Year in Review: Management of Myelofibrosis

A CME/MOC-Accredited Live Webinar

Wednesday, April 30, 2025
5:00 PM – 6:00 PM ET

Faculty

Professor Claire Harrison
John Mascarenhas, MD

Moderator

Neil Love, MD

RTP Year in Review 2025

Faculty

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

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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

Commercial Support

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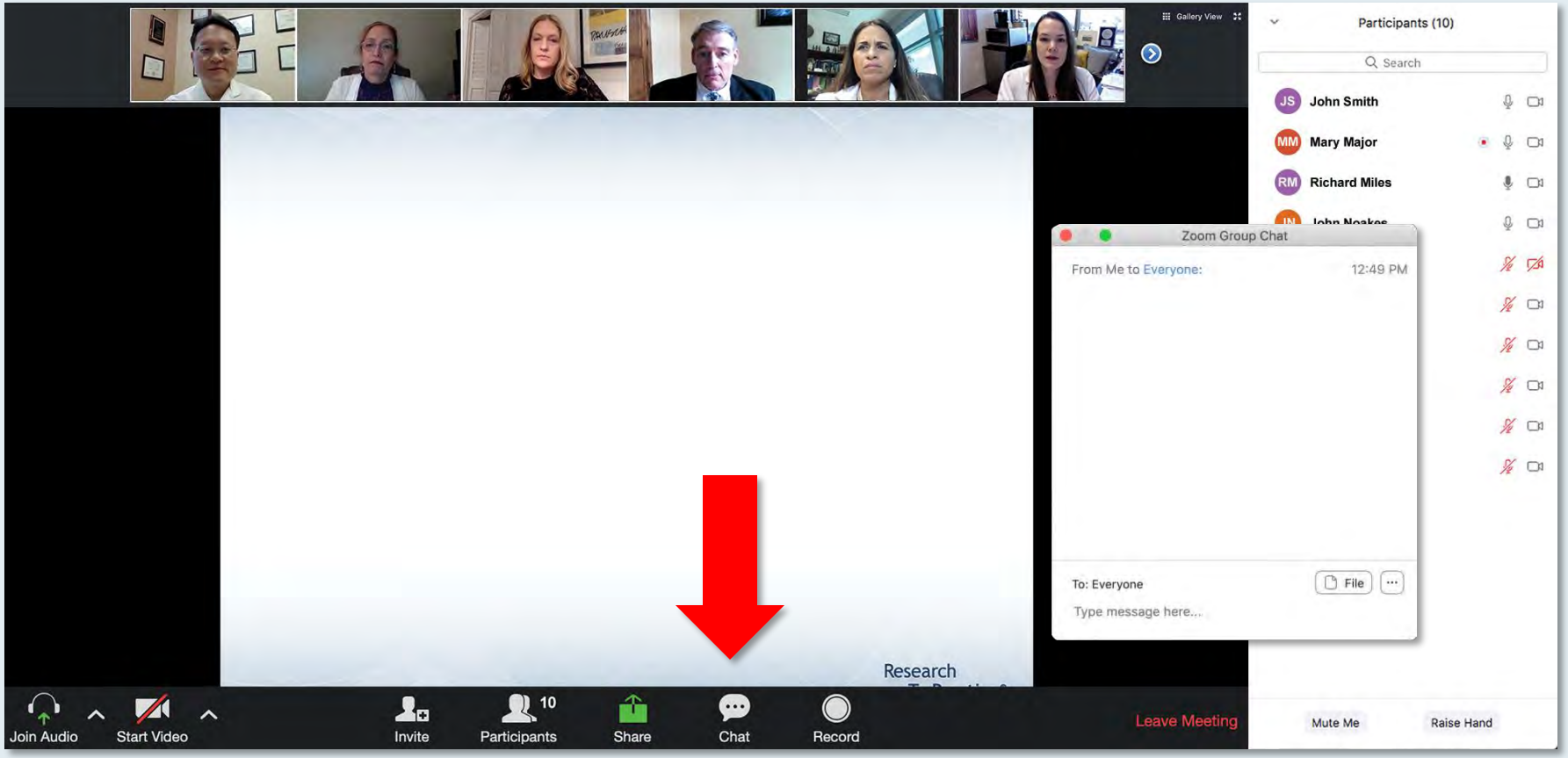

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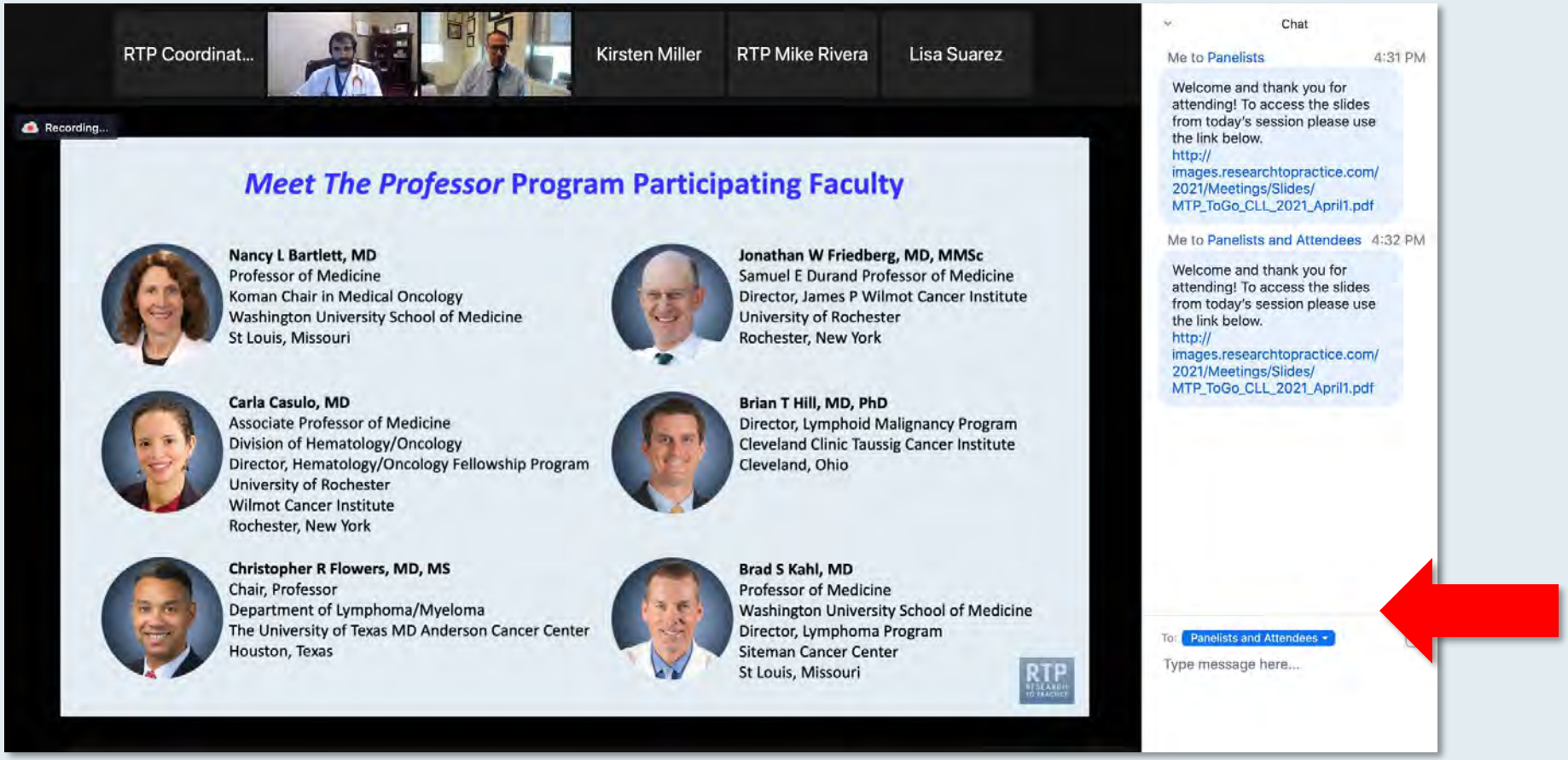

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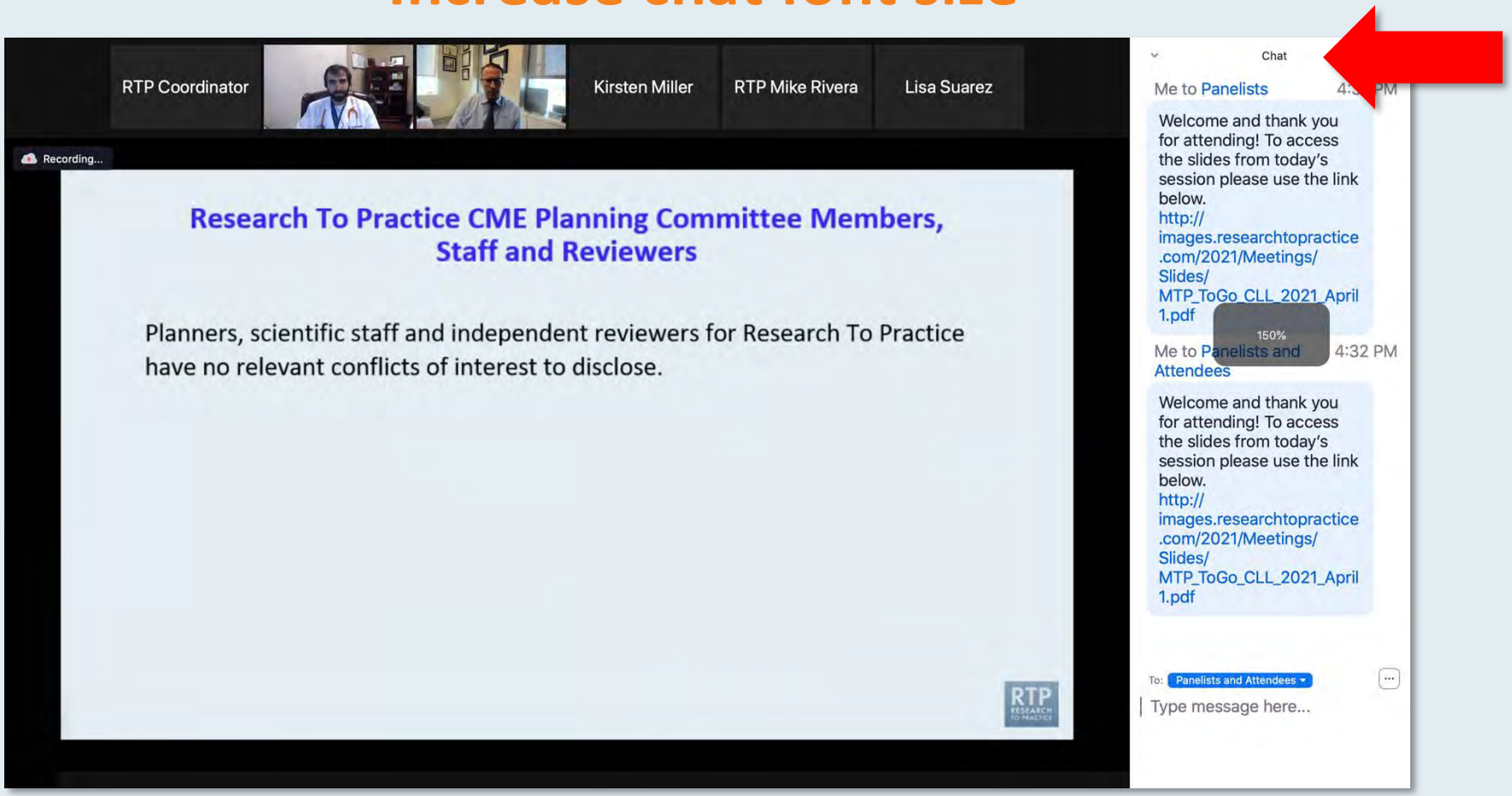

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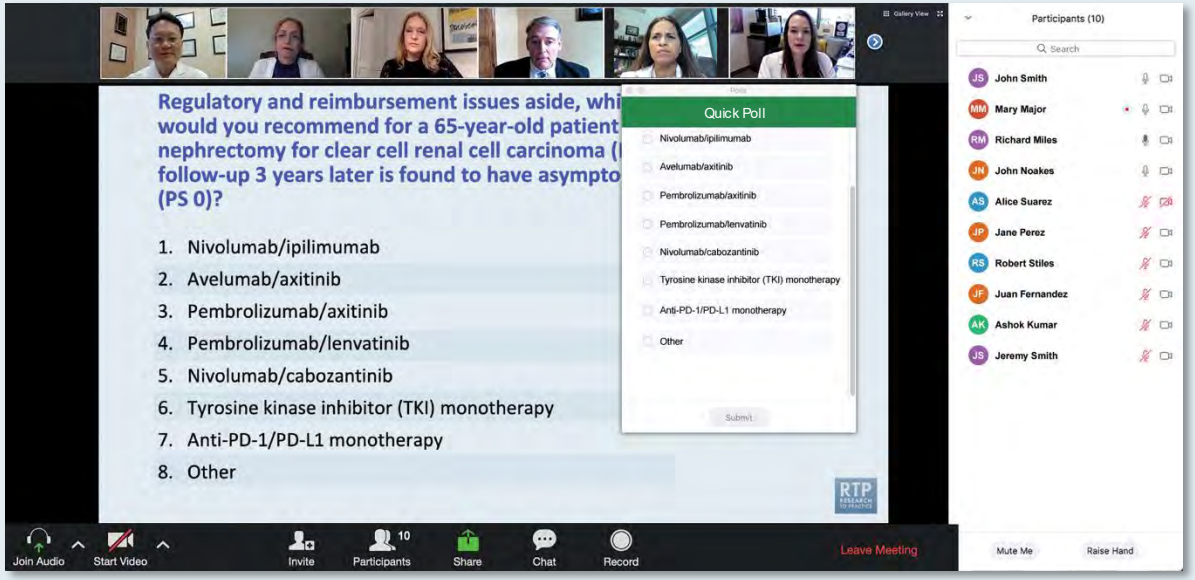

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WITH DR NEIL LOVE

Myelofibrosis — An Interview with Dr Raajit K Rampal on Key Presentations from the 66th American Society of Hematology (ASH) Annual Meeting

DR RAAJIT K RAMPAL

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

Management of Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Thursday, May 8, 2025
5:00 PM – 6:00 PM ET

Faculty

Meletios-Athanasios (Thanos) C Dimopoulos, MD
Robert Z Orlowski, MD, PhD

Moderator

Neil Love, MD

RTP Year in Review 2025

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

Therapeutic Targets Beyond EGFR for Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, May 15, 2025

5:00 PM – 6:00 PM ET

Faculty

Jessica J Lin, MD

Joel W Neal, MD, PhD

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Practical Perspectives: Experts Review Actual Cases of Patients with Advanced Gastroesophageal Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, May 21, 2025
5:00 PM – 6:00 PM ET

Faculty

Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

AGENDA

Year in Review: Management of Myelofibrosis

INTRODUCTION:

- The New Trastuzumab?
- Off-the-Shelf Allo T-Reg Cell Infusions?

MODULE 1: Myelofibrosis 2025 — JAK Inhibitors (Ruxolitinib)

MODULE 2: BET Inhibitors — Pelabresib

MODULE 3: Navtemadlin

MODULE 4: Selinexor and Elritercept

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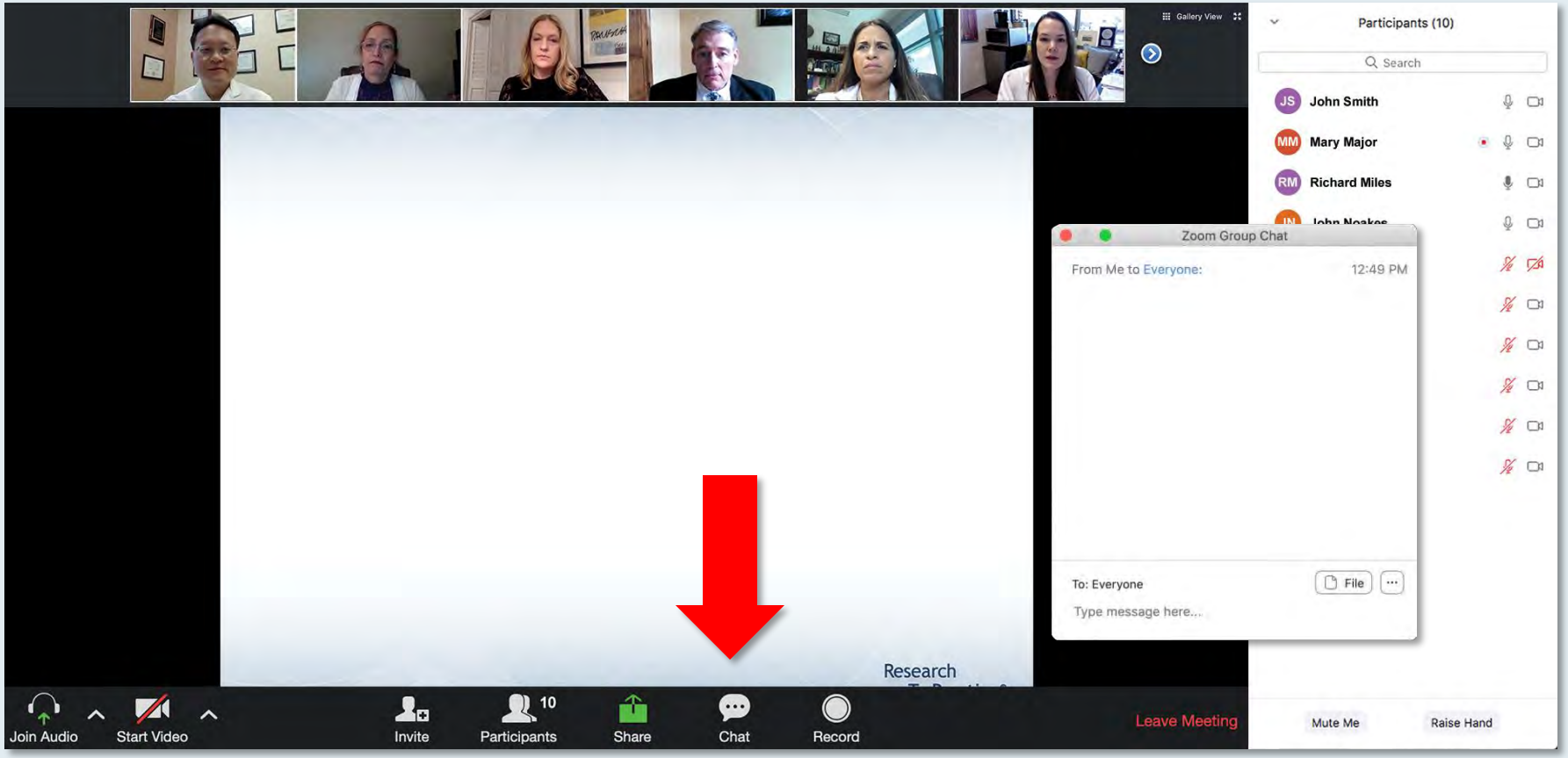

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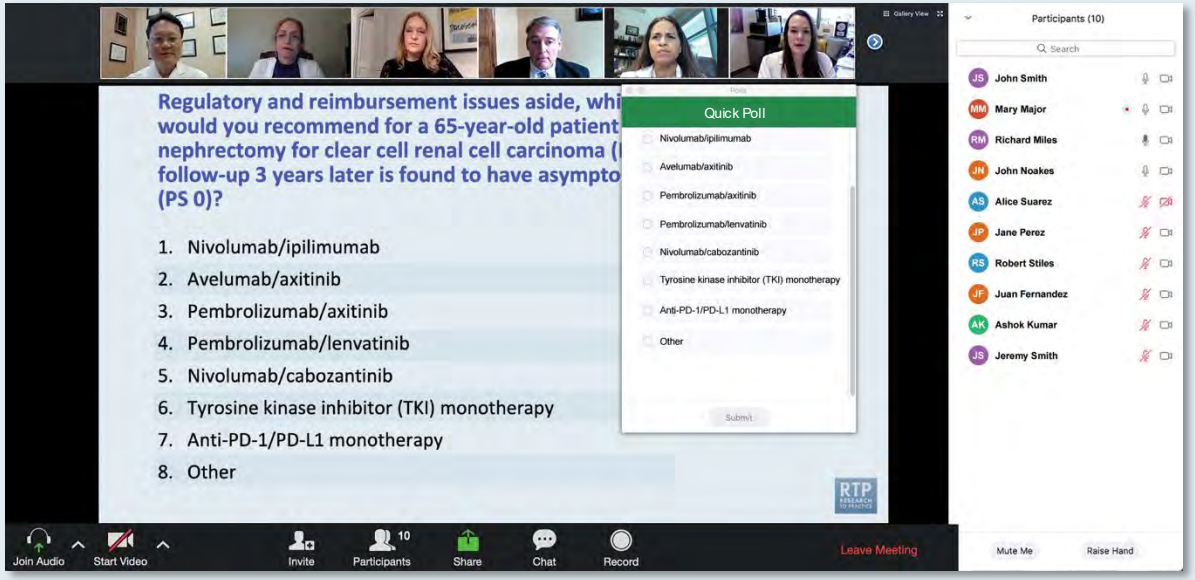

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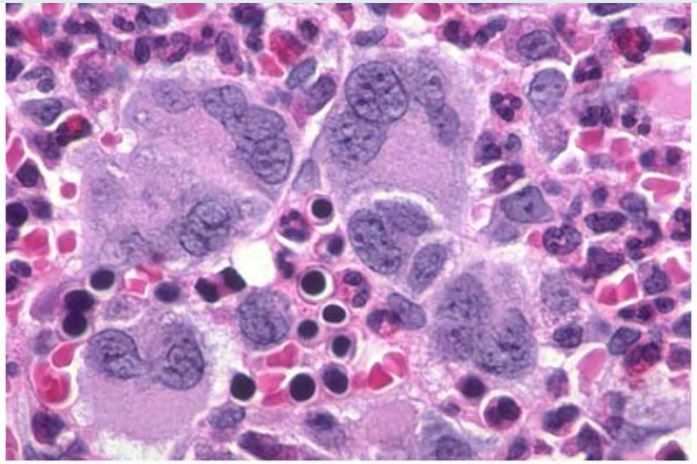
Year in Review

Current Management of Myelofibrosis

Professor Claire Harrison
Deputy Chief Medical Officer — Research, Data and Analytics
Professor of Myeloproliferative Neoplasms
Guy's and St Thomas' NHS Foundation Trust
London, United Kingdom



Year in Review Live Webinar | Myelofibrosis Edition

John Mascarenhas, MD
Professor of Medicine
Icahn School of Medicine at Mount Sinai
New York, NY

Icahn School of Medicine at Mount Sinai

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Key Datasets

Professor Claire Harrison

- Palandri F et al. Clinical outcomes of **ruxolitinib treatment in 595 intermediate-1 risk patients** with myelofibrosis: The **RUX-MF Real-World Study**. *Cancer* 2024;130(24):4257-66.
- Breccia M et al. Dosing and clinical outcomes of **ruxolitinib in patients with myelofibrosis in a real-world setting**: Interim results of the **Italian observational study (ROMEI)**. *Cancer* 2025;131(7):e35801.
- Vachhani P et al. Clinical outcomes in patients with myelofibrosis treated with **ruxolitinib and anemia-supporting medications**. ASH 2024;Abstract 4546.
- Gupta V et al. Safety and efficacy **of fedratinib in patients with myelofibrosis previously treated with ruxolitinib**: Primary analysis of **FREEDOM trial**. *Leuk Lymphoma* 2024;65(9):1314-24.
- Harrison CN et al. Efficacy and safety of **fedratinib in patients with myelofibrosis previously treated with ruxolitinib (FREEDOM2):** Results from a multicentre, open-label, randomised, controlled, phase 3 trial. *Lancet Haematol* 2024;11(10).
- Koschmieder S et al. Myelofibrosis management in routine clinical practice with a focus on patients with cytopenias: **Recommendations from a global consensus group**. *Leukemia* 2024;38(8):1831-8.

Key Datasets

Professor Claire Harrison (continued)

- Gagelmann N et al. Consistency of spleen and symptom reduction regardless of cytopenia in patients with **myelofibrosis treated with pacritinib**. *Clin Lymphoma Myeloma Leuk* 2024;24(11):796-803.
- 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.
- Gupta V et al. **Momelotinib vs ruxolitinib** in myelofibrosis patient subgroups by baseline hemoglobin levels in the **SIMPLIFY-1 trial**. *Leuk Lymphoma* 2024;65(7):965-77.
- Harrison CN et al. **Momelotinib versus continued ruxolitinib or best available therapy** in JAK inhibitor-experienced patients with myelofibrosis and anemia: Subgroup analysis of **SIMPLIFY-2**. *Adv Ther* 2024;41(9):3722-35.
- Harrison CN et al. Longitudinal assessment of **transfusion intensity** in patients with JAK inhibitor-naive or -experienced myelofibrosis treated with **momelotinib**. *Clin Lymphoma Myeloma Leuk* 2025;25(3):199-211.

Key Datasets

John Mascarenhas, MD

- Mascarenhas J et al. Updated results from the **phase 3 Manifest-2 study of pelabresib in combination with ruxolitinib** for Janus kinase inhibitor–naïve patients with myelofibrosis. ASH 2024;Abstract 3178.
- Watts JM et al. Safety and efficacy of **bromodomain and extra-terminal inhibitor INCB057643** in patients with relapsed or refractory myelofibrosis and other advanced myeloid neoplasms: A phase 1 study. ASH 2024;Abstract 658.
- Duan M et al. The efficacy and safety of **selinexor in combination with ruxolitinib** in ruxolitinib-treated myelofibrosis patients: The interim analysis of a prospective, open-label, multicenter, parallel-cohort, phase 2 study. ASH 2024;Abstract 1002.
- Mascarenhas J et al. **Selinexor plus ruxolitinib** in JAK inhibitor treatment-naive myelofibrosis: **SENTRY phase 3 study design**. *Future Oncol* 2025;21(7):807-13.
- Mascarenhas J et al. Trial update from **IMproveMF**, an ongoing, open-label, dose-escalation and -expansion, phase 1/1B trial to evaluate the safety, pharmacokinetics, and clinical activity of the novel combination of **imetelstat with ruxolitinib** in patients with intermediate-1, intermediate-2, or high-risk myelofibrosis (MF). ASH 2024;Abstract 998.

Key Datasets

John Mascarenhas, MD (continued)

- Mascarenhas J et al. **Imetelstat versus best available therapy** in patients with intermediate-2 or high-risk myelofibrosis relapsed or refractory to Janus kinase inhibitor in **IMpactMF, a randomized, open-label, phase 3 trial.** ASH 2024;Abstract 1808.1.
- Mascarenhas J et al. Results from the randomized, multicenter, global **phase 3 BOREAS study**: **Navtemadlin versus best available therapy** in JAK inhibitor relapsed/refractory myelofibrosis. ASH 2024;Abstract 1000.
- Mascarenhas J et al. **Disease-modifying activity of navtemadlin** correlates with clinical responses in a randomized, multicenter, global **phase 3 study (BOREAS)** in JAK-inhibitor relapsed/refractory myelofibrosis. ASH 2024;Abstract 483.
- Vachhani P et al. **POIESIS**: A randomized, double-blind, placebo-controlled, multicenter, global **phase 3 study of navtemadlin as add-on to ruxolitinib** in JAK inhibitor-naïve patients with myelofibrosis who have a suboptimal response to ruxolitinib. ASH 2024;Abstract 1808.2.
- Harrison C et al. Hematological improvement and other clinical benefits of **elritercept as monotherapy and in combination with ruxolitinib** in participants with myelofibrosis from the ongoing **phase 2 Restore trial**. ASH 2024;Abstract 997.
- Masarova L et al. A phase Ib, open-label study of **add on therapy with CK0804** in participants with myelofibrosis and suboptimal response to ruxolitinib. ASH 2024;Abstract 999.

AGENDA

Year in Review: Management of Myelofibrosis

INTRODUCTION:

- The New Trastuzumab?
- Off-the-Shelf Allo T-Reg Cell Infusions?

MODULE 1: Myelofibrosis 2025 — JAK Inhibitors (Ruxolitinib)

MODULE 2: BET Inhibitors — Pelabresib

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MODULE 4: Selinexor and Elritercept

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New Biology of Myelofibrosis

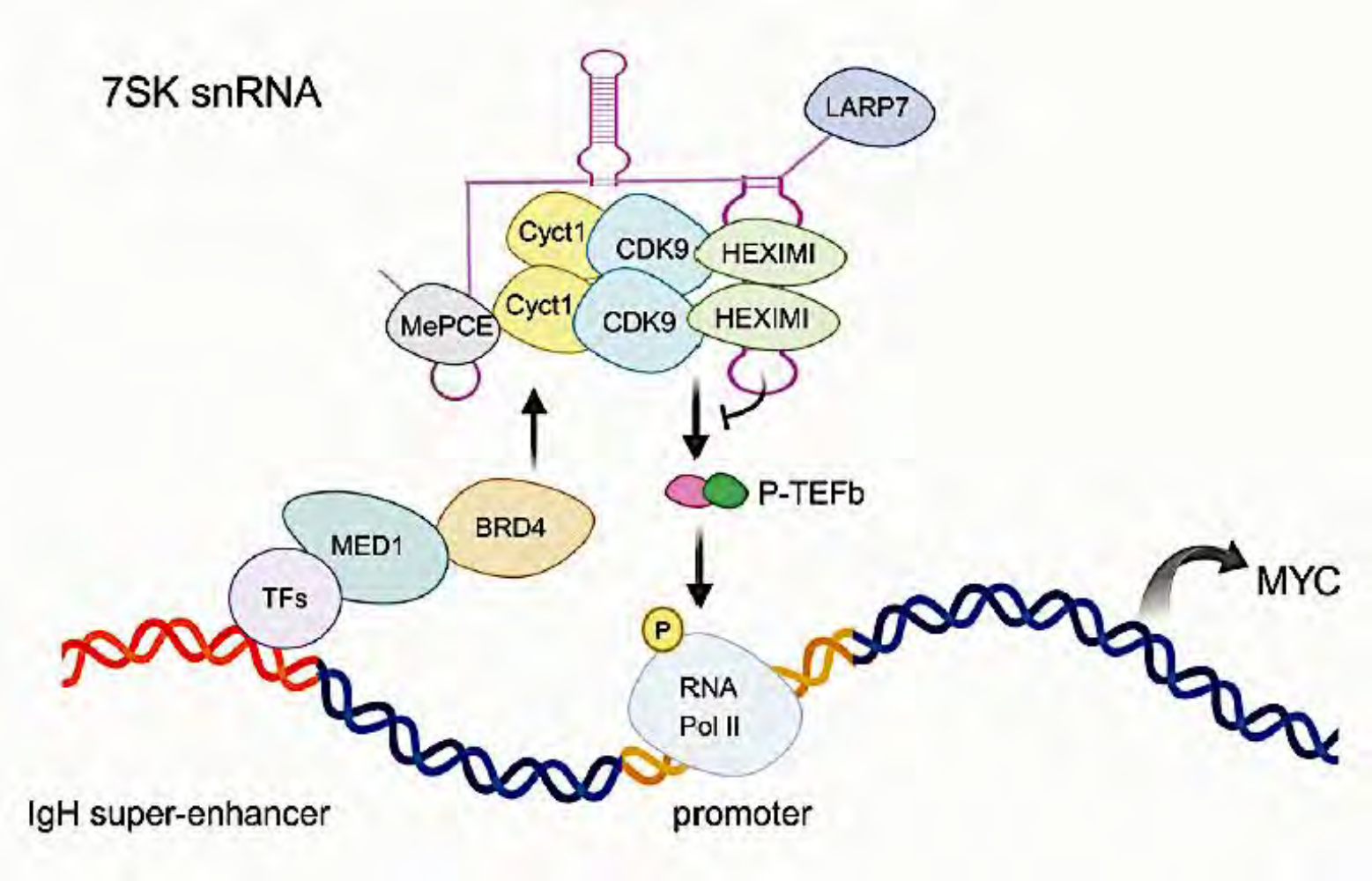
REVIEW ARTICLE OPEN

Bromodomain and extraterminal (BET) proteins: biological functions, diseases and targeted therapy

Zhi-Qiang Wang[1], Zhao-Cong Zhang[1], Yu-Yang Wu[2], Ya-Nan Pi[1], Sheng-Han Lou[3], Tian-Bo Liu[1], Ge Lou[1]✉ and Chang Yang[1]✉

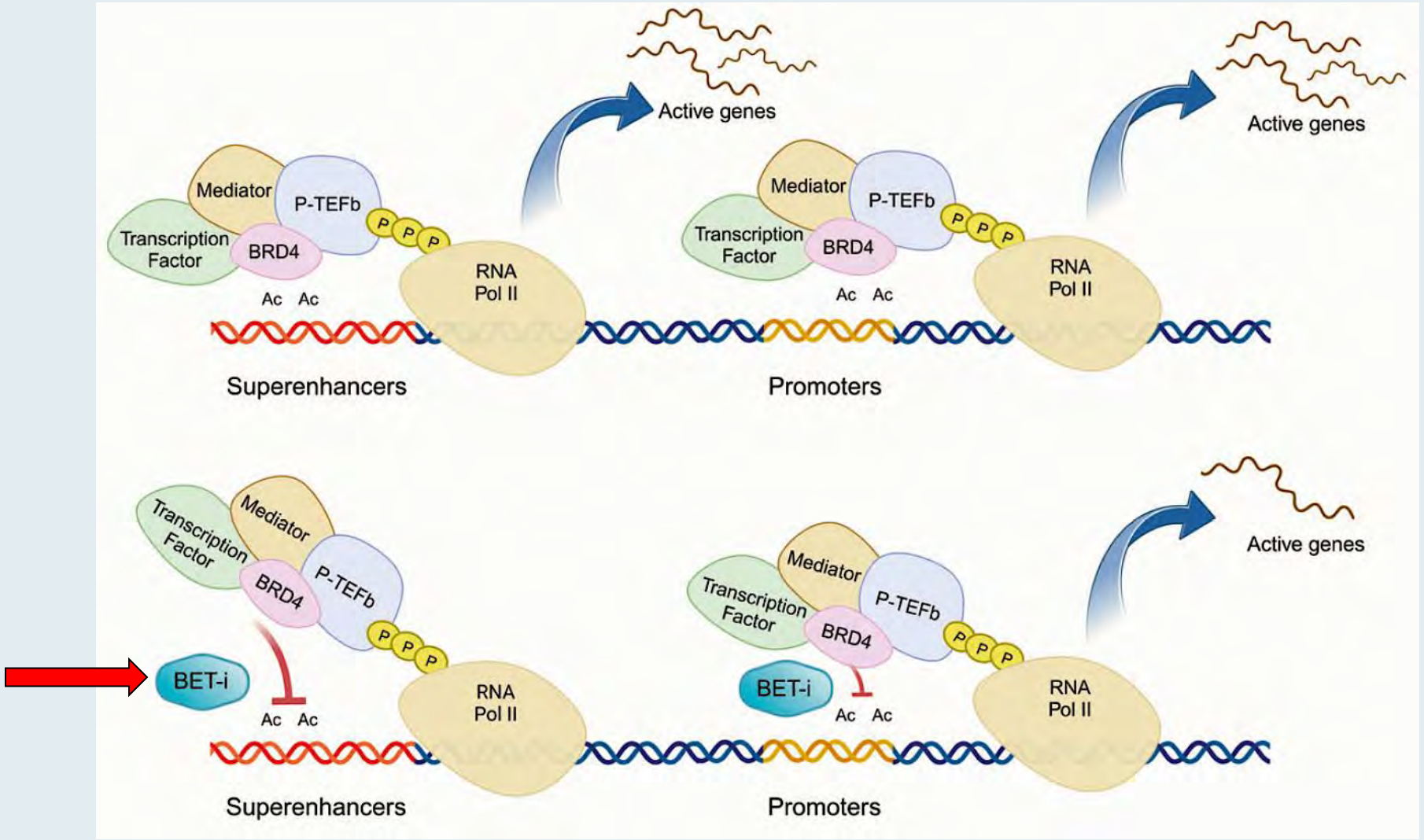
Signal Transduct Target Ther 2023;8(1):420.

Mechanism by Which BRD4 Promotes Transcriptional Elongation



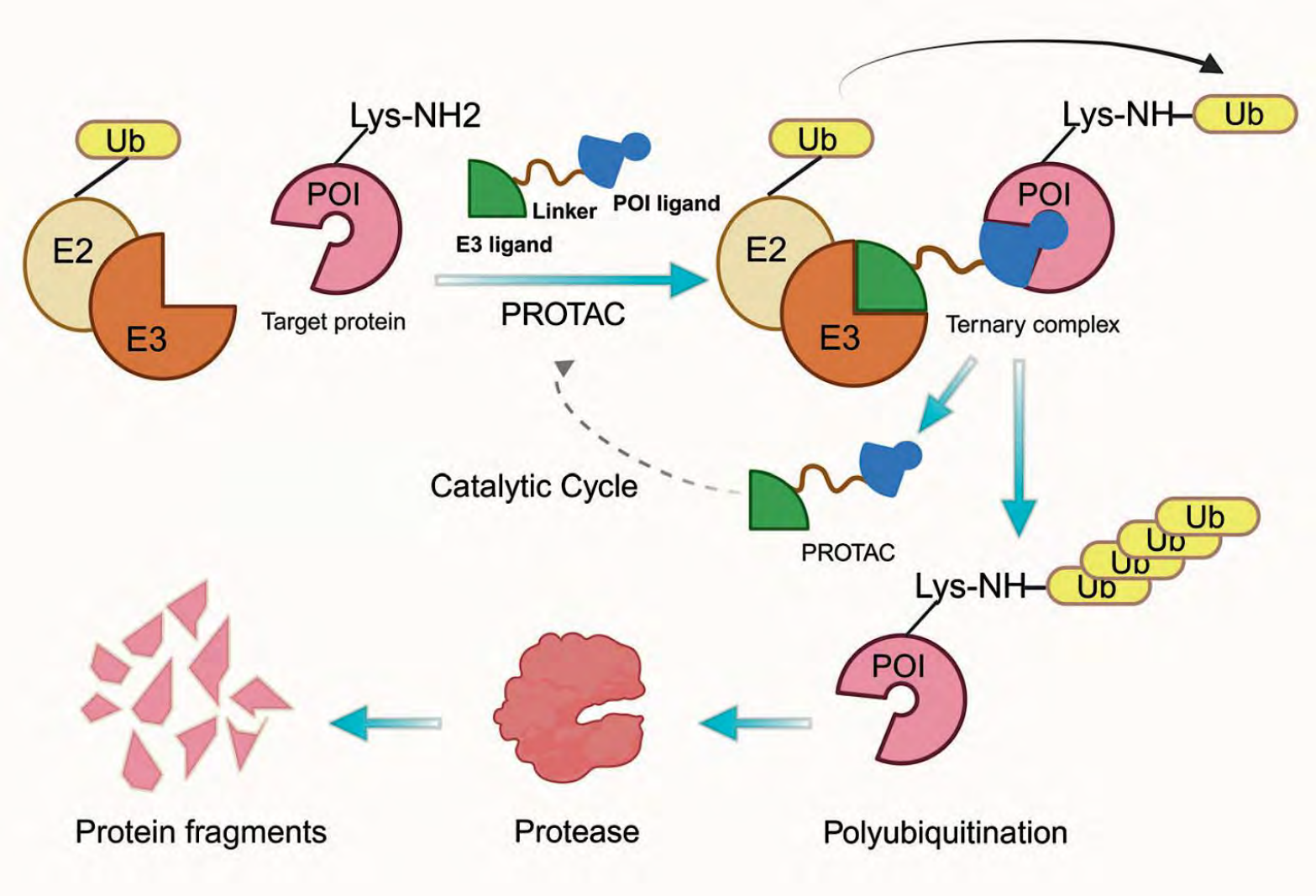
Wang Z-Q et al. *Signal Transduct Target Ther* 2023;8(1):420.

Mechanism of Action of BET Inhibitors



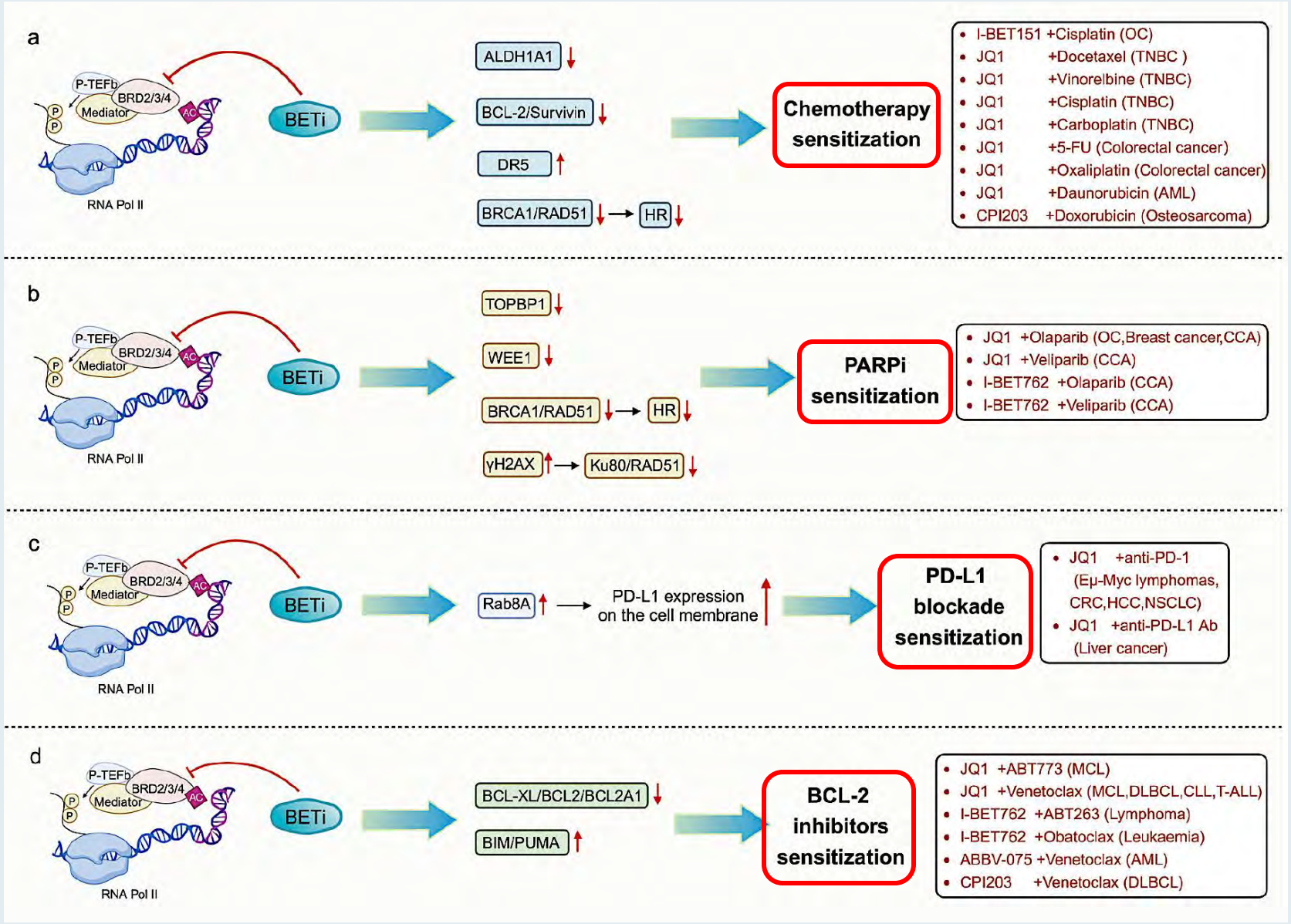
Wang Z-Q et al. *Signal Transduct Target Ther* 2023;8(1):420.

Mechanism of Proteolysis Targeting Chimera (PROTAC)



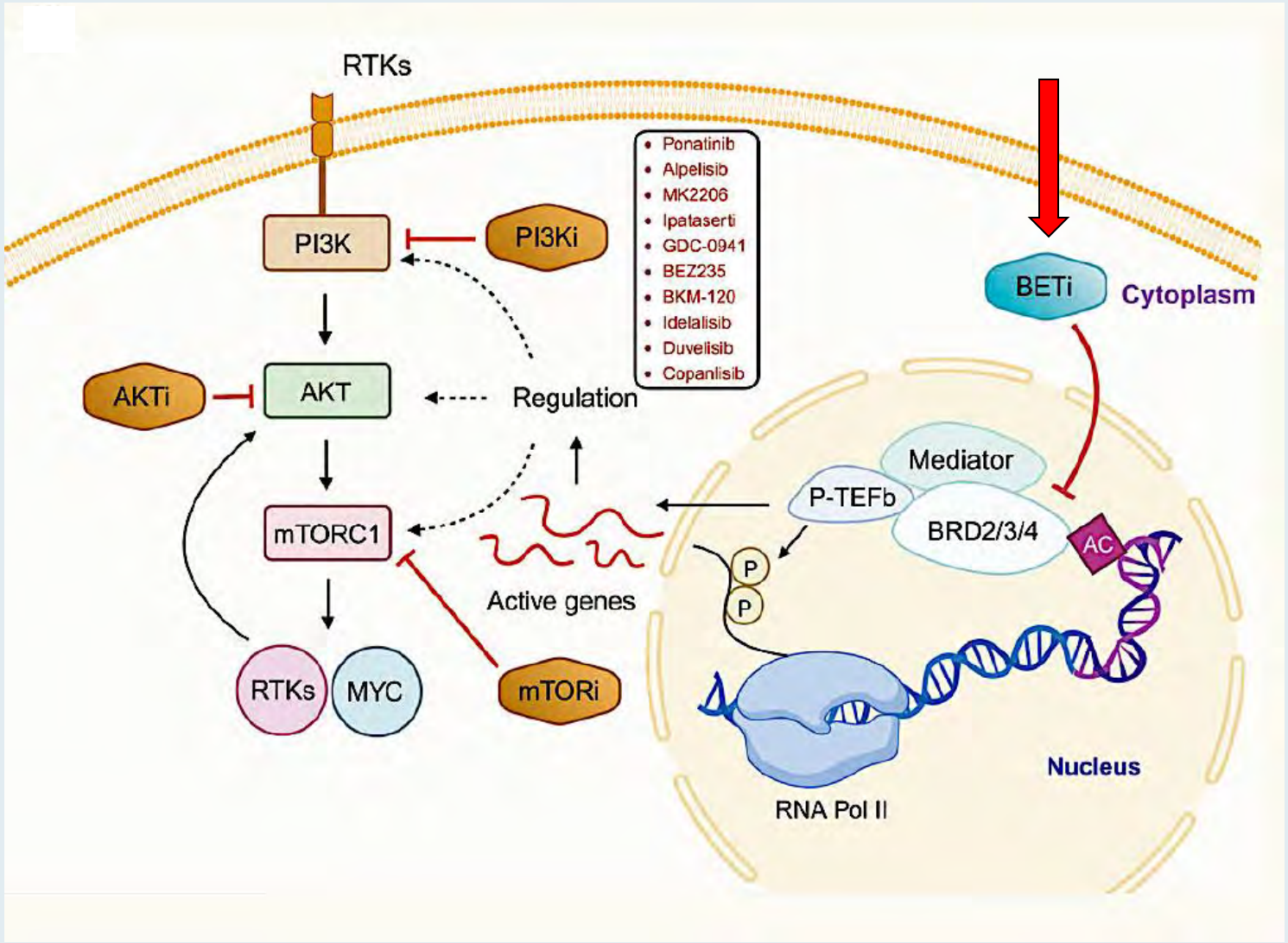
Wang Z-Q et al. *Signal Transduct Target Ther* 2023;8(1):420.

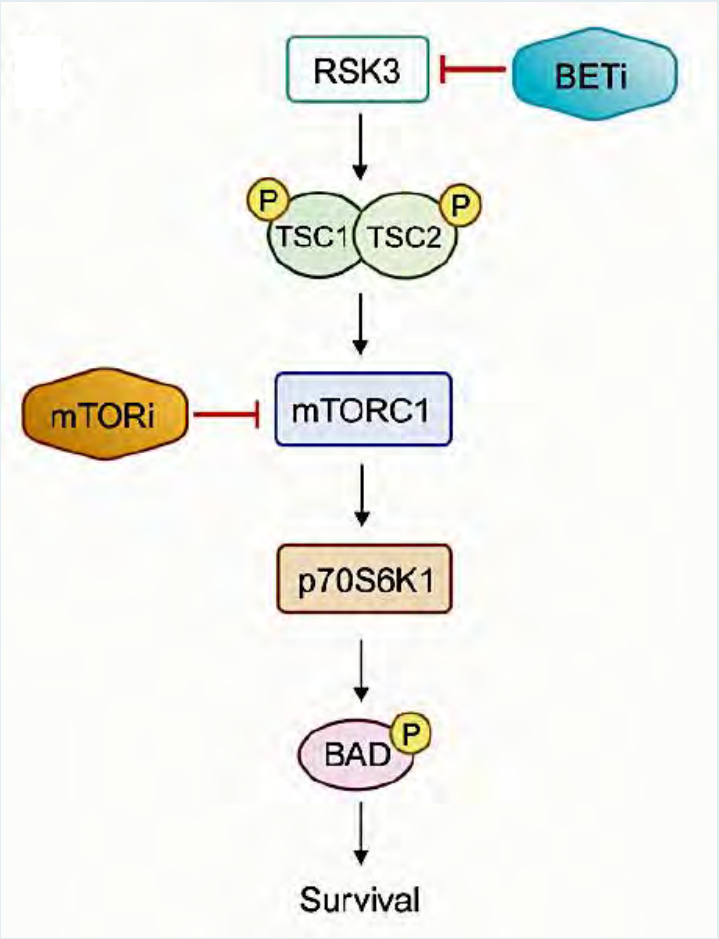
BET Inhibitors May Synergize with a Variety of Antitumor Agents



Wang Z-Q et al. *Signal Transduct Target Ther* 2023;8(1):420.

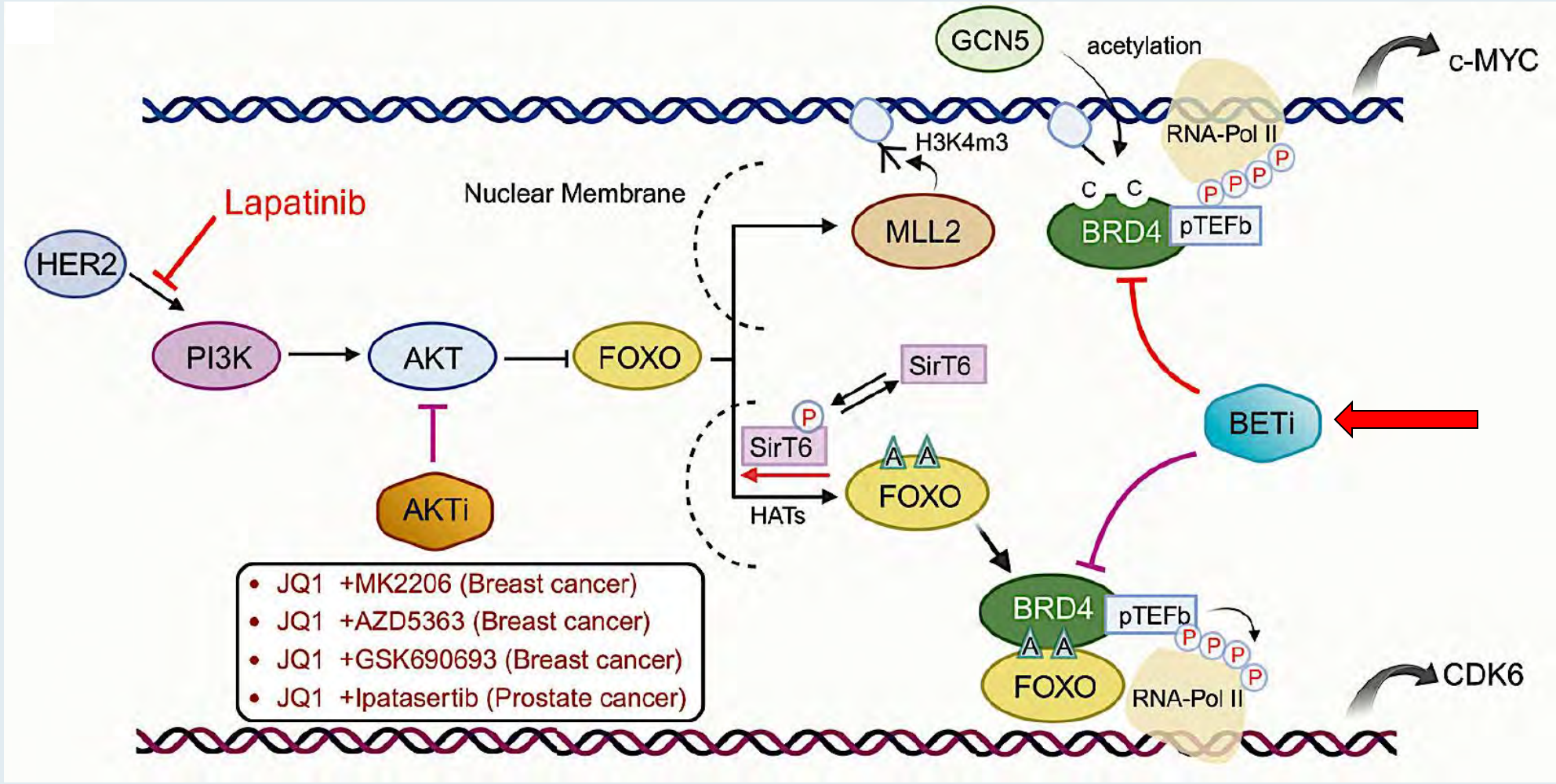
BET Inhibitors' Synergism with PI3K and mTOR Inhibitors





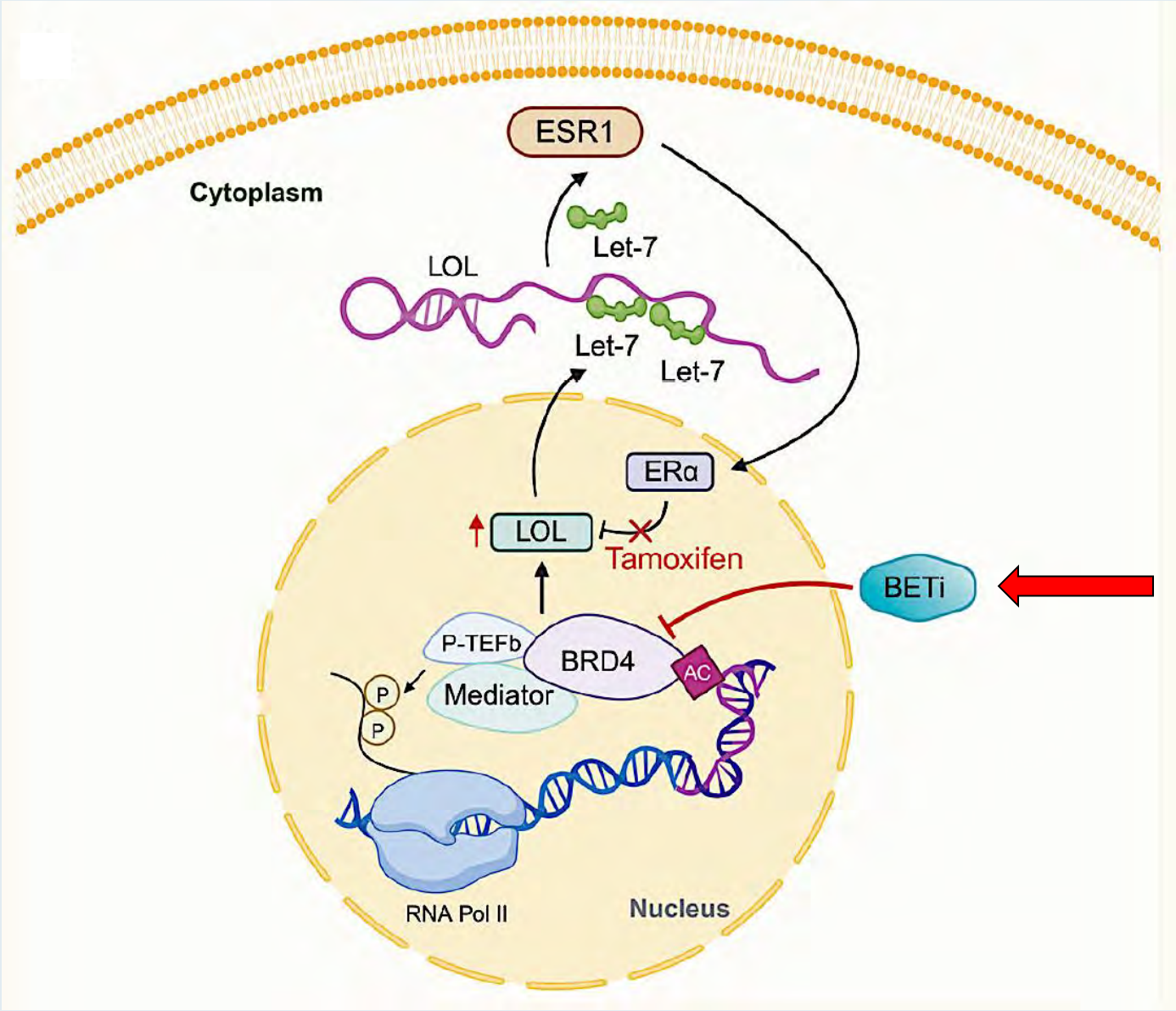
Wang Z-Q et al. *Signal Transduct Target Ther* 2023;8(1):420.

BET Inhibitors' Synergism with Lapatinib and AKT Inhibitors



Wang Z-Q et al. *Signal Transduct Target Ther* 2023;8(1):420.

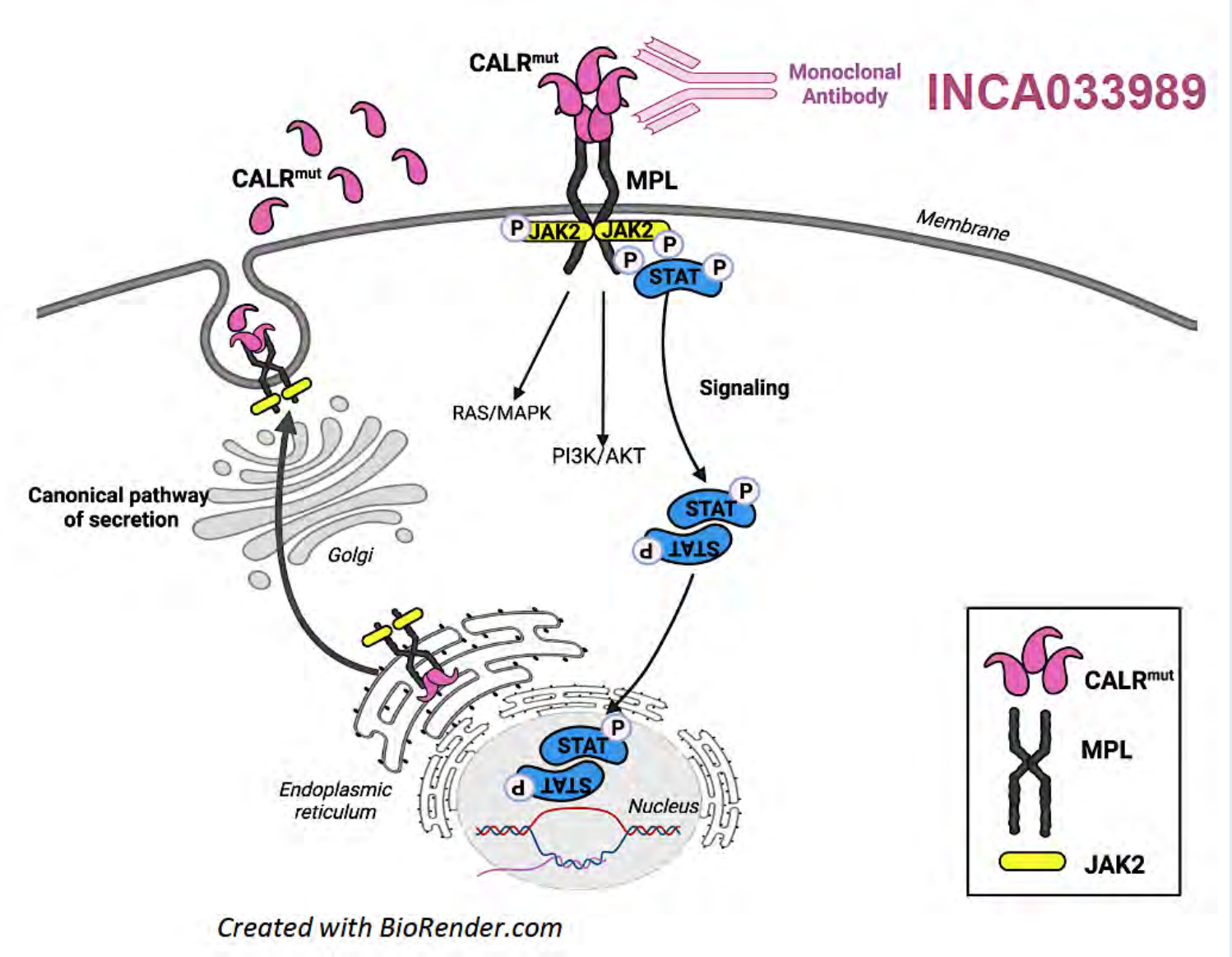
BET Inhibition Resensitizes ER-Positive Breast Cancer Cells to Tamoxifen



Wang Z-Q et al. *Signal Transduct Target Ther* 2023;8(1):420.

Novel Antibody Targeting Calreticulin

INCA033989: Mechanism of Action



Marty C et al. EHA 2024;Abstract P1002.

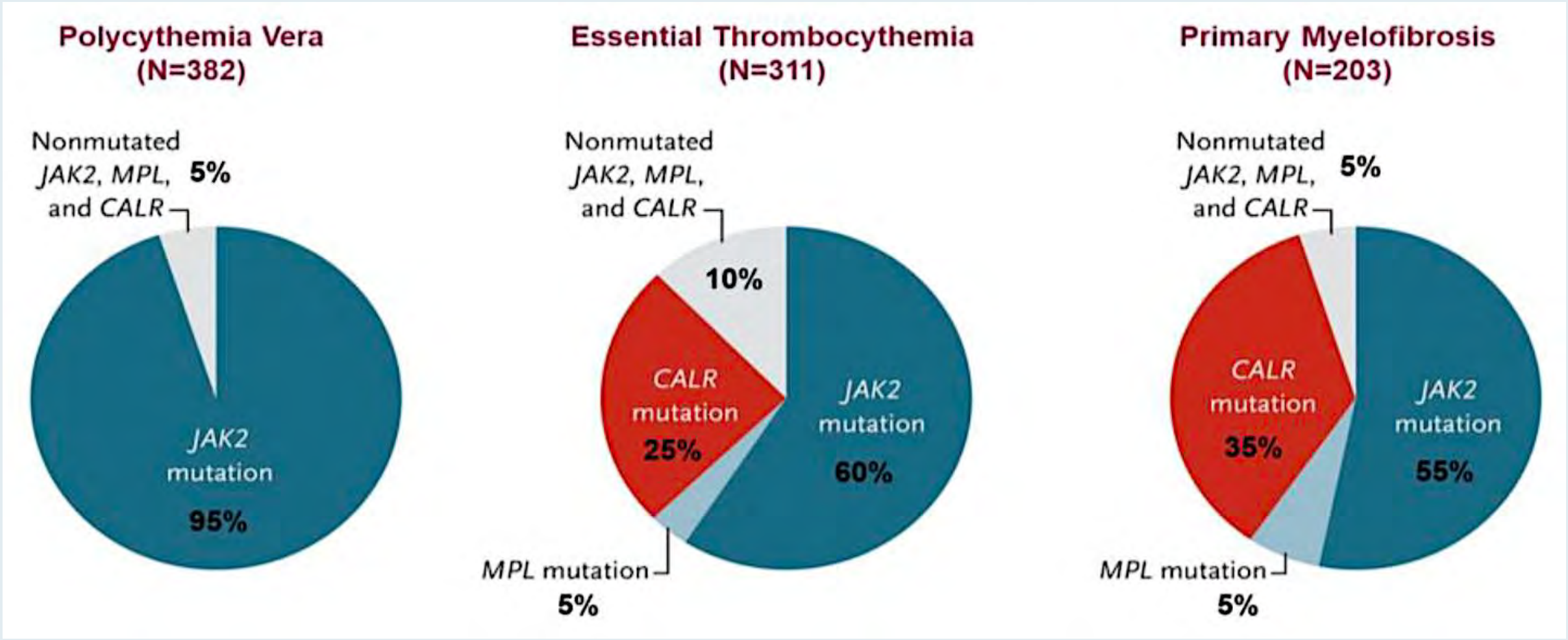
MYELOID NEOPLASIA

Selective targeting of mutated calreticulin by the monoclonal antibody INCA033989 inhibits oncogenic function of MPN

Edimara S. Reis,[1] Rebecca Buonpane,[1] Hamza Celik,[1] Caroline Marty,[2-4] Angela Lei,[1] Fatoumata Jobe,[1] Mark Rupar,[1] Yue Zhang,[1] Darlise DiMatteo,[1] Rahel Awdew,[1] Bianca L. Ferreira,[5] Lynn Leffet,[1] Lu Lu,[1] Elodie Rosa,[2-4] Maxime Evrard,[2-4] Gaurang Trivedi,[1] Brittney Wass,[1] April Horsey,[1] Xin He,[1] Maryanne Covington,[1] Alla Volgina,[1] Florence Pasquier,[2-4,6] Laurence Legros,[7] Guillemette Fouquet,[8] William Vainchenker,[2-4] Yan-ou Yang,[1] Breann Barker,[1] Jing Zhou,[1] Shaun Stewart,[1] Ian S. Hitchcock,[5] Dashyant Dhanak,[1] Ricardo Macarron,[1] Isabelle Plo,[2-4] Horacio Nastri,[1] and Patrick A. Mayes[1]

Blood 2024;144(22):2336-48.

Driver Mutations in Myeloproliferative Neoplasms



Stubbs MC et al. ASH 2023;Abstract 860.

Novel Regulatory T-Cell Infusion Therapy

ASH | Annual Meeting & Exposition

Abstract # 999

A Phase Ib, Open-label Study of Add-On Therapy with CK0804 in Participants with Myelofibrosis and Suboptimal Response to Ruxolitinib

Lucia Masarova, MD, *Meixian Huang, Swati Goel, MD, Sharon Bledsoe, Naveen Pemmaraju, MD, Tapan M. Kadia, MD, Prithviraj Bose, MD, Jo Ishizawa, MD, Phd, Guillermo Montalban-bravo, MD, Mi-ae Lyu, Tara Sadeghi, Simrit Parmar, MBBS, Christopher R. Flowers, MD, MS and Hagop M. Kantarjian, MD*

Phase 1b Study of CK0804: CXCR4 Enriched, Non-HLA matched, Cryopreserved, Multi-Dose, Treg Therapy in MF Patients with Suboptimal Response to Ruxolitinib

Eligible patients

Age > 18 years with PMF/ PPV-MF or PET-MF by IWG MRT criteria.

On ruxolitinib for at least 3 months and stable dose for 8 weeks and presence of:

- disease-related symptoms, as determined by a MPN SAF TSS score of ≥10 points

OR

- splenomegaly of ≥5 cm below the costal margin by physical examination or by ultrasound or MRI.

OR

- new grade ≥2 anemia or thrombocytopenia or neutropenia

- **Primary Objective**: Safety of the add-on CK0804 to ruxolitinib
- **Secondary Objective**: Efficacy of the add-on CK0804 to ruxolitinib
- **Exploratory Objective**: PB and BM immune reconstitution; longitudinal serum biomarker and plasma inflammatory cytokines analysis

Safety Run-In

Every 28 days x 6 infusions of 100 million Tregs per dose;
N=9

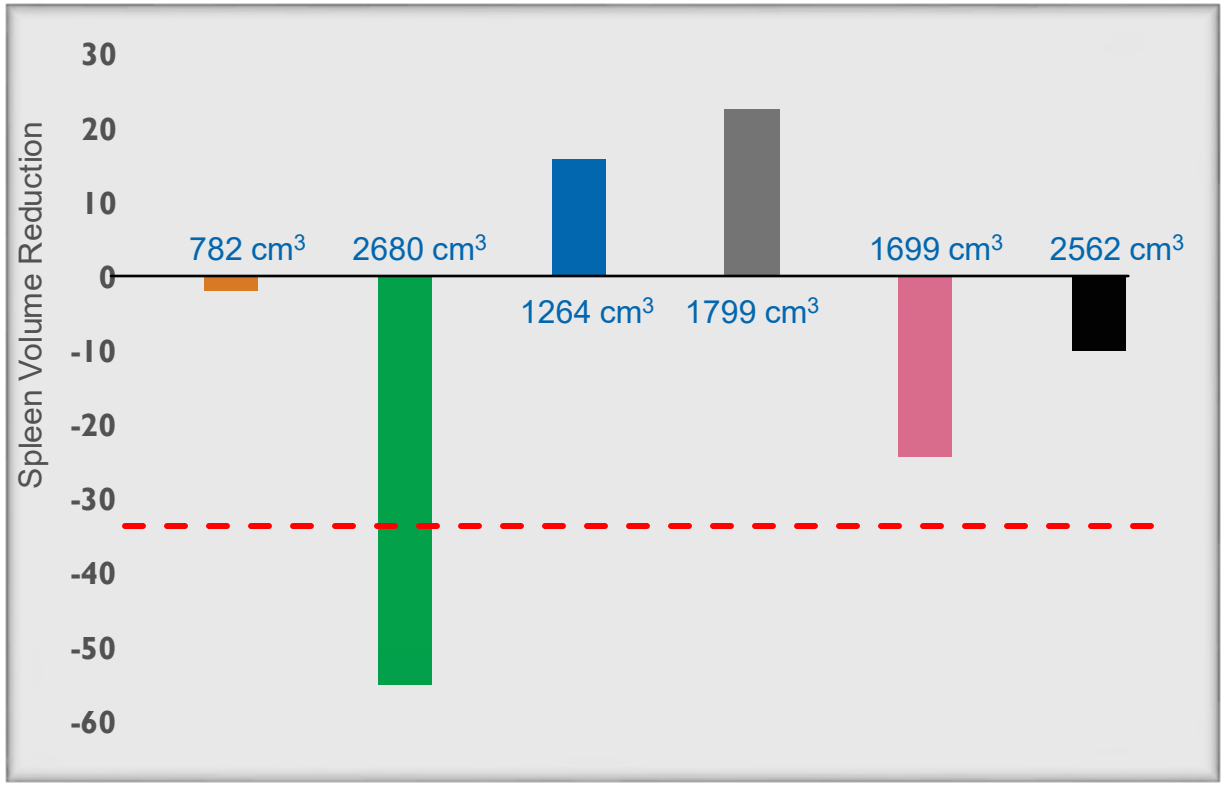
Expansion Cohort 1

Every 7 days x 4 infusions; then
Every 28 days x 5 infusions
N=6

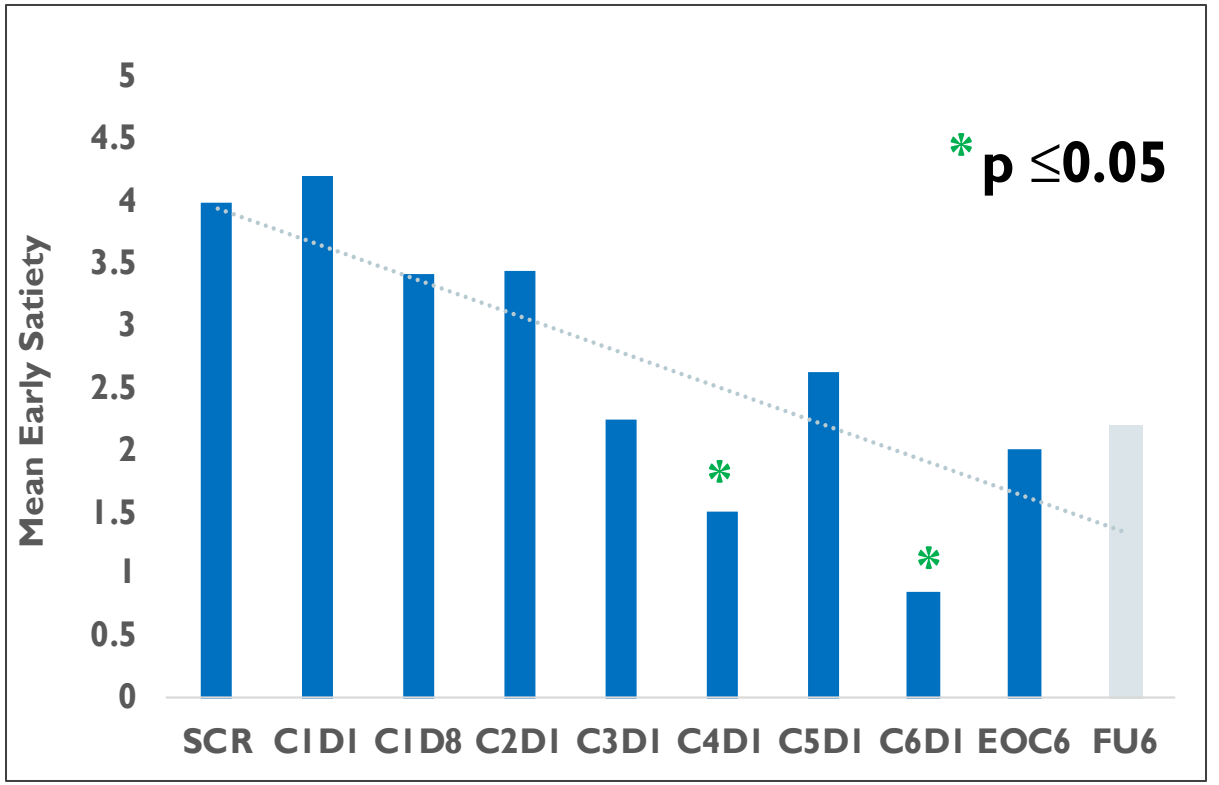
Courtesy of John Mascarenhas, MD

Masarova et al. ASH 2024;Abstract 999

Spleen Volume Change (Best); n=6



MPN SAF TSS: Early Satiety; n=6



Maximum SVR = EOC6 in all pt

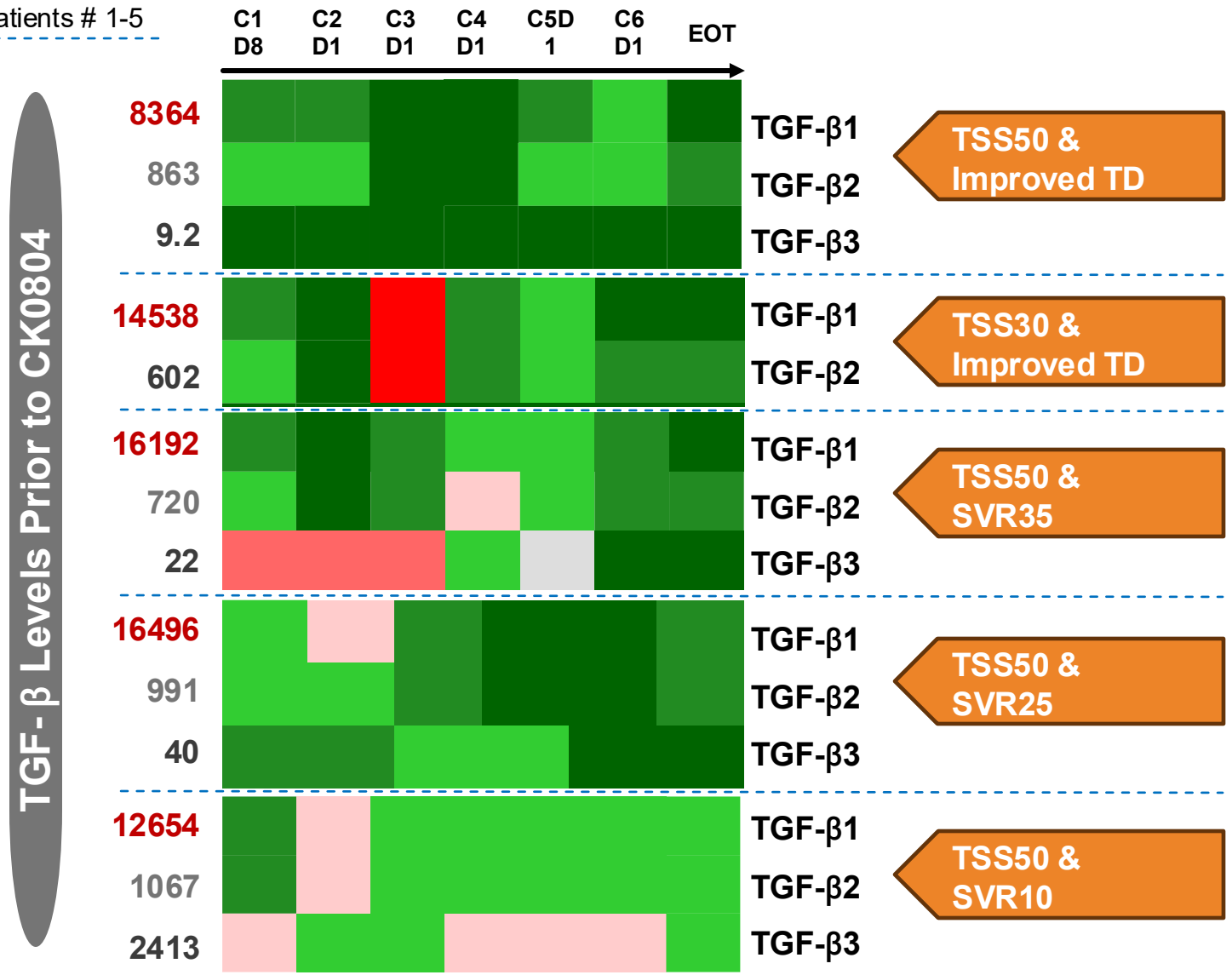
The Early Satiety subset score

	Mean	95% CI Lower	95% CI Upper
Baseline	4.0	2.0	5.5
C4D1	1.8	0	4.0
EOC6	2.1	0.5	5.0

Masarova et al. ASH 2024;Abstract 999

Courtesy of John Mascarenhas, MD

Reduction of TGF-β Levels Correlates with Clinical Response [n=5]



TGFβ Baseline Levels [9]	Median (range)	Ref.
TGFβ1 (ng/ml)	11629 (5935-25630)	<2
TGFβ2 (ng/ml)	574 (336-1035)	<0.2
TGFβ3 (ng/ml)	382 (9.3-2503)	<0.1

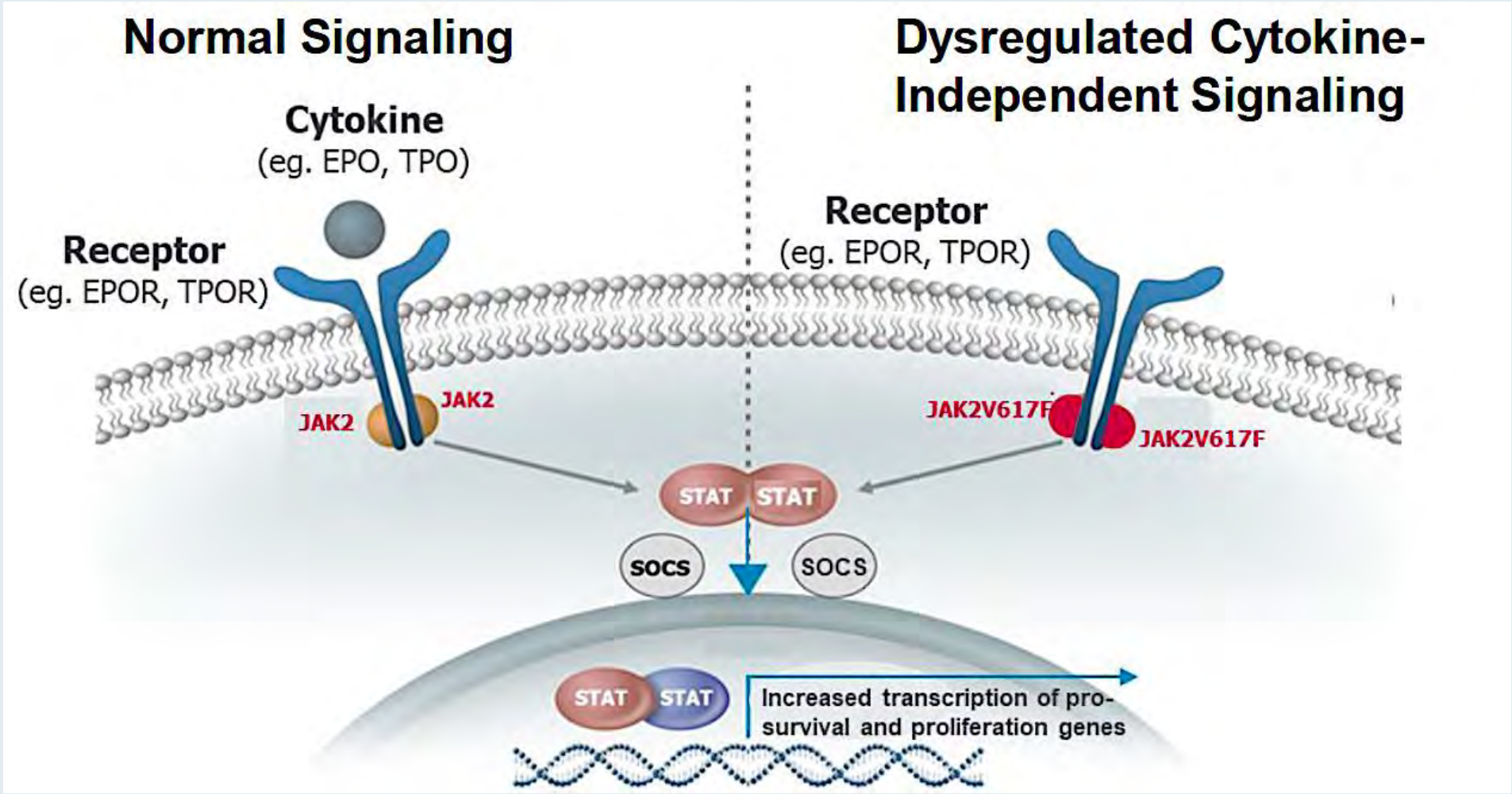
- Increase > 50%
- Increase 25- 50%
- Increase 0 - 25%
- Decrease 0 - 25%
- Decrease 25- 50%
- Decrease > 50%

Courtesy of John Mascarenhas, MD

Masarova et al. ASH 2024;Abstract 999

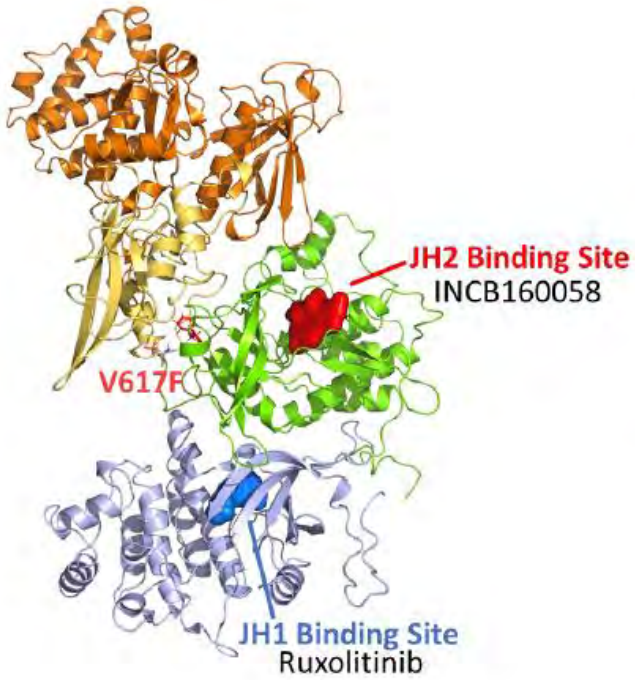
Selective JAK Inhibitors

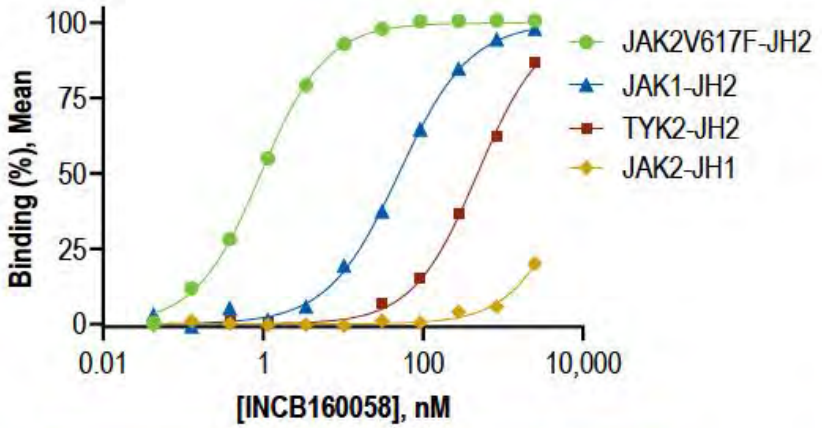
Potential Therapeutic Option: Selective Targeting of JAK2V617F



Stubbs MC et al. ASH 2023;Abstract 860.

INCB160058 Is a Selective Pseudokinase (JH2)-Binding Inhibitor of JAK2V617F





	Selectivity for JAK2V617F-JH2
JAK2-JH1	>2500×
JAK1-JH2	50×
TYK2-JH2	500×

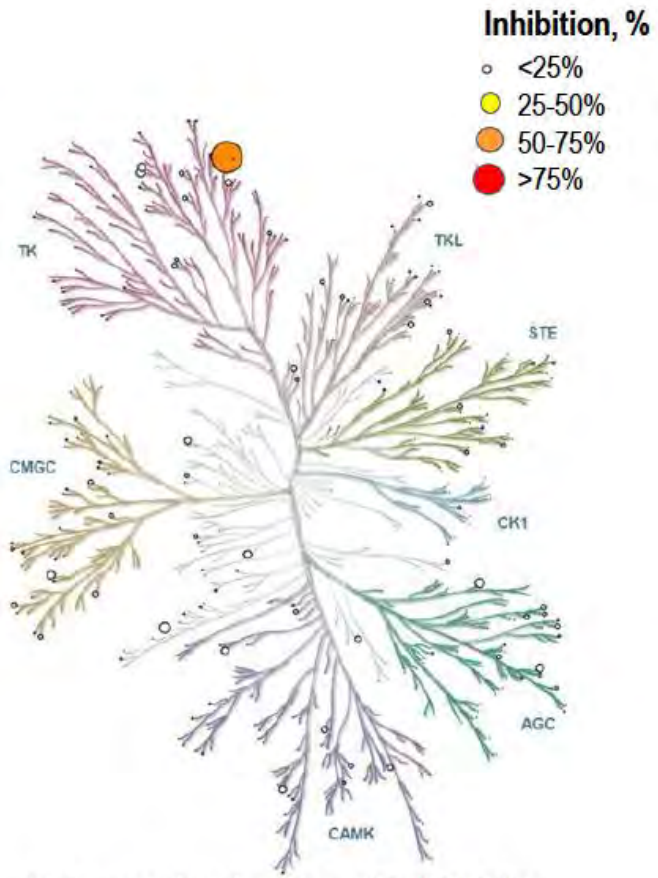
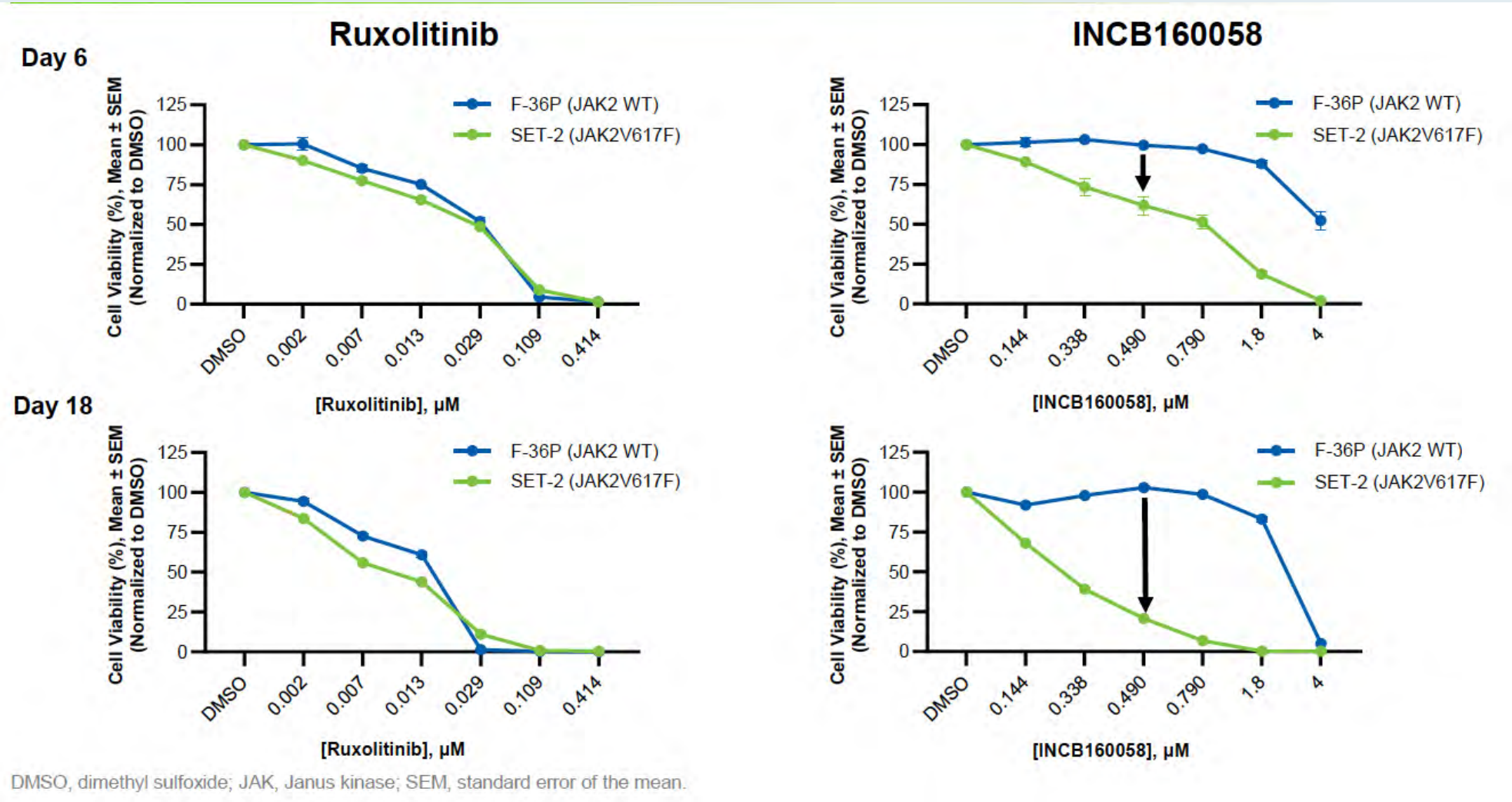


Image reproduced courtesy of Cell Signaling Technology, Inc (www.cellsignal.com).

Stubbs MC et al. ASH 2023;Abstract 860.

INCB160058 Selectively Inhibits Growth of JAK2V617F-Expressing Cells



DMSO, dimethyl sulfoxide; JAK, Janus kinase; SEM, standard error of the mean.

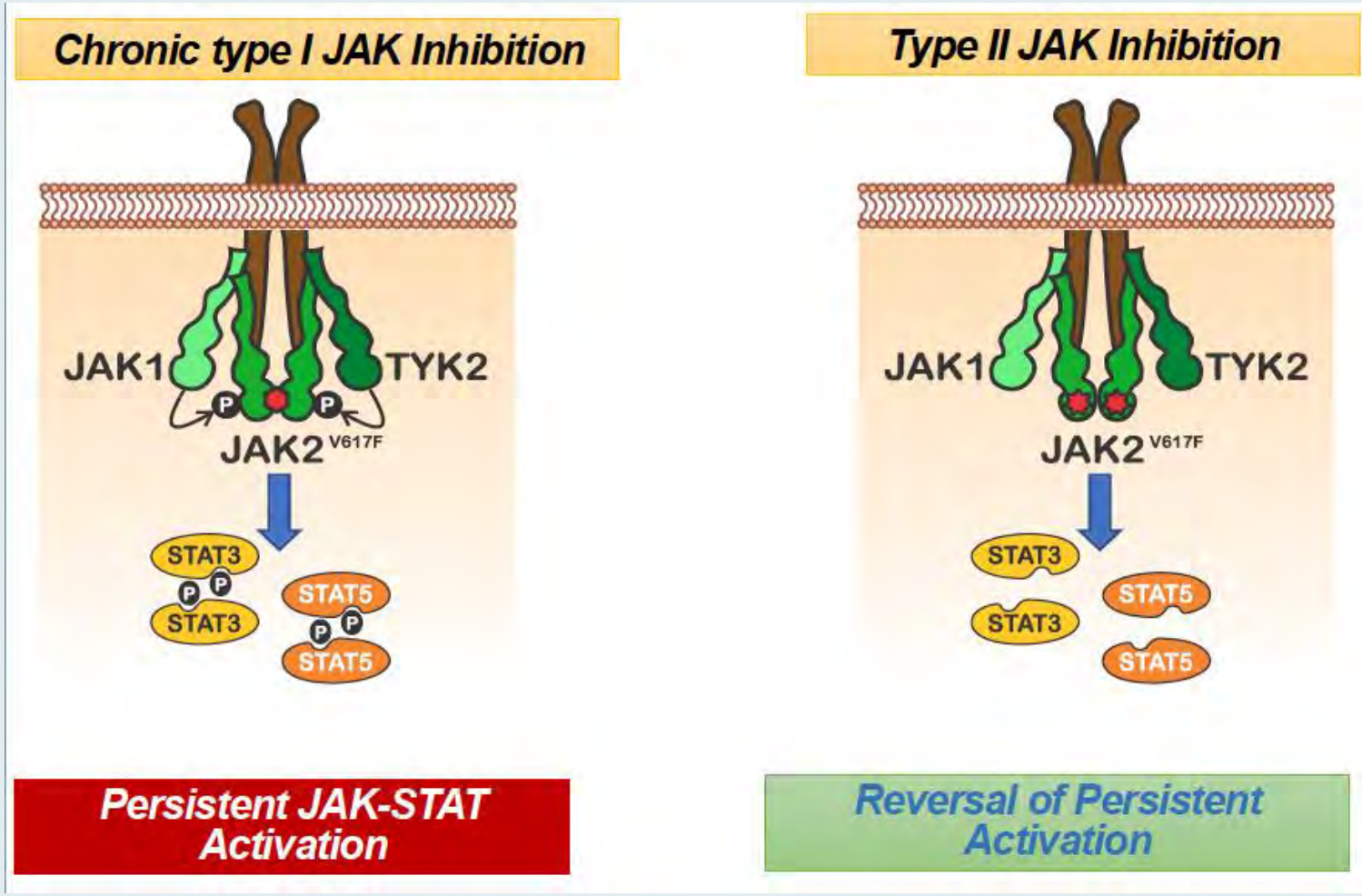
Stubbs MC et al. ASH 2023;Abstract 860.

Summary of Preclinical Findings with INCB160058

- INCB160058 is a potent and selective JAK2 pseudokinase domain binder
- Pseudokinase binding offers a new mechanism of action for selective inhibition of JAK2V617F, with potential to eradicate mutant clones
- INCB160058 inhibits cytokine-independent activity of JAK2V617F while sparing wild-type JAK2
- In vitro, INCB160058 selectively targets JAK2V617F-harboring cell lines as well as myeloproliferative neoplasm patient-derived CD34-positive cells, repressing phosphorylated STAT5 levels and slowing cell growth
- In vivo, INCB160058 maintains its selective nature, reducing human JAK2V617F-derived cell engraftment; erythropoietic cells and proinflammatory cytokines were selectively reduced

Stubbs MC et al. ASH 2023;Abstract 860.

Potential of Type II JAK Inhibitors



Mascarenhas J et al. ASH 2024;Abstract 3147.1.

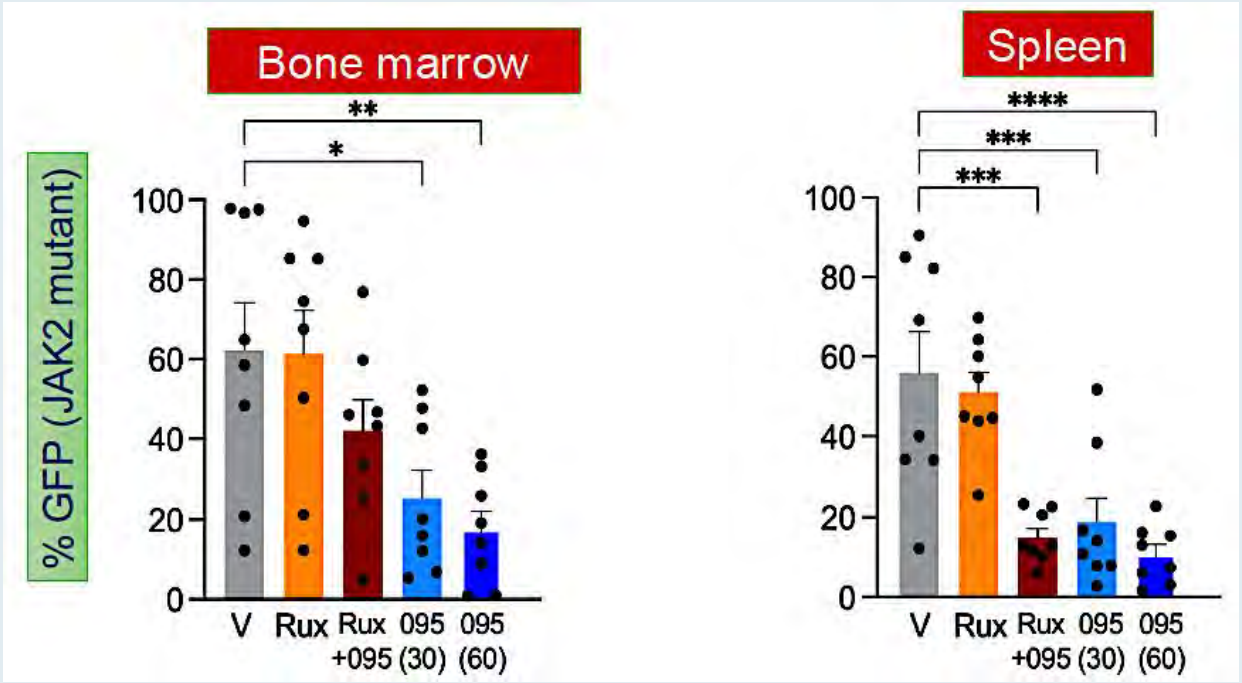
AJ1-11095 Preclinical Data

- AJ1-11095 was designed through computational and structure-based methods to specifically bind the Type II (inactive) conformation of JAK2

- AJ1-11095 is highly selective for JAK2 compared with other JAK family members (JAK1, JAK3, TYK2)

- Cell line experiments and murine models of MPN show potent activity of AJ1-11095 both as initial therapy and post ruxolitinib treatment (ruxolitinib persistence model)

- AJ1-11095 ("095") also induces reduction in the mutant clone in preclinical MPN models



Mascarenhas J et al. ASH 2024;Abstract 3147.1.

AGENDA

Year in Review: Management of Myelofibrosis

INTRODUCTION:

- The New Trastuzumab?
- Off-the-Shelf Allo T-Reg Cell Infusions?

MODULE 1: Myelofibrosis 2025 — JAK Inhibitors (Ruxolitinib)

MODULE 2: BET Inhibitors — Pelabresib

MODULE 3: Navtemadlin

MODULE 4: Selinexor and Elritercept

RTP Year in Review 2025

Dosing and clinical outcomes of ruxolitinib in patients with myelofibrosis in a real-world setting: Interim results of the Italian observational study (ROMEI)

Breccia et al

Prospective multicentre study in Italy enrolling MF patients treated with ruxolitinib - 508 patients enrolled

Prior work from this study confirmed in its 24-week findings, the beneficial effect of ruxolitinib in improving symptoms and QOL (primary endpoints) and reducing spleen size. A favorable safety profile was observed, consistent with results from clinical studies. The interim results in the ROMEI study indicated high adherence (60%–75%) to oral ruxolitinib at 24 weeks.
However, **one third (25%–40%) of the patients receiving ruxolitinib may be undertreated** owing to suboptimal adherence, potentially undermining disease control and survival outcomes.

This paper presents an interim analysis at 12 months based upon outcomes of patients according to starting dose of ruxolitinib.

AsEx – as expected for platelet count n = 174
LtEx – less than expected n= 132

TABLE 1 Distribution of patients according to the expected starting dose group (baseline platelet count).

Ruxolitinib expected starting dose group	Platelets at baseline (10^9/L) class	Starting dose	*N* (%)
As expected (AsEx, *N* = 174)	50–<75	5 mg bid (10 mg/day)	8 (4.6)
	75–<100	10 mg bid (20 mg/day)	5 (2.9)
	100–200	15 mg bid (30 mg/day)	24 (13.8)
	>200	20 mg bid (40 mg/day)	137 (78.7)
Lower than expected (LtEx; *N* = 132)	50–<75	<5 mg bid (<10 mg/day)	0
	75–<100	<10 mg bid (<20 mg/day)	10 (7.6)
	100–200	<15 mg bid (<30 mg/day)	29 (22.0)
	>200	<20 mg bid (<40 mg/day)	93 (70.5)

bid, twice daily.

Courtesy of Professor Claire Harrison

Discussion Question

What is the optimal dosing strategy for initial treatment with ruxolitinib?

Clinical outcomes of ruxolitinib treatment in 595 intermediate-1 risk patients with myelofibrosis: The RUX-MF Real-World Study

Francesca Palandri MD, PhD[1] | Elena M. Elli MD[2] | Erika Morsia MD[3] | Giulia Benevolo MD[4] | Mario Tiribelli MD[5] | Eloise Beggiato MD[6] | Massimiliano Bonifacio MD[7] | Mirko Farina MD[8] | Bruno Martino MD[9] | Giovanni Caocci MD[10] | Novella Pugliese MD[11] | Alessia Tieghi MD[12] | Monica Crugnola MD[13] | Gianni Binotto MD[14] | Francesco Cavazzini MD[15] | Elisabetta Abruzzese MD[16] | Alessandra Iurlo MD[17] | Alessandro Isidori MD[18] | Costanza Bosi MD[19] | Veronica Guglielmana MD[2] | Marta Venturi MD[20] | Alessandra Dedola MD[20] | Michele Loffredo MD[20] | Gabriele Fontana MD[20] | Andrea Duminuco MD[21] | Alessia Moioli MD[7] | Luca Tosoni MD[5] | Emilia Scalzulli MD[22] | Daniele Cattaneo MD[17] | Roberto M. Lemoli MD[23,24] | Daniela Cilloni MD[25] | Monica Bocchia MD[26] | Fabrizio Pane MD[11] | Florian H. Heidel MD[27] | Nicola Vianelli MD[1] | Michele Cavo MD[1,20] | Giuseppe A. Palumbo MD[28] | Filippo Branzanti MSc[20] | Massimo Breccia MD[22]

Courtesy of Professor Claire Harrison

Discussion Question

How do you decide when to start ruxolitinib treatment?

LETTER OPEN

Myelofibrosis management in routine clinical practice with a focus on patients with cytopenias: recommendations from a global consensus group

Steffen Koschmieder[1], Prithviraj Bose[2], Martin H. Ellis[3], Vikas Gupta[4], Jean-Jacques Kiladjian[5], John Mascarenhas[6], Vikram Mathews[7], Francesco Passamonti[8] and Claire Harrison[9]✉

Aims to assess:

- Defining the thresholds for anemia, and when to initiate/ modify treatment
- Defining the threshold for thrombocytopenia and when to initiate/modify treatment
- Defining JAKi failure and what would warrant switching treatment
- How and when to determine prognosis in patients with MF
- Unmet needs in MF clinical trials

Courtesy of Professor Claire Harrison

Question 8:
What Criteria Should be Used to Define a Patient who is Relapsed, Refractory, or Intolerant to JAK Inhibitor Treatment?

Clinical Recommendation 8

- There are existing criteria for ruxolitinib that are used in clinical trials to determine if a patient is relapsed, refractory, or intolerant to treatment (Table 2)
- However, in clinical practice, it may be difficult to distinguish exactly between ruxolitinib intolerance and relapse, as often these can coexist
- Criteria for other JAK inhibitors are likely to be similar

Table 2: Criteria for Ruxolitinib Failure Used in the Re-analysis of the JAKARTA-2, PAC203, and FREEDOM Trials (Adapted From Bose P, Verstovsek S. Hemasphere. 2020;4:e424)

Relapsed	Ruxolitinib for ≥3 months with spleen regrowth (defined as <10% SVR or <30% decrease in spleen size by palpation from baseline) following an initial response*
Refractory	Ruxolitinib for ≥3 months with <10% SVR or <30% decrease in spleen size by palpation from baseline
Intolerant	Ruxolitinib for ≥28 days complicated by development of RBC transfusion requirement (≥2 units/month for two consecutive months); or Grade ≥3 thrombocytopenia, anemia, hematoma/hemorrhage or other, non-hematologic adverse events while on ruxolitinib

Courtesy of Professor Claire Harrison

*Response to ruxolitinib is defined as ≥35% reduction in spleen volume from baseline or ≥50% reduction in spleen size for baseline spleen sizes >10cm below LCM, a non-palpable spleen for baseline spleen sizes between 5–10cm below LCM, or not eligible for spleen response for baseline spleen <5cm below LCM (Harrison CN, et al. Am J Hematol. 2020;95:594–603).

JAK, Janus kinase; LCM, left costal margin; RBC, red blood cell; SVR, spleen volume reduction.

Discussion Questions

How do you determine if a patient has relapsed/refractory disease?

What is the optimal way to identify intolerance to JAK inhibitor therapy?

Question 3:
Which Current and Emerging Treatments to Improve Anemia Should be Considered for: • MF-Related Anemia? • Treatment-Related Anemia?

Clinical Recommendation 3

Once other causes such as disease progression have been excluded: for MF-related anemia, JAK inhibition with momelotinib or pacritinib, danazol, luspatercept, ESAs, IMiD®, or conventional combination therapies, such as JAK inhibition plus ESAs, danazol, luspatercept, or IMiD®, may overcome the necessity of dose adjustments/interruptions, which may be associated with ruxolitinib or fedratinib*

In the future, novel combination therapies may deliver these benefits

Splenectomy can be considered as a last resort in select cases of refractory disease-related anemia.
For treatment-related anemia, consider dose reduction of current therapy for 4–6 weeks.

*Only ruxolitinib, fedratinib, pacritinib, and momelotinib are approved treatments for MF.

MEDIAN SCORE

CONSENSUS

All current and emerging treatment options for MF- and treatment-related anemia should be considered

Courtesy of Professor Claire Harrison

ESA, erythropoietin-stimulating agent; Hb, hemoglobin; IMiD, immunomodulatory drugs; JAK, Janus kinase; MF, myelofibrosis.

Koschmieder Leukemia 2024

Question 4:
Aside From Access and Reimbursement, What Factors Guide Selection of JAK Inhibitor Therapy in Patients With MF and Anemia?

Clinical Recommendation 4

- Factors guiding selection of JAK inhibitor monotherapy would include:


Baseline Hb


Likely tolerance of anemia


Baseline thrombocytopenia


MF-related symptoms

- For some agents, consideration of drug-specific adverse events (immunosuppression, skin cancer, infection risk, nutritional status, tolerance of GI toxicity, neurotoxicity, cardiovascular adverse events) is also a factor

Courtesy of Professor Claire Harrison

GI, gastrointestinal; Hb, hemoglobin; JAK, Janus kinase; MF, myelofibrosis.

Koschmieder Leukemia 2024

Clinical Outcomes in Patients with Myelofibrosis Treated with Ruxolitinib and Anemia-Supporting Medications

Vachhani ASH 2024; Abstract 4546

- The large (N=2233), single-arm, phase 3b, expanded-access JUMP trial evaluated safety and efficacy of ruxolitinib treatment for patients with MF in a setting similar to routine clinical practice.
- This post hoc analysis included patients with BL anemia (hemoglobin [Hb] <12.0 g/dL or Hb <10.0 g/dL) who were not receiving supportive care for anemia at enrollment but initiated an ESA or danazol within 3 months of enrollment and remained on that therapy for ≥3 months. Clinical outcomes evaluated were spleen length response.
- 101 (7.3%) initiated an ESA (n=98) or danazol (n=3) within 3 months of enrollment (52 [6.9%] with Hb<10.0g/dL) and were included in this analysis.
- For the Hb<12.0 g/dL cohort, time from enrollment to first dose of an ESA or danazol was 43.0 (2–91) days.
- For the Hb<10.0 g/dL subgroup, time to first dose of ESA or danazol was 34 (2–90) days.

Courtesy of Professor Claire Harrison

Momelotinib vs. ruxolitinib in myelofibrosis patient subgroups by baseline hemoglobin levels in the SIMPLIFY-1 trial

Vikas Gupta, Stephen Oh, Timothy Devos, Viviane Dubruille, John Catalano, Tim C. P. Somervaille, Uwe Platzbecker, Pilar Giraldo, Hiroshi Kosugi, Tomasz Sacha, Jiri Mayer, Arpad Illes, Catherine Ellis, Zhaohui Wang, Francisco J. Gonzalez Carreras, Bryan Strouse & Ruben Mesa

- Anemia is a key hallmark of MF and often results in poor quality of life and under dosing of ruxolitinib. This is a *post hoc* analysis of the SIMPLIFY-1 study.

- This study was the only trial to perform a head to head analysis of JAK inhibitors.

Courtesy of Professor Claire Harrison

Momelotinib versus Continued Ruxolitinib or Best Available Therapy in JAK Inhibitor-Experienced Patients with Myelofibrosis and Anemia: Subgroup Analysis of SIMPLIFY-2

Claire N. Harrison · Alessandro M. Vannucchi · Christian Recher · Francesco Passamonti · Aaron T. Gerds · Juan Carlos Hernandez-Boluda · Abdulraheem Yacoub · Shireen Sirhan · Catherine Ellis · Bharat Patel · Bryan Strouse · Uwe Platzbecker

Post hoc analysis of SIMPLIFY 2

The patient subgroups for the present analysis were defined by either:

- Hb of < 100 g/L
- *or* transfusion status, ie all patients who were non-TI.

Transfusion independence is absence of RBC transfusions and no Hb of < 80 g/L in the 12 weeks before randomization.

As few patients received anemia supportive therapies other than RBC transfusions (e.g., ESAs), results in the small subgroup of the overall intent-to-treat (ITT) population who did were also summarized.

Courtesy of Professor Claire Harrison

Longitudinal Assessment of Transfusion Intensity in Patients With JAK Inhibitor–Naive or –Experienced Myelofibrosis Treated With Momelotinib

Claire N. Harrison,[1] Ruben Mesa,[2] Moshe Talpaz,[3] Vikas Gupta,[4] Aaron T. Gerds,[5] Andrew Perkins,[6] Yeow Tee Goh,[7] Maria Laura Fox,[8] Donal McLornan,[9] Jeanne Palmer,[10] Lynda Foltz,[11] Alessandro Vannucchi,[12] Steffen Koschmieder,[13] Francesco Passamonti,[14] Sung-Eun Lee,[15] Catherine Ellis,[16] Bryan Strouse,[16] Francisco J. Gonzalez Carreras,[17] Stephen T. Oh[18]

- In this descriptive analysis, the impact of momelotinib on RBC transfusion burden over time was further characterized across JAK inhibitor–naive and –experienced patients.

- To further visualize changes to RBC transfusion burden during treatment, patients were arrayed in ordinal bins jointly based on their baseline- and treatment-period intensities of RBC units per 28 days: exactly zero units, >0 to 1 unit, >1 to 2 units, >2 to 3 units, >3 to 4 units, and >4 units.

Courtesy of Professor Claire Harrison

Discussion Question

How do you choose between JAK inhibitors as initial therapy for patients with anemia?

Discussion Question

How do you determine when to switch from ruxolitinib to momelotinib for patients with anemia?

Discussion Question

If a patient is receiving ruxolitinib and is going to switch to momelotinib, does the ruxolitinib need to be tapered down?

AGENDA

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INTRODUCTION:

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- Off-the-Shelf Allo T-Reg Cell Infusions?

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MODULE 2: BET Inhibitors — Pelabresib

MODULE 3: Navtemadlin

MODULE 4: Selinexor and Elritercept

RTP Year in Review 2025

Abstract number: 3178

John Mascarenhas
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Courtesy of John Mascarenhas, MD

Updated Results From the Phase 3 MANIFEST-2 Study of Pelabresib in Combination With Ruxolitinib for Janus Kinase Inhibitor–Naïve Patients With Myelofibrosis

John Mascarenhas,[1] Sebastian Grosicki,[2] Dominik Chraniuk,[3] Elisabetta Abruzzese,[4] Prithviraj Bose,[5] Aaron Gerds,[6] Alessandro M. Vannucchi,[7] Francesca Palandri,[8] Sung-Eun Lee,[9] Vikas Gupta,[10] Alessandro Lucchesi,[11] Stephen T. Oh,[12] Andrew T. Kuykendall,[13] Andrea Patriarca,[14] Alberto Álvarez-Larrán,[15] Ruben Mesa,[16] Jean-Jacques Kiladjian,[17] Moshe Talpaz,[18] Morgan Harris,[19] Sarah-Katharina Kays,[20] Tabea Kräft,[20] Qing Li,[21] Anna-Maria Jegg,[20] Claire Harrison,[22] Raajit K. Rampal[23]

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Presentation #658

Safety and Efficacy of Bromodomain and Extra-Terminal Inhibitor INCB057643 in Patients With Relapsed or Refractory Myelofibrosis and Other Advanced Myeloid Neoplasms: A Phase 1 Study

Justin Watts, MD,[1] Anthony M. Hunter, MD,[2] Alessandro M. Vannucchi, MD,[3] Vikas Gupta, MD, FRCP,[4] Srinivas K. Tantravahi, MD,[5] Alessandra Iurlo, MD, PhD,[6] Brandon McMahon, MD,[7] Francesca Palandri, MD, PhD,[8] María T. Gómez-Casares, MD,[9] Junichiro Yuda, MD, PhD,[10] Emma Searle, MD, PhD,[11,12] Anna B. Halpern, MD,[13,14] Rosa Ayala Diaz, MD,[15] Akihiro Tomita, MD, PhD,[16] Blanca Xicoy, MD,[17] Prithviraj Bose, MD,[18] Brandi Reeves, MD,[19] Xuejun Chen, PhD,[20] Lea Burke, MS,[20] Feng Zhou, PhD,[20] Fred Zheng, MD,[20] Pankit Vachhani, MD[21]

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66th American Society of Hematology (ASH) Annual Meeting & Exposition; December 7–10, 2024; San Diego, CA, USA

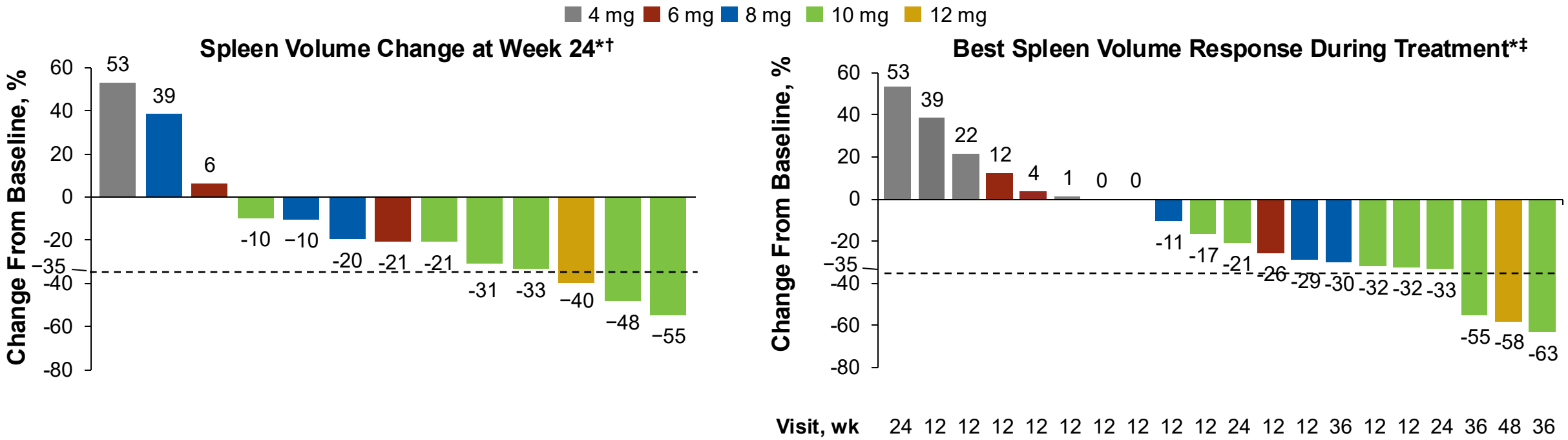
Courtesy of John Mascarenhas, MD

Efficacy – Monotherapy

Spleen Volume Response in Individual Patients With MF (n=25)

Courtesy of John Mascarenhas, MD

- Week 24 SVR35 achieved by 3/7 patients receiving INCB057643 ≥10 mg and 3/20 all evaluable patients
- Of 23 evaluable patients, BOR SVR35 achieved by 3 patients; SVR25 achieved by 9 patients



BOR, best overall response; MF, myelofibrosis; SVR35, 35% reduction from baseline in spleen volume.
* Dotted line represents response criteria threshold. † 7 evaluable patients (4-mg, n=4 and 6-mg, n=3) discontinued from treatment before Week 24; 5 patients were ongoing (6-mg, n=3 and 10-mg, n=2) and not evaluable because they were not followed up long enough and had no Week 24 assessment. ‡ 3 evaluable patients (6-mg n=2 and 10-mg n=1) discontinued from treatment before first postbaseline (Week 12) spleen volume assessment or missed the assessment; 2 patients (6-mg) were not evaluable because they were not followed up long enough to reach the first postbaseline spleen volume assessment

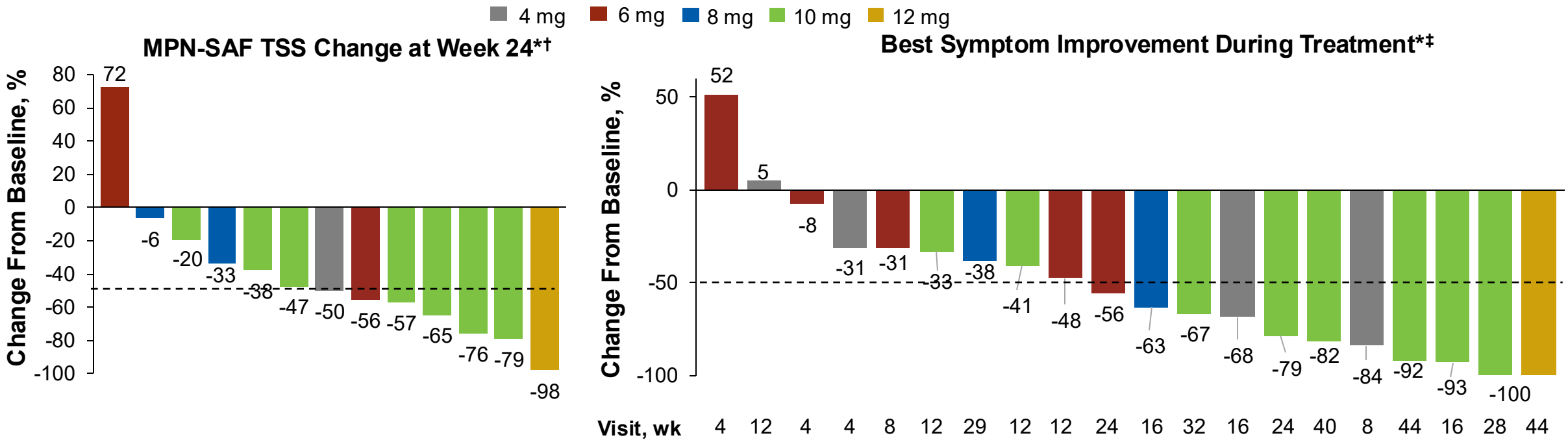
Watts ASH 2024;Abstract 658

Efficacy – Monotherapy

Symptom Response in Individual Patients With MF (n=25)

Courtesy of John Mascarenhas, MD

- Week 24 TSS50 achieved by 5/8 evaluable patients receiving INCB057643 ≥10 mg; 7/19 all evaluable patients
- BOR TSS50 achieved by 11/20 evaluable patients



BOR, best overall response; MF, myelofibrosis; MPN, myeloproliferative neoplasm; TSS50, ≥50% reduction from baseline in Myeloproliferative Neoplasm Symptom Assessment Form total symptom score.

* Dotted line represents response criteria threshold. † 6 evaluable patients (4-mg, n=3 and 6-mg, n=3) discontinued from treatment before Week 24; 6 patients were not evaluable: 1 (4-mg) was missing baseline data, 4 were ongoing (6-mg, n=3; 10-mg, n=1) but not followed up long enough and had no Week 24 assessment, 1 of which (6-mg) and 1 additional (8-mg) had baseline TSS <5. ‡ 5 patients not evaluable: 2 were ongoing but not followed long enough (6 mg), 2 had baseline TSS <5 (6-mg and 8-mg, n=1 each), and 1 did not have baseline data (4 mg).

Watts ASH 2024;Abstract 658

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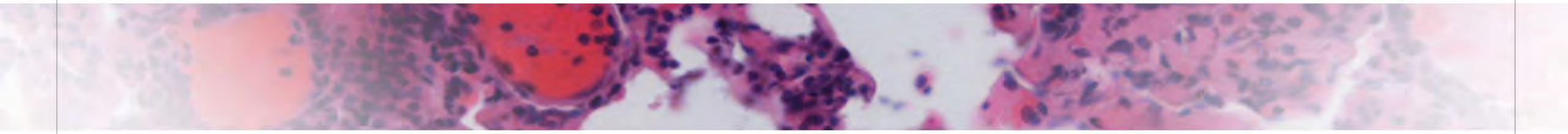

Trial Update from IMproveMF, an Ongoing, Open-label, Dose-Escalation and -Expansion Phase 1/1b Trial to Evaluate the Safety, Pharmacokinetics, and Clinical Activity of the Novel Combination of Imetelstat with Ruxolitinib in Patients with Intermediate-1, Intermediate-2, or High-Risk Myelofibrosis

John O. Mascarenhas, MD,[1] Salman Otoukesh, MD,[2] Terrence Bradley, MD,[3] Bart L. Scott, MD,[4] Habte A. Yimer, MD,[5] Souria Dougherty, MBA,[6] Lixian Peng, PhD,[6] Fei Huang, PhD,[6] Ying Wan, MD, PhD,[6] Faye M. Feller, MD,[6] Vivian Rodolf, MD,[6] Judy Ho, BS,[6] Tymara Berry, MD,[6] Andrew T. Kuykendall, MD[7]

[1]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [3]University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA; [4]Fred Hutchinson Cancer Center, Seattle, WA, USA; [5]Texas Oncology/US Oncology Research, Tyler, TX, USA; [6]Geron Corporation, Foster City, CA, USA; [7]Moffitt Cancer Center, Tampa, FL, USA

Courtesy of John Mascarenhas, MD

Presentation 998 | Presented at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA

Imetelstat Combined With Ruxolitinib Was Well Tolerated

- No DLTs[a] were reported at any imetelstat dose level within the first 28 days of cycle 1

Any-grade TEAEs in ≥15% of patients

Preferred term, n (%)	Total (N=17)
Patients with ≥1 TEAE	**15 (88)**
Pain in extremity	7 (41)
Nausea	6 (35)
ALT increased	5 (29)
Anemia	5 (29)
Thrombocytopenia[b]	4 (24)
Fatigue	4 (24)
AST increased	3 (18)
Neutropenia[c]	3 (18)

Grade 3 TEAEs

Preferred term, n (%)	Total (N=17)
Patients with ≥1 grade 3 TEAE	**8 (47)**
Anemia[d]	4 (24)
Neutropenia[c]	3 (18)
Leukopenia[e]	2 (12)
Abdominal pain	1 (6)
Fatigue	1 (6)
Pneumonia[f]	1 (6)
Epistaxis[f]	1 (6)

- No grade 4 or 5 events were reported

ALT, alanine aminotransferase; AST, aspartate aminotransferase; DLT, dose-limiting toxicity; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
[a]Toxicities determined by the investigator to be possibly, probably, or definitely related to imetelstat treatment, and not attributable to the underlying disease, or toxicities with ruxolitinib increasing in grade and/or clinically significant from before imetelstat initiation. [b]Combined term includes decreased platelet count. [c]Combined term includes decreased neutrophil count. [d]One was a SAE considered related to study treatments and resulted in dose reduction to 6.0 mg/kg. [e]Combined term includes decreased white blood cell count. [f]SAE considered to be related to underlying disease and resolved without dose modification.

Courtesy of John Mascarenhas, MD
Mascarenhas et al. ASH 2024;Abstract 998

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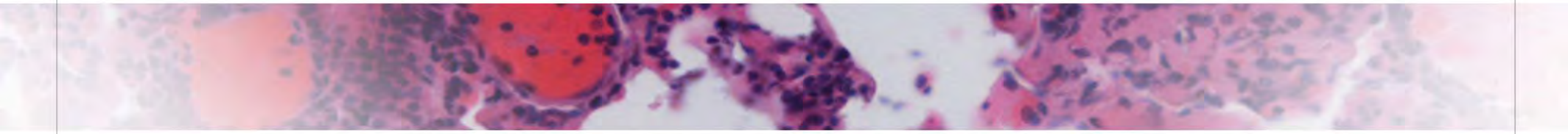


Imetelstat Versus Best Available Therapy in Patients with Intermediate-2 or High-Risk Myelofibrosis Relapsed or Refractory to Janus Kinase Inhibitor in IMpactMF, a Randomized, Open-label, Phase 3 Trial

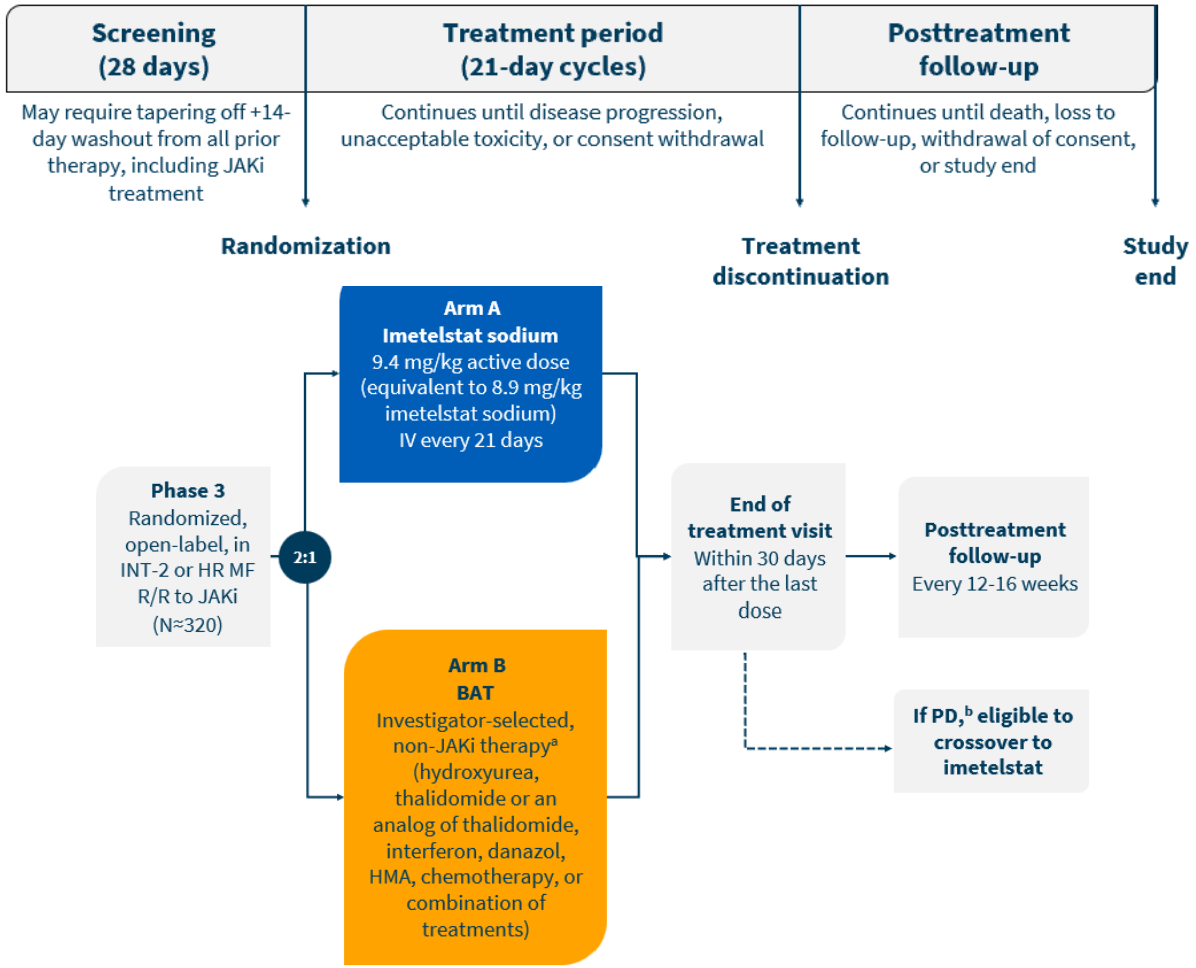
John O. Mascarenhas, MD,[1] Claire Harrison, MD,[2] Prithviraj Bose, MD,[3] Jean-Jacques Kiladjian, MD, PhD,[4] Alessandro Lucchesi, MD, PhD,[5] Alessandro M. Vannucchi, MD,[6] Tymara Berry, MD,[7] Jennifer Riggs, MPH,[7] Lixian Peng, PhD,[7] Fei Huang, PhD,[7] Ying Wan, MD, PhD,[7] Vivian Rodolf, MD,[7] Judy Ho, BS,[7] Shyamala Navada, MD,[7] Rami S. Komrokji, MD[8]

[1]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Guy's and St Thomas' National Health Service Foundation Trust, London, UK; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Hôpital Saint-Louis, Assistance Publique-Hôpitaux de Paris, Université Paris Cité, Paris, France; [5]Hematology Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori," Meldola, Italy; [6]University of Florence, Florence, Italy; [7]Geron Corporation, Foster City, CA, USA; [8]H. Lee Moffitt Cancer Center, Tampa, FL, USA

Courtesy of John Mascarenhas, MD

Poster 1808.1 | Presented at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA

IMpactMF Phase 3 Study Design



- An interim analysis is planned when ~35% of the planned enrolled patients have died (early 2026)
- The final analysis is planned when >50% of the planned enrolled patients have died (early 2027)

BAT, best available therapy; HMA, hypomethylating agent; HR, high risk; INT, intermediate; IV, intravenous; JAKi, Janus kinase inhibitor; MF, myelofibrosis; PD, progressive disease; R/R, relapsed or refractory.
[a]Hematopoietic stem cell transplantation or splenectomy are not to be permitted as BAT. [b]Must demonstrate ≥25% increase in spleen volume from baseline during the study or a palpable increase in splenomegaly after 6 months of BAT.

Courtesy of John Mascarenhas, MD

Mascarenhas ASH 2024;Abstract 1808.1

Study End Points

PRIMARY END POINT
Overall survival

SECONDARY END POINTS

- Symptom response rate at week 24 (≥50% reduction in TSS measured by MFSAF v4.0)
- PFS
- Spleen response rate at week 24 (≥35% spleen volume reduction by MRI or CT)
- Complete remission, partial remission, clinical improvement, spleen response, symptom response, and anemia response per modified 2013 IWG-MRT criteria
- Time to and duration of responses
- Reduction in the degree of bone marrow fibrosis
- Safety
- PK and immunogenicity of imetelstat
- PROs as measured by the EORTC QLQ-C30 and EuroQol-EQ-5D (EQ-5D-5L) questionnaires

EXPLORATORY END POINTS

- Association between baseline cytogenetic and mutational status and clinical responses; change in mutant allele burden (molecular response)
- Correlation between baseline TA, TL, or hTERT and OS, symptom response, or spleen response

BAT, best available therapy; CT, computed tomography; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 items; hTERT, human telomerase reverse transcriptase; IWG-MRT, International Working Group-Myeloproliferative Neoplasms Research and Treatment; MFSAF, Myelofibrosis Symptom Assessment Form; MRI, magnetic resonance imaging; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; PRO, patient-reported outcome; TA, telomerase activity; TL, telomere length; TSS, Total Symptom Score.

Courtesy of John Mascarenhas, MD
Mascarenhas ASH 2024;Abstract 1808.1

AGENDA

Year in Review: Management of Myelofibrosis

INTRODUCTION:

- The New Trastuzumab?
- Off-the-Shelf Allo T-Reg Cell Infusions?

MODULE 1: Myelofibrosis 2025 — JAK Inhibitors (Ruxolitinib)

MODULE 2: BET Inhibitors — Pelabresib

MODULE 3: Navtemadlin

MODULE 4: Selinexor and Elritercept

RTP Year in Review 2025

Abstract #1000

9 December 2024

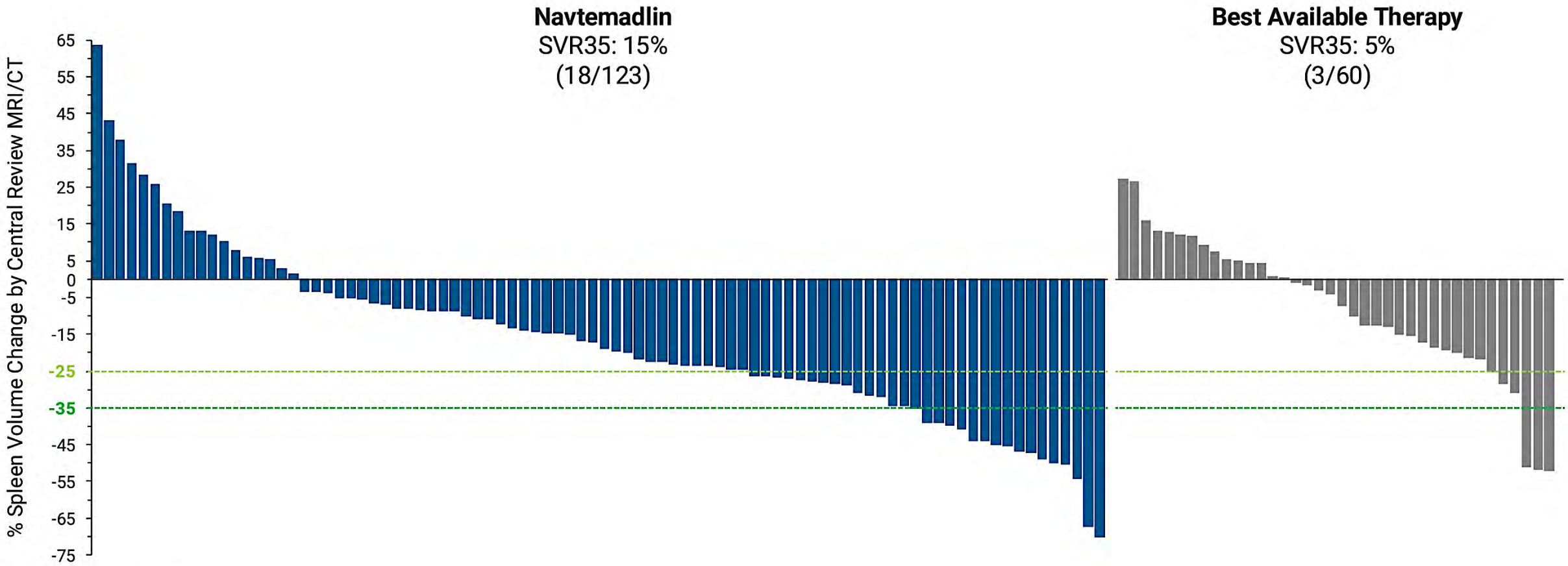
Results from the Randomized, Multicenter, Global Phase 3 Study BOREAS: Navtemadlin Versus Best Available Therapy in JAK Inhibitor Relapsed/Refractory Myelofibrosis

John O. Mascarenhas, MD[1]; Viola Maria Popov, MD, PhD, MSc[2]; Sanjay Mohan, MD[3]; Zübeyde Nur Özkurt, Prof.[4]; Jean-Jacques Kiladjian, MD, PhD[5]; Haifa Kathrin Al-Ali[6]; Andrew Charles Perkins, MBBS, PhD[7]; Zhuying Huang, PhD[8]; Hope Qamoos, NP[8]; Jesse McGreivy, MD[8]; Wayne Rothbaum, MA[8]; Srdan Verstovsek, MD, PhD[8] and Maciej Kaźmierczak, MD, PhD[9]

[1]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY. [2]Colentina Clinical Hospital Bucharest, Hematology Department, Pitesti, Arges, Romania. [3]The Vanderbilt Clinic, Nashville, TN. [4]Gazi University, Faculty of Medicine, Department of Hematology, Ankara, Turkey. [5]Hopital Saint-Louis, Paris, France. [6]University Hospital Halle, Halle (Saale), Germany. [7]The Alfred Hospital and Monash University, Melbourne, Australia. [8]Kartos Therapeutics, Inc., Redwood City, CA. [9]University of Medical Sciences, Poznan, Poland.

SVR35 at Week 24 (ITT Population)

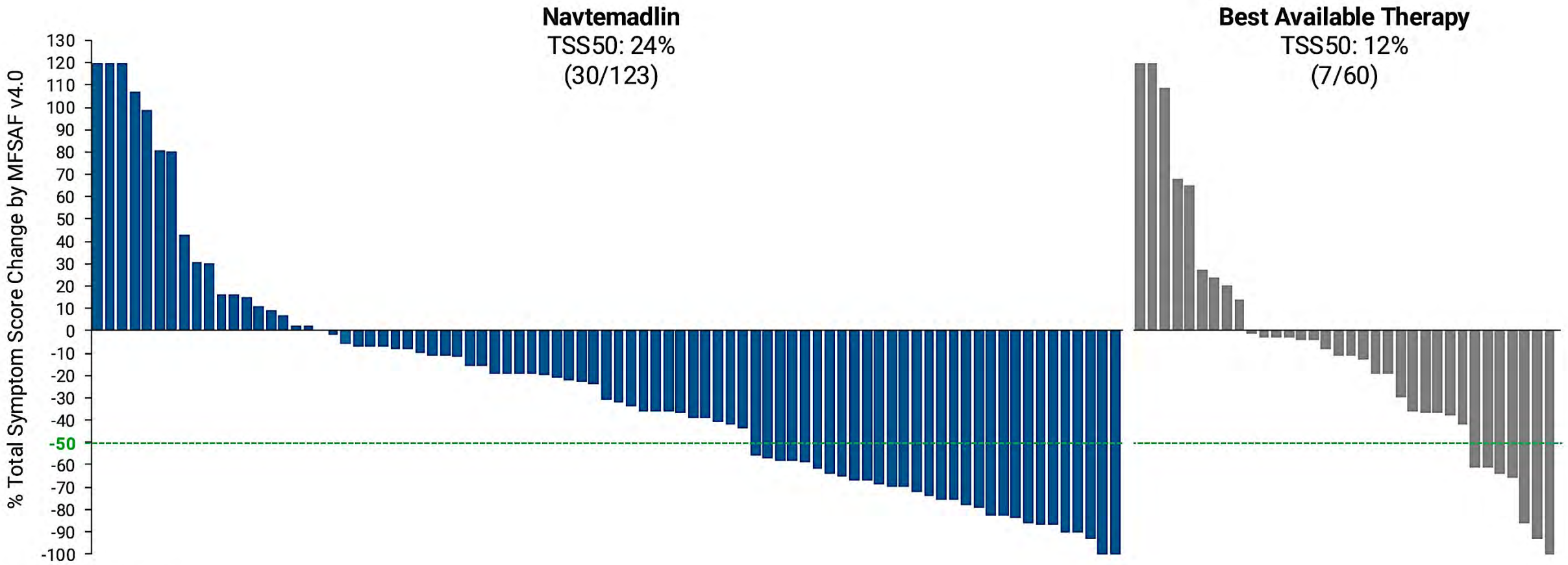
Spleen Volume Reduction by Central Review MRI/CT – Baseline to Week 24



Data cut-off: 30 Sep 2024.
Note: Navtemadlin dosed at 240 mg QD (Days 1-7/28-day cycle). ITT is all randomized subjects. Figure represents subjects with baseline and Week 24 data.
Navtemadlin vs BAT, p=0.0815. SVR25: Navtemadlin, 27% (33/123); BAT, 10% (6/60). BAT SVR35 responders received hydroxyurea (2) and lenalidomide (1).
Abbreviations: BAT, best available therapy; CT, computed tomography; ITT, intention-to-treat; MRI, magnetic resonance imaging; SVR35, spleen volume reduction ≥35%.

TSS50 at Week 24 (ITT Population)

Total Symptom Score Reduction by MFSAF v4.0 – Baseline to Week 24

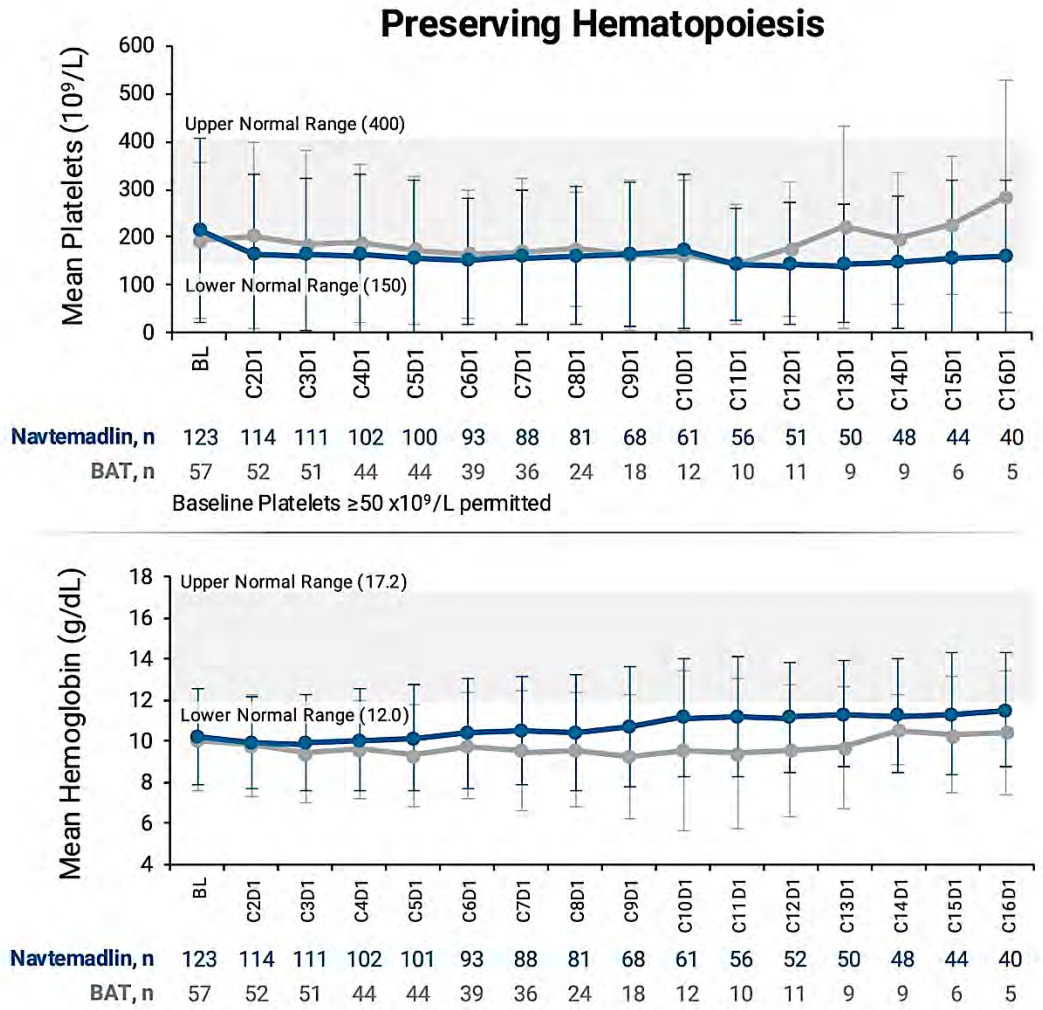


Data cut-off: 30 Sep 2024.
Note: Navtemadlin dosed at 240 mg QD (Days 1-7/28-day cycle). ITT is all randomized subjects. Figure represents subjects with baseline and Week 24 data. Navtemadlin vs BAT, p=0.0507.
Week 24 TSS assessment includes Week 23 scores for subjects who stopped TSS at the start of Week 24 (n=2).
Abbreviations: BAT, best available therapy; ITT, intention-to-treat; MFSAF, myelofibrosis symptom assessment form; TSS, total symptom score; TSS50, total symptom score reduction ≥50%.

Treatment-Emergent Adverse Events

	Navtemadlin n = 123[1]		Best Available Therapy n = 57[1,2]	
Preferred Term, n (%)	**All Grade**	**Grade 3/4**	**All Grade**	**Grade 3/4**
TEAE Occurring in ≥ 10%[1]				
Thrombocytopenia[3]	57 (46)	45 (37)	18 (32)	14 (25)
Nausea	52 (42)	5 (4)	3 (5)	–
Diarrhea	50 (41)	7 (6)	9 (16)	1 (2)
Anemia	44 (36)	35 (29)	16 (28)	16 (28)
Neutropenia[4]	37 (30)	31 (25)	10 (18)	7 (12)
Constipation	25 (20)	1 (1)	2 (4)	–
Vomiting	31 (25)	3 (2)	1 (2)	–
Decreased Appetite	22 (18)	–	4 (7)	1 (2)
Fatigue	19 (15)	4 (3)	7 (12)	2 (4)
Peripheral Edema	15 (12)	–	7 (12)	1 (2)
Asthenia	16 (13)	2 (2)	5 (9)	1 (2)
Abdominal Pain, Upper	13 (11)	2 (2)	1 (2)	–
Pruritus	7 (6)	–	6 (11)	–

Median time on study, months (range): Navtemadlin 15.6 (0.23, 39.9); BAT 6.5 (0.03, 30.5)



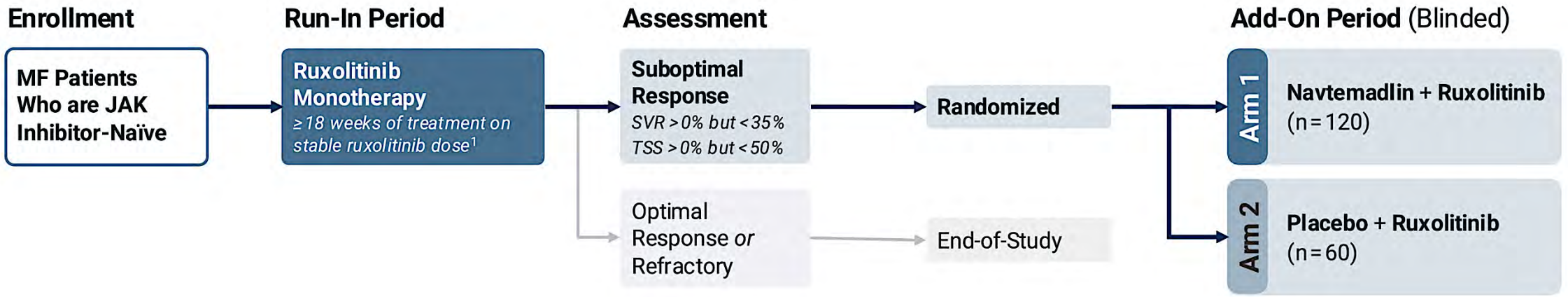
Data cut-off: 30 Sep 2024.

Note: Navtemadlin dosed at 240 mg QD (Days 1-7/28-day cycle).

[1]Safety dataset is all subjects who received ≥1 dose of study treatment. [2]One subject randomized to BAT, first cycle was navtemadlin. [3]Combined terms: thrombocytopenia and platelet count decrease. [4]Combined terms: neutropenia and neutrophil count decrease. Abbreviations: BAT, best available therapy; BL, baseline; C, cycle; D, day; QD, once daily; TEAE, treatment-emergent adverse event.

Navtemadlin in Suboptimal Responders to Ruxolitinib

A Phase 3 Randomized, Double-Blind, Add-On Study Evaluating the Safety and Efficacy of Navtemadlin and Ruxolitinib vs Placebo and Ruxolitinib in JAK Inhibitor-Naïve Patients With Myelofibrosis Who Have a Suboptimal Response to Ruxolitinib Treatment



Run-In Period (N = 600)

Key Inclusion Criteria

- Primary or secondary MF by WHO criteria
- Int-1, Int-2, or High-risk disease by IPSS
- Spleen volume ≥ 450 cm^3
- Platelet count ≥ 100 x 10^9/L

Add-On Period (N = 180)

Key Inclusion Criteria

- *TP53*^{WT} by central testing
- Treatment with a stable dose of ruxolitinib
- Suboptimal response to ruxolitinib run-in

Endpoints

Co-Primary Endpoints

- Targeted SVR and TSS reduction 24 weeks after randomization

Note: Navtemadlin dosed at 240 mg QD (Days 1-7/28-day cycle). Target enrollment from 220 sites across 19 countries.
[1]Stable ruxolitinib is ≥5 mg BID that does not require treatment hold or dose adjustment during the eight weeks prior to add-on navtemadlin or placebo.
Abbreviations: BID, twice daily; Int, intermediate; IPSS, International Prognostic Scoring System; JAK, Janus kinase; MF, myelofibrosis; TSS, total symptom score; WHO, World Health Organization; WT, wild-type.

AGENDA

Year in Review: Management of Myelofibrosis

INTRODUCTION:

- The New Trastuzumab?
- Off-the-Shelf Allo T-Reg Cell Infusions?

MODULE 1: Myelofibrosis 2025 — JAK Inhibitors (Ruxolitinib)

MODULE 2: BET Inhibitors — Pelabresib

MODULE 3: Navtemadlin

MODULE 4: Selinexor and Elritercept

RTP Year in Review 2025

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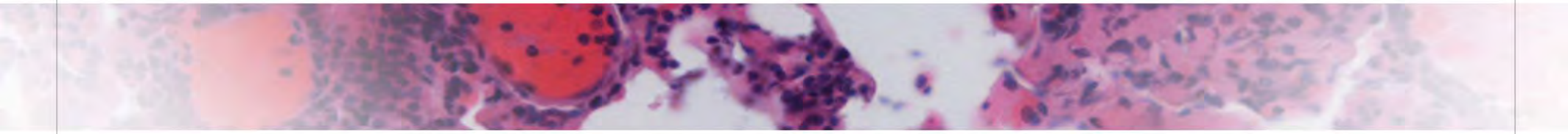

The Efficacy and Safety of Selinexor in Combination with Ruxolitinib in Ruxolitinib-Treated Myelofibrosis Patients: the Interim Analysis of a Prospective, Open-Label, Multicenter, Parallel-Cohort, Phase 2 Study

Minghui Duan, Lan Ma , Qiuling Wu, Hong Liang, Wei Wang, Shaoling Wu, Lijun Mu, Hai Lin, Hebing Zhou, Hong-Xia Shi, MD, Jinghua Wang, Hongmei Jing

Courtesy of John Mascarenhas, MD

Hematological Improvement and Other Clinical Benefits of Elritercept as Monotherapy and in Combination with Ruxolitinib in Participants with Myelofibrosis from the Ongoing Phase 2 RESTORE Trial

Claire Harrison, MD, FRCP, FRCPath

Professor of Myeloproliferative Neoplasms and Deputy Chief Medical Officer (Research, Data, and Analytics) of the Guy's and St. Thomas' NHS Foundation Trust, UK

Courtesy of John Mascarenhas, MD

RESTORE

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

Management of Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Thursday, May 8, 2025
5:00 PM – 6:00 PM ET

Faculty

Meletios-Athanasios (Thanos) C Dimopoulos, MD
Robert Z Orlowski, MD, PhD

Moderator

Neil Love, MD

RTP Year in Review 2025

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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.

Information on how to obtain CME and ABIM MOC credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP Year in Review 2025