# What I Tell My Patients: Integrating New Research Information into Current Clinical Care

*A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress*

# Myelofibrosis

**Saturday, April 27, 2024**
**12:15 PM – 1:45 PM**

## Faculty

**Ilene Galinsky, NP**
**Andrew T Kuykendall, MD**
**Sara M Tinsley-Vance, PhD, APRN, AOCN**
**Abdulraheem Yacoub, MD**

## Moderator

**Neil Love, MD**

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# Faculty

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Senior Adult Leukemia Program
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Westwood, Kansas

## Moderator

**Neil Love, MD**
Research To Practice
Miami, Florida

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# Ms Galinsky — Disclosures

| | |
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| **Consulting Agreements** | AbbVie Inc, CTI Biopharma, a Sobi company, Novartis |

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# Dr Kuykendall — Disclosures

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| **Contracted Research** | Blueprint Medicines, Bristol Myers Squibb, Geron, Janssen Biotech Inc, Protagonist Therapeutics, MorphoSys |
| **Data and Safety Monitoring Board/Committee** | Geron |

# Dr Tinsley-Vance — Disclosures

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# Dr Yacoub — Disclosures

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## Commercial Support

This activity is supported by educational grants from CTI Biopharma, a Sobi company, GSK, and Incyte Corporation.

## Research To Practice NCPD Planning Committee Members, Staff and Reviewers

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

**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.**

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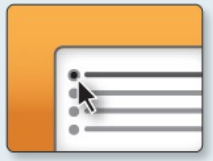
# Clinicians in the Meeting Room

**Networked iPads are available.**

**Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.**



**Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.**

**Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.**

***For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.***

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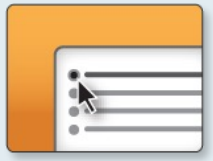
# Clinicians Attending via Zoom

**Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.**



**Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.**

**Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.**

**Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.**

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# Clinicians in the Meeting Room

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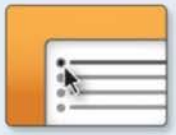
**Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.**



**Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.**

**Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.**

**Complete Your Evaluation: Tap the NCPD Evaluation button to complete your evaluation electronically to receive credit for your participation.**

***For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.***

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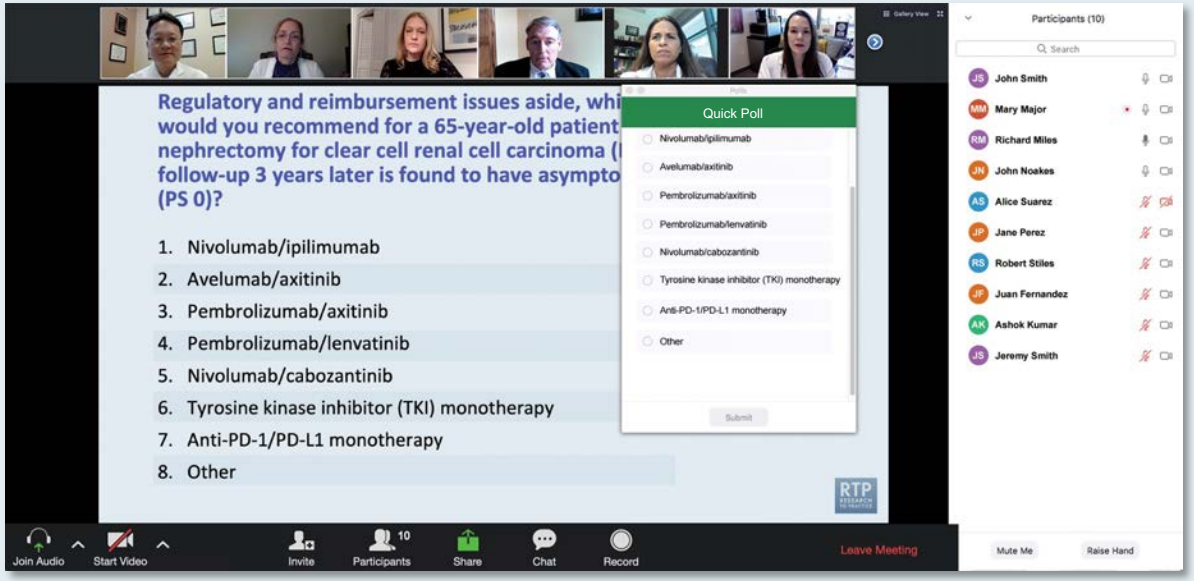
# Clinicians, Please Complete the Pre- and Postmeeting Surveys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# About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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# “What I Tell My Patients”
# Sixteenth Annual RTP-ONS NCPD Symposium Series

| | |
|---|---|
| Wednesday<br>April 24 | **Hormone Receptor–Positive Breast Cancer**<br>6:00 PM – 8:00 PM ET |
| Thursday<br>April 25 | **Endometrial Cancer**<br>6:00 AM – 7:30 AM ET |
| | **Antibody–Drug Conjugates**<br>12:15 PM – 1:45 PM ET |
| | **Chronic Lymphocytic Leukemia and Bispecific Antibodies in Lymphoma**<br>6:00 PM – 8:00 PM ET |
| Friday<br>April 26 | **Head and Neck Cancer**<br>6:00 AM – 7:30 AM ET |
| | **Non–Small Cell Lung Cancer with an EGFR Mutation**<br>12:15 PM – 1:45 PM ET |
| | **Ovarian Cancer**<br>6:00 PM – 7:30 PM ET |
| Saturday<br>April 27 | **Hepatobiliary Cancers**<br>6:00 AM – 7:30 AM ET |
| | **Myelofibrosis**<br>12:15 PM – 1:45 PM ET |
| | **Gastroesophageal and Colorectal Cancers**<br>6:00 PM – 8:00 PM ET |
| Wednesday,<br>May 1 | **LIVE WEBINAR — Prostate Cancer**<br>7:00 PM – 8:00 PM ET |

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# Consulting Nurse Faculty

**Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC**
The University of Texas
MD Anderson Cancer Center
Houston, Texas

**Kathleen D Burns, RN, MSN, AGACNP-BC, OCN**
City of Hope Comprehensive Cancer Center
Duarte, California

**Sonia Glennie, ARNP, MSN, OCN**
Swedish Cancer Institute Center for Blood Disorders
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**Jessica Mitchell, APRN, CNP, MPH**
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**Tiffany A Richards, PhD, ANP-BC, AOCNP**
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**Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC**
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Los Angeles, California

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## Moderator

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# Agenda

**Introduction**

**Module 1:** Biology of Myelofibrosis (MF)

**Module 2:** Role of Available and Investigational JAK inhibitors in the Management of MF

**Module 3:** Promising Agents and Strategies for Patients with MF

# Agenda

**Introduction**

**Module 1:** Biology of Myelofibrosis (MF)

**Module 2:** Role of Available and Investigational JAK inhibitors in the Management of MF

**Module 3:** Promising Agents and Strategies for Patients with MF

# Consulting Nursing Faculty Comments

## Financial stressors on patients

Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC

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# Agenda

Introduction

**Module 1: Biology of Myelofibrosis (MF)**

**Module 2: Role of Available and Investigational JAK inhibitors in the Management of MF**

**Module 3: Promising Agents and Strategies for Patients with MF**

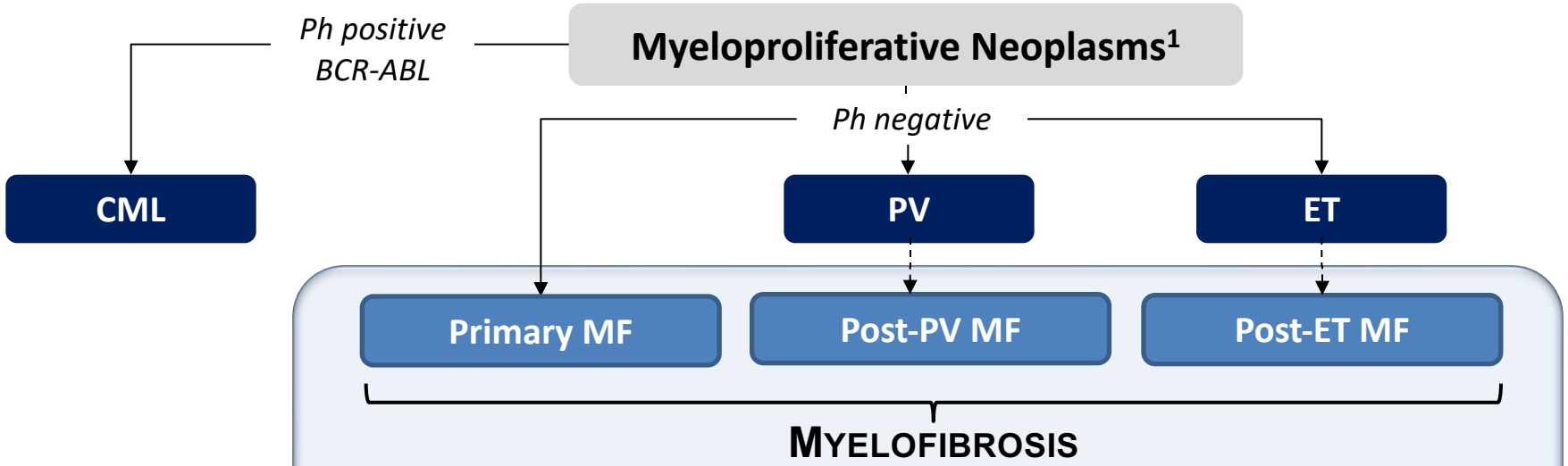
# The Biology of MF

**Dr Kuykendall**
Tampa, Florida

**Dr Yacoub**
Westwood, Kansas

- **Typical presentation, symptoms and clinical course of MF; differences between primary and secondary disease**
- **Clinical significance of the JAK-STAT pathway in MF development**
- **Appropriate risk stratification for patients with MF; advantages and limitations of available scoring systems**
- **Establishing goals of care; identification of patients who may be appropriate for allogeneic stem cell transplant**
- **Effectiveness of various interventions, such as transfusions, erythropoiesis-stimulating agents, growth factors and splenectomy, in addressing common symptoms of MF**

# 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]

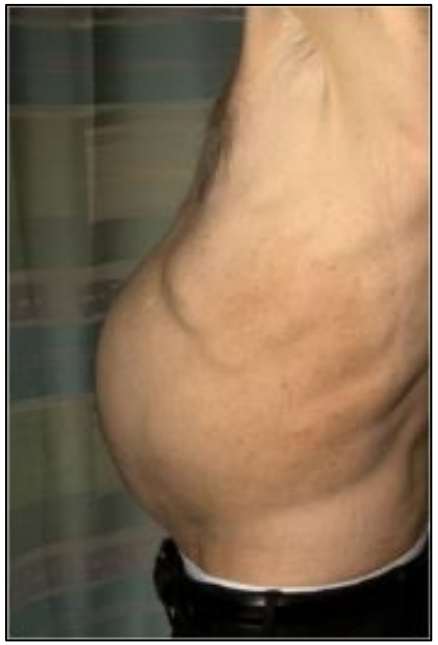
MF, myelofibrosis
PV, polycythemia vera
ET, essential thrombocythemia
CML, chronic myeloid leukemia

[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

# Myelofibrosis: Clinical Manifestations[1]

| | |
|---|---|
| **Constitutional symptoms** | Fatigue, weight loss, cachexia, pruritus, night sweats, bone/joint pain, low-grade fever, cough |
| **Marked hepatosplenomegaly** | Early satiety, abdominal discomfort, painful splenic infarcts, portal hypertension, cachexia |
| **Nonhepatosplenic extramedullary hematopoiesis (rare)** | Cord compression, ascites, pulmonary hypertension, pulmonary embolism, lymphadenopathy, skin tumors |
| **Thrombohemorrhagic complications** | |
| **Marked leukocytosis or thrombocytosis; severe anemia, thrombocytopenia, neutropenia; hyperuricemia** | |
| **Increased risk of leukemic transformation** | |



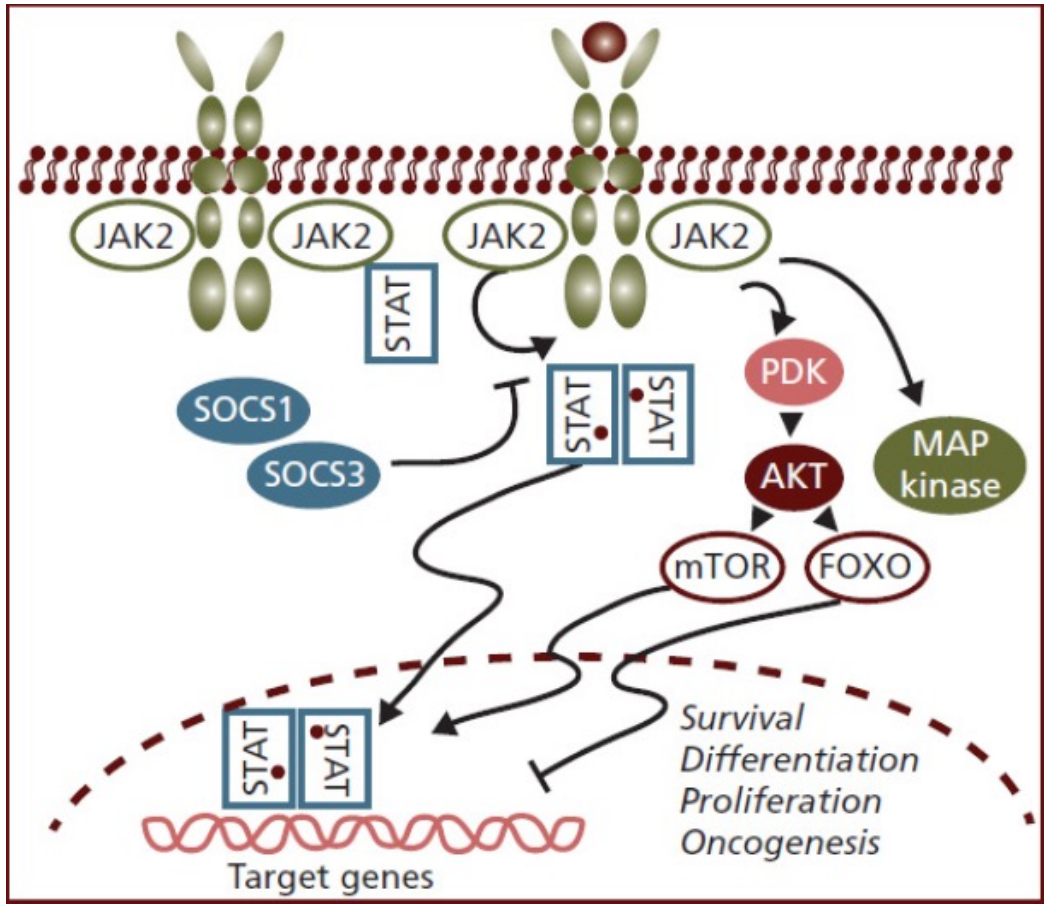
Splenomegaly[2]

1. Barbui T et al. *J Clin Oncol*. 2011;29:761-770. 2. Image provided courtesy of S. Verstovsek.

Courtesy of Rami Komrokji, MD

# JAK-STAT Pathway Constitutively Activated in Myelofibrosis

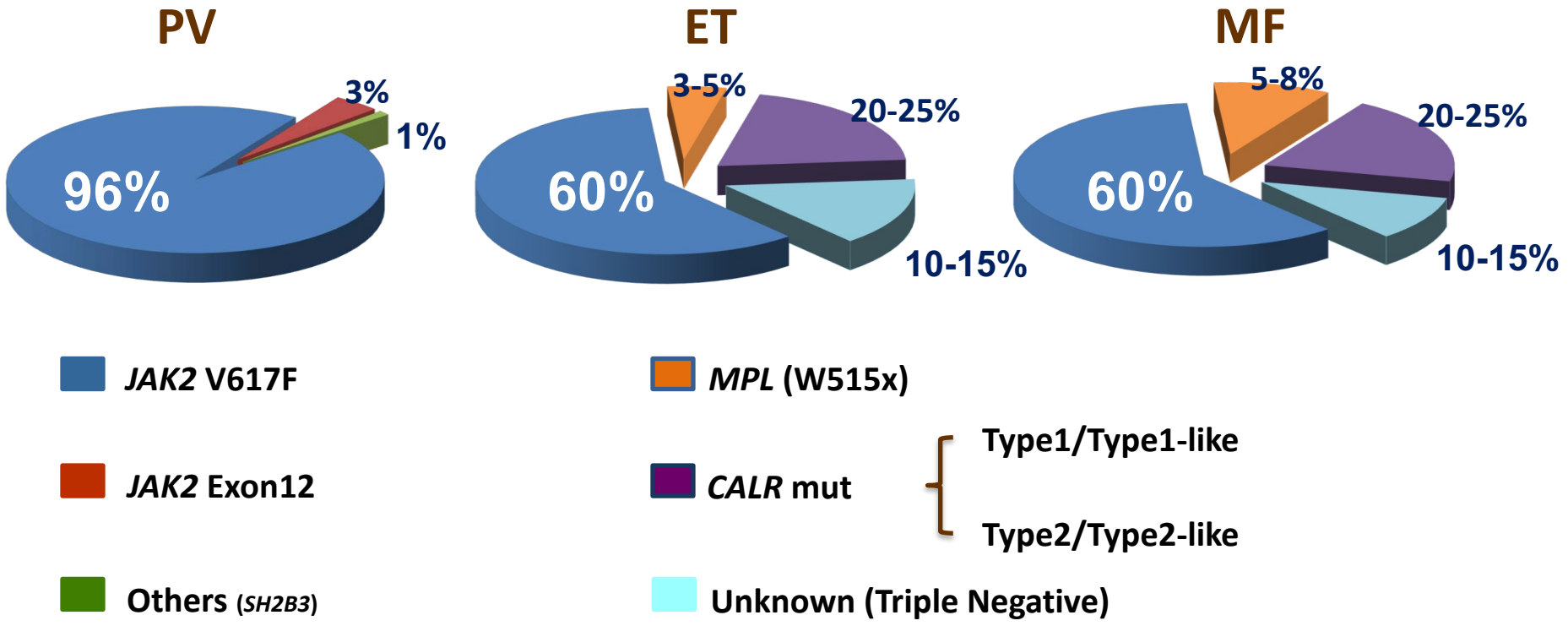
- JAK-STAT pathway implicated in normal hematopoiesis[1]
- An activating mutation in the pseudokinase domain of *Janus kinase 2* (*JAK2*) was identified in approximately 50% of MF patients
- Dysregulation of JAK-STAT, regardless of *JAK* mutation status, is a key pathologic feature of MF and other MPNs[1,2]




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 (they 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

# *Ilene Galinsky, NP*

**What I tell my patients with MF about myeloproliferative neoplasms – how they are defined and diagnosed and the goals of treatment, including allotransplant**

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# Quality of Life in MPNs

* Individualized based on your goals and values
* Optimal symptom management
* Shared decision-making
  * Enhanced by understanding of MPN
* Improved communication

Courtesy of Sara M Tinsley-Vance, PhD, APRN, AOCN

## Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS)

| Symptom | 1 to 10 (0 if absent) ranking<br>1 is most favorable and 10 least favorable |
|---|---|
| Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during past 24 hours* | (No Fatigue) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |

| Circle the one number that describes how, during the past week how much difficulty you have had with each of the following symptoms | |
|---|---|
| Filling up quickly when you eat (Early satiety) | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |
| Abdominal discomfort | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |
| Inactivity | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |
| Problems with concentration – Compared to prior to my MPD | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |
| Numbness/Tingling (in my hands and feet) | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |
| Night sweats | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |
| Itching (pruritus) | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |
| Bone pain (diffuse not joint pain or arthritis) | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |
| Fever (>100 F) | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Daily) |
| Unintentional weight loss last 6 months | (Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable) |

* Question used with permission from the MD Anderson Cancer Center Brief Fatigue Inventory ©

**About this form**

The article describes the development and use of this form as published in the November 20, 2012 edition of the *Journal of Clinical Oncology*.

Incyte

- You are a key member of your healthcare team
- Assist your healthcare team in recognition and evaluation of your symptoms
- This tool can help you evaluate how symptoms change over time
- Discuss your symptoms with your healthcare team and focus on how it affects your normal routine

Emanuel, R.M., Dueck, A.C., Geyer, H.L., Kiladjian, J.J., Slot,S., Zweegman, S., te Boekhorst, P.A., … Mesa. R.A. (2012).Myeloproliferative neoplasm (MPN) symptom assessment form total symptom score: prospective international assessment of an abbreviated symptom burden scoring system among patient with MPNs. Journal of Clinical Oncology, 30(33), 4098–4103.

Courtesy of Sara M Tinsley-Vance, PhD, APRN, AOCN

# Identify Goals of Treatment

- Individualized to what is most important to you
- Improve symptoms and overall quality of life
  - Fatigue
  - Concentration Problems
  - Early Satiety
  - Inactivity
  - Night Sweats
  - Pruritus (Itching)
  - Bone Pain
  - Abdominal Discomfort
  - Weight Loss
  - Fever
- Reduction in spleen size
- Delay progression of MPN to later stages of disease and transformation to acute myelogenous leukemia
- Sometimes cure is the goal through allogeneic transplant

Emanuel, R.M., Dueck, A.C., Geyer, H.L., Kiladjian, J.J., Slot,S., Zweegman, S., te Boekhorst, P.A., … Mesa. R.A. (2012). Myeloproliferative neoplasm (MPN) symptom assessment form total symptom score: prospective international assessment of an abbreviated symptom burden scoring system among patient with MPNs. Journal of Clinical Oncology, 30(33), 4098–4103. Mesa, R.A., Scherber, R.M., & Geyer, H.L. (2015). Reducing symptom burden in patients with myeloproliferative neoplasms in the era of Janus kinase inhibitors. Leukemia & Lymphoma, 56(7), 1989–1999.

Courtesy of Sara M Tinsley-Vance, PhD, APRN, AOCN

# Anemia Management

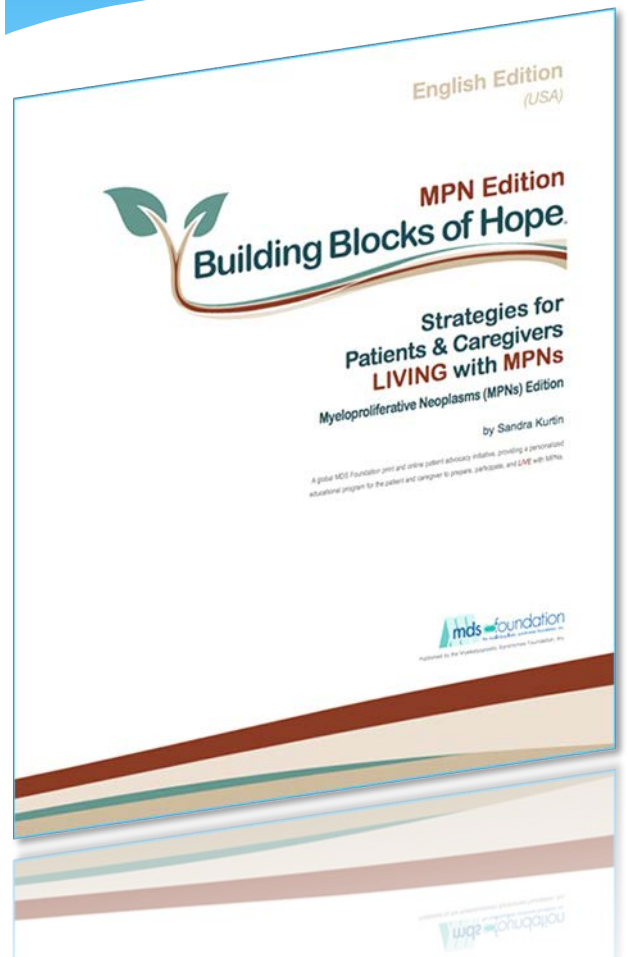
* Monitor complete blood count
* Recognize  symptoms of anemia (increasing fatigue, shortness of breath)
* Communicate symptoms to healthcare team – could be related to anemia
* Review medications at each visit
* Consider other  causes of anemia aside from myelofibrosis (bleeding, nutrition, worry)
* Transfuse  as needed to minimize impact of anemia on quality of life
* Involve your support team in education

Fowkles , Sabrina et al. Myeloproliferative neoplasms (MPNs) – Part 2: A nursing guide to managing the symptom burden of MPNs. Canadian Oncology Nursing Journal / Revue canadienne de soins infirmiers en oncologie, [S.l.], v. 28, n. 4, p. 276-281, Oct. 2018. ISSN 2368-8076. Available at:

<http://canadianoncologynursingjournal.com/index.php/conj/article/view/931>. Date accessed: 19 Mar. 2020.

Courtesy of Sara M Tinsley-Vance, PhD, APRN, AOCN

# Strategies to Improve Understanding




* Written communication reinforces verbal communication
  * *These are complicated diseases that are difficult to explain to others*
* *Online Resources*
  * *MDS Foundation Building Blocks of Hope MPN Edition*
  * *Voices of MPN*
  * *MPN Research*
  * *Leukemia and Lymphoma Society -MPN*

Courtesy of Sara M Tinsley-Vance, PhD, APRN, AOCN

# Agenda

Introduction

Module 1: Biology of Myelofibrosis (MF)

**Module 2: Role of Available and Investigational JAK inhibitors in the Management of MF**

Module 3: Promising Agents and Strategies for Patients with MF

# The Role of Ruxolitinib in Therapy for MF

**Dr Kuykendall**
Tampa, Florida

**Dr Yacoub**
Westwood, Kansas

- **Published research database with ruxolitinib for patients with intermediate- and high-risk MF; impact on symptom control and survival**
- **Common side effects and toxicities associated with ruxolitinib, such as thrombocytopenia, anemia, neutropenia and infection; appropriate monitoring of blood counts**
- **Initial dosing of ruxolitinib and dose-modification strategies for patients with treatment-related toxicity, preexisting thrombocytopenia or inadequate initial response**
- **Importance of gradual tapering versus abrupt discontinuation of ruxolitinib**

# Ruxolitinib

## Mechanism of action

- Janus-associated kinase (JAK) 1/2 inhibitor

## Indication in myelofibrosis

- For the treatment of intermediate- or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera (PV) myelofibrosis and post-essential thrombocythemia (ET) myelofibrosis in adults

## Recommended dosing for myelofibrosis

- Starting dose based on patient's baseline platelet count:
  - Greater than 200 x $10^9$/L: 20 mg given orally twice daily
  - 100 x $10^9$/L to 200 x $10^9$/L: 15 mg given orally twice daily
  - 50 x $10^9$/L to less than 100 x $10^9$/L: 5 mg given orally twice daily
- Monitor complete blood counts every 2 to 4 weeks until doses are stabilized, and then as clinically indicated. Modify or interrupt dosing for thrombocytopenia.

Ruxolitinib package insert, 1/2023.

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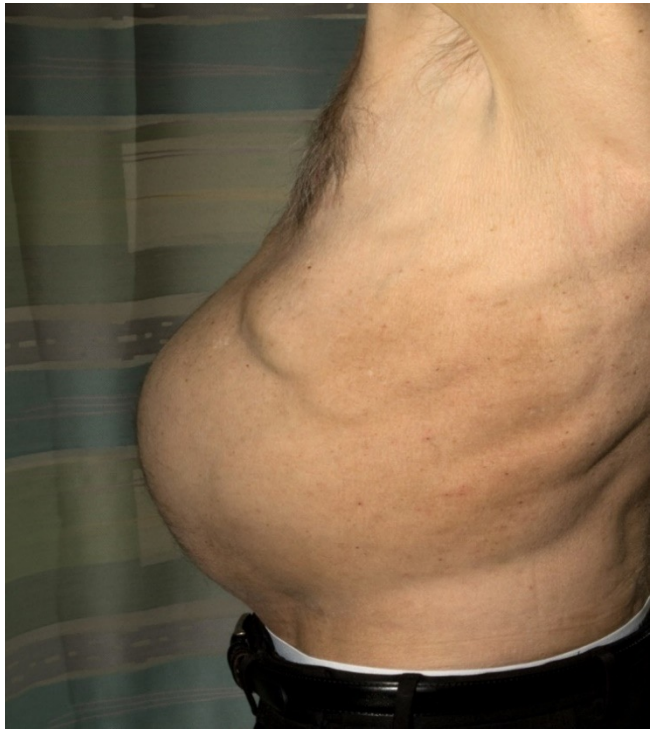
# JAK Inhibitor Specificities

| 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 |

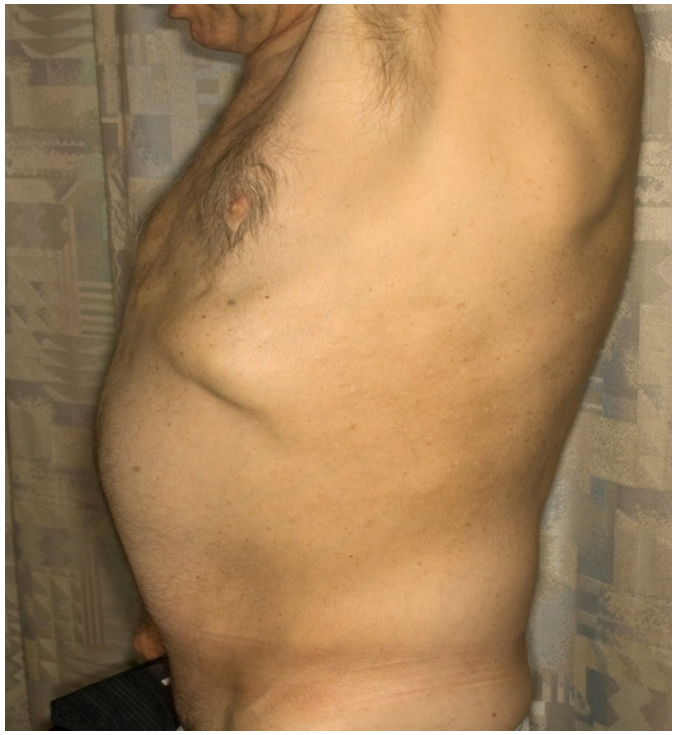
CSF1R, colony stimulating factor 1 receptor; FLT, FMS-like tyrosine kinase; IRAK, interleukin-1 receptor-associated kinase; ITD, internal tandem duplication; TYK, tyrosine kinase.
Singer J, et al. *Blood.* 2014;124:1874; Mascarenhas JO, et al. *Haematologica.* 2017;102:327-335. Jadwiga J. et al. *Blood.*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

Courtesy of John O Mascarenhas, MD.

# What Does Ruxolitinib Do?



**Patient Before Ruxolitinib Therapy**



**After 2 Months of Therapy**

***It is good for spleen and symptoms***

Courtesy of Rami Komrokji, MD

2012;366:799-807

The NEW ENGLAND JOURNAL of MEDICINE

**COMFORT-I**

ORIGINAL ARTICLE

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

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

The NEW ENGLAND JOURNAL of MEDICINE

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

**COMFORT-II**

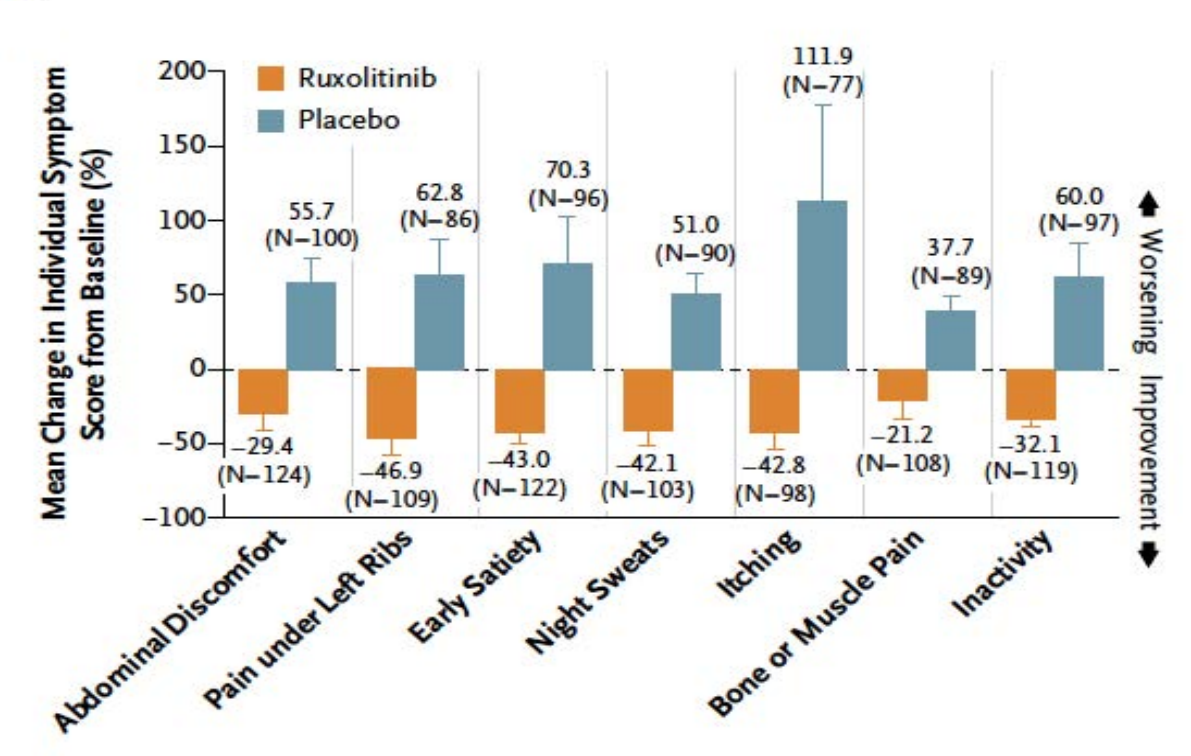
# JAK Inhibition with Ruxolitinib versus Best Available Therapy for Myelofibrosis

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

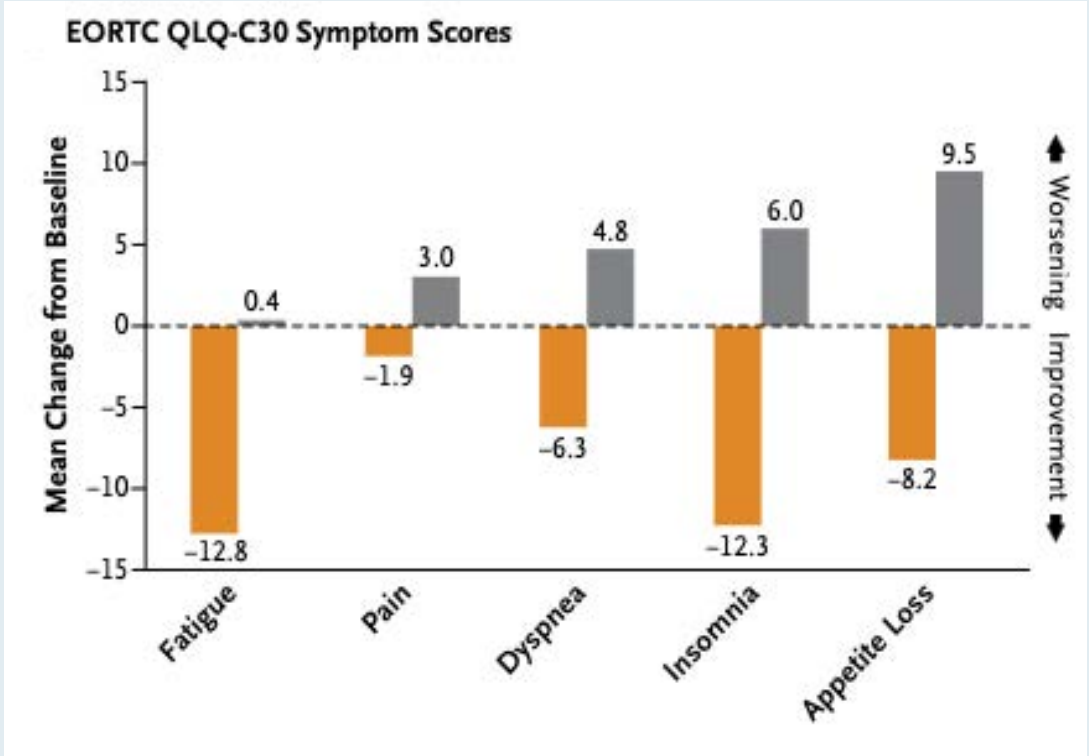
RTP RESEARCH TO PRACTICE

# COMFORT-I and COMFORT-II: Symptom Responses with Ruxolitinib

## COMFORT-I




## COMFORT-II




Verstovsek S et al. *New Engl J Med* 2012;366:799. Harrison C et al. *New Engl J Med* 2012;366:787.

RTP RESEARCH TO PRACTICE

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

Journal of Hematology & Oncology

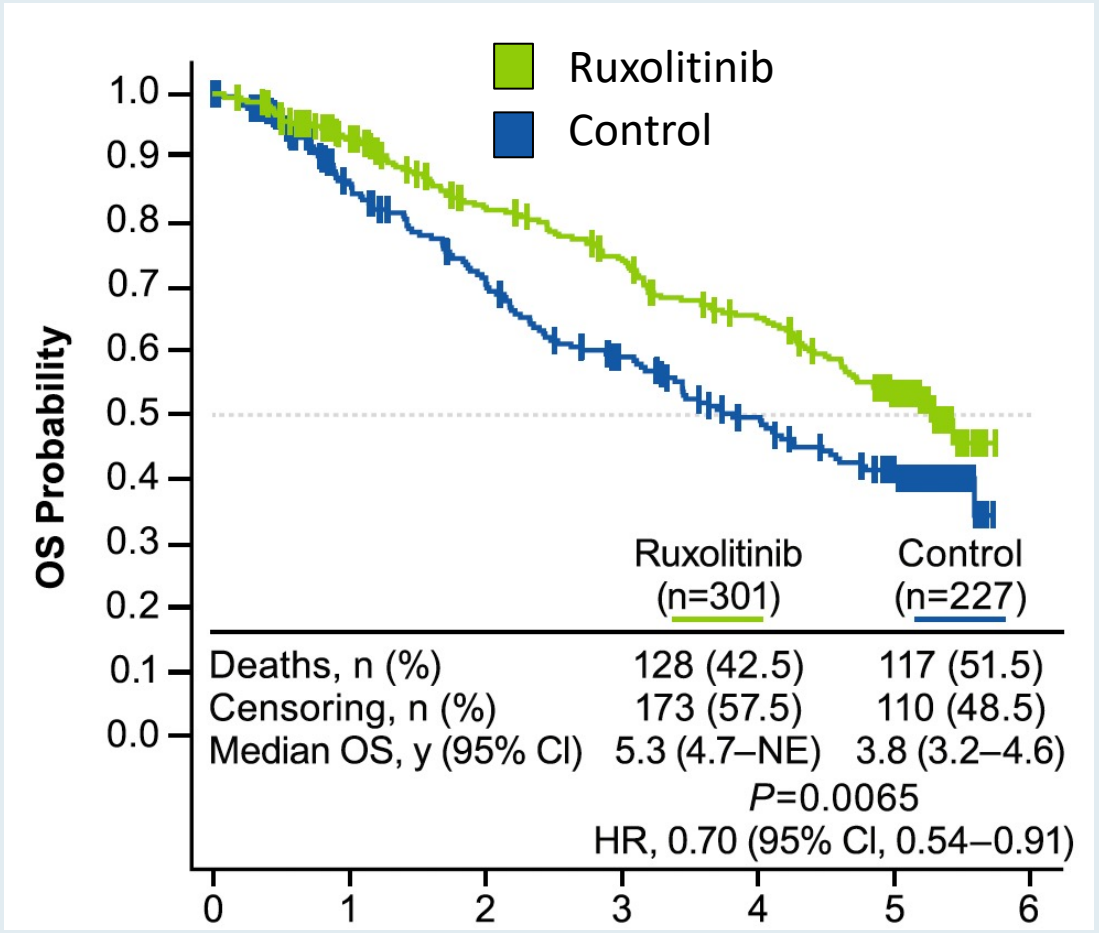
RESEARCH Open Access

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

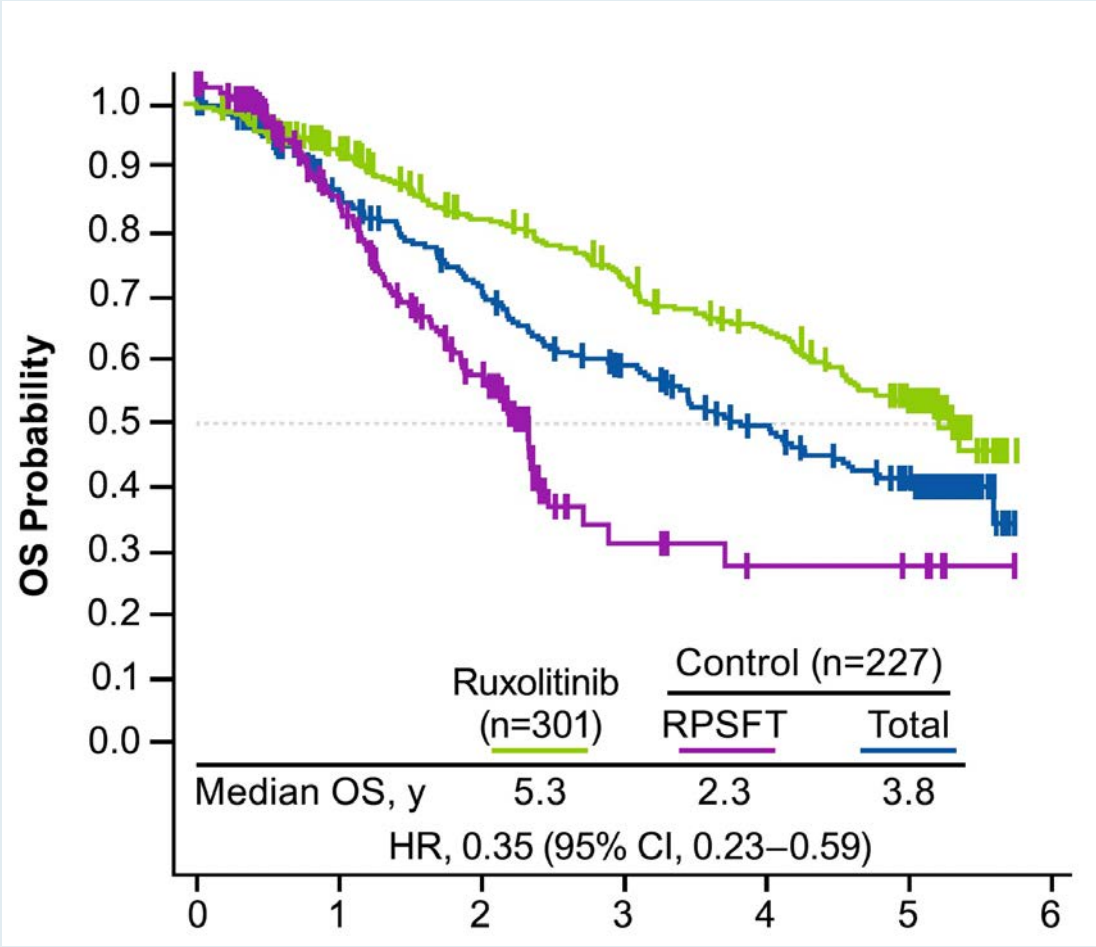
Srdan Verstovsek[1*], Jason Gotlib[2], Ruben A. Mesa[3], Alessandro M. Vannucchi[4], Jean-Jacques Kiladjian[5], Francisco Cervantes[6], Claire N. Harrison[7], Ronald Paquette[8], William Sun[9], Ahmad Naim[9], Peter Langmuir[9], Tuochuan Dong[10], Prashanth Gopalakrishna[11] and Vikas Gupta[12]

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

## OS (5-year ITT population)




## OS (corrected for crossover)




OS = overall survival; ITT = intention to treat

Verstovsek S et al. *J Hematol Oncol* 2017;10:156.

RTP RESEARCH TO PRACTICE

# *Sara M Tinsley-Vance, PhD, APRN, AOCN*

**What I tell my patients who are about to begin treatment with ruxolitinib**

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# Fedratinib in the Management of MF

**Dr Kuykendall**
Tampa, Florida

**Dr Yacoub**
Westwood, Kansas

- **Mechanistic similarities and differences between fedratinib and ruxolitinib**
- **Efficacy and safety outcomes reported in key studies of fedratinib for newly diagnosed or previously treated MF; selection of patients for fedratinib therapy**
- **Incidence of encephalopathy with fedratinib; assessment of thiamine levels and thiamine supplementation for patients receiving this agent**
- **Rates of gastrointestinal (GI) adverse events reported with fedratinib; early implementation of mitigation strategies to prevent GI toxicity**
- **Spectrum, frequency and severity of other toxicities associated with fedratinib; optimal approach to monitoring and management**

# Fedratinib

## Mechanism of action

- JAK2 and FLT3 inhibitor

## Indication

- For patients with intermediate-2 or high-risk primary or secondary (post-PV or post-ET) MF

## Recommended dosing

- 400 mg PO once daily with or without food for patients with a baseline platelet count greater than or equal to 50 x $10^9$/L
- Reduce dose for patients taking strong CYP3A inhibitors or with severe renal impairment

Fedratinib package insert, 5/2023.

# 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.

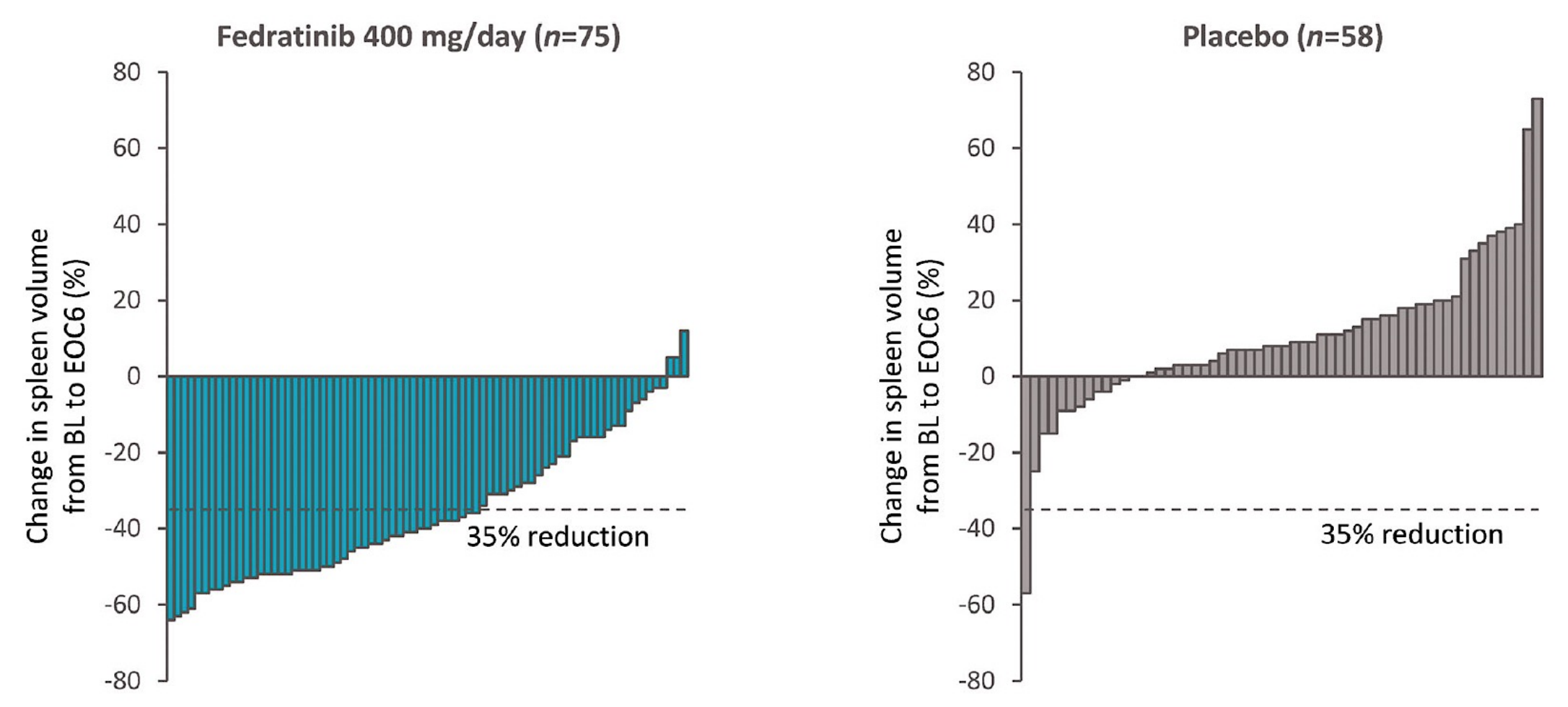
bjh short report

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

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

*Br J Haematol* 2021;195:244-8

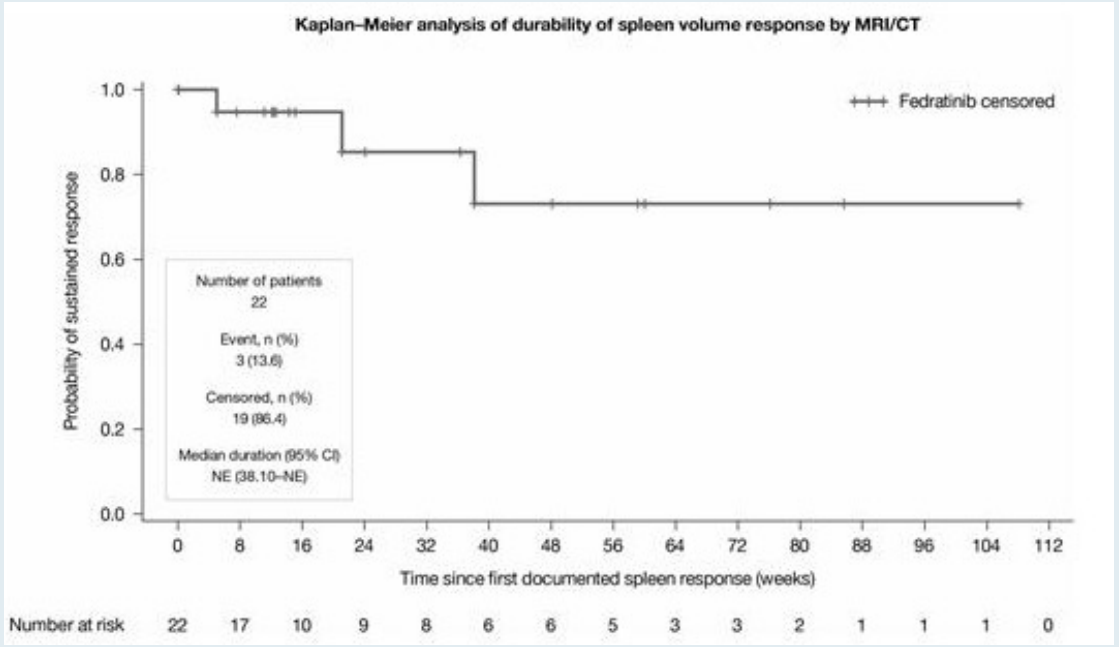
# JAKARTA: Change in Spleen Volume from Baseline to End of Cycle 6

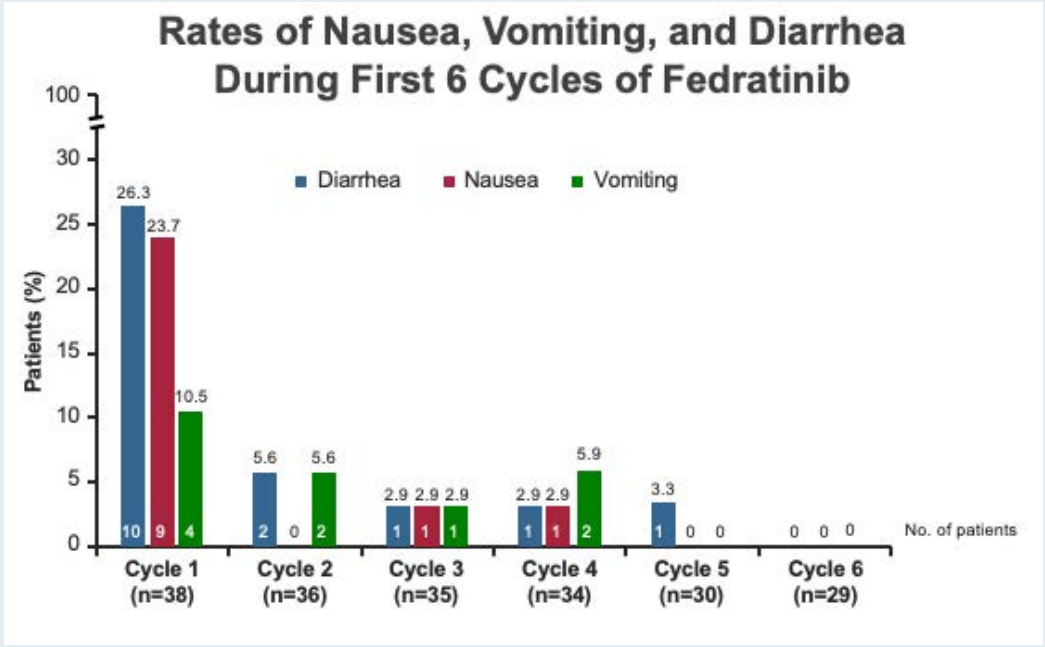



Pardanani A et al. *Br J Haematol* 2021;195:244-8.

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

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




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

Gupta V et al. ASH 2022;Abstract 1711.

RTP RESEARCH TO PRACTICE

# JAKARTA: Selected Adverse Events

| | Fedratinib 400 mg (n = 96) | | Placebo (n = 95) | |
|---|---|---|---|---|
| **Adverse events** | **All grades** | **Grade ≥3** | **All grades** | **Grade ≥3** |
| Diarrhea | 66% | 5% | 16% | 0 |
| Nausea | 62% | 0 | 15% | 0 |
| Anemia | 40% | 30% | 14% | 7% |
| Vomiting | 39% | 3.1% | 5% | 0 |
| Fatigue | 19% | 5% | 16% | 1.1% |
| **Laboratory parameters** | | | | |
| Anemia | 74% | 34% | 32% | 10% |
| Thrombocytopenia | 47% | 12% | 26% | 10% |
| Neutropenia | 23% | 5% | 13% | 3.3% |
| **Biochemistry** | | | | |
| Lipase increased | 35% | 10% | 7% | 2.2% |

No patient receiving fedratinib 400 mg/day experienced Wernicke encephalopathy

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

# Fedratinib Warning: Encephalopathy, Including Wernicke

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

Fedratinib package insert, May 2023.

RTP RESEARCH TO PRACTICE

# *Ilene Galinsky, NP*

**What I tell my patients who are about to begin treatment with fedratinib**

RTP
RESEARCH
TO PRACTICE

# The Role of Pacritinib in MF Treatment

**Dr Kuykendall**
Tampa, Florida

**Dr Yacoub**
Westwood, Kansas

- **Implications of the mechanistic differences between pacritinib and other approved JAK inhibitors for its safety in cytopenic patients**
- **Key efficacy and safety findings with pacritinib for MF, including for patients with baseline thrombocytopenia**
- **FDA approval of pacritinib for patients with MF and severe thrombocytopenia; optimal use in clinical practice and ongoing investigations**
- **Potential utility of pacritinib for patients with MF and severe anemia**
- **Reported risk of hemorrhage and other adverse events with pacritinib; importance of holding therapy before planned surgical and invasive procedures**

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RESEARCH
TO PRACTICE

# JAK Inhibitor Specificities

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|---|---|---|---|---|
| Kinase | Pacritinib | Ruxolitinib | Fedratinib | Momelotinib |
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| *CSF1R* | 39.5 | >3000 | 220 | – |
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CSF1R, colony stimulating factor 1 receptor; FLT, FMS-like tyrosine kinase; IRAK, interleukin-1 receptor-associated kinase; ITD, internal tandem duplication; TYK, tyrosine kinase.
Singer J, et al. *Blood.* 2014;124:1874; Mascarenhas JO, et al. *Haematologica.* 2017;102:327-335. Jadwiga J. et al. *Blood.* 2018 132 (Supplement 1): 2559. Duenas-Perez AB et al. *Ther Adv Hematol.* 2015: 186-201

Courtesy of John O Mascarenhas, MD

# Pacritinib

## Mechanism of action

- Oral inhibitor of JAK2, FLT3 and IRAK1 kinases

## Indication

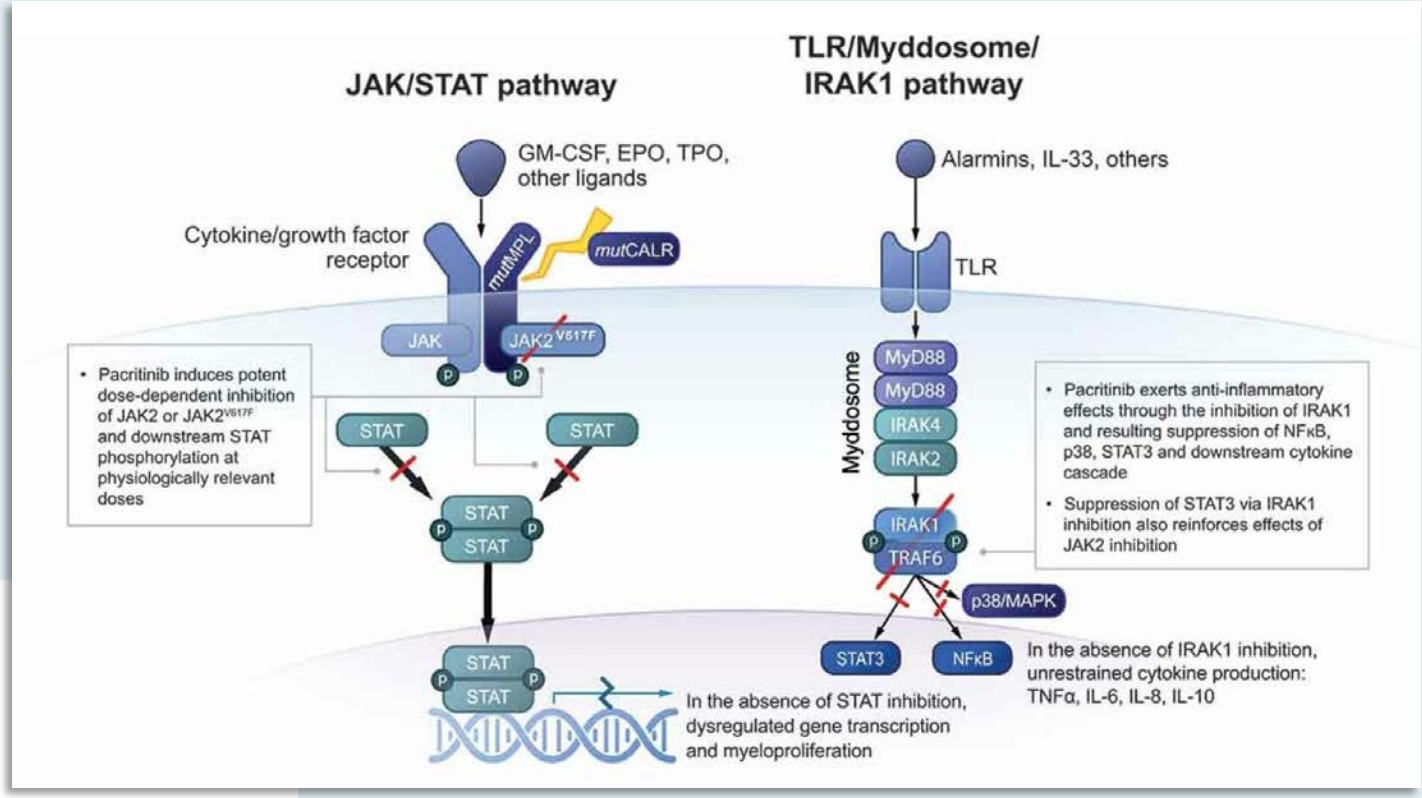
- For patients with intermediate or high-risk primary or secondary (post-PV or post-ET) myelofibrosis with a platelet count below 50 x $10^9$/L

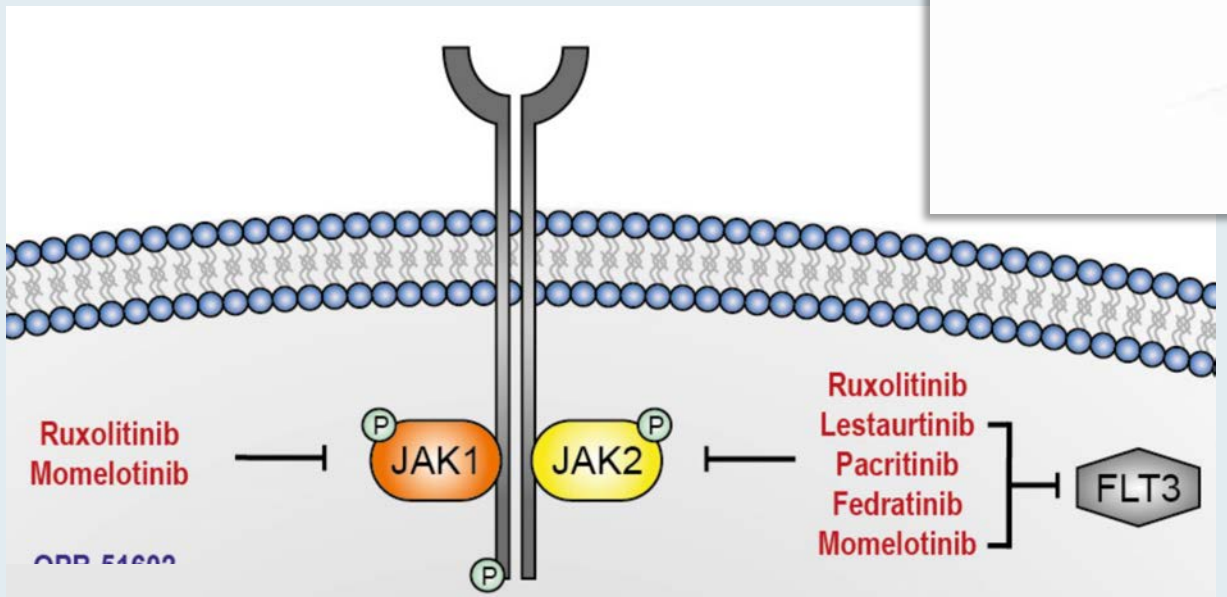
## Recommended dosing

- 200 mg PO BID, with or without food

Pacritinib package insert, 8/2023.

# Pacritinib Mechanism of Action: JAK2/FLT3/IRAK1 Inhibitor




Mascarenhas J. *Expert Rev Hematol* 2022;15(8):671-84. Moser B et al. *Biomedicines* 2021;9(8):1051.

RTP RESEARCH TO PRACTICE

Research

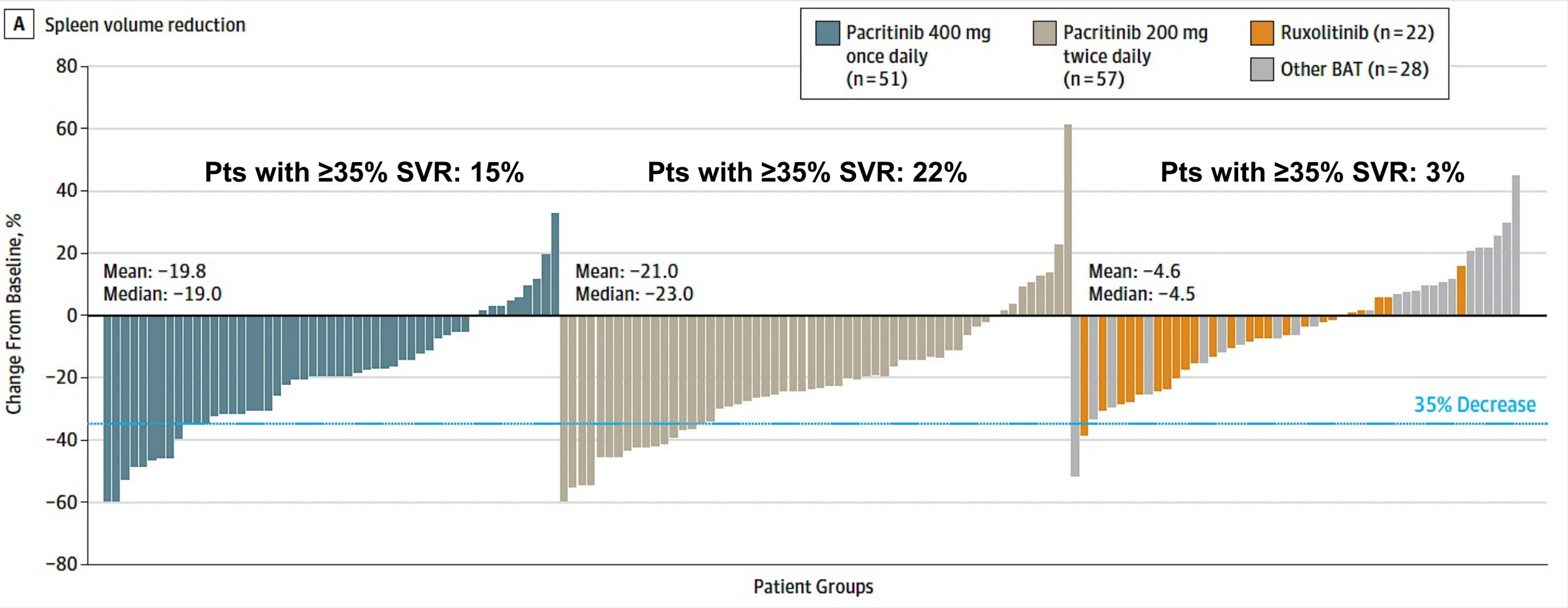
2018;4(5):652-9

JAMA Oncology | Original Investigation

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

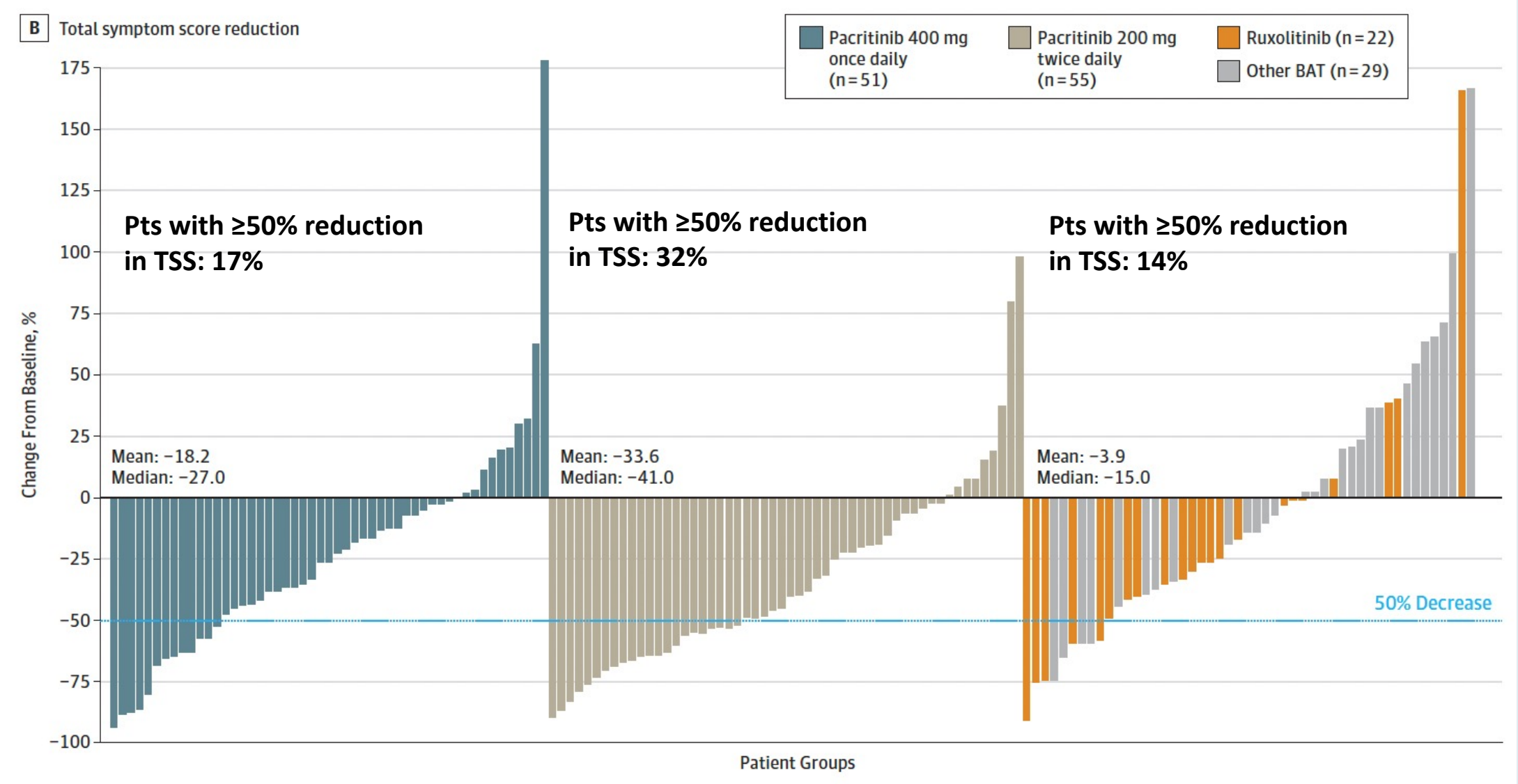
John Mascarenhas, MD; Ronald Hoffman, MD; Moshe Talpaz, MD; Aaron T. Gerds, MD; Brady Stein, MD; Vikas Gupta, MD, FRCP, FRCPath; Anita Szoke, MD; Mark Drummond, MBChB, PhD, FRCPath; Alexander Pristupa, MD; Tanya Granston, PhD; Robert Daly, PhD; Suliman Al-Fayoumi, PhD; Jennifer A. Callahan, MS; Jack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

# PERSIST-2 Trial: Spleen Volume Reduction (SVR)




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

# PERSIST-2: Reduction in Total Symptom Score (TSS)




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

# PERSIST-2: Adverse Event Profile of Pacritinib

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

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

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

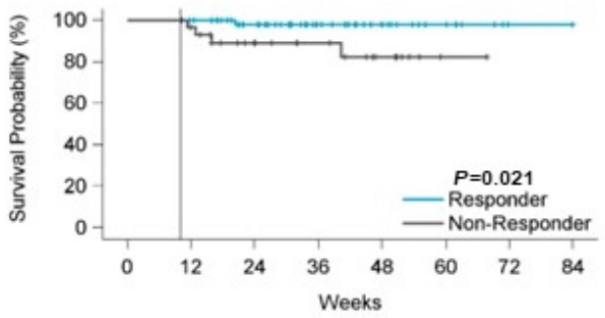
Ajufo H et al.

ASH 2023;Abstract 3207.

# PERSIST-2: OS Stratified by TSS Response

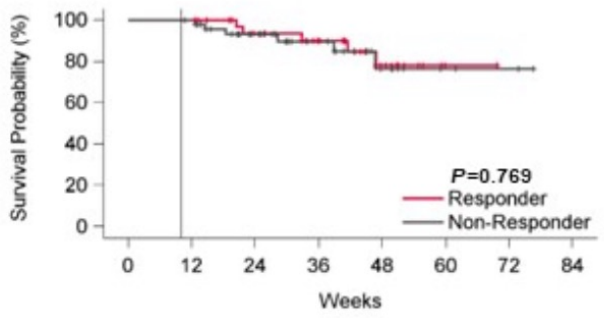
**Figure 1. Landmark survival analysis based on week 12 Total Symptom Score (TSS) reduction.**
Survival stratified by varying thresholds of TSS (v2.0, excluding tiredness) response (≥10%, ≥20%, ≥50%) for pacritinib 200 mg BID (A, C, E) and BAT (B, D, F).

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



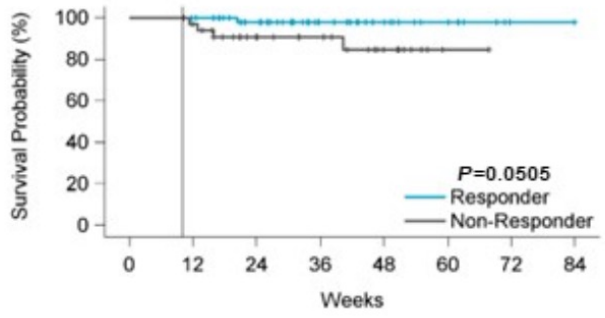

| N | | | | | | | |
|---|---|---|---|---|---|---|---|
| Responder | 59 | 44 | 27 | 15 | 8 | 1 | 0 |
| Non-Responder | 30 | 18 | 14 | 8 | 1 | 0 | 0 |

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



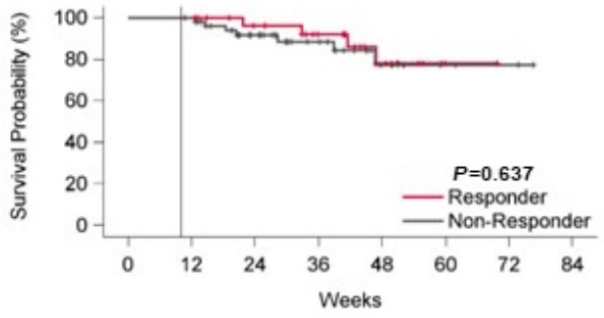

| N | | | | | | | |
|---|---|---|---|---|---|---|---|
| Responder | 36 | 28 | 21 | 10 | 1 | 0 | 0 |
| Non-Responder | 48 | 32 | 20 | 8 | 3 | 2 | 0 |

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



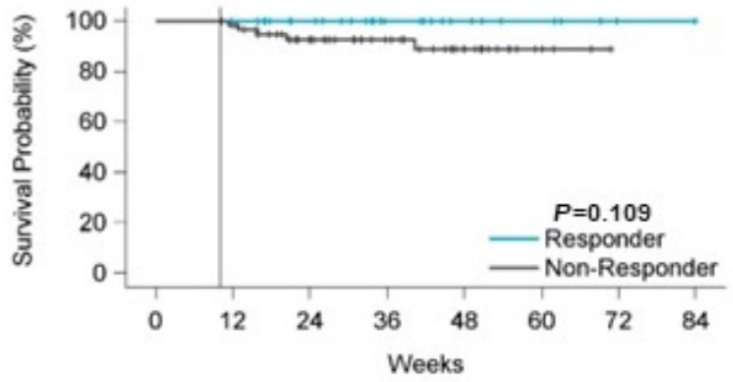

| N | | | | | | | |
|---|---|---|---|---|---|---|---|
| Responder | 54 | 41 | 24 | 14 | 8 | 1 | 0 |
| Non-Responder | 35 | 21 | 17 | 9 | 1 | 0 | 0 |

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



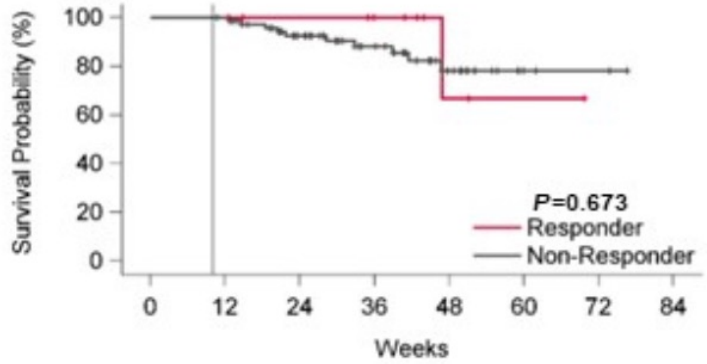

| N | | | | | | | |
|---|---|---|---|---|---|---|---|
| Responder | 31 | 25 | 18 | 9 | 1 | 0 | 0 |
| Non-Responder | 53 | 35 | 23 | 9 | 3 | 2 | 0 |

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




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

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




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

Ajufo H et al. ASH 2023;Abstract 3207.

RTP RESEARCH TO PRACTICE

REGULAR ARTICLE

blood advances

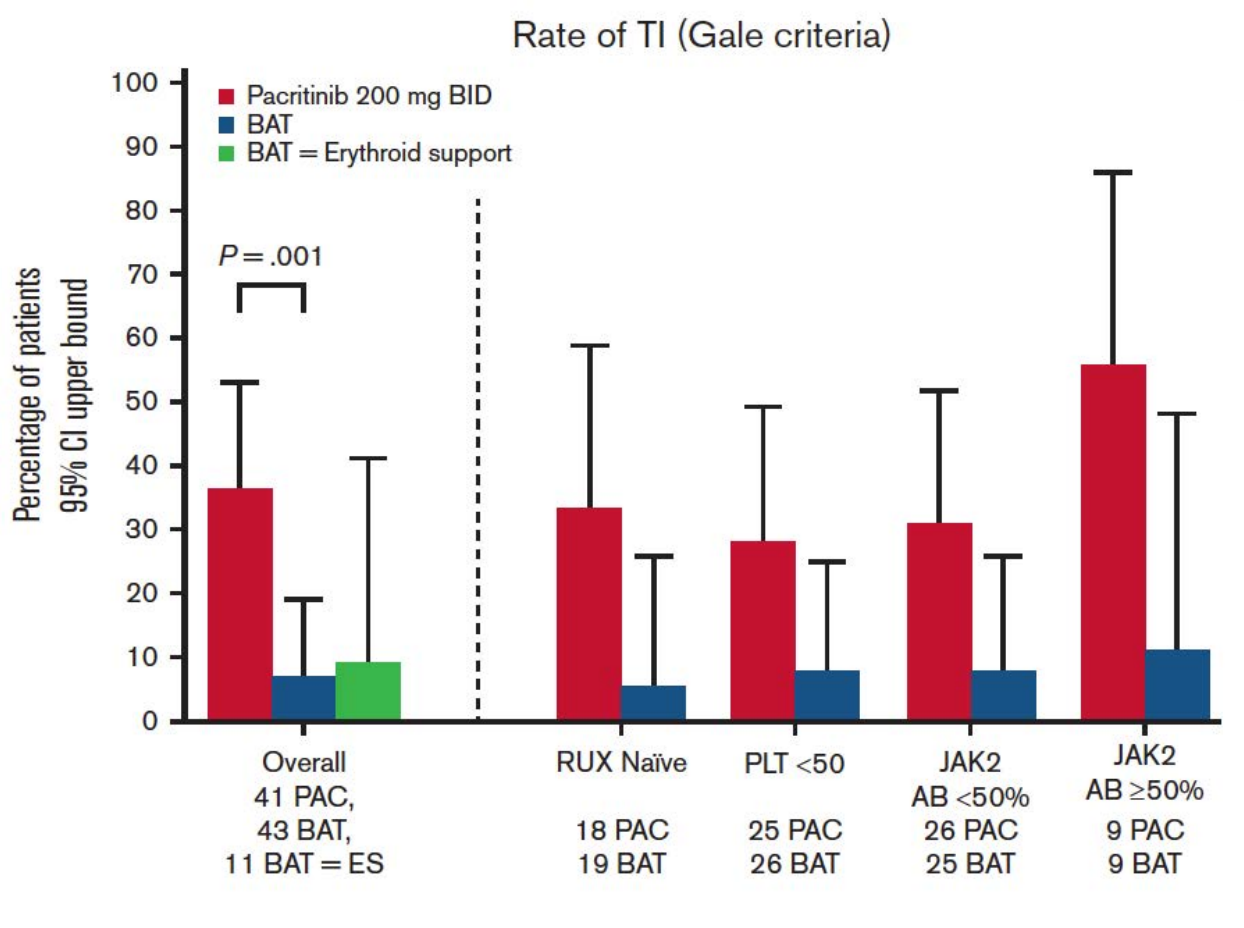
# Pacritinib is a potent ACVR1 inhibitor with significant anemia benefit in patients with myelofibrosis

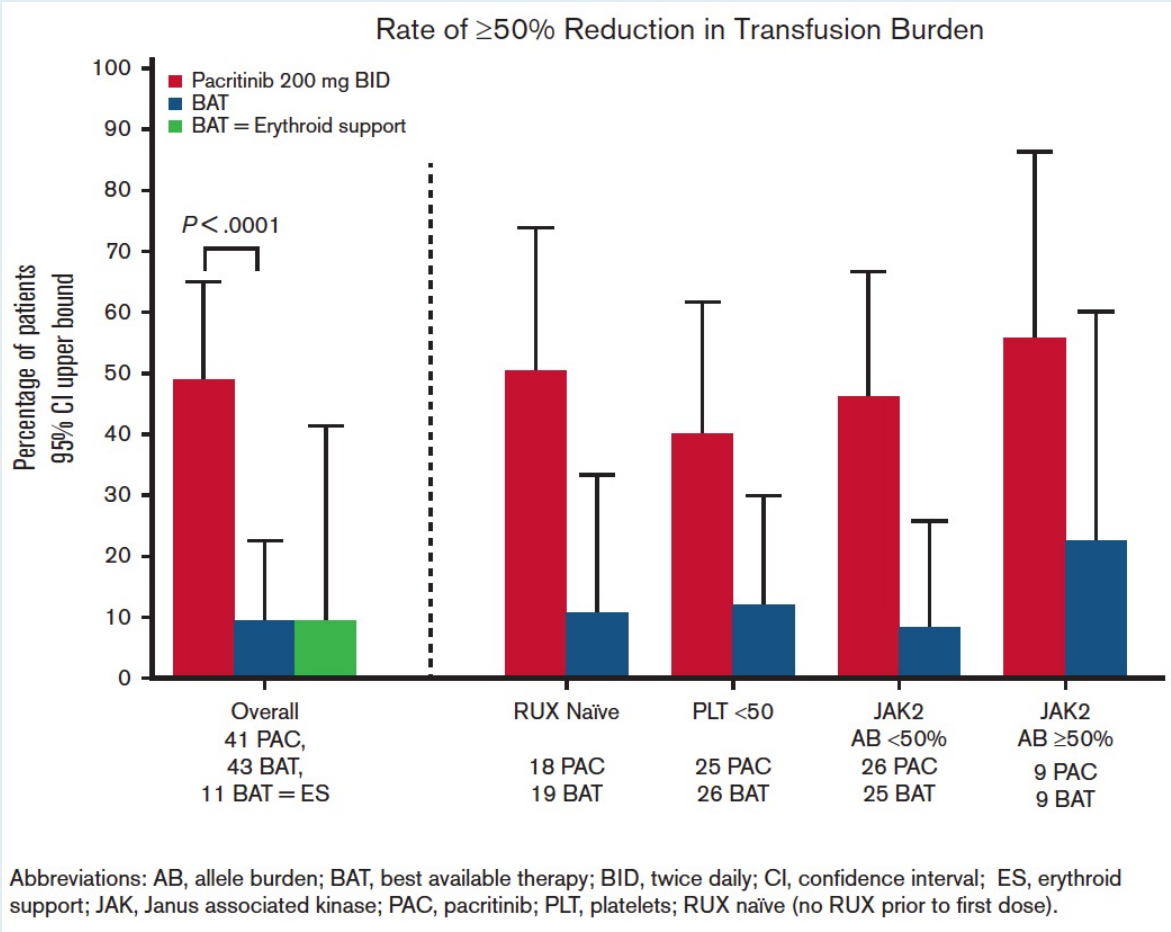
Stephen T. Oh,[1] Ruben A. Mesa,[2] Claire N. Harrison,[3] Prithviraj Bose,[4] Aaron T. Gerds,[5] Vikas Gupta,[6] Bart L. Scott,[7] Jean-Jacques Kiladjian,[8] Alessandro Lucchesi,[9] Tim Kong,[1] Sarah A. Buckley,[10] Shanthakumar Tyavanagimatt,[10] Bryan G. Harder,[10] Karisse Roman-Torres,[10] Jennifer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

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

2023;7(19):5835-42

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




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

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

RTP RESEARCH TO PRACTICE

# *Sara M Tinsley-Vance, PhD, APRN, AOCN*

**What I tell my patients who are about to begin treatment with pacritinib**

RTP
RESEARCH
TO PRACTICE

# The Current Utility of Momelotinib in Therapy for MF

**Dr Kuykendall**
Tampa, Florida

**Dr Yacoub**
Westwood, Kansas

- **Rationale for the activity of momelotinib in patients with MF and anemia**
- **Historical data sets with momelotinib for treatment-naïve and previously treated MF**
- **Key clinical trial findings supporting the FDA approval of momelotinib for symptomatic, anemic patients with MF who have previously received a JAK inhibitor**
- **Tolerability and toxicity profile of momelotinib; recognition and management of commonly occurring adverse events, such as anemia, thrombocytopenia, infections and peripheral neuropathy**

# JAK Inhibitor Specificities

| JAK and FLT3 Kinases $IC_{50}$ (nM) | | | | |
|---|---|---|---|---|
| Kinase | Pacritinib | Ruxolitinib | Fedratinib | Momelotinib |
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Courtesy of John O Mascarenhas, MD

# Momelotinib

## Mechanism of action

- **Highly selective JAK1/2 and activin A receptor, Type 1 (ACVR1) inhibitor**

## Indication

- **For treatment of intermediate or high-risk myelofibrosis, including primary or secondary myelofibrosis (post-PV or post-ET), in adults with anemia**

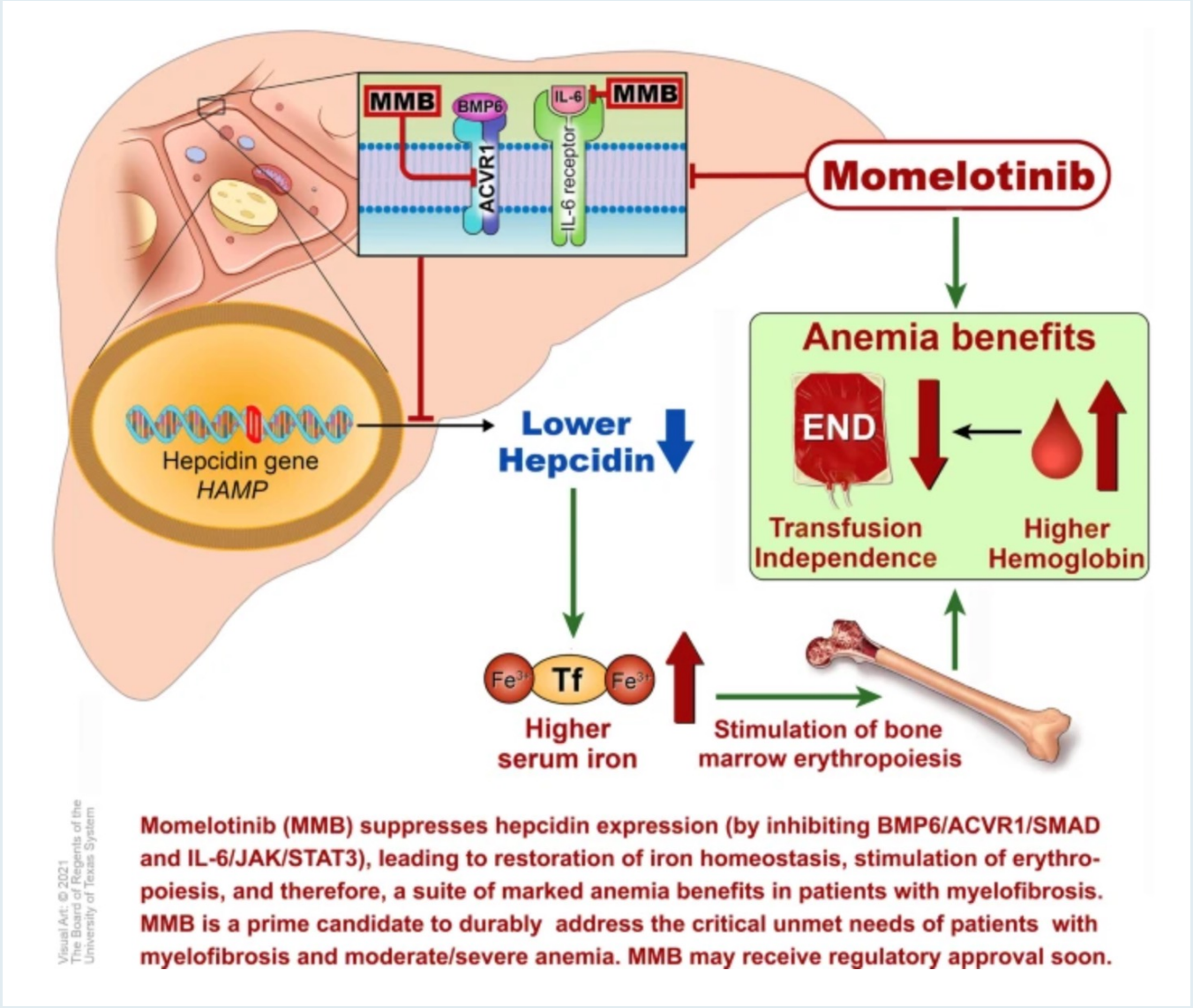
## Recommended dosing

- **200 mg PO once daily, with or without food**
- **Severe hepatic impairment (Child-Pugh class C): Reduce the starting dose to 150 mg PO once daily**

Momelotinib package insert, 9/2023.

RTP RESEARCH TO PRACTICE

# Proposed Mechanism of Momelotinib for MF with Anemia




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

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."

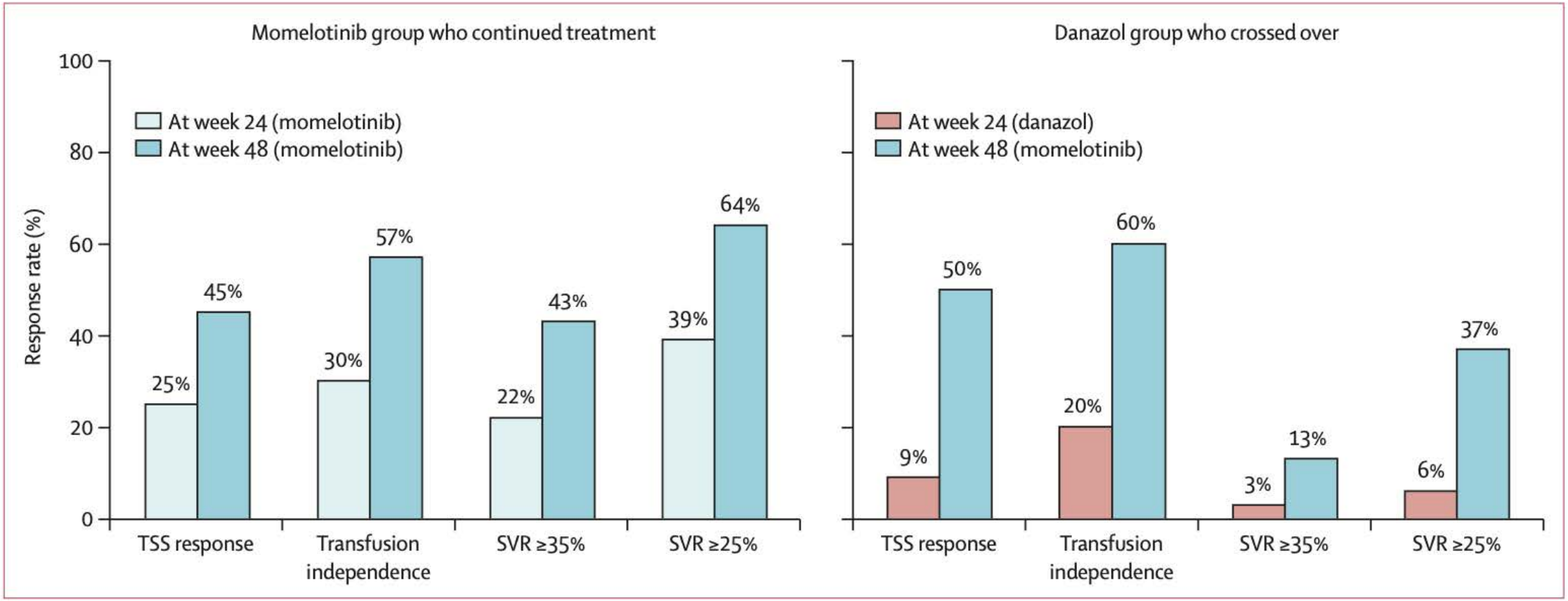
https://ascopost.com/news/september-2023/fda-approves-momelotinib-for-patients-with-myelofibrosis-and-anemia/

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

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

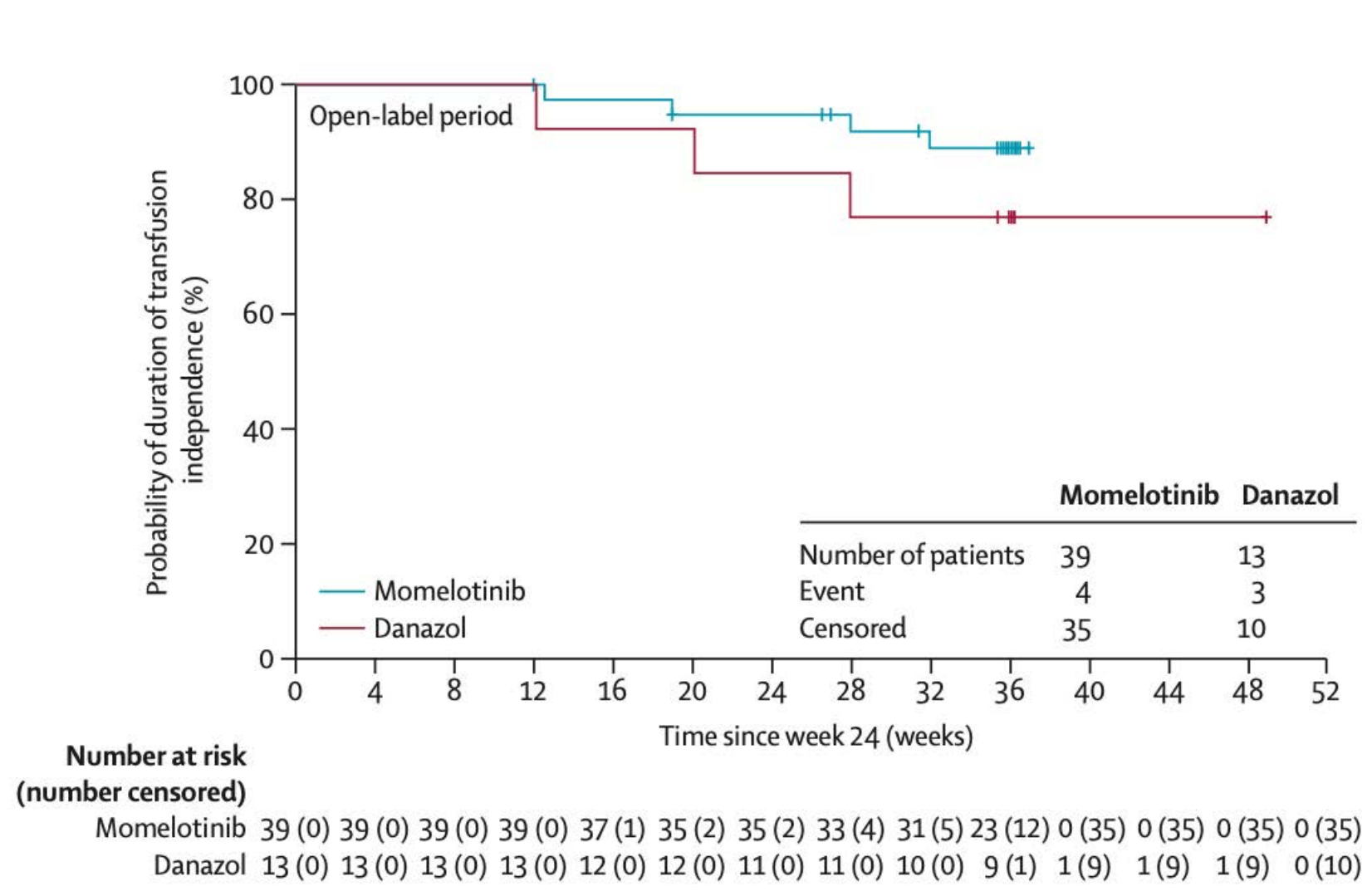
***Lancet Haematol* 2023;10(9):e735-46**

# MOMENTUM: Summary of Response Rates at Weeks 24 and 48




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

# MOMENTUM: Duration of Transfusion Independence Response




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

# MOMENTUM: Treatment-Emergent Adverse Events

| | Momelotinib group (n=130) | | Danazol group (n=65) | |
|---|---|---|---|---|
| | Any grade | Grade ≥3 | Any grade | Grade ≥3 |
| **Non-haematological abnormalities (preferred term)** | | | | |
| Diarrhoea | 29 (22%) | 0 | 6 (9%) | 1 (2%) |
| Nausea | 21 (16%) | 3 (2%) | 6 (9%) | 2 (3%) |
| Asthenia | 17 (13%) | 1 (1%) | 6 (9%) | 1 (2%) |
| Pruritus | 14 (11%) | 2 (2%) | 7 (11%) | 0 |
| Weight decreased | 14 (11%) | 0 | 4 (6%) | 0 |
| Blood creatinine increased | 10 (8%) | 1 (1%) | 10 (15%) | 2 (3%) |
| Dyspnoea | 10 (8%) | 3 (2%) | 9 (14%) | 1 (2%) |
| Peripheral oedema | 10 (8%) | 2 (2%) | 9 (14%) | 0 |
| Fatigue | 8 (6%) | 1 (1%) | 7 (11%) | 2 (3%) |
| Acute kidney injury | 6 (5%) | 4 (3%) | 8 (12%) | 6 (9%) |
| **Haematological abnormalities*** | | | | |
| Anaemia | 129 (99%) | 79 (61%) | 65 (100%) | 49 (75%) |
| Thrombocytopenia | 99 (76%) | 36 (28%) | 40 (62%) | 17 (26%) |
| Neutropenia | 38 (29%) | 16 (12%) | 17 (26%) | 6 (9%) |

Data are n (%). *Haematological abnormalities are based on laboratory values. The data shown are for events of the worst grade during the 24-week randomised treatment phase of the study, regardless of whether this grade was a change from baseline.

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

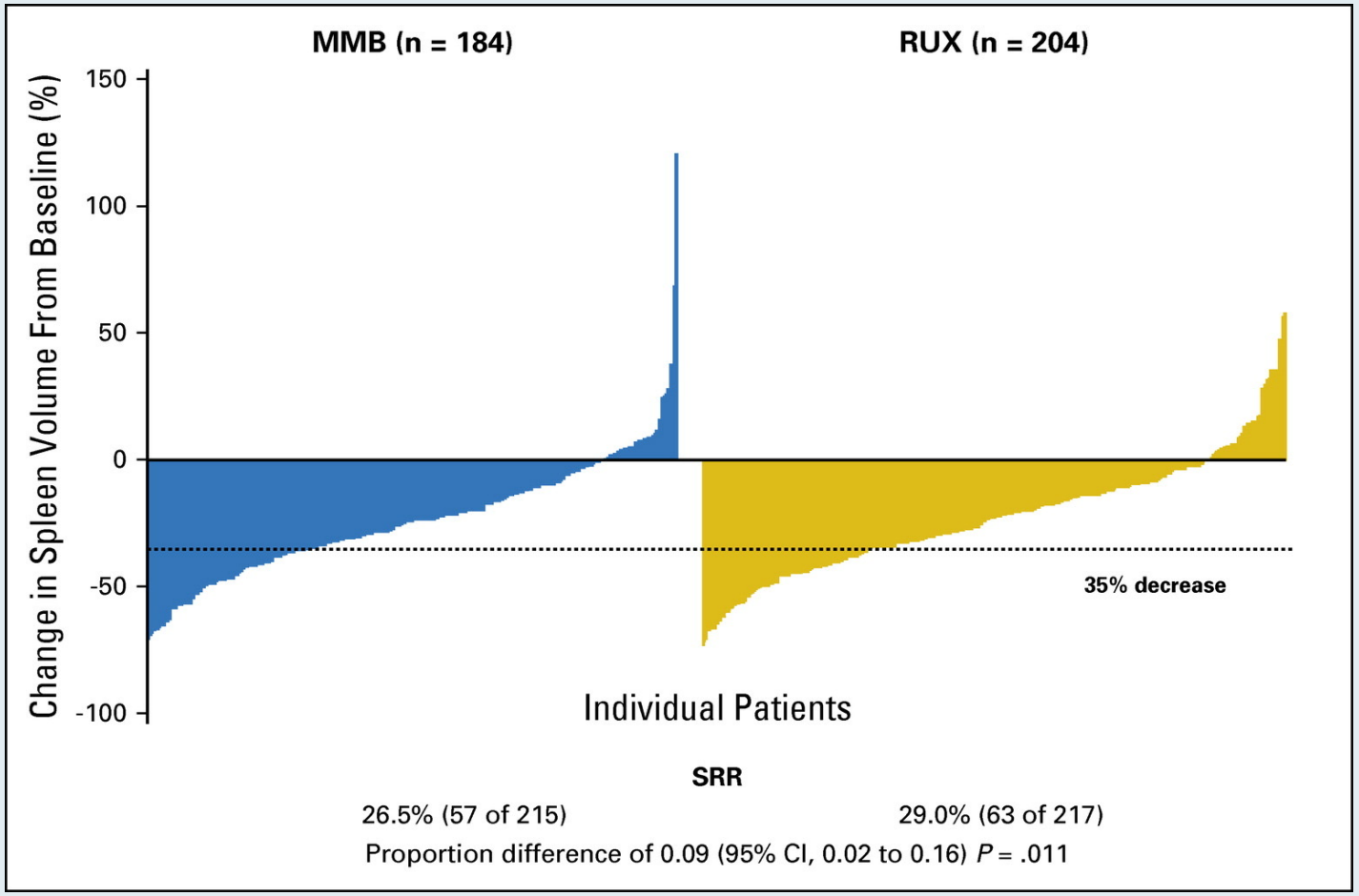
# SIMPLIFY-1: A Phase III Randomized Trial of Momelotinib Versus Ruxolitinib in Janus Kinase Inhibitor–Naïve Patients With Myelofibrosis

**Authors**: Ruben A. Mesa, Jean-Jacques Kiladjian, John V. Catalano, Timothy Devos, Miklos Egyed, Andrzei Hellmann, Donal McLornan, Kazuya Shimoda, Elliott F. Winton, Wei Deng, Ronald L. Dubowy, Julia D. Maltzman, Francisco Cervantes, and Jason Gotlib SHOW FEWER | AUTHORS INFO & AFFILIATIONS

**Publication**: Journal of Clinical Oncology • Volume 35, Number 34

*JCO* 35, 3844-3850(2017)

# SIMPLIFY-1: Primary Endpoint (Change in Spleen Volume)




Mesa RA et al. *JCO* 35, 3844-3850(2017)

# SIMPLIFY-1: Adverse Events

| Treatment-Emergent Adverse Event | Double-Blind Phase | |
|---|---|---|
| | Momelotinib (n = 214) | Ruxolitinib (n = 216) |
| Thrombocytopenia | 40 (18.7) | 63 (29.2) |
| Diarrhea | 38 (17.8) | 43 (19.9) |
| Headache | 37 (17.3) | 43 (19.9) |
| Dizziness | 34 (15.9) | 25 (11.6) |
| Nausea | 34 (15.9) | 8 (3.7) |
| Fatigue | 31 (14.5) | 26 (12.0) |
| Anemia | 29 (13.6) | 82 (38.0) |
| Abdominal pain | 22 (10.3) | 24 (11.1) |

NOTE. Data presented as No. (%).

Mesa RA et al. *JCO* 35, 3844-3850(2017)

# *Ilene Galinsky, NP*

**What I tell my patients who are about to begin treatment with momelotinib**

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# Agenda

Introduction

Module 1: Biology of Myelofibrosis (MF)

Module 2: Role of Available and Investigational JAK inhibitors in the Management of MF

**Module 3: Promising Agents and Strategies for Patients with MF**

# Promising Agents and Strategies for Patients with MF

**Dr Kuykendall**
Tampa, Florida

**Dr Yacoub**
Westwood, Kansas

- **Educating patients on the potential advantages of participating in a clinical research study of a novel strategy**
- **Mechanism of antitumor activity of navitoclax and biological rationale for its evaluation in patients with MF, including in tandem with JAK2 inhibition**
- **Recently presented efficacy and safety findings with navitoclax in combination with ruxolitinib versus ruxolitinib alone for patients with previously untreated MF**
- **Potential role of navitoclax in the up-front setting and ongoing evaluation for relapsed/refractory disease**
- **Tolerability profile of navitoclax in published clinical investigations**

# Promising Agents and Strategies for Patients with MF (Continued)

**Dr Kuykendall**
Tampa, Florida

**Dr Yacoub**
Westwood, Kansas

- **Scientific justification for the inhibition of BET proteins for MF; mechanism of action of pelabresib**
- **Recently presented findings with the combination of pelabresib and ruxolitinib for JAK inhibitor-naïve MF**
- **Early results with and ongoing evaluations of other BET inhibitors, such as INCB057643 and BMS-986158, as monotherapy and in combination with JAK inhibitors**
- **Available data with luspatercept as monotherapy or combined with a JAK2 inhibitor for patients with MF and anemia; current nonresearch role, if any**

**Dr Kuykendall**
Tampa, Florida

# Promising Agents and Strategies for Patients with MF (Continued)

**Dr Yacoub**
Westwood, Kansas

- **Potential role of ACVR1/ALK2 inhibition in alleviating anemia for patients with MF; mechanism of action of zilurgisertib**
- **Preliminary data with and ongoing investigation of zilurgisertib as monotherapy and combined with ruxolitinib for patients with anemia due to MF**
- **Early activity and safety data with and ongoing investigation of other novel agents and strategies for MF, such as imetelstat, navtemadlin, selinexor, bomedemstat and ropeginterferon alfa-2b**

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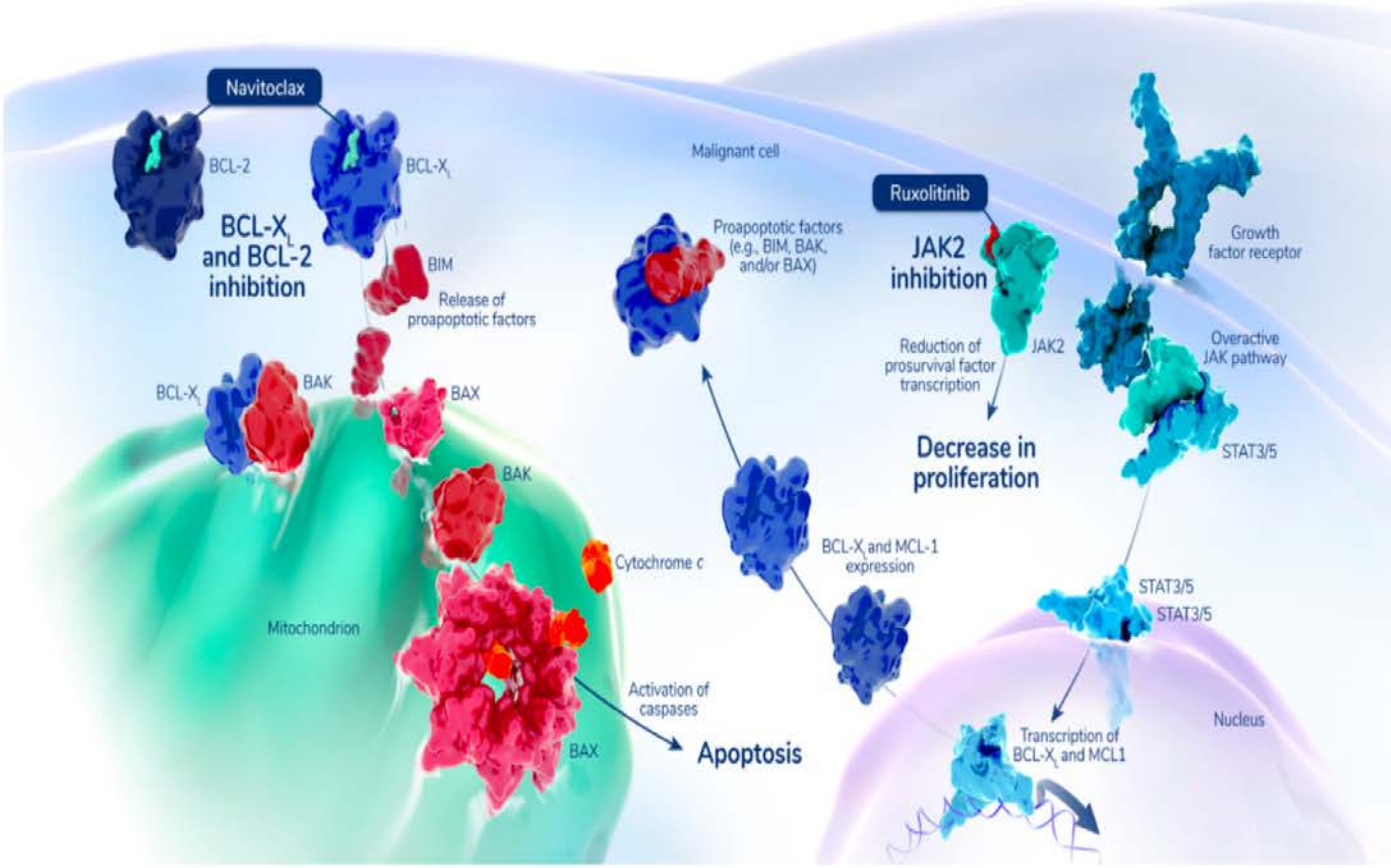
# Navitoclax Mechanism of Action in Myelofibrosis

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

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



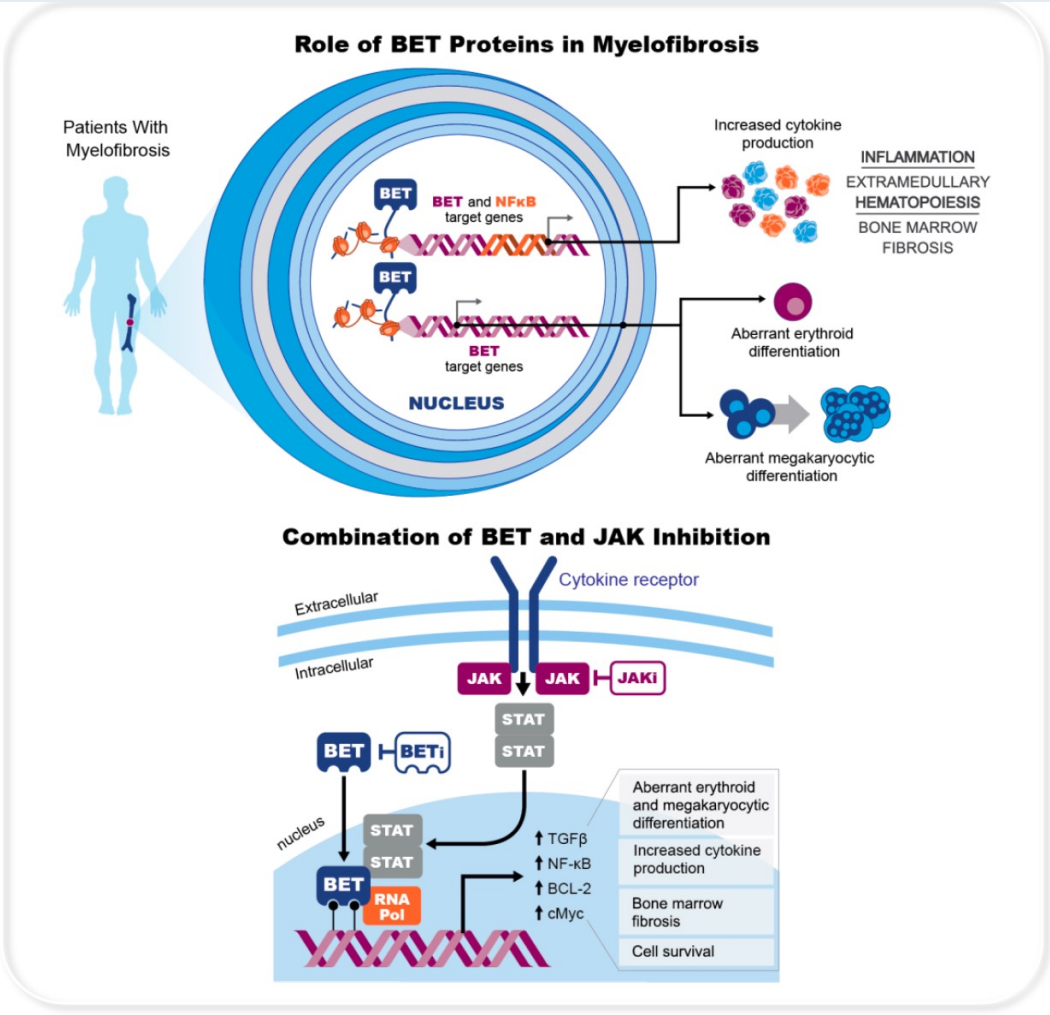



1. Tse C, et al. *Cancer Res*. 2008;68(9):3421–3428; 2. Waibel M, et al. *Cell Rep*. 2013;5:1047–1059; 3. Harrison et al. *J Clin Oncol*. 2022;40:1671–1680.
BCL-$X_L$, B-cell lymphoma-extra large; BCL-2, B-cell lymphoma 2; JAK2, Janus kinase 2; JAKi, Janus kinase inhibitor; MF, myelofibrosis.

Pemmaraju N et al. ASH 2023;Abstract 620.

# Simultaneous Inhibition of BET and JAK in Myelofibrosis

## A Potential Therapeutic Approach to Address Heterogeneous Disease Pathology

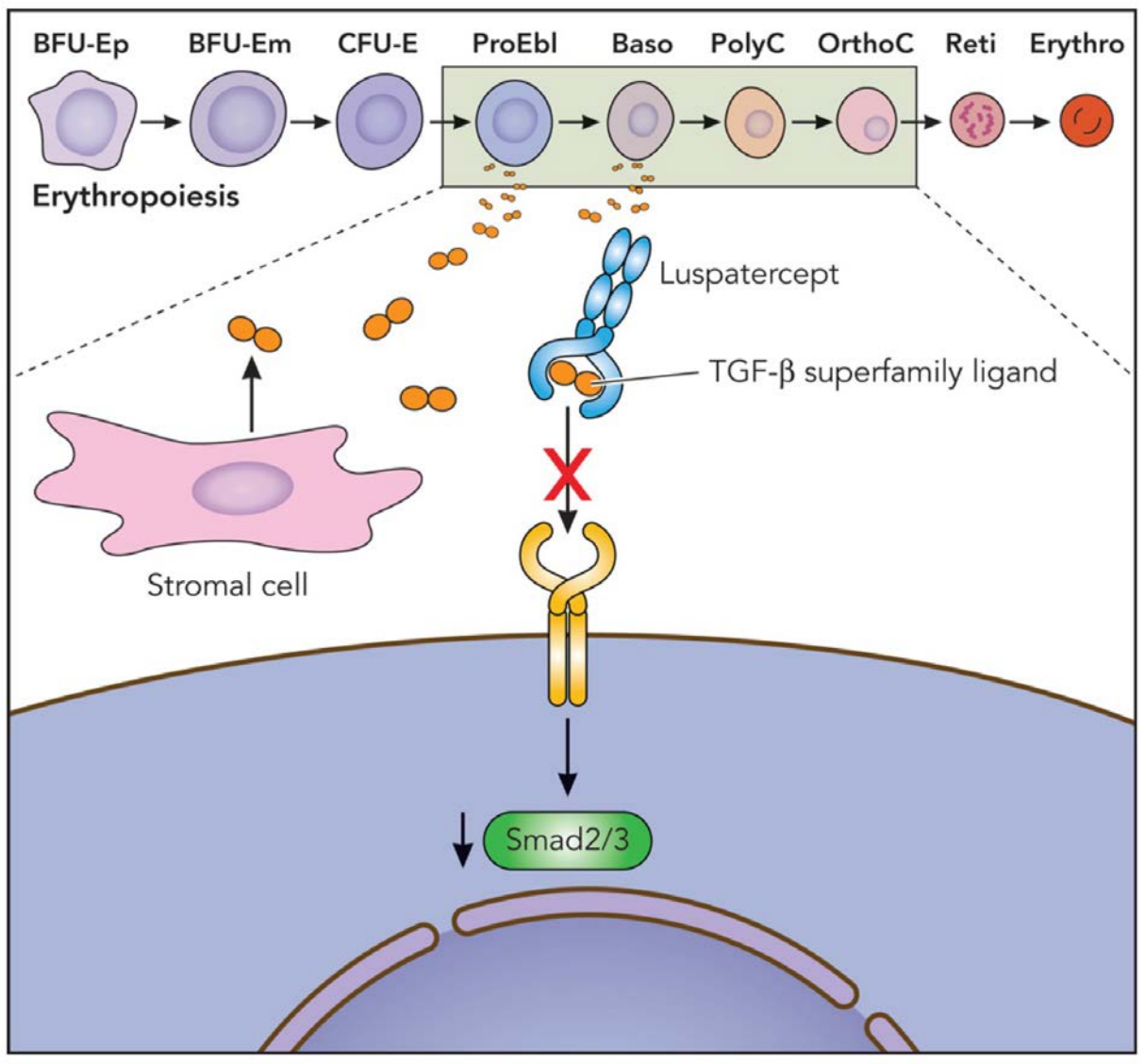



- JAK inhibition with ruxolitinib is the standard of care in patients with higher risk MF who are ineligible for HSCT, but unmet medical need persists due to limited efficacy with currently available JAKi monotherapy, high rates of discontinuation and toxicities[1]
- Preclinical data indicated synergistic effects of BET and JAK inhibition in MF[2]
- Pelabresib, a BET inhibitor, downregulates the expression of genes that contribute to the heterogenous pathology of MF[3–7]



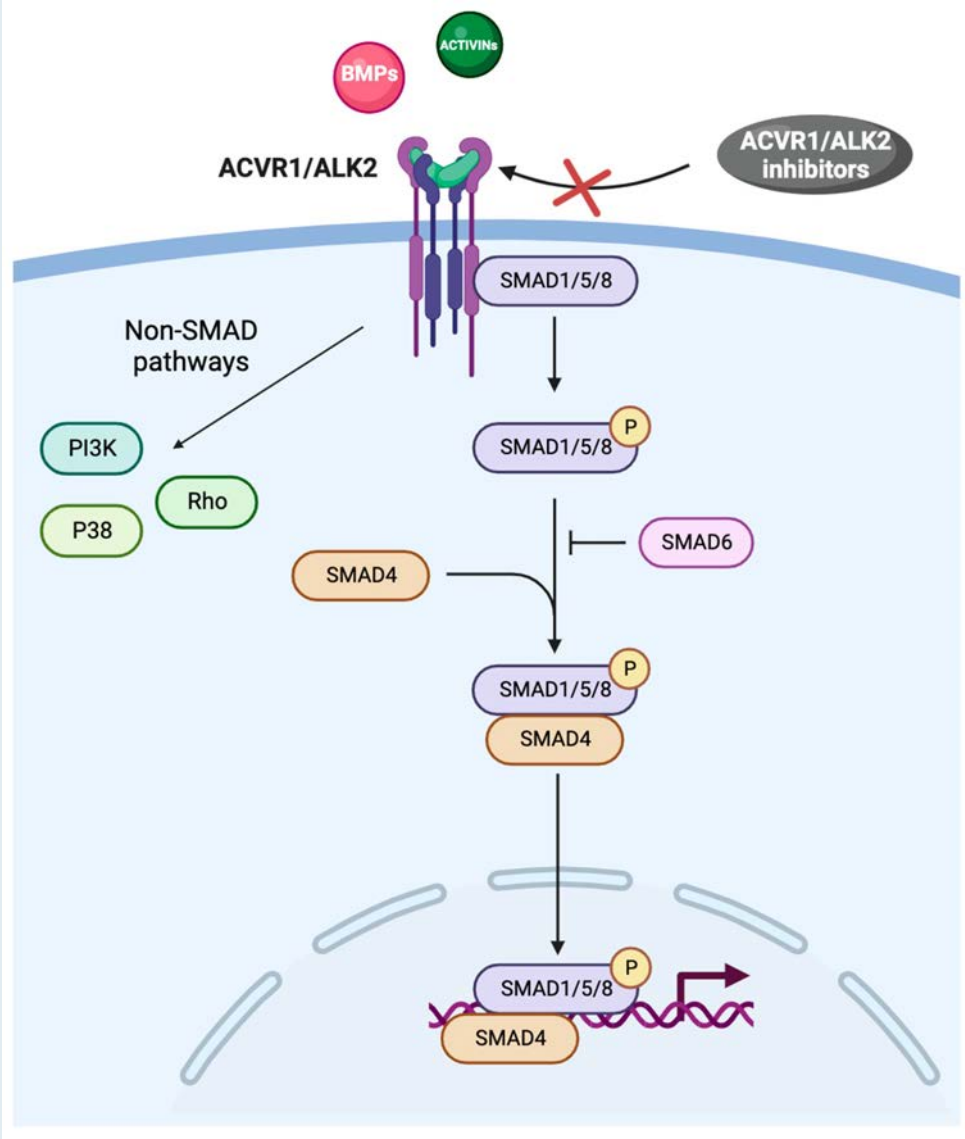
Mascarenhas J et al. ASH 2022;Abstract 238.

# Luspatercept Mechanism of Action in Anemia




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

# 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.

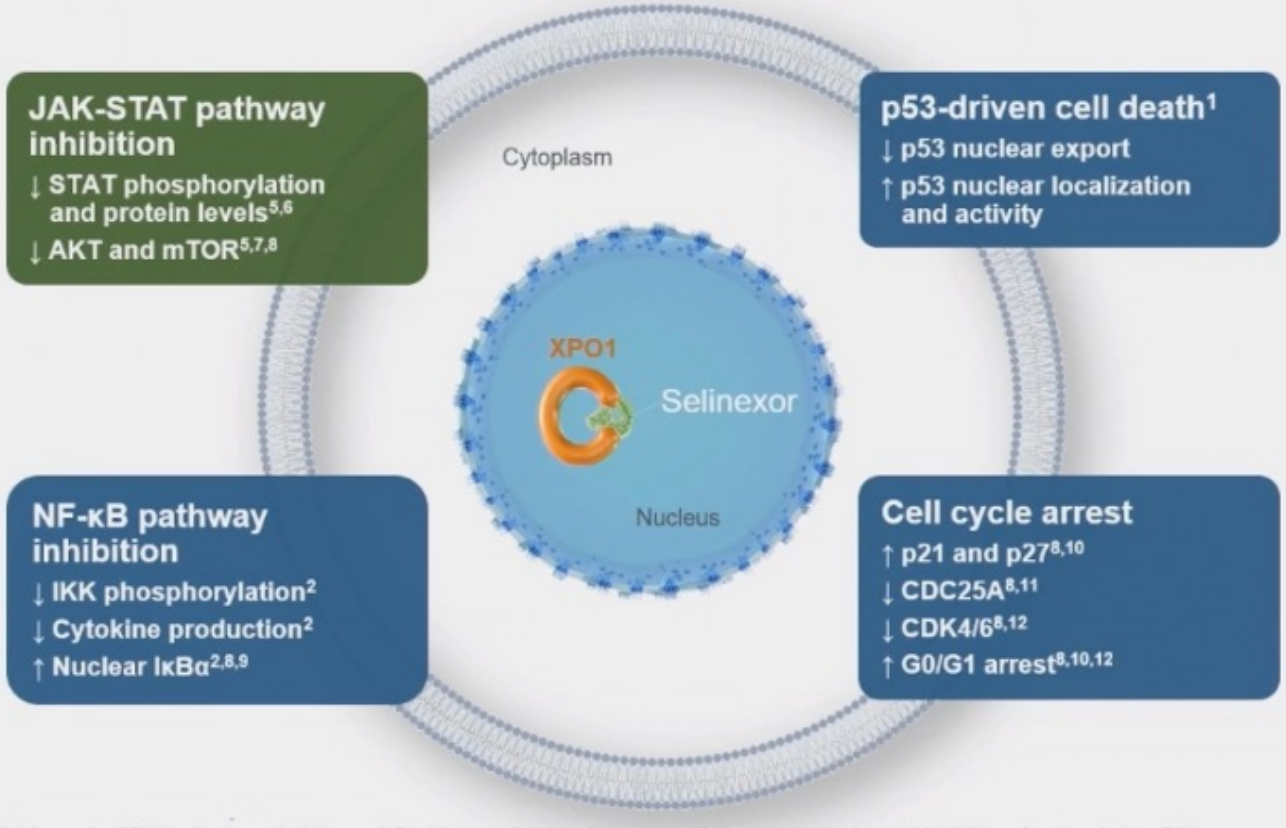
RTP RESEARCH TO PRACTICE

# 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)

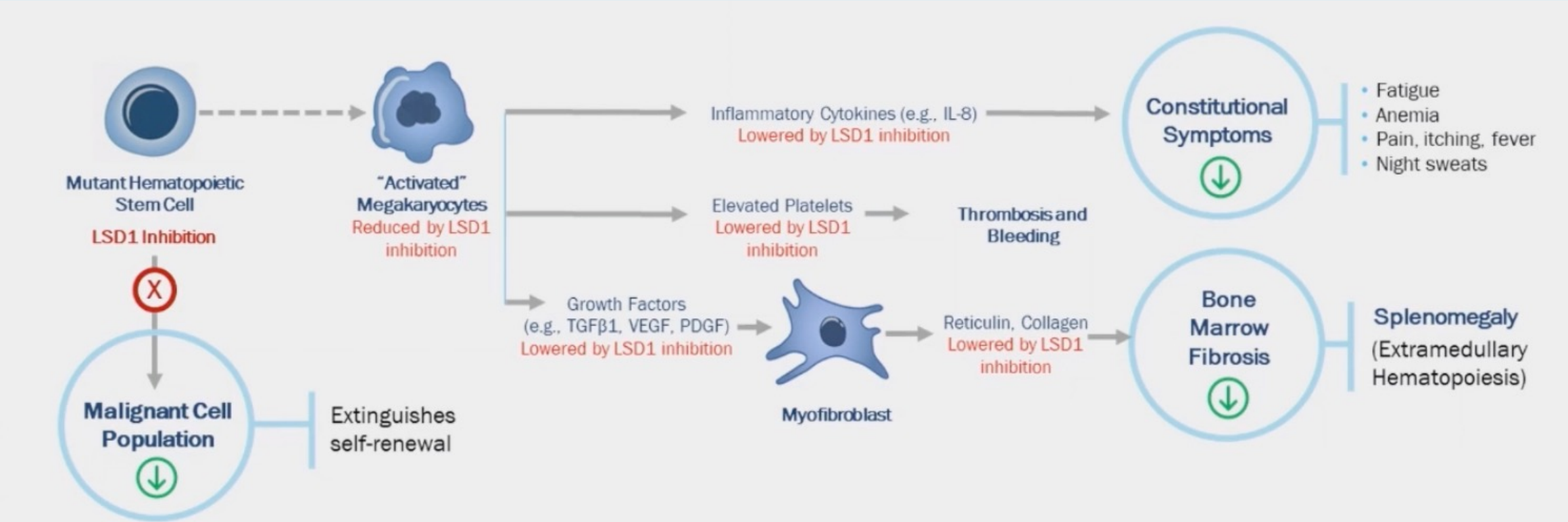
AKT, protein kinase B; CD, cluster of differentiation; CDC, cell division cycle; CDK, cyclin-dependent kinase; IκBα, inhibitor of nuclear factor kappa-B kinase subunit alpha; IKK, inhibitor of nuclear factor-κB kinase; mTOR, mammalian target of rapamycin; NF-κB, nuclear factor κ-light-chain-enhancer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

RTP RESEARCH TO PRACTICE

# Bomedemstat Mechanism of Action





Gill H, Yacoub A, Pettit KM, et al. A phase 2 study of the LSD1 inhibitor Img-7289 (bomedemstat) for the treatment of advanced myelofibrosis. Blood. 2021 Nov 23;138:139.
Gill H. Lysine-specific demethylase 1 (LSD1/KDM1A) inhibition as a target for disease modification in myelofibrosis. Cells. 2022 Jul 3;11(13):2107.
Pettit KM, Gill H, Yacoub A, et al. A phase 2 study of the LSD1 inhibitor bomedemstat (IMG-7289) for the treatment of advanced myelofibrosis (MF): updated results and genomic analyses. Blood. 2022 Nov:9717-20.
Rienhoff Jr HY, Gill H. Bomedemstat as an investigative treatment for myeloproliferative neoplasms. Expert Opinion on Investigational Drugs. 2023 Oct 3;32(10):879-86.


Gill H et al. ASH 2023;Abstract 621.

RTP RESEARCH TO PRACTICE

# *Sara M Tinsley-Vance, PhD, APRN, AOCN*

**What I tell my patients about the logistics and potential benefits of enrolling on a clinical trial**

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# Consulting Nursing Faculty Comments

## Trip to LEGOLAND

**Amy Goodrich, CRNP**

# APPENDIX

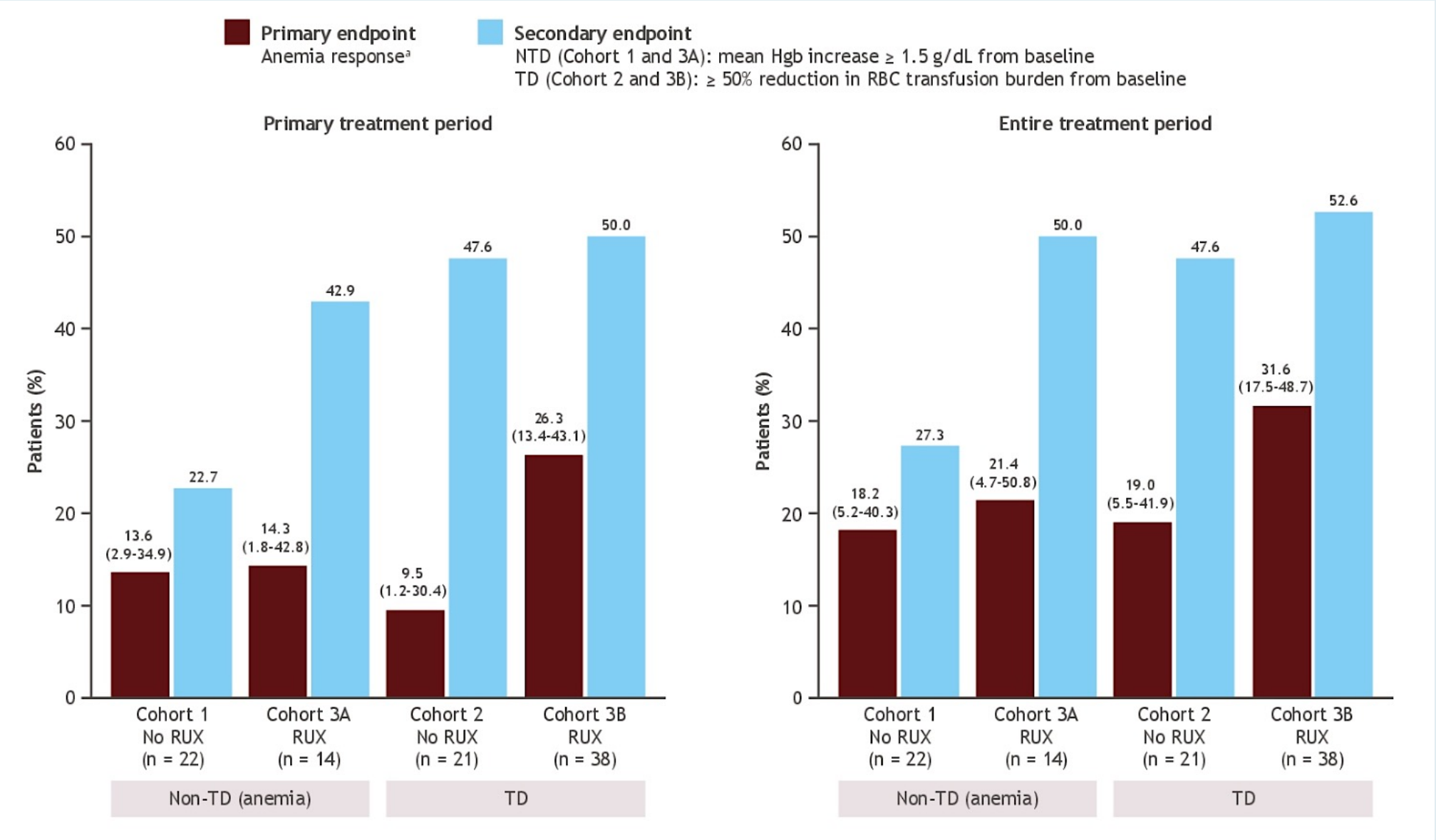
# Promising Agents and Strategies for Patients with MF

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

Gerds AT et al.

ASCO 2023;Abstract 7016.

# ACE-536-MF-001: Efficacy Results




Gerds AT et al. ASCO 2023;Abstract 7016.

# 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. [a]Duration 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.

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

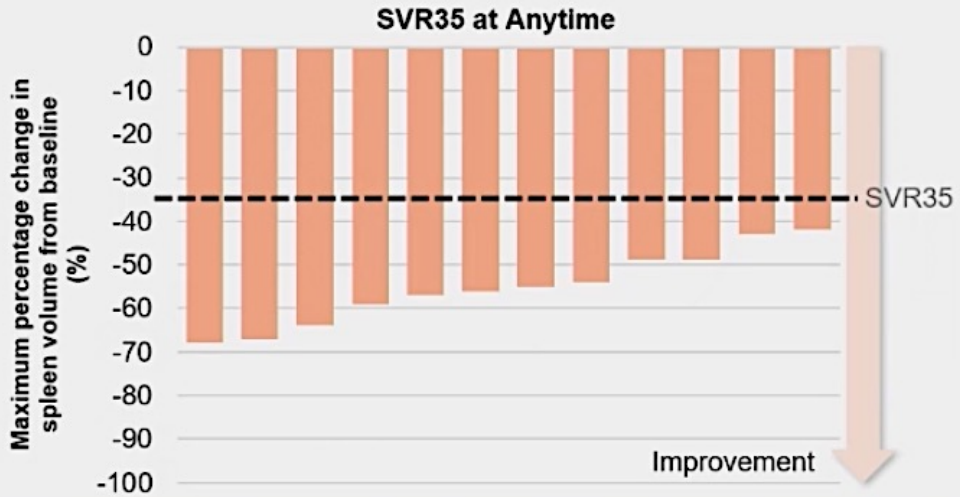
Srinivas K Tantravahi,[1] Ashwin Kishtagari,[2] Keri Maher,[3] Sanjay Mohan,[2] Josef T Prchal,[1] Xulong Wang,[4] Kamal Chamoun,[5] Christopher J Walker,[4] Pietro Taverna,[4] Steve Kye,[4] Haris Ali[6]

[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

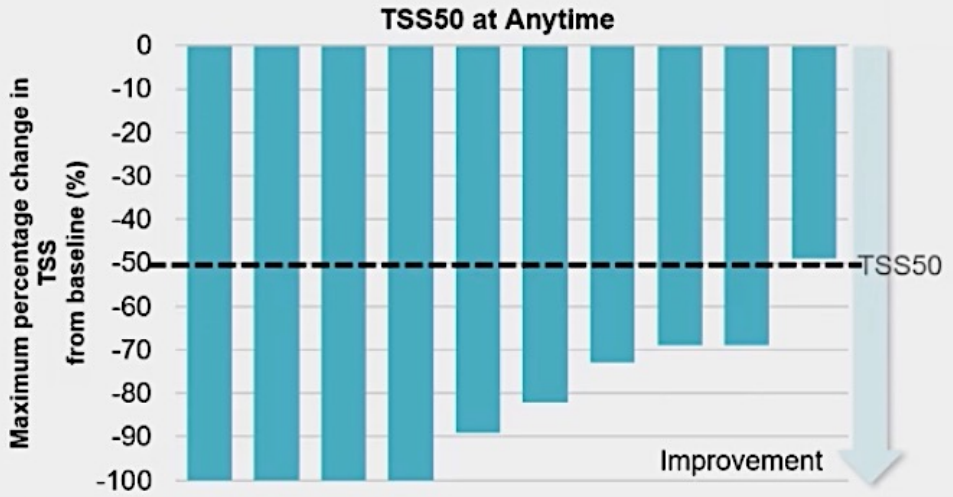
# XPORT-MF-034: Phase I Long-Term Follow-Up of SVR and TSS with Selinexor and Ruxolitinib

| | | 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)** |




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

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




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

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



Tantravahi S et al. ASH 2023;Abstract 622.

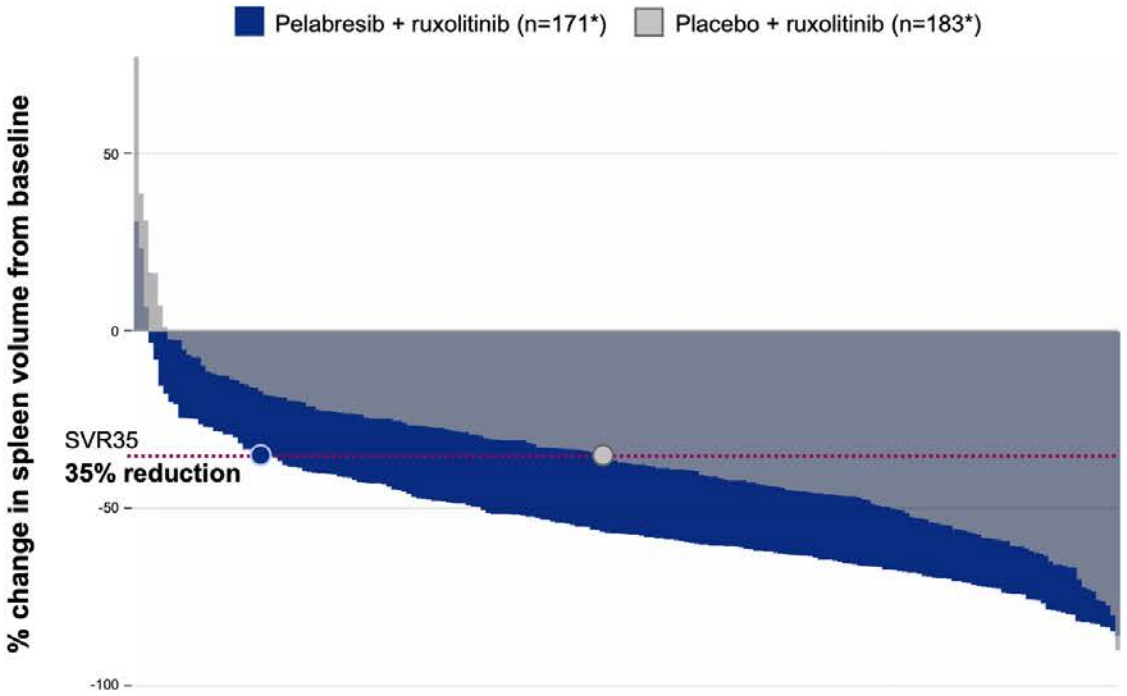
# Pelabresib in combination with ruxolitinib for Janus kinase inhibitor treatment-naïve patients with myelofibrosis: results of the MANIFEST-2 randomized, double-blind, Phase 3 study

**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**



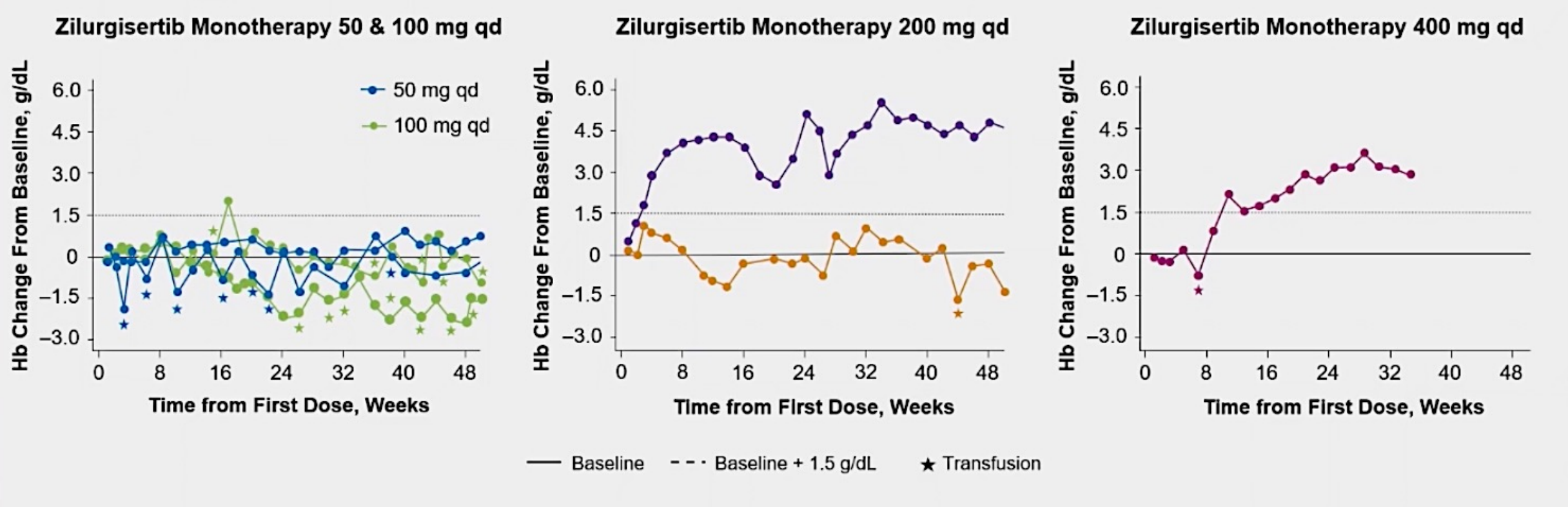
Rampal R et al. ASH 2023;Abstract 628.

# Phase 1/2 Study of the Activin Receptor-like Kinase-2 Inhibitor Zilurgisertib (INCB000928, LIMBER-104) as Monotherapy or With Ruxolitinib in Patients With Anemia due to Myelofibrosis

Sanjay Mohan, MD, MSCI,[1] Stephen T. Oh, MD, PhD,[2] Jean-Jacques Kiladjian, MD, PhD,[3] Masahiro Takeuchi, MD, PhD,[4] Jason Gotlib, MD, MS,[5] Ellen Ritchie, MD,[6] Taizo Shimomura, MD, PhD,[7] Paola Guglielmelli, MD, PhD,[8] Anthony M. Hunter, MD,[9] Francesca Palandri, MD, PhD,[10] Francoise Boyer, MD,[11] Alessandro Rambaldi, MD,[12] Takehiko Mori, MD,[13] Tomoki Ito, MD,[14] Betty Lamothe, PhD,[15] Yan-ou Yang, PhD,[15] Yi Cui, PhD,[15] Francis Seguy, MSc,[16] Amanda McBride, MD, PhD,[15] Prithviraj Bose, MD[17]

**ASH 2023;Abstract 624**

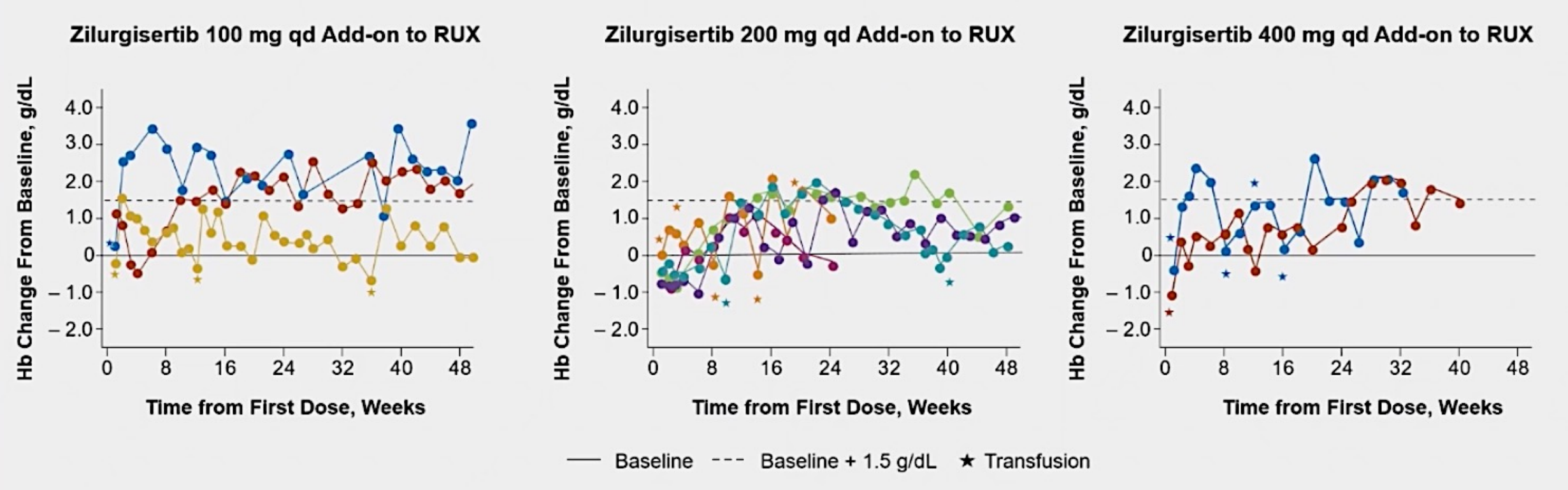
# LIMBER-104: Results with Zilurgisertib as Monotherapy




Mohan S et al. ASH 2023;Abstract 624.

RTP RESEARCH TO PRACTICE

# LIMBER-104: Results with Zilurgisertib in Combination with Ruxolitinib




Mohan S et al. ASH 2023;Abstract 624.

RTP RESEARCH TO PRACTICE

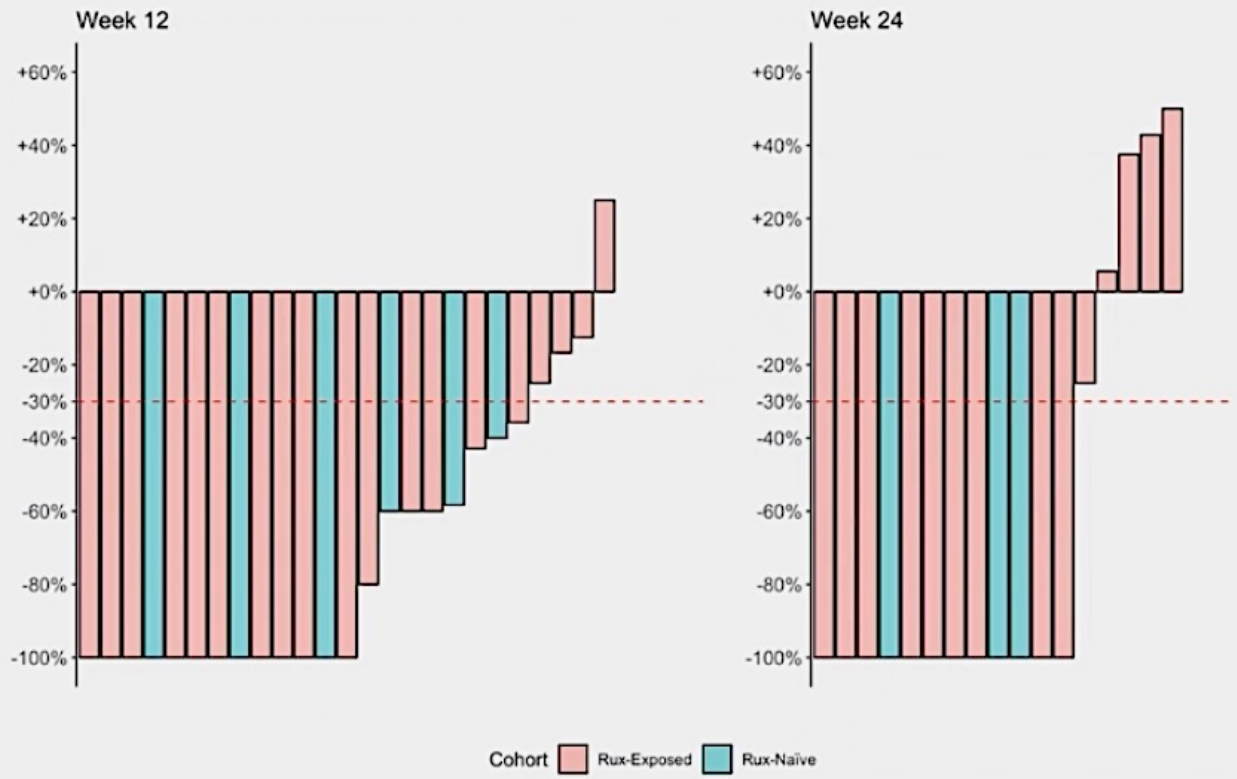
# Phase 2 Study to Assess the Safety and Efficacy of Bomedemstat (MK3543) in Combination with Ruxolitinib in Patients with Myelofibrosis

**Harinder Gill**[1], Lester Au[1], Garret M.K. Leung[1], Dorothy Y.Y. Tsai[1], Rita Yim[1], Lynn Chin[1], Vivian Li[1], Paul Lee[1], Rock Y.Y. Leung[2], Elaine Y.P. Lee[3], Hugh Young Rienhoff Jr[4], Yok-Lam Kwong[1]

ASH 2023;Abstract 621

# Spleen Responses with Bomedemstat

## Responses – Spleen length at Week 12 and 24




| | Week 12 | Week 24 |
|---|---|---|
| Total no. of patient | 25 | 17 |
| No. of patient in Cohort A | 19 | 14 |
| No. of patient in Cohort B | 6 | 3 |
| No. of patients with 30% reduction in Cohort A | 13 | 9 |
| No. of patients with 30% reduction in Cohort B | 5 | 3 |

**≥30% reduction in spleen length at Week 12:**

- Rux-exposed=68.4%
- Rux-naïve=83.3%

**≥30% reduction in spleen length at Week 24:**

- Rux-exposed=64.3%
- Rux-naïve=100%

Gill H et al. ASH 2023;Abstract 621.

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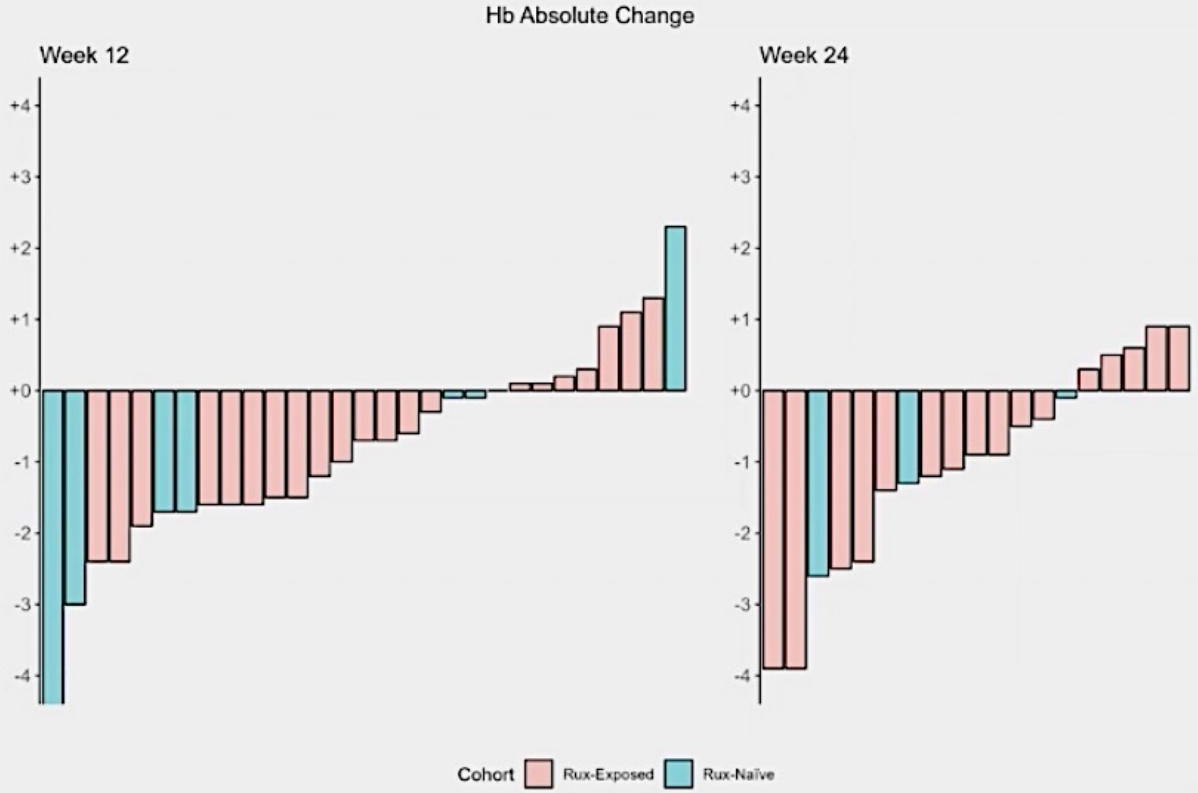
# Hemoglobin Responses with Bomedemstat

## Responses – changes in Hb at Week 12 and 24




**Stable (Δ <± 1.0 g/dL) or improved Hb (>1.0 g/dL) at Week 12**
**Rux-exposed=13/22 (59.9%)**
**Rux-naïve=3/7 (42.9%)**

**Stable (Δ <± 1.0 g/dL) or improved Hb (>1.0 g/dL) at Week 24**
**Rux-exposed=9/16 (56.3%)**
**Rux-naïve=1/3 (33.3%)**

**3 out 5 patients had reductions (60%) in RBC transfusion requirements at Week 24 with 1 patient being transfusion independent**

| | Week 12 | Week 24 |
|---|---|---|
| Total no. of patient | 29 | 19 |
| No. of patient in Cohort A | 22 | 16 |
| No. of patient in Cohort B | 7 | 3 |

Gill H et al. ASH 2023;Abstract 621.

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# What I Tell My Patients: Integrating New Research Information into Current Clinical Care

*A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress*

# Myelofibrosis

**Saturday, April 27, 2024**
**12:15 PM – 1:45 PM**

## Faculty

**Ilene Galinsky, NP**
**Andrew T Kuykendall, MD**
**Sara M Tinsley-Vance, PhD, APRN, AOCN**
**Abdulraheem Yacoub, MD**

## Moderator

**Neil Love, MD**

RTP RESEARCH TO PRACTICE

# What I Tell My Patients: Integrating New Research Information into Current Clinical Care

*A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress*

# Gastroesophageal and Colorectal Cancers

**Saturday, April 27, 2024**
**6:00 PM – 8:00 PM**

## Faculty

**Deanna A Griffie, MSN, AGNP-C**
**Caroline Kuhlman, MSN, APRN-BC**
**Manish A Shah, MD**
**John Strickler, MD**

## Moderator

**Neil Love, MD**

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

## *To Claim NCPD Credit*

*In-person attendees: Please refer to the program syllabus for the NCPD credit link or QR code.*

*Virtual attendees: The NCPD credit link is posted in the chat room.*

*NCPD/ONCC credit information will be emailed to each participant within 1 to 2 business days.*

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