Year in Review: Myelofibrosis

A CME/MOC-Accredited Live Webinar

Tuesday, May 14, 2024
5:00 PM – 6:00 PM ET

Faculty

Aaron T Gerds, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

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

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by an educational grant from GSK.

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, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI Biopharma, a Sobi company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, 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, Kronos Bio Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.

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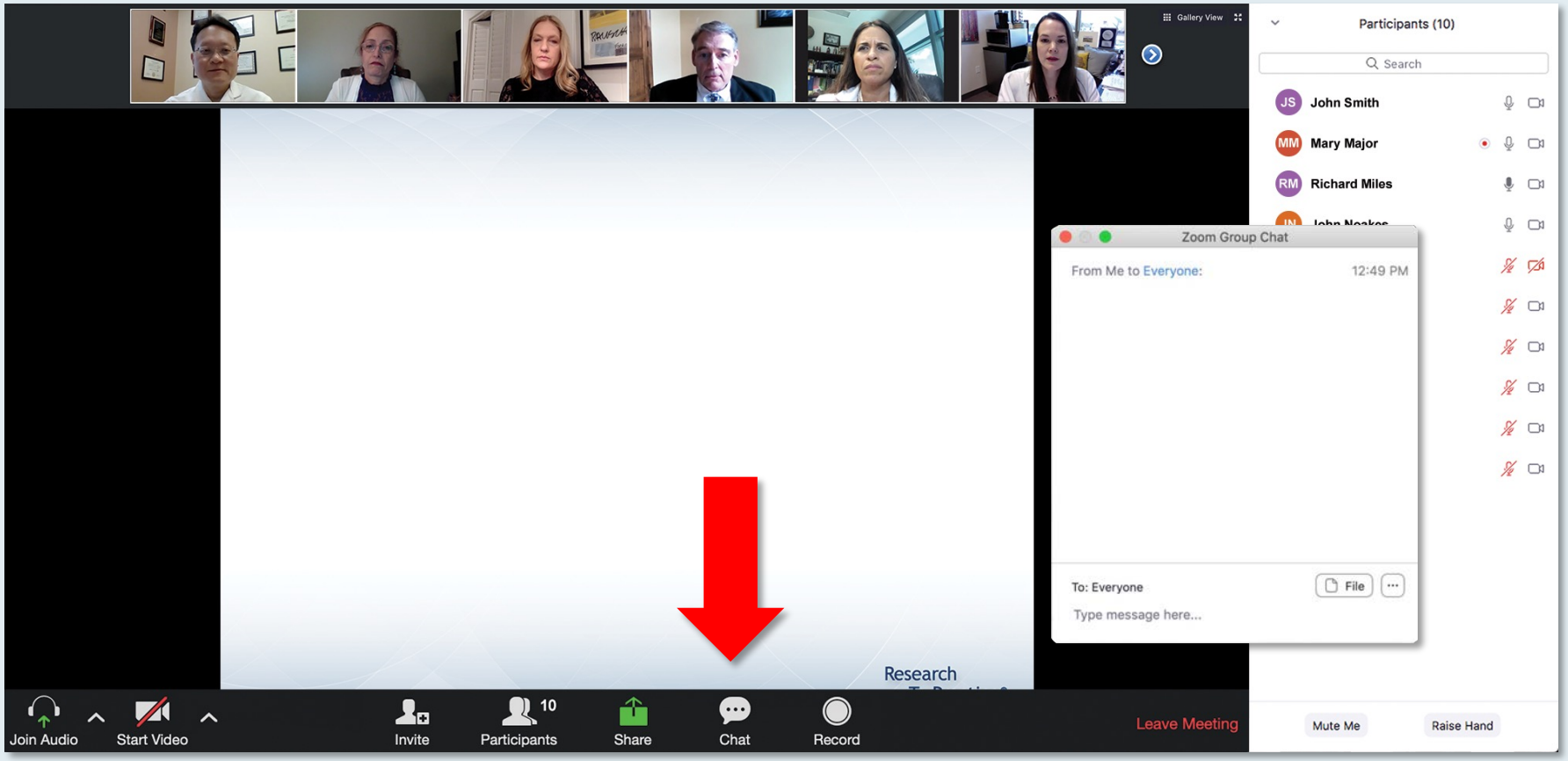
Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Gerds — Disclosures

Consulting Agreements	AbbVie Inc, Agios Pharmaceuticals Inc, Disc Medicine, GSK, PharmaEssentia, Rain Oncology

We Encourage Clinicians in Practice to Submit Questions



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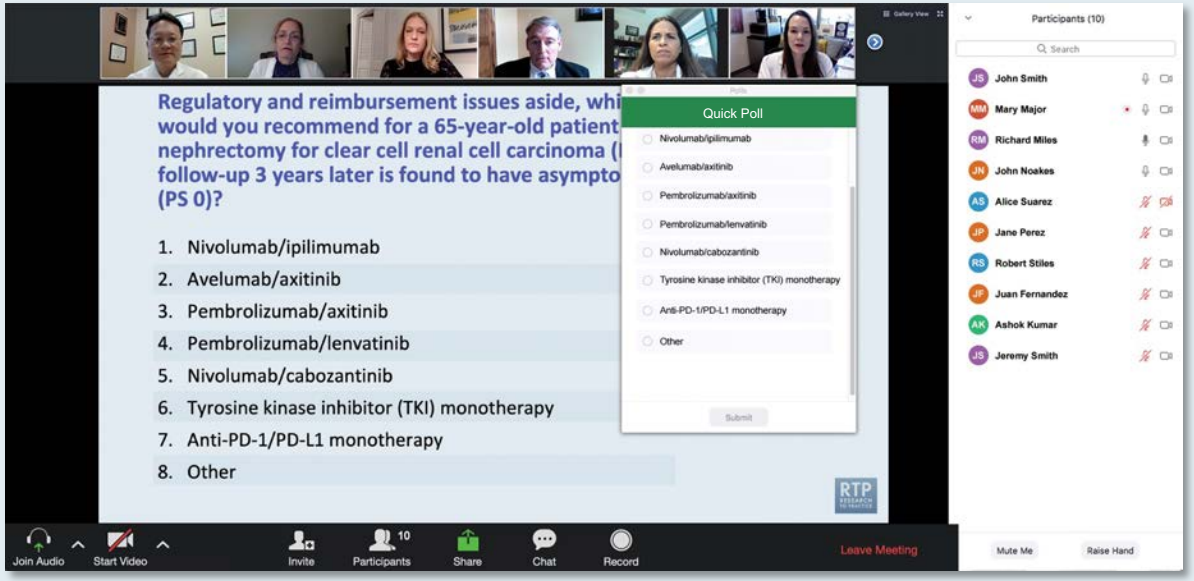

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Meet The Professor: Optimizing the Management of Myelofibrosis — Part 2 of a 2-Part Series

DR RUBEN A MESA

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Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

Hepatobiliary Cancers

Friday, May 31, 2024

11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)

Faculty

Robin K (Katie) Kelley, MD

Additional faculty to be announced

Antibody-Drug Conjugates in Lung Cancer

Saturday, June 1, 2024

6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

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Non-Small Cell Lung Cancer with an EGFR Mutation

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Multiple Myeloma

Sunday, June 2, 2024

6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty

Rafael Fonseca, MD
María-Victoria Mateos, MD, PhD
Elizabeth O'Donnell, MD

LIVE WEBCAST

Colorectal Cancer

Monday, June 3, 2024

7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

Faculty

Scott Kopetz, MD, PhD
John Strickler, MD

Ovarian and Endometrial Cancer

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Mansoor Raza Mirza, MD
Ritu Salani, MD, MBA
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Metastatic Breast Cancer

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7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

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Aditya Bardia, MD, MPH
Harold J Burstein, MD, PhD
Professor Giuseppe Curigliano, MD, PhD
Sara A Hurvitz, MD, FACP
Joyce O'Shaughnessy, MD
Hope S Rugo, MD

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Bispecific Antibodies in Lymphoma

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Tycel Phillips, MD

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INTRODUCTION: Myelofibrosis (MF) for Oncology "Newbies"

MODULE 1: Biology of MF

MODULE 2: Management of Anemia in MF

MODULE 3: Novel Strategies for MF

MODULE 4: Journal Club

Thank you for joining us!

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

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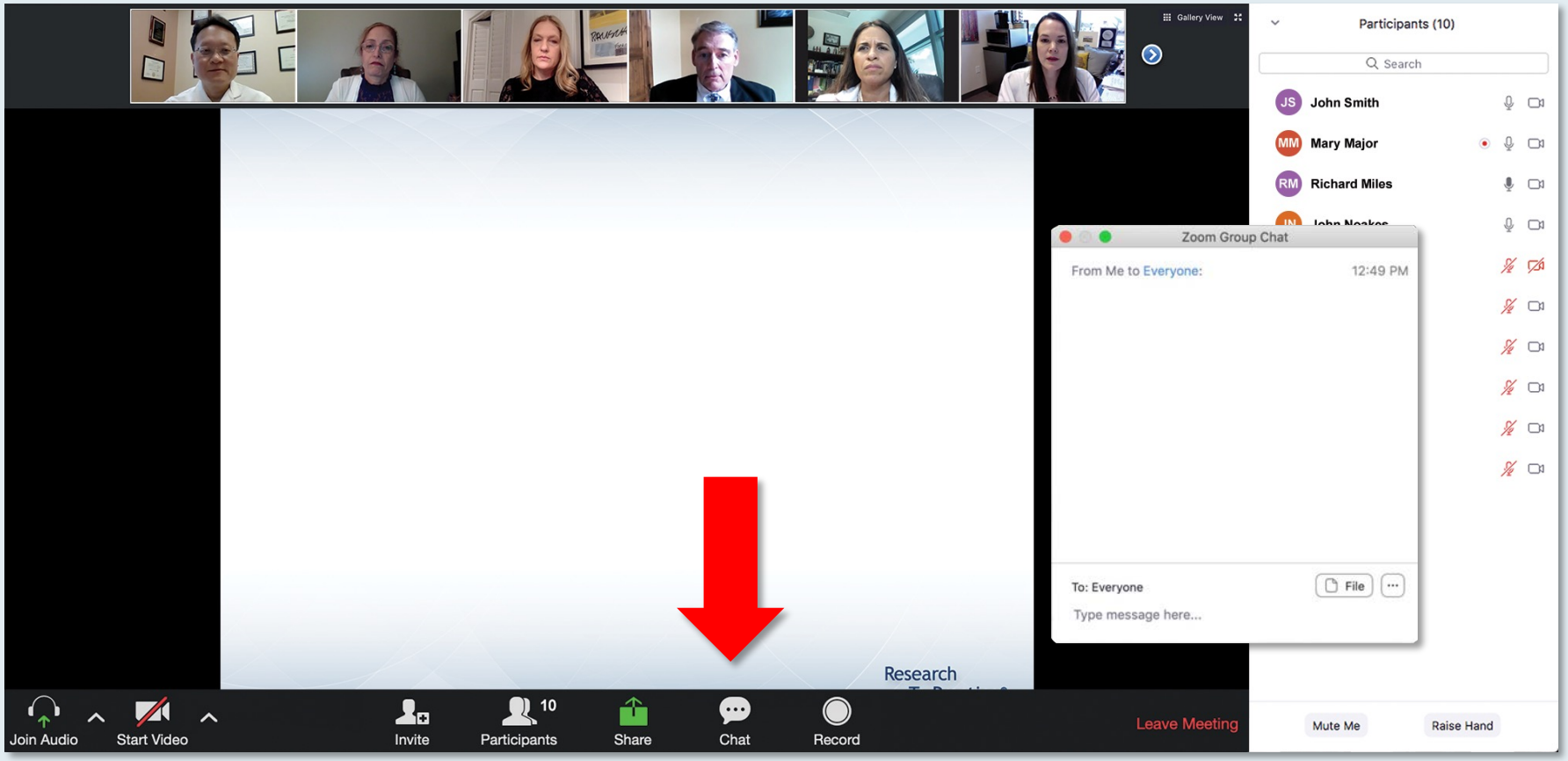
We Encourage Clinicians in Practice to Submit Questions



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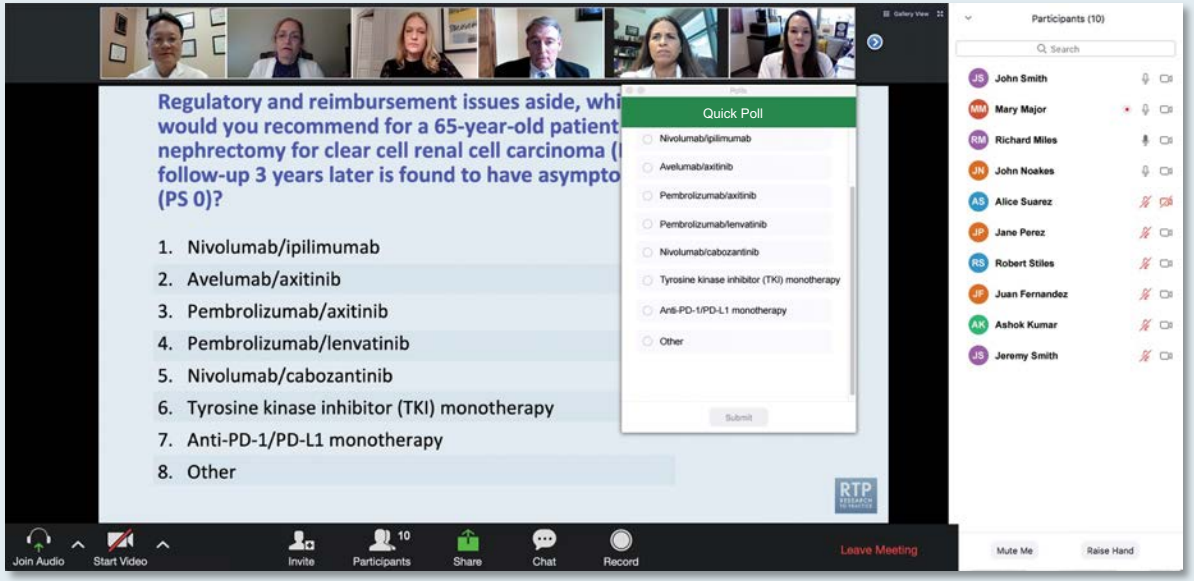

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This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

Key Data Sets

- Chase ML et al. Consensus recommendations on peripheral blood smear review: Defining curricular standards and fellow competency. *Blood Adv* 2023;7(13):3244-52.
- Chase ML et al. Development of consensus guidelines for hematology fellow competency in peripheral blood smear review utilizing nominal group technique 3204. *Blood* 2022; 140(Supplement 1):10781-3.
- Mendez LF et al. Mediterranean diet intervention in patients with myeloproliferative neoplasm. *Blood* 2022;140(Suppl 1):3972-3.
- Verstovsek S et al. MOMENTUM Study Investigators. Momelotinib versus danazol in symptomatic patients with anaemia and MF (MOMENTUM): Results from an international, double-blind, randomised, controlled, phase III study. *Lancet* 2023;401(10373):269-80.
- Gerds AT et al. 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. *Lancet Haematol* 2023;10(9):e735-46.
- Verstovsek S et al. Momelotinib long-term safety and survival in MF: Integrated analysis of phase III randomized controlled trials. *Blood Adv* 2023;7(14):3582-91.

Key Data Sets

- Gangat N et al. Predictors of anemia response to momelotinib therapy in myelofibrosis and impact on survival. *Am J Hematol* 2023;98:282-89.
- Pemmaraju N et al. 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. ASH 2023;Abstract 620.
- Rampal R et al. 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. ASH 2023;Abstract 628.
- Tantravahi S et al. Selinexor plus ruxolitinib in JAK inhibitor (JAKi)-naïve patients with myelofibrosis: Long-term follow-up from XPORT-MF-034 suggestive of disease modification. ASH 2023;Abstract 622.
- Mesa R et al. Clinical outcomes of patients with myelofibrosis after immediate transition to momelotinib from ruxolitinib. *Haematologica* 2024;109(2):676-81.
- Harrison CN et al. Clinical effectiveness and safety of momelotinib compared with continued ruxolitinib or best available therapy in patients with myelofibrosis who required RBC transfusions: Subgroup analysis of the phase 3 Simplify-2 study. ASH 2023;Abstract 2189.

Key Data Sets

- Gupta V et al. Long-term survival adjusted for treatment crossover in patients (pts) with myelofibrosis (MF) treated with momelotinib (MMB) vs danazol (DAN) in the MOMENTUM trial. ASCO 2024;Abstract 6571.
- Kuzmanovic T et al. Identification and management of clonal hematopoiesis of indeterminate potential (CHIP) in cancer survivors: The Cleveland Clinic experience. ASCO 2023;Abstract 7010.
- Scandura JM et al. A phase 2 study to evaluate the efficacy and safety of selinexor monotherapy in patients with JAK inhibitor-naïve myelofibrosis and moderate thrombocytopenia (XPORT-MF-044). ASH 2023;Abstract 3211.
- Scandura JM et al. Phase 2 study evaluating selinexor monotherapy in patients with JAKi-naïve myelofibrosis and moderate thrombocytopenia. ASCO 2024;Abstract TPS6593.
- Gerds AT et al. Ruxolitinib for myelofibrosis in elderly non-transplant patients: Healthcare resource utilization and costs. *J Med Econ* 2023;26(1):843-9.
- Mishra R et al. Risk of myelodysplastic syndromes (MDS) in adolescents and young adults with cancers treated with chemotherapy with or without radiotherapy. ASH 2023;Abstract 2351.
- Pemmaraju N et al. Ten years after ruxolitinib approval for myelofibrosis: A review of clinical efficacy. *Leuk Lymphoma* 2023;64(6):1063-81.

Agenda

INTRODUCTION: Myelofibrosis (MF) for Oncology "Newbies"

MODULE 1: Biology of MF

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REGULAR ARTICLE

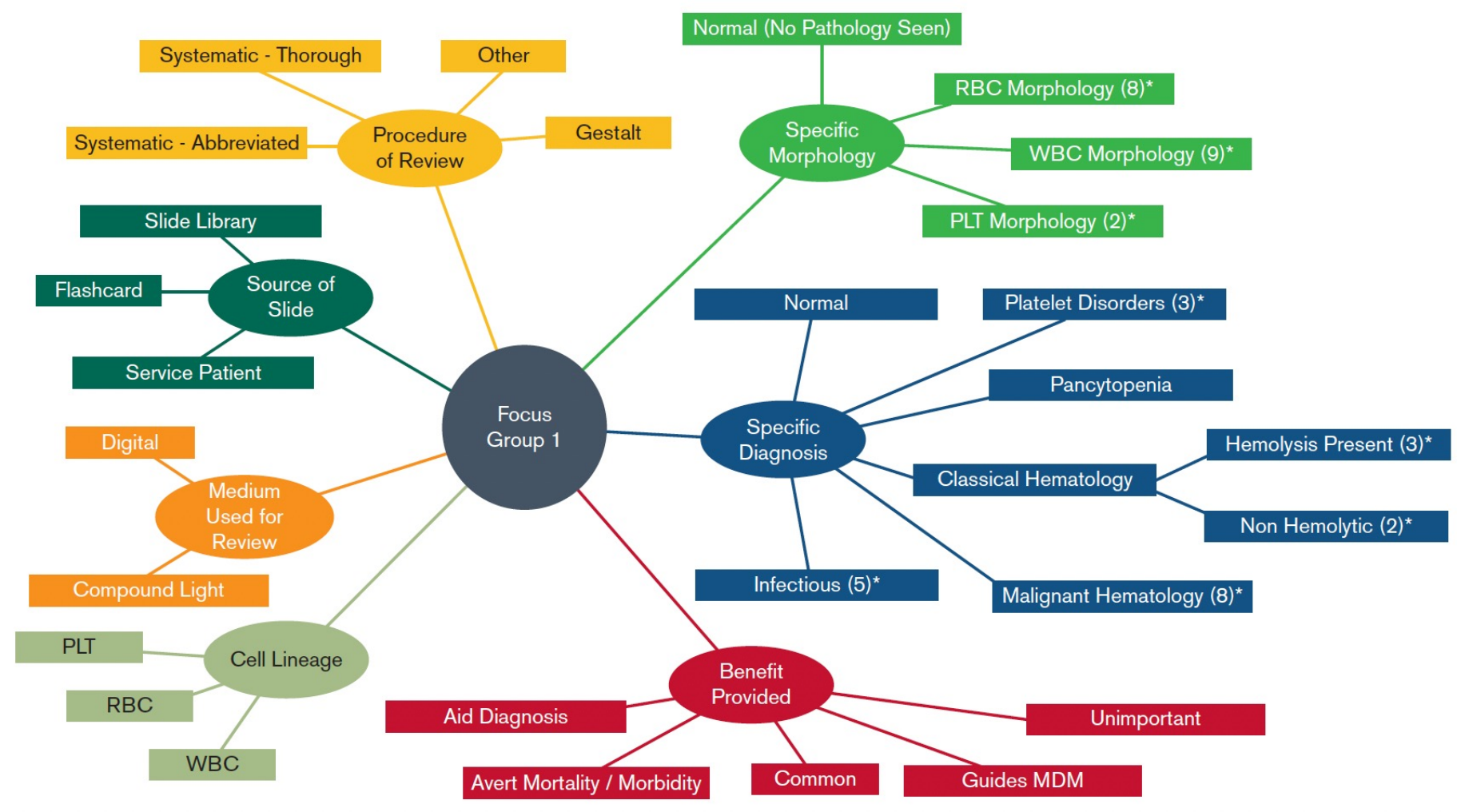
blood advances

Consensus recommendations on peripheral blood smear review: defining curricular standards and fellow competency

Matthew L. Chase,[1] Reed Drews,[2] Marc S. Zumberg,[3] Leslie R. Ellis,[4] Erin G. Reid,[5] Aaron T. Gerds,[6] Alfred I. Lee,[7] Gabriela S. Hobbs,[8] Jonathan Berry,[1] and Jason A. Freed[2]

2023;7(13):3244-52

Participant Statement Coding



Chase ML et al. *Blood Adv* 2023;7(13):3244-52.


Focus Group 1
Procedure at Review
Systematic - Thorough
Other
Systematic - Abbreviated
Gestalt
Source of Slide
Slide Library
Flashcard
Service Patient
Medium Used for Review
Digital
Compound Light
Cell Lineage
PLT
RBC
WBC
Specific Morphology
Normal (No Pathology Seen)
RBC Morphology (8)*
WBC Morphology (9)*
PLT Morphology (2)*
Specific Diagnosis
Normal
Platelet Disorders (3)*
Pancytopenia
Classical Hematology
Hemolysis Present (3)*
Non Hemolytic (2)*
Infectious (5)*
Malignant Hematology (8)*
Benefit Provided
Aid Diagnosis
Avert Mortality / Morbidity
Common
Unimportant
Guides MDM

Agenda

INTRODUCTION: Myelofibrosis (MF) for Oncology “Newbies”

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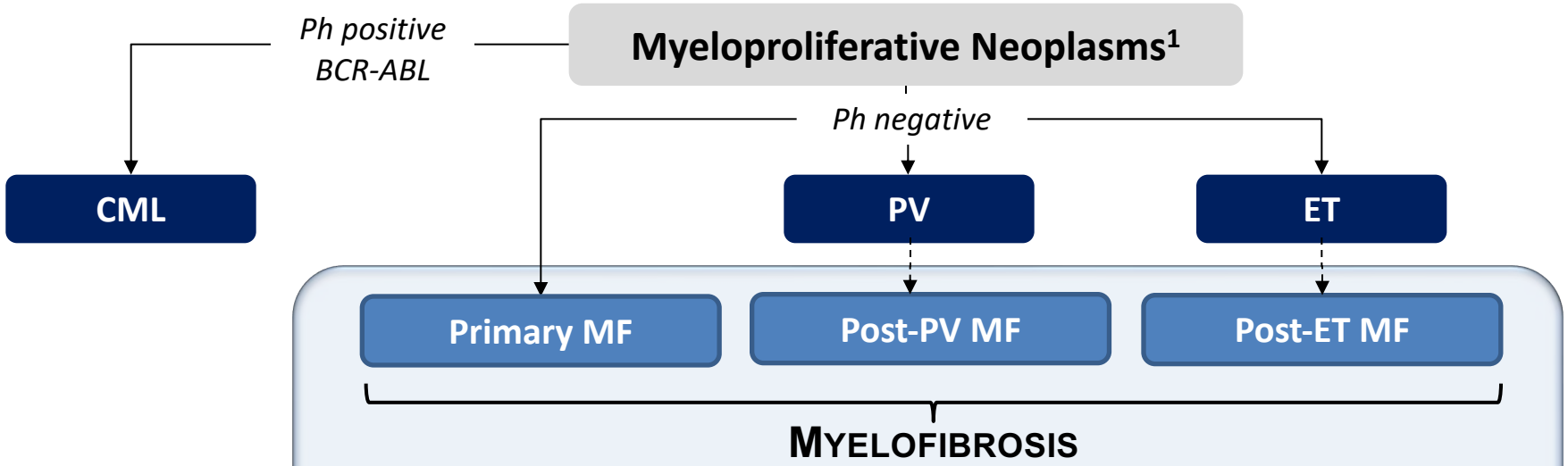
Overview of Myelofibrosis (MF)



MF prevalence

- Approximately 16,000 to 18,500 patients in the United States[2]

MF is characterized by

- Bone marrow fibrosis, cytopenias, and constitutional symptoms[3]
- Splenomegaly[4]

MF natural history

- Time course of disease progression is highly variable but frequently characterized by a period of stable disease followed by a late stage with rapid clinical progression[5,6]

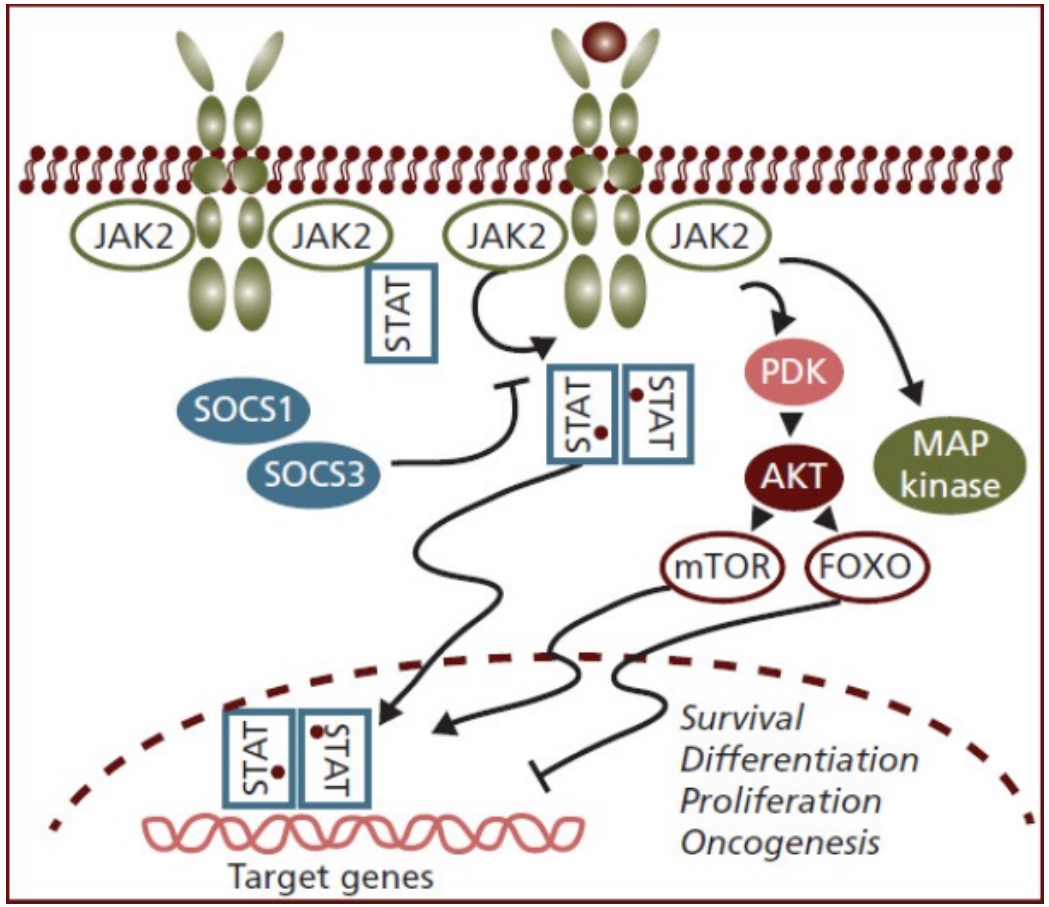
MF, myelofibrosis
PV, polycythemia vera
ET, essential thrombocythemia
CML, chronic myeloid leukemia

[1]Tefferi A, Vardiman JW. *Leukemia*. 2008;22:14-22; [2]Data on file, Incyte Corporation; [3]Verstovsek S. *Clin Can Res*. 2010;16:1988-1996; [4]Mesa RA. *Blood*. 2009;113(22):5394-5400; [5]Cervantes F, et al. *Blood*. 2009;113:2895-2901; [6]Tam CS, et al. *J Clin Oncol*. 2009;27:5587-5593.

Courtesy of Rami Komrokji, MD

JAK-STAT Pathway Constitutively Activated in Myelofibrosis

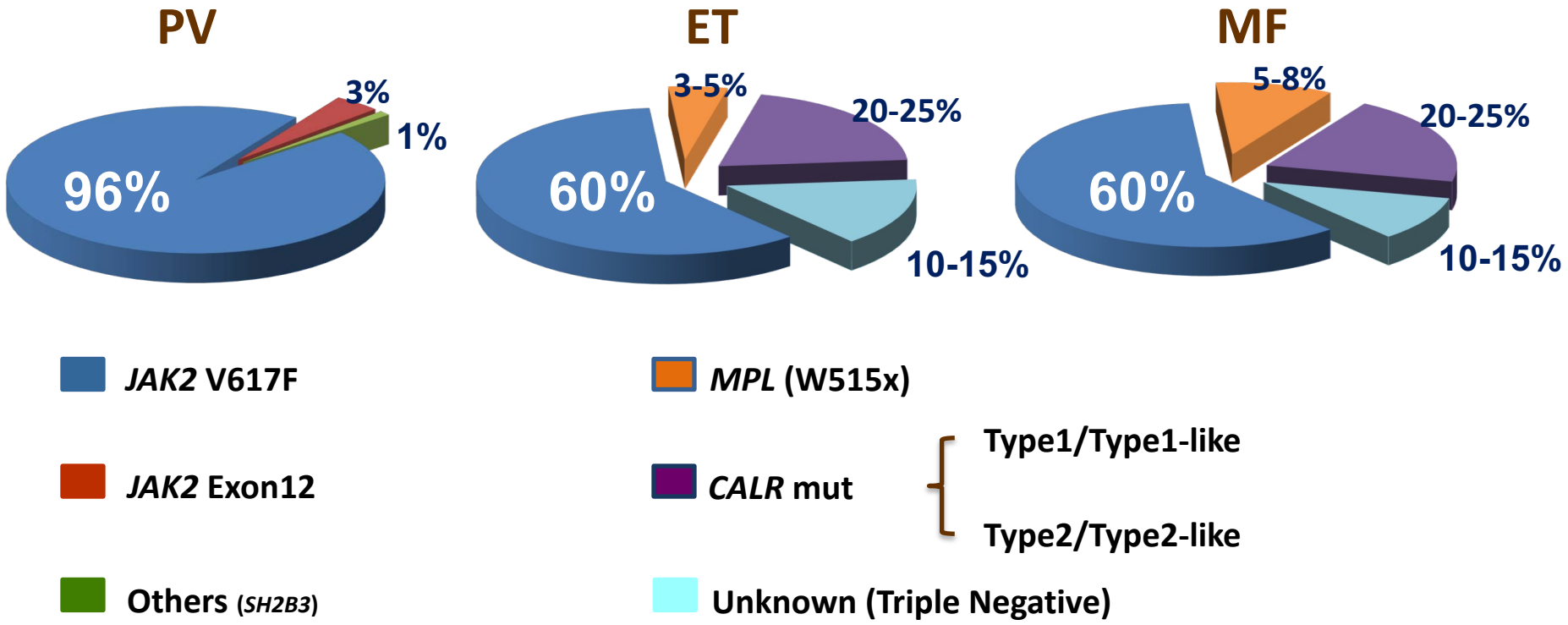
- JAK-STAT pathway implicated in normal hematopoiesis[1]
- An activating mutation in the pseudokinase domain of *Janus kinase 2* (*JAK2*) was identified in approximately 50% of MF patients
- Dysregulation of JAK-STAT, regardless of *JAK* mutation status, is a key pathologic feature of MF and other MPNs[1,2]



1. Vannucchi AM et al. *CA Cancer J Clin*. 2009;59:171-191. 2. Anand S et al. *Blood*. 2011;118:1610-1621.

Courtesy of Rami Komrokji, MD

Phenotypic Driver Mutations (activate JAK-STAT pathway) in MPNs



Klampfl T, et al. *NEJM* 2013;369(25):2379-90; Nangalia J, et al. *NEJM* 2013;369(25):2391-405.

Courtesy of Rami Komrokji, MD

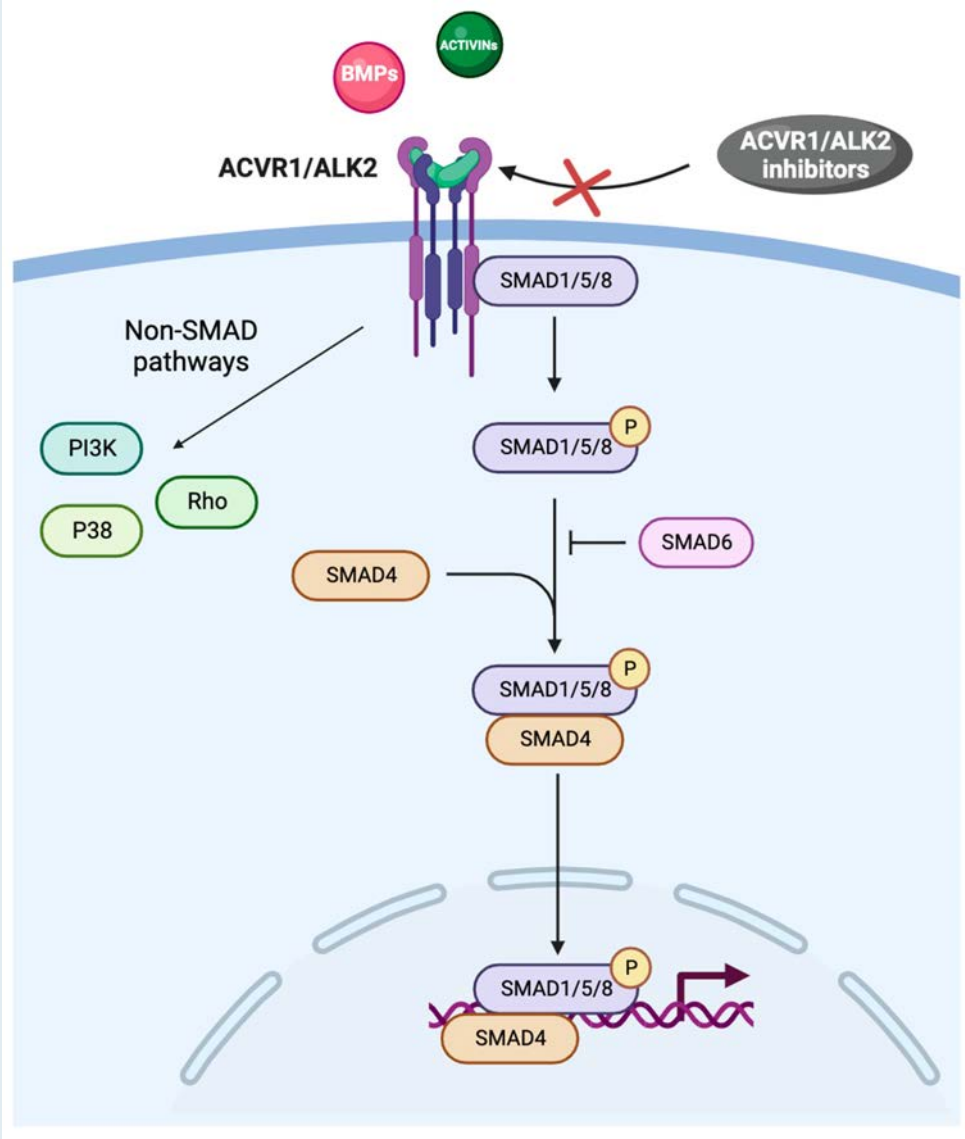
JAK Inhibitor Specificities

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

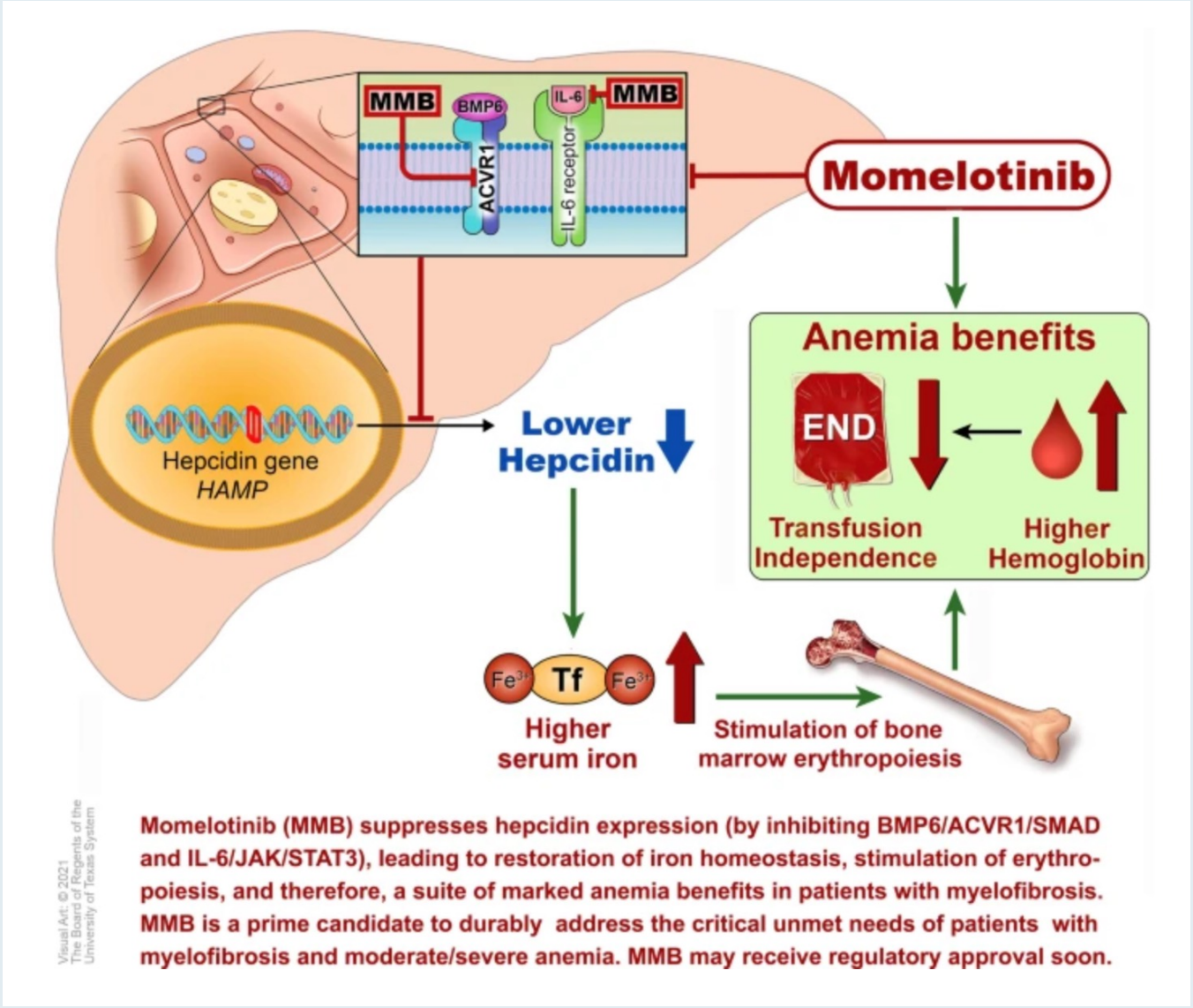
Courtesy of John O Mascarenhas, MD.

ACVR1 Is an Emerging Biomarker in MF and Anemia



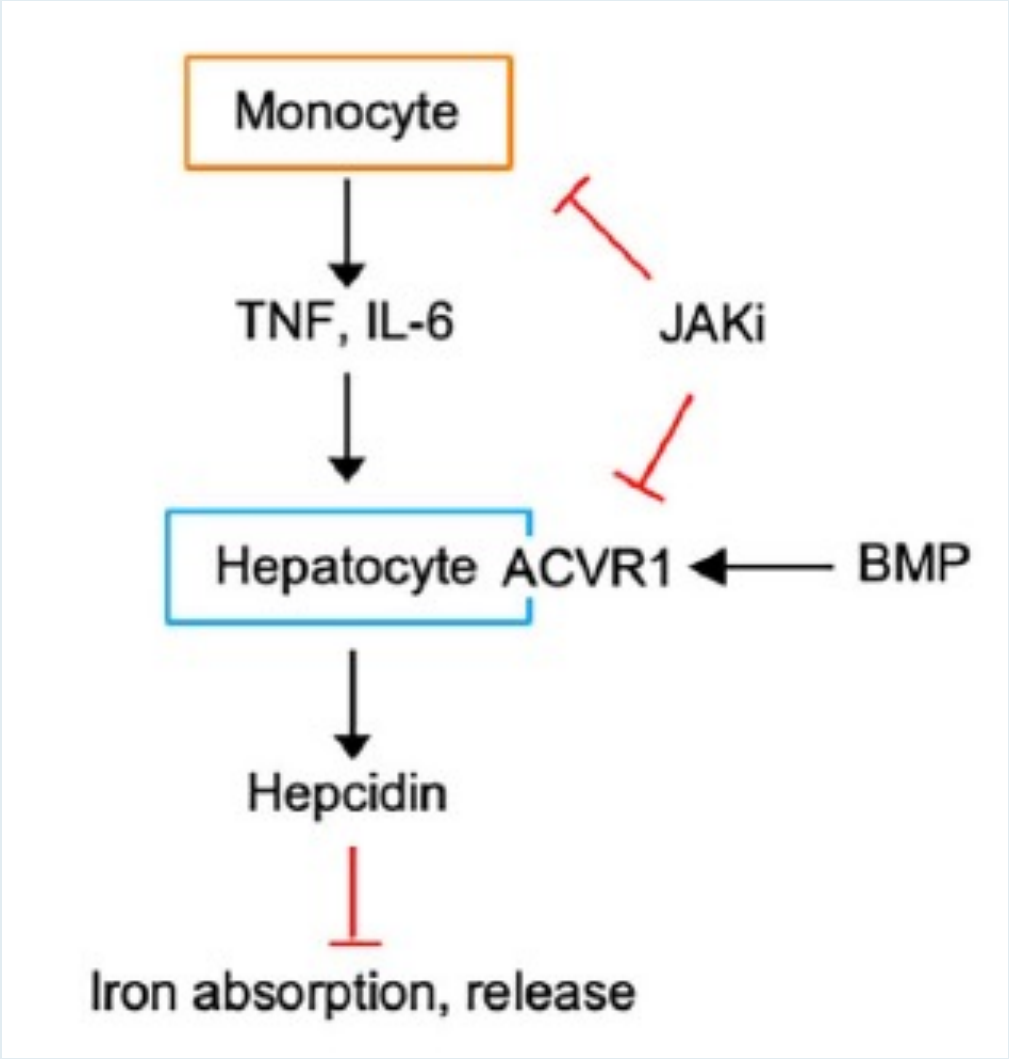
Oh ST et al. *Blood Adv* 2023;7(19):5835-42; Duminuco A et al. *Cancers* 2024;16(1):154.

Proposed Mechanism of Momelotinib for MF with Anemia



Chifotides HT et al. *J Hematol Oncol* 2022;15(1):7.

Hepcidin Regulation



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

The NEW ENGLAND JOURNAL of MEDICINE

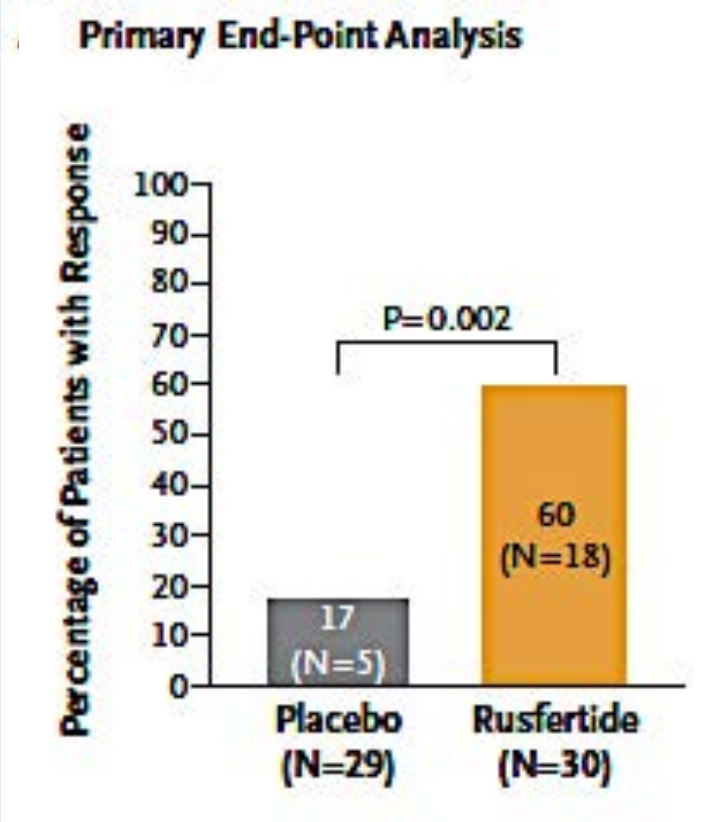
ORIGINAL ARTICLE

Rusfertide, a Hepcidin Mimetic, for Control of Erythrocytosis in Polycythemia Vera

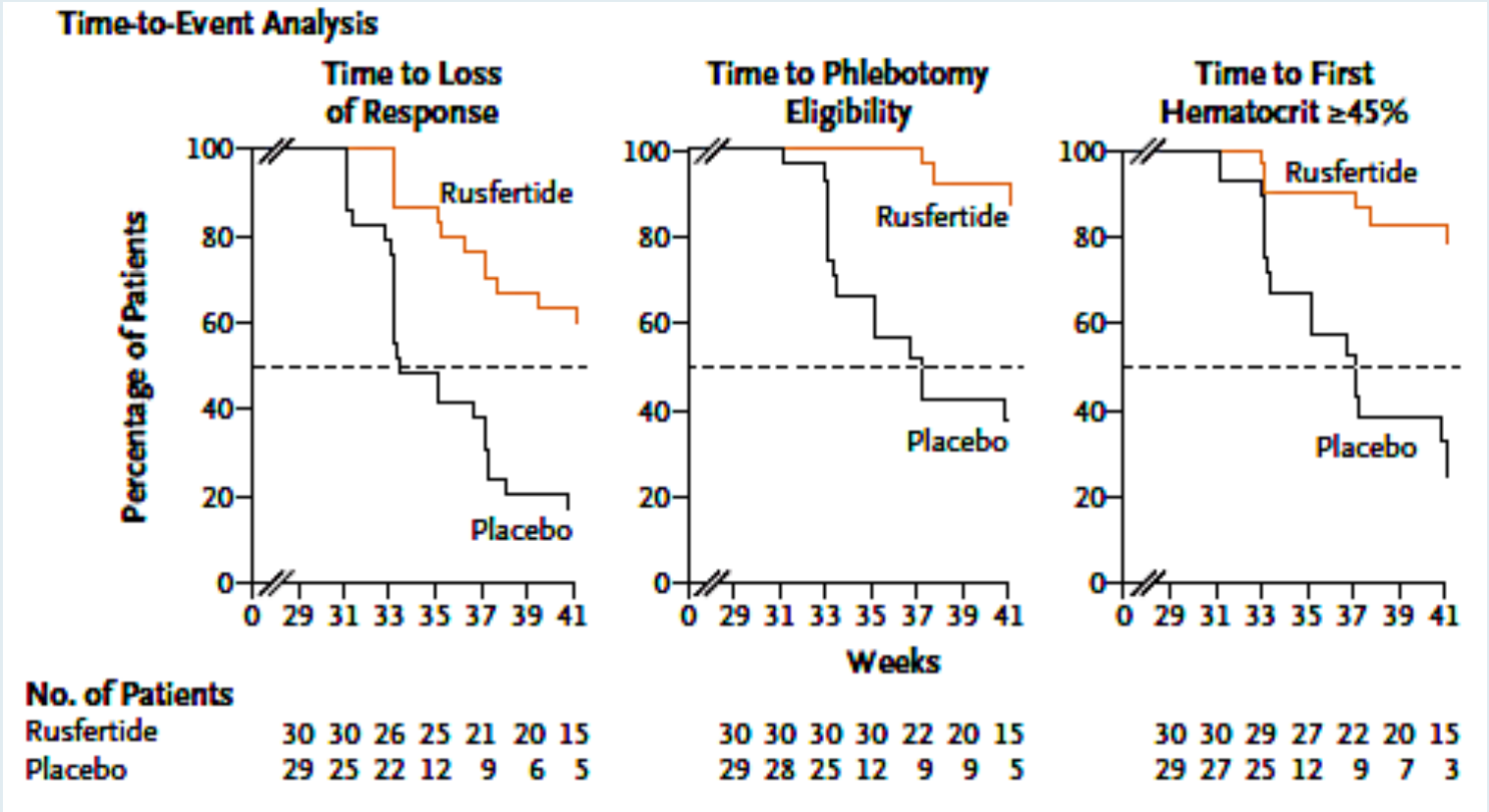
M. Kremyanskaya, A.T. Kuykendall, N. Pemmaraju, E.K. Ritchie, J. Gotlib, A. Gerds, J. Palmer, K. Pettit, U.K. Nath, A. Yacoub, A. Molina, S.R. Saks, N.B. Modi, F.H. Valone, S. Khanna, S. Gupta, S. Verstovsek, Y.Z. Ginzburg, and R. Hoffman, for the REVIVE Trial Investigators*

2024 February 22;390(8):723-35

REVIVE Trial: Clinical Efficacy of Rusfertide in Patients with Polycythemia Vera



Response defined by hematocrit control, absence of phlebotomy and completion of the trial regimen during part 2.



Analysis of times until the loss of response, phlebotomy eligibility and a first hematocrit of at least 45% during part 2. The dashed lines indicate the median time to the event.

Kremyanskaya M et al. *N Engl J Med* 2024;390(8):723-35 .

Phase 3 Study VERIFY (NCT05210790): Rusfertide vs Placebo in Patients With PV[1,2]

≈250 Patients with PV Are Being Randomized Globally[1]

Key Eligibility:[1-3]

- Age ≥18 years
- Meet revised 2016 WHO criteria for diagnosis of PV
- ≥3 phlebotomies due to inadequate HCT control in 28 weeks[a] before randomization OR ≥5 phlebotomies due to inadequate HCT control within 1 year prior to randomization

N=250

R 1:1

Part 1A: Double-Blind[1,2]

32 weeks (Weeks 0-32)

- **Placebo + ongoing therapy**
- **Rusfertide + ongoing therapy** *Starting dose: 20 mg SC Q1W*

CRT may be decreased or stopped but not increased

Part 1B: Open-Label[1,2]

20 weeks (Weeks 32-52)

Goal: Assess durability of responses through Week 52

Rusfertide + ongoing therapy

CRT may be decreased or stopped but not increased

Part 2: Open-Label[1,2]

104 weeks (Weeks 52-156)[c]

Goal: Assess long-term safety

Rusfertide + PV therapy

Dose of CRT may be changed or new CRT may be initiated

Key Endpoints:[1,4,5]

- Proportion of patients achieving response, defined as absence of phlebotomy eligibility[b] (Weeks 20-32)
- Mean number of phlebotomies (Weeks 0-32)

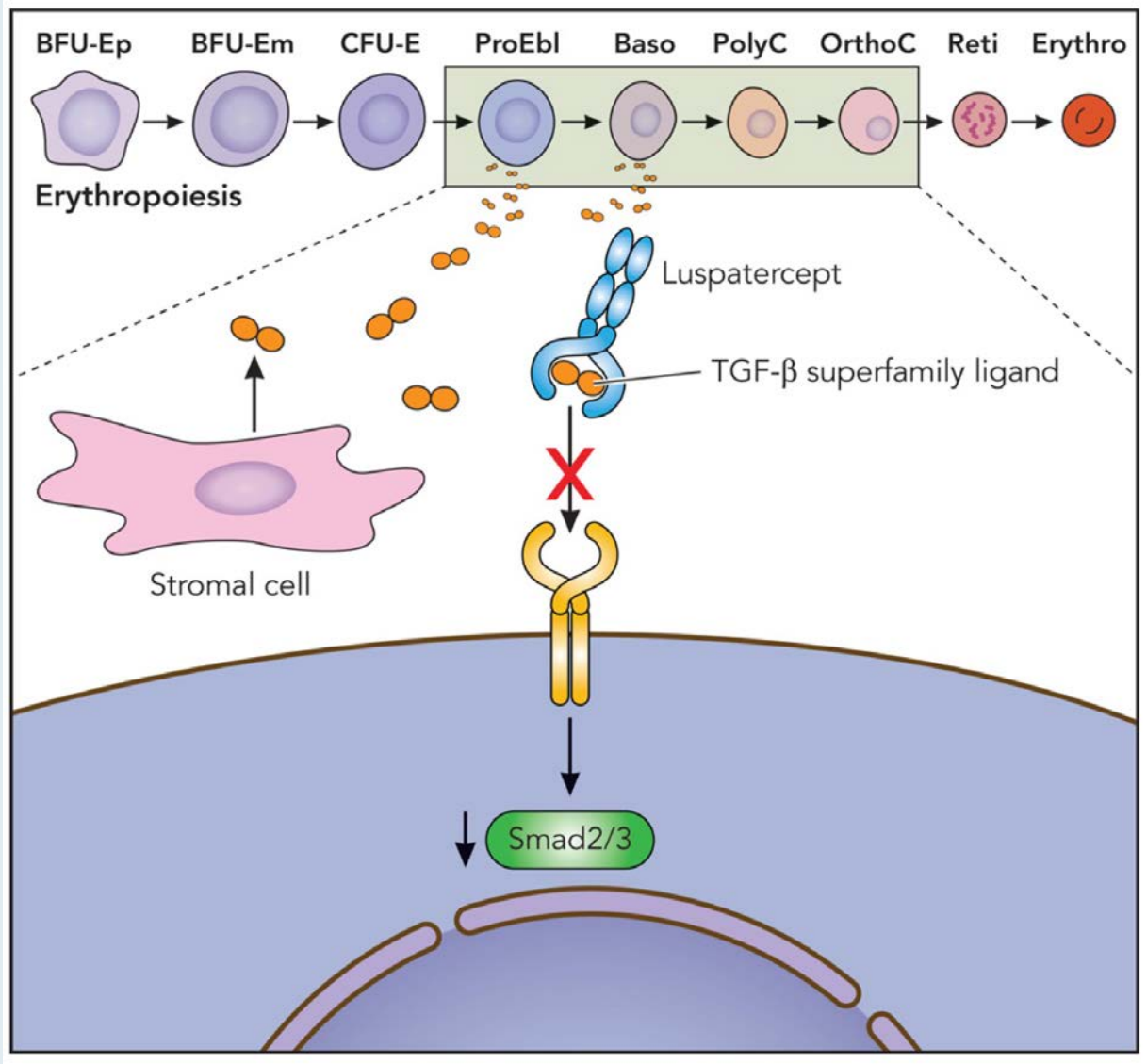
[a]Defined as 28 weeks in protocol amendment 3.1, but previously published as 6 months.[2,3] [b]Phlebotomy eligibility defined as confirmed HCT ≥45% that is ≥3% higher than baseline, or HCT ≥48%.[1]

CRT, cytoreductive therapy; **HCT**, hematocrit; **PV**, polycythemia vera; **Q1W**, once a week; **R**, randomized; **SC**, subcutaneous; **WHO**, World Health Organization.

1. ClinicalTrials.gov. NCT05210790. https://clinicaltrials.gov/ct2/show/NCT05210790 **2.** Verstovsek S, et al. 64th American Society of Hematology (ASH) Annual Meeting; December 2022. TiP poster presentation. **3.** Protagonist Therapeutics. Protocol Number: PTG-300-11, Protocol Amendment 3.1. July 25, 2023. **4.** Protagonist Therapeutics. Press release. Published March 22, 2021. https://feeds.issuerdirect.com/news-release.html?newsid=6535012005620858 **5.** EU Clinical Trials Register. 2021-004732-29. https://www.clinicaltrialsregister.eu/ctr-search/trial/2021-004732-29/HU.

Data cutoff: 17 October 2023

Luspatercept Mechanism of Action in Anemia



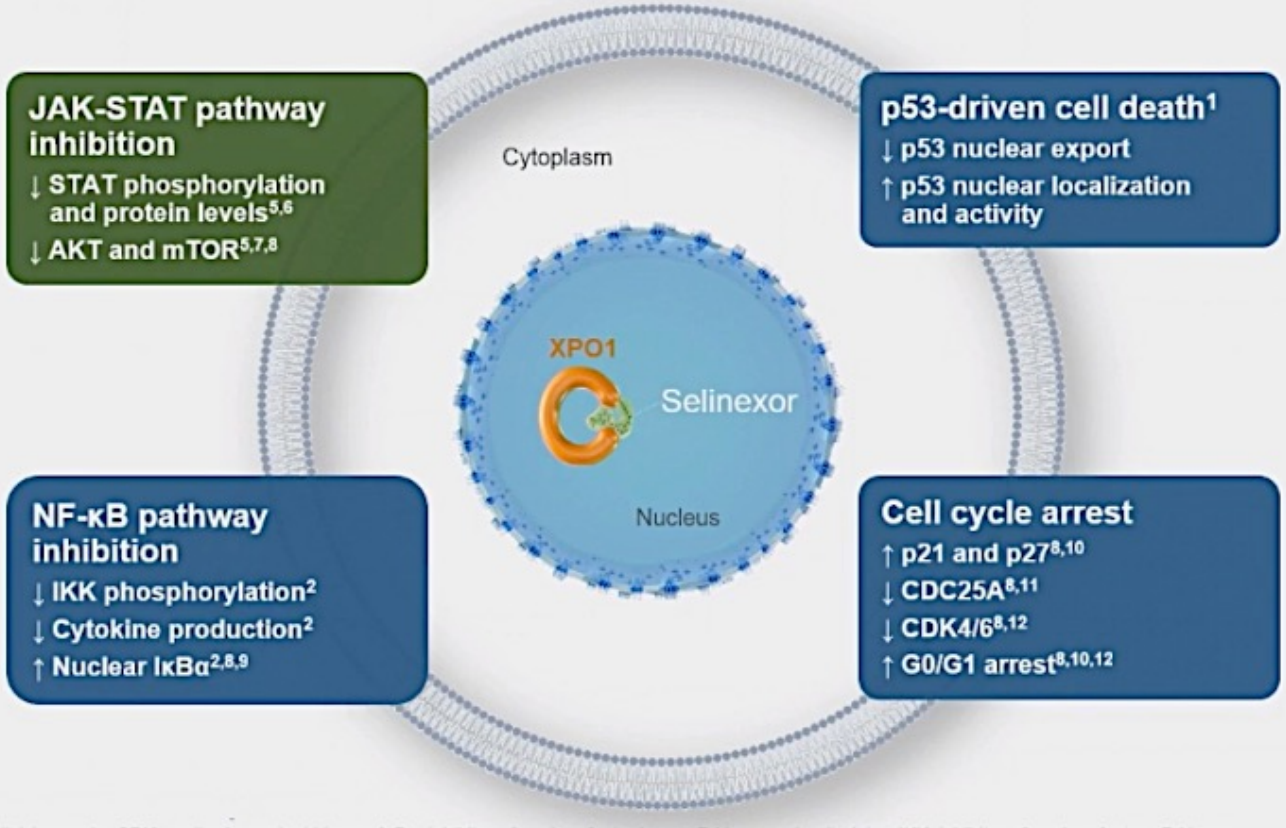
Kubasch AS et al. *Blood Adv* 2021;5(5):1565-75.

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.

Agenda

INTRODUCTION: Myelofibrosis (MF) for Oncology “Newbies”

MODULE 1: Biology of MF

MODULE 2: Management of Anemia in MF

MODULE 3: Novel Strategies for MF

MODULE 4: Journal Club

A 78-year-old man with symptomatic MF receives ruxolitinib 10 mg BID but develops severe anemia and cardiac symptoms. Ruxolitinib dose is decreased to 5 mg BID with no change in symptoms. Platelet count = 77,000/µL, Hgb = 6.16 g/dL, WBC = 32,500/µL with 2% blasts, spleen is 12 cm below left costal margin. 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	 Dr Oh	Switch to momelotinib
 Dr Kuykendall	Switch to momelotinib	 Dr Palmer	Switch to momelotinib
 Dr Mesa	Switch to momelotinib	 Dr Yacoub	Switch to momelotinib

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/

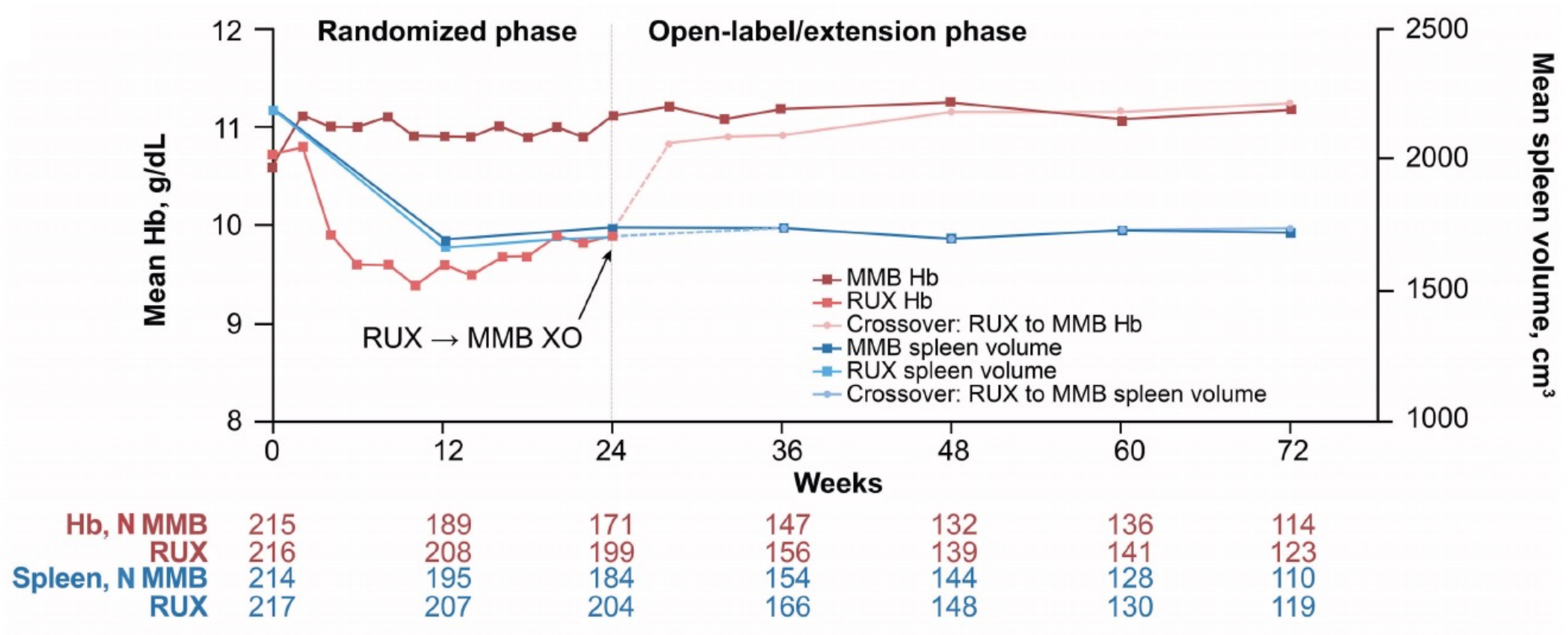
LETTER TO THE EDITOR

Clinical outcomes of patients with myelofibrosis after immediate transition to momelotinib from ruxolitinib

Mesa R et al. *Haematologica* 2024 February 1;109(2):676-81

SIMPLIFY-1 Trial: Clinical Efficacy of Momelotinib After Immediate Crossover from Ruxolitinib

Hemoglobin and Spleen Volume Dynamics



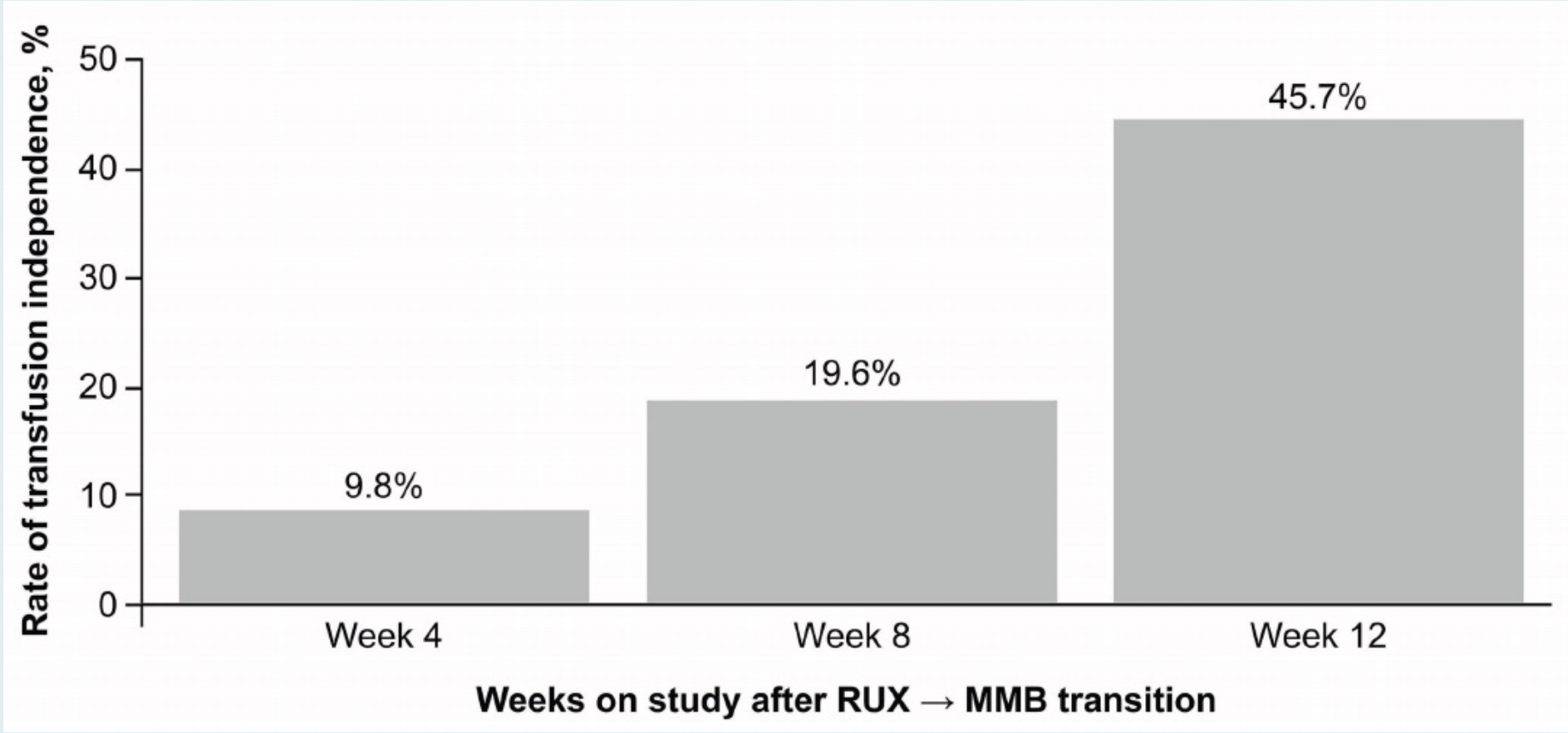
Hb, N MMB	215	189	171	147	132	136	114
RUX	216	208	199	156	139	141	123
Spleen, N MMB	214	195	184	154	144	128	110
RUX	217	207	204	166	148	130	119

MMB = momelotinib; RUX = ruxolitinib; XO = crossover

Mesa R et al. *Haematologica* 2024 February 1;109(2):676-81.

SIMPLIFY-1: Clinical Efficacy of Momelotinib After Immediate Crossover from Ruxolitinib

Transfusion Independence Rate After Transition to Open-Label Momelotinib

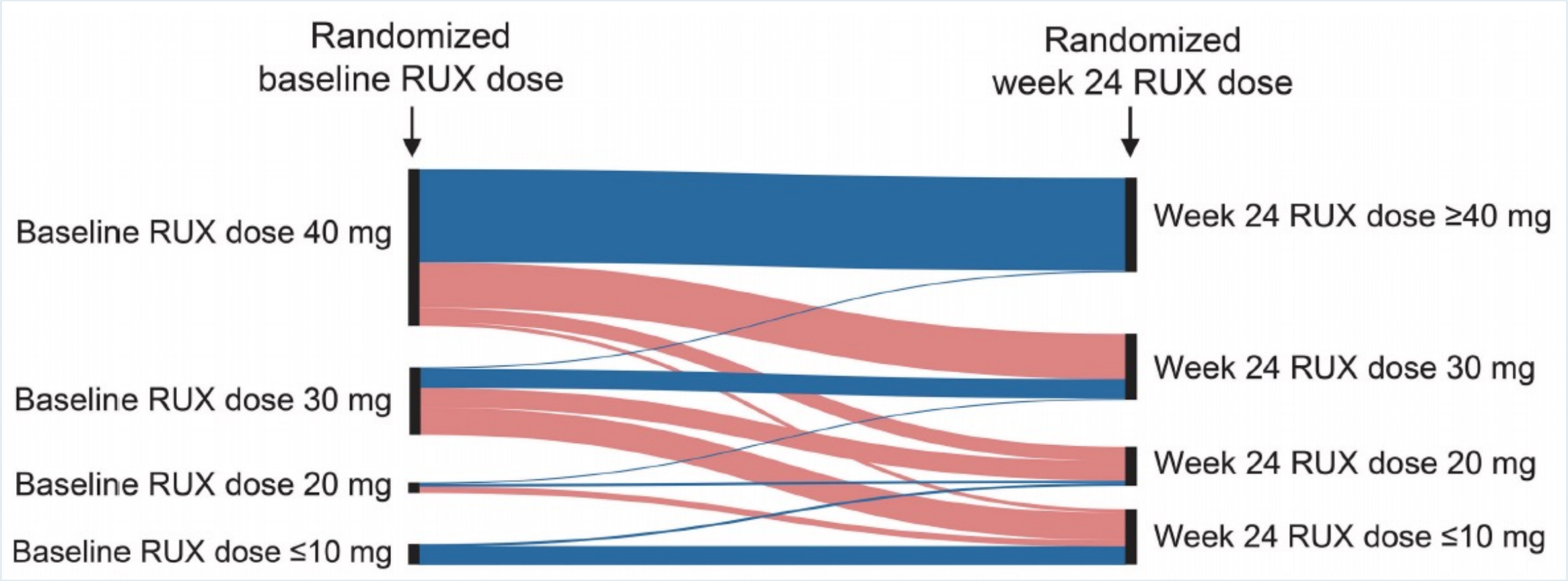


MMB = momelotinib; RUX = ruxolitinib; XO = crossover

Mesa R et al. *Haematologica* 2024 February 1;109(2):676-81.

SIMPLIFY-1: Dosing for Patients Randomly Assigned to Ruxolitinib

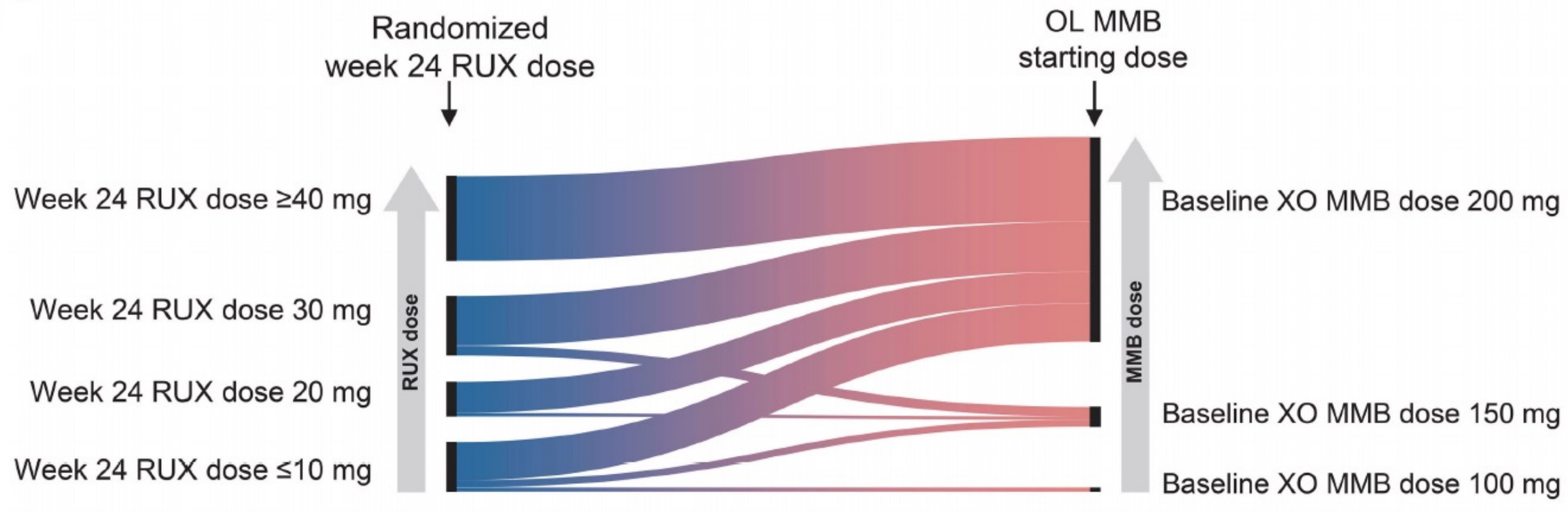
Dosing from Baseline to Week 24 of Ruxolitinib Treatment



Mesa R et al. *Haematologica* 2024 February 1;109(2):676-81.

SIMPLIFY-1: Dosing for Patients Randomly Assigned to Ruxolitinib

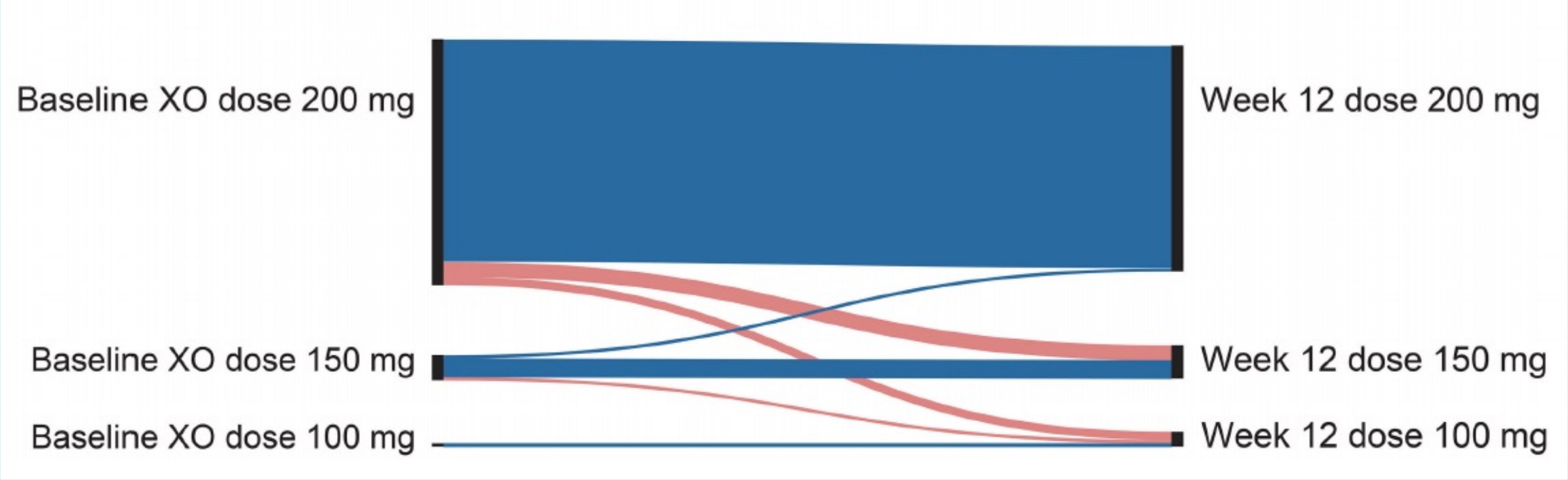
Dosing at Crossover from Ruxolitinib → Momelotinib



Mesa R et al. *Haematologica* 2024 February 1;109(2):676-81.

SIMPLIFY-1: Dosing for Patients Randomly Assigned to Ruxolitinib

Dosing from Baseline Momelotinib at Crossover to Week 12 of Open-Label Momelotinib Treatment



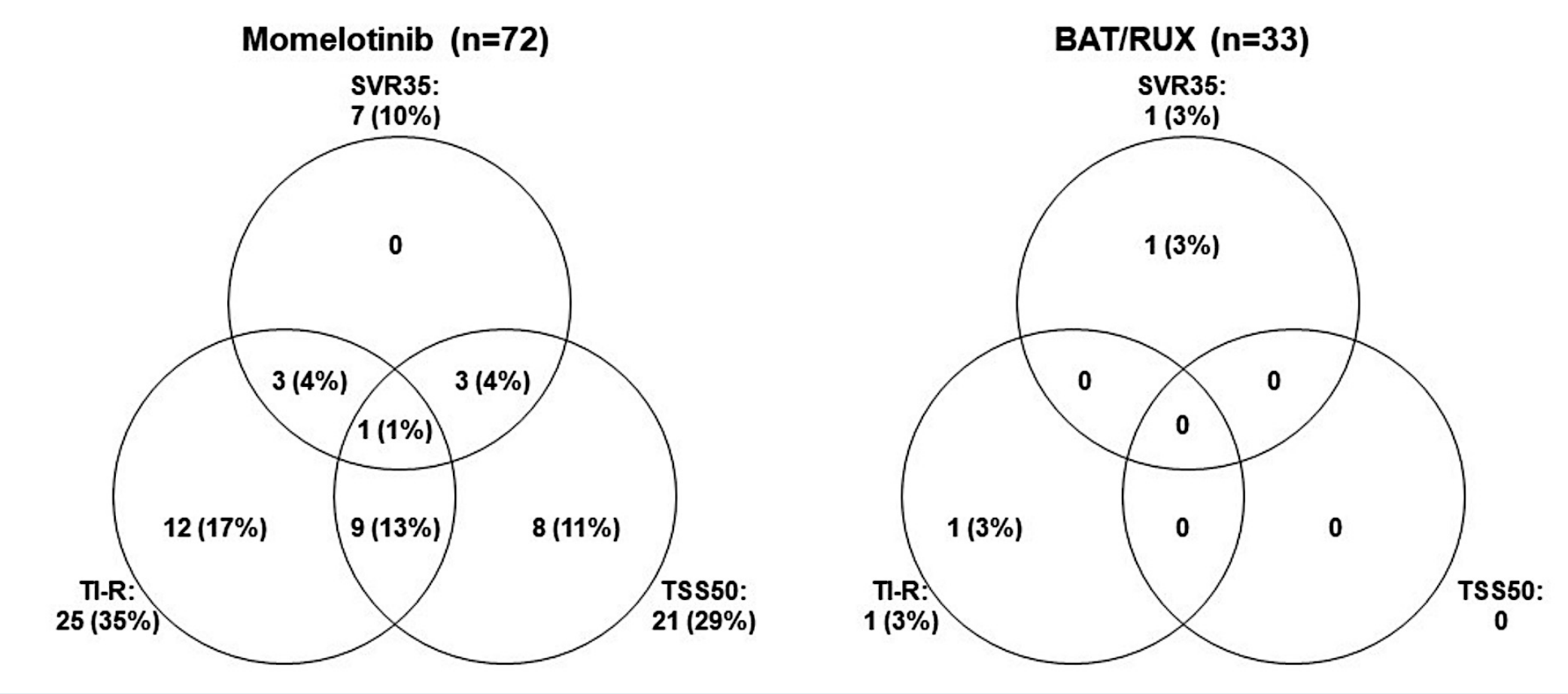
Mesa R et al. *Haematologica* 2024 February 1;109(2):676-81.

Clinical Effectiveness and Safety of Momelotinib Compared with Continued Ruxolitinib or Best Available Therapy in Patients with Myelofibrosis Who Required RBC Transfusions: Subgroup Analysis of the Phase 3 Simplify-2 Study

Claire N Harrison, Alessandro Maria Vannucchi, Christian Recher, Francesco Passamonti, Aaron T. Gerds, Juan Carlos Hernandez Boluda, Abdulraheem Yacoub, Shireen Sirhan, Jun Kawashima, Bharat Patel, Bryan Strouse, Uwe Platzbecker

ASH 2023;Abstract 2189

SIMPLIFY-2: Responses at Week 24 for Transfusion-Dependent Patients at Baseline



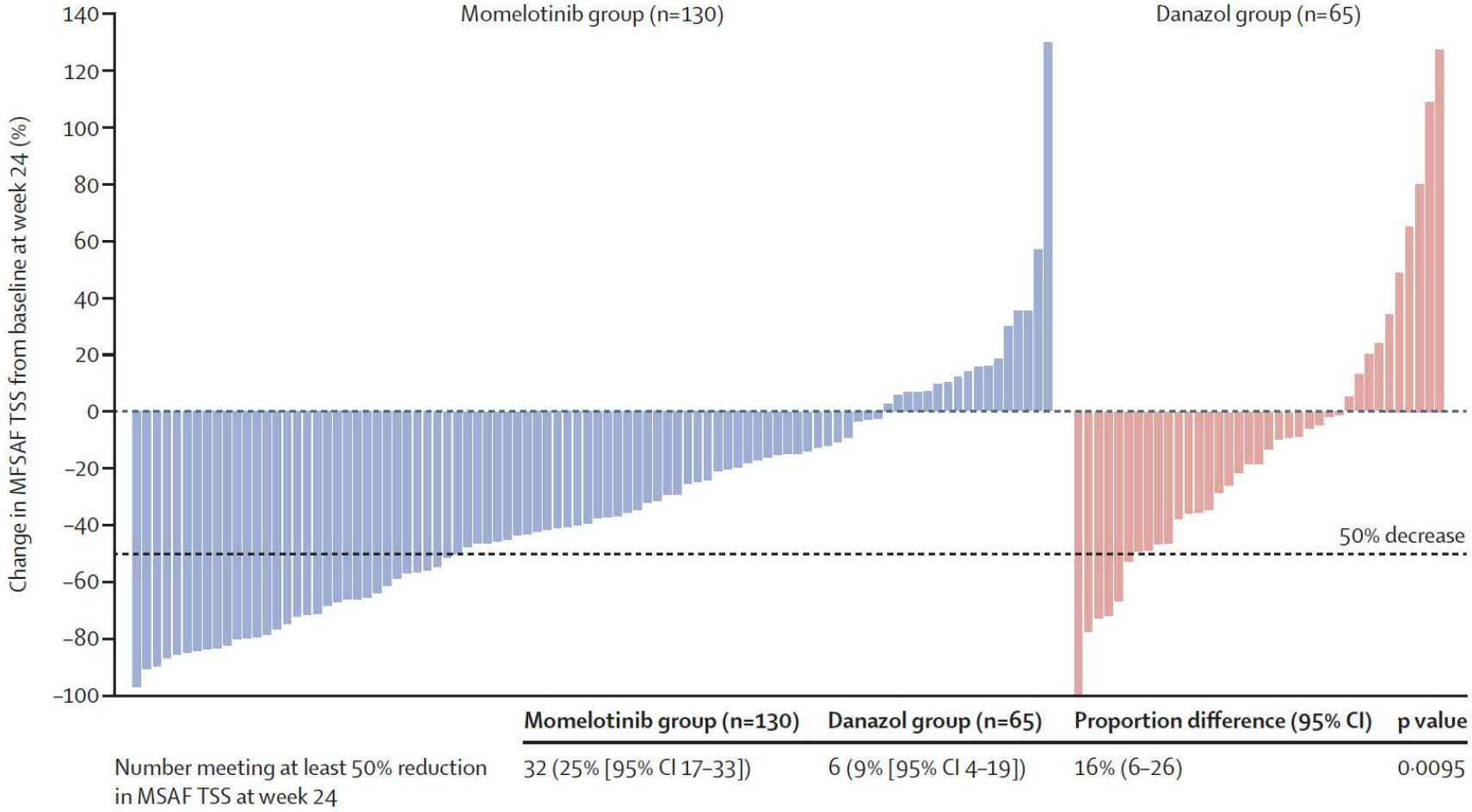
Harrison CN et al. ASH 2023;Abstract 2189.

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

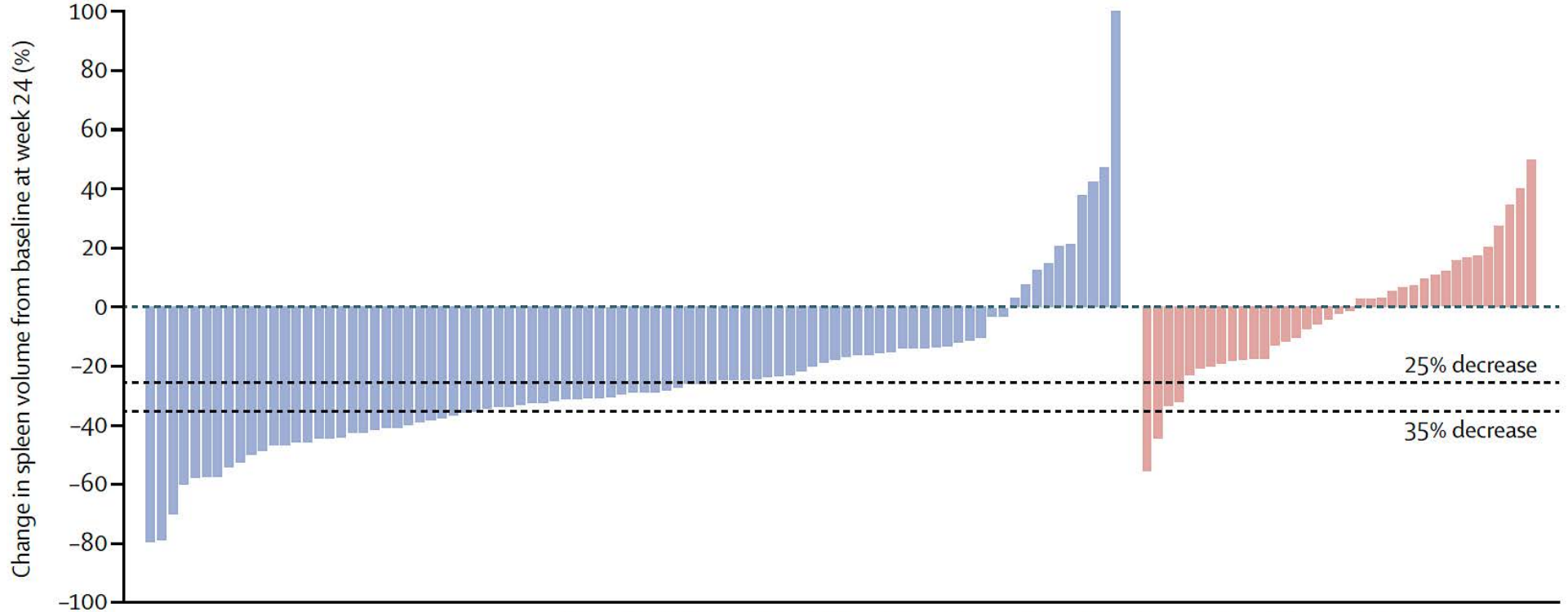


	Momelotinib group (n=130)	Danazol group (n=65)	Proportion difference (95% CI)	p value
Number meeting at least 50% reduction in MSAF TSS at week 24	32 (25% [95% CI 17–33])	6 (9% [95% CI 4–19])	16% (6–26)	0·0095

MFSAF=Myelofibrosis Symptom Assessment Form TSS=total symptom score

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

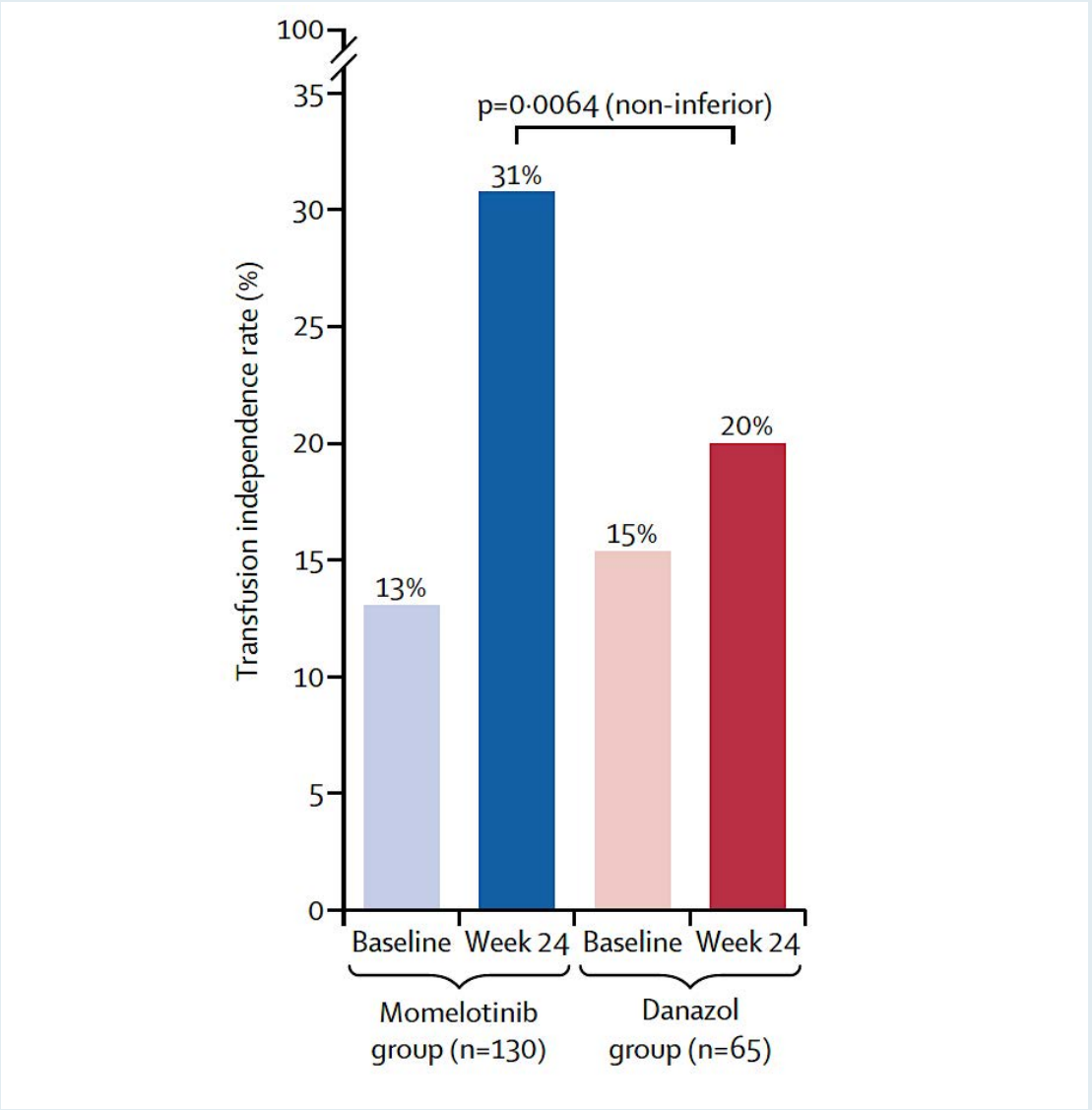
MOMENTUM: Percent Change of Spleen Volume from Baseline to Week 24 for Each Patient



	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

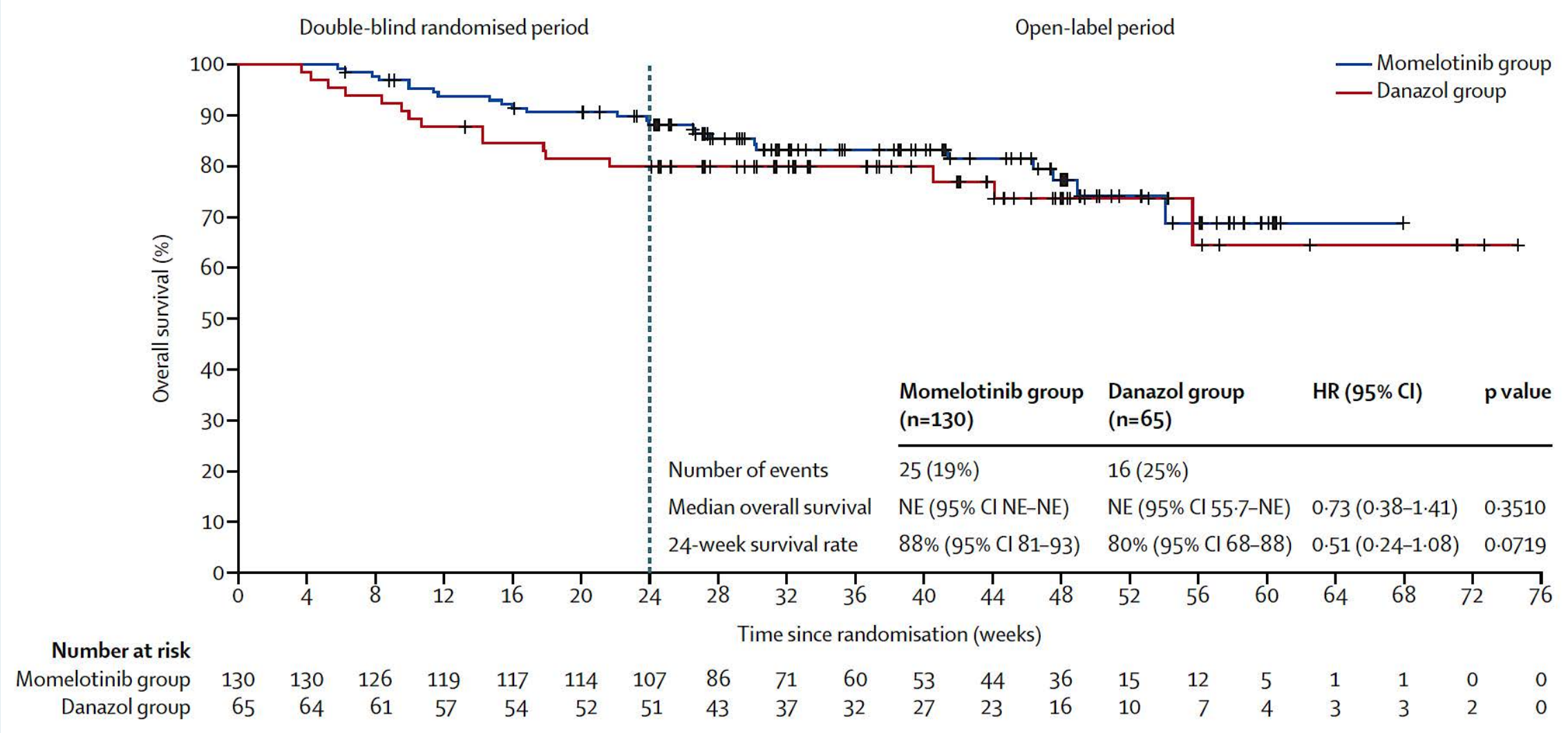
Verstovsek S et al. *Lancet* 2023;401:269-80.

MOMENTUM: Change in Transfusion Independence Rate from Baseline to Week 24



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

MOMENTUM: Overall Survival (ITT Population)



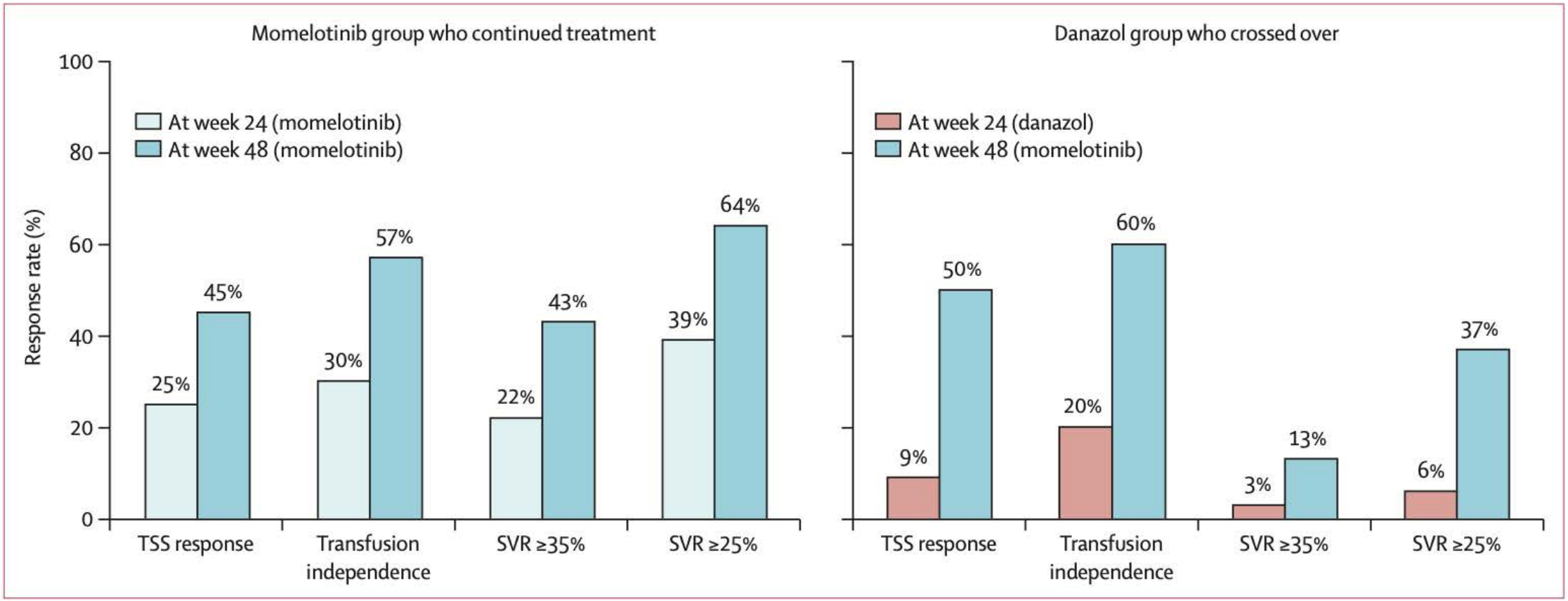
	Momelotinib group (n=130)	Danazol group (n=65)	HR (95% CI)	p value
Number of events	25 (19%)	16 (25%)		
Median overall survival	NE (95% CI NE–NE)	NE (95% CI 55·7–NE)	0·73 (0·38–1·41)	0·3510
24-week survival rate	88% (95% CI 81–93)	80% (95% CI 68–88)	0·51 (0·24–1·08)	0·0719

Number at risk

Momelotinib group	130	130	126	119	117	114	107	86	71	60	53	44	36	15	12	5	1	1	0	0
Danazol group	65	64	61	57	54	52	51	43	37	32	27	23	16	10	7	4	3	3	2	0

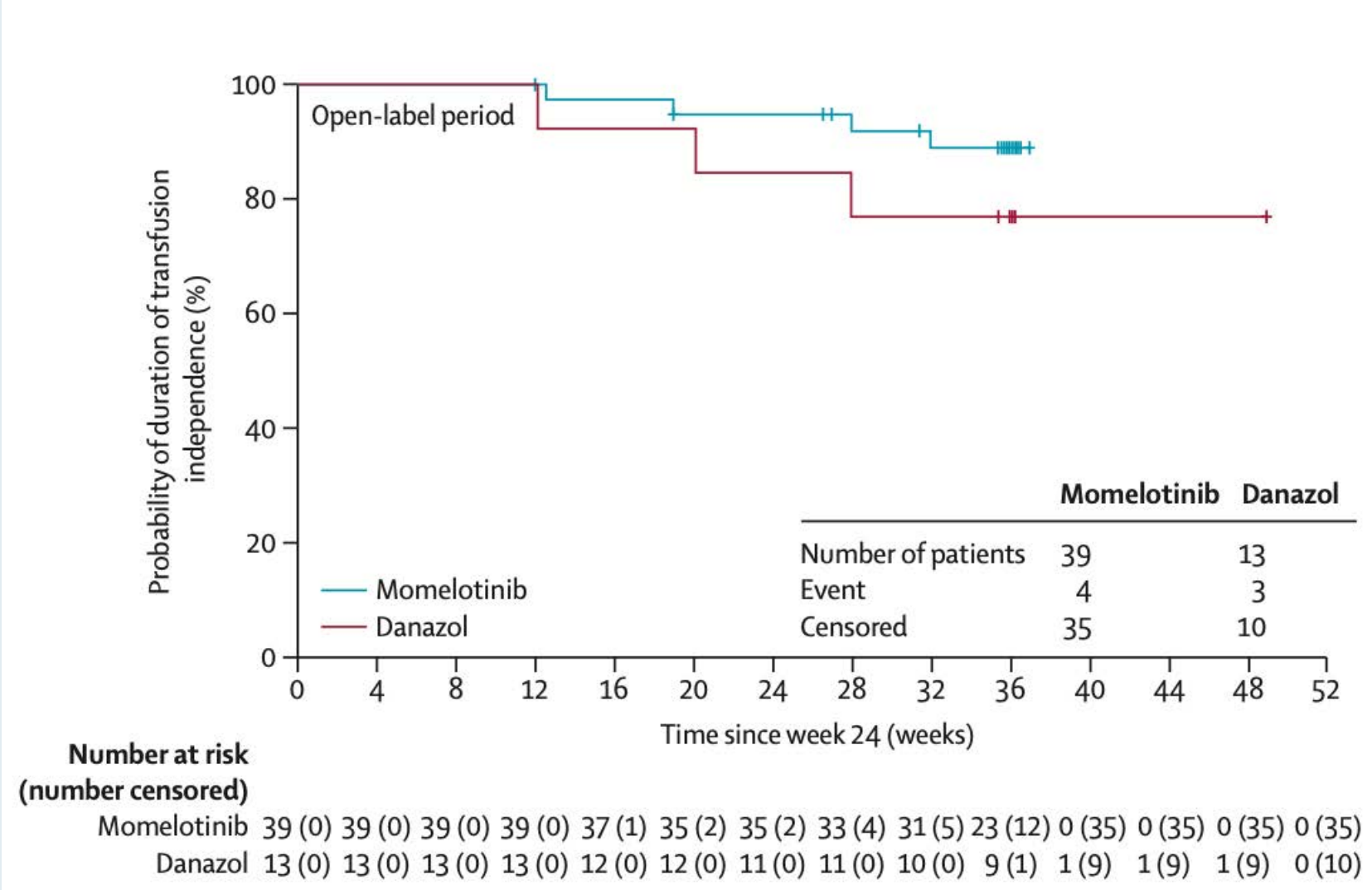
Verstovsek S et al. *Lancet* 2023;401:269-80.

MOMENTUM Updated Analysis: Summary of Response Rates at Weeks 24 and 48



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

MOMENTUM Updated Analysis: : Duration of Transfusion Independence Response



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

Long-Term Survival Adjusted for Treatment Crossover in Patients (pts) with Myelofibrosis (MF) Treated with Momelotinib (MMB) vs Danazol (DAN) in the MOMENTUM Trial

Gupta V et al.

ASCO 2024;Abstract 6571.

REGULAR ARTICLE

blood advances

Momelotinib long-term safety and survival in myelofibrosis: integrated analysis of phase 3 randomized controlled trials

Srdan Verstovsek,[1] Ruben Mesa,[2] Vikas Gupta,[3] David Lavie,[4] Viviane Dubruille,[5] Nathalie Cambier,[6] Uwe Platzbecker,[7] Marek Hus,[8] Blanca Xicoy,[9] Stephen T. Oh,[10] Jean-Jacques Kiladjian,[11] Alessandro M. Vannucchi,[12] Aaron Gerds,[13] Miklos Egyed,[14] Jiří Mayer,[15,16] Tomasz Sacha,[17] Jun Kawashima,[18] Marc Morris,[18] Mei Huang,[18] and Claire Harrison[19]

2023;7(14):3582-91

Overall Survival (OS) and Safety of Momelotinib from Pooled Analysis of SIMPLIFY-1, SIMPLIFY-2 and MOMENTUM Studies

Pooled analysis of overall survival	
2-year OS rate	76.5%
4-year OS rate	59.6%
6-year OS rate	51.1%
Median OS	Not reached

- The most common nonhematologic treatment-emergent adverse event occurring in ≥20% of patients was diarrhea (any grade, 27% and Grade ≥3, 3%).
- The most common reason for momelotinib discontinuation was thrombocytopenia (4% discontinuation rate).

AE	Momelotinib (N = 725), n (%)	
	Any-grade AE	Grade ≥3 AE
AEs of clinical importance*		
Infections (SOC)	402 (55.4)	154 (21.2)
Opportunistic infections (similar PTs)	40 (5.5)	11 (1.5)
Malignancies (similar PTs)	97 (13.4)	53 (7.3)
AML/malignant transformation (similar PTs)	22 (3.0)	22 (3.0)
Nonmelanoma skin cancer (similar PTs)	35 (4.8)	4 (0.6)
MACE (similar PTs)	57 (7.9)	48 (6.6)
Thrombocytopenia (similar PTs)	181 (25.0)	119 (16.4)
Neutropenia (similar PTs)	49 (6.8)	38 (5.2)
Anemia (similar PTs)	170 (23.4)	107 (14.8)
Thromboembolism (SMQ)	64 (8.8)	39 (5.4)
Hemorrhage (SMQ)	207 (28.6)	49 (6.8)
Peripheral neuropathy (SMQ)	107 (14.8)	9 (1.2)

Data cutoff: 3 December 2021.
Includes AEs reported between the first momelotinib dose date and 30 days after the last momelotinib dose date.

AE = adverse event; MACE = major adverse cardiovascular event

Verstovsek S et al. *Blood Adv* 2023;7(14):3582-91.

DOI: 10.1002/ajh.26778

RESEARCH ARTICLE

AJH WILEY

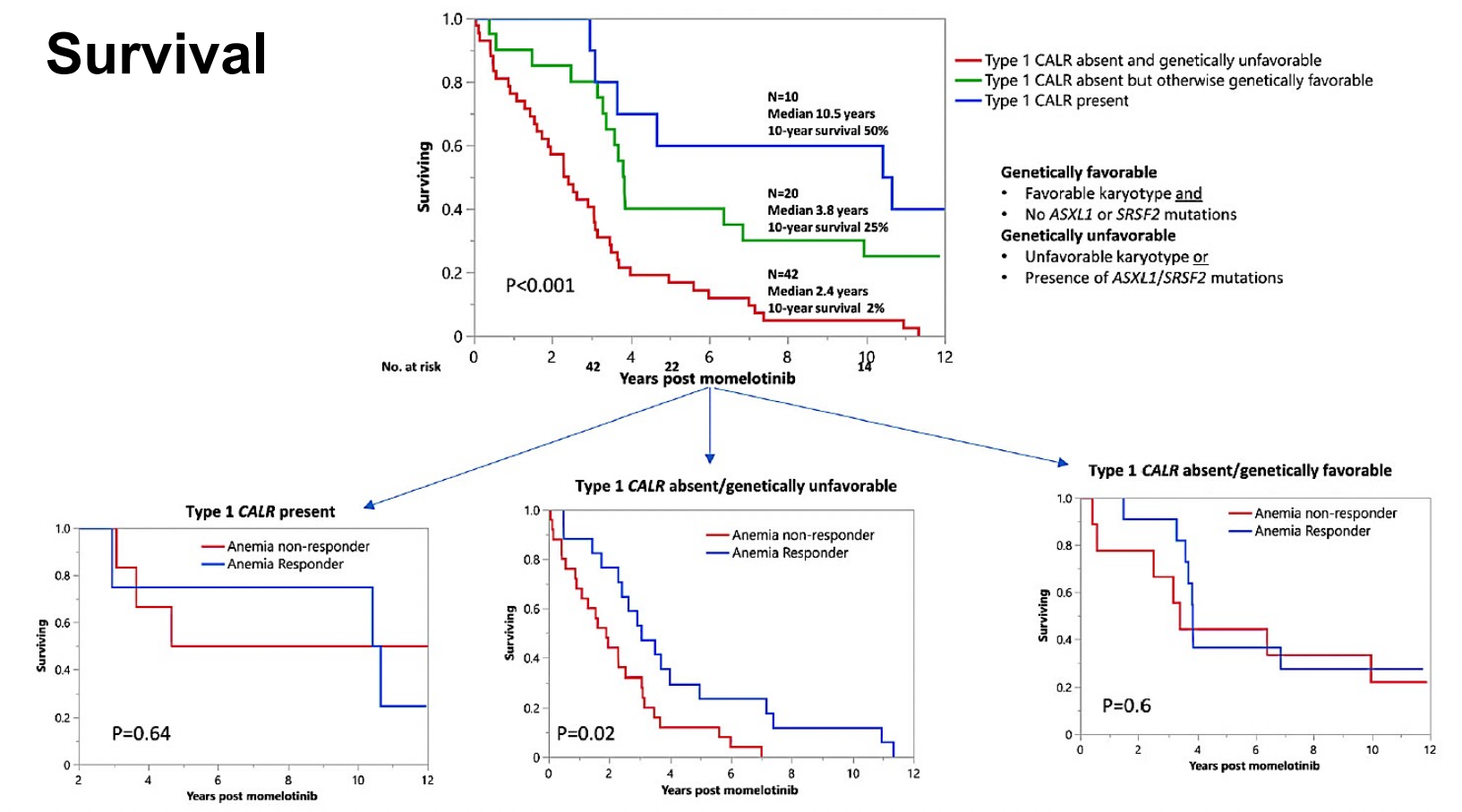
Predictors of anemia response to momelotinib therapy in myelofibrosis and impact on survival

Naseema Gangat | Kebede H. Begna | Aref Al-Kali | William Hogan | Mark Litzow | Animesh Pardanani | Ayalew Tefferi

Am J Hematol 2023;98:282-89

Predictors of Anemia Response to Momelotinib and Impact on Survival

- **Anemia response to momelotinib** favorably impacted by:
  - Post-ET MF variant
  - Lower serum ferritin level
  - Shorter time from diagnosis to initiation of momelotinib
  - Serum ferritin level <55 mcg/L
  - Time from diagnosis to initiation of momelotinib of <23 months



- In addition to achieving an anemia response, overall survival with momelotinib was favorably affected by the presence of type 1/CALR mutations and the absence of ASXL1/SRSF2 mutations

Gangat N et al. *Am J Hematol* 2023;98:282-89.

Agenda

INTRODUCTION: Myelofibrosis (MF) for Oncology “Newbies”

MODULE 1: Biology of MF

MODULE 2: Management of Anemia in MF

MODULE 3: Novel Strategies for MF

MODULE 4: Journal Club

ASCO 2024 Highlights

- Rampal R et al. Updated safety and efficacy data from the phase 3 MANIFEST-2 study of pelabresib in combination with ruxolitinib for JAK inhibitor treatment-naïve patients with myelofibrosis. Abstract 6502.

- Braish B et al. Impact of JAK2 allele burden on MF outcome in the era of ruxolitinib. Abstract 6514.

- Mascarenhas J et al. Phase 3 randomized double-blind study evaluating selinexor, an XPO1 inhibitor, plus ruxolitinib in JAKi-naïve myelofibrosis. Abstract TPS6594 .

- Scandura JM et al. Phase 2 study evaluating selinexor monotherapy in patients with JAKi-naïve myelofibrosis and moderate thrombocytopenia. Abstract TPS6593 .

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

TRANSFORM-1: Efficacy Outcomes with Navitoclax and Ruxolitinib for Treatment-Naïve Myelofibrosis

- Time to first SVR_{35} response was similar in NAV + RUX arm compared with PBO + RUX [median (range): 12.3 (10.1–48.3) vs 12.4 (11.3–72.3) weeks]

	NAV + RUX (N=125)	PBO + RUX (N=127)	Response rate difference (95% CI; P-value)
SVR_{35} at Week 24; n (%)	79 (63.2)	40 (31.5)	**31.0 (19.5–42.5); P<0.0001**
Duration of study follow-up; median (range) months	14.8 (1.0–29.5)	14.9 (0.0–28.8)	
SVR_{35} at any time on-study; n (%)	96 (76.8)	53 (41.7)	**34.6 (23.6–45.6); P<0.0001***
Time to first SVR_{35} response; median (range) weeks	12.3 (10.1–48.3)	12.4 (11.3–72.3)	
Subjects who lost SVR_{35} response; n/N (%)	18/96 (18.8)	14/53 (26.4)	
12-month duration of SVR_{35} rate; % (95% CI)	76.7 (64.7, 85.0)	76.9 (59.8, 87.4)	

*Nominal P-value. ᵃDuration of SVR35 is the time from the first date of SVR35 to the first assessment where SVR35 is not maintained and the spleen volume is ≥25% increased from nadir (the lowest spleen volume in the previous assessments), confirmed relapse, or leukemic transformation per IWG criteria, whichever is earlier.
CI, confidence interval; IWG, International Working Group; NAV, navitoclax; PBO, placebo; RUX, ruxolitinib; SVR_{35}, spleen volume reduction of ≥35%.

Pemmaraju N et al. ASH 2023;Abstract 620.

TRANSFORM-1: Safety Outcomes with Navitoclax and Ruxolitinib for Treatment-Naïve Myelofibrosis

	NAV + RUX (N=124)[a] N (%)		PBO + RUX (N=125)[a] N (%)	
Any AE	124 (100)		121 (97)	
Any AE grade ≥3	105 (85)		87 (70)	
Most common AEs (>30% patients receiving NAV)	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Thrombocytopenia	112 (90)	63 (51)	62 (50)	19 (15)
Anemia	74 (60)	57 (46)	61 (49)	49 (39)
Neutropenia	56 (45)	47 (38)	7 (6)	5 (4)
Diarrhea	42 (34)	6 (5)	17 (14)	0
Bleeding/hemorrhagic events	30 (24)	2 (2)	27 (22)	7 (6)
COVID-19	26 (21)	1 (1)	23 (18)	7 (6)
Contusion	13 (10)	0	7 (6)	0
Abdominal pain	11 (9)	1 (1)	8 (6)	1 (1)
Abdominal pain upper	9 (7)	1 (1)	10 (8)	1 (1)
Bone pain	9 (7)	0	6 (5)	0
Any serious AE	32 (26)		40 (32)	
AEs leading to dose reduction				
Navitoclax/placebo	101 (81)		39 (31)	
Ruxolitinib	112 (90)		76 (61)	
AE leading to dose interruption				
Navitoclax/placebo	87 (70)		44 (35)	
Ruxolitinib	78 (63)		41 (33)	
All deaths	13 (10)		13 (10)	
Deaths ≤30 days following last dose of study drug	6 (5)		5 (4)	

- Most commons AEs were thrombocytopenia, anemia, neutropenia, and diarrhea
- Most common serious AEs reported were
  - COVID-19 pneumonia and pneumonia in 3 patients each with NAV + RUX and 2 each with PBO + RUX
- Dose reductions and interruptions were mostly due to thrombocytopenia, none were due to bleeding

Pemmaraju N et al. ASH 2023;Abstract 620.

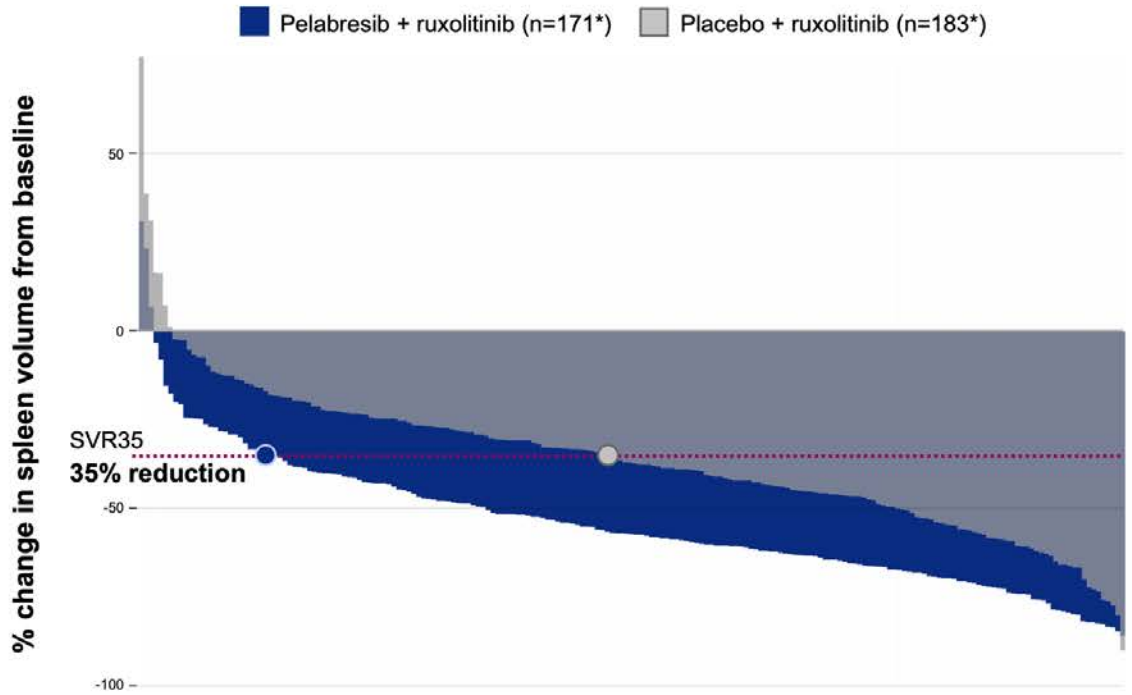
Pelabresib in combination with ruxolitinib for Janus kinase inhibitor treatment-naïve patients with myelofibrosis: results of the MANIFEST-2 randomized, double-blind, Phase 3 study

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*

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.

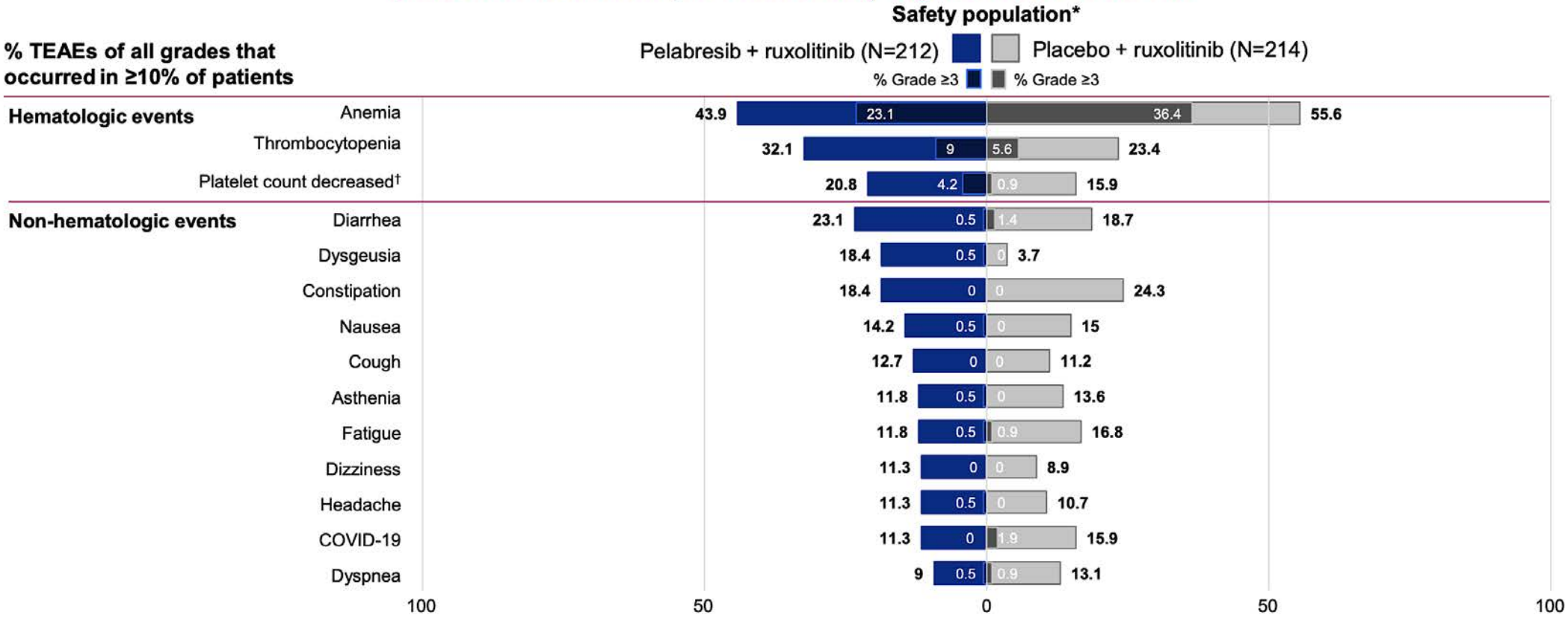
Rampal R, et al. ASH 2023. Oral 628

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: Safety Outcomes with Pelabresib and Ruxolitinib for Treatment-Naïve Myelofibrosis

Adverse events of anemia were reported less frequently with pelabresib + ruxolitinib combination than with placebo + ruxolitinib; no new safety signals were observed



Preliminary Analyses from Data cut off: August 31, 2023. TEAE, treatment-emergent adverse event. *Safety population: received at least one dose of study drug. †Platelet count decreased was classified under the system organ class of investigation. TEAEs are regardless of relationship to study drug. A TEAE for the double-blinded treatment period is defined as an adverse event that has a start date on or after the first dose of the pelabresib/placebo and before 30 days after the last dose of pelabresib/placebo or before the start of alternative (off-study) treatment for MF, whichever occurs first. MF, myelofibrosis; COVID-19, coronavirus disease 2019.

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.

Updated Safety and Efficacy Data from the Phase 3 MANIFEST-2 Study of Pelabresib in Combination with Ruxolitinib for JAK Inhibitor Treatment-Naïve Patients with Myelofibrosis

Rampal R et al.

ASCO 2024;Abstract 6502 (Oral).

May 31, 2024

3:09 PM – 3:21 PM CDT

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]

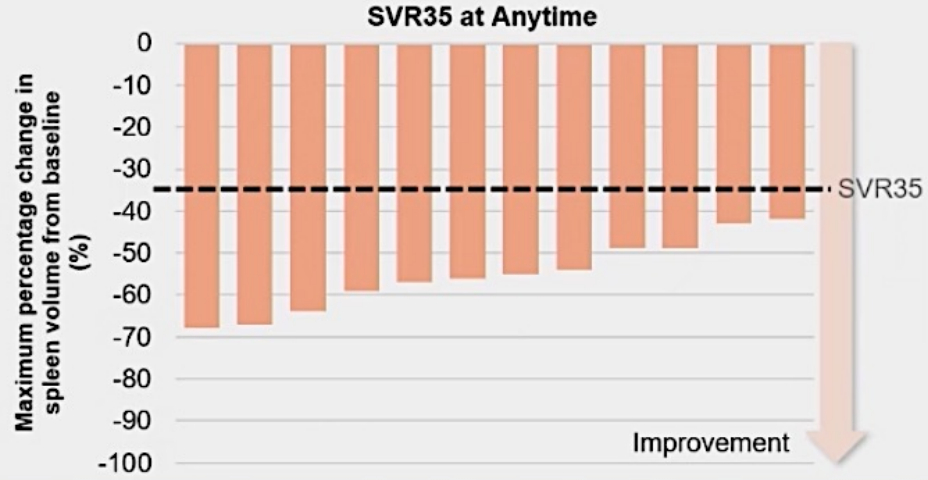
[1]Division of Hematology and Hematologic Malignancies, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA
[2]Vanderbilt Ingram Cancer Center, Nashville, TN, USA
[3]VCU Massey Cancer Center, Richmond, VA, USA
[4]Karyopharm Therapeutics, Newton, MA, USA
[5]Formerly of Karyopharm Therapeutics,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

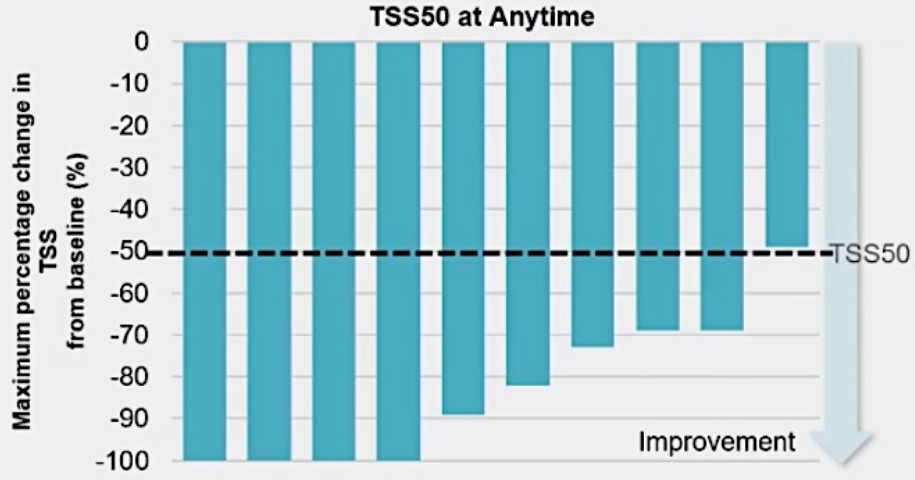
ASH 2023;Abstract 622

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)**

		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)**





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

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 s

*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 Wee
§Two patients discontinued prior to Week 24, and one had missing data.

Tantravahi S et al. ASH 2023;Abstract 622.

XPORT-MF-034: Phase I Treatment-Emergent Adverse Events with Selinexor 60 mg per Week

TEAEs	Selinexor 60 mg QW + ruxolitinib (N = 14)
Any grade (≥ 30% overall), n (%)	
Nausea	11 (78.6)
Anemia	9 (64.3)
Thrombocytopenia	9 (64.3)
Fatigue	8 (57.1)
Constipation	7 (50.0)
Vomiting	7 (50.0)
Dyspnea	5 (35.7)
Headache	5 (35.7)
Hyponatremia	5 (35.7)
Leukopenia	5 (35.7)
Neutropenia	5 (35.7)
Grade 3+ (> 5%), n (%)	
Anemia	6 (42.9)
Thrombocytopenia	4 (28.6)
Back pain	2 (14.3)
Neutropenia	1 (7.1)
Atrial fibrillation	1 (7.1)
Leukopenia	1 (7.1)
Treatment-related AEs leading to treatment discontinuations, n (%)	
Thrombocytopenia, Grade 3	1 (7.1)
Peripheral neuropathy, Grade 3	1 (7.1)

Prophylactic Antiemetic use Reduced the Incidence and Severity of Nausea

Nausea was transient in nature with a median duration ~2 cycles

64% Patients in the 60 mg cohort received one prophylactic antiemetic

67% Of these patients had nausea (Grade 1 only)

Versus

100% Patients without antiemetic prophylaxis had nausea (Grades 1–3)

2.5 kg Median weight gain at Week 24

Median Hemoglobin (Hgb) Levels and Platelet Counts Were Generally Stable

46% Transfusion-independent patients had stable Hb levels†

Median Hgb levels (g/dL) **9.9** Baseline **8.8** Week 12 **9.1** Week 24

Median platelet levels ($\times 10^9$/L) **220** Baseline **135** Week 12 **137** Week 24

Tantravahi S et al. ASH 2023;Abstract 622.

A Phase 2 Study to Evaluate the Efficacy and Safety of Selinexor Monotherapy in Patients with JAK Inhibitor-Naïve Myelofibrosis and Moderate Thrombocytopenia (XPORT-MF-044)

Sandura JM et al.

ASH 2023;Abstract 3211.

Phase 2 Study Evaluating Selinexor Monotherapy in Patients with JAKi-Naïve Myelofibrosis and Moderate Thrombocytopenia

Sandura JM et al.

ASCO 2024;Abstract TPS6593.

Mediterranean Diet Intervention in Patients with Myeloproliferative Neoplasm

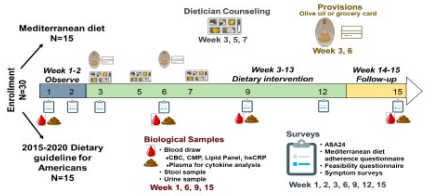
Laura Mendez Luque[1], Hellen Nguyen[1], Jenny Nguyen[1], Alexander Himstead[2], Elena Heide[2], Melinda Lem[2], Robyn Scherber[3], Chelsea McKinney[1], Ruben Mesa[3], Lari Wenzel[1], Andrew Odegaard[4], Angela Fleischman[1]

1. Chao Family Comprehensive Cancer Center, University of California, Irvine; 2. University of California, Irvine School of Medicine; 3. Mays Cancer Center, UT Health San Antonio;
4. Department of Epidemiology, University of California, Irvine

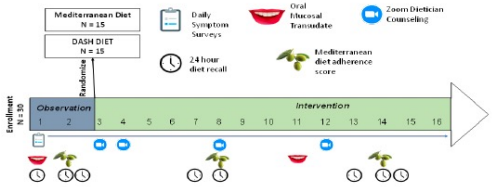
BACKGROUND

Myeloproliferative Neoplasm (MPN) is a chronic incurable blood cancer characterized by high inflammation, debilitating symptoms such as fatigue, and blood clots. A Mediterranean Diet reduces inflammatory biomarkers and improves outcomes in cardiovascular disease, therefore we predict that a Mediterranean diet may also prove beneficial in chronic blood cancers such as MPN.

CLINICAL TRIALS WE'VE PERFORMED AT UCI

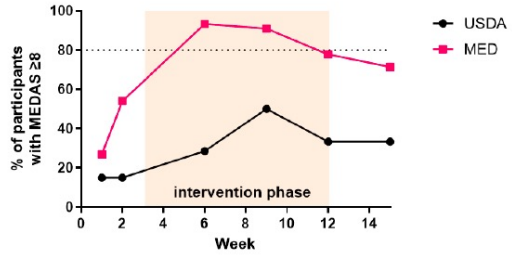


In our first study we randomized 30 MPN patients to either Mediterranean or standard US Diet guidelines with in person dietician counseling.

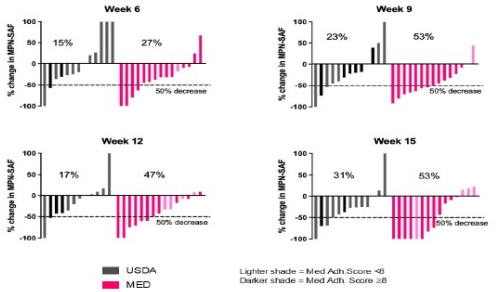


In our second study we randomized 30 MPN patients to either a Mediterranean or DASH diet with zoom based dietician counseling. This was a fully remote study.

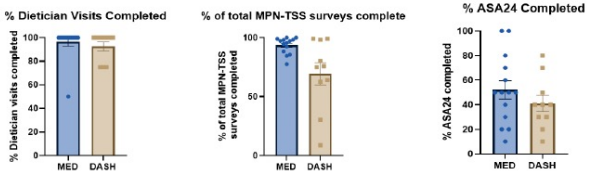
RESULTS



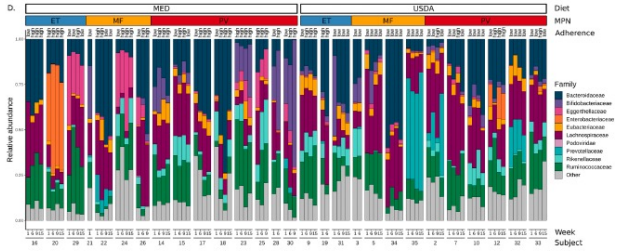
MPN patients can adopt a Mediterranean diet eating pattern. We measured adherence to a Mediterranean diet using a 14-point questionairre called the MEDAS, with a score of ≥ 8 regarded as good adherence to a Mediterranean diet. The majority of people in the MED group achieved good adherence to a Mediterranean diet, whereas people in the USDA arm did not.



Dietary intervention reduces symptom burden in MPN patients. We measured symptom burden using the MPN-TSS, a 10 point survey covering the most common MPN associated symptoms. Reductions were seen in both diet groups, however more so in the MED diet group.



A fully online diet intervention is feasible in MPN patients. We had almost 100% attendance at dietician visit and MPN patients are willing to perform daily online symptom assessements. However, for more time intense online activities such as 24 hour diet recalls (ASA24) alternative methods such as phone calls are necessary



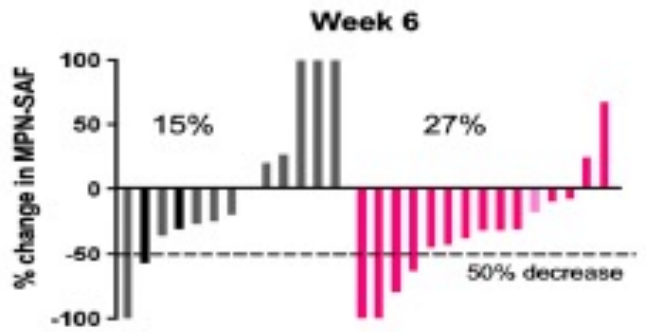
Gut microbiome signature of MPN patients. We collected stool samples at multiple time points during the study. We did not detect any significant changes in the gut microbiome with our diet intervention.

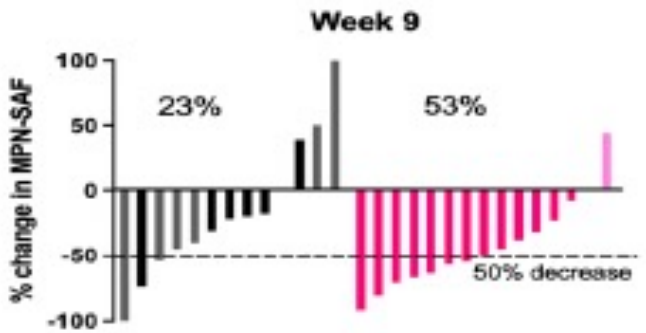
CONCLUSIONS/FUTURE DIRECTIONS

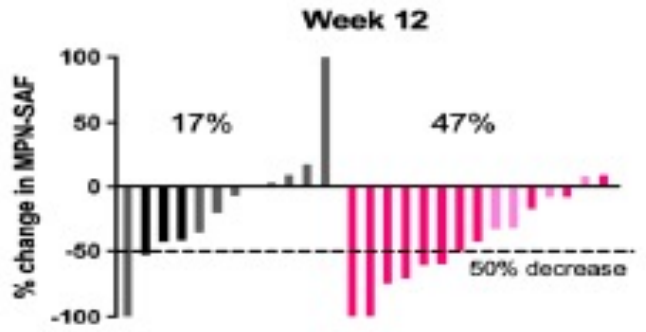
- Patients with myeloproliferative neoplasms can easily adopt a Mediterreanean Diet eating pattern
- Fully online based diet intervention studies are feasible in the myeloproliferative neoplasm patient population
- Diet interventions may be a low risk, low cost approach to improve symptom burden in chronic blood cancers

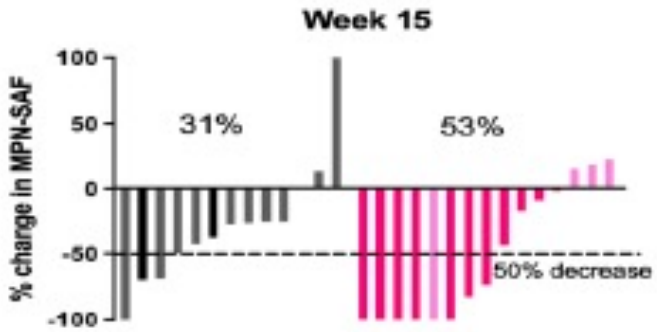
Mendez LF et al. *Blood* 2022;140(Suppl 1):3972-3.

Diet Intervention and Symptom Burden









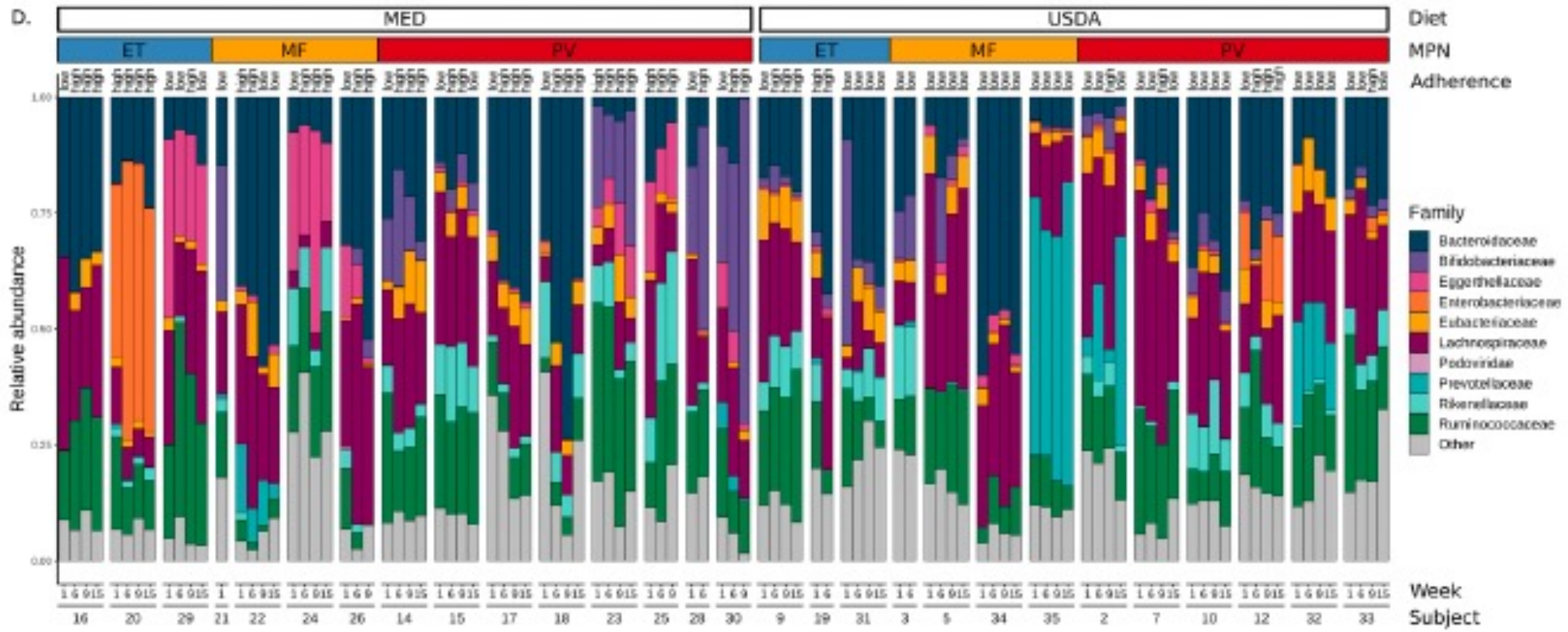
USDA
MED

Lighter shade = Med Adh.Score <8
Darker shade = Med Adh. Score ≥8

Dietary intervention reduces symptom burden in MPN patients. We measured symptom burden using the MPN-TSS, a 10 point survey covering the most common MPN associated symptoms. Reductions were seen in both diet groups, however more so in the MED diet group.

Mendez LF et al. *Blood* 2022;140(Suppl 1):3972-3.

Gut Microbiome Signature



Gut microbiome signature of MPN patients. We collected stool samples at multiple time points during the study. We did not detect any significant changes in the gut microbiome with our diet intervention.

Mendez LF et al. *Blood* 2022;140(Suppl 1):3972-3.

Abstract 7010: Identification and management of clonal hematopoiesis of indeterminate potential (CHIP) in cancer survivors: The Cleveland Clinic experience

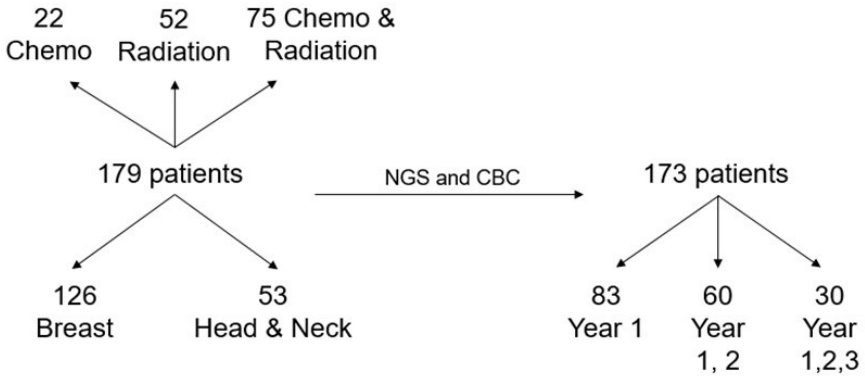
Teodora Kuzmanovic, Donna Horvath, Maurice Slaughter, Natalya Karasik, David Bosler, MD, Halle Moore, MD, Jame Abraham, MD, Jessica Geiger, MD, Pauline Funchain, MD Aaron T. Gerds, MD, Anjali S. Advani, MD, Sudipto Mukherjee, MD, MPH, Mikkael A. Sekeres, MD, MS, Jaroslaw P. Maciejewski, MD, PhD, Brian Bolwell, MD, Hetty E. Carraway, MD, MBA, Bhumika J. Patel, MD and Abhay Singh, MD, MPH

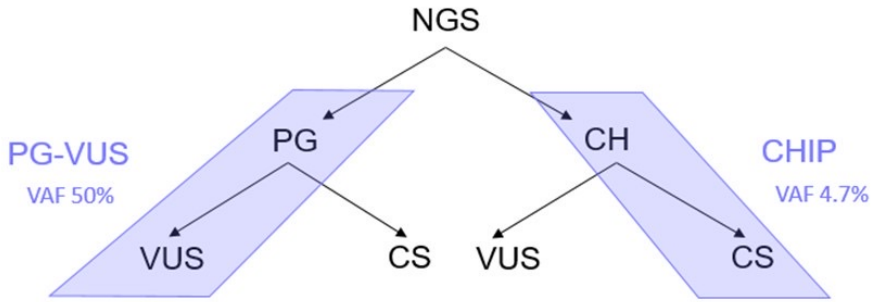
Cleveland Clinic | Cleveland Clinic Cancer Center

ASCO 2023

Background and Design

- Background
  - CHIP can be seen in healthy individuals and cancer patients
  - Associated with cardiovascular disease and hematologic neoplasm risk
- Design
  - 10 year prospective study
  - Annual NGS/CBC
  - CHIP + patients referred to CHIP clinic and Preventive Cardiology

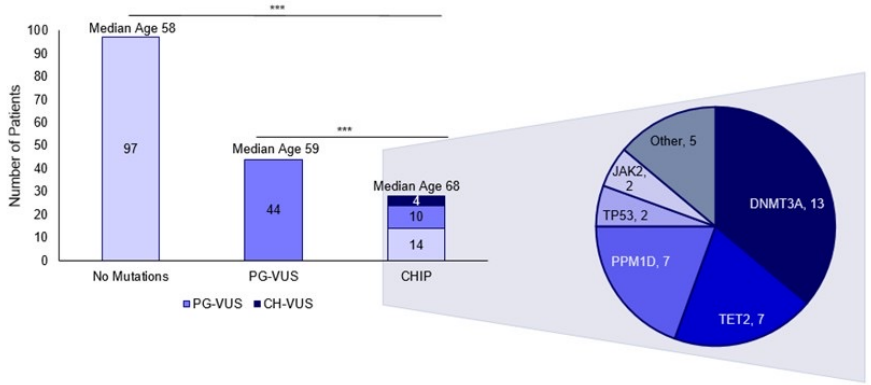




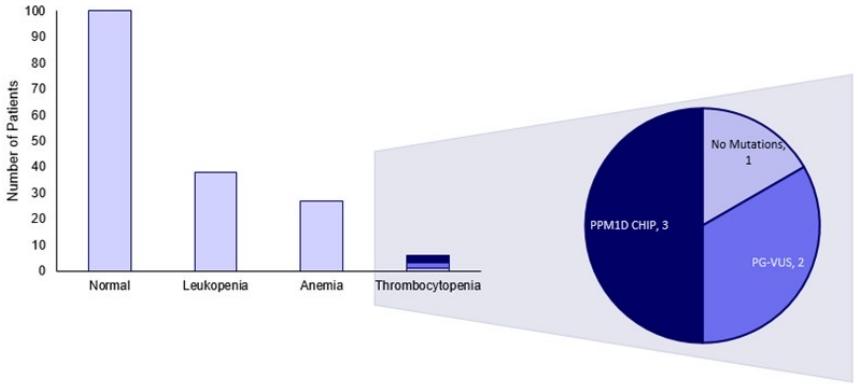
PG, potentially germline; **VUS**, variant of uncertain significance; **CS**, clinically significant; **CH**, clonal hematopoiesis; **VAF**, variant allele frequency

Kuzmanovic T et al. ASCO 2023;Abstract 7010.

Results: NGS and CBC



CHIP in 16% of patients, half co-occurring with VUS. CHIP patients are older, with *DNMT3A*, *TET2*, and *PPM1D* as most frequent mutations



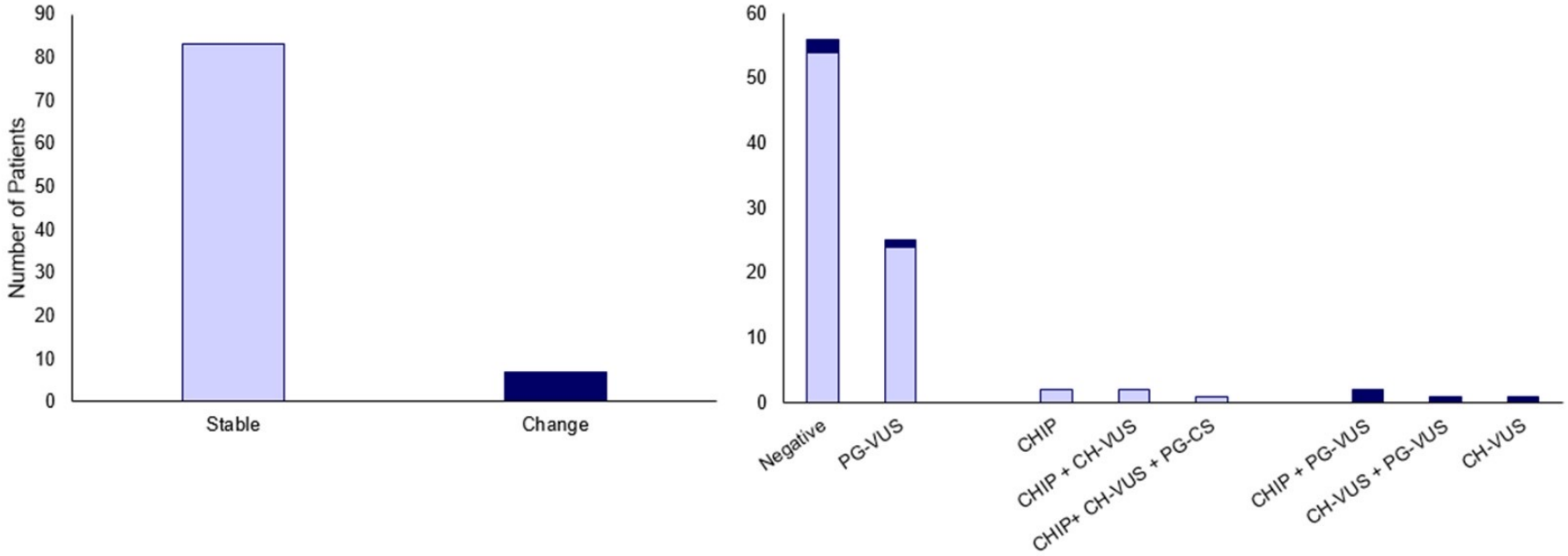
Most patients had normal CBC (58%), some mild stable leukopenia (22%) and anemia (15%). Thrombocytopenia seen in 6 patients, half with *PPM1D* CHIP

Structure of *PPM1D*. Dark blue, residues of interest including: loop 39-95, hinge 155-166, flap 219-295, and nuclear localization signal 535-552. White dots, transitions; black dots, deletions, duplications, transversions.

PPM1D mutations clustered at C-terminal domain. CHIP arising from DNA transversions, deletions, duplications following chemoradiation *vs.* PG-VUS from transitions.

Kuzmanovic T et al. ASCO 2023;Abstract 7010.

Results: Serial NGS



- Majority of patients had stable NGS
- Presence of 2+ categories (e.g., CHIP + CH-VUS) portended 10x increased likelihood for clonal evolution (somatic acquisition, disappearance on NGS) *vs.* single/no mutations, p=0.0053
- CHIP/CH-VUS + PG-VUS all had change in NGS on serial analysis, $p=2.9 \times 10^{-4}$

Kuzmanovic T et al. ASCO 2023;Abstract 7010.

CHIP and Preventive Cardiology

Patient	Cardiology Visit	CVD Comorbidities	CVD Medication	NGS Classification	PG Mutations	CH and CHIP Mutations	Serial NGS Status
1	Yes	HTN, HLD	Yes	CHIP		***DNMT3A***	Stable
2	Yes	T2D, HTN, HLD	Yes	CHIP + CH-VUS		***PPM1D***, *SUZ12*	Stable
3	Yes	HTN, HLD	Yes	CHIP + PG-VUS	*CUX1*	***TET2, TP53, PPM1D****	Worse, Better (Overall Stable)
4	Yes	HTN	Yes	CHIP + PG-VUS	*GATA2*	***TP53****	Better
5	Yes	T2D, HTN, HLD	Yes	CH-VUS + PG-VUS	*KMT2A*	*CUX1****, ***JAK2*****	Worse; Better (Overall Better)
6	No	HTN	Yes	CHIP		***DNMT3A***	Stable
7	No	None	No	CHIP + CH-VUS + PG-CS	*TET2*	***PPM1D***, *DNMT3A, RAD21*	Stable
8	No	HTN, HLD	Lifestyle Modification	CHIP and CH+VUS		***GNAS***, *ZRSR2*	Stable

CHIP and Preventive Cardiology. Genes in bold, CHIP mutations. HTN, hypertension, HLD, hyperlipidemia, T2D, type 2 diabetes. **PPM1D* appeared in year 2 and disappeared in year 3. ***TP53* appeared in year 1 and disappeared in years 2 and 3. **** *CUX1* appeared in year 1 and disappeared in years 2 and 3.***** *JAK2* appeared in year 2 and disappeared in year 3

- Most patients had CVD risk factors
- Those with risk factors were on medications (statin, antihypertensives) or lifestyle modifications
- CHIP is dynamic
- Preventive cardiology interventions potentially stabilize or improve CHIP

Kuzmanovic T et al. ASCO 2023;Abstract 7010.

Summary

- CHIP is common in cancer survivors, seen in 16% of patients.
- Most patients had normal CBC. Some had mild stable lymphopenia, anemia. Half of the patients with thrombocytopenia had *PPM1D* CHIP.
- Eighteen percent of PG-VUS identified were also found in hematologic neoplasm literature and patients. These represent rare variants.
- Serial testing shows overall NGS stability; evolution is more common with multiple co-occurring aberrations (CHIP/CH-VUS + PG-VUS).
- Management of CHIP patients with CVD comorbidities using statin, antihypertensives may promote clonal stability.

Kuzmanovic T et al. ASCO 2023;Abstract 7010.

Agenda

INTRODUCTION: Myelofibrosis (MF) for Oncology "Newbies"

MODULE 1: Biology of MF

MODULE 2: Management of Anemia in MF

MODULE 3: Novel Strategies for MF

MODULE 4: Journal Club

Taylor & Francis
Taylor & Francis Group

Journal of Medical Economics

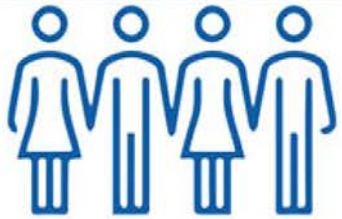
ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/ijme20

Ruxolitinib for myelofibrosis in elderly non-transplant patients: healthcare resource utilization and costs

Aaron T. Gerds, Jingbo Yu, Anne Shah, Ann Xi, Shambhavi Kumar, Robyn Scherber & Shreekant Parasuraman

2023;26(1):843-9.

Cost of Medical Care and Survival with Ruxolitinib



Study population

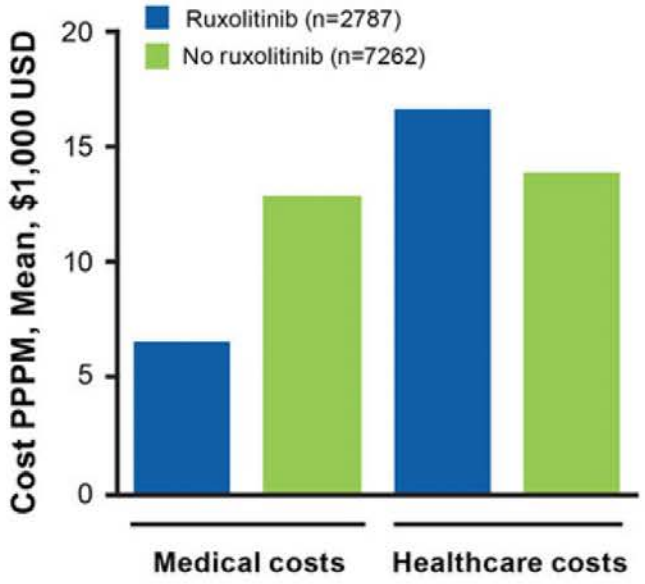
10,049 Medicare beneficiaries with myelofibrosis

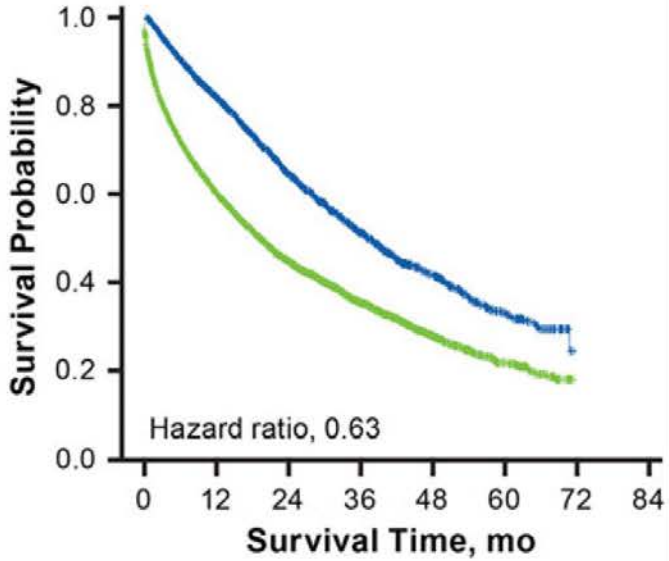
Comparing patients who

Received ruxolitinib
vs
Those who did not

Assessments

- Healthcare resource utilization
- Direct healthcare costs
- Overall survival



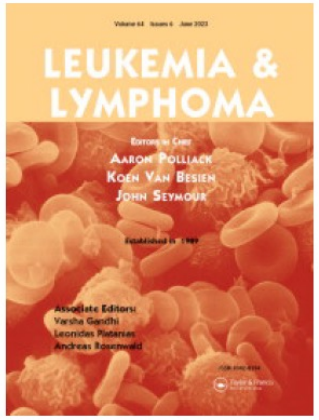


Patients treated with ruxolitinib:

- Visited hospitals, doctors' offices, and other services less often and stayed in the hospital for a shorter time when they visited
- Spent about half as much on these medical services, but more at the pharmacy
- Lived longer, with median OS about doubled

PPPM, price per patient per month; USD, United States Dollar

Gerds AT et al. *J Med Econ* 2023;26(1):843-9.



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Taylor & Francis Group

Leukemia & Lymphoma

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

Ten years after ruxolitinib approval for myelofibrosis: a review of clinical efficacy

Naveen Pemmaraju, Prithviraj Bose, Raajit Rampal, Aaron T. Gerds, Angela Fleischman & Srdan Verstovsek

2023;64(6):1063-81

Risk of Myelodysplastic Syndromes (MDS) in Adolescents and Young Adults with Cancers Treated with Chemotherapy with or without Radiotherapy

Mishra E et al.

ASH 2023;Abstract 2351.

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

Hepatobiliary Cancers

Friday, May 31, 2024

11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)

Faculty

Robin K (Katie) Kelley, MD

Additional faculty to be announced

Antibody-Drug Conjugates in Lung Cancer

Saturday, June 1, 2024

6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty

Rebecca S Heist, MD, MPH

Luis Paz-Ares, MD, PhD

Jacob Sands, MD

Non-Small Cell Lung Cancer with an EGFR Mutation

Friday, May 31, 2024

6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)

Faculty

Jonathan W Goldman, MD

Corey J Langer, MD

Joel W Neal, MD, PhD

Zofia Piotrowska, MD, MHS

Joshua K Sabari, MD

Helena Yu, MD

Prostate Cancer

Saturday, June 1, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Neeraj Agarwal, MD, FASCO

Emmanuel S Antonarakis, MD

Andrew J Armstrong, MD, ScM

Tanya B Dorff, MD

Matthew R Smith, MD, PhD

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

Multiple Myeloma

Sunday, June 2, 2024

6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty

Rafael Fonseca, MD
María-Victoria Mateos, MD, PhD
Elizabeth O'Donnell, MD

LIVE WEBCAST

Colorectal Cancer

Monday, June 3, 2024

7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

Faculty

Scott Kopetz, MD, PhD
John Strickler, MD

Ovarian and Endometrial Cancer

Sunday, June 2, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Floor J Backes, MD
Mansoor Raza Mirza, MD
Ritu Salani, MD, MBA
Angeles Alvarez Secord, MD, MHSc

Metastatic Breast Cancer

Monday, June 3, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Aditya Bardia, MD, MPH
Harold J Burstein, MD, PhD
Professor Giuseppe Curigliano, MD, PhD
Sara A Hurvitz, MD, FACP
Joyce O'Shaughnessy, MD
Hope S Rugo, MD

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

LIVE WEBCAST

Bispecific Antibodies in Lymphoma

Tuesday, June 4, 2024

7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

Faculty

Ian W Flinn, MD, PhD

Tycel Phillips, MD

Additional faculty to be announced

Thank you for joining us!

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

RTP Year in Review 2024