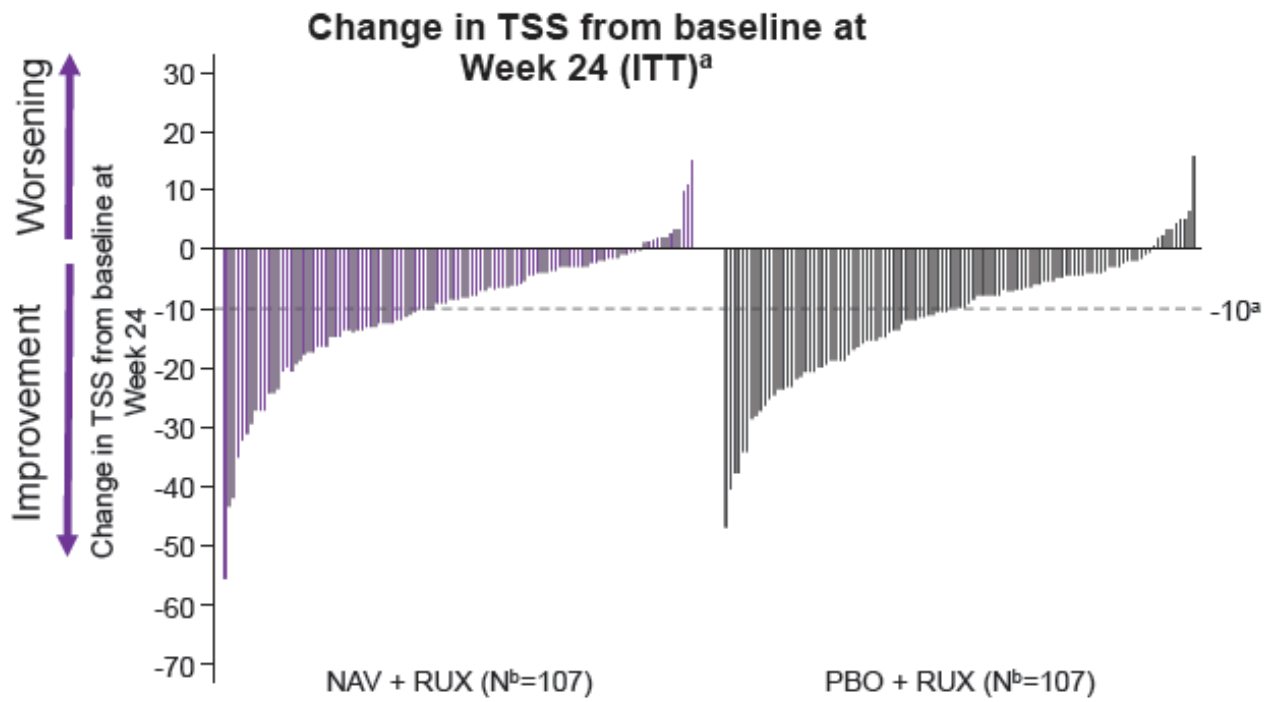
[a]Number of patients with available percent change in SVR_{35W24}.
ITT, intention-to-treat; NAV, navitoclax; PBO, placebo; RUX, ruxolitinib; SVR, spleen volume reduction; SVR_{35W24}, SVR of ≥35% at Week 24.

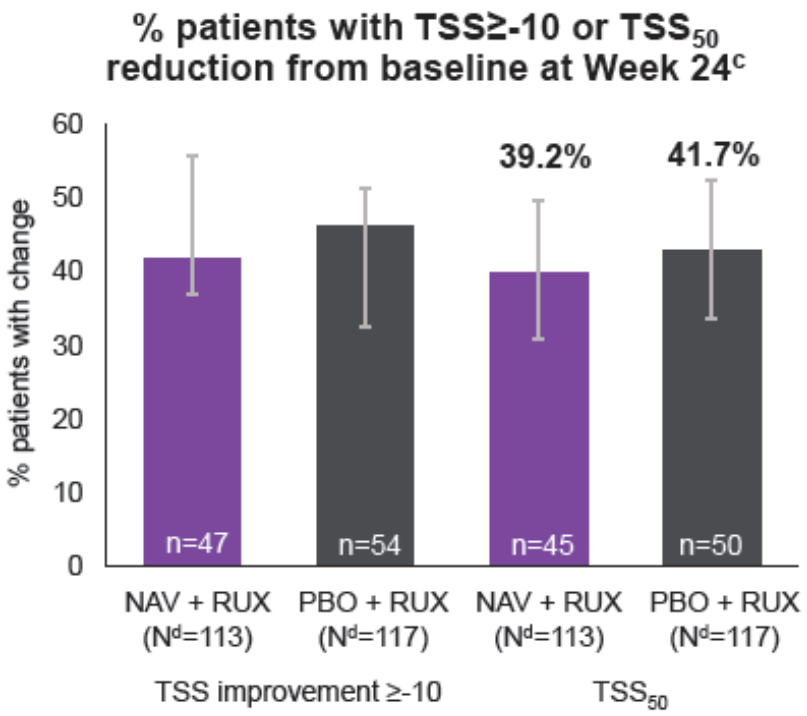
Pemmaraju N et al. ASH 2023;Abstract 620.

RTP RESEARCH TO PRACTICE

TRANSFORM-1: TSS Responses with Navitoclax and Ruxolitinib

- At Week 24, the mean change in TSS from baseline was -9.7 (95% CI: -11.8, -7.6) with NAV + RUX compared with -11.1 (95% CI: -13.2, -9.1) with PBO + RUX arm in ITT population (P=0.2852)





[a]TSS was calculated based on reporting on the Myelofibrosis Symptom Assessment Form v4.0. A 10-point improvement (scale: 0–70) was estimated to be the level of change in TSS that patients would perceive to be meaningful improvement in MF-related symptoms; [b]Number of patients with available data for change in TSS at Week 24; [c]Error bars represent 95% CI. [d]Includes patients with baseline TSS ≥12 or at least 2 symptoms with a baseline symptom score ≥3 with TSS available at baseline and week 24. CI, confidence interval; ITT, intention-to-treat; NAV, navitoclax; RUX, ruxolitinib; TSS, total symptom score

Pemmaraju N et al. ASH 2023;Abstract 620.

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Based on your personal clinical experience and/or knowledge of available data, what is your global perspective on the overall efficacy of pelabresib in the management of MF?

 Dr Gerds	Remarkable SVR in combination w/rux, some anemia responses
 Dr Mesa	Good combination benefit for splenomegaly
 Dr Oh	Additive spleen response in combination w/rux, some activity for anemia, minor effect on sxs

SVR = spleen volume reduction; rux = ruxolitinib; sxs = symptoms

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and/or knowledge of available data, what is your global perspective on the tolerability of pelabresib in the management of MF?

 Dr Gerds	Very tolerable; need to monitor for marrow suppression
 Dr Mesa	Relatively well tolerated
 Dr Oh	Well tolerated overall, some GI toxicity

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and/or knowledge of available data, what is your global perspective on the overall efficacy of navitoclax in the management of MF?

 Dr Gerds	Remarkable SVR in combination w/rux in high-risk pts
 Dr Mesa	Helpful in additive way for splenomegaly
 Dr Oh	Moderate efficacy for spleen response but no effect on sxs

SVR = spleen volume reduction; rux = ruxolitinib; sxs = symptoms

Based on your personal clinical experience and/or knowledge of available data, what is your global perspective on the tolerability of navitoclax in the management of MF?

 Dr Gerds	Must carefully manage cytopenias in early tx
 Dr Mesa	Some toxicity issues with GI and platelets
 Dr Oh	Thrombocytopenia is limiting

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Oh

MODULE 1: Case Presentations

- Dr Mushtaq: 70-year-old woman with symptomatic primary MF receives ruxolitinib
- Dr Bhatnagar: 69-year-old woman, a Jehovah's Witness with multiple comorbidities, presents with splenomegaly and anemia and is diagnosed with primary MF
- Dr Morganstein: 75-year-old woman s/p pacritinib for 4 years on trial, now with disease progression with massive splenomegaly and thrombocytopenia (20K-30K)
- Dr Palmer: 57-year-old woman is diagnosed with symptomatic primary MF – normal cytogenetics, JAK2 and DNMT3A mutations
- Dr Palmer (continued): 57-year-old woman has progressive MF after ruxolitinib and fedratinib – repeat NGS shows JAK2, DNMT3A, IDH2 and TET2 mutations
- Dr Bhatnagar: 69-year-old woman with primary MF who discontinued ruxolitinib due to onset of CHF now has possible AML transformation
- Dr Palmer: 69-year-old woman with well controlled MF on ruxolitinib 10 mg BID x 3 years develops increasing anemia and splenomegaly

Dr Rao Mushtaq
(Thornton, Colorado)

Dr Jeanne Palmer
(Phoenix, Arizona)

Case Presentation: 70-year-old woman with symptomatic primary MF receives ruxolitinib

Questions for Dr Oh

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Received: 13 March 2023 | Accepted: 3 April 2023
DOI: 10.1002/ajh.26935

RESEARCH ARTICLE

Comprehensive profiling of clinical JAK inhibitors in myeloproliferative neoplasms

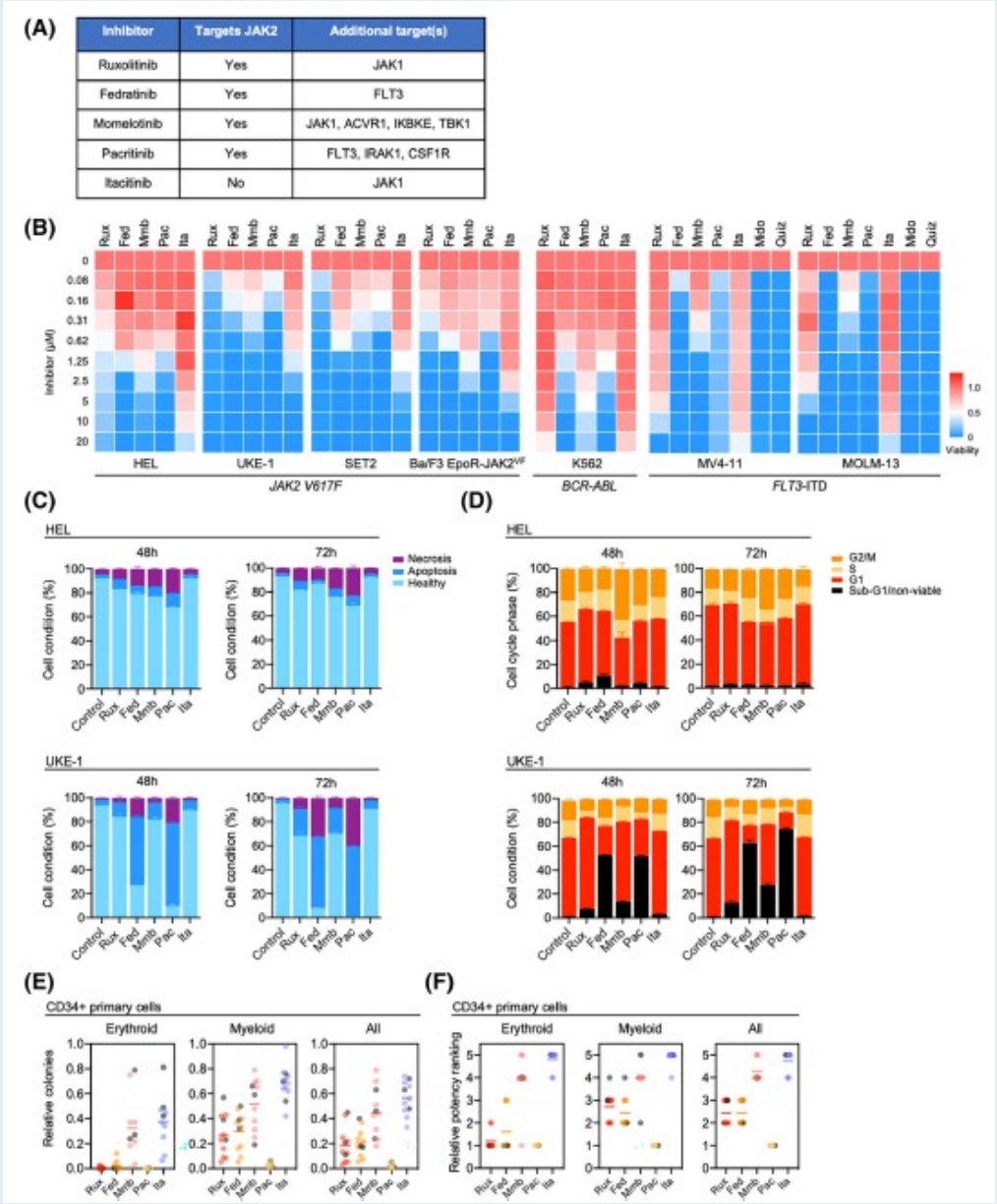
Tim Kong[1] | LaYow Yu[1] | Angelo B. A. Laranjeira[1] | Daniel A. C. Fisher[1] | Fan He[1] | Maggie J. Cox[1] | Stephen T. Oh[1,2,3]

Am J Hematol 2023;98(7):1029-42

In Vitro Efficacy of JAK Inhibitors

(A)

Inhibitor	Targets JAK2	Additional target(s)
Ruxolitinib	Yes	JAK1
Fedratinib	Yes	FLT3
Momelotinib	Yes	JAK1, ACVR1, IKBKE, TBK1
Pacritinib	Yes	FLT3, IRAK1, CSF1R
Itacitinib	No	JAK1



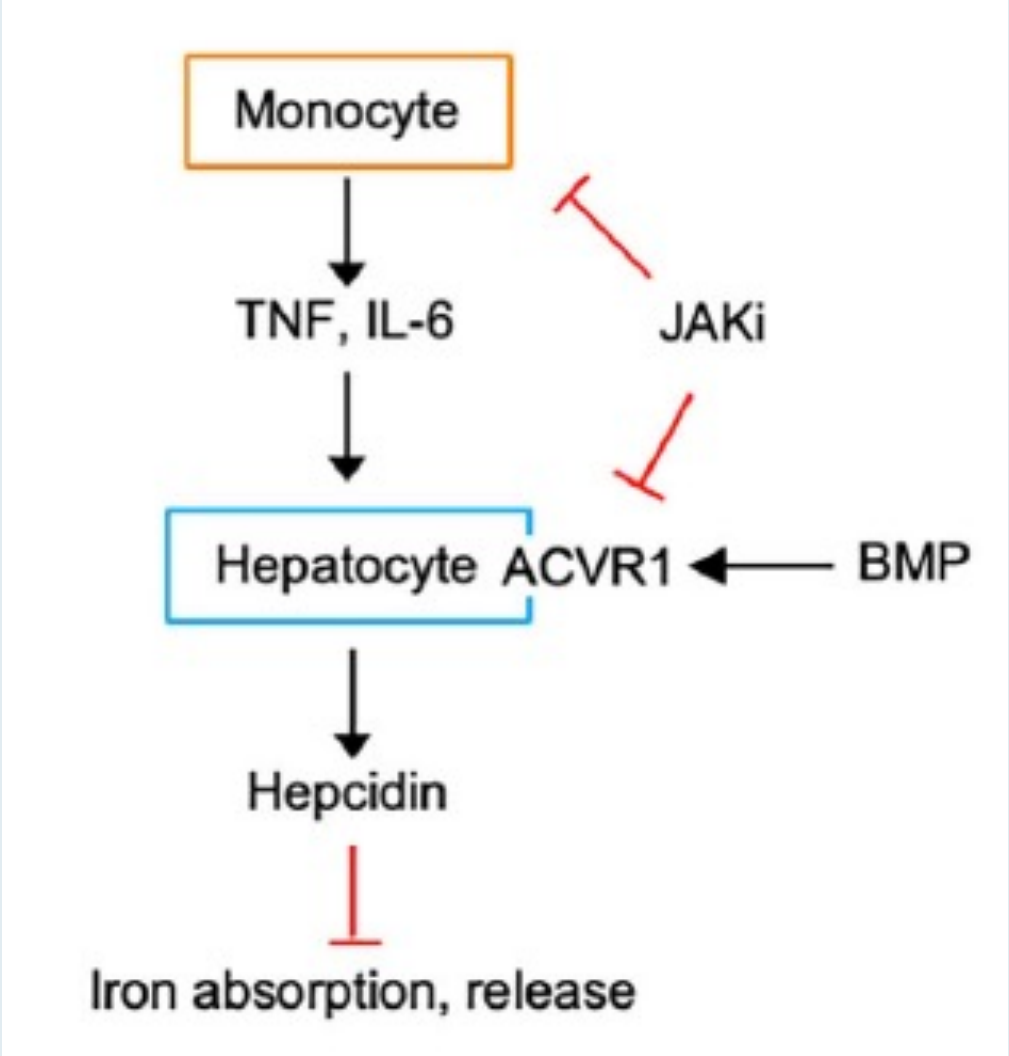
Kong T et al. *Am J Hematol* 2023;98(7):1029-42.

Primary and Secondary Targets of JAK Inhibitors

Inhibitor	Targets JAK2	Additional target(s)
Ruxolitinib	Yes	JAK1
Fedratinib	Yes	FLT3
Momelotinib	Yes	JAK1, ACVR1, IKBKE, TBK1
Pacritinib	Yes	FLT3, IRAK1, CSF1R
Itacitinib	No	JAK1

Kong T et al. *Am J Hematol* 2023;98(7):1029-42.

Hepcidin Regulation



Kong T et al. *Am J Hematol* 2023;98(7):1029-42.

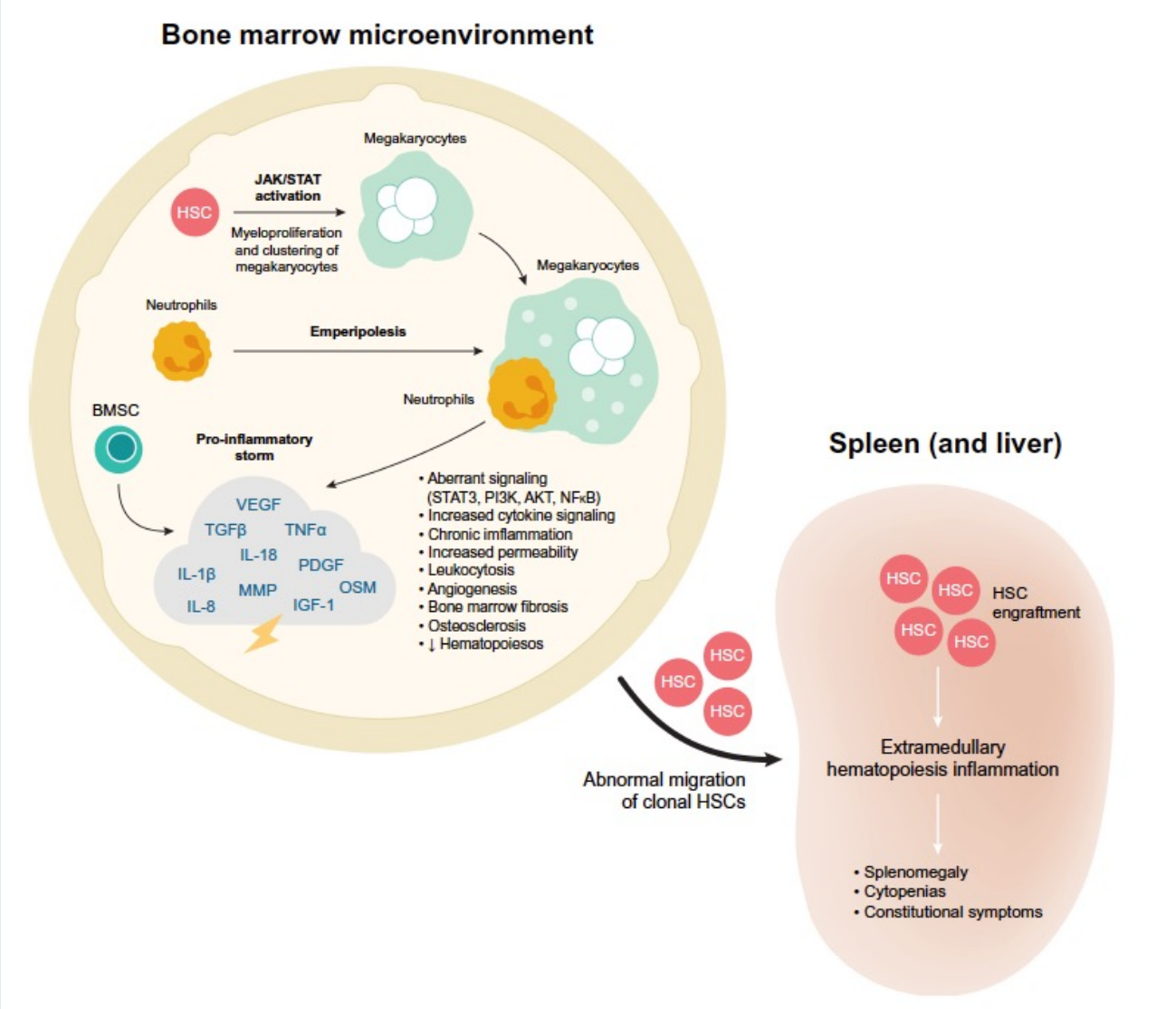
Cancer 2022;128(13):2420-32

Review Article

Defining disease modification in myelofibrosis in the era of targeted therapy

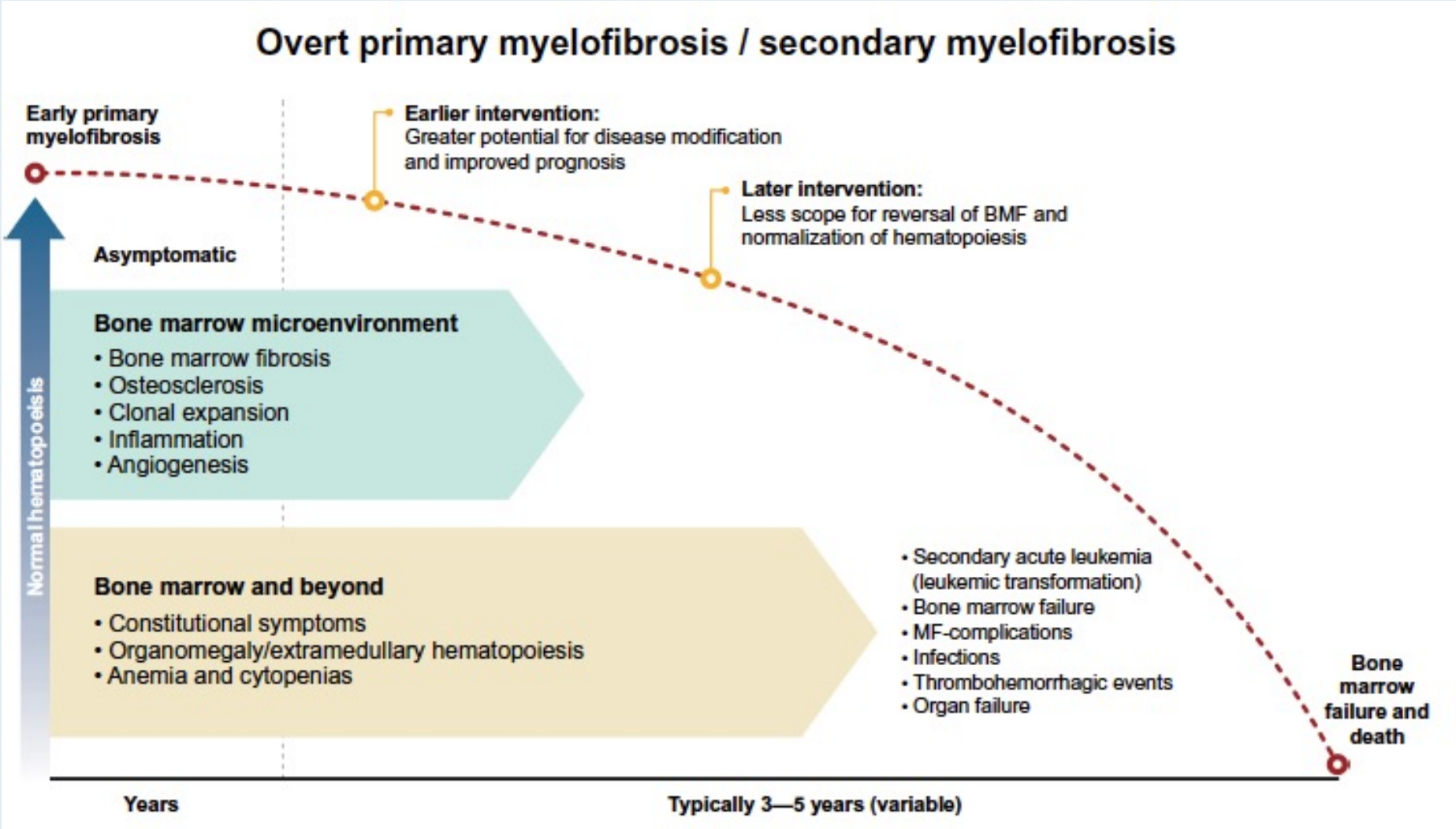
Naveen Pemmaraju, MD [1]; Srdan Verstovsek, MD, PhD[1]; Ruben Mesa, MD, FACP [2]; Vikas Gupta, MD[3]; Jacqueline S. Garcia, MD[4]; Joseph M. Scandura, MD [5]; Stephen T. Oh, MD[6]; Francesco Passamonti, MD[7]; Konstanze Döhner, MD[8]; and Adam J. Mead, MD[9]

Overview of Myelofibrosis Disease Pathology



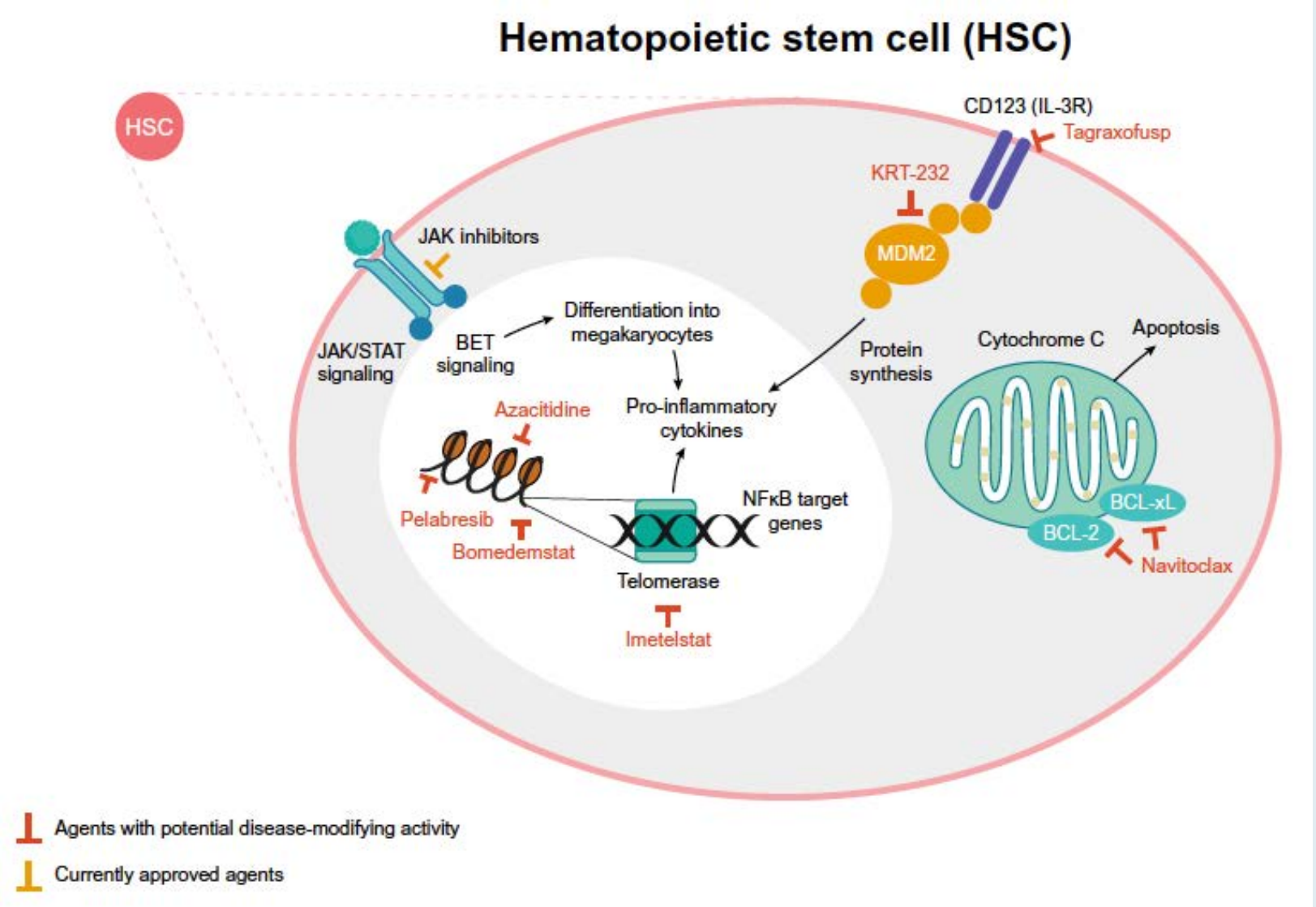
Pemmaraju N et al. *Cancer* 2022;128(13):2420-32.

Natural History of Myelofibrosis and Potential Time Points for Intervention



Pemmaraju N et al. *Cancer* 2022;128(13):2420-32.

Novel and Potentially Disease-Modifying Therapeutic Targets in Myelofibrosis



Pemmaraju N et al. *Cancer* 2022;128(13):2420-32.

Case Presentation: 69-year-old woman, a Jehovah's Witness with multiple comorbidities, presents with splenomegaly and anemia and is diagnosed with primary MF

Dr Tina Bhatnagar (Wheeling, West Virginia)

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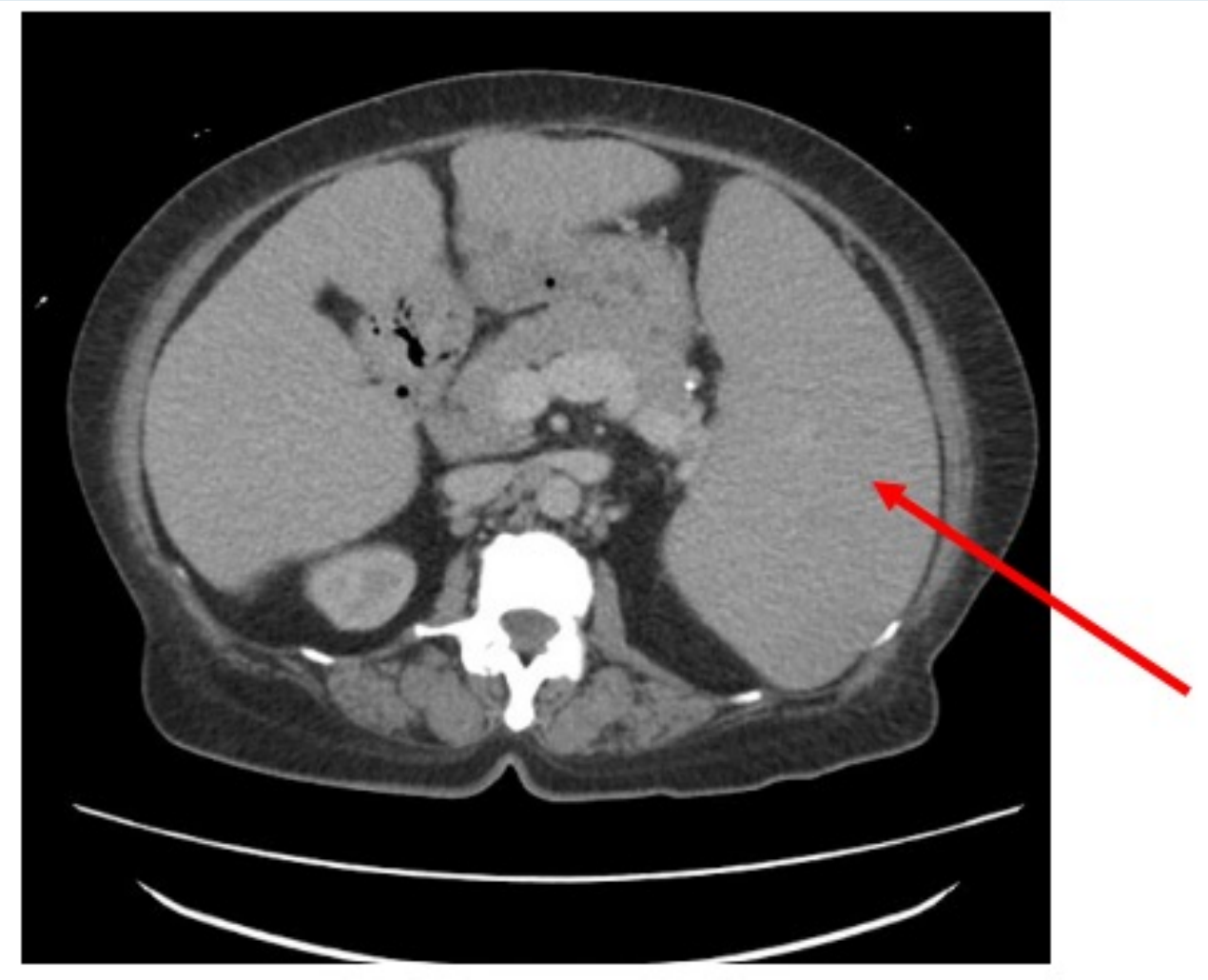
CT Scan at Diagnosis
Splenomegaly and Cirrhotic Liver Morphology



Lab Work After Momelotinib for 4 Months

1m ago | All Rows | Time Mark

CBC	2024 1/8/24 13:10	1/5/24 14:28	2023 12/4/23 13:21	11/2/23 14:07	10/19/23 14:42
WBC	15.0 ▲	16.1 ▲	11.6 ▲	10.4	8.8
HGB	6.3 ⏬	6.0 ⏬	7.8 ▼	8.4 ▼	8.4 ▼
HCT	20.5 ▼	19.5 ▼	24.9 ▼	26.1 ▼	26.9 ▼
PLATELET COUNT (AUTO)	95 ▼		117 ▼	127 ▼	
PLATELET COUNT	125 ▼	103 ▼	117 ▼	172	182

Case Presentation: 75-year-old woman s/p pacritinib for 4 years on trial, now with disease progression with massive splenomegaly and thrombocytopenia (20K-30K)

Dr Neil Morganstein (Summit, New Jersey)

case reports

Long-Term Hematologic Improvement in a Patient With Cytopenic Myelofibrosis Treated With Pacritinib

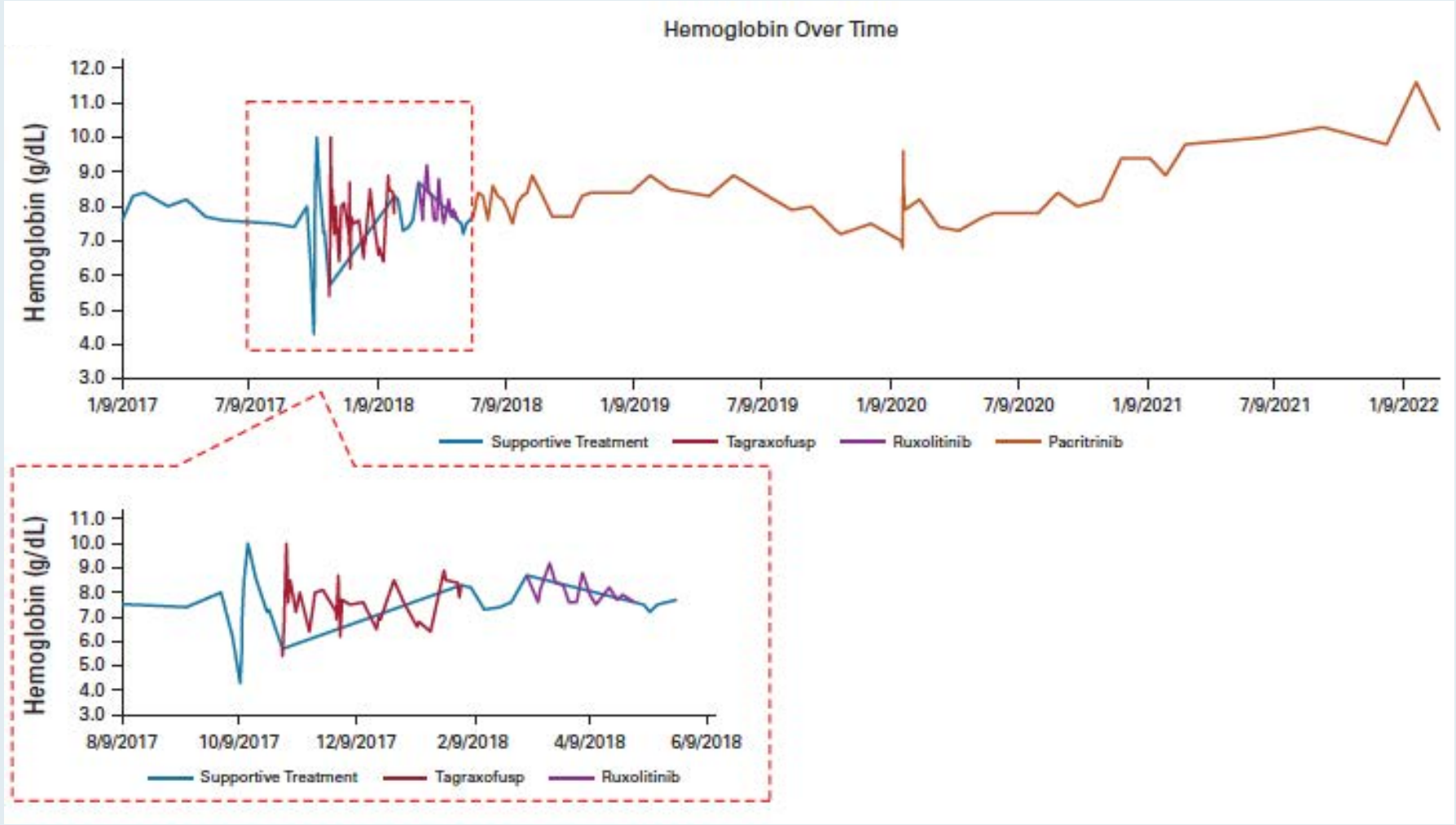
Abdulraheem Yacoub, MD[1]; Ruben A. Mesa, MD[2]; and Stephen T. Oh, MD, PhD[3]

JCO Precis Oncol 7:e2200523.

JCO Precis Oncol 2023;7:e2200523.

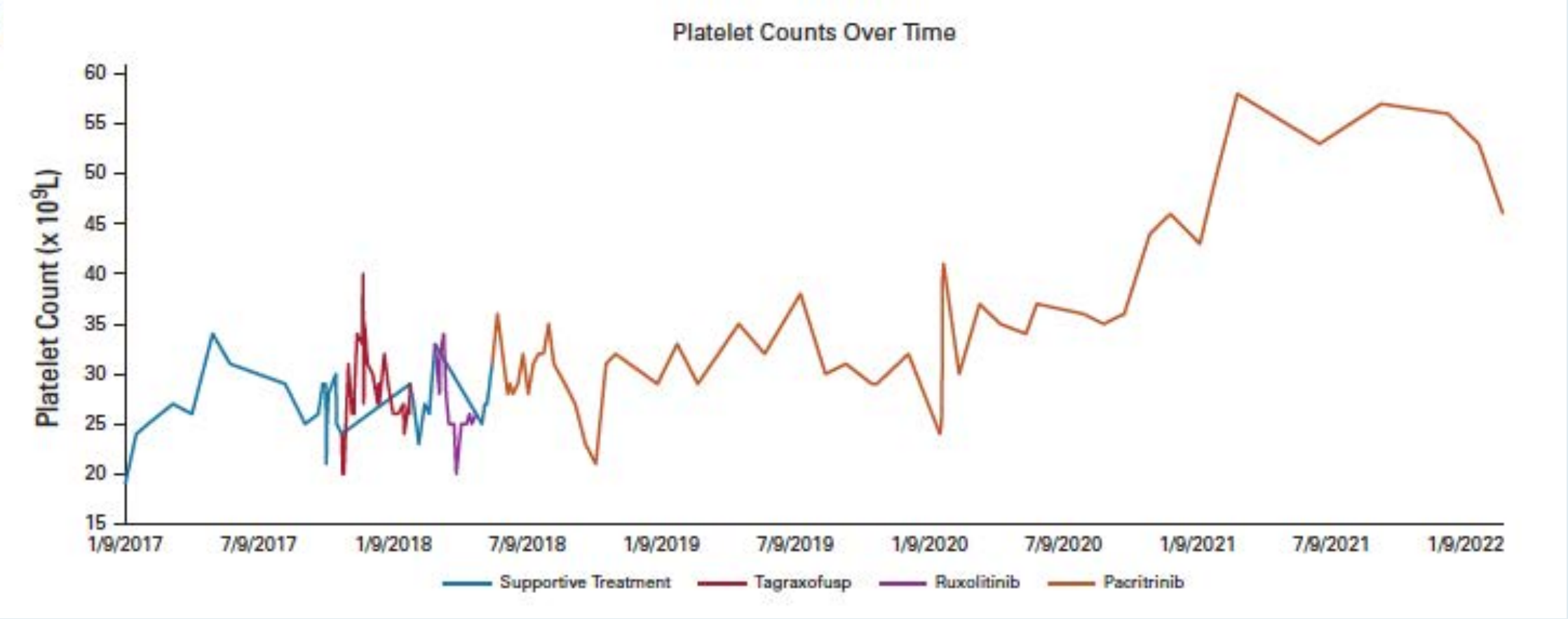
JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Case Report: Hemoglobin Levels over Time for a Patient with MF and Profound Cytopenias Who Received Pacritinib for 4 Years



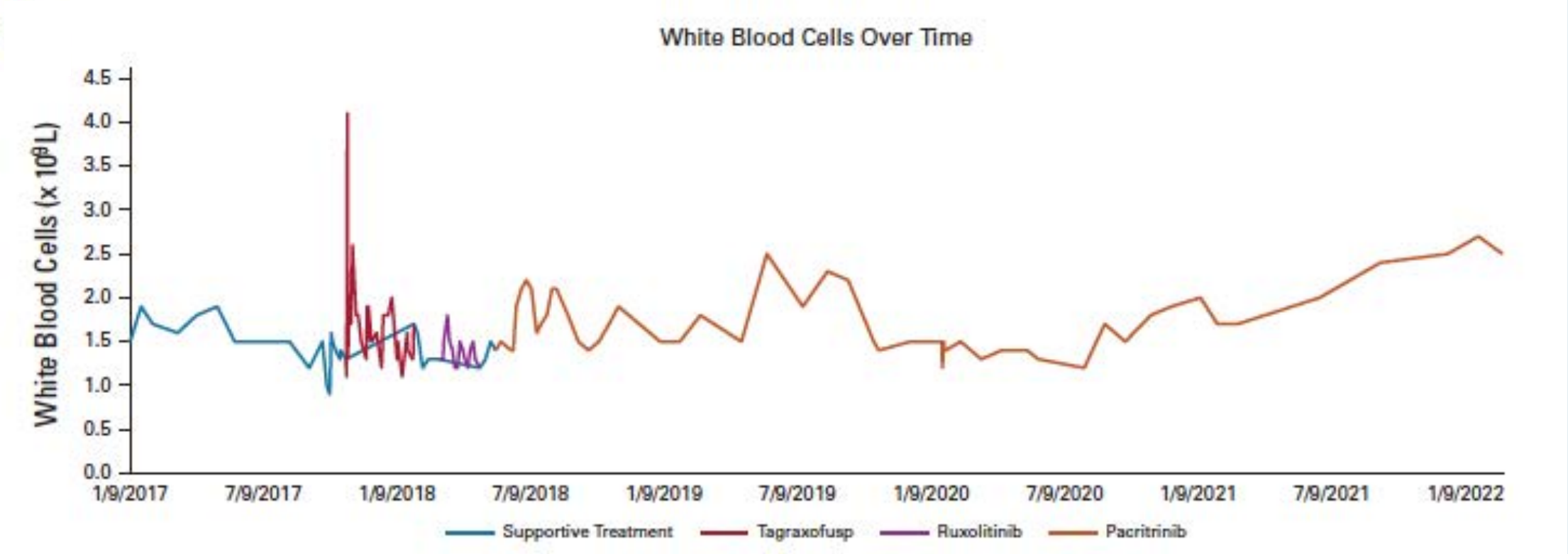
Yacoub A et al. *JCO Precis Oncol* 2023;7:e2200523.

Case Report: Platelet Counts over Time for a Patient with MF and Profound Cytopenias Who Received Pacritinib for 4 Years



Yacoub A et al. *JCO Precis Oncol* 2023;7:e2200523.

Case Report: White Blood Cells over Time for a Patient with MF and Profound Cytopenias Who Received Pacritinib for 4 Years



Yacoub A et al. *JCO Precis Oncol* 2023;7:e2200523.

Received: 24 August 2022 | Accepted: 21 September 2022

DOI: 10.1002/jha2.591

eJHaem

British Society for Haematology

SHORT REPORT

Risk-adjusted safety analysis of the oral JAK2/IRAK1 inhibitor pacritinib in patients with myelofibrosis

Naveen Pemmaraju[1] | Claire Harrison[2] | Vikas Gupta[3] | Srdan Verstovsek[1] | Bart Scott[4] | Stephen T. Oh[5] | Francesca Palandri[6] | Haifa Kathrin Al-Ali[7] | Marta Sobas[8] | Mary Frances McMullin[9] | Ruben Mesa[10] | Sarah Buckley[11] | Karisse Roman-Torres[11] | Alessandro Vannucchi[12] | Abdulraheem Yacoub[13]

2022;3(4):1345-51

Case Presentation: 57-year-old woman is diagnosed with symptomatic primary MF – normal cytogenetics, JAK2 and DNMT3A mutations

Dr Jeanne Palmer (Phoenix, Arizona)

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Case Presentation (Continued): 57-year-old woman has progressive MF after ruxolitinib and fedratinib – repeat NGS shows JAK2, DNMT3A, IDH2 and TET2 mutations

Dr Jeanne Palmer (Phoenix, Arizona)

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Case Presentation: 69-year-old woman with primary MF who discontinued ruxolitinib due to onset of CHF now has possible AML transformation

Dr Tina Bhatnagar (Wheeling, West Virginia)

Initial Bone Marrow Biopsy Results

Final Diagnosis

A. BONE MARROW, CORE BIOPSY AND CLOT SECTION:

- JAK2-positive myeloproliferative neoplasm, favor primary myelofibrosis. (See comment)
- Hypercellular marrow (approximately 95% cellularity) with:
  - No increase in blasts.
  - Trilineage hematopoiesis increased and left-shifted.
  - Numerous atypical megakaryocytes with clustering.
  - Moderate reticulin fibrosis.

Case Presentation: 69-year-old woman with well controlled MF on ruxolitinib 10 mg BID x 3 years develops increasing anemia and splenomegaly

Dr Jeanne Palmer (Phoenix, Arizona)

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Meet The Professor with Dr Oh

INTRODUCTION: ASH 2023 Update

MODULE 1: Case Presentations

MODULE 2: Faculty Survey

MODULE 3: Appendix

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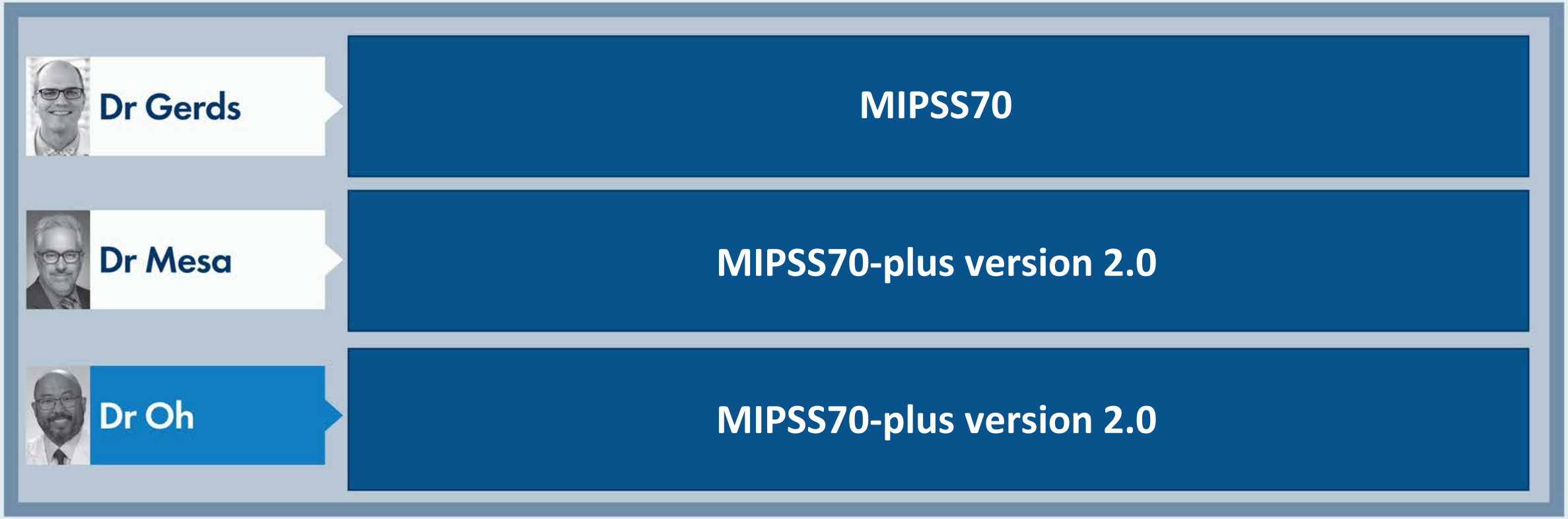
Which prognostic tool do you typically use for your patients with myelofibrosis (MF)?



What was the age of a recent patient from your practice who received fedratinib for MF and what prior treatment(s) had they received?

	Age	Prior treatment(s)
 Dr Gerds	65 years	Ruxolitinib
 Dr Mesa	65 years	Ruxolitinib
 Dr Oh	~50 years	Ruxolitinib

For the patient in the previous scenario who received fedratinib for MF, how much benefit did the patient derive from treatment? What side effects, if any, did the patient experience?

	Treatment benefit	Side effects
 Dr Gerds	A great deal	Mild nausea, mild diarrhea
 Dr Mesa	Some	Nausea, diarrhea
 Dr Oh	Some	GI toxicity

What was the age of a recent patient from your practice who received pacritinib for MF and what prior treatment(s) had they received?

	Age	Prior treatment(s)
 Dr Gerds	76 years	Ruxolitinib + pelabresib
 Dr Mesa	72 years	Ruxolitinib
 Dr Oh	~50 years	Ruxolitinib

For the patient in the previous scenario who received pacritinib for MF, how much benefit did the patient derive from treatment? What side effects, if any, did the patient experience?

	Treatment benefit	Side effects
 Dr Gerds	Some	None
 Dr Mesa	Some	GI effects
 Dr Oh	Some	GI toxicity

What was the age of a recent patient from your practice who received momelotinib for MF and what prior treatment(s) had they received?

	Age	Prior treatment(s)
 Dr Gerds	64 years	Ruxolitinib, fedratinib
 Dr Mesa	58 years	Ruxolitinib
 Dr Oh	~65 years	Ruxolitinib

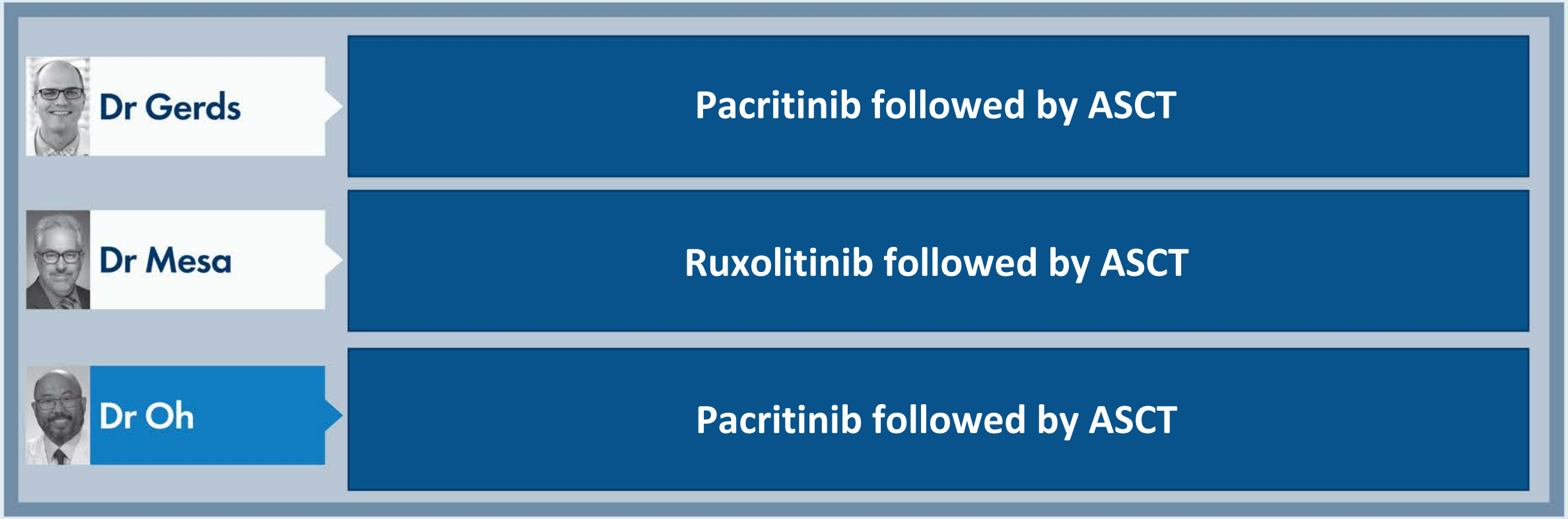
For the patient in the previous scenario who received momelotinib for MF, how much benefit did the patient derive from treatment? What side effects, if any, did the patient experience?

	Treatment benefit	Side effects
 Dr Gerds	A great deal	Flushing of hands and face
 Dr Mesa	A great deal	Not much
 Dr Oh	Some	Nothing significant

A 75-year-old man presents with fatigue, drenching night sweats, weight loss and abdominal pain and is diagnosed with MF. Platelet count = 110,000/µL, Hgb = 11.1 g/dL, WBC = 18,000/µL with 2% blasts. Regulatory and reimbursement issues aside, which treatment would you most likely recommend (assuming the patient is not a transplant candidate)?

 Dr Gerds	Ruxolitinib
 Dr Mesa	Ruxolitinib
 Dr Oh	Ruxolitinib

A 55-year-old man presents with fatigue, drenching night sweats, weight loss, bone pain and a spleen measurement of 20 cm with significant abdominal symptoms and is diagnosed with MF. Platelet count = 44,000/µL, Hgb = 8.1 g/dL, WBC = 36,000/µL with 2% blasts. Genomic profiling is positive for JAK2 V617F, TET2 and ASXL1 mutations. Regulatory and reimbursement issues aside, which treatment would you most likely recommend?



ASCT = allogeneic stem cell transplant

A 62-year-old woman presents with primary MF, constitutional symptoms and splenomegaly, with a baseline platelet count of <50,000/µL. Regulatory and reimbursement issues aside, which treatment would you most likely recommend (assuming the patient is not a transplant candidate)?

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Regulatory and reimbursement issues aside, 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 changes would you most likely try (assuming normal renal and hepatic function and a platelet count >200,000/µL)?

 Dr Gerds	Fedratinib
 Dr Mesa	Escalate dose of ruxolitinib
 Dr Oh	Escalate dose of ruxolitinib

RTP RESEARCH TO PRACTICE

Before a patient starts on fedratinib, which nutritional elements must be evaluated and repleted, and monitored at what frequency?

	Nutritional element(s)	Monitoring frequency
 Dr Gerds	Thiamine	Q3m
 Dr Mesa	Thiamine	Q6m
 Dr Oh	Thiamine	Q6m

When administering the JAK inhibitor fedratinib to a patient with MF, how do you generally approach the prevention and management of associated toxicities?

 Dr Gerds	Prescribe antiemetic and OTC antidiarrheal and thiamine
 Dr Mesa	Administer thiamine and prophylactic antiemetic/ antidiarrheal agents
 Dr Oh	Prophylactic antiemetic, antidiarrheal as needed

A 75-year-old woman with MF receives ruxolitinib 15 mg BID for 2 years with good response. However, at a recent follow-up visit she is experiencing worsening cytopenias, new-onset splenomegaly and an increased symptom burden. Platelet count = 76,000/µL, Hgb = 6.7 g/dL. Regulatory and reimbursement issues aside, which treatment would you most likely recommend (assuming the patient is not a transplant candidate)?

 Dr Gerds	Switch to momelotinib 200 mg once a day
 Dr Mesa	Switch to momelotinib 200 mg once a day
 Dr Oh	Switch to momelotinib 200 mg once a day

RTP RESEARCH TO PRACTICE

Based on current clinical trial data and your personal experience, how would you indirectly compare the overall efficacy and tolerability of pacritinib to that of ruxolitinib and fedratinib for patients with MF?

	Efficacy	Tolerability
 Dr Gerds	Available data are insufficient at this time	Ruxolitinib is most tolerable
 Dr Mesa	Available data are insufficient at this time	Ruxolitinib is most tolerable
 Dr Oh	Ruxolitinib is most efficacious	Ruxolitinib is most tolerable

When administering the JAK inhibitor pacritinib to a patient with MF, how do you generally approach the prevention and management of associated toxicities?

 Dr Gerds	Frequent blood counts, antiemetic and antidiarrheal meds, check EKG to monitor for QTc
 Dr Mesa	Nausea and diarrhea prophylaxis
 Dr Oh	Prophylactic antiemetic, antidiarrheal as needed

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

 Dr Gerds	No
 Dr Mesa	No
 Dr Oh	No

In your experience, what are the most important tolerability issues associated with momelotinib?

 Dr Gerds	GI side effects, thrombocytopenia, rebound symptoms when changing tx to momelotinib
 Dr Mesa	GI issues, but they are mild
 Dr Oh	Generally well tolerated

Meet The Professor with Dr Oh

INTRODUCTION: ASH 2023 Update

MODULE 1: Case Presentations

MODULE 2: Faculty Survey

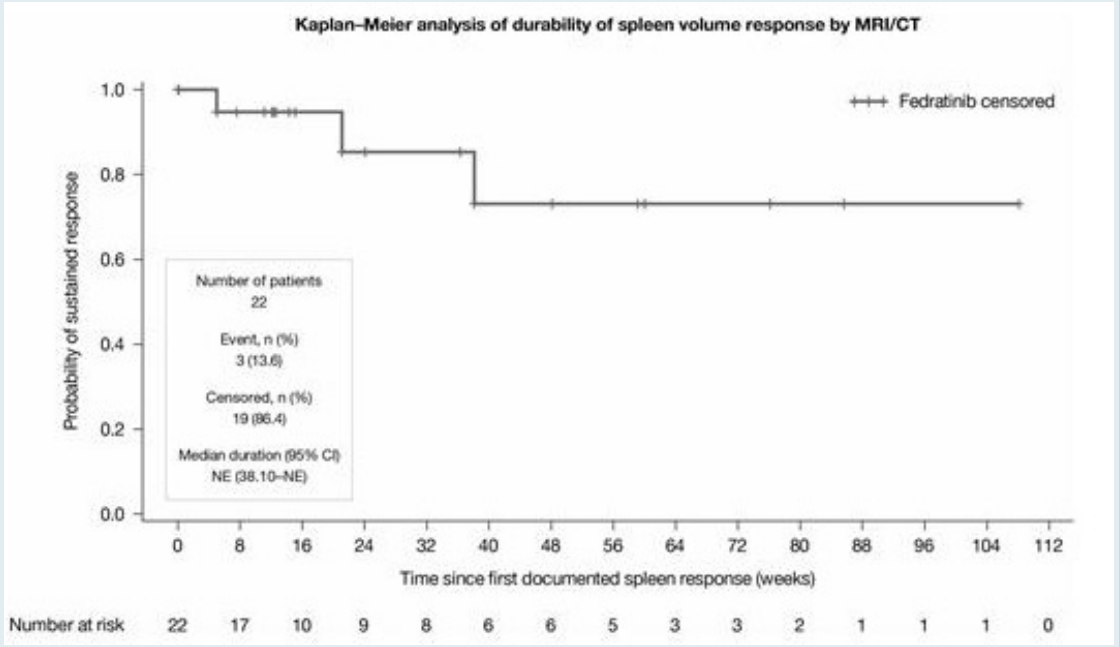
MODULE 3: Appendix

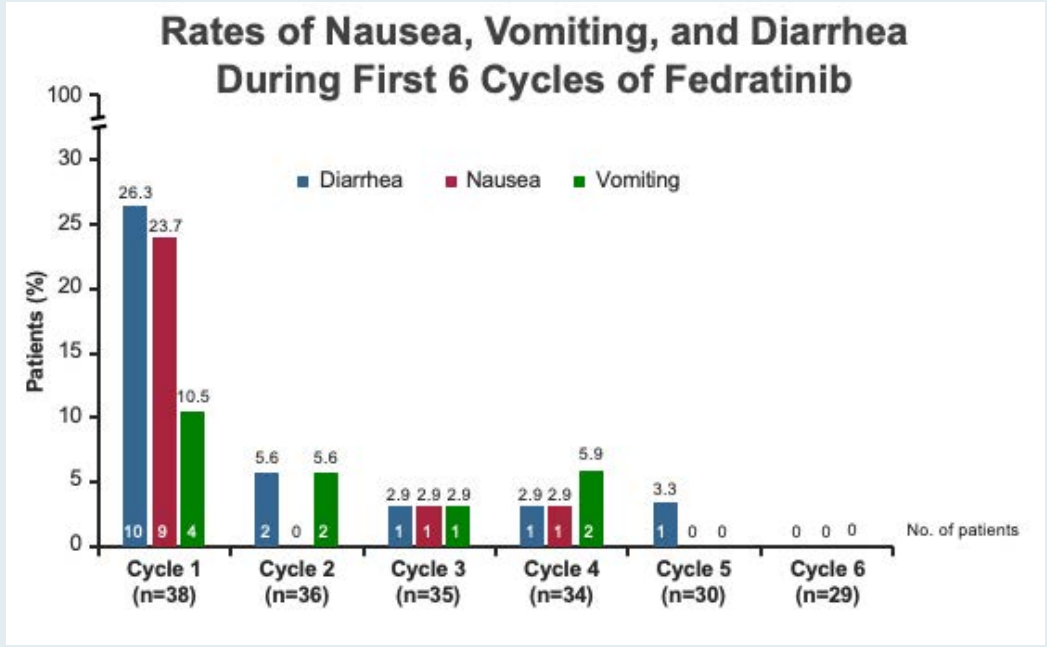
RTP
RESEARCH
TO PRACTICE

Current Clinical Decision-Making for Patients with Myelofibrosis (MF) in the Absence of Severe Cytopenias

Phase IIIB FREEDOM Trial of Fedratinib for Patients with Primary, Post-PV or Post-ET Myelofibrosis Previously Treated with Ruxolitinib

FREEDOM included proactive strategies to mitigate gastrointestinal (GI) adverse events, thiamine level decreases and potential encephalopathy





- Clinically relevant and durable spleen responses were observed
- Most GI AEs were Grade 1/2 and occurred during cycle 1, and decreased in subsequent cycles
- 6 patients with Grade 1/2 decreases in thiamine levels after initial tx were treated and deficiencies were resolved at next assessment; no patients required tx discontinuation due to low thiamine levels

Gupta V et al. ASH 2022;Abstract 1711.

RTP RESEARCH TO PRACTICE

Management of MF in Patients with Thrombocytopenia

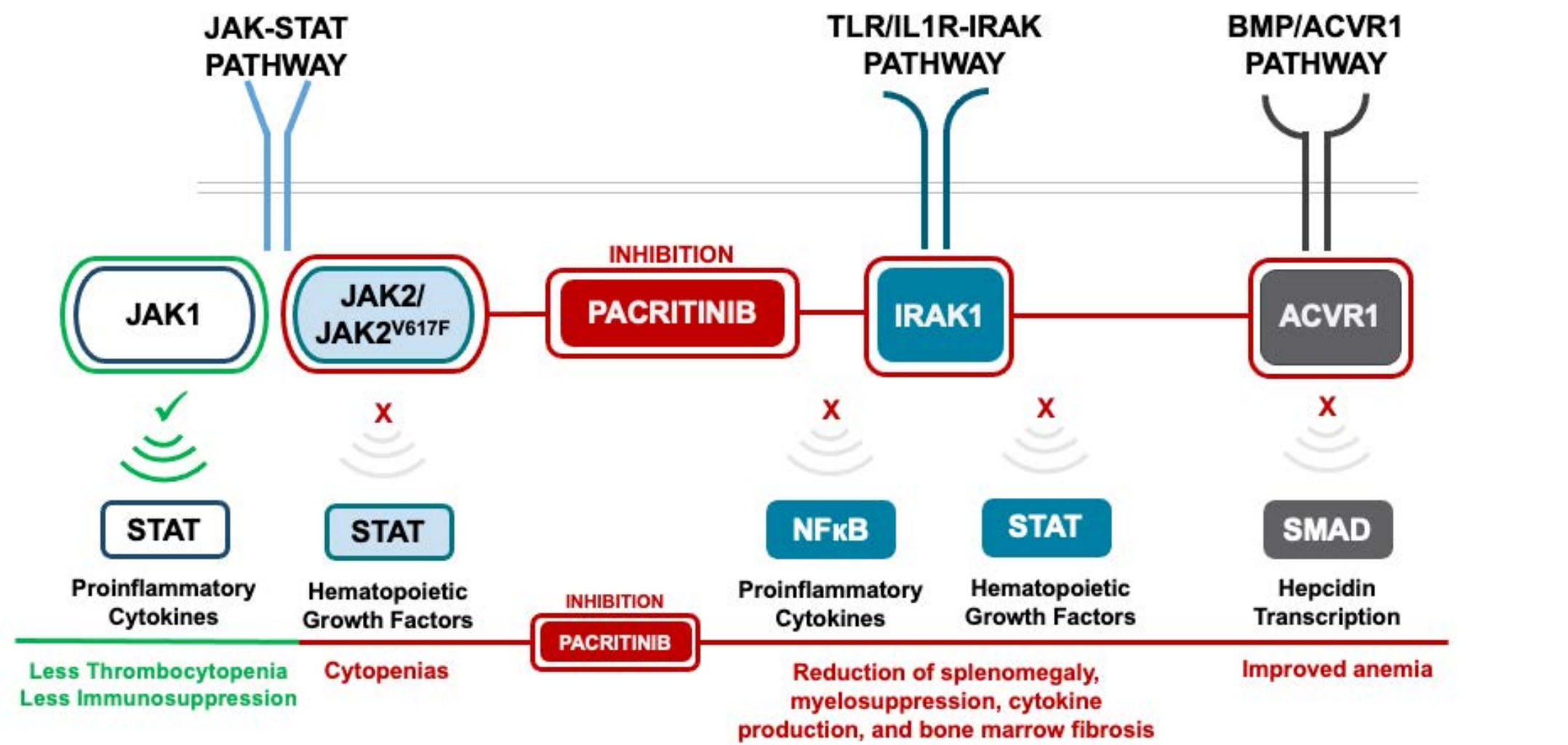
JAK Inhibitor Specificities

JAK and FLT3 Kinases IC_{50} (nM)				
Kinase	Pacritinib	Ruxolitinib	Fedratinib	Momelotinib
JAK1	1280	3.4	18	11
JAK2	6.0	4.5	1.1	18
$JAK2^{V617F}$	9.4	NR	NR	–
Non-tyrosine Kinases of Interest IC_{50} (nM)				
CSF1R	39.5	>3000	220	–
IRAK1	13.6	290	620	NR
ACVR1	16.7	>1000	273	52.5

CSF1R, colony stimulating factor 1 receptor; FLT, FMS-like tyrosine kinase; IRAK, interleukin-1 receptor-associated kinase; ITD, internal tandem duplication; TYK, tyrosine kinase.
Singer J, et al. *Blood.* 2014;124:1874; Mascarenhas JO, et al. *Haematologica.* 2017;102:327-335. Jadwiga J. et al. *Blood.* 2018 132 (Supplement 1): 2559. Duenas-Perez AB et al. *Ther Adv Hematol.* 2015: 186-201

Courtesy of John O Mascarenhas, MD

Pacritinib Inhibits JAK2, IRAK1 and ACVR1 (Sparing JAK1)



1. Jarochoa J. et al. Blood 2018; 132(supplement 1)"2559. 2. Mascarenhas J, et al. Haematologica 2017; 102(2): 327-335 3. Singer J et al. Abstract #1874 Oral presentation ASH2014 4. Fisher D. et al Leukemia 2019; 333(8) 1978-1996 5. Lay HY, et al. Blood Adv 2019; 3(2): 122-131 6. Balka KR, et al. J Leukoc Biol 2019; 105 (2): 339-351 6. Oh S. et al. Oral Presentation ASH2022 Abstract #628 Pacritinib exhibits inhibitory activity against additional cellular kinases (such as CSF1R and IRKA1), although the clinical relevance is unknown ACVR1= Activin A receptor type 1

Courtesy of John O Mascarenhas, MD

RTP RESEARCH TO PRACTICE

Pacritinib Granted Accelerated Approval for Myelofibrosis 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. 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

Research

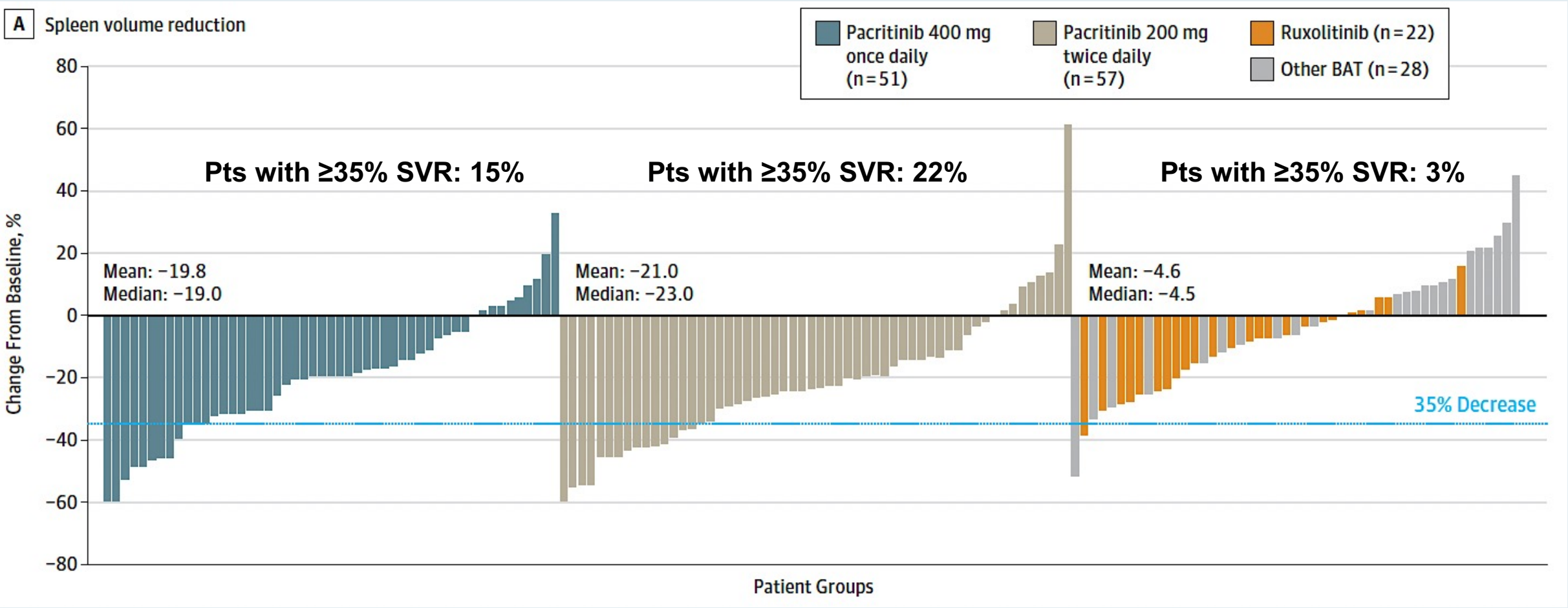
2018;4(5):652-9

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 (SVR)



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

PERSIST-2: Adverse Event Profile of Pacritinib

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

Mascarenhas J et al. *JAMA Oncol* 2018;4:652-59.

Impact of Symptom Benefit and Transfusion Response on Survival in Myelofibrosis Patients Treated with Pacritinib: PERSIST-2 Landmark Survival Analysis

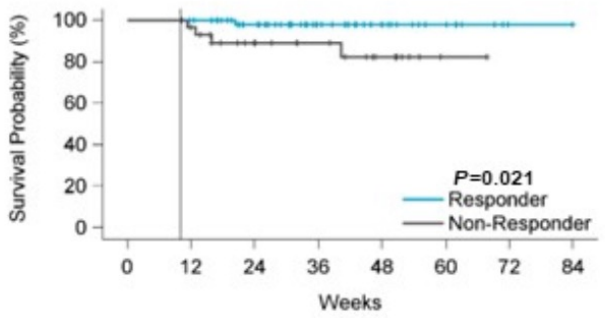
Ajufo H et al.

ASH 2023; Abstract 3207.

PERSIST-2: OS Stratified by TSS Response

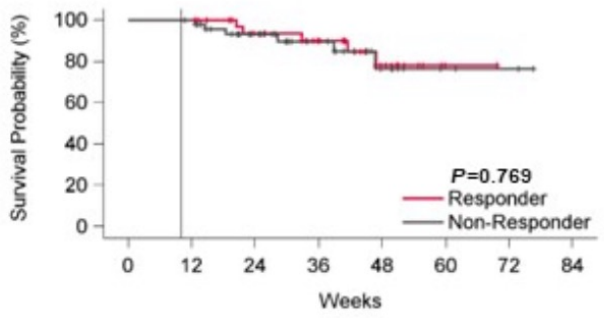
Figure 1. Landmark survival analysis based on week 12 Total Symptom Score (TSS) reduction.
Survival stratified by varying thresholds of TSS (v2.0, excluding tiredness) response (≥10%, ≥20%, ≥50%) for pacritinib 200 mg BID (A, C, E) and BAT (B, D, F).

(a) PAC 200 mg BID: OS stratified by **≥10%** TSS Response



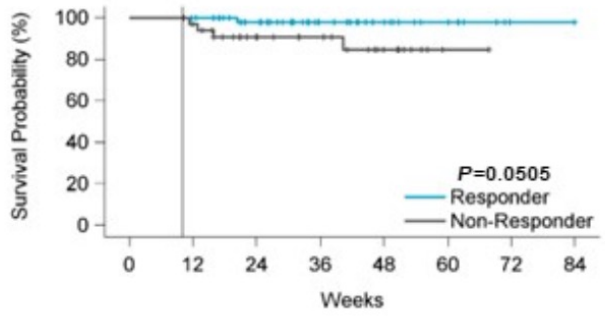
N							
Responder	59	44	27	15	8	1	0
Non-Responder	30	18	14	8	1	0	0

(b) BAT (including RUX): OS stratified by **≥10%** TSS Response



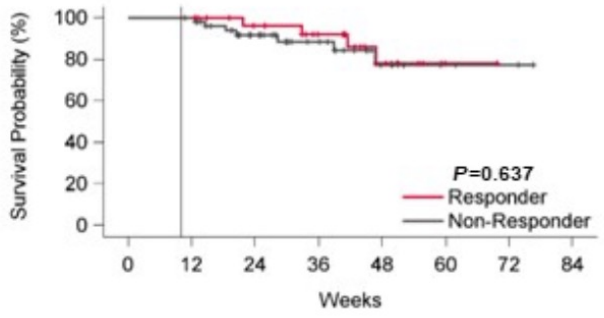
N							
Responder	36	28	21	10	1	0	0
Non-Responder	48	32	20	8	3	2	0

(c) PAC 200 mg BID: OS stratified by **≥20%** TSS Response



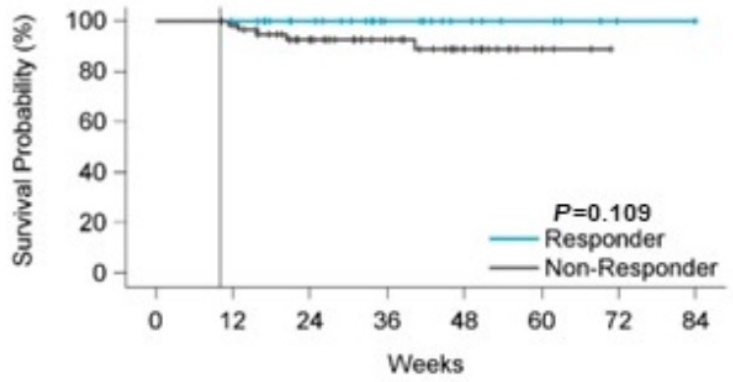
N							
Responder	54	41	24	14	8	1	0
Non-Responder	35	21	17	9	1	0	0

(d) BAT (including RUX): OS stratified by **≥20%** TSS Response



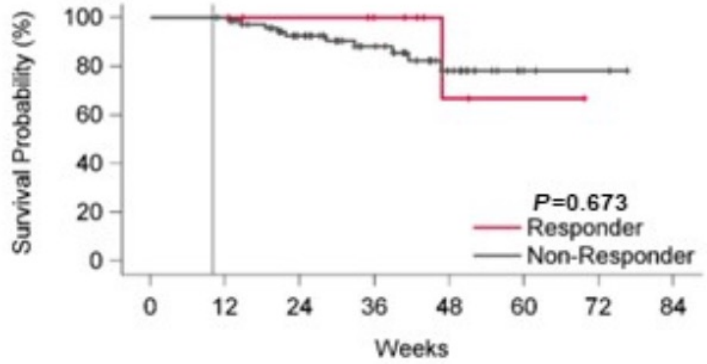
N							
Responder	31	25	18	9	1	0	0
Non-Responder	53	35	23	9	3	2	0

(e) PAC 200 mg BID: OS stratified by **≥50%** TSS Response



N							
Responder	29	22	13	8	5	1	0
Non-Responder	60	40	28	15	4	0	0

(f) BAT (including RUX): OS stratified by **≥50%** TSS Response



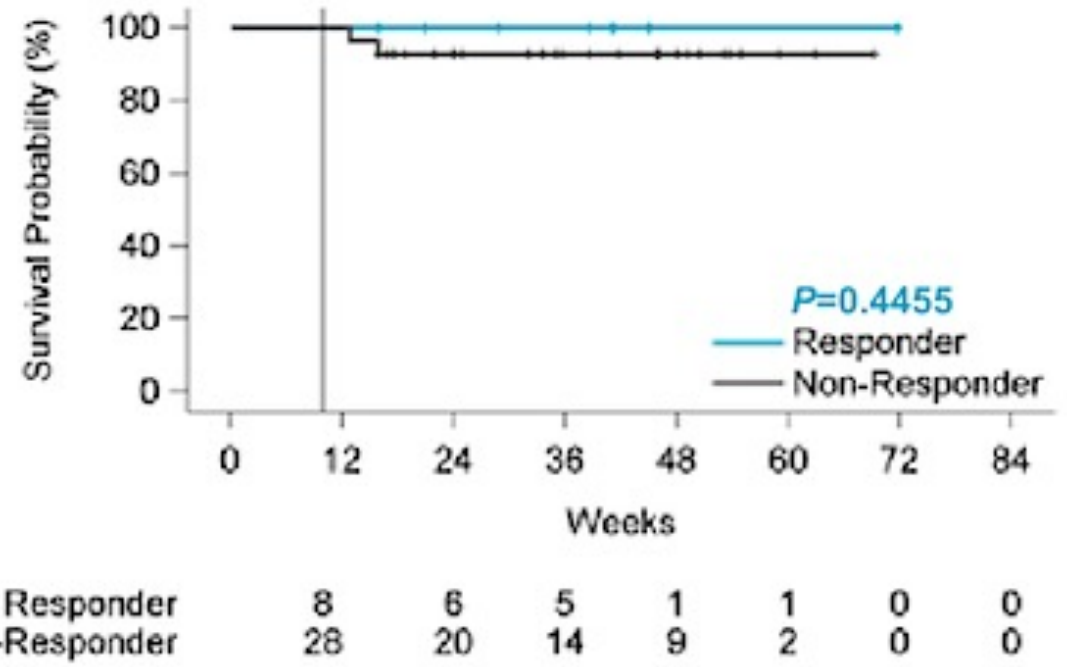
N							
Responder	10	8	6	2	1	0	0
Non-Responder	74	52	35	16	3	2	0

Ajufo H et al. ASH 2023;Abstract 3207.

RTP RESEARCH TO PRACTICE

PERSIST-2: OS Analysis Based on Transfusion Independence (TI)

Figure 2. OS analysis based on TI response for PAC



PAC, pacritinib, OS, overall survival, TI, transfusion independence.

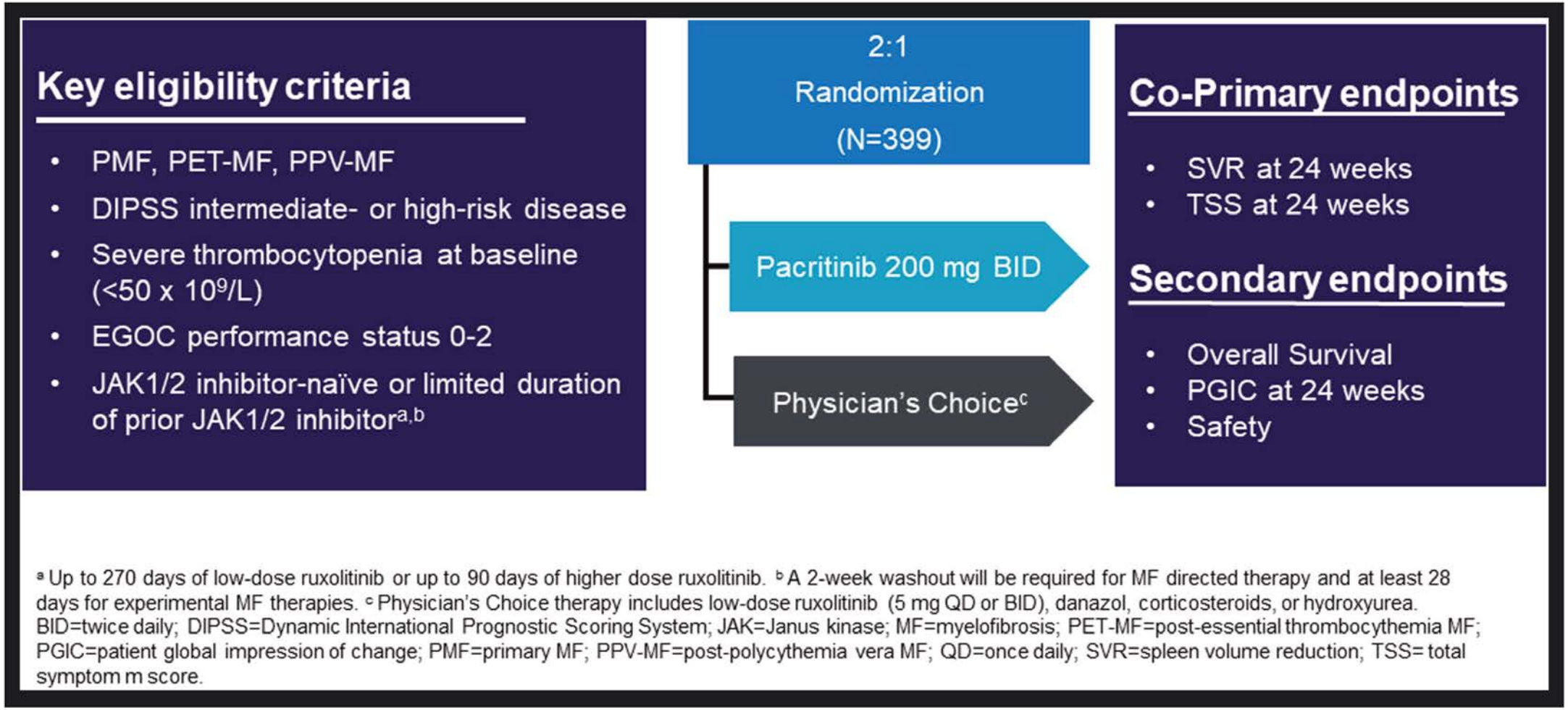
No clear association between transfusion response and death

- Among 36 patients on PAC who received RBC transfusions at baseline, 7 achieved TI over at least a 12-week period up to the time of the landmark analysis.
  - There were no deaths among TI responders compared to 2 (6.9%) among TI non-responders.
- There were too few TI responders on BAT (only 2 out of 38) to assess the impact on survival.

Ajufo H et al. ASH 2023;Abstract 3207.

RTP RESEARCH TO PRACTICE

PACIFICA: An Ongoing Phase III Trial of Pacritinib versus Physician's Choice for Patients with Primary or Secondary Myelofibrosis and Severe Thrombocytopenia



Mascarenhas J et al. *Blood* 2022; 140(Supplement 1):9592-4.

Available and Emerging Options for Patients with MF and Anemia

REGULAR ARTICLE

blood advances

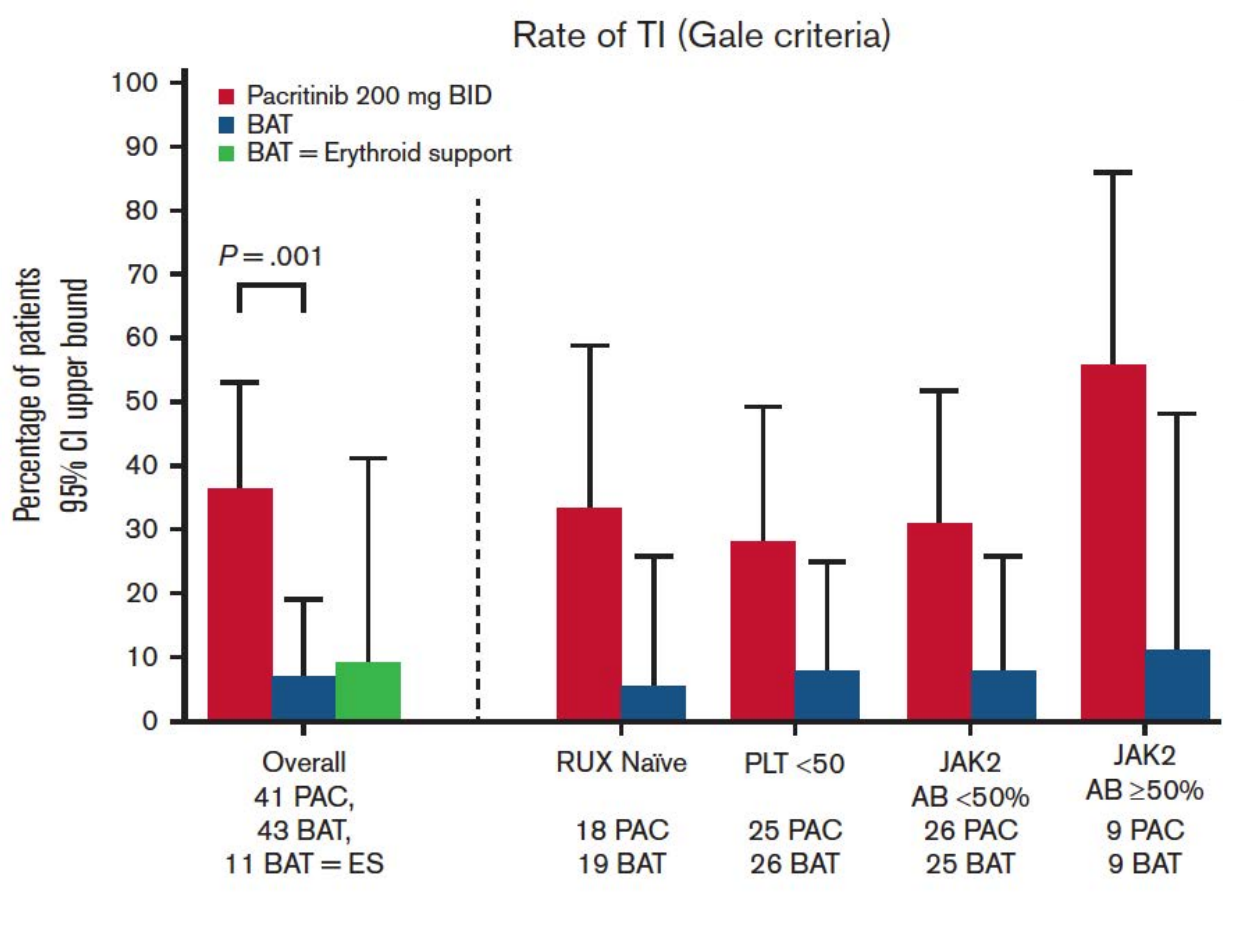
Pacritinib is a potent ACVR1 inhibitor with significant anemia benefit in patients with myelofibrosis

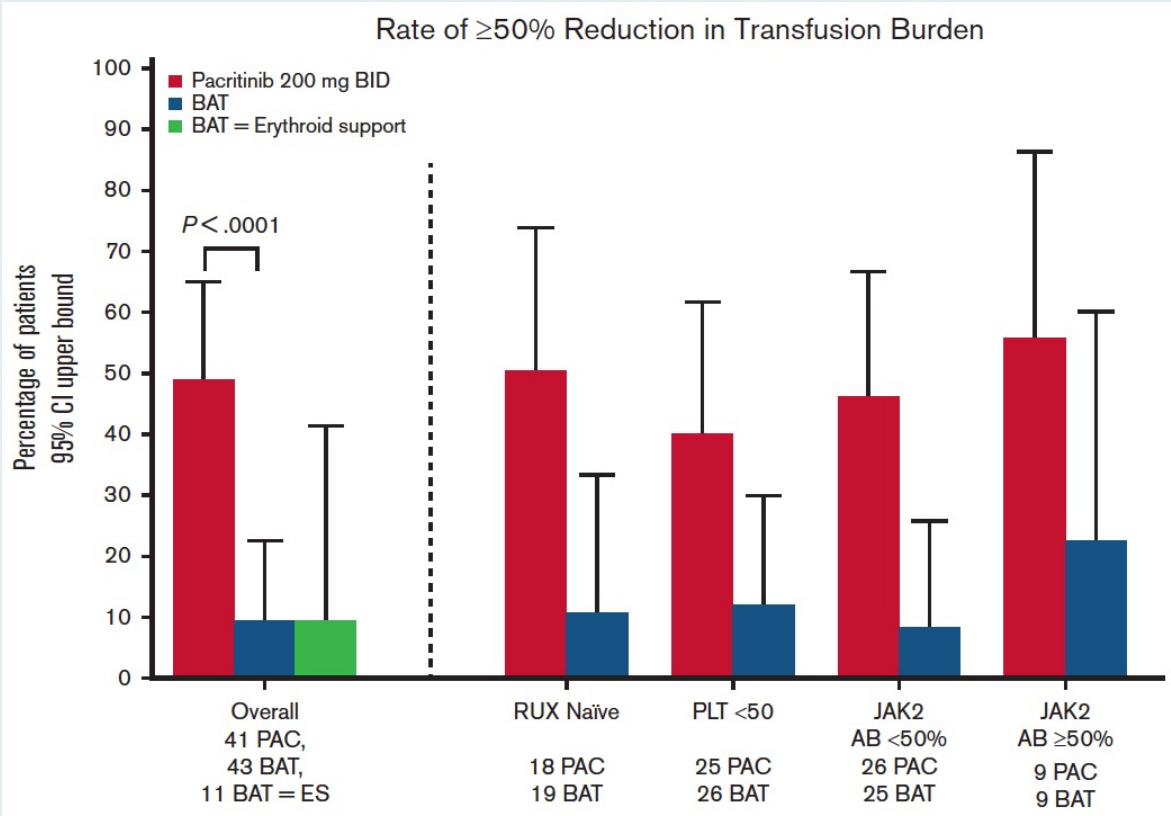
Stephen T. Oh,[1] Ruben A. Mesa,[2] Claire N. Harrison,[3] Prithviraj Bose,[4] Aaron T. Gerds,[5] Vikas Gupta,[6] Bart L. Scott,[7] Jean-Jacques Kiladjian,[8] Alessandro Lucchesi,[9] Tim Kong,[1] Sarah A. Buckley,[10] Shanthakumar Tyavanagimatt,[10] Bryan G. Harder,[10] Karisse Roman-Torres,[10] Jennifer Smith,[10] Adam R. Craig,[10] John Mascarenhas,[11] and Srdan Verstovsek[4]

[1]Washington University School of Medicine, St. Louis, MO; [2]Atrium Health Wake Forest Baptist Comprehensive Cancer Center, Winston-Salem, NC; [3]Guy's and St Thomas' NHS Trust, London, United Kingdom; [4]The University of Texas MD Anderson Cancer Center, Houston, TX; [5]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH; [6]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; [7]Fred Hutchinson Cancer Research Center, Seattle, WA; [8]Hôpital Saint- Louis, Université de Paris, Paris, France; [9]Hematology Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori," Meldola, Italy; [10]CTI BioPharma Corp., Seattle, WA; and [11]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY

2023;7(19):5835-42

PERSIST-2: Transfusion Independence (TI) and Transfusion Reduction with Pacritinib





Abbreviations: AB, allele burden; BAT, best available therapy; BID, twice daily; CI, confidence interval; ES, erythroid support; JAK, Janus associated kinase; PAC, pacritinib; PLT, platelets; RUX naïve (no RUX prior to first dose).

Oh ST et al. *Blood Adv* 2023;7(19):5835-42.

RTP RESEARCH TO PRACTICE

Momelotinib Granted Approval for Myelofibrosis with Anemia

Press Release: September 15, 2023

"On September 15, 2023, the FDA approved momelotinib for the treatment of intermediate- or high-risk myelofibrosis, including primary myelofibrosis or secondary myelofibrosis (post–polycythemia vera and post–essential thrombocythemia), in adults with anemia.

The FDA approval of momelotinib is supported by data from the pivotal MOMENTUM study (NCT04173494) and a subpopulation of adults with anemia from the SIMPLIFY-1 phase III trial (NCT01969838).

MOMENTUM was designed to evaluate the safety and efficacy of momelotinib vs danazol for the treatment and reduction of key manifestations of myelofibrosis in an anemic, symptomatic, JAK inhibitor–experienced patient population. The MOMENTUM trial met all its primary and key secondary endpoints, demonstrating statistically significant response with respect to constitutional symptoms, splenic response, and transfusion independence in patients treated with momelotinib vs danazol."

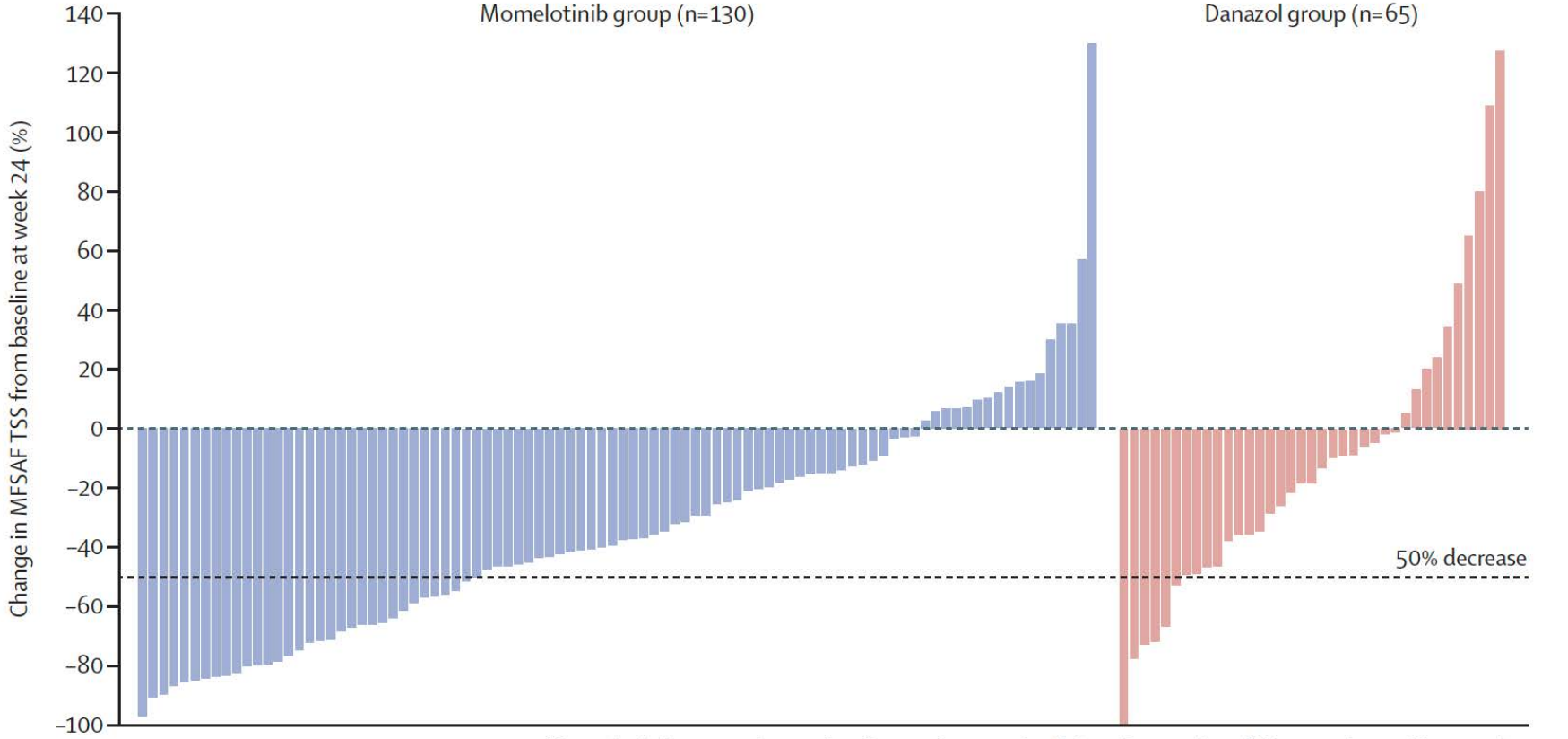
https://ascopost.com/news/september-2023/fda-approves-momelotinib-for-patients-with-myelofibrosis-and-anemia/

Lancet 2023;401;269-80

Momelotinib versus danazol in symptomatic patients with anaemia and myelofibrosis (MOMENTUM): results from an international, double-blind, randomised, controlled, phase 3 study

*Srdan Verstovsek, Aaron T Gerds, Alessandro M Vannucchi, Haifa Kathrin Al-Ali, David Lavie, Andrew T Kuykendall, Sebastian Grosicki, Alessandra Iurlo, Yeow Tee Goh, Mihaela C Lazaroiu, Miklos Egyed, Maria Laura Fox, Donal McLornan, Andrew Perkins, Sung-Soo Yoon, Vikas Gupta, Jean-Jacques Kiladjian, Nikki Granacher, Sung-Eun Lee, Luminita Ocroteala, Francesco Passamonti, Claire N Harrison, Barbara J Klencke, Sunhee Ro, Rafe Donahue, Jun Kawashima, Ruben Mesa, on behalf of MOMENTUM Study Investigators**

MOMENTUM: Percent Change of TSS from Baseline to Week 24 for Each Patient



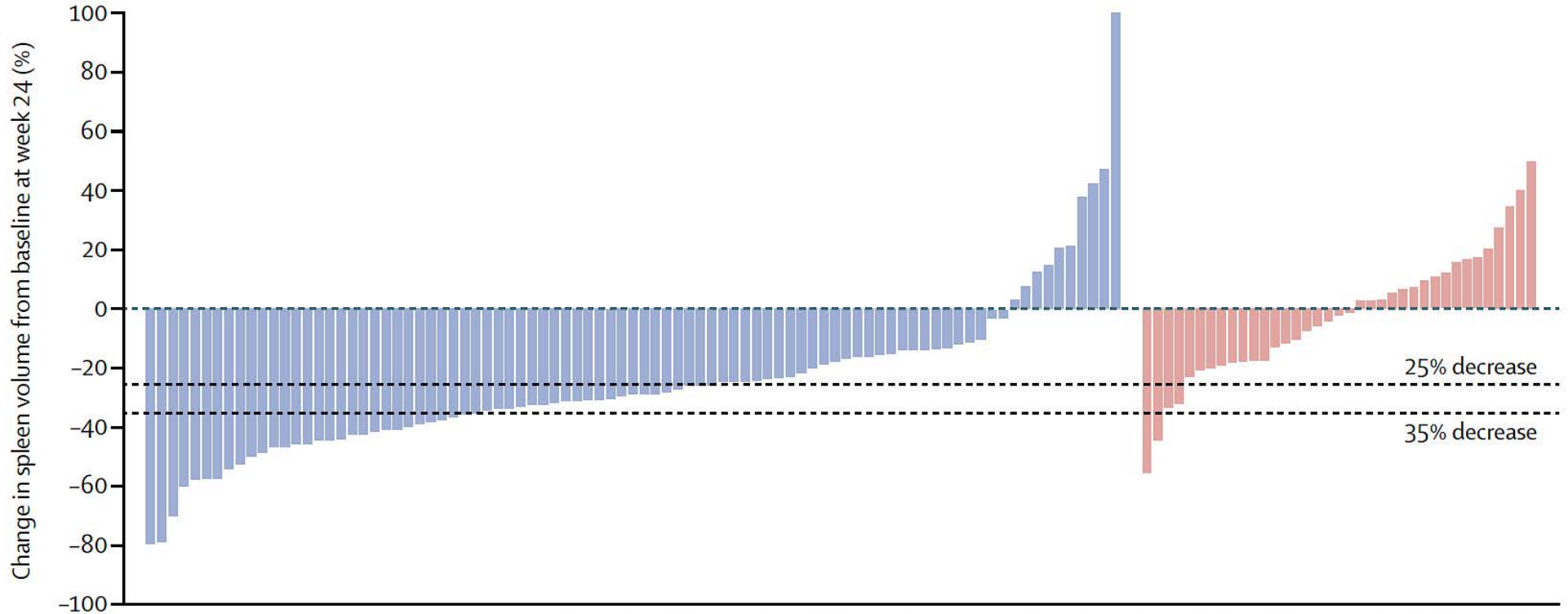
	Momelotinib group (n=130)	Danazol group (n=65)	Proportion difference (95% CI)	p value
Number meeting at least 50% reduction in MSAF TSS at week 24	32 (25% [95% CI 17–33])	6 (9% [95% CI 4–19])	16% (6–26)	0·0095

MFSAF=Myelofibrosis Symptom Assessment Form TSS=total symptom score

Verstovsek S et al. *Lancet* 2023;401:269-80.

RTP RESEARCH TO PRACTICE

MOMENTUM: Percent Change of Spleen Volume from Baseline to Week 24 for Each Patient



	Momelotinib group (n=130)	Danazol group (n=65)	Proportion difference (95% CI)	p value
Number meeting at least 25% reduction in spleen volume	52 (40% [95% CI 32–49])	4 (6% [95% CI 2–15])	34% (24–45)	<0·0001
Number meeting at least 35% reduction in spleen volume	30 (23% [95% CI 16–31])	2 (3% [95% CI 0–11])	19% (11–28)	0·0006

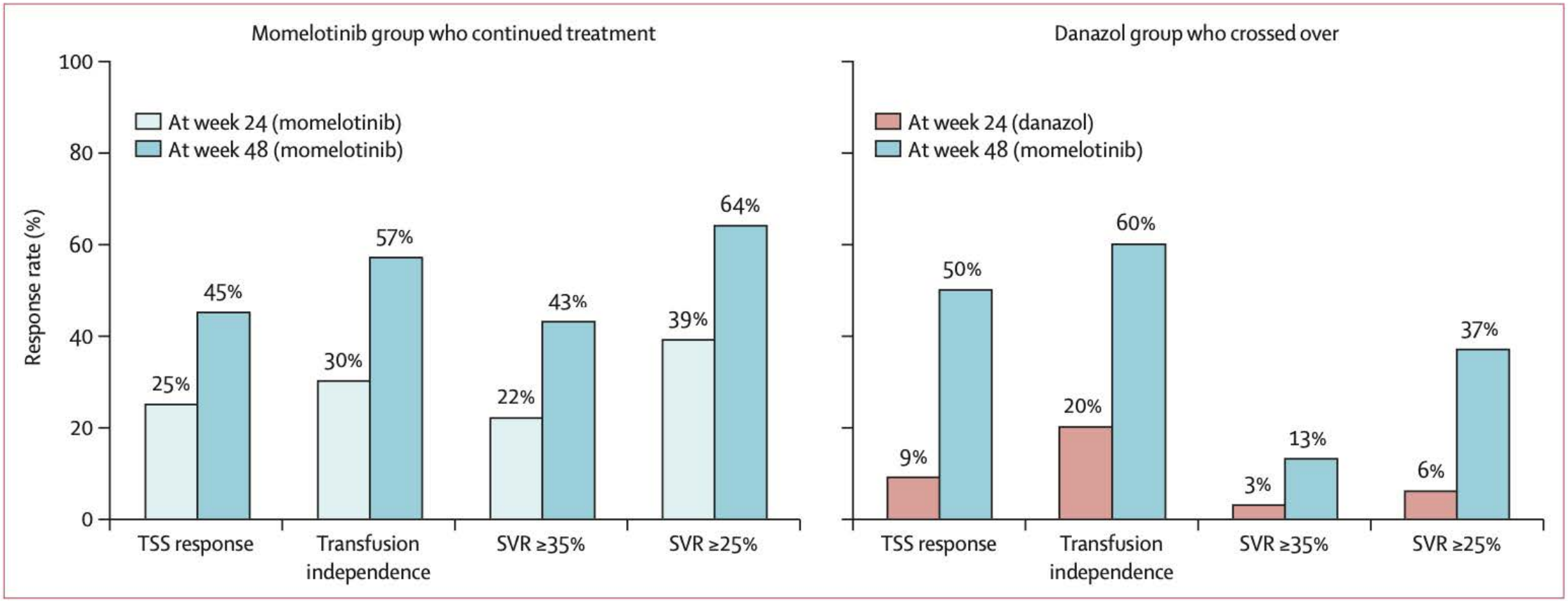
Verstovsek S et al. *Lancet* 2023;401:269-80.

Momelotinib versus danazol in symptomatic patients with anaemia and myelofibrosis previously treated with a JAK inhibitor (MOMENTUM): an updated analysis of an international, double-blind, randomised phase 3 study

Aaron T Gerds, Srdan Verstovsek, Alessandro M Vannucchi, Haifa Kathrin Al-Ali, David Lavie, Andrew T Kuykendall, Sebastian Grosicki, Alessandra Iurlo, Yeow Tee Goh, Mihaela C Lazaroiu, Miklos Egyed, Maria Laura Fox, Donal McLornan, Andrew Perkins, Sung-Soo Yoon, Vikas Gupta, Jean-Jacques Kiladjian, Nikki Granacher, Sung-Eun Lee, Luminita Ocroteala, Francesco Passamonti, Claire N Harrison, Stephen Oh, Barbara J Klencke, Jing Yu, Rafe Donahue, Jun Kawashima, Ruben Mesa

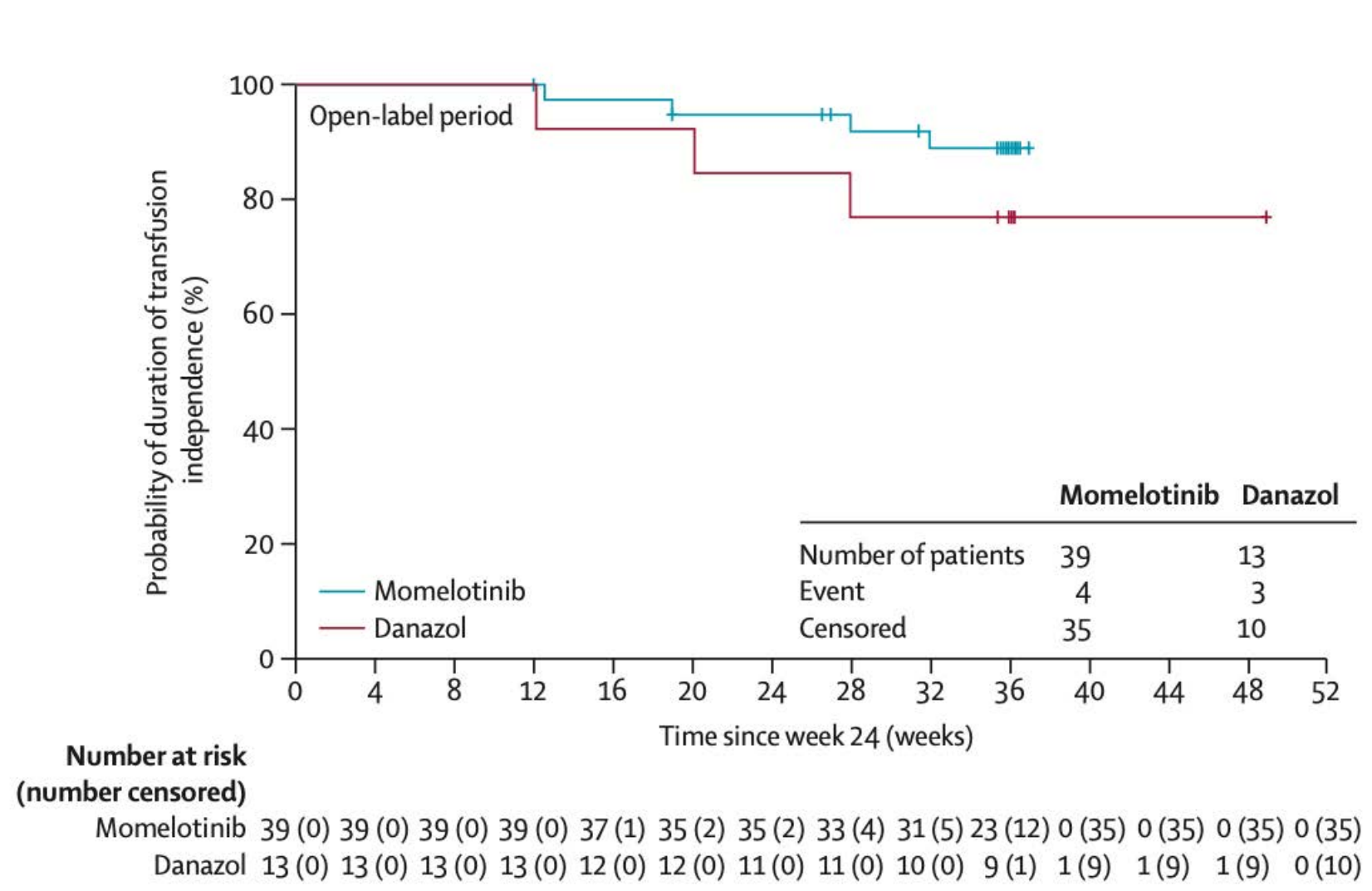
***Lancet Haematol* 2023;10(9):e735-46**

MOMENTUM: Summary of Response Rates at Weeks 24 and 48



Gerds AT et al. *Lancet Haematol* 2023;10(9):e735-46.

MOMENTUM: Duration of Transfusion Independence Response



Gerds AT et al. *Lancet Haematol* 2023;10(9):e735-46.

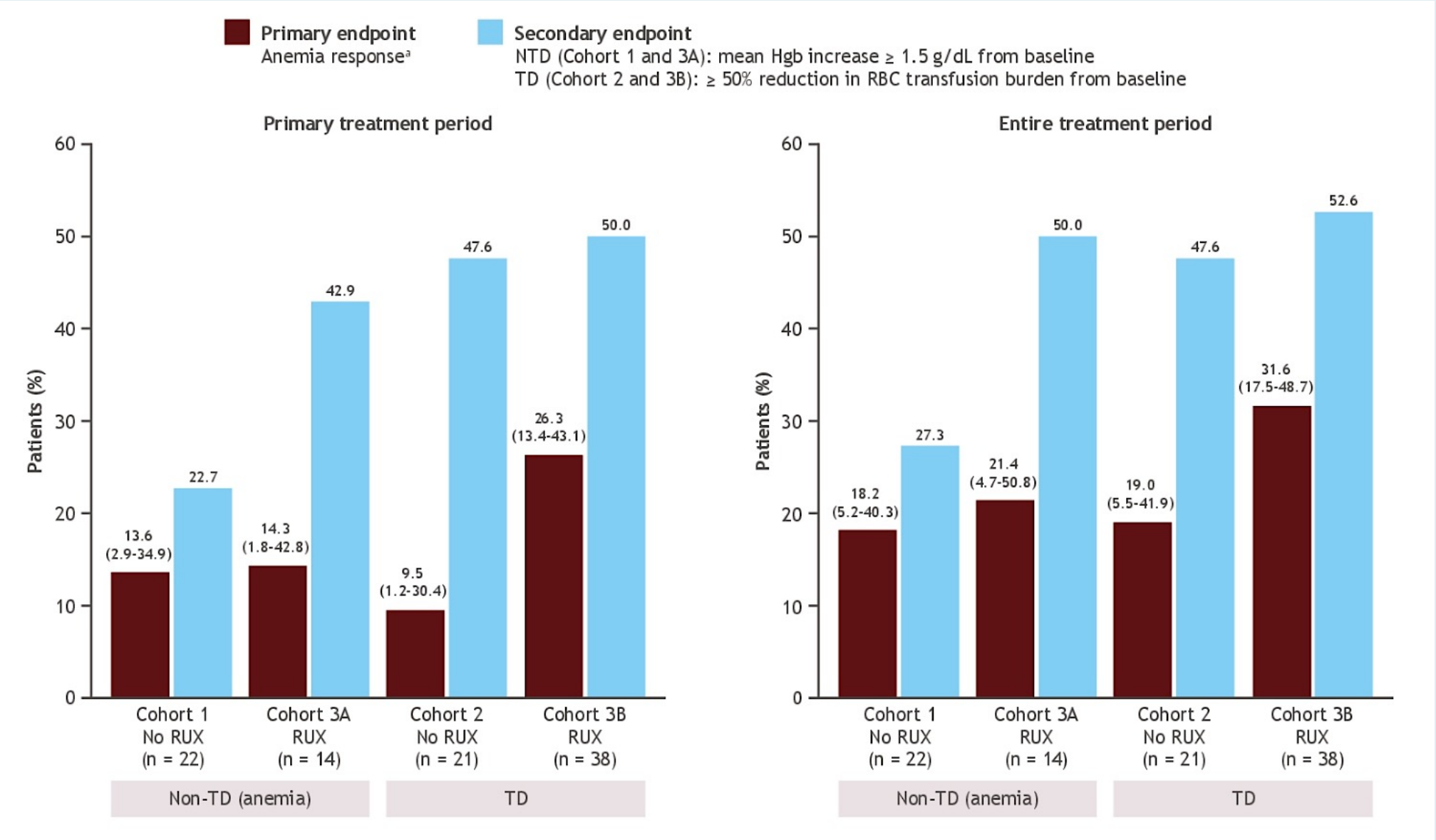
RTP RESEARCH TO PRACTICE

Safety and Efficacy of Luspatercept for the Treatment of Anemia in Patients with Myelofibrosis: Results from the ACE-536-MF-001 Study

Gerds AT et al.

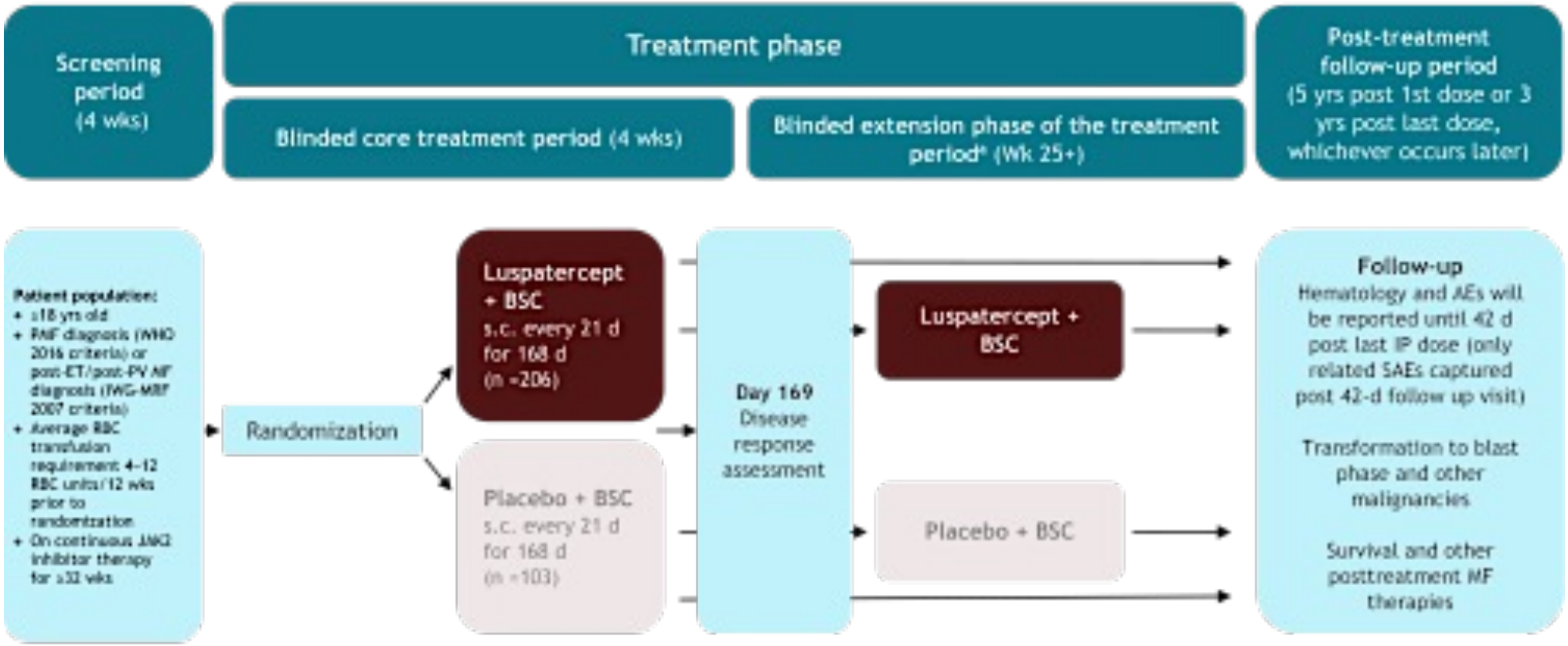
ASCO 2023;Abstract 7016.

ACE-536-MF-001: Efficacy Results



Gerds AT et al. ASCO 2023;Abstract 7016.

INDEPENDENCE: A Phase III Study of Luspatercept for MPN-Associated Myelofibrosis in Patients Receiving JAK2 Inhibitor Therapy



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; yr, year.

*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 weeks 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.

Mesa R et al. EHA 2021;Abstract PB1702.

MPN = myeloproliferative neoplasm

RTP RESEARCH TO PRACTICE

Future Directions in MF Management

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RESEARCH
TO PRACTICE

Selinexor Plus Ruxolitinib in JAK Inhibitor (JAKi)-Naïve Patients With Myelofibrosis: Long-Term Follow-up From XPORT-MF-034 Suggestive of Disease Modification

Srinivas K Tantravahi,[1] Ashwin Kishtagari,[2] Keri Maher,[3] Sanjay Mohan,[2] Josef T Prchal,[1] Xulong Wang,[4] Kamal Chamoun,[5] Christopher J Walker,[4] Pietro Taverna,[4] Steve Kye,[4] Haris Ali[6]

[1]Division of Hematology and Hematologic Malignancies, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA
[2]Vanderbilt Ingram Cancer Center, Nashville, TN, USA
[3]VCU Massey Cancer Center, Richmond, VA, USA
[4]Karyopharm Therapeutics, Newton, MA, USA
[5]Formerly of Karyopharm Therapeutics, Newton, MA, USA
[6]City of Hope Comprehensive Cancer Center, Duarte, CA, USA

ASH 2023;Abstract 622

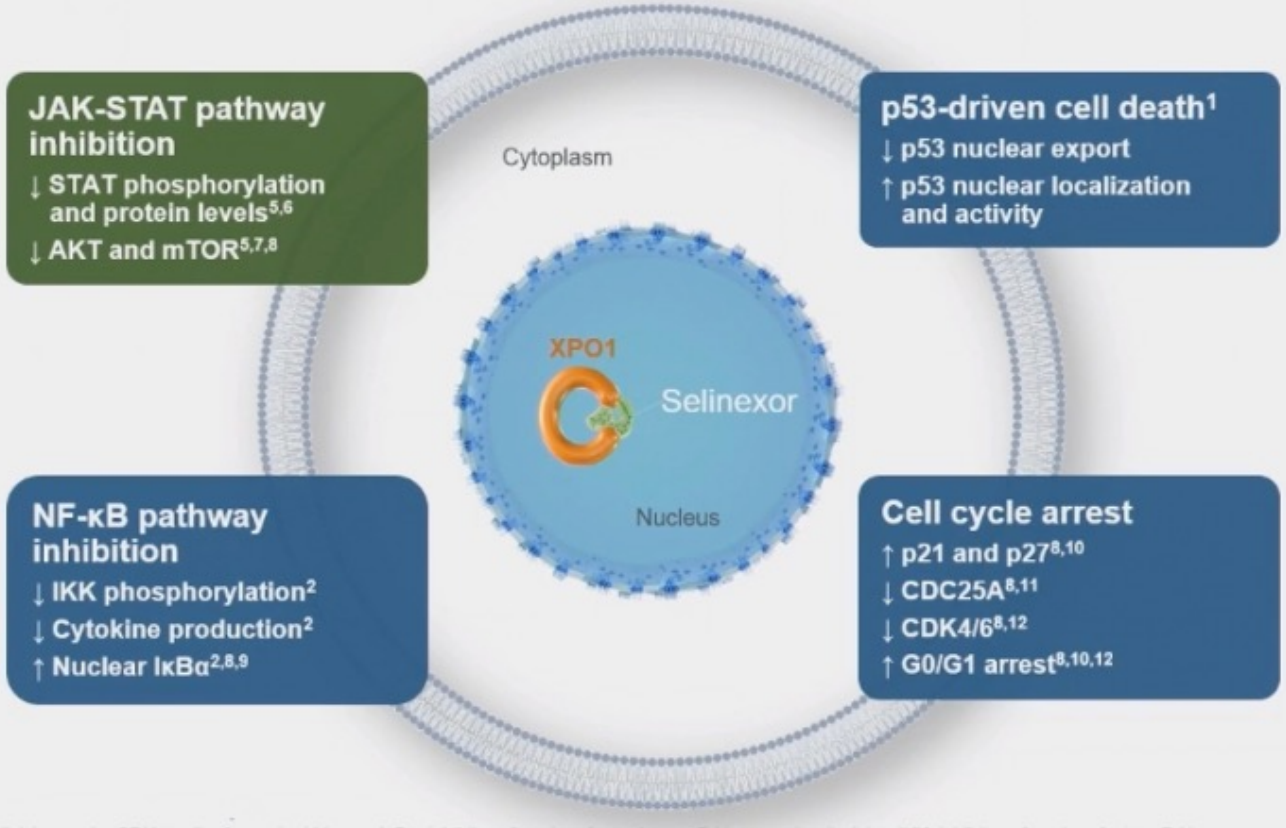
Selinexor Mechanism of Action in Myelofibrosis

XPO1 Inhibition is a fundamental mechanism of action that may target both JAK/STAT and non-JAK/STAT pathways in MF

Selinexor inhibits XPO1-mediated nuclear cargo protein export that may lead to:

- Increased malignant cell death[1]
- Reduced inflammation[2]
- Apoptosis of *JAK2*-mutated MF CD34+ cells but not healthy donor cells[3]
- Synergism with ruxolitinib and other therapeutic agents in cell lines with or without *JAK2*^{V617F} and *TP53* mutations[4]

Poster 1792
Lu M, et al. Use of Combination Therapies Including the XPO1 Inhibitor Selinexor Is a Potential Effective Therapeutic Strategy to Treat Myelofibrosis Patients
Saturday, December 9, 2023: 6:00 PM–8:00 PM
Halls G–H (San Diego Convention Center)



AKT, protein kinase B; CD, cluster of differentiation; CDC, cell division cycle; CDK, cyclin-dependent kinase; IκBα, inhibitor of nuclear factor kappa-B kinase subunit alpha; IKK, inhibitor of nuclear factor-κB kinase; mTOR, mammalian target of rapamycin; NF-κB, nuclear factor κ-light-chain-enhancer of activated B cells; pXX, tumor suppressor protein XX; XPO1, exportin 1.

1. Yan D, et al. *Clin Cancer Res*. 2019;25(7):2323-2335. 2. Kashyap T, et al. *Oncotarget*. 2016;7(48):78883-78895. 3. Lu M, et al. Poster presented at: 65th ASH Annual Meeting and Exposition; December 9–12, 2023; San Diego, CA. Abstract 1792. 4. Maloof M, et al. Poster presented at: 15th International Congress for Myeloproliferative Neoplasms (MPN); November 2–3, 2023; Brooklyn, NY. 5. Walker CJ, et al. *Blood*. 2013;122(17):3034-3044. 6. Cheng Y, et al. *Mol Cancer Ther*. 2014;13(3):675-686. 7. Argueta C, et al. *Oncotarget*. 2018;9(39):25529-25544. 8. Gandhi UH, et al. *Clin Lymphoma Myeloma Leuk*. 2018;18(5):335-345. 9. Turner JG, et al. *Oncotarget*. 2016;7(48):78896-78909. 10. Gravina GL, et al. *BMC Cancer*. 2015;15:941. 11. Garg M, et al. *Oncotarget*. 2017;8(5):7521-7532. 12. Tan M, et al. *Am J Physiol Renal Physiol*. 2014;307(11):F1179-F1186.

Tantravahi S et al. ASH 2023;Abstract 622.

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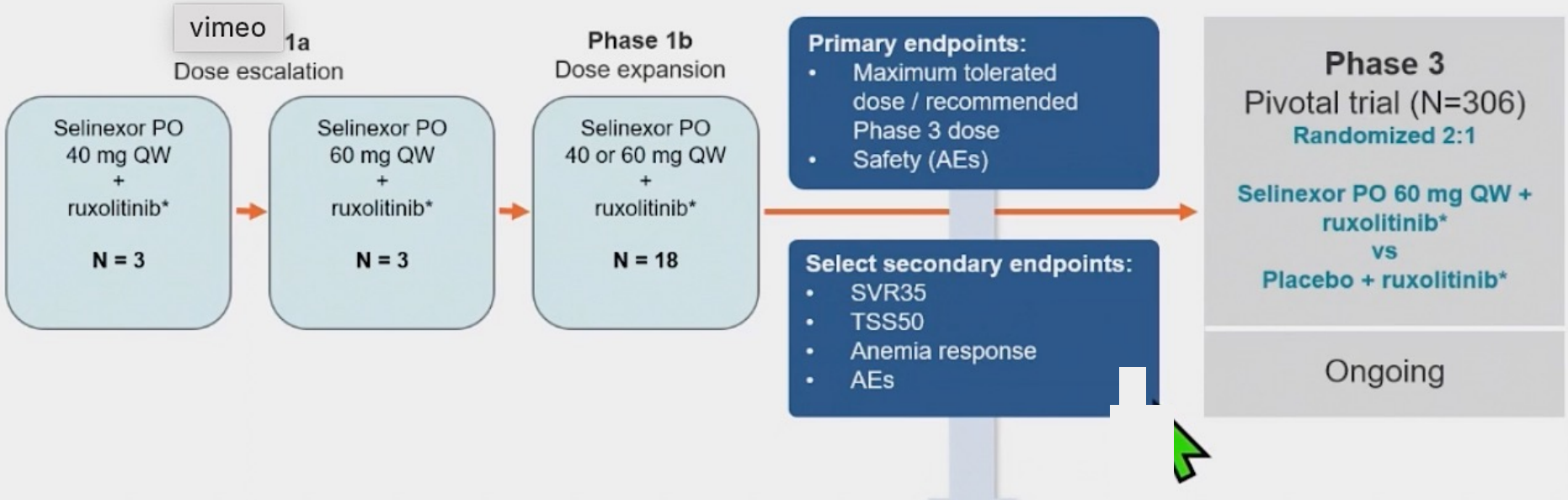
XPORT-MF-034 Phase I/III Study Design



Select inclusion criteria:

- Spleen volume of ≥ 450 cm^3 by magnetic resonance imaging or computed tomography
- Dynamic International Prognostic Scoring System (DIPSS) intermediate-1 and symptomatic, intermediate-2, or high risk
- Eastern Cooperative Oncology Group 0–2
- Platelet count ≥ 100×10^9/L

Data cutoff: August 1, 2023

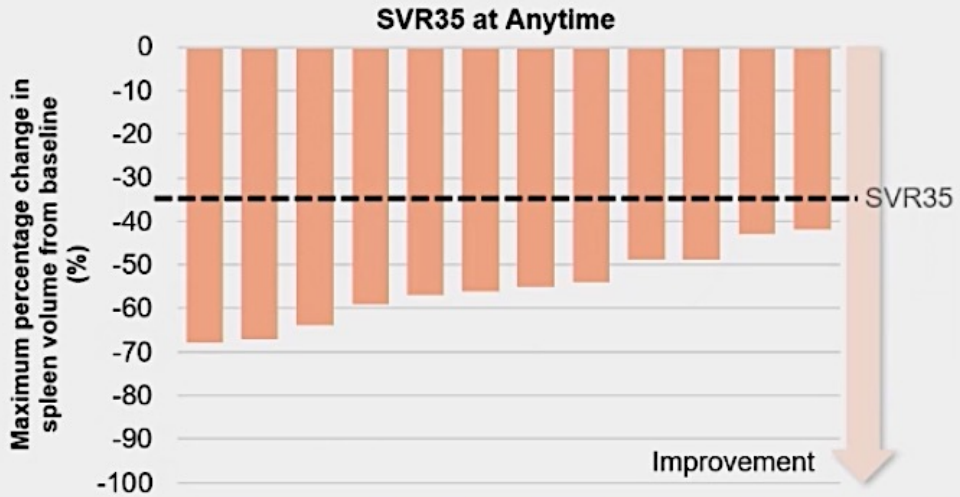
- Safety
- Durability of SVR35/TSS50 responses
- Disease modification as assessed by biomarkers and VAF

AE, adverse event; DIPSS, Dynamic International Prognostic Scoring System; PO, by mouth; QW, once-weekly dosing; VAF, variant allele frequency.
*Ruxolitinib dosing per label

Tantravahi S et al. ASH 2023;Abstract 622.

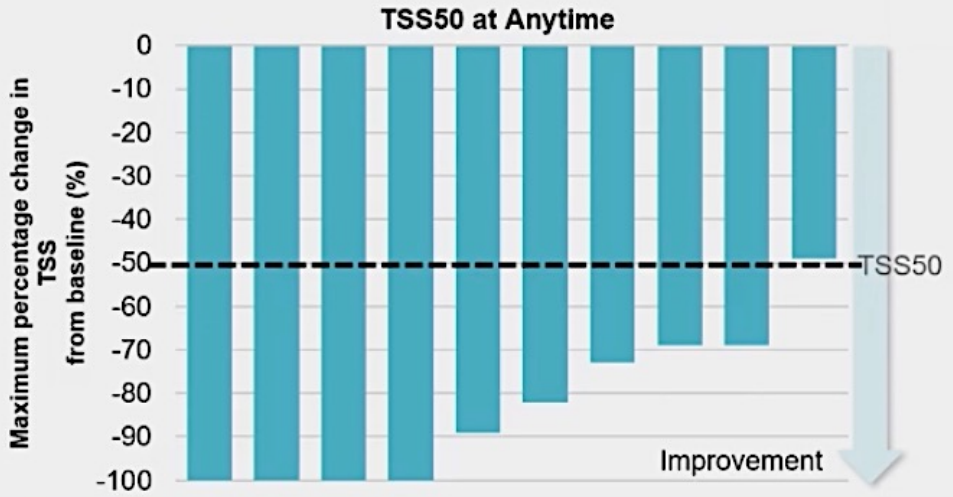
XPORT-MF-034: Phase I Long-Term Follow-Up of SVR and TSS with Selinexor and Ruxolitinib

		SVR35
Population	Timepoint	Selinexor 60 mg QW + ruxolitinib n (%)
Efficacy evaluable	Week 12	10/12† (83)
	Week 24	**11/12 (92)**
Intent-to-treat	Week 12	10/14 (71)
	Week 24	**11/14 (79)**



All patients in the efficacy evaluable population treated with selinexor 60 mg QW achieved an SVR35 at anytime

		TSS50
Population	Timepoint	Selinexor 60 mg QW + ruxolitinib n (%)
Efficacy evaluable	Week 12	8/10‡ (80)
	Week 24	**7/9§ (78)**
Intent-to-treat	Week 12	8/12 (67)
	Week 24	**7/12 (58)**

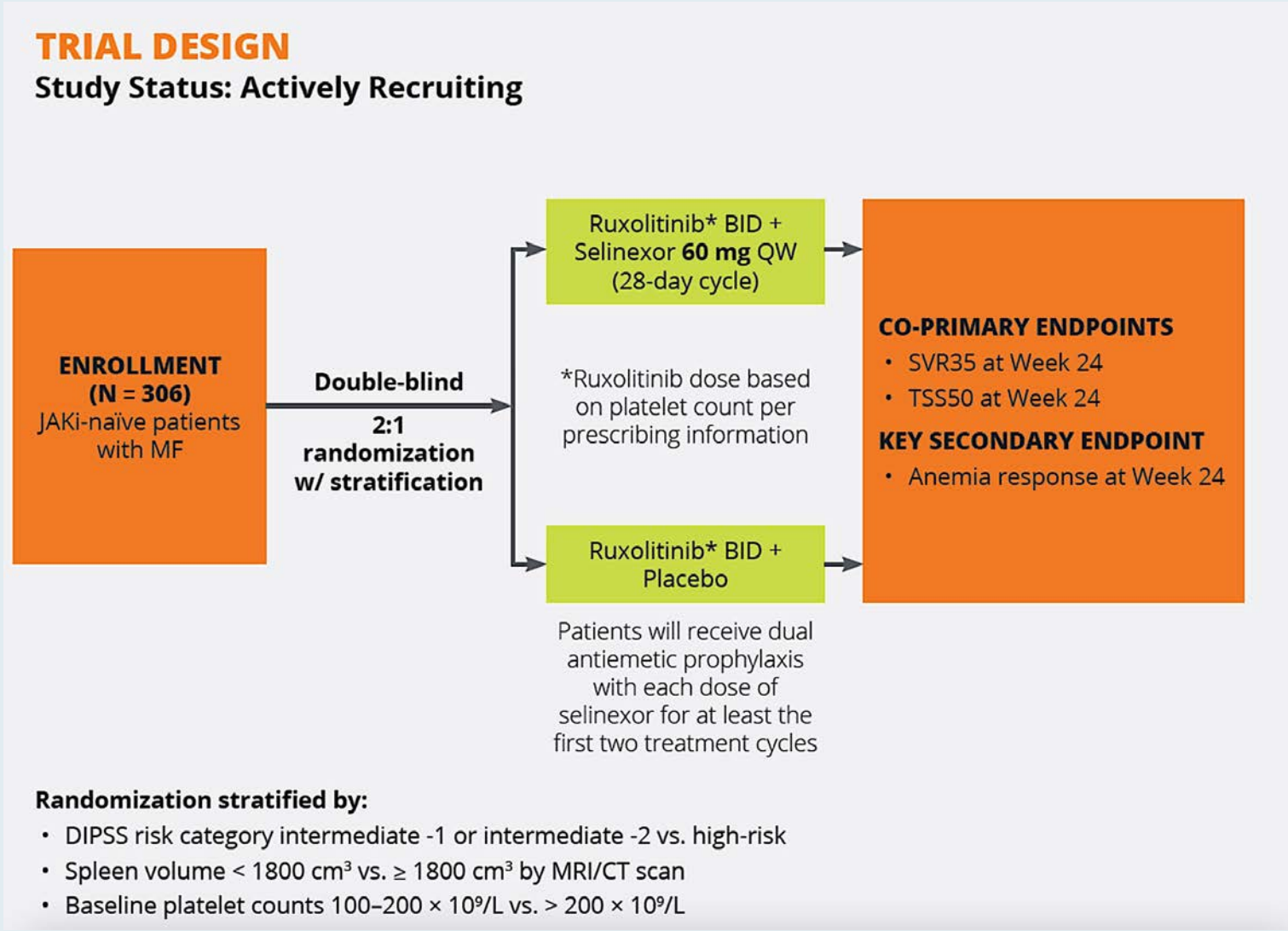


90% of patients in the efficacy evaluable population treated with selinexor 60 mg QW achieved an TSS50 at anytime

SVR, spleen volume reduction; TSS, total symptom score.
*Data cutoff date: August 01, 2023; †Two patients discontinued prior to Week 24; ‡One patient discontinued prior to Week 12; one patient with missing data at Week 12, who subsequently discontinued prior to Week 24; §Two patients discontinued prior to Week 24, and one had missing data.

Tantravahi S et al. ASH 2023;Abstract 622.

XPORT-MF-034: An Ongoing Phase III Trial of Selinexor and Ruxolitinib versus Ruxolitinib for JAK Inhibitor-Naïve Myelofibrosis



Maher K et al. ASH 2023;Abstract 3209.

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Third Annual **National General Medical Oncology Summit**

Friday, March 22, 2024

6:30 PM – 7:00 PM

Welcome Reception

7:00 PM – 9:00 PM

Keynote Session: ER-Positive Metastatic Breast Cancer

Erika Hamilton, MD
Kevin Kalinsky, MD, MS
Joyce O'Shaughnessy, MD
Hope S Rugo, MD

Special Feature: Clinicians with Breast Cancer

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Chronic Lymphocytic Leukemia

Tuesday, February 6, 2024
5:00 PM – 6:00 PM ET

Faculty

Lindsey Roeker, MD

Jeff Sharman, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

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

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