Atrium Health

Wake Forest University School of Medicine

NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

WE WORK AS ONE

Targets and Treatments of MPNs

2023 Indy Review

Ruben A. Mesa, MD, FACP
President, Enterprise Cancer Service Line Atrium Health
Executive Director Atrium Health Wake Forest Baptist Comprehensive Cancer Center
Enterprise Senior Vice President Atrium Health
Vice Dean for Cancer Programs – Wake Forest School of Medicine
Professor of Medicine
Ruben.Mesa@Atriumhealth.org

Disclosures – Ruben Mesa, MD

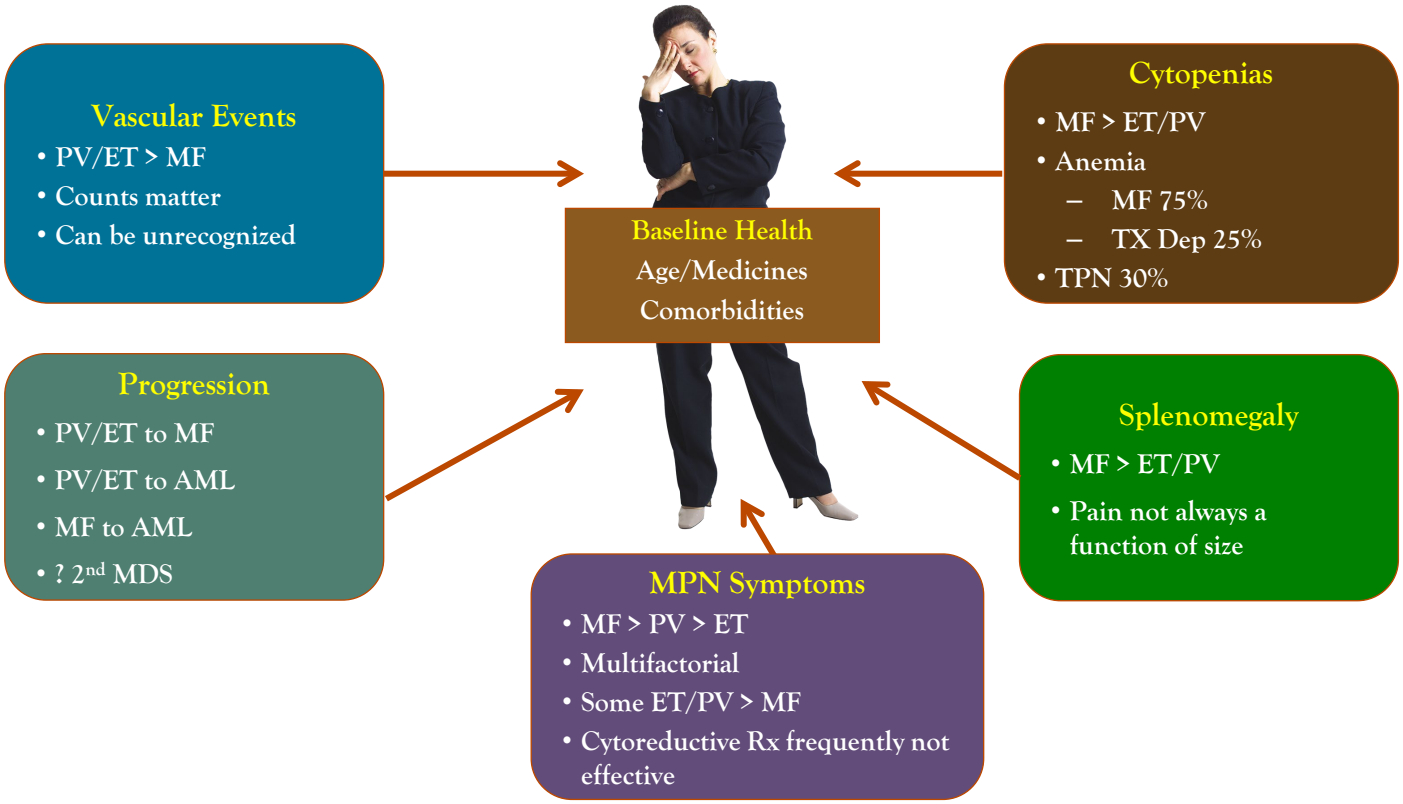
- Consultant (Honoraria) over past 3 years
  - Novartis
  - Sierra Oncology
  - Genentech
  - Sierra
  - Blueprint
  - Geron
  - Telios
  - CTI
  - Incyte
  - BMS
  - Abbvie
  - GSK
- Research Support
  - Incyte
  - Sierra
  - CTI
  - BMS
  - Abbvie
  - Genentech
  - Blueprint
  - Morphosys

Therapy of MPNs 2023

- Goals and Targets
- ET and PV
- JAK Inhibitors as Foundation
- Non JAKi MOA
- Putting it all Together

Assessing MPN Burden

WHO Diagnosis Does Not Tell Whole Story



Therapy of MPNs 2023

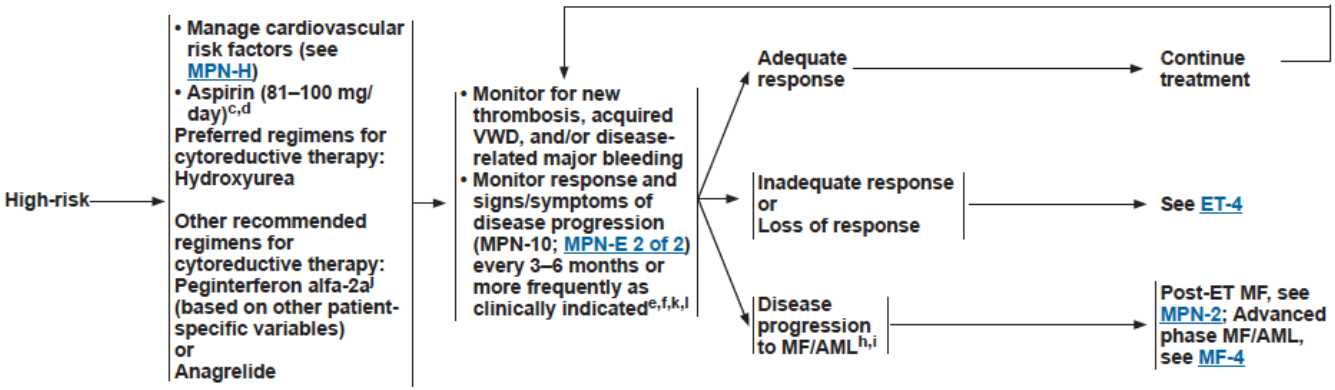
- Goals and Targets
- ET and PV
- JAK Inhibitors as Foundation
- Non JAKi MOA
- Putting it all Together

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2021
Essential Thrombocythemia
NCCN Evidence Blocks™

NCCN Guidelines Index
Table of Contents
Discussion

TREATMENT FOR HIGH-RISK ESSENTIAL THROMBOCYTHEMIA[a]



See Evidence Blocks on ET-4A

American Society *of* Hematology

Helping hematologists conquer blood diseases worldwide

Phase 2 Study of the LSD1 Inhibitor IMG-7289 (Bomedemstat) for the Treatment of Essential Thrombocythemia (ET)

Francesca Palandri, MD, PhD[1*], David M Ross, MBBS, PhD, FRACP, FRCPA[4*], Tara Cochrane, MBBS, FRCPA, FRACP[5], Steven W Lane, MD, PhD[6], Stephen R Larsen, MBBS PhD FRACP FRCPA[7], Aaron T. Gerds, MD[8*], Anna B. Halpern, MD[9], Jake Shortt, FRACP, FRCPA, PhD[10], James M. Rossetti, DO[11], Kristen M. Pettit, MD[12], James Liang[20], Adam Mead, MBBChir[21], Monia Marchetti, MD[22], Alessandro Vannucchi, MD[23], Andrew Wilson, MD[24], Joachim R. Göthert, MD[25], Merit Hanna[26], Amber Jones, MA[13*], Jennifer Peppe, BA[14*], Georges Natsoulis, Ph.D.[15*], Willis Navarro, MD[16], Wan-Jen Hong, MD[16], William S. Stevenson, MBBS, PhD[17], Claire N. Harrison, DM[18], Mosne Talpaz, MD[12], Nicola Vianelli, MD[2,3], and Hugh Young Rienhoff Jr., MD[19]

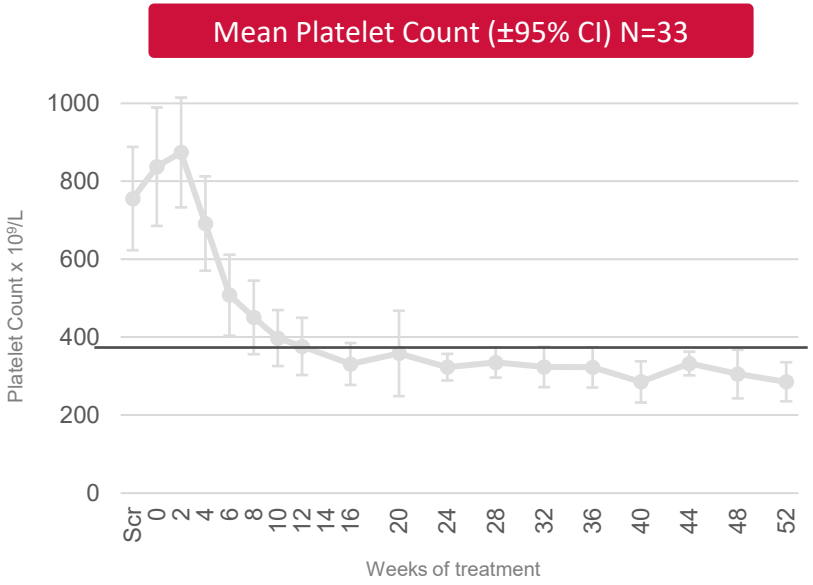
[1]Institute of Hematology "L. & A. Seràgnoli", Sant'Orsola-Malpighi University Hospital, Bologna, Italy; [2]Azienda Ospedaliero-Universitaria S.Orsola-Malpighi di Bologna, Bologna, Italy; [3]Institute of Hematology "L. & A. Seragnoli", Azienda Ospedaliero-Universitaria di Bologna, Via Albertoni 15, Bologna, Italy; [4]Department of Haematology, Royal Adelaide Hospital and SA Pathology, Adelaide, SA, Australia; [5]Department of Haematology, Gold Coast University Hospital, Southport, Australia; [6]QIMR Berghofer Medical Research Institute, Brisbane, Australia; [7]Institute of Haematology, Royal Prince Alfred Hospital, Sydney, NSW, Australia; [8]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH; [9]Department of Medicine, Division of Hematology, University of Washington, Seattle, WA; [10]Monash Haematology, Monash Health, Clayton, VIC, Australia; [11]UPMC Hillman Cancer Center, Pittsburgh, PA; [12]Department of Internal Medicine, Division of Hematology/Oncology, University of Michigan, Ann Arbor, MI; [13]Imago Biosciences Inc., Chilton Polden, GBR; [14]Imago BioSciences, Inc., San Carlos, CA; [15]Imago Biosciences, Inc., San Carlos, CA; [16]Imago BioSciences, San Carlos, CA; [17]Kolling Institute of Medical Research, Royal North Shore Hospital, Sydney, Australia; [18]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; [19]Imago Biosciences, San Francisco; [20]Middlemore Clinical Trials, Auckland, New Zealand; [21]MRC Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, United Kingdom; [22]Azienda Ospedaliera Nazionale SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy; [23]University of Florence, AOU Careggi, CRIMM, Center for Research and Innovation of Myeloproliferative Neoplasms, Italy, Florence, Italy; [24]University College Hospital, NHS Foundation Trust, London, United Kingdom; [25]Department of Hematology, West German Cancer Center (WTZ), University Hospital Essen, Essen, Germany; [26]North Shore Hospital. Waitemata District Health Board, Auckland, New Zealand.

Abstract #386: Bomedemstat in ET

Atrium Health

Wake Forest University School of Medicine

Primary Objective: Reduction in Platelet Count



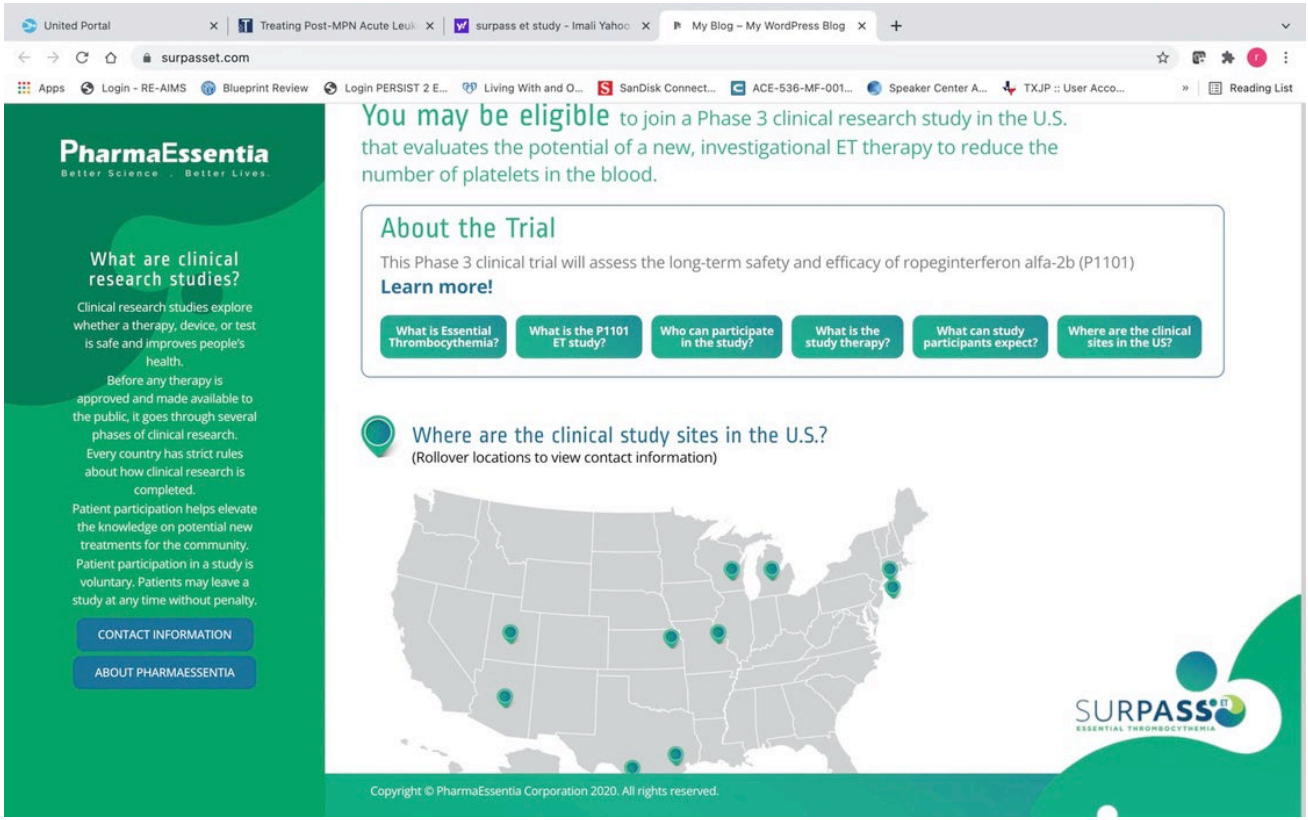
In the 29 patients treated for >6 weeks:

- 100% patients experienced a reduction in platelets
- 93% of patients achieved a platelet count of ≤400 x 10^9/L
- Response Rate*: 90% (26/29)

*Platelet count ≤400 x 10^9/L without thromboembolic events

Data cut-off date: 01 Nov 2021

SURPASS ET Study: 2L for ET NCT 04285086 (Clinicaltrials.GOV)



SurpassET.com

Atrium Health

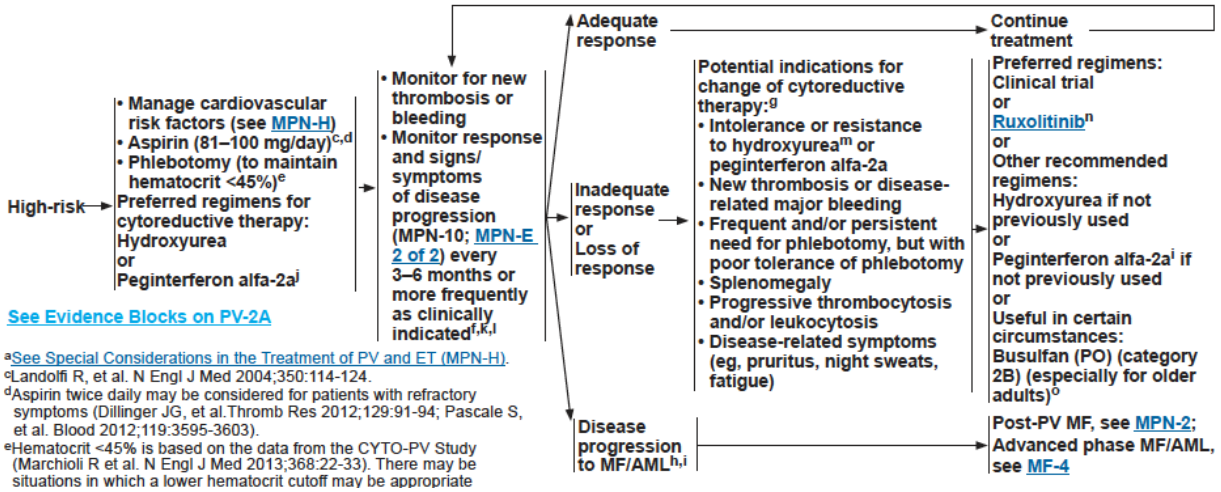
Wake Forest University School of Medicine

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2021
Polycythemia Vera
NCCN Evidence Blocks™

NCCN Guidelines Index
Table of Contents
Discussion

TREATMENT FOR HIGH-RISK POLYCYTHEMIA VERA[a]

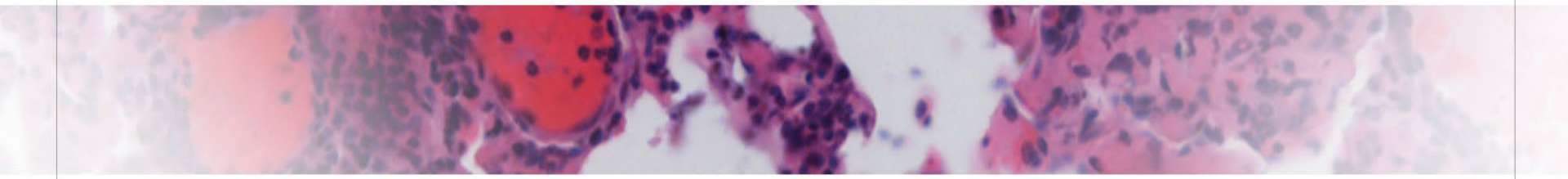


[a] See Special Considerations in the Treatment of PV and ET (MPN-H).
[c] Landolfi R, et al. N Engl J Med 2004;350:114-124.
[d] Aspirin twice daily may be considered for patients with refractory symptoms (Dillinger JG, et al.Thromb Res 2012;129:91-94; Pascale S, et al. Blood 2012;119:3595-3603).
[e] Hematocrit <45% is based on the data from the CYTO-PV Study (Marchioli R et al. N Engl J Med 2013;368:22-33). There may be situations in which a lower hematocrit cutoff may be appropriate

Atrium Health
Wake Forest University School of Medicine

American Society *of* Hematology

Helping hematologists conquer blood diseases worldwide



ROPEGINTERFERON ALFA-2B ACHIEVES PATIENT-SPECIFIC TREATMENT GOALS IN POLYCYTHEMIA VERA: FINAL RESULTS FROM THE PROUD-PV/CONTINUATION-PV STUDIES

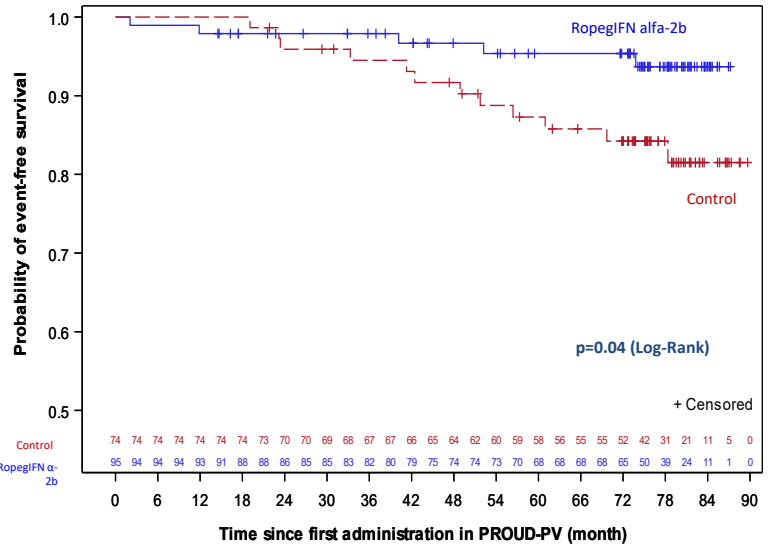
Heinz Gisslinger, MD, Christoph Klade, PhD, Pencho Georgiev, MD, Dorota Krochmalczyk, MD, Liana Gercheva-Kyuchukova, MD, Miklos Egyed, MD, Petr Dulicek, MD, Arpad Illes, MD, Halyna Pylypenko, MD, Lylia Sivcheva, MD, Jiří Mayer, MD, Vera Yablokova, MD, Kurt Krejcy, MD, Victoria Empson, MSc, Hans C. Hasselbalch, MD, Robert Kralovics, PhD and Jean-Jacques Kiladjian, MD PhD, for the PROUD-PV Study Group

Atrium Health

Wake Forest University School of Medicine

Event-free survival

Risk events: death, disease progression and thromboembolic events



The probability of event-free survival was significantly higher among patients treated with ropeginterferon alfa-2b compared to the control arm (maximum treatment period 7.3 years)

Atrium Health

Wake Forest University School of Medicine

WARNING: RISK OF SERIOUS DISORDERS

See full prescribing information for complete boxed warning.

Risk of Serious Disorders: Interferon alfa products may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor closely and withdraw therapy with persistently severe or worsening signs or symptoms of the above disorders.

----------ADVERSE REACTIONS----------

The most common adverse reactions reported in > 40% of patients were influenza-like illness, arthralgia, fatigue, pruritus, nasopharyngitis, and musculoskeletal pain (6).

Things to watch for

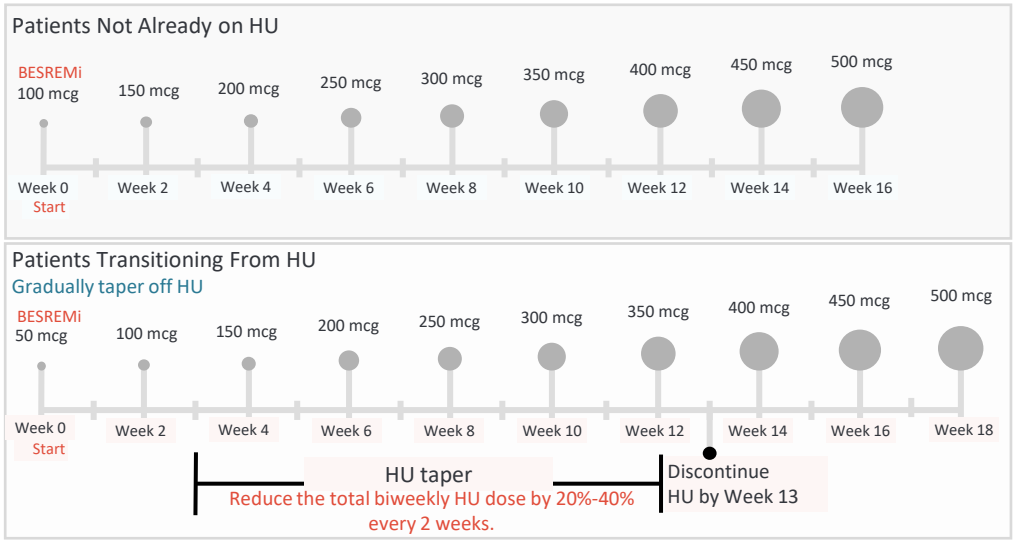
- Mood side effects (i.e. depression)
- Blood counts dropping too much
- Elevated liver function tests
- Rare autoimmune side effects
- Rare endocrine or cardiac side effects

Package insert: RoPEG INF 2021

----------CONTRAINDICATIONS----------

- Existence of, or history of severe psychiatric disorders, particularly severe depression, suicidal ideation or suicide attempt (4)
- Hypersensitivity to interferon or to any component of BESREMi (4)
- Hepatic impairment (Child-Pugh B or C) (4)
- History or presence of active serious or untreated autoimmune disease (4)
- Immunosuppressed transplant recipients (4)

Recommended BESREMi Dose Titration



Increase the dose of BESREMi **by 50 mcg every 2 weeks (up to a maximum of 500 mcg)** until hematologic parameters are stabilized.

Besremi. Package insert. PharmaEssentia Corporation; 2021.

Atrium Health

Wake Forest University School of Medicine

2022 ASCO® ANNUAL MEETING

Rusfertide (PTG-300) Treatment in Phlebotomy-Dependent Polycythemia Vera

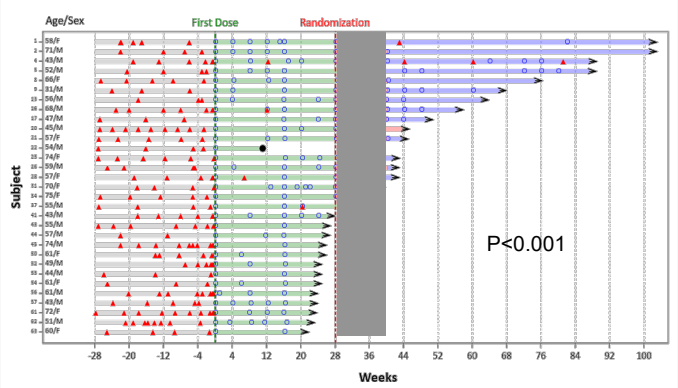
The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York; Protagonist Therapeutics, Newark, CA

Atrium Health

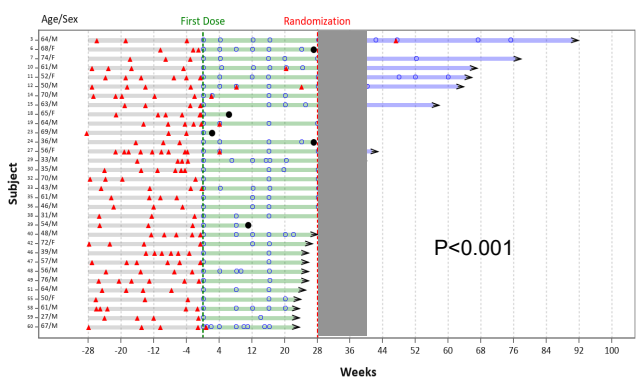
Wake Forest University School of Medicine

Effect of Rusfertide on Reducing Phlebotomy Frequency

PHLEBOTOMY ONLY (N=31, 49%)



PHLEBOTOMY + CYTOREDUCTIVE (N=32,



Median Dose 40-60 mg/week

During the first 28 weeks of treatment, **84% of patients did not require a phlebotomy,** 14% required one and 2% required two phlebotomies.

Data cut off Sept 30, 2021

Ron Hoffman. Abstract # 7003

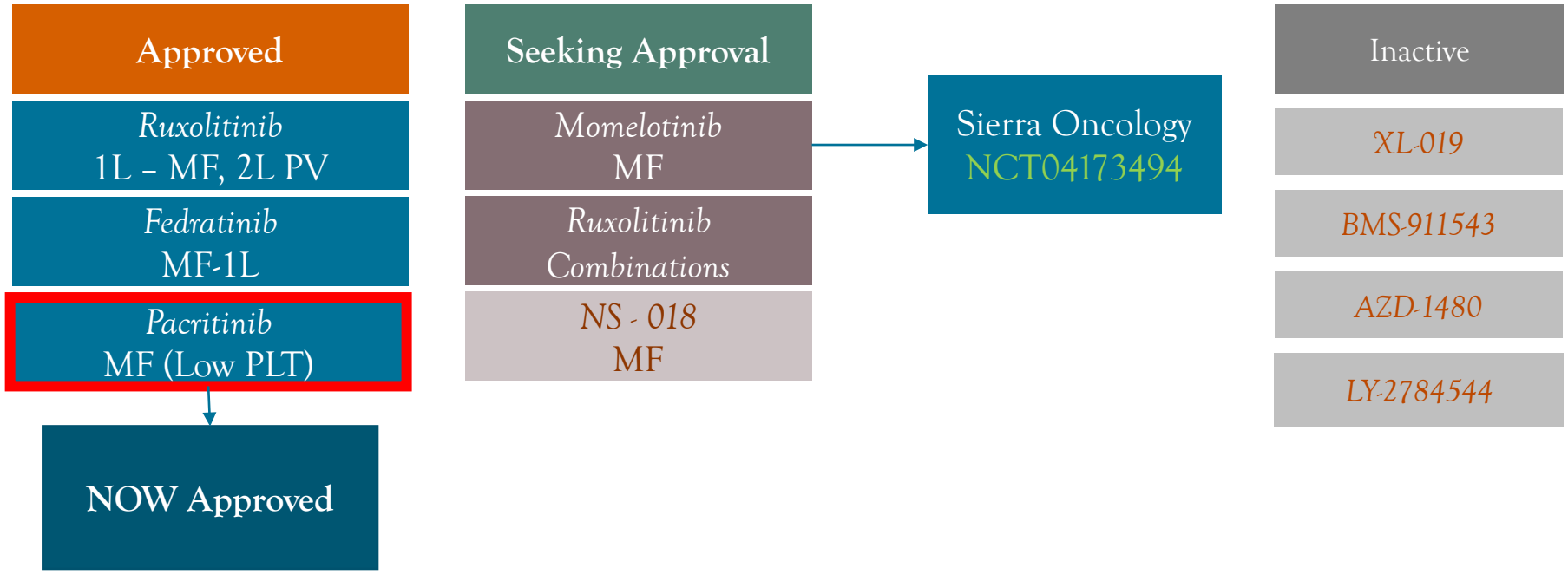
Atrium Health

Wake Forest University School of Medicine

Therapy of MPNs 2023

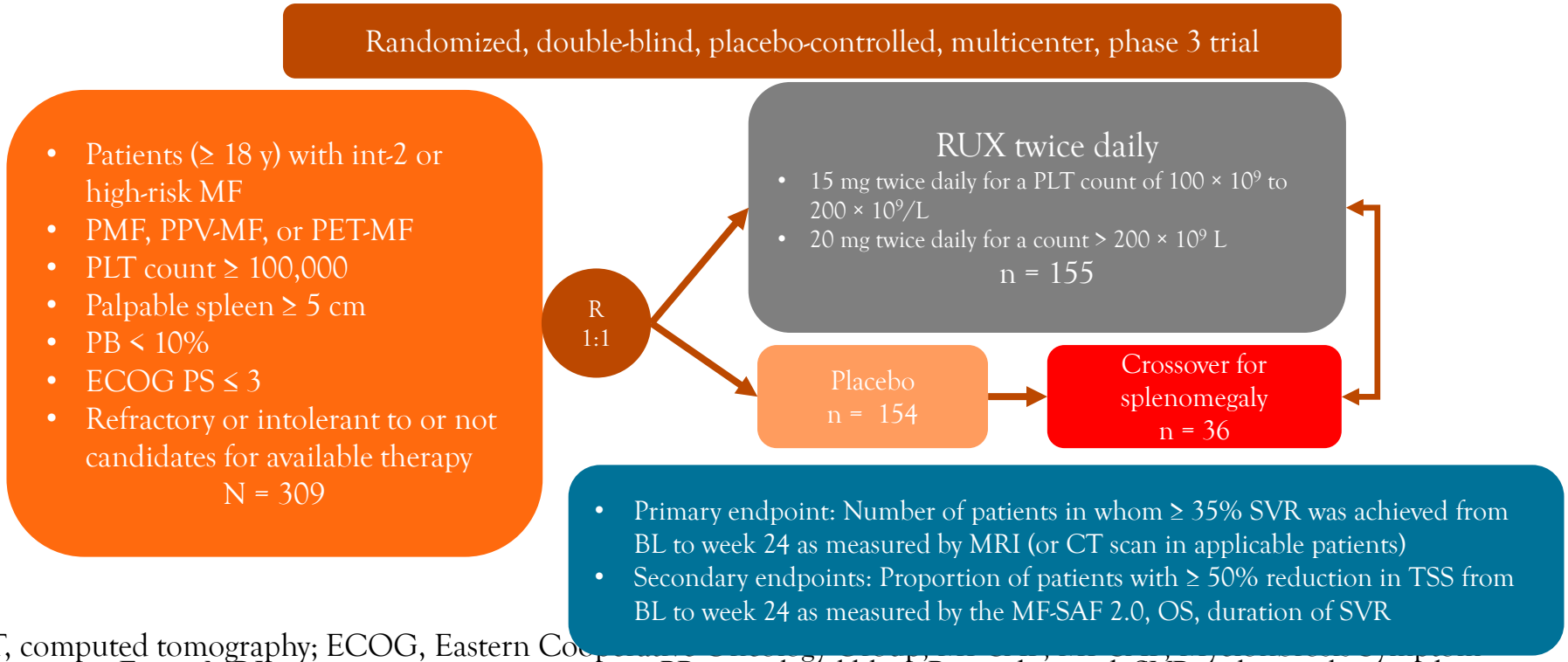
- Goals and Targets
- ET and PV
- JAK Inhibitors as Foundation
- Non JAKi MOA
- Putting it all Together

JAK Inhibitor Landscape 2023



Ruxolitinib FDA Approved (MF) November 16,2011

COMFORT-I Study Design



CT, computed tomography; ECOG, Eastern Co[illegible] Assessment Form; MRI, magnetic resonance imaging; PB, peripheral blast; R, randomized; SVR, spleen volume reduction.

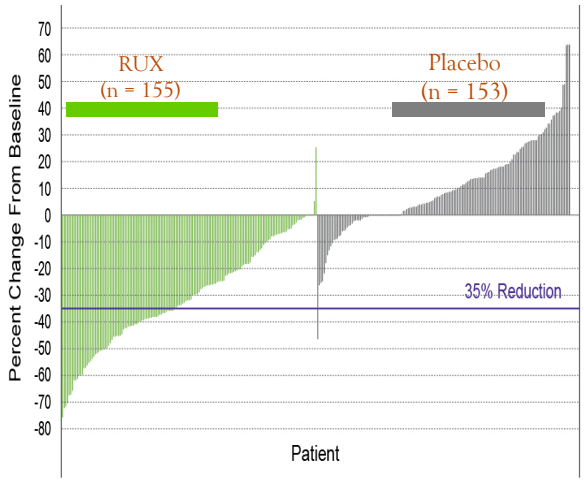
Verstovsek S, et al. N Engl J Med. 2012;366:799-807.

COMFORT-I

Results

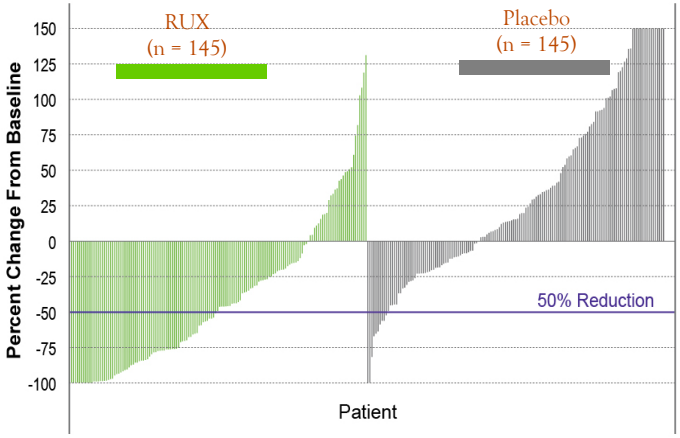
- Primary endpoint: the proportion of patients in whom ≥ 35% SVR was achieved from BL to week 24 (as measured by MRI or CT scan)
  - 41.9% in RUX group reached the primary endpoint vs 0.7% in the placebo group ($P < .0001$)
  - A similar proportion of patients in the RUX group had a ≥ 50% reduction in palpable spleen length
- SVR responses were seen with RUX in *JAK2* V617F-positive patients and *JAK2* V617F-negative patients, relative to placebo

SVR at 24 Weeks



OR, 134.4 (95% CI: 18, 1004.9); $P < .0001$

TSS at 24 Weeks



OR, 15.3 (95% CI: 6.9, 33.7); $P < .0001$

OR, odds ratio.

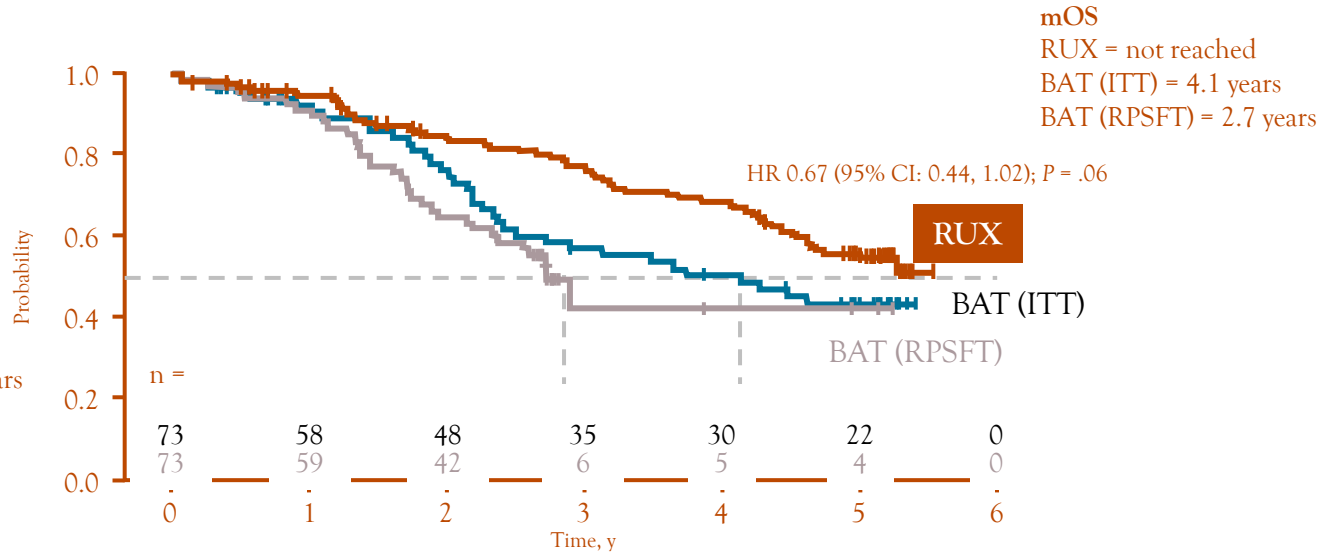
Verstovsek S, et al. N Engl J Med. 2012;366:799-807.

COMFORT-II: 5-Year* Final Study Results

RUX vs BAT in MF

33% reduced risk of death among patients treated with RUX vs those treated with BAT

Most patients in the BAT arm crossed over to receive ruxolitinib



*Median follow-up: 4.3 years

ITT, intent to treat; RPSFT, rank-preserving structural failure time.

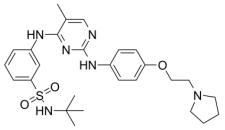
Modified from Harrison CN, et al. Blood. 2015;126(23):59.

Fedratinib FDA Approved (MF)
August 16,2019

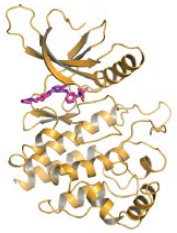
Fedratinib

INREBIC® (Fedratinib)

- Oral, JAK2-selective inhibitor recently approved in the US for treatment of intermediate-2 or high-risk primary or secondary (post-PV or post-ET) MF with **platelet counts ≥50 × 10^9/L**[3]
- Fedratinib has higher inhibitory activity for JAK2 over JAK1, JAK3, and TYK2[4]
- Fedratinib was investigated for treatment of MF in JAK-inhibitor-naïve patients in the phase III JAKARTA trial, and in patients previously treated with RUX in the phase II JAKARTA2 trial
- JAKARTA and JAKARTA2 allowed enrollment of patients with platelet counts of ≥50 × 10^9/L at study entry



FEDRATINIB



JAK2 KINASE DOMAIN – Fedratinib Complex[7]

1. Jakafi (ruxolitinib) prescribing information. Incyte Corporation; 05/2019. 2. Center for Drug Evaluation and Research. Clinical Pharmacology Genomics Group Review; 2011.
3. INREBIC® (fedratinib) prescribing information. Celgene Corporation; 08/2019. 4. Wernig et al. *Cancer Cell*. 2008;13:311–20. 5. Pardanani et al. *JAMA Oncol*. 2015;1(5):643–51.
6. Harrison et al. *Lancet Haematol*. 2017;4:e317–24. 7. Hantschel O. *ACS Chem Biol*. 2015;10(1):234-45.
BL, baseline ET, essential thrombocythemia; JAK, Janus kinase; MF, myelofibrosis; MPN, myeloproliferative neoplasm; PV, polycythemia vera; RUX, ruxolitinib.

FREEDOM: Fedratinib Safety Data

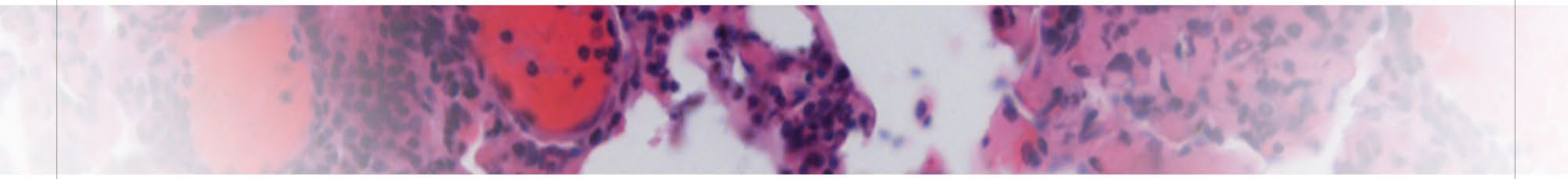
Any grade AEs	Patients, %
At least one TEAE	89.5%
Serious AEs	7.9%
Anemia	60.5%
Thrombocytopenia	34.2%
GI-related	
Nausea	39.5%
Vomiting	18.4%
Diarrhea	39.5%

- Most GI AEs were grade 1/2, and decreased in subsequent cycles.
- No pts required tx discontinuation due to low thiamine levels.
- There were no cases of WE reported.
- Few deaths occurred during tx and follow-up; none were related to study medication.

Gupta et al ASH 2022

Pacritinib FDA Approved (MF)
February 28th, 2022

American Society *of* Hematology
Helping hematologists conquer blood diseases worldwide



Pacritinib Is a Potent ACVR1 Inhibitor with Significant Anemia Benefit in Patients with Myelofibrosis

Session 634. Myeloproliferative Syndromes: Clinical and Epidemiological: Towards Personalized Medicine in Myeloproliferative Neoplasms and Mastocytosis: New and Repurposed Drugs for Unmet Clinical Needs

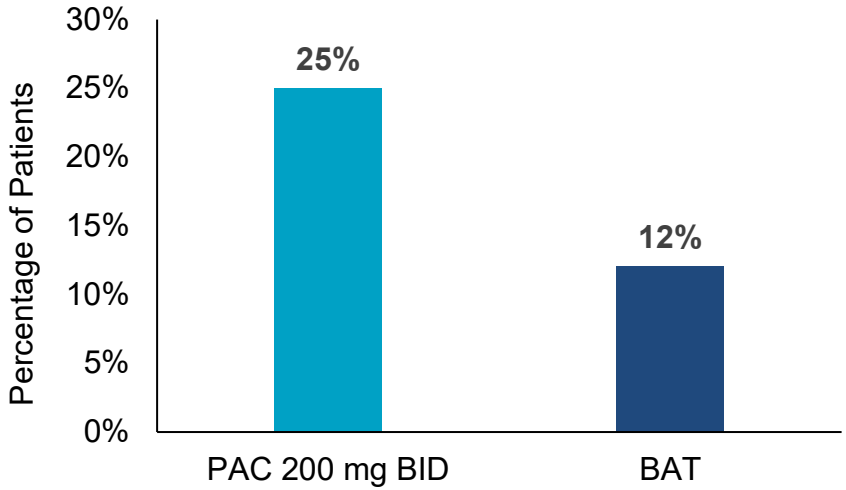
Dec 11, 2022, #628

Pacritinib in Cytopenic Myelofibrosis

- Approved in patients with MF who have a platelet count <50x10^9/L
- Able to be administered at the full approved dose (200 mg BID) regardless of cytopenias[1-3]
- Demonstrated hemoglobin improvement in randomized PERSIST-2 study[2]
- The mechanism behind / extent of anemia benefit has not been fully described

Clinical Improvement in Hemoglobin[2]

PERSIST-2, Week 24



IWG criteria: among patients with baseline hemoglobin <10 g/dL, increase of ≥2.0 g/dL or RBC transfusion independence for ≥8 weeks

BAT=best available therapy; BID=twice daily; IWG= ; MF=myelofibrosis; RBC=red blood cell.

[1] Mesa R, et al. *Lancet Oncology*; 2017. [2] Mascarenhas J, et al. *JAMA Oncol*. 2018;4(5):652-659. [3] Gerds A, et al. *Blood Advances*. 2020;4(22):5825-35.

Abstract 628 ASH 2022

Pacritinib is a Potent ACVR1 Inhibitor

- **Pacritinib is ~4x more potent** than momelotinib against ACVR1

	+ Control LDN 193189[a]	PAC C_{max} 213 nM	MMB C_{max} 168 nM	FED C_{max} 275 nM	RUX C_{max} 47 nM
Replicate 1 ACVR1 IC_{50} (nM)	**20.4**	**22.6**	**70.2**	**312.0**	**>1000**
Replicate 2 ACVR1 IC_{50} (nM)	**32.4**	**10.8**	**34.9**	**235.0**	**>1000**
Mean ACVR1 IC_{50} (nM)	**26.4**	**16.7**	**52.6**	**273.5**	**>1000**
Potency[b] (C_{max}:IC_{50})	**N/A**	**12.7**	**3.2**	**1.0**	**<0.01**

Legend

Higher potency

Lower potency

[a]LDN 193189 is an ACVR1 inhibitor.

[b]C_{max} is the maximum unbound plasma concentration at the clinical recommended dose in humans.

ACVR1= Activin A receptor type 1; FED=fedratinib; IC_{50}=half maximal inhibitory concentration; MOM=momelotinib; PAC=pacritinib; RUX=ruxolitinib.

Abstract 628 ASH 2022

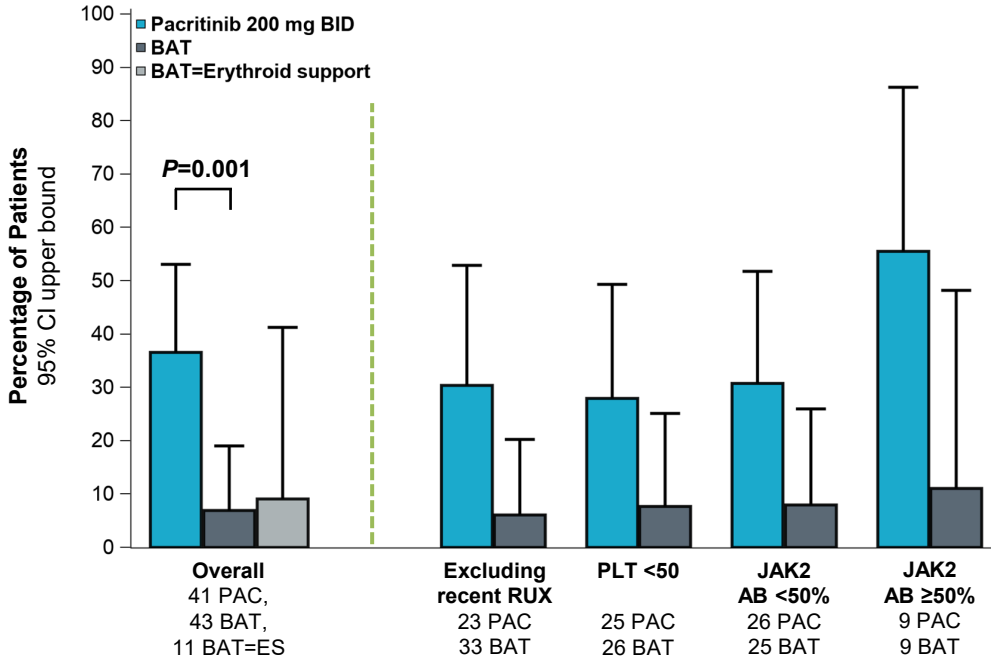
More Pacritinib Patients Achieved TI

TI Conversion Rate

Pacritinib N=41	BAT N=43	*P*-value
37%	7%	0.001

- TI conversion better on pacritinib than BAT, including patients receiving erythroid support agents as BAT
  - Erythroid support agents were prohibited on the pacritinib arm

Rate of TI (Gale criteria) through Week 24

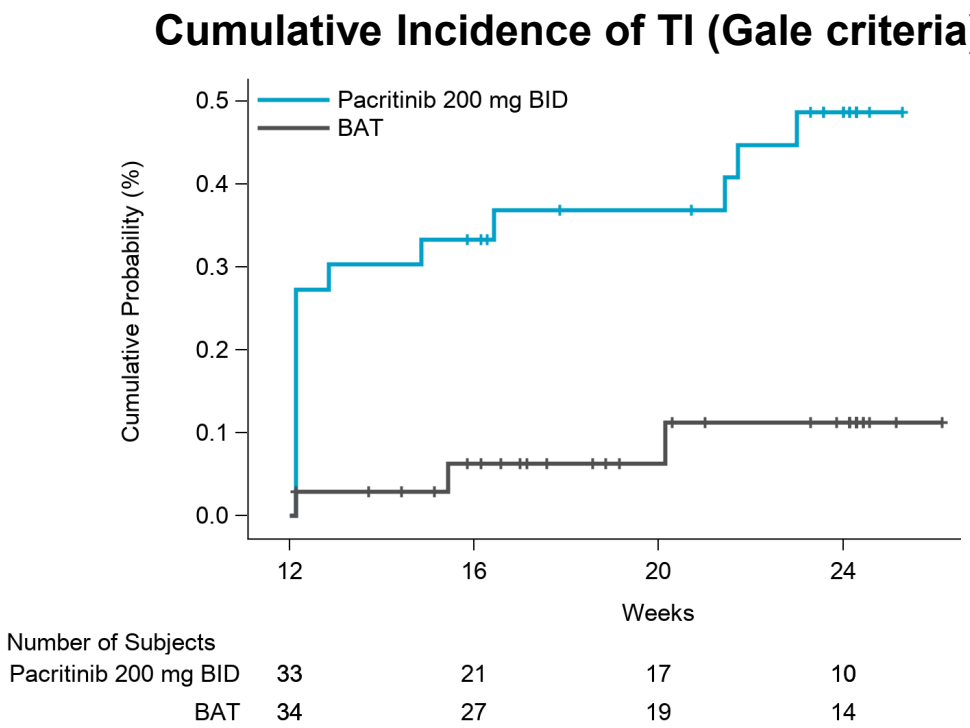


AB=allele burden; BAT=best available therapy; ES=erythroid support; JAK=Janus associated kinase; PAC=pacritinib; PLT=platelets; recent RUX=no ruxolitinib in prior 30 days; TI=transfusion independence.

Abstract 628 ASH 2022

TI Conversion Can Occur Late in Treatment

- Many responses occurred early during treatment
- Some responses occurred after several months on treatment



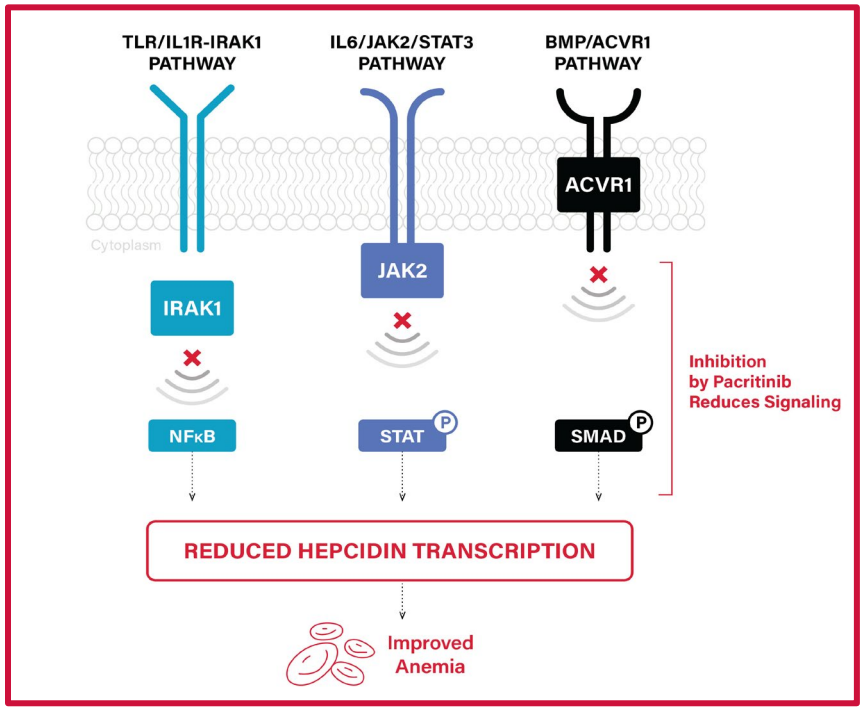
BAT=best available therapy; BID=twice daily; TI=transfusion independence.

Abstract 628 ASH 2022

Hypothesized Mechanism of Anemia Benefit

- **Potent, 24-hour inhibition of ACVR1** may function in conjunction with IRAK1 and JAK2 inhibition to reduce levels of hepcidin

- Hepcidin reduction ameliorates anemia of inflammation that occurs in myelofibrosis

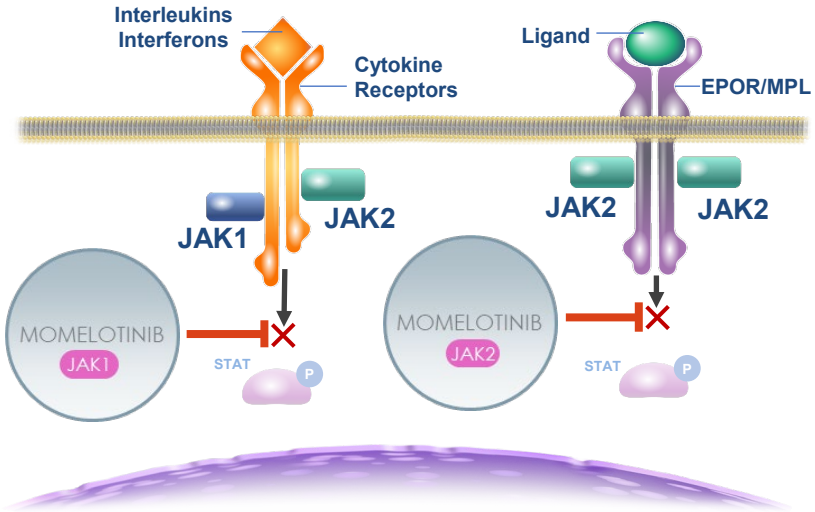


ACVR1= Activin A receptor type 1; JAK2=Janus associated kinase 2; IL6=interleukin-6; IRAK=interleukin receptor-associated kinase.

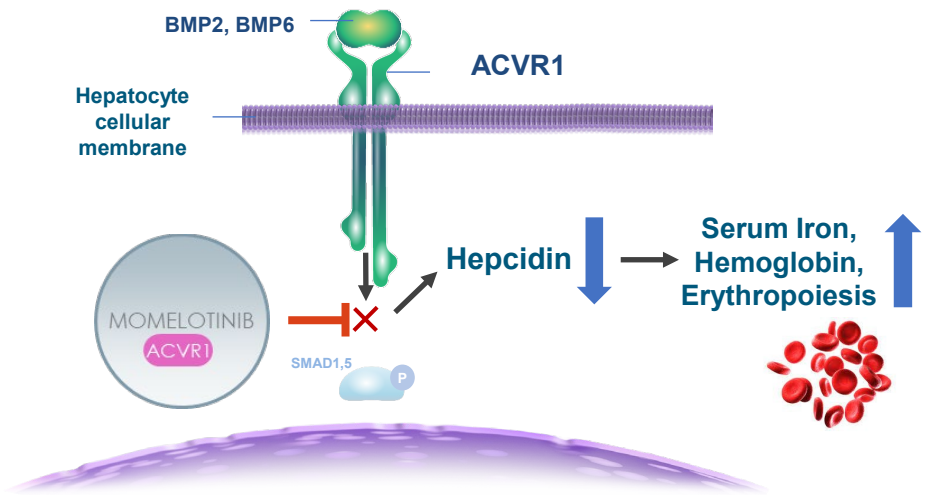
Abstract 628 ASH 2022

Momelotinib
Seeking Approval

Momelotinib Inhibits JAK1, JAK2 and ACVR1 to Address MF Symptoms, Spleen, and Anemia



Dysregulated **JAK-STAT signaling** in MF drives overproduction of inflammatory cytokines, **bone marrow fibrosis, systemic symptoms,** and clonal proliferation resulting in extramedullary hematopoiesis and **splenomegaly**.[1,2]



Chronic inflammation also drives hyperactivation of **ACVR1**, elevated **hepcidin**, dysregulated iron metabolism, and **anemia** of MF.[3,4]

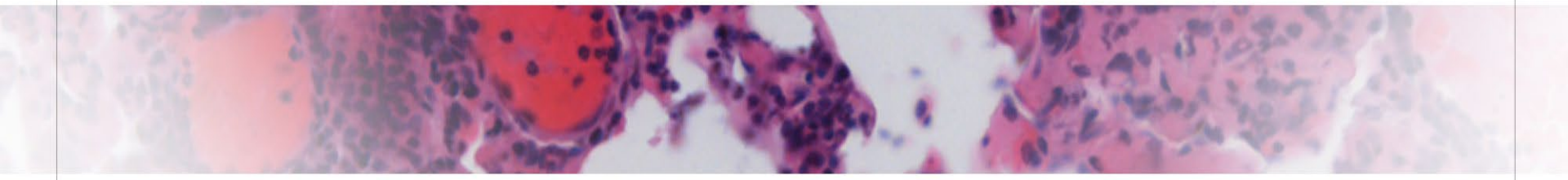
ACVR1=activin A receptor type 1; BMP=bone morphogenic protein; EPOR=erythropoietin receptor; JAK=Janus kinase; MMB=momelotinib; MPL=myeloproliferative leukemia protein; STAT=signal transducer and activator of transcription.

1. Chifotides HT, et al. *J Hematol Oncol*. 2022;15(1):7; 2. Verstovsek S, et al. *Future Oncol*. 2021;17(12):1449-1458; 3. Asshoff M, et al. *Blood*. 2017;129(13):1823-1830; 4. Oh S, et al. *Blood Adv*. 2020;4(18):4282-4291.

PRESENTED BY:
Ruben Mesa, MD, FACP
Director, Mays Cancer Center at UT Health San Antonio MD Anderson

American Society *of* Hematology

Helping hematologists conquer blood diseases worldwide



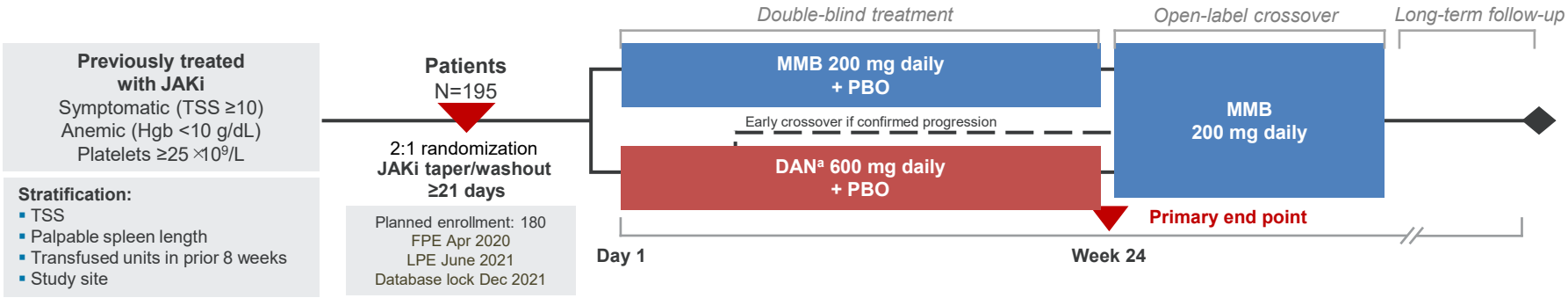
Updated Results from the Momentum Phase 3 Study of Momelotinib (MMB) Versus Danazol (DAN) in Symptomatic and Anemic Myelofibrosis (MF) Patients Previously Treated with a JAK Inhibitor

Aaron T. Gerds,[1] Ruben A. Mesa,[2] Alessandro M. Vannucchi,[3] Haifa Kathrin Al-Ali,[4] David Lavie,[5] Andrew Kuykendall,[6] Sebastian Grosicki,[7] Alessandra Iurlo,[8] Yeow Tee Goh,[9] Mihaela Lazaroiu,[10] Miklos Egyed,[11] Maria Laura Fox,[12] Donal P. McLornan,[13] Andrew Charles Perkins,[14] Sung-Soo Yoon,[15] Vikas Gupta,[16] Jean-Jacques Kiladjian,[17] Rafe Donahue,[18] Jun Kawashima,[18] Srdan Verstovsek[19]

[1]Cleveland Clinic Taussig Cancer Center, Cleveland, OH, USA; [2]UT Health San Antonio MD Anderson Cancer Center, San Antonio, TX, USA; [3]University of Florence, Firenze, Italy; [4]University Hospital of Halle (Saale), Halle, Germany; [5]Hadassah University Medical Center, Jerusalem, Israel; [6]Moffitt Cancer Center, Tampa, FL, USA; [7]Medical University of Silesia, Katowice, Poland; [8]Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Milan, Italy; [9]Singapore General Hospital, Singapore; [10]Policlinica de Diagnostic Rapid, Brasov, Romania; [11]Somogy County Kaposi Mór General Hospital, Kaposvár, Hungary; [12]Vall d'Hebron University Hospital, Barcelona, Spain; [13]Guy's and St Thomas' NHS Foundation Trust, London, UK; [14]Australian Centre for Blood Diseases and Alfred Hospital, Monash University, Melbourne, VIC, Australia; [15]Seoul National University Hospital, Seoul, South Korea; [16]Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada; [17]Université de Paris, AP-HP, Hôpital Saint-Louis, Centre d'Investigations Cliniques, Paris, France; [18]Sierra Oncology, Inc., San Mateo, CA, USA; [19]The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Presentation 627 | Presented at the 64 American Society of Hematology Annual Meeting & Exposition, New Orleans, LA, USA | December 10-13, 2022

MOMENTUM Is an Ongoing Phase 3 Study of Momelotinib Versus DAN in Symptomatic, Anemic, JAKi-Experienced Patients



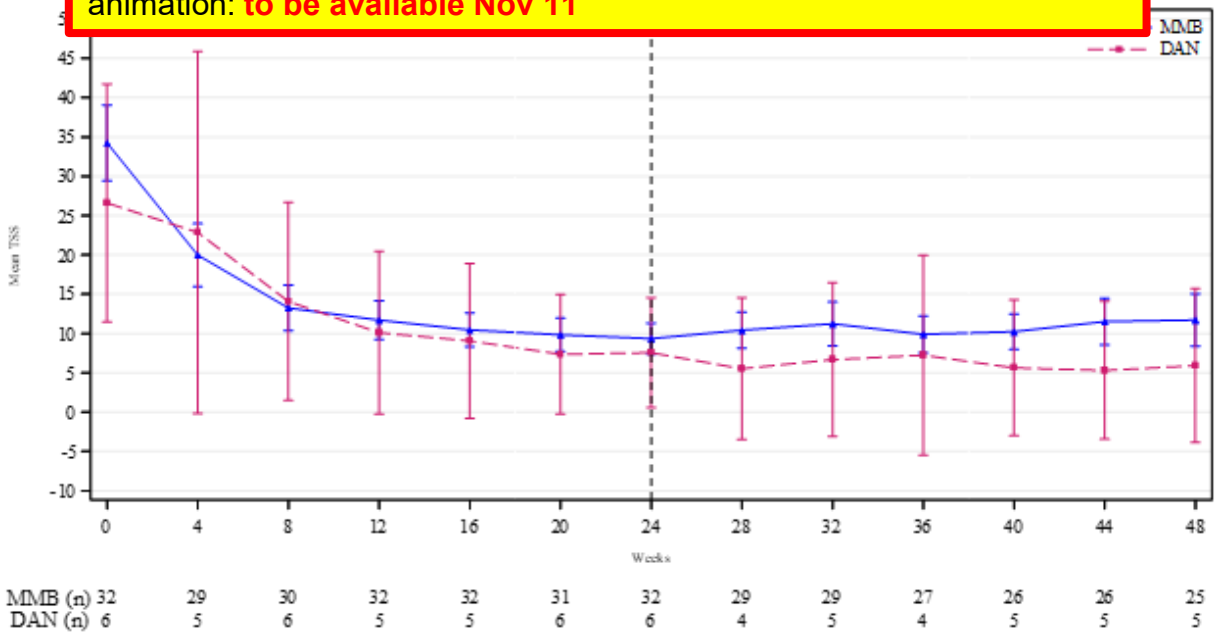
MOMENTUM Topline Results at Week 24: All Primary and Key Secondary End Points Met[1,2]

	MFSAF TSS[b] response rate (primary end point)	TI response[c] rate	SRR[d] (35% reduction)
MMB (N=130)	32 (24.6%)	40 (30.8%)	30 (23.1%)
DAN (N=65)	6 (9.2%)	13 (20.0%)	2 (3.1%)
	P =.0095 (superior)	1-sided *P* =.0064 (noninferior)	*P* =.0006 (superior)

ClinicalTrials.gov: NCT04173494.
[a]Danazol was selected as an appropriate comparator given its use to ameliorate anemia in patients with MF.[3-5] [b]TSS response defined as achieving ≥50% reduction in TSS over the 28 days immediately before the end of week 24 compared with baseline. [c]TI response defined as not requiring red blood cell transfusion in the last 12 weeks of the 24-week randomized period, with all Hgb levels during the 12-week interval of ≥8 g/dL. [d]SRR defined as achieving a ≥25% or ≥35% reduction in spleen volume from baseline.
DAN, danazol; Hgb, hemoglobin; JAKi, Janus kinase inhibitor; MF, myelofibrosis; MFSAF, Myelofibrosis Symptom Assessment Form; MMB, momelotinib; PBO, placebo; SRR, splenic response rate; TI, transfusion independence; TSS, total symptom score.
1. Mesa R, et al. Abstract presented at: 2022 ASCO Annual Meeting; June 3-6, 2022; Chicago, IL and Virtual. Abstract 7002. 2. Verstovsek S, et al. Abstract presented at: 2022 EHA Congress; June 9-12; 2022; Vienna, Austria and Virtual. Abstract S195. 3. Chifotides HT, et al. *J Hematol. Oncol.* 2022;15(1):7. 4. Naymagon L, et al. *Hemasphere.* 2017;1(1):e1. 5. Vannucchi AM, et al. *Ann Oncol.* 2015;26(suppl 5):v85-v99.

Sustained Responses Were Observed in Week 24 Symptom Responders[a]

PLACEHOLDER: Sierra to replace figure with the individual patient animation: **to be available Nov 11**



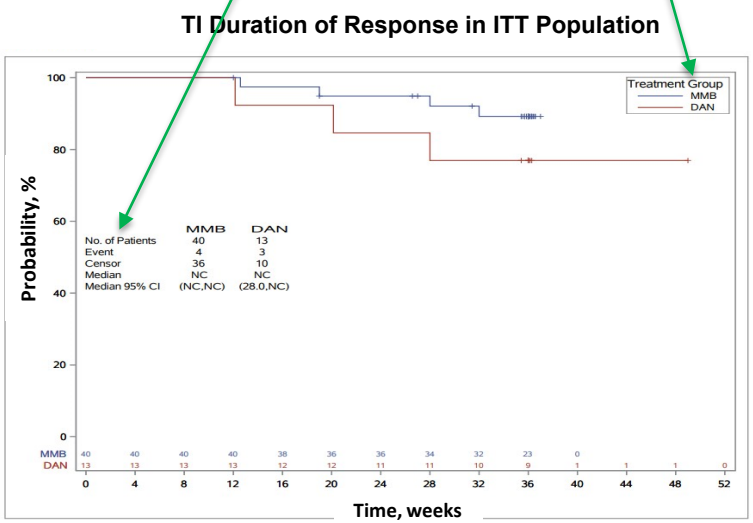
Of TSS responders at week 24, 1 of 32 (3%) MMB→MMB patients and 0 of 6 (0%) DAN→MMB patients had TSS ≥baseline in OL

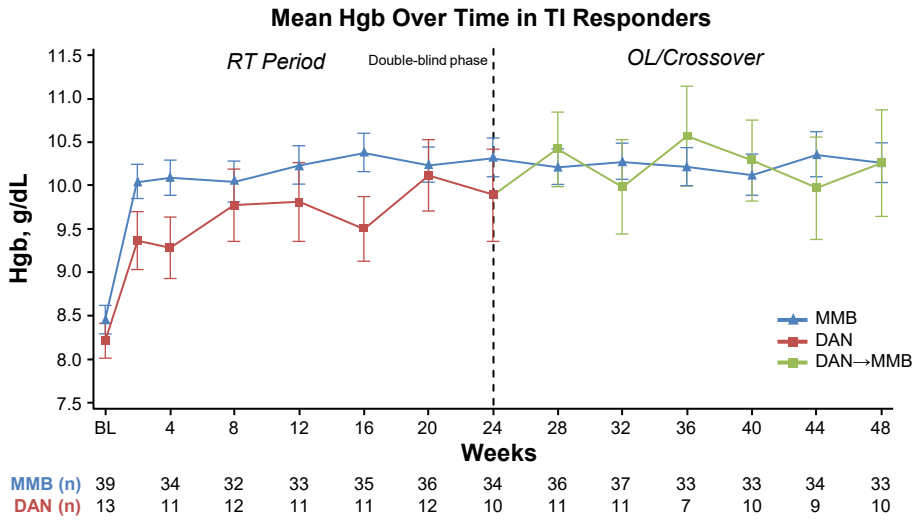
[a]Defined as the proportion of patients who achieve ≥50% reduction in TSS over the 28 days immediately before the end of week 24 compared with baseline.
DAN, danazol; MMB, momelotinib; OL, open-label; TSS, total symptom score.

Gerds et. al. ASH 2022

Sustained Responses Were Observed in Week 24 TI Response[a]

LW Creative to redraw and replace text in graphs with sentence case during redrawal/recreation



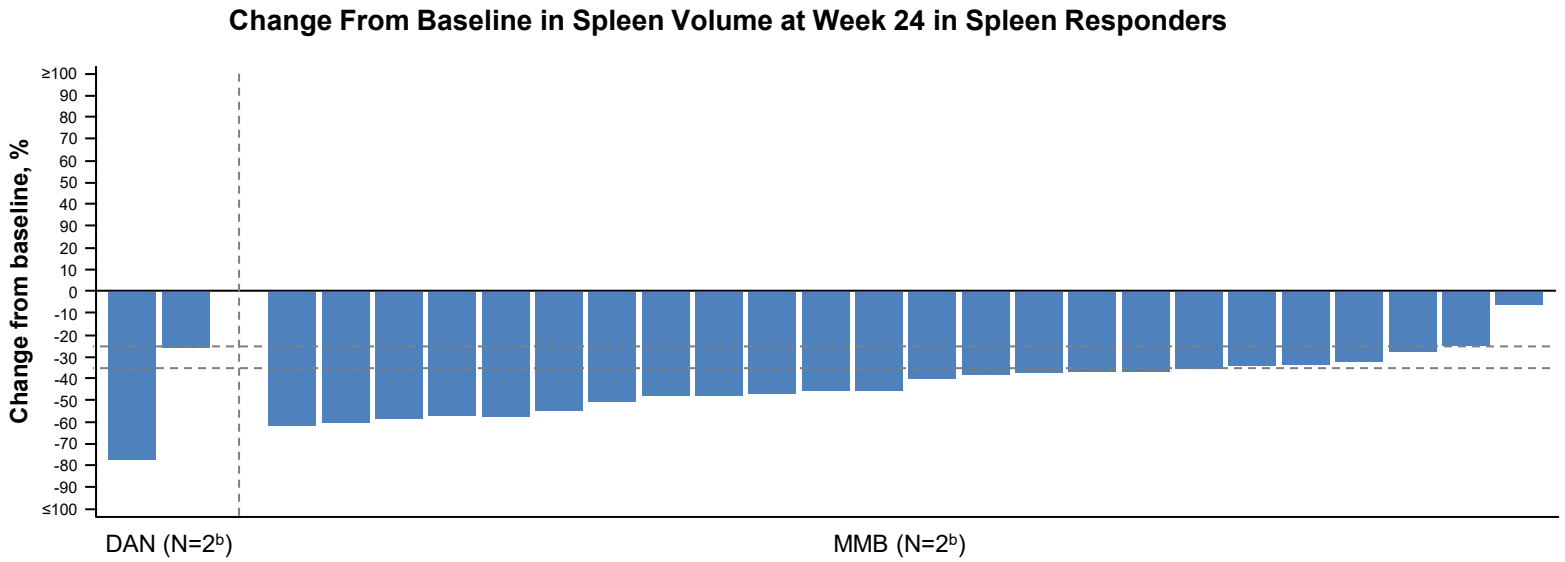


Of TI responders at week 24, 4 of 40 (10%) MMB→MMB patients and 3 of 13 (23%) DAN→MMB patients had an RBC transfusion or Hgb <8 g/dL in OL

[a]Defined as not requiring RBC transfusion in the prior 12 weeks and Hgb levels ≥8 g/dL.
BL, baseline; DAN, danazol; Hgb, hemoglobin; ITT, intention-to-treat; MMB, momelotinib; OL, open-label; RBC, red blood cell; RT, randomized treatment; TI, transfusion independence.

Gerds et. al. ASH 2022

Sustained Responses Were Observed in Week 24 Spleen Responders[a]

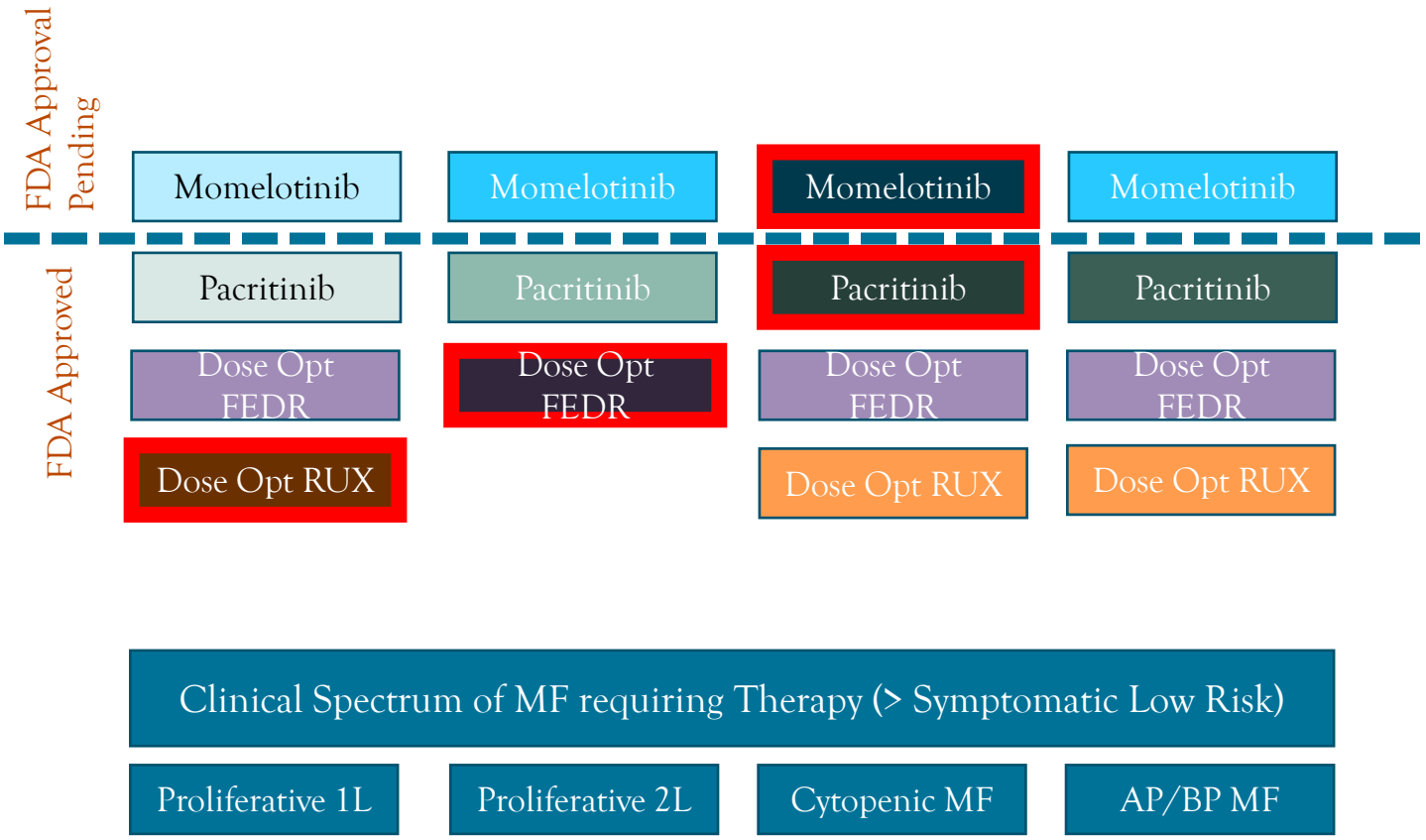


Of SRR35 responders at week 24 who had a week 48 scan, 0 of 24 (0%) MMB→MMB patients and 0 of 2 (0%) DAN→MMB patients had splenic volume ≥ baseline at week 48

[a]Defined as the proportion of patients who have a reduction in spleen volume of ≥35% from baseline. [b]N is the number of patients with percent change in spleen volume at week 48 available.
DAN, danazol; MMB, momelotinib; SRR35, splenic response rate >35%.

Gerds et. al. ASH 2022

Step 1 for MF Management: Optimize JAK Inhibition



R Mesa developed Slide

A selection of novel agents/targets being developed in MPN particularly MF

Cell-cycle Checkpoint

- P2 Imetelstat | Telomerase Inhibitor (*Geron*)
- P1 Alisertib | Aurora Kinase Inhibitor (*Takeda*)

Anti-fibrotic

- P2 PRM-151 | Pentraxin-2 (*Promedior*)

Receptor Ab / ADC

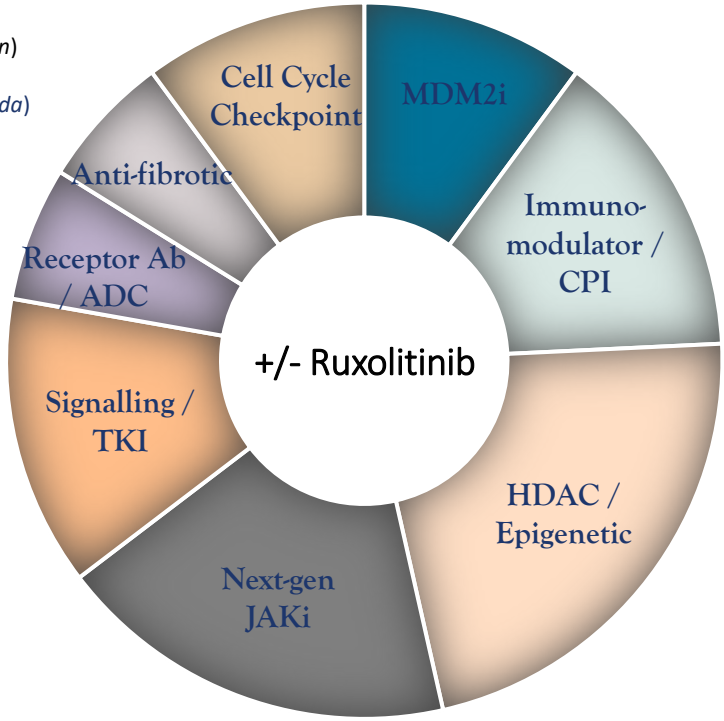
- P2 SL-401 | CD123-toxin (*Stemline*)

Signaling / TKI

- P2 Glasdegib | Hedgehog (*Pfizer*)
- P2 Sonidegib | Hedgehog (*Sun*)
- P2 INCB'465 | PI3Ki (*Incyte*)
- P2 LCL1 I SMAC/IAP (Novartis)

Next-gen JAKi

- P3 Fedratinib | JAK2 (*Celgene*)
- P3 Pacritinib | JAK2/FLT3 (*CTI Bio*)
- P3 Momelotinib | JAK2/1/ACVR1 (*Sierra*)
- P2 Itacitinib | JAK1 (*Incyte*)



Slide Courtesy of Prof Claire Harrison

Apoptosis/MDM2/BCL

- P1 KRT-232 (*Kartos Therapeutics*)
- P2 Idasanutlin / RG7388 (*Roche*)
- P1 Navitoclax | BCL2 inhibition (*Abbvie*)

Immuno-modulator / CPI

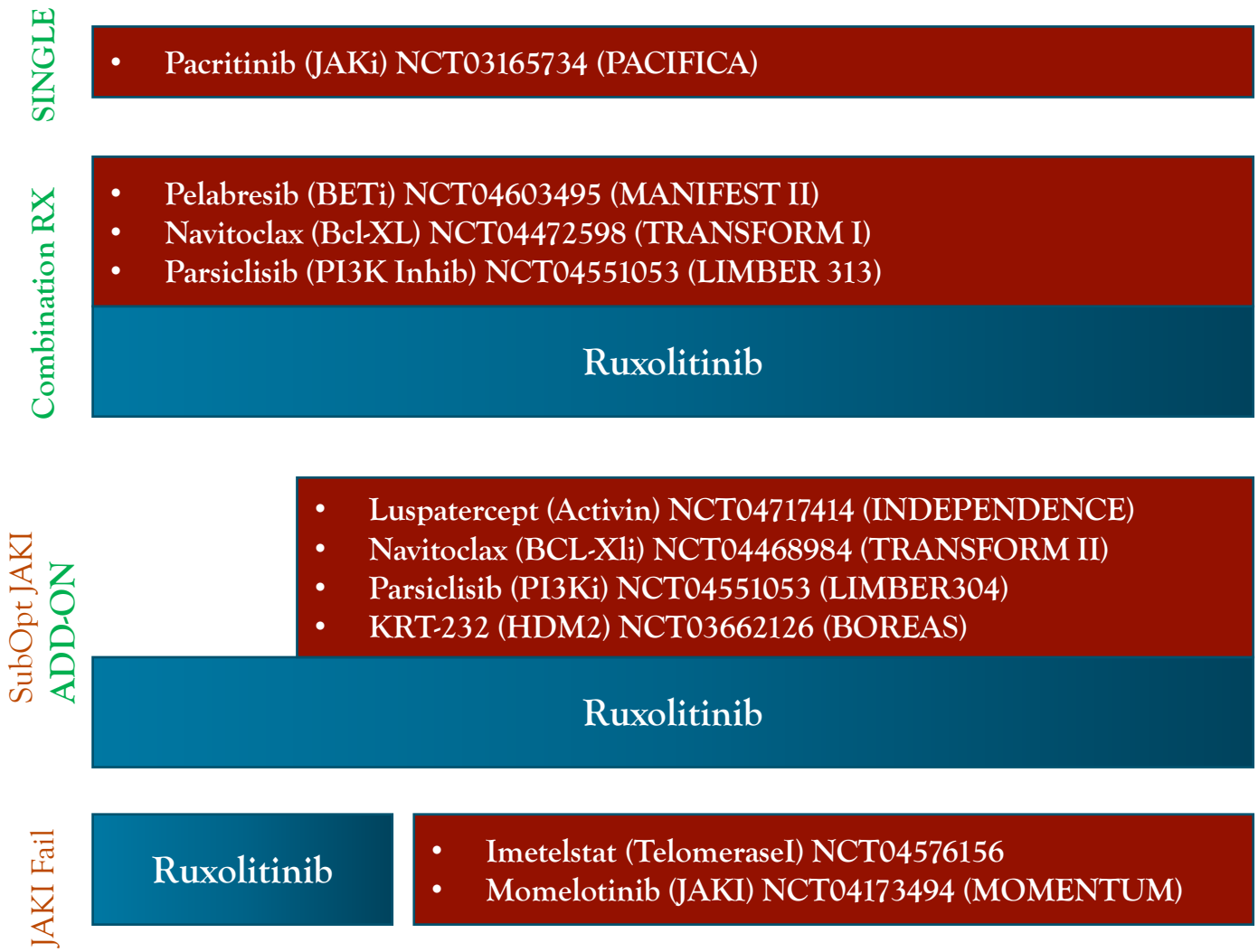
- P3 Pegasys | IFN-α2a (ESR/Roche)
- P3 Ropeg-IFN-α2b (*PharmaEssentia*)
- P2 Nivolumab / Pembrolizumab | PD-1 (*BMS / MRK*)

HDAC / Epigenetic

- P3 Azacytidine | HMA (*ESR/Celgene*)
- P3 Panobinostat | HDAC (*Novartis*)
- P2 Givinostat I HDAC (Italfama)
- P2 IMG-7289 | LSD1 (*Imago*)
- P1 CPI-0610 | BETi (*Constellation*)
- P1 PU-H71 | HSP90i (*Samus*)

PHASE OF DEVELOPMENT (IN MPN): P1 P2 P3

Current Phase III trials in MF



Therapy of MPNs 2023

- Goals and Targets
- ET and PV
- JAK Inhibitors as Foundation
- Non JAKi MOA
- Putting it all Together

What is Precise and Personalized Cancer Care?

Molecular Features of Disease
-Multi-Omic
-Dx, treatment, survivorship

Communication
Social DOH
Health Literacy

Individual Health Factors In Treatment Planning?

Geography
Employment
Financial Pressures

Individualized Supportive Care Needs?

Individual Cultural Value Factors In Treatment Planning?

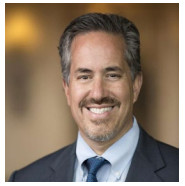
Individualized Survivorship?

Disease impact
Symptoms
QoL?

MPN Patient Community

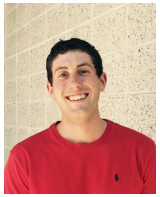
MPN Group	Focus	Website
MPN Research Foundation	RES-ED-ADV	www.Mpnresearchfoundation.org
Leukemia and Lymphoma Society*	RES-ED-ADV	www.lls.org
MPN Advocacy & Education International*	ED-ADV	www.mpnadvocacy.com
MPN Education Foundation*	ED-COMM	www.mpninfo.org
AAMDS Foundation	ED	www.aamds.org
MPN Voice	ED	www.mpnvoice.org.uk
MPN HUB*	ED	www.mpn-hub.com
MPN Advocates Network	ED-ADV	www.mpn-advocates.net
Global MPN Scientific Foundation*	RES-ED-ADV	www.gmpnsf.org
MPN Forum Facebook Group	ED-COMM	https://www.facebook.com/groups/ourmpnforum/

MPN QoL STUDY GROUP








Atrium Health

Wake Forest University School of Medicine