



Strategie condivise
per la Mielofibrosi

23 giugno 2025 • Milano

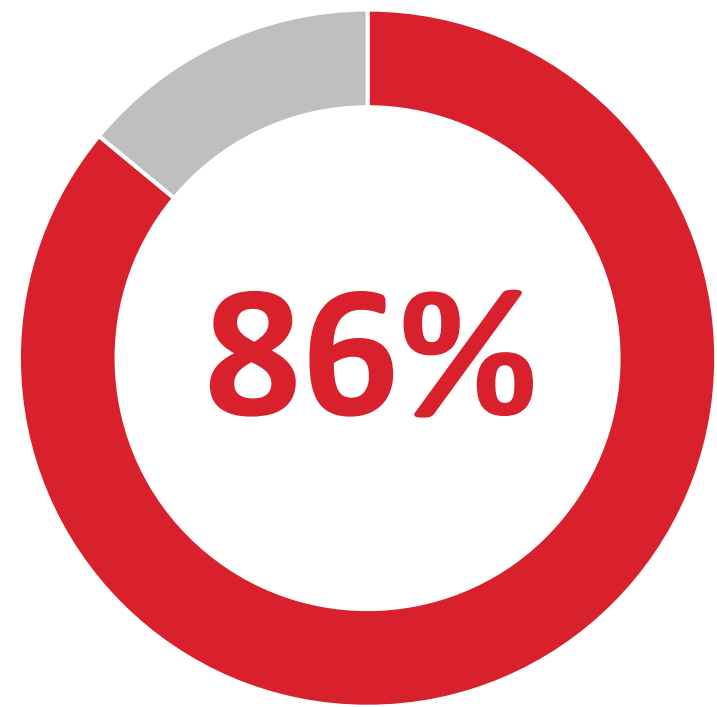
Unmet medical needs nei pazienti con mielofibrosi e anemia

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degli STUDI
di CATANIA

Effects of Anemia Are Associated With a Significant Burden on Patients



of patients with MF would most like **fatigue/tiredness** improved.^{1,a} Patients with MF and anemia have **higher mean total symptom scores** than those without anemia
(29.6 vs 22.3; $P<.001$)²



- **Hemoglobin levels and transfusion dependency** significantly correlate with **worse quality of life**^{3,4}



Ability to work and productivity are typically impaired in patients with high symptom burden^{1,2}



RBC transfusions may cause⁵⁻⁷:

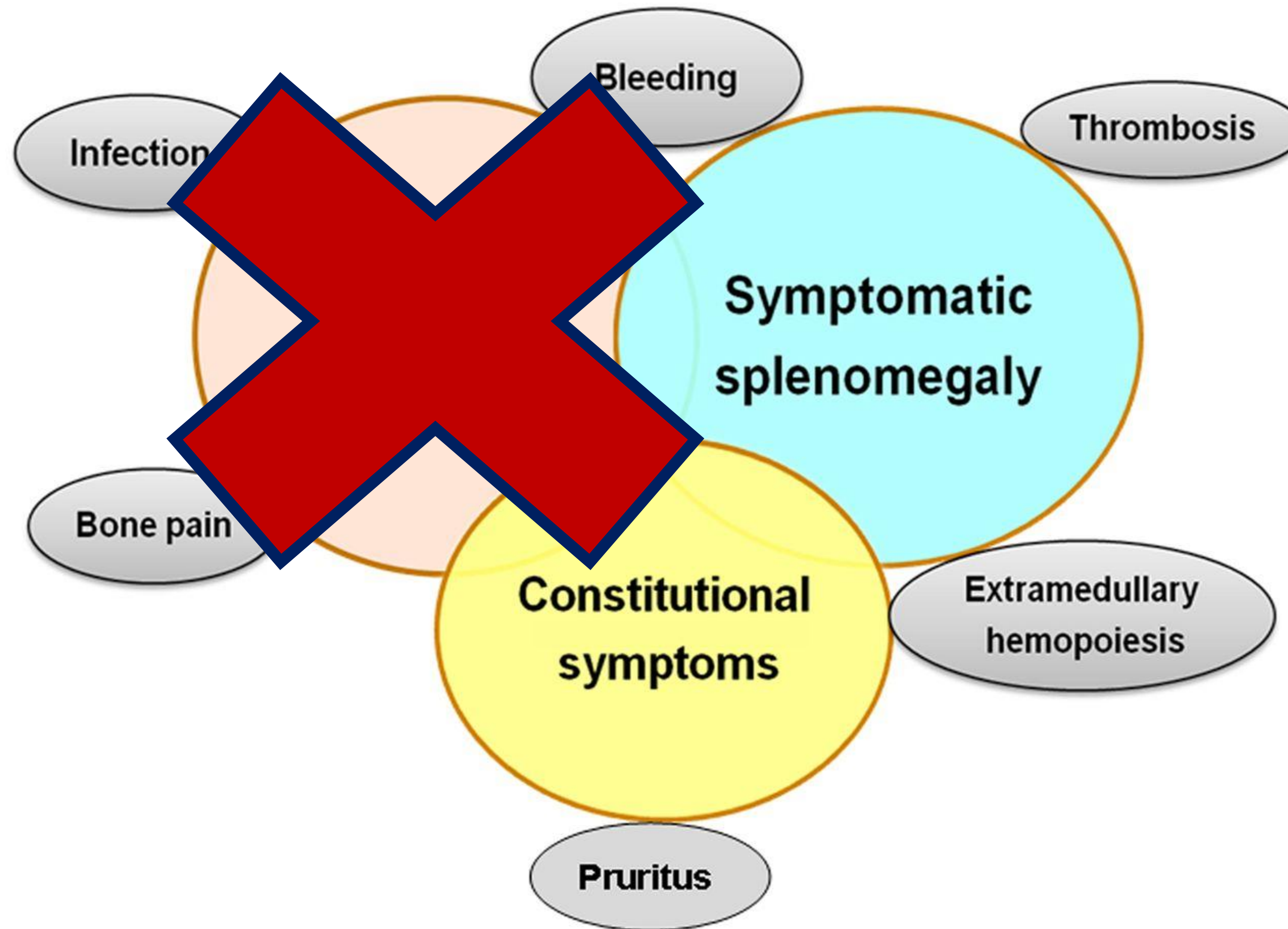
- **Iron overload**
- **Time burden** to receive treatment
- **Burden on healthcare resources**

MF, myelofibrosis; RBC, red blood cell.

^a The data shown are based on a global online survey of patients with MF and physicians conducted from April 2016 to October 2016.

1. Harrison CN, et al. *Ann Hematol*. 2017;96(10):1653-1665.
2. Scotch AH, et al. *Leuk Res*. 2017;63:34-40.
3. Mesa RA, et al. *Cancer*. 2007;109(1):68-76.
4. Tefferi A, et al. *Clin Ther*. 2014;36(4):560-566.
5. Wood JC, *Am J Hematol*. 2007;82(12 suppl):1132-1135.
6. Shreay S, et al. *Support Care Cancer*. 2013;21(5):1335-40.
7. Gerds A, et al. ASH 2022. Poster 1729.

Therapy of Myelofibrosis

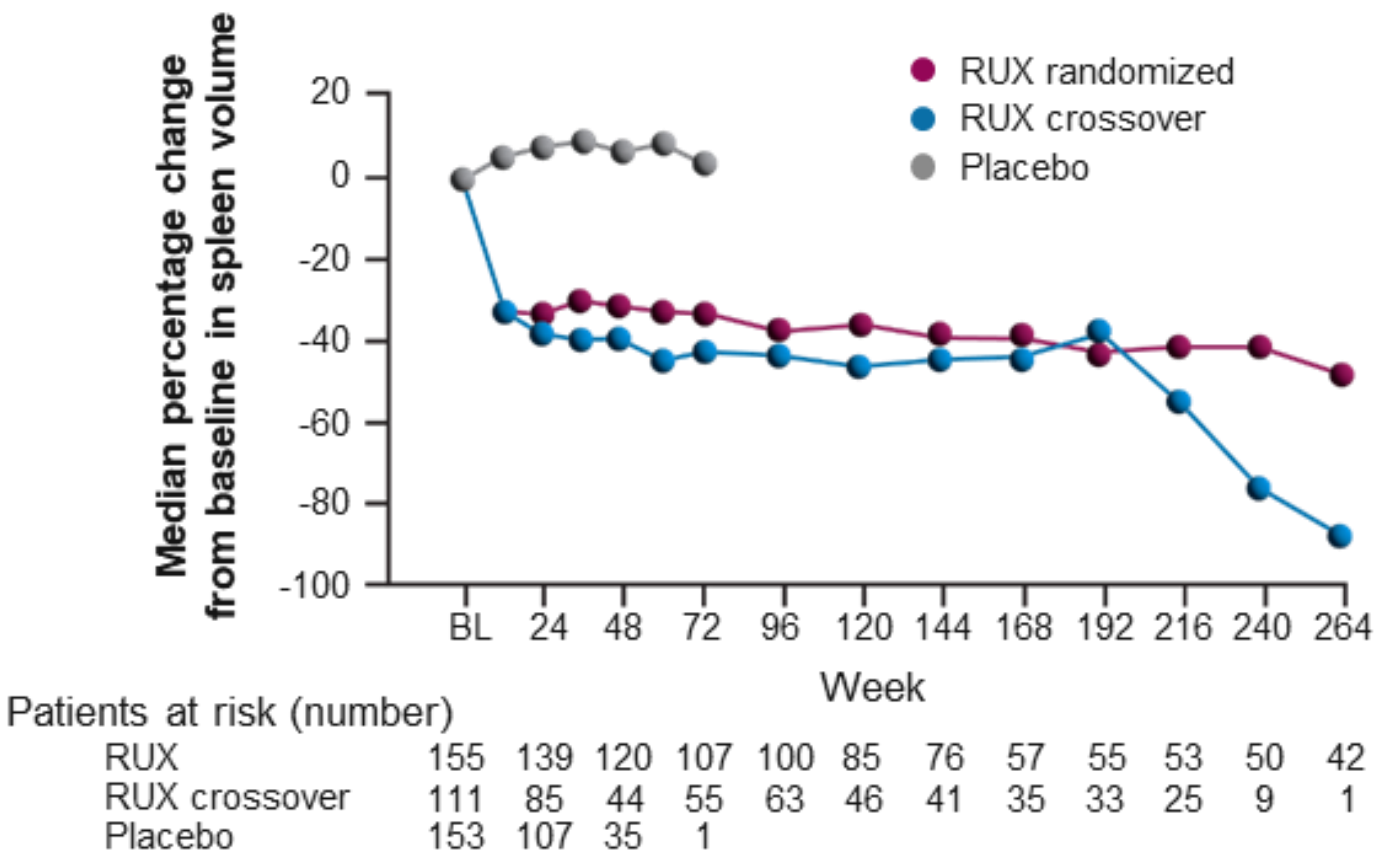


What Are the Benefits of Ruxolitinib in Myelofibrosis?

Splenomegaly

Evidence of therapeutic benefit based on SVR35

COMFORT-I Study: Randomized, double-blind, placebo-controlled, phase 3 study | 5-year analysis | n=309

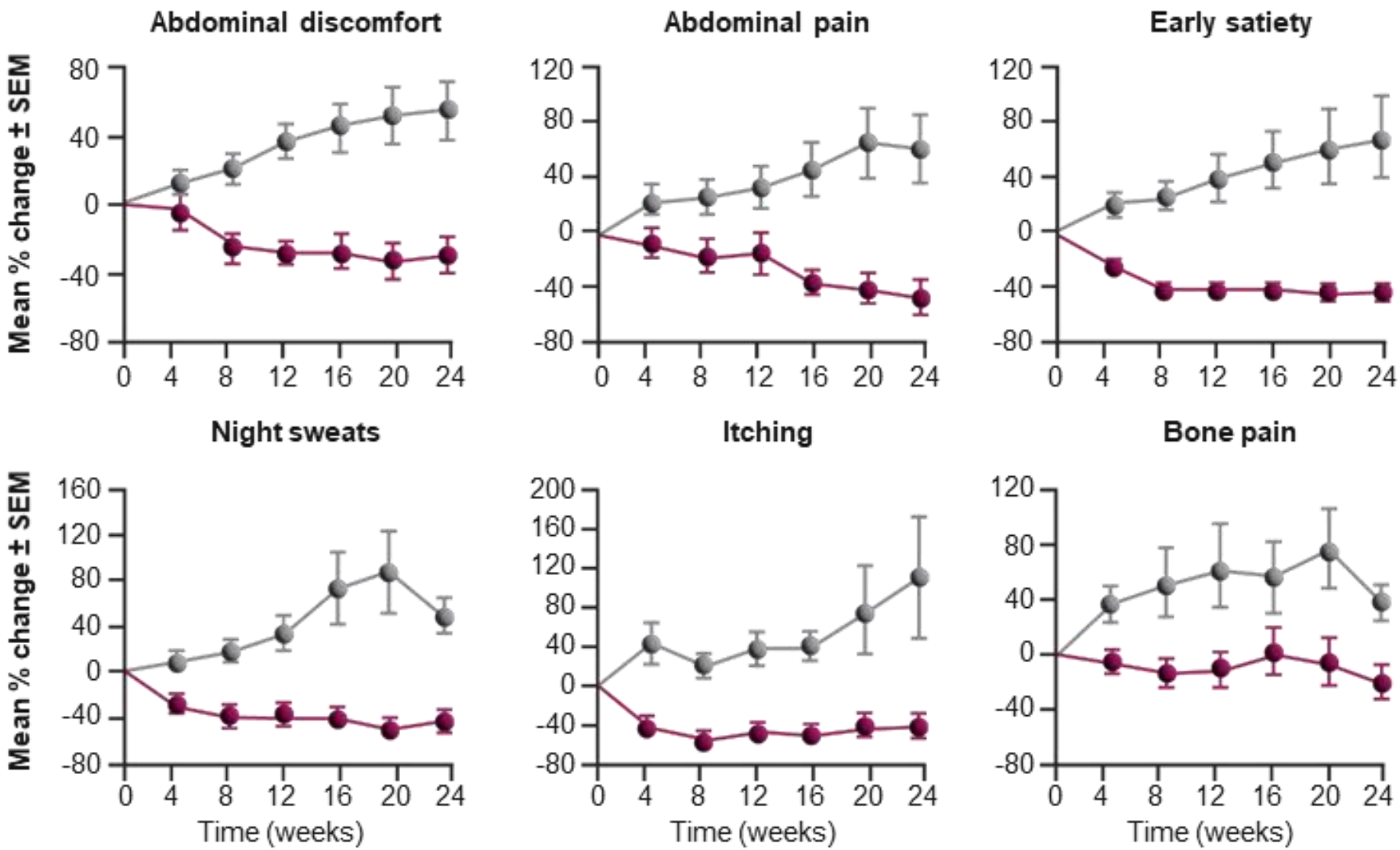


Among patients originally randomized to RUX, 59.4% (92/155) achieved a $\geq 35\%$ reduction in spleen volume at any time during the study
50% of patients maintained the response at 5 years

Symptoms

Evidence of therapeutic benefit based on TSS50

COMFORT-I Study

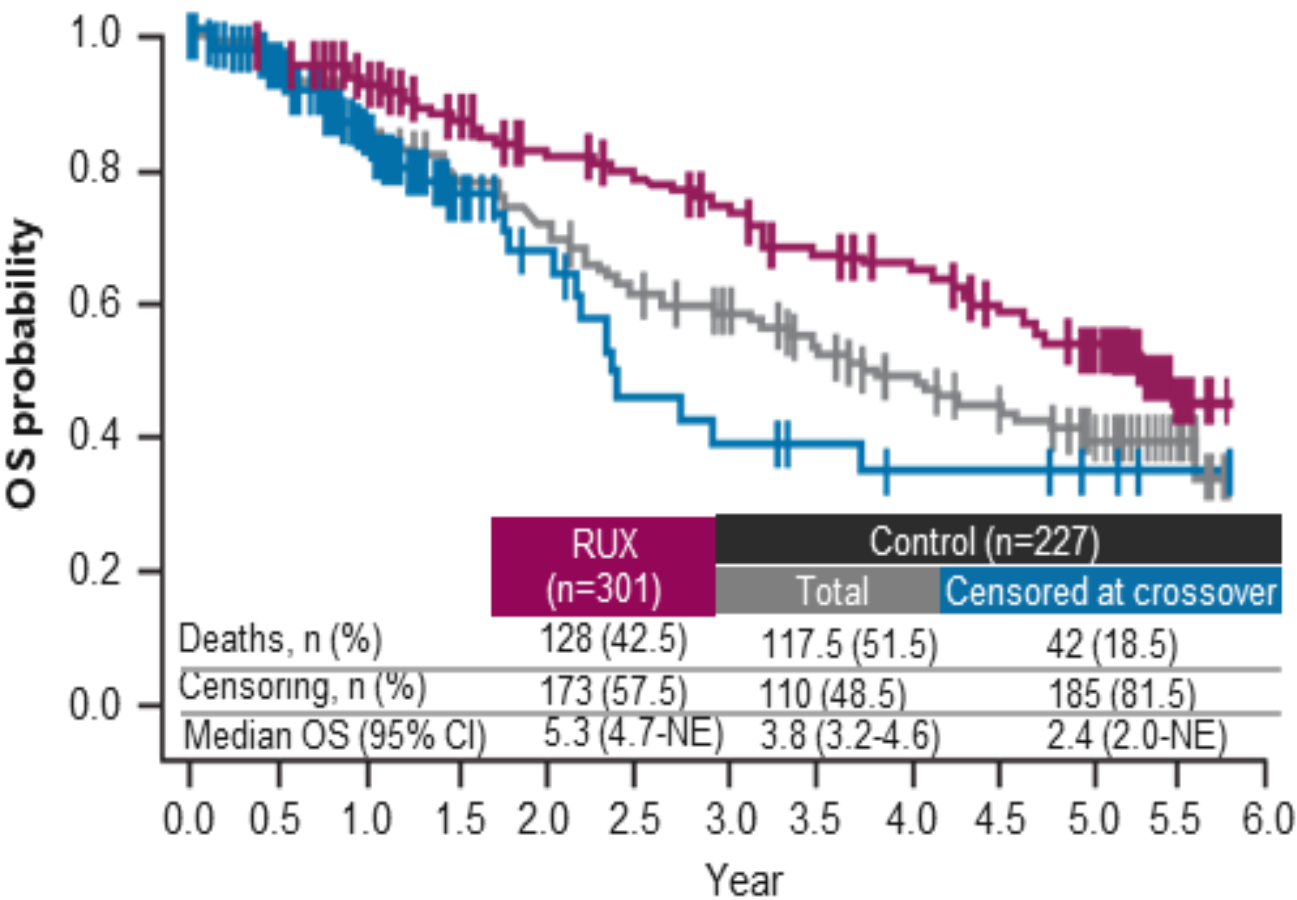


Individual symptom scores, as assessed by the modified MFSAF v2.0 at each 4-week timepoint in patients receiving RUX, showed **improvement relative to baseline**

Survival

Some evidence of survival benefit for ruxolitinib

COMFORT I and COMFORT-II Studies (Randomized, open-label, active-controlled, phase 3 study with crossover) | 5-year pooled analysis of overall survival



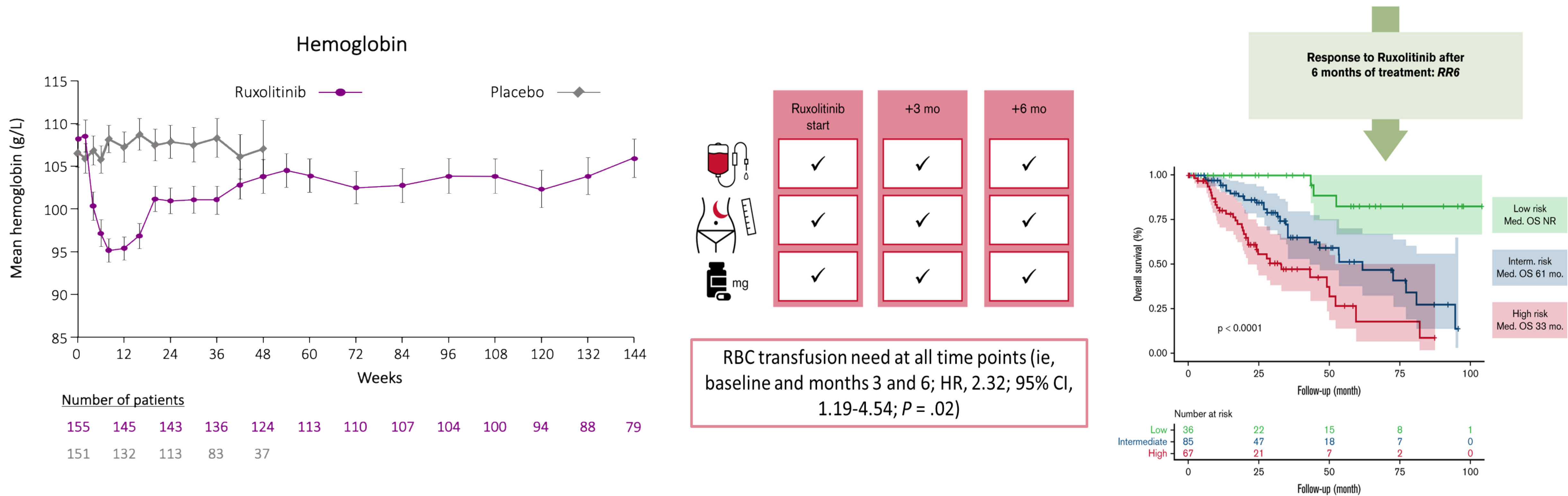
MFSAF, myelofibrosis symptom assessment form; RUX, ruxolitinib; SVR35, $\geq 35\%$ spleen volume reduction from baseline; TSS50, $\geq 50\%$ improvement in Total Symptom Score from baseline.

[1] JAKAFI (ruxolitinib). U.S. Prescribing Information. January 2023. [2] JAKAVI (ruxolitinib). Summary of Product Characteristics. May 2022. [3] Verstovsek S, et al. *J Hematol Oncol*. 2017;10(1):55. [4] ClinicalTrials.gov COnTrolled MyeloFibrosis Study With ORal JAK Inhibitor Treatment: The COMFORT-I Trial. Available at: <https://clinicaltrials.gov/ct2/show/NCT00952289>. Accessed June 2, 2023. [5] Mesa RA, et al. *J Clin Oncol*. 2013;31(10):1285-1292. [6] Verstovsek S, et al. *J Hematol Oncol*. 2017;10(1):156. [7] ClinicalTrials.gov Controlled Myelofibrosis Study With Oral Janus-associated Kinase (JAK) Inhibitor Treatment-II: The COMFORT-II Trial. Available at: <https://clinicaltrials.gov/ct2/show/NCT00934544>. Accessed June 2, 2023.



A prognostic model to predict survival after 6 months of ruxolitinib in patients with MF

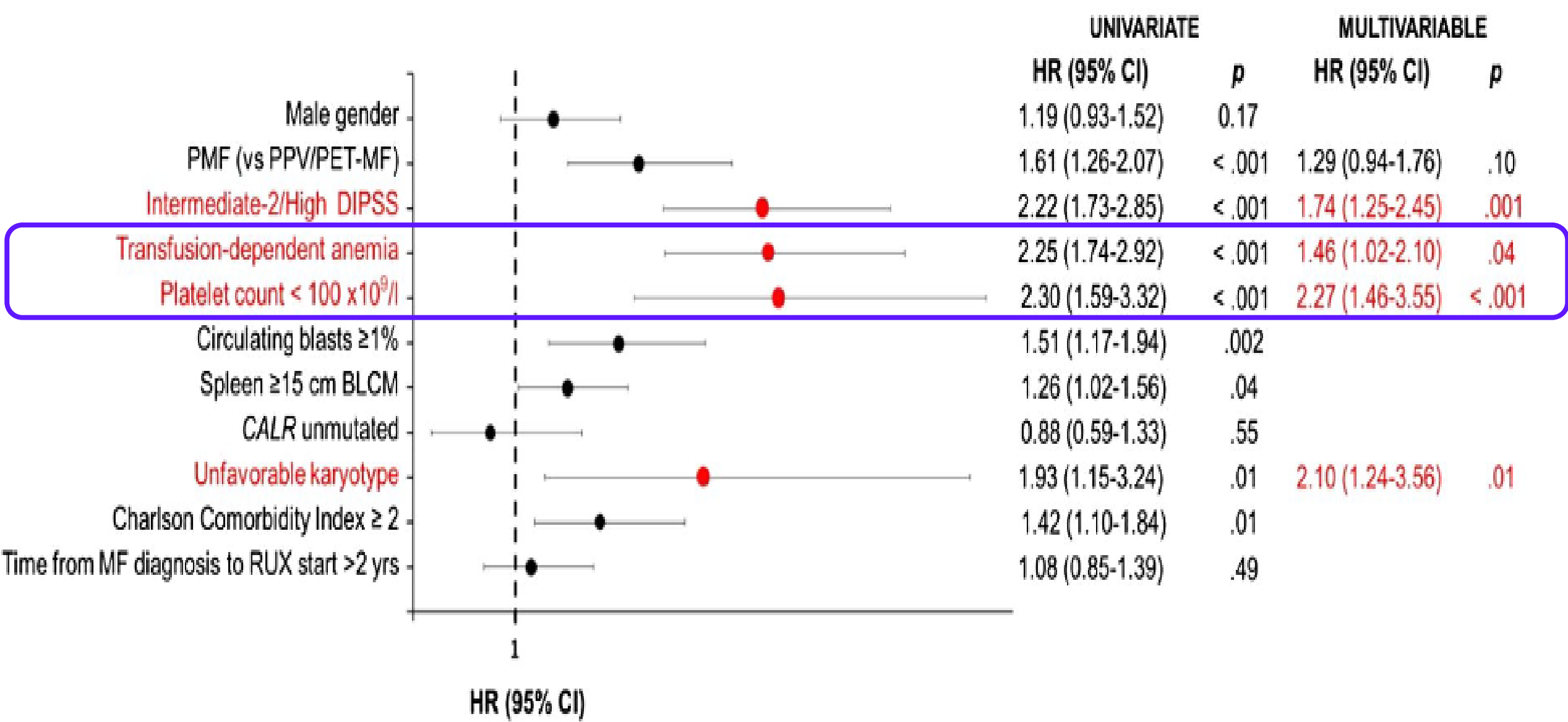
Median 3-year follow-up of COMFORT-I in patients with int-2 or high-risk MF randomized to RUX or pbo



CI, confidence interval; HR, hazard ratio; Med, medium; NR, not reached; OS, overall survival; pbo, placebo; RBC, red blood cell RUX, ruxolitinib.
References: 1. Verstovsek S, et al. *Haematologica* 2015; 100:479-488. 2. Maffioli M et al. *Blood Adv.* 2022;6(6):1855-1864

Real-World Evidence on Ruxolitinib Use

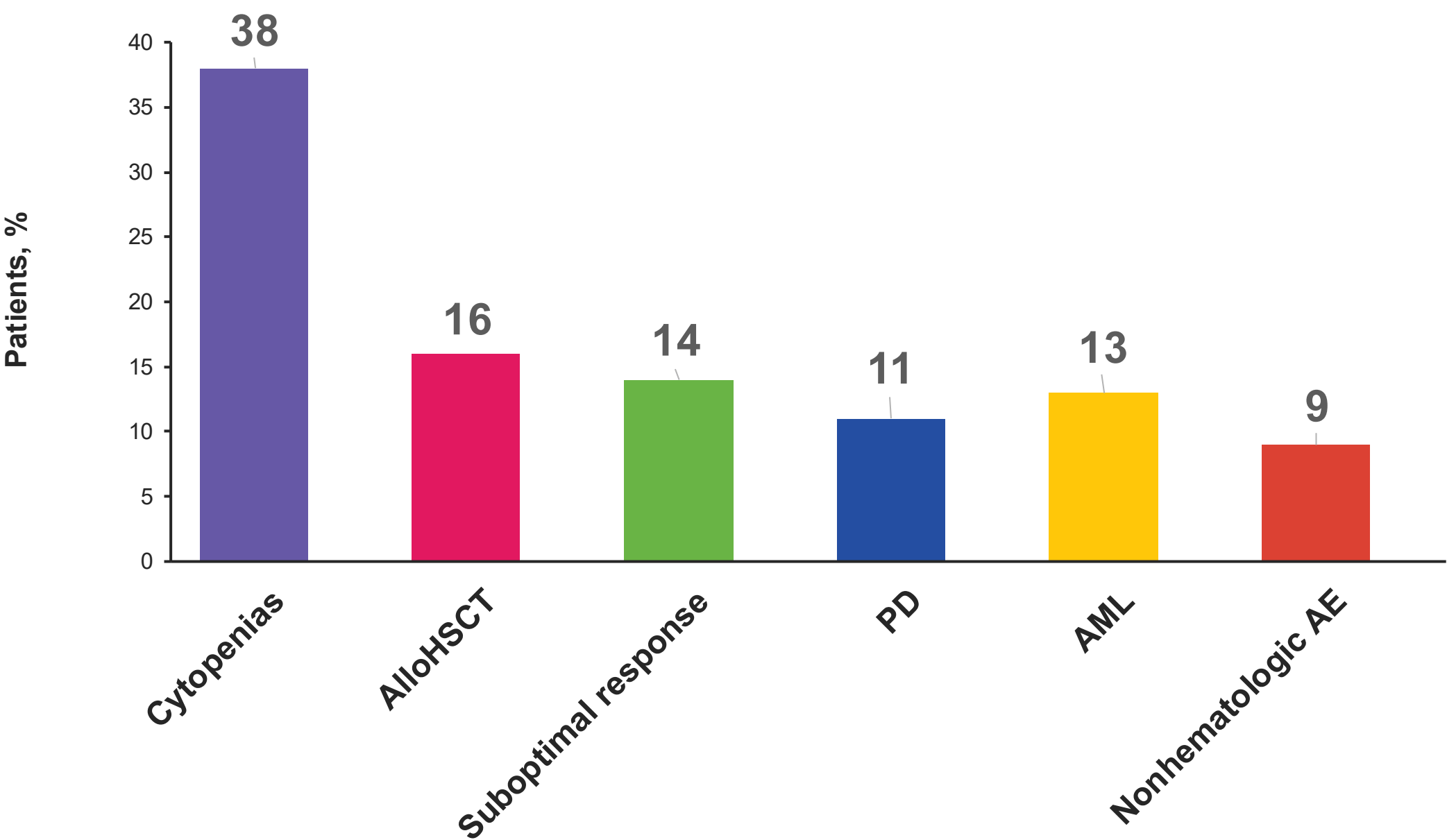
Baseline Risk Factors for Ruxolitinib Discontinuation



BLCM indicates below the left costal margin; PMF, primary myelofibrosis; PPV/PET-MF, postpolycythemia vera/postessential thrombocythemia myelofibrosis.

The 3 top clinical reasons for stopping ruxolitinib in patients with MF in chronic phase: inadequately controlled splenomegaly (including the lack or loss of a spleen response; 34.8%), **anemia/thrombocytopenia (17.4%)**, and infectious events (9.2%)

Real-World Study Showing Reasons for Ruxolitinib Discontinuation



AE, adverse event; alloHSCT, allogeneic hematopoietic stem cell transplant; AML, acute myeloid leukaemia; PD, progressive disease; PLT, platelet.

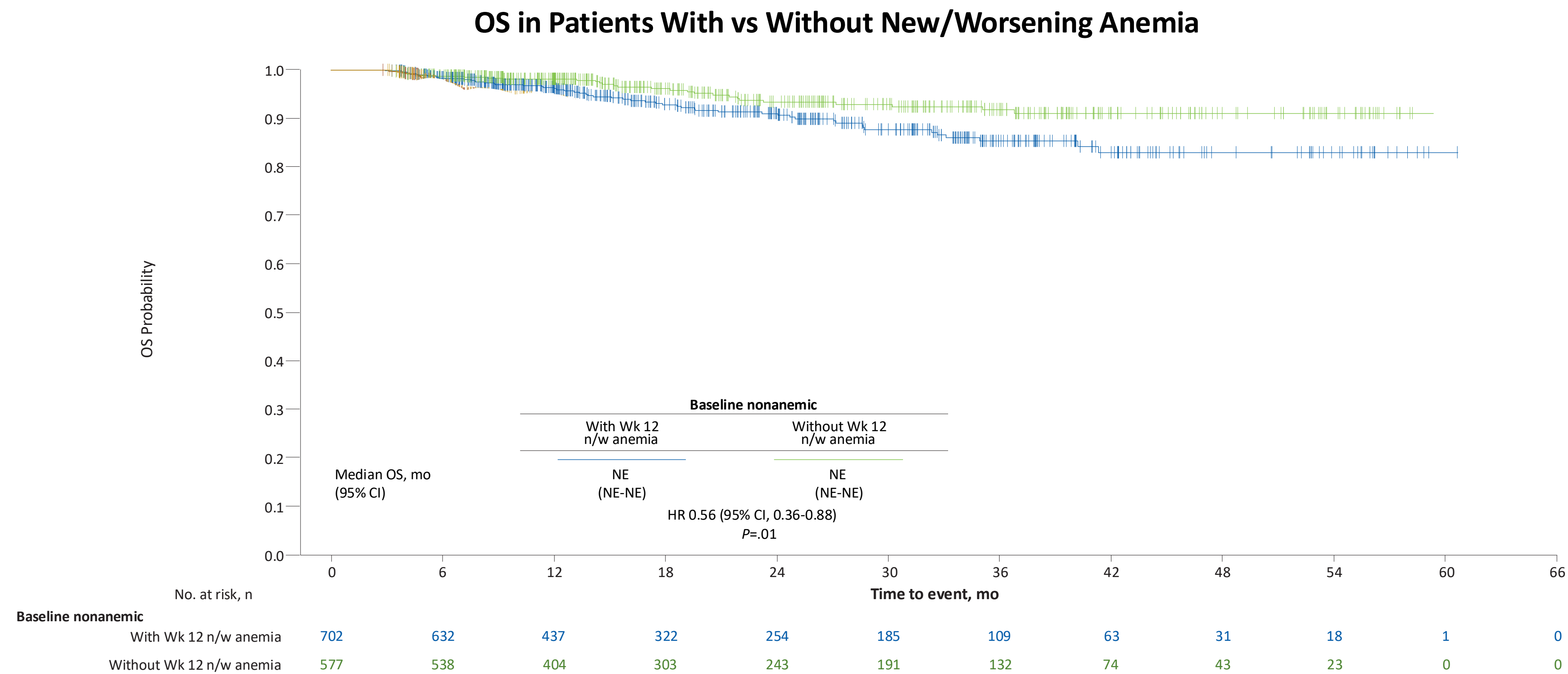
In a real-world analysis, the most common reason for ruxolitinib discontinuation was cytopenias (n=24; 38%). Most commonly due to anemia (n=21; 33%)

Palandri F et al. Cancer. 2020 Mar 15;126(6):1243-1252.

Kuykendall AT. Ann Hematol. 2018;97(3):435-441.



Ruxolitinib: Post Hoc Analysis of the JUMP Expanded-Access Phase 3b Trial in Patients With and Without New/Worsening Anemia at Week 12 of Treatment



Reprinted from Gupta V, et al. Blood. 2023;142 (Suppl 1):5174. Copyright © 2023 The American Society of Hematology. Published by Elsevier Inc.

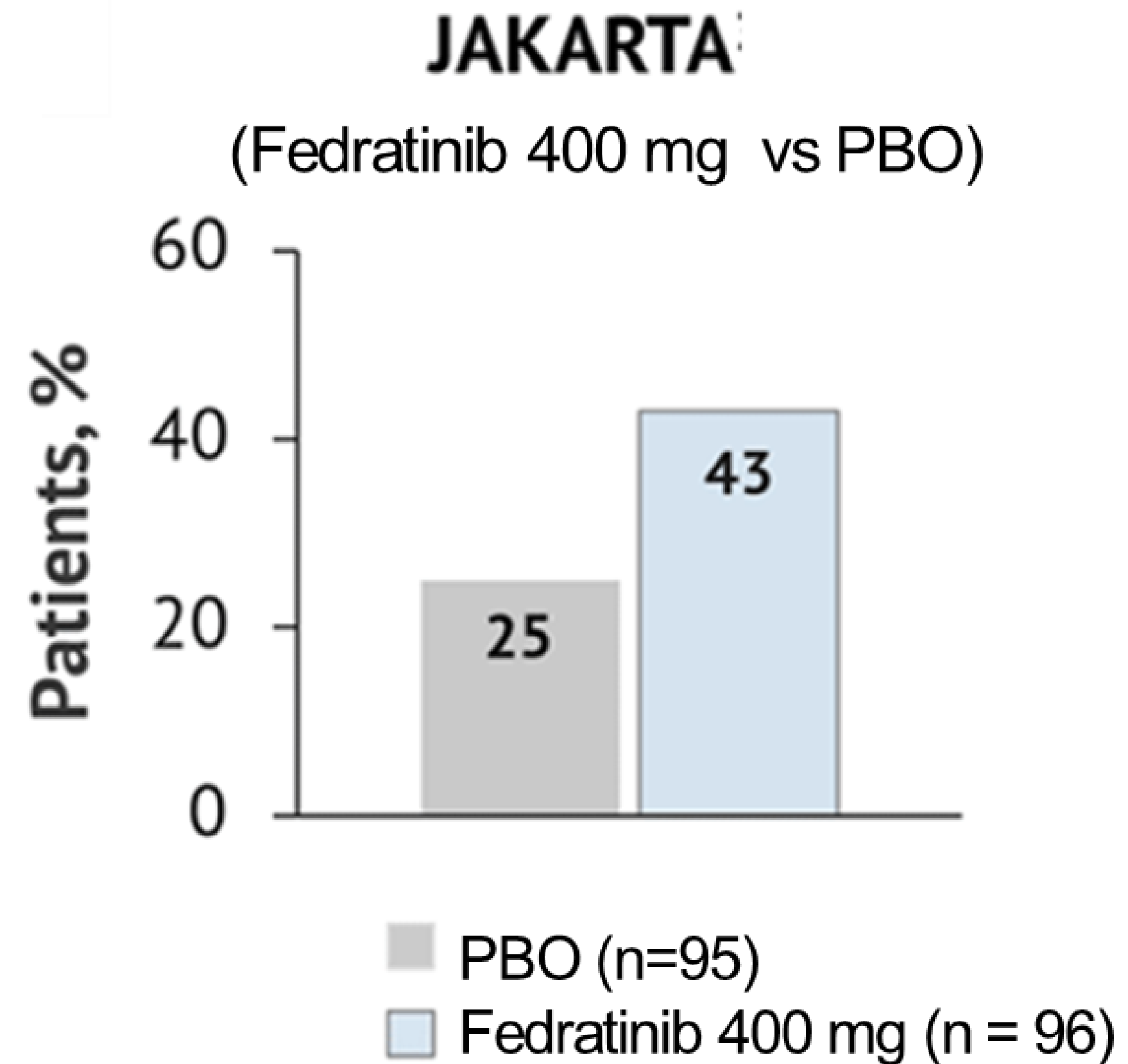
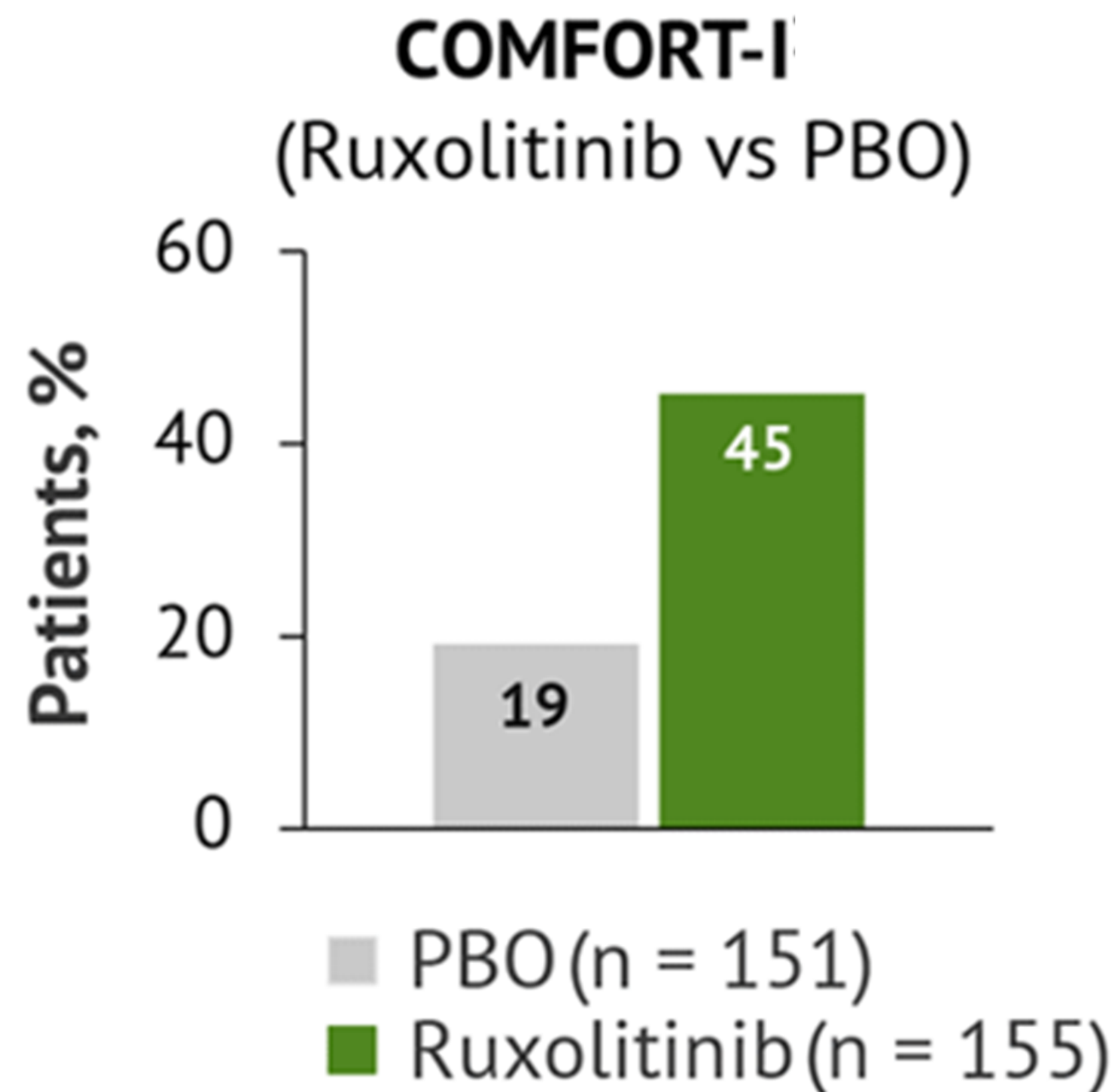
BID, twice daily; FACT-Lym, Functional Assessment of Cancer Therapy-Lymphoma; Hb, hemoglobin; HR, hazard ratio; Int, intermediate; MF, myelofibrosis; NE, not estimable; n/w, new or worsening; OS, overall survival; PLT, platelet; SLR, spleen length response; Wk, week.

^a Outcomes were stratified by the presence or absence of new or worsening anemia following ruxolitinib initiation, defined as Hb $\geq$ 1.5 g/dL decrease from baseline, or new transfusion requirement at weeks 4, 8, or 12. ^b Nonanemic defined as Hb >10 g/dL.



COMFORT-I and JAKARTA Studies Focus on Anemia Symptoms Observations

Rates of grade 3/4 anemia observed in phase 3 trials with ruxolitinib and fedratinib in pts with INT-2 or High risk MF



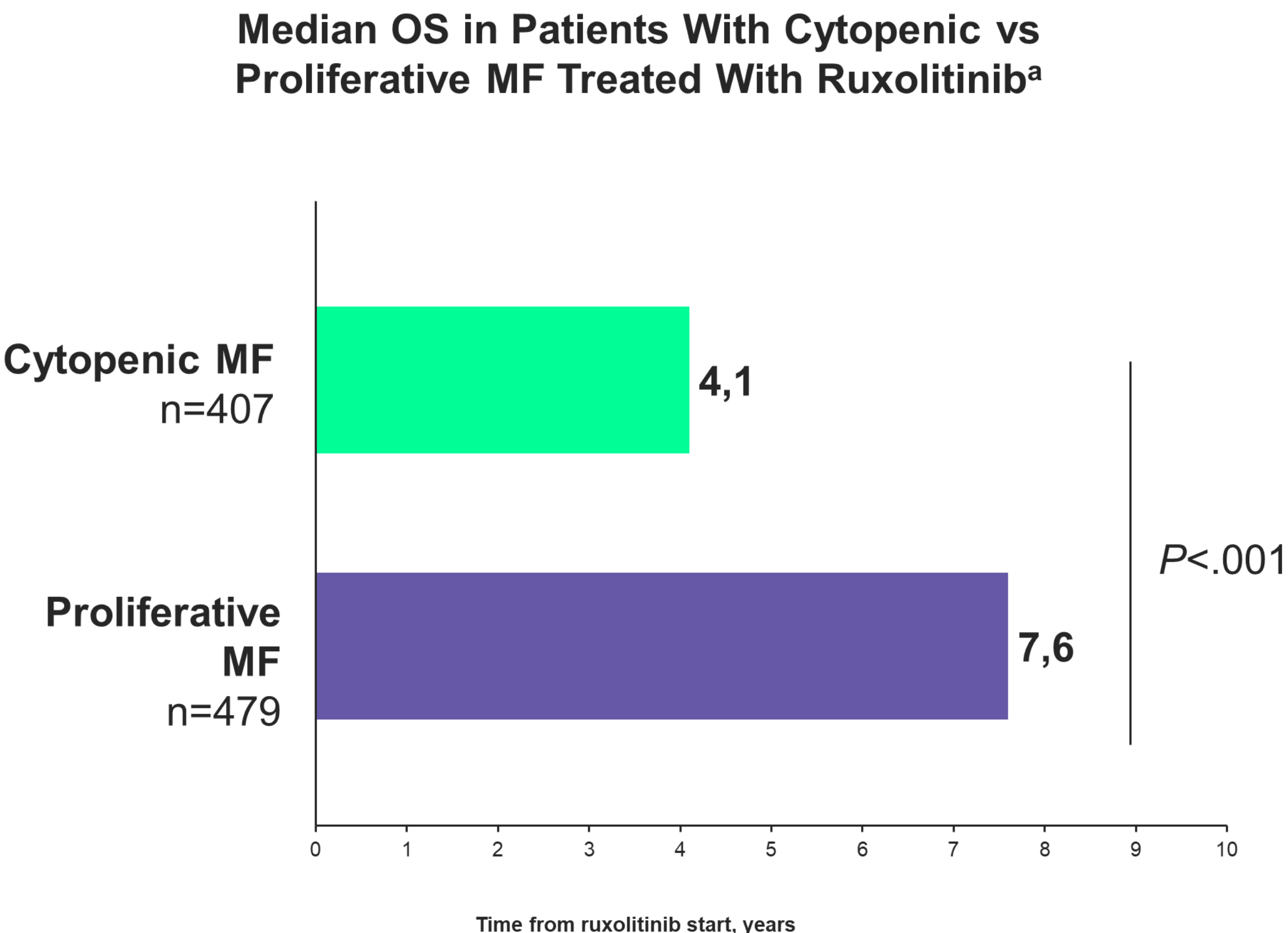
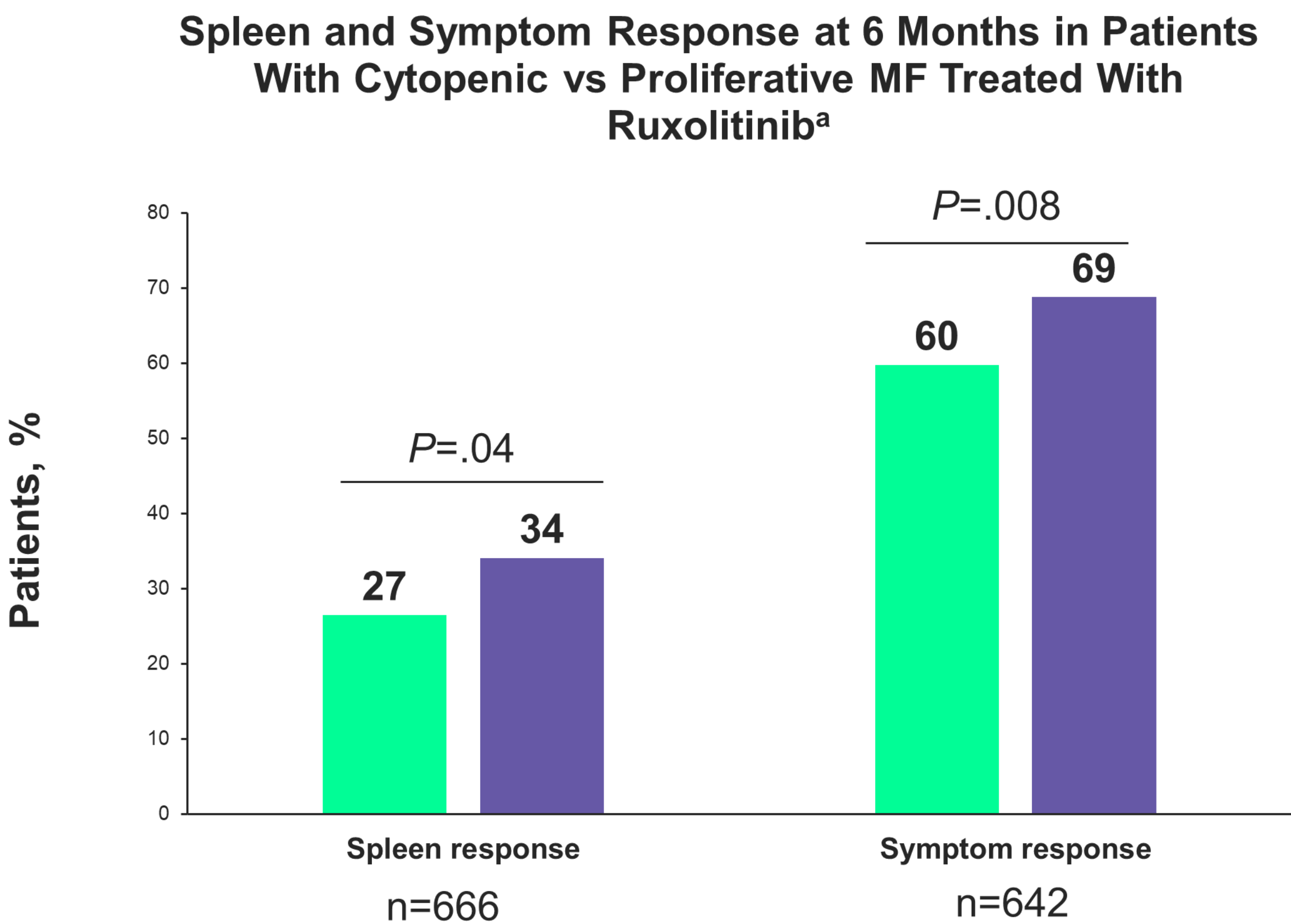
COMFORT-I: phase 3, randomized, double-blind, placebo-controlled study of ruxolitinib vs placebo in patients with intermediate-2 or high-risk myelofibrosis; n = 305 total, with 151 ruxolitinib and 154 placebo. The primary endpoint was proportion of patients with spleen volume reduction of 35% or more at 24 weeks., and the study also reported overall survival as a secondary endpoint.

JAKARTA: phase 3, 1:1:1 randomized, placebo-controlled study of fedratinib vs placebo in patients with intermediate-2 or high-risk myelofibrosis; the updated report describes n = 96 fedratinib 400 mg, n= 97 fedratinib 500mg and n = 95 placebo in the randomized treatment period, total n= 289. Primary efficacy point is focused on 35% reduction in spleen volume from baseline and secondary endpoint is 50% reduction in total symptom score at week 24.

JAKI, Janus Kinase inhibitor; MF, myelofibrosis; PBO, placebo; pts, patients; INT-2, intermediate-2.

References: 1. Verstovsek S et al. N Engl J Med. 2012 Mar 1;366(9):799-807. 2. Pardanani A et al. JAMA Oncol. 2015 Aug;1(5):643-51.

Ruxolitinib Retrospective Study (EU): Clinical Outcomes for Cytopenic vs Myeloproliferative MF at Baseline



Retrospective study of outcomes in 886 ruxolitinib-treated patients with MF.

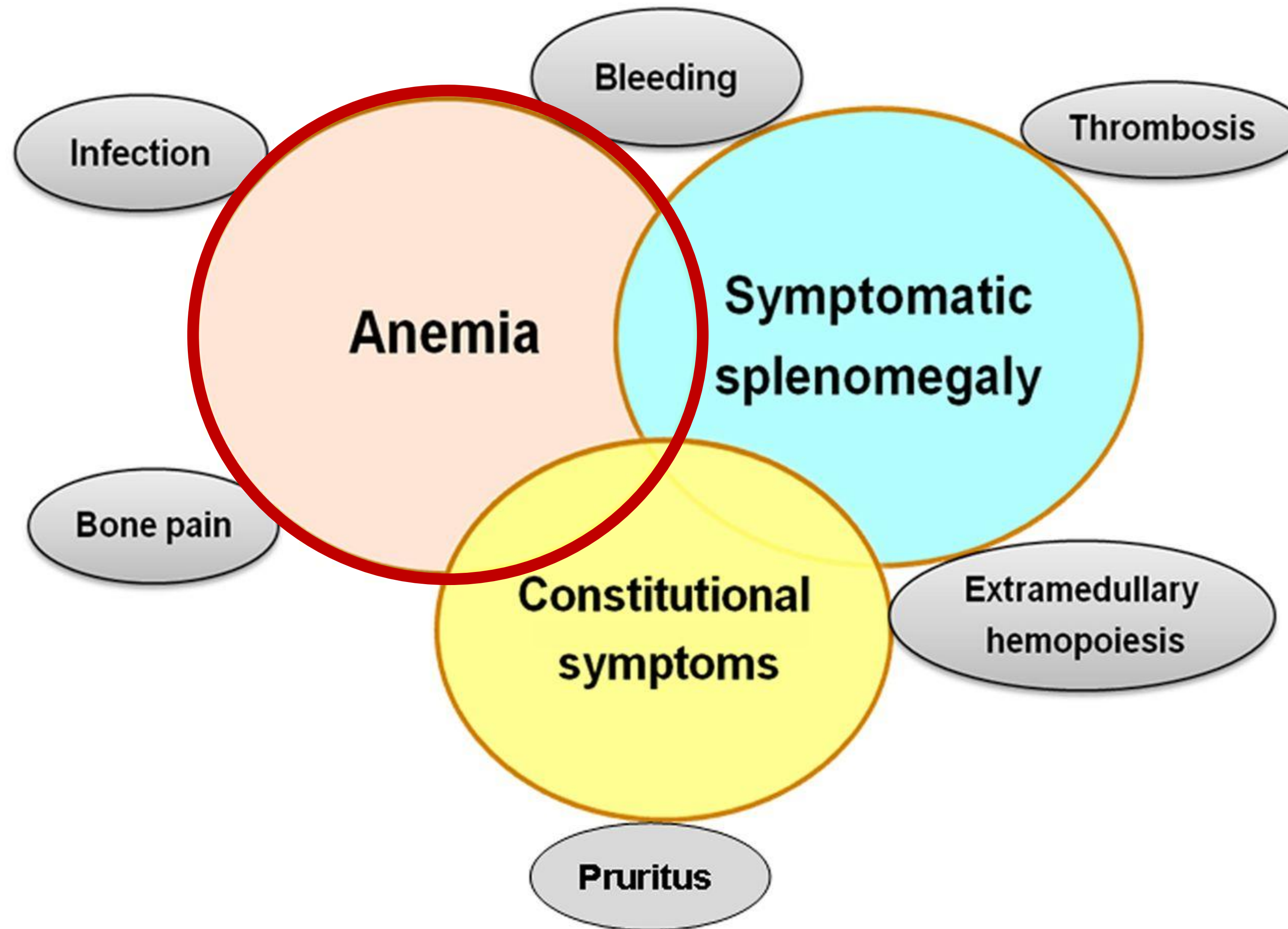
MF, myelofibrosis; OS, overall survival; RUX, ruxolitinib.

^a Cytopenias at ruxolitinib start were defined as follows: white blood cell $<4 \times 10^9/L$, hemoglobin <11 g/dL for men and <10 g/dL for women, and platelets $<100 \times 10^9/L$. The cytopenic phenotype was defined by the presence of at least 1 cytopenia. Patients not included in the cytopenic group were considered as having a proliferative phenotype.

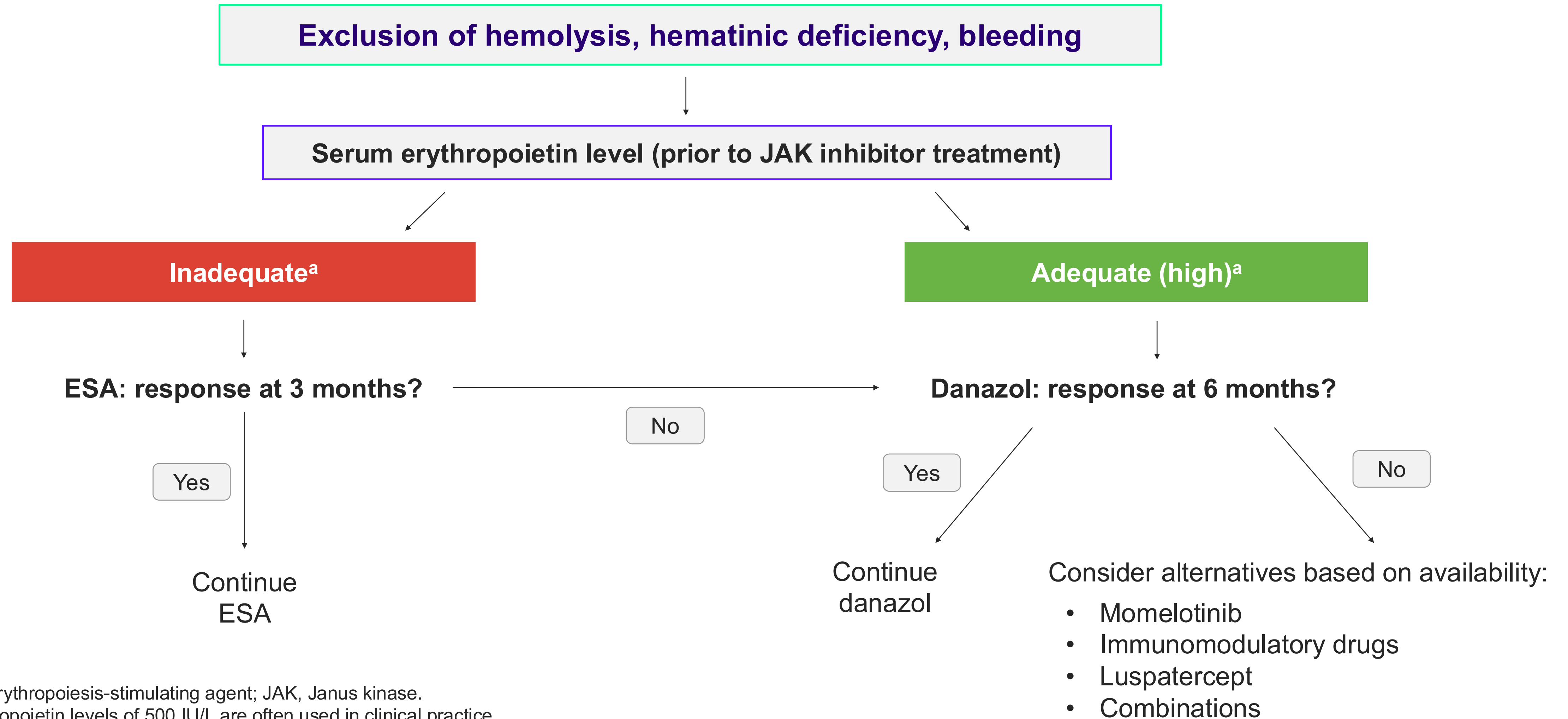
■ Cytopenic MF ■ Proliferative MF



Therapy of Myelofibrosis



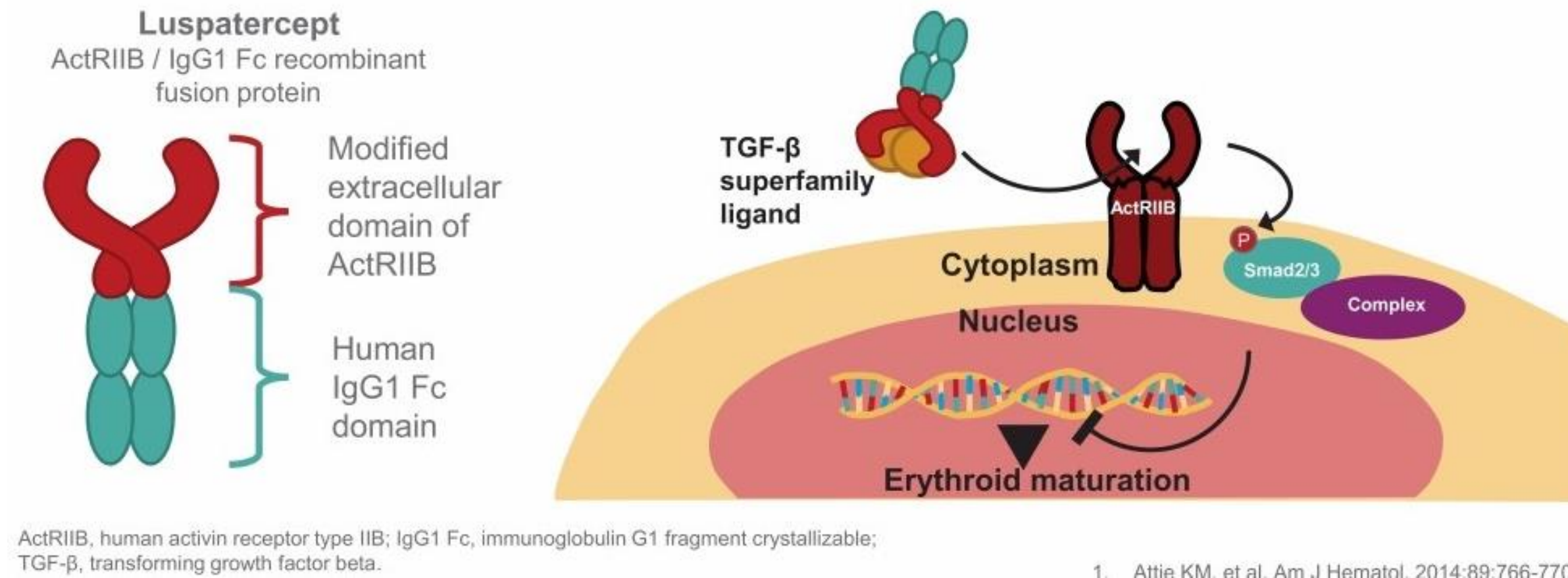
British Society for Haematology Guidelines for Patients With Myelofibrosis and Anemia



ESA, erythropoiesis-stimulating agent; JAK, Janus kinase.

^a Erythropoietin levels of 500 IU/L are often used in clinical practice.

Luspatercept



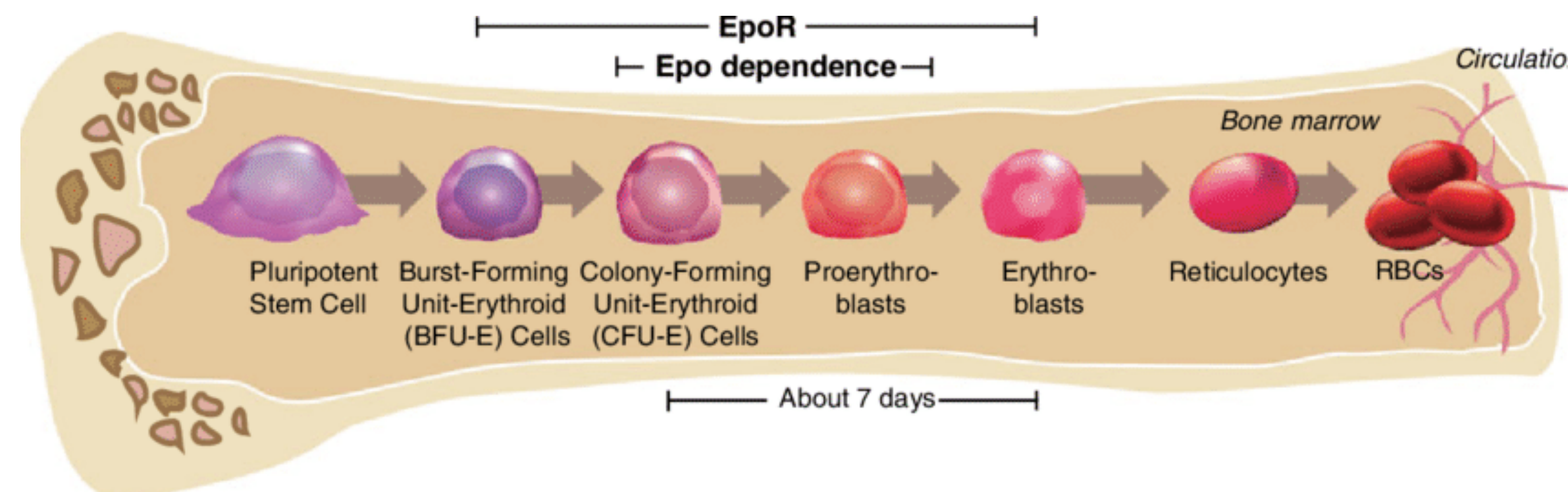
Selective inhibitor of TGF- β superfamily ligands



Aberrant Smad 2/3 signaling inhibition



Late Erythroid Maturation (non EPO-dependent)



INDEPENDENCE: Luspatercept in Patients With MF and Anemia Receiving JAK Inhibitor Therapy

- International, double-blind, randomized phase III trial



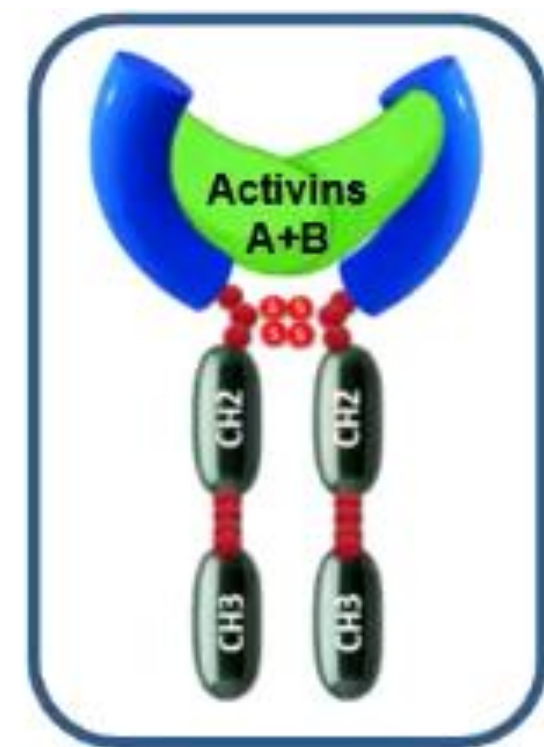
*Transfusion frequency 4-12 RBC units/12 wk prior to randomization with no interval of >6 wk without a transfusion; transfusions scored in determining eligibility when given for treatment of symptomatic anemia with pretransfusion Hgb ≤ 9.5 g/dL or asymptomatic anemia with pretransfusion Hgb ≤ 7 g/dL.

PRESS RELEASE (July 18, 2025): the Phase 3 INDEPENDENCE trial **did not meet its primary endpoint**, defined as RBC transfusion independence over any ≥ 12 -week interval within the first 24 weeks (**p = 0.0674**).

Secondary endpoints demonstrated **quantitative improvements** with luspatercept, including a higher proportion of patients achieving: (i) **$\geq 50\%$ reduction in transfusion burden (≥ 4 RBC units)** and (ii) **hemoglobin increase ≥ 1 g/dL with ≥ 12 consecutive weeks of transfusion independence**.

The **safety profile was consistent** with prior studies. Regulatory interactions with FDA and EMA are planned.

Elritercept (KER-050) is designed to target disorders of ineffective hematopoiesis including myelofibrosis

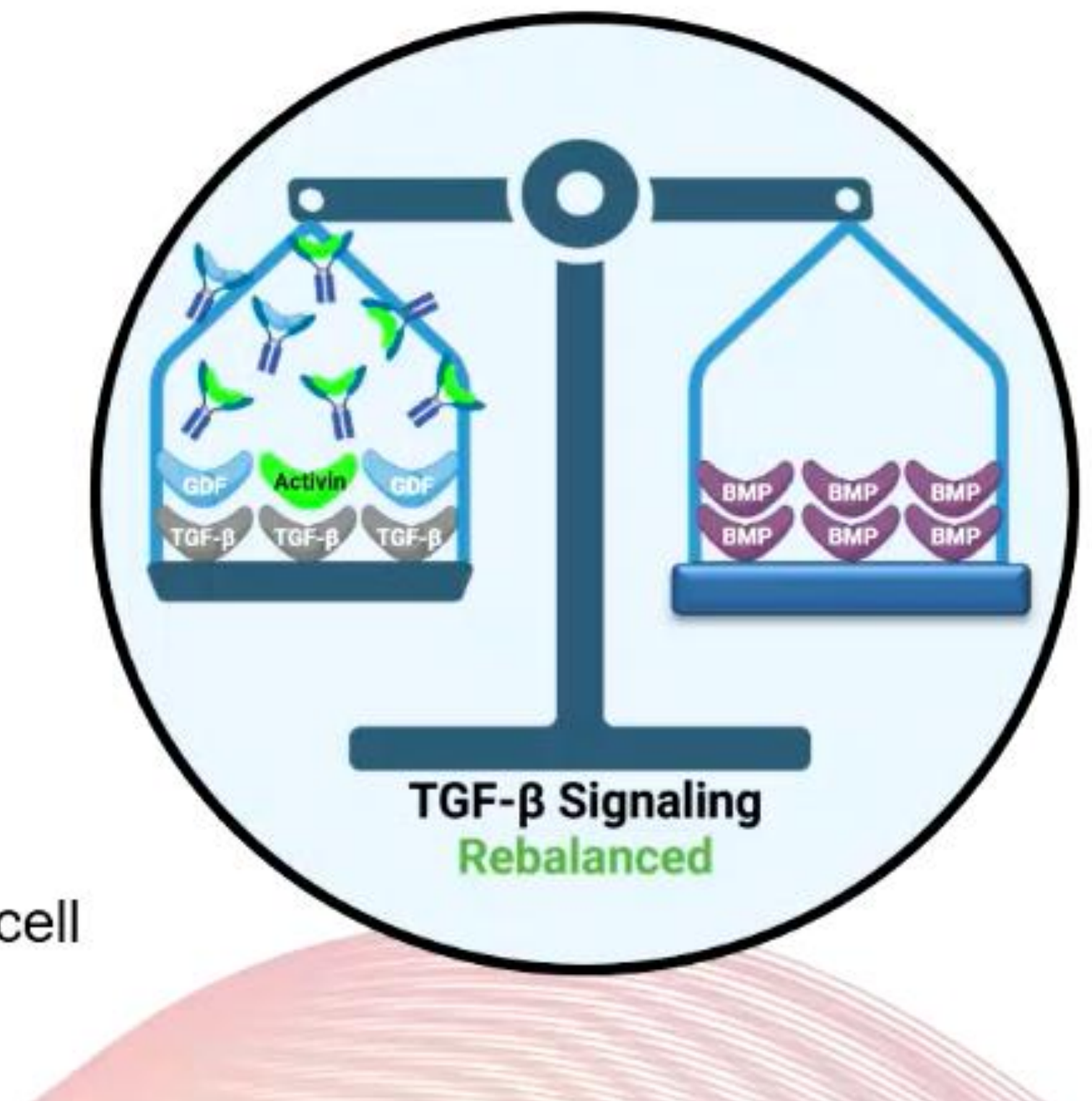


Elritercept

- Designed to inhibit select TGF-beta superfamily ligands, including **Activin A**, which has been associated with **ineffective hematopoiesis, inflammation, disease pathogenesis and progression**^{1,2,3}

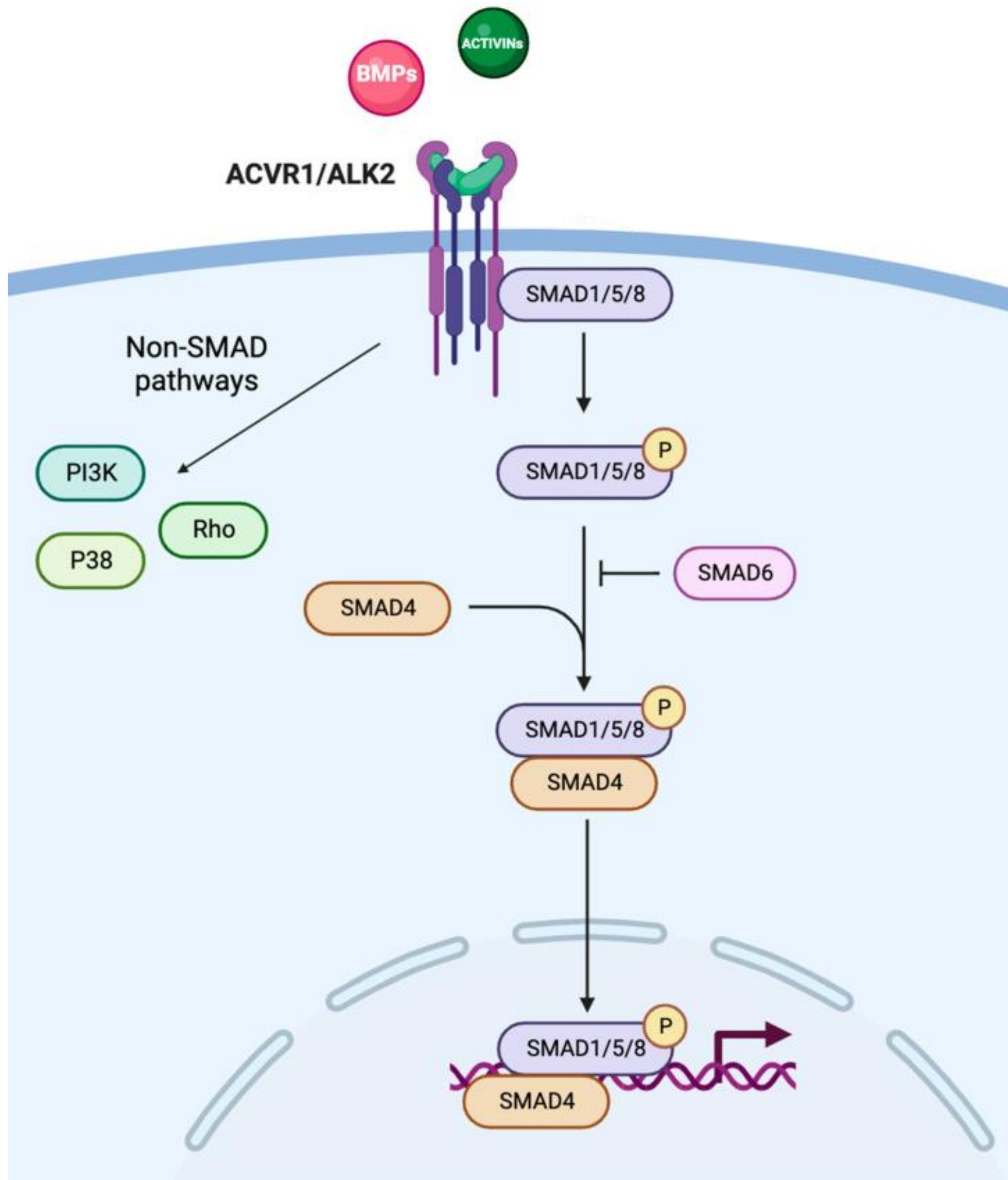
Preclinical data showed that the research form of **elritercept** (RKER-050):

- induced erythropoiesis in mouse model of myelofibrosis⁴
- reversed ruxolitinib-associated reductions in hemoglobin, hematocrit, and red blood cell (RBC) count⁵
- increased platelet counts⁶



1. Verma A et al., J Clin Invest 2020. Portale F et al., Haematologica 2019. 3, Phillips D et al., Cytokine Growth Factor Rev 2009. 4 Moses et al., EHA 2023. 5. Nathan et al., ASH 2021. 6. Moses et al. Gordon Research Conference: Cell Biology of Megakaryocyte and Platelets, 2023. Modified from Harrison C et al., EHA 2024. TGF-b = Transforming Growth Factor beta.

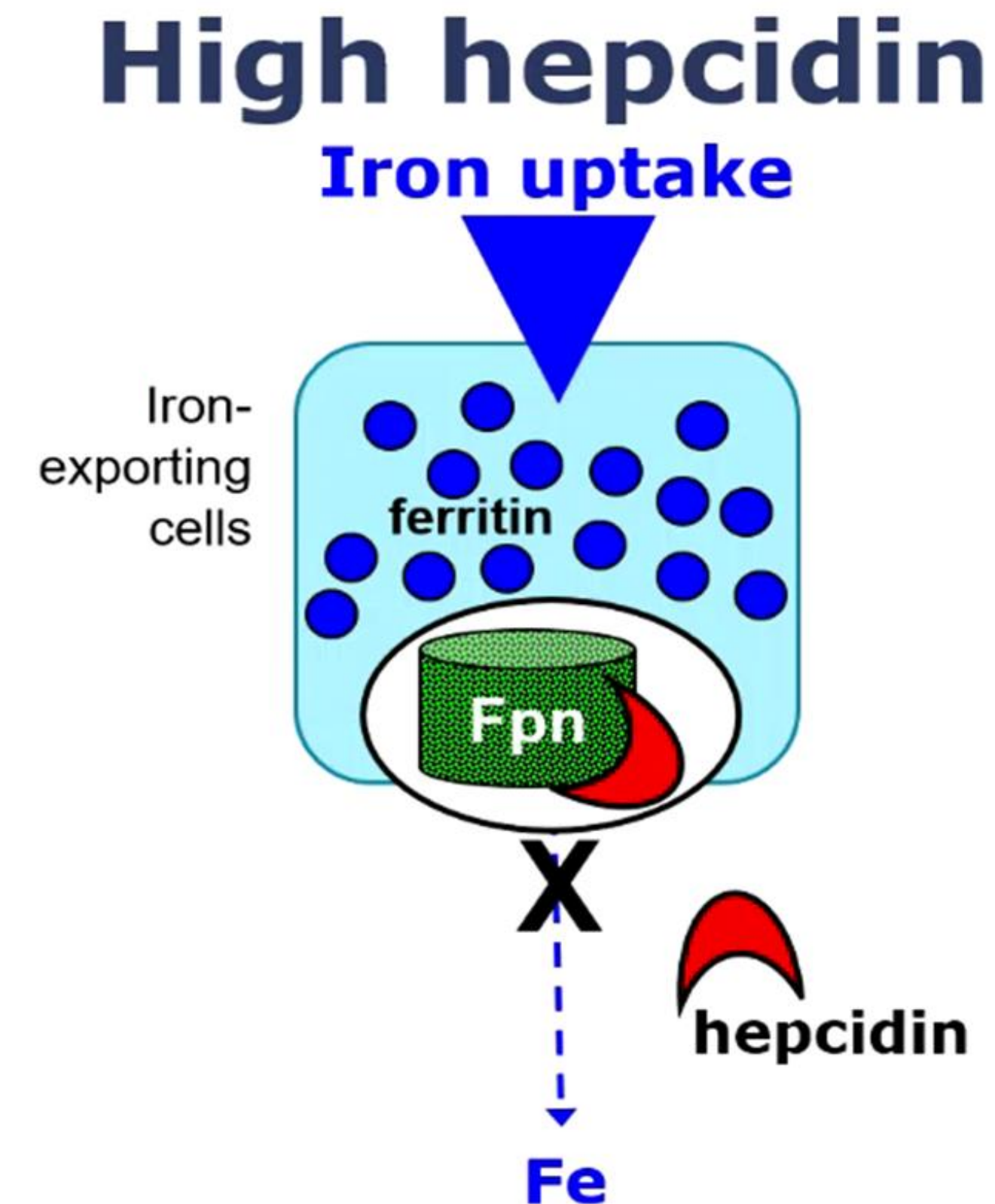
ACVR1



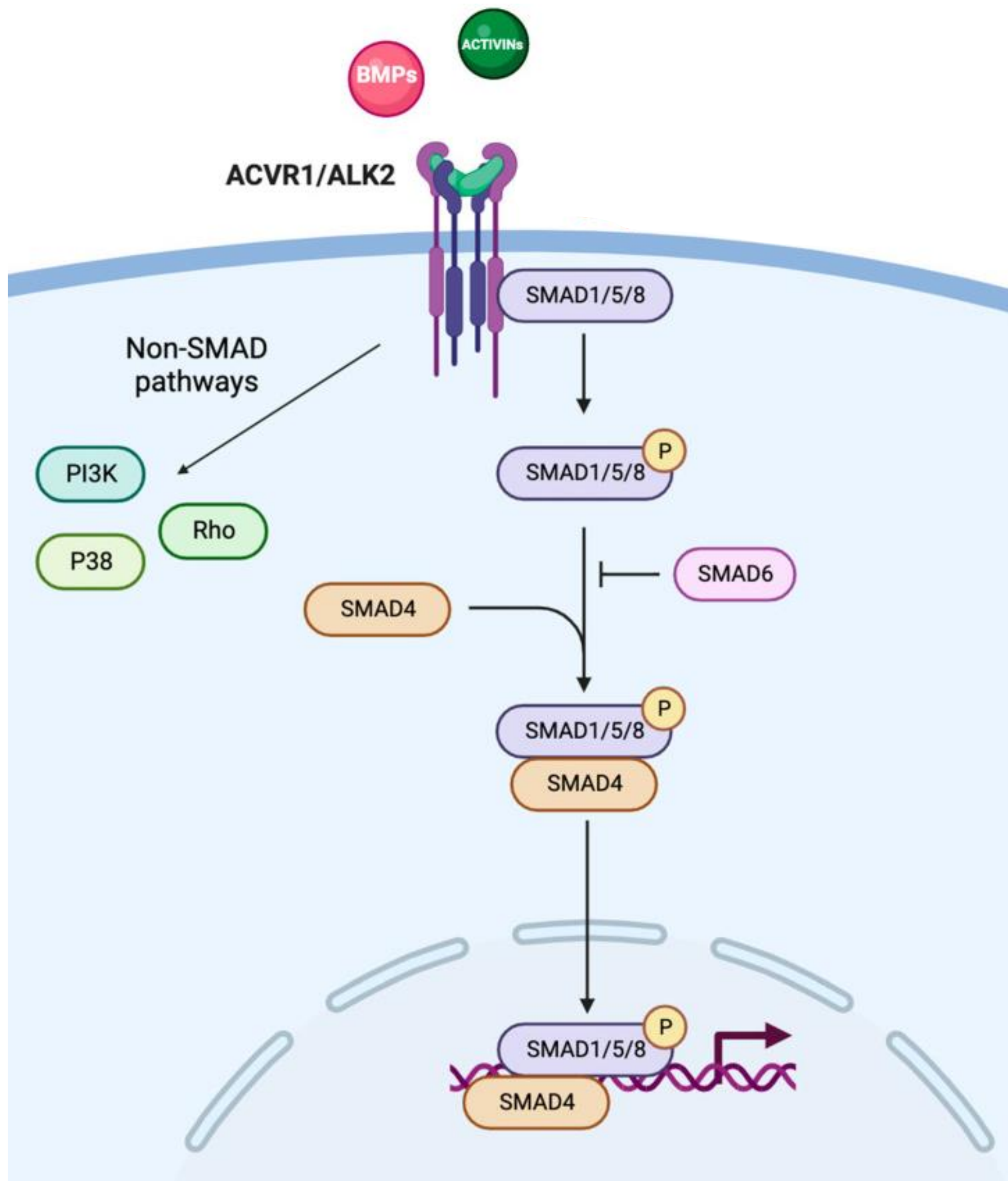
The **ACVR1** receptor functions in the **development and regulation** of the bone, heart, cartilage, nervous, and reproductive systems

In other diseases, dysregulated ACVR1 signaling has been linked to **cardiac malformations**, alterations in the **reproductive system**, and certain **cancers**

ACVR1 is a key regulator of **hepcidin** production and is expressed on the surface of hepatocytes; **hepcidin** is a peptide hormone secreted in the liver that serves as a **master iron regulator**



ACVR1

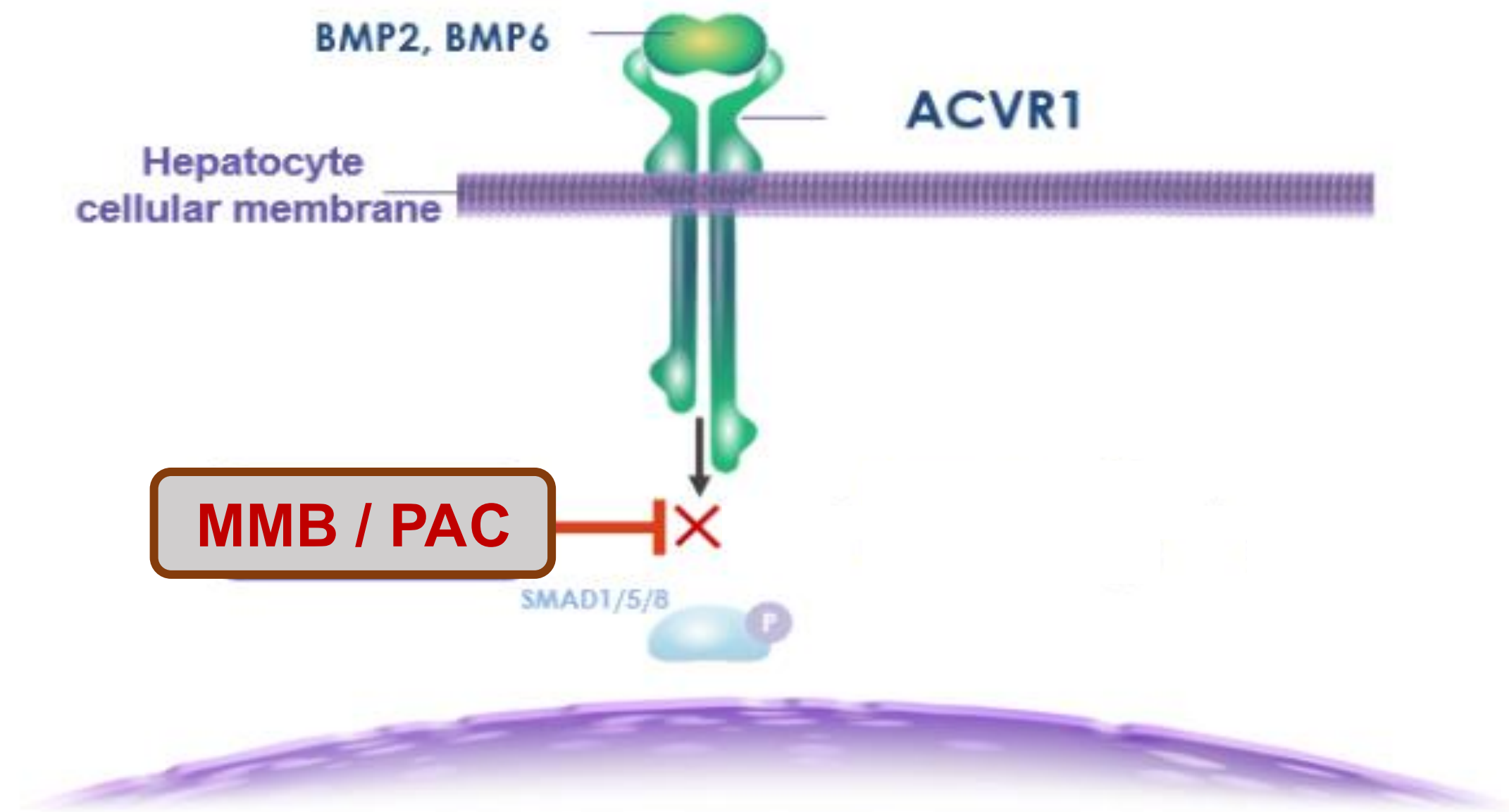


In MF, chronically **activated ACVR1 signaling** leads to markedly **elevated hepcidin levels**

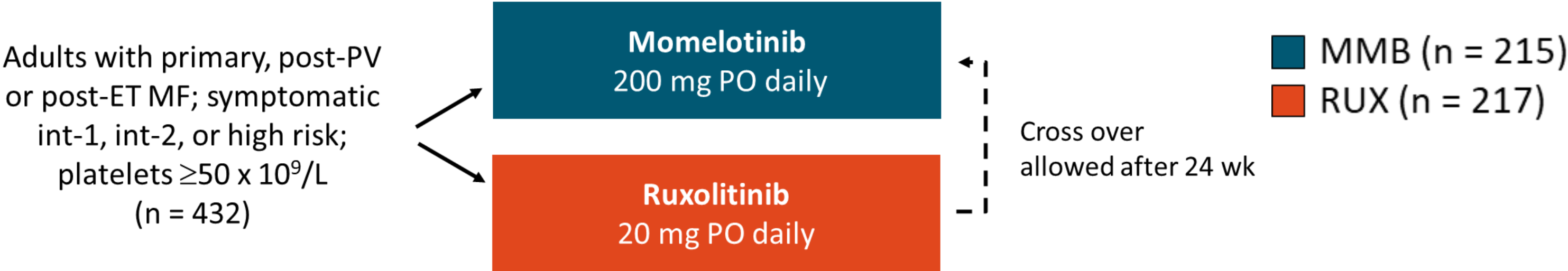
Elevated hepcidin levels inhibit iron transport and iron homeostasis, driving iron-restricted anemia and anemia of MF

Upregulation of **inflammatory cytokines** in the bone marrow disrupts erythropoiesis and is associated with upregulation of circulating hepcidin; cytokines associated with anemia include **TGF- β , IL-2, IL-6, and TNF- α**

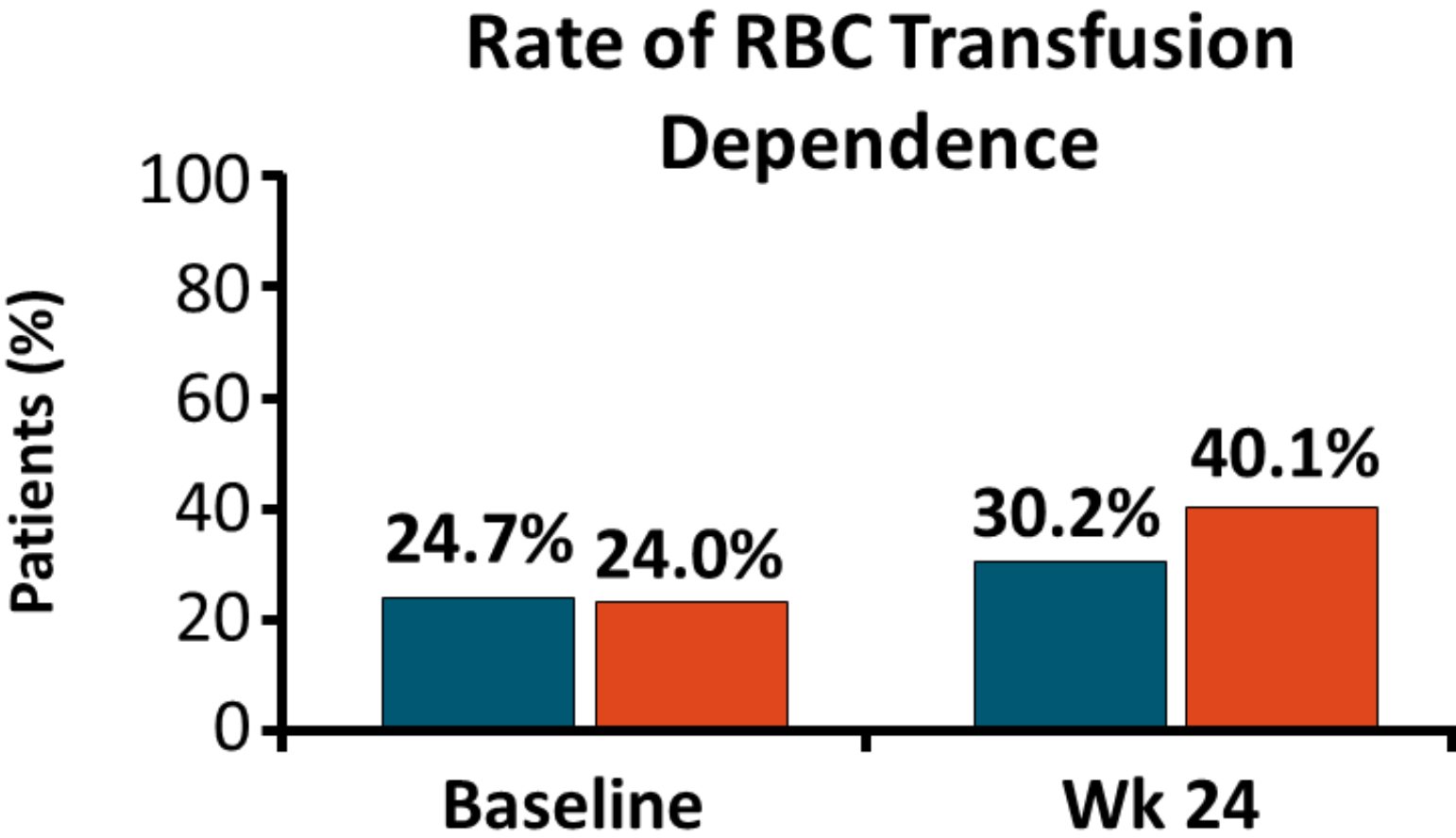
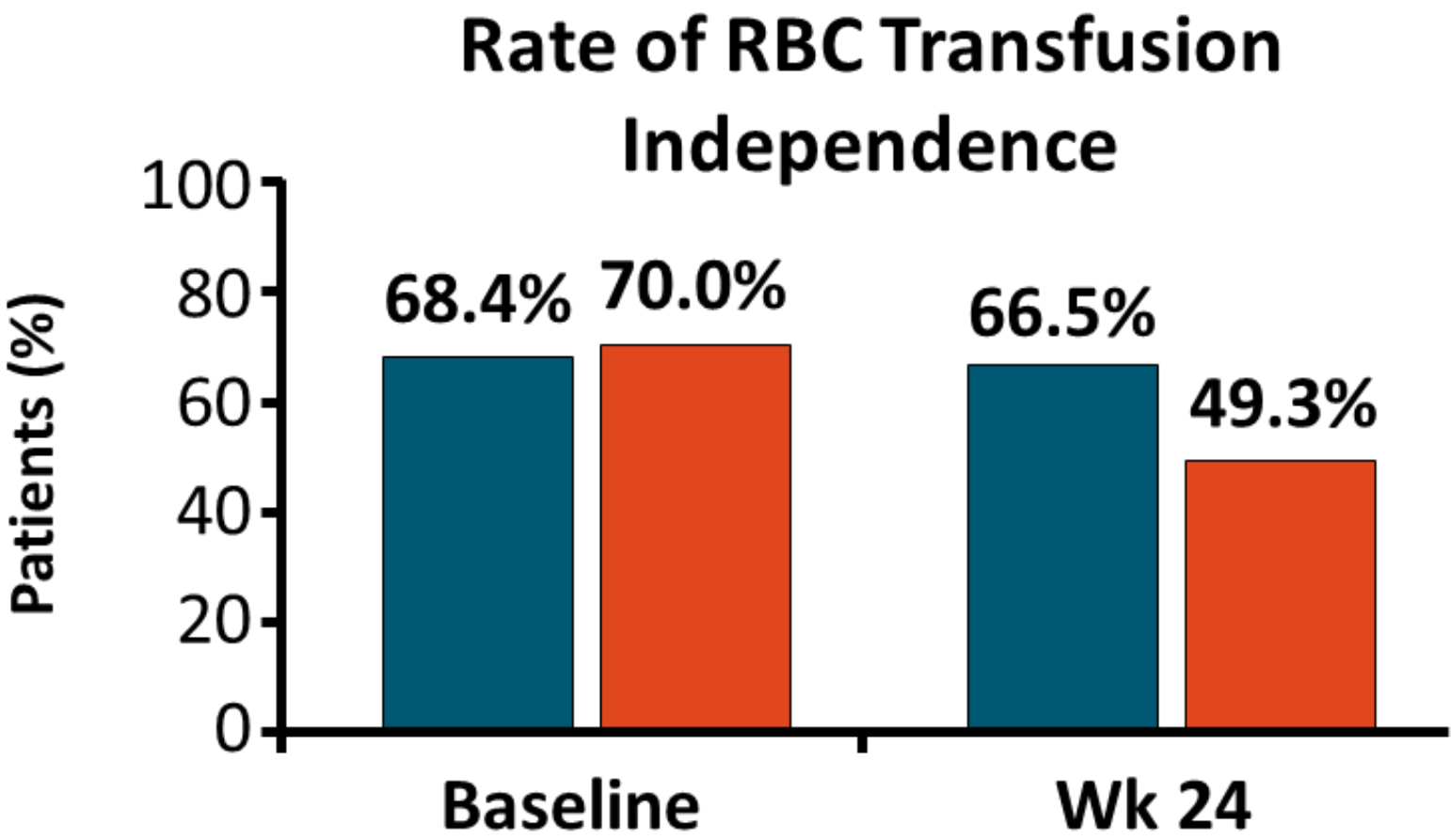
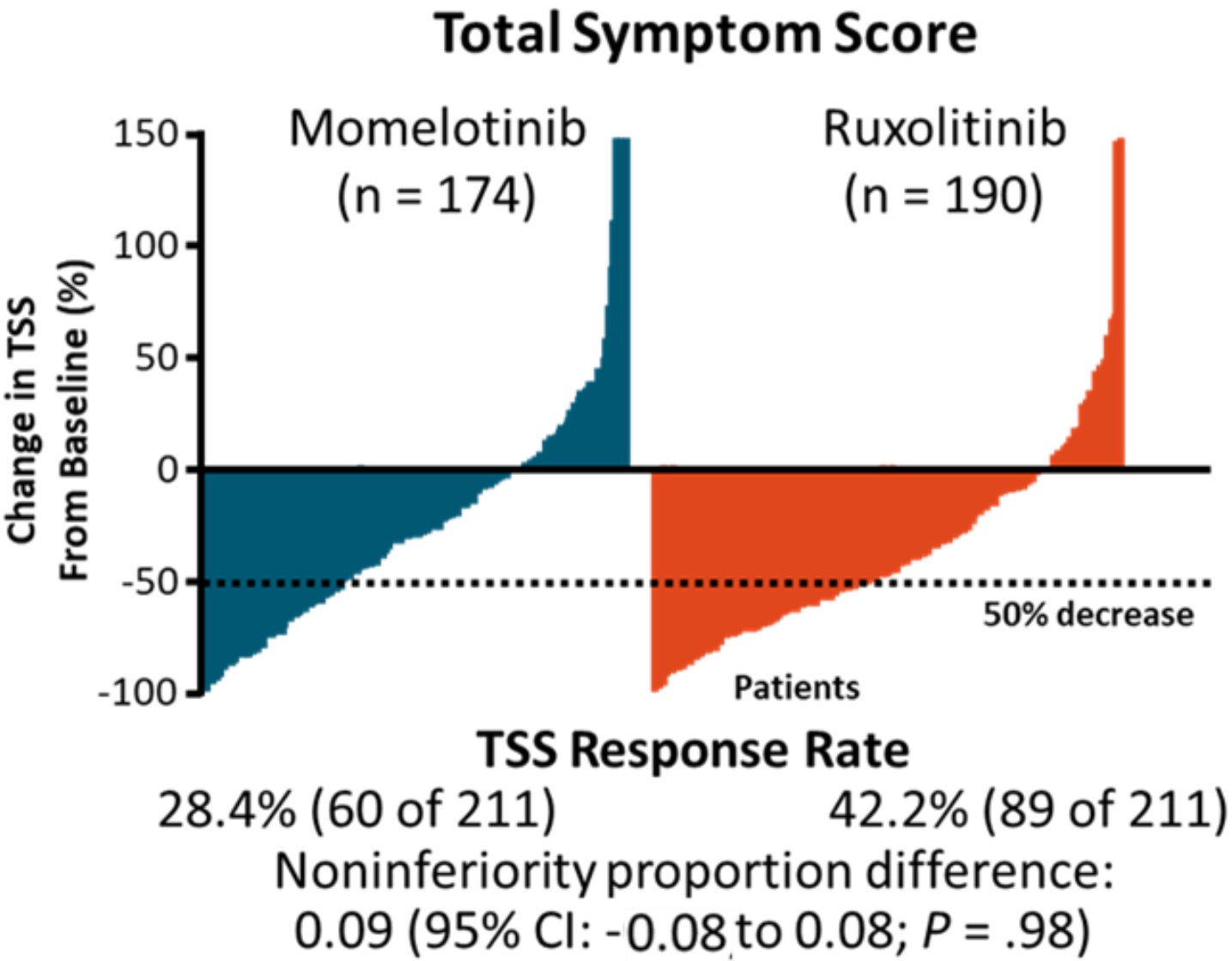
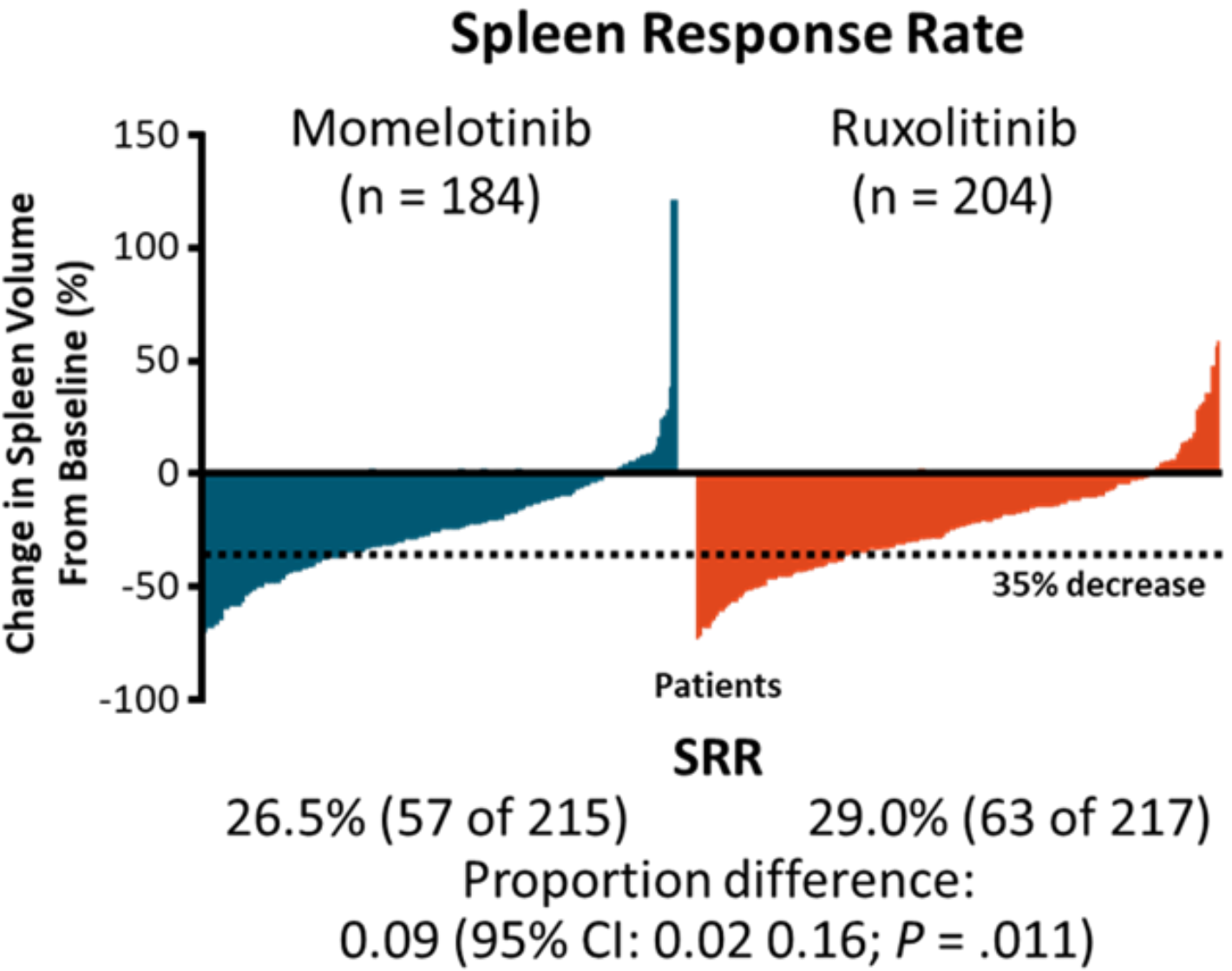
Inhibiting ACVR1 results in **decreased hepcidin** transcription and an increase in **iron availability**, thereby improving iron-restricted anemia



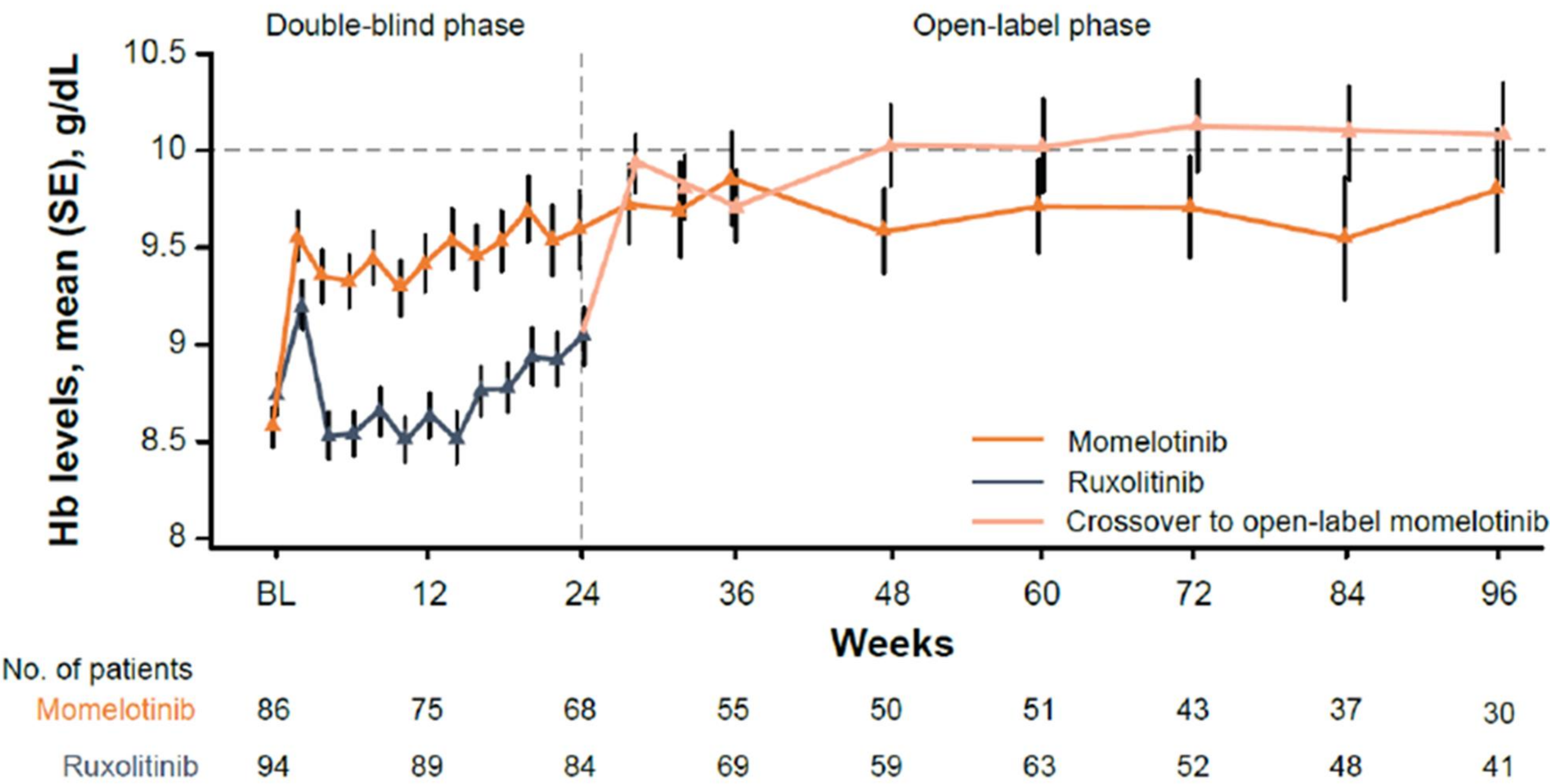
SIMPLIFY-1: Phase III Trial of Mometotinib vs Ruxolitinib for JAK Inhibitor–Naive MF



- **Primary endpoint:** SVR $\geq 35\%$ at Wk 24 (assessed by MRI or CT)
- **Secondary endpoints:** TSS response rate at Wk 24, RBC transfusion-independence rate at Wk 24, RBC transfusion-dependence rate at Wk 24, and rate of RBC transfusions



SIMPLIFY-1 (JAKi-naive MF patients)
Mean Hb levels over time in the moderate and severe anemia subgroup (Hb <10 g/dl) in JAKi-naive patients treated with momelotinib or ruxolitinib



In the momelotinib arm, mean Hb levels increased by weeks 2 to 4 in anemic subgroup

Figure depicts results through week 96, although the study continued beyond this time point.

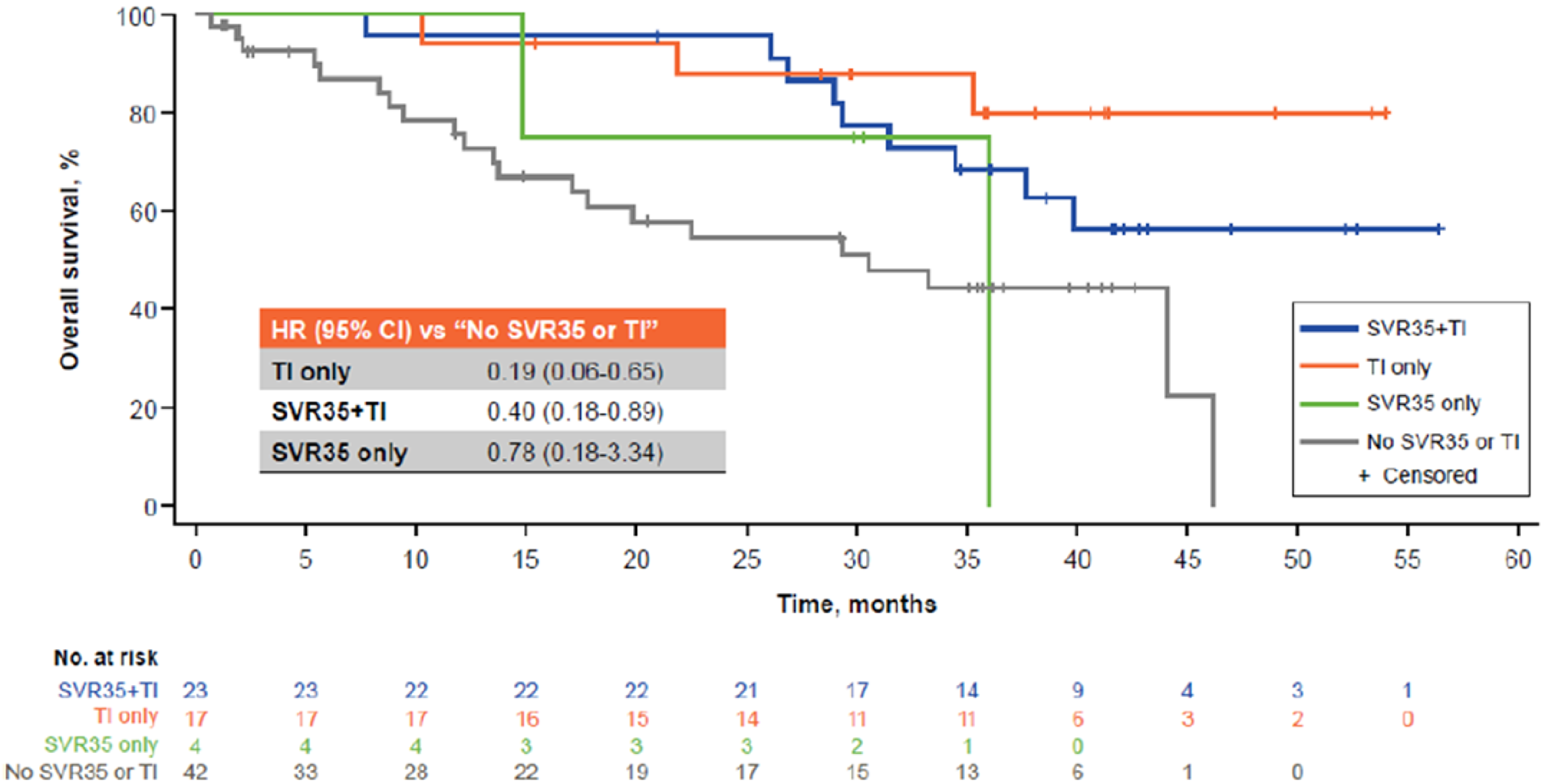
Gupta V et al. Leuk Lymphoma. 2024 Jul;65(7):965-977. Erratum in: Leuk Lymphoma. 2024 Jul;65(7):ii-iii.



Impact of Dual Spleen Response and Transfusion Independence on Survival in JAK Inhibitor-naïve Patients with Myelofibrosis and Anemia

A Subgroup Analysis of SIMPLIFY-1 in JAK-naïve Patients with Baseline Hb < 10 g/dl randomized to Momelotinib

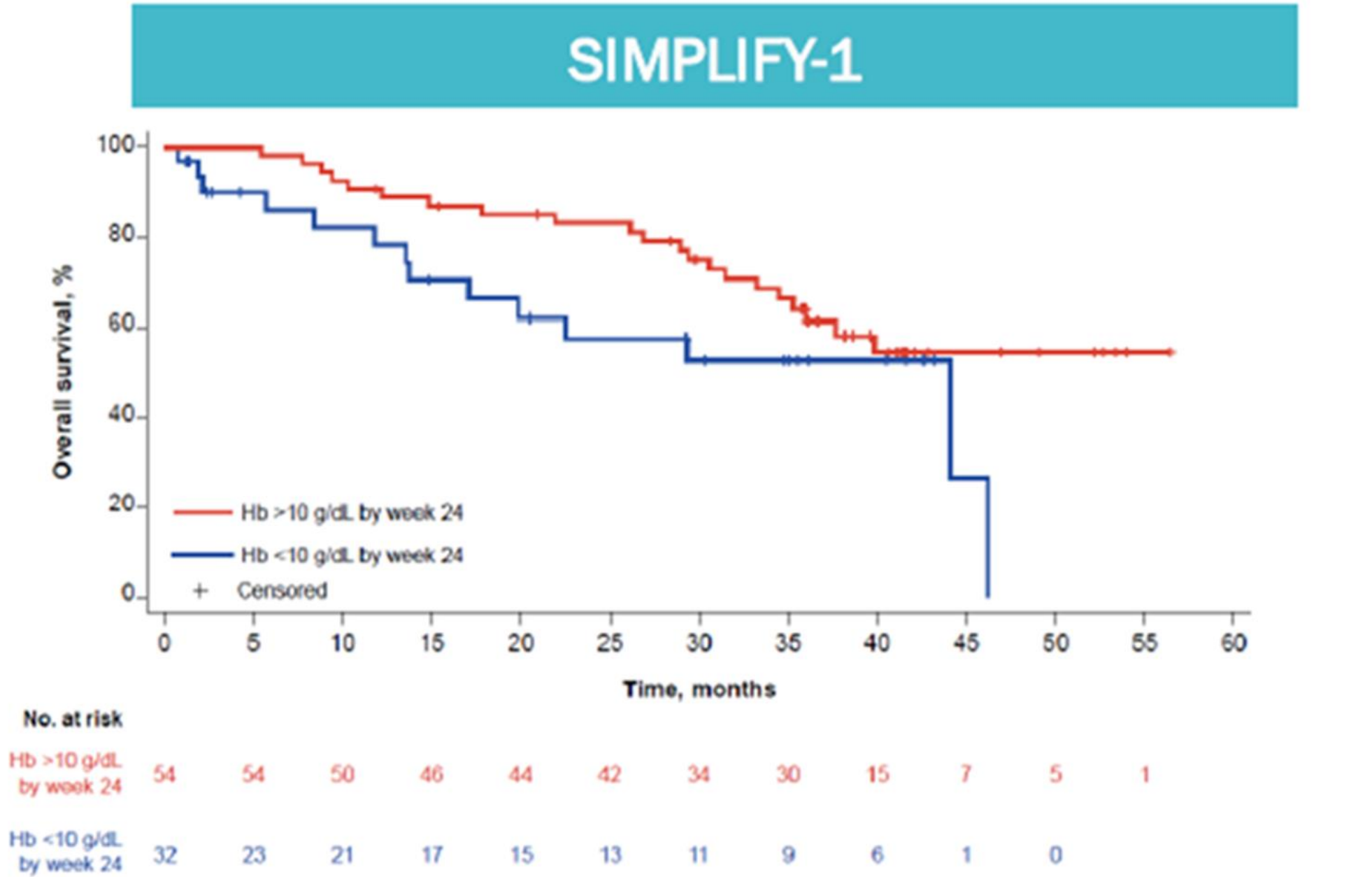
OS from Treatment Initiation based on Week 24 SVR35 and/or TI



Survival Impact and Kinetics of Haemoglobin Improvement with Momelotinib in Patients with Myelofibrosis and Moderate to Severe Anaemia

Post Hoc Analyses of SIMPLIFY-1 (JAKi-naïve)

Overall Survival based on achieving Hb >10 g/dl



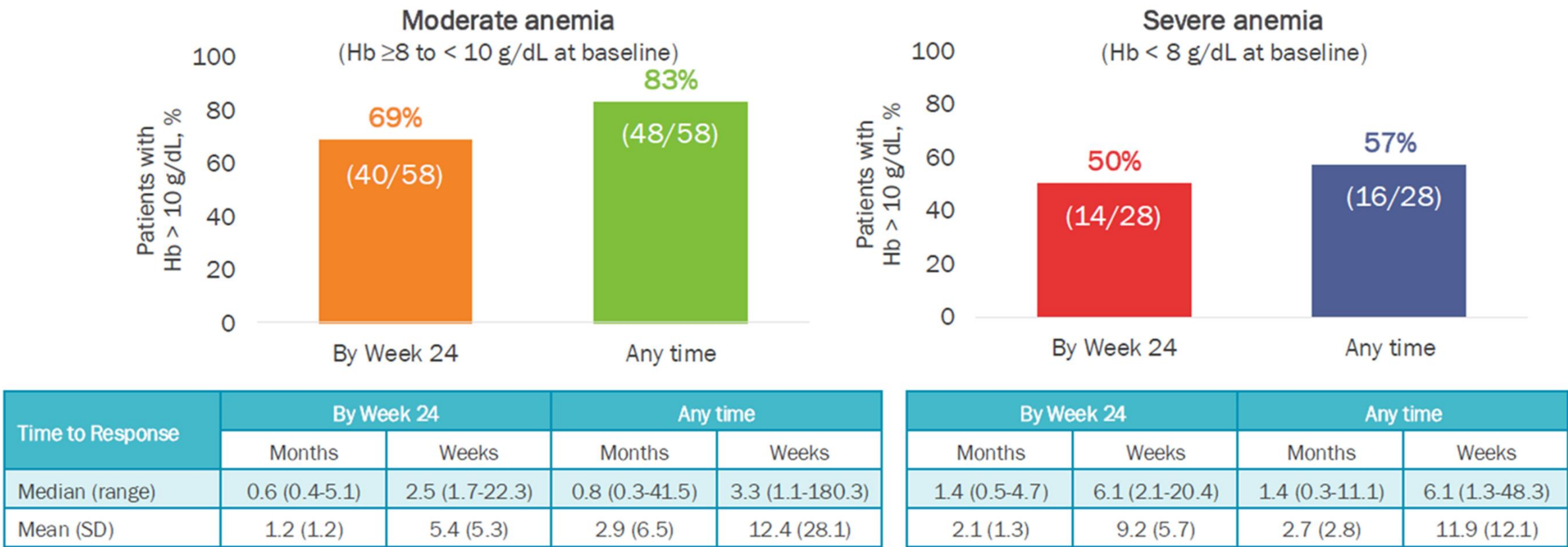
Hb > 10 g/dL by Week 24 ^a	Yes (n=54)	No (n=32)
Median, months (95% CI)	NR (35.3-NE)	44.1 (13.7-NE)
HR (95% CI)	0.57 (0.27-1.06)	

a. Defined based on patients who achieved Hb >10 g/dl by Week 24, excluding all Hb values in the 4 weeks post transfusion.

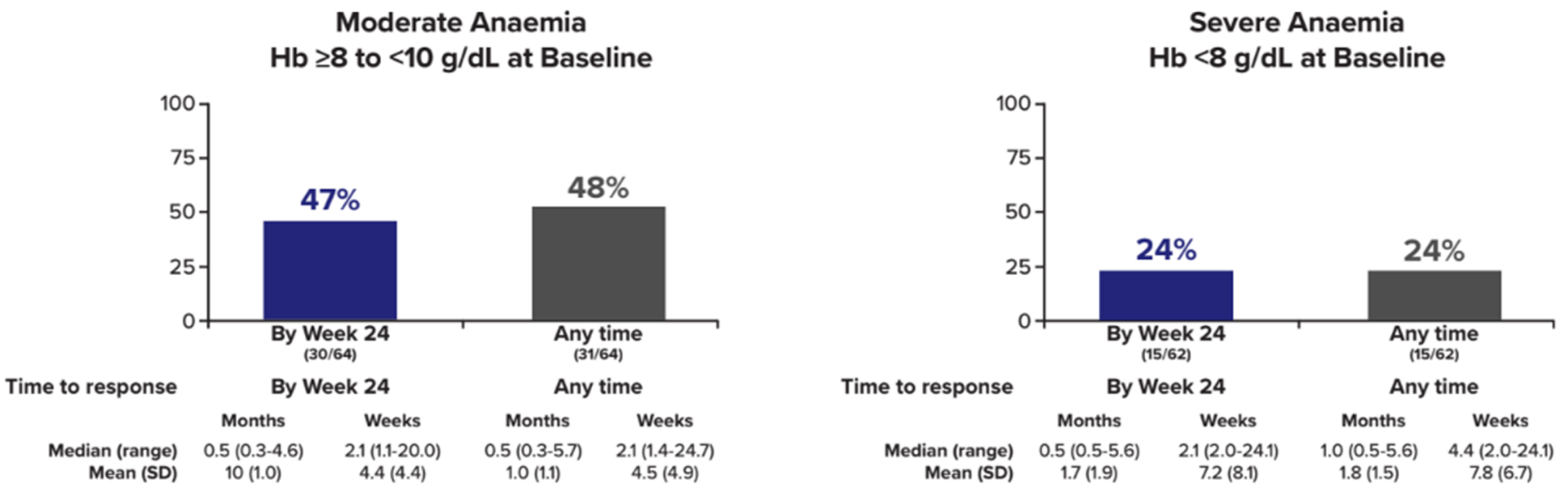


Rates and Kinetics (Time to Hb >10 g/dl) of Hemoglobin Improvement in Momelotinib treated patients

SIMPLIFY-1 (JAKi-naive)



MOMENTUM (JAKi-experienced)



In MOMENTUM, 47% and 24% of patients treated with Momelotinib with baseline moderate and severe anemia, respectively, achieved Hb >10 g/dl by week 24

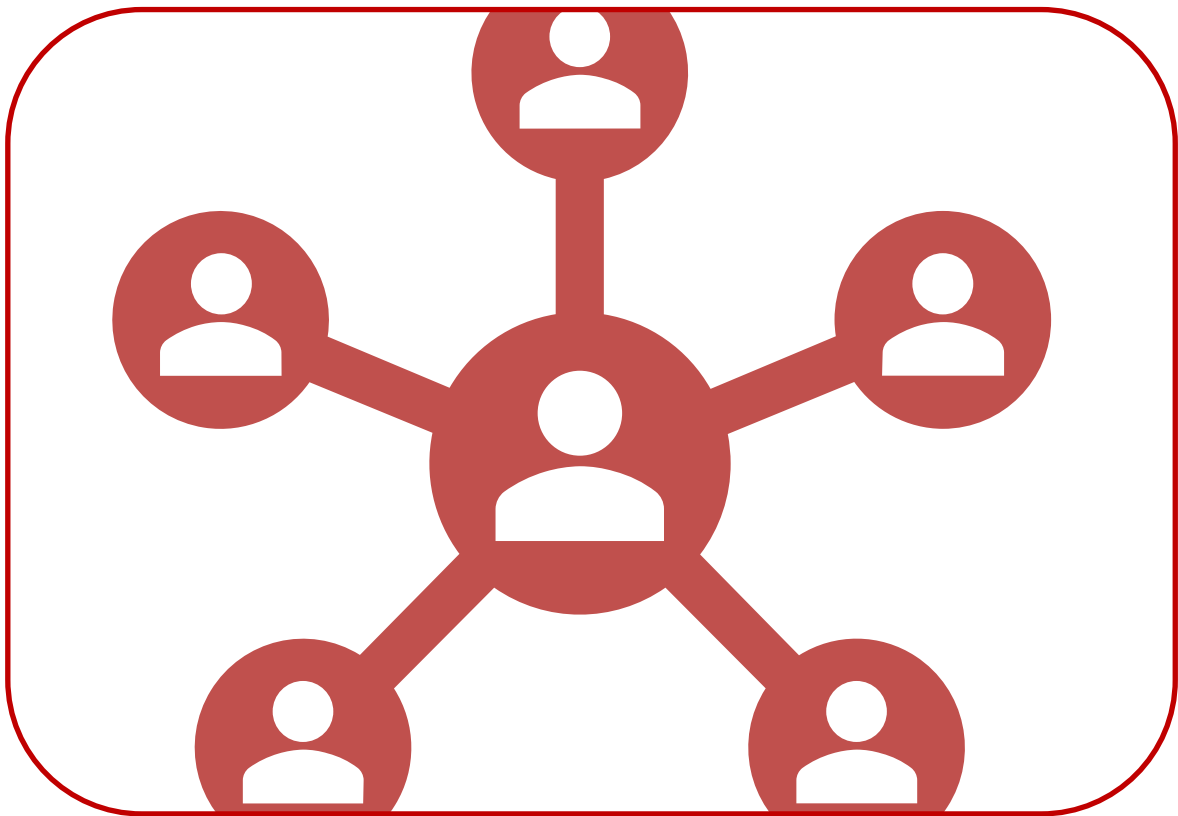
Respective mean (SD) times to first occurrence were 1.0 (1.0) and 1.7 (1.9) months



Retrospective data collection of MF patients treated with 2nd-line MMB, after RUX failure

Study Design

Data source



RUX-MF network*

n = 125



Additional Italian Centers*
(≥4 pts)

n = 64



Moffitt Cancer Center (USA)

n = 32

All information merged into an RUX-MF–like centralized database
All patients were followed until death or to data cut-off date (November 2025)

*All Italian patients received MMB through the Managed Access Program (MAP)
MMB: momelotinib; RUX: ruxolitinib; MF: myelofibrosis; USA: United States of America

Retrospective data collection of MF patients treated with 2nd-line MMB, after RUX failure

Characteristics at Momelotinib Start (n. 221)

Table 1: Baseline Characteristics of the Study Cohort

Characteristic	n. 221
Age, mean (±SD), years	72.2 (8.4)
Age >65 years, n. (%)	181 (81.9%)
Age >75 years, n. (%)	96 (43.4%)
Male sex, n (%)	126 (57.0%)
Primary MF, n (%)	130 (58.8%)
Post-PV MF, n. (%)	40 (18.1%)
Post-ET MF, n. (%)	51 (23.1%)
Hemoglobin, mean (±SD), g/dL	8.8 (1.2)
Hemoglobin <10 g/dL, n (%)	207 (93.7%)
Hemoglobin <8 g/dL, n (%)	130 (58.8%)
RBC transfusion requirement, n (%)	129 (58.4%)
RBC transfusion dependence, n (%)	92 (41.6%)
Platelets, mean (±SD), x10 ⁹ /L	172.8 (160.4)
Platelets <200 x10 ⁹ /L, n. (%)	155 (70.1%)
Platelets <100 x10 ⁹ /L, n. (%)	92 (41.6%)
Platelets <50 x10 ⁹ /L, n. (%)	29 (13.1%)
Cytopenic phenotype, n (%)	215 (97.3%)
Peripheral blasts count, mean (±SD), %	1.1 (1.6)
Peripheral blasts ≥3%, n. (%)	32 (14.5%)
Peripheral blasts ≥1%, n. (%)	95 (43.0%)

Spleen length, mean (±SD), cm below costal margin	7.8 (6.5)
Palpable spleen, n (%)	191 (86.4%)
Spleen ≥5 cm, n. (%)	145 (65.6%)
Spleen ≥10 cm, n. (%)	77 (34.8%)
Total Symptoms Score (TSS), mean (±SD)	20.0 (15.3)
TSS ≥1, n (%)	194 (87.8%)
TSS ≥20, n (%)	97 (43.9%)
Driver mutation, n. (%)	
JAK2	138 (62.4%)
CALR	54 (24.4%)
MPL	25 (11.3%)
Triple Negative	4 (1.8%)
CALR type 1 / type 1-like, n. (%)	24 (10.9%)
CALR non-type-1 or unknown	30 (13.6%)
CALR wild-type	167 (75.6%)
High Molecular Risk mutations, n. (%)	29/66 (43.9%)
ASXL1	20 (30.3%)
EZH2	3 (4.5%)
SRSF2	6 (9.1%)
IDH1/2	3 (4.5%)
U2AF1	5 (7.6%)
DIPSS risk score, n. (%)	
Intermediate-1	24 (10.9%)
Intermediate-2	141 (63.8%)
High	56 (25.3%)

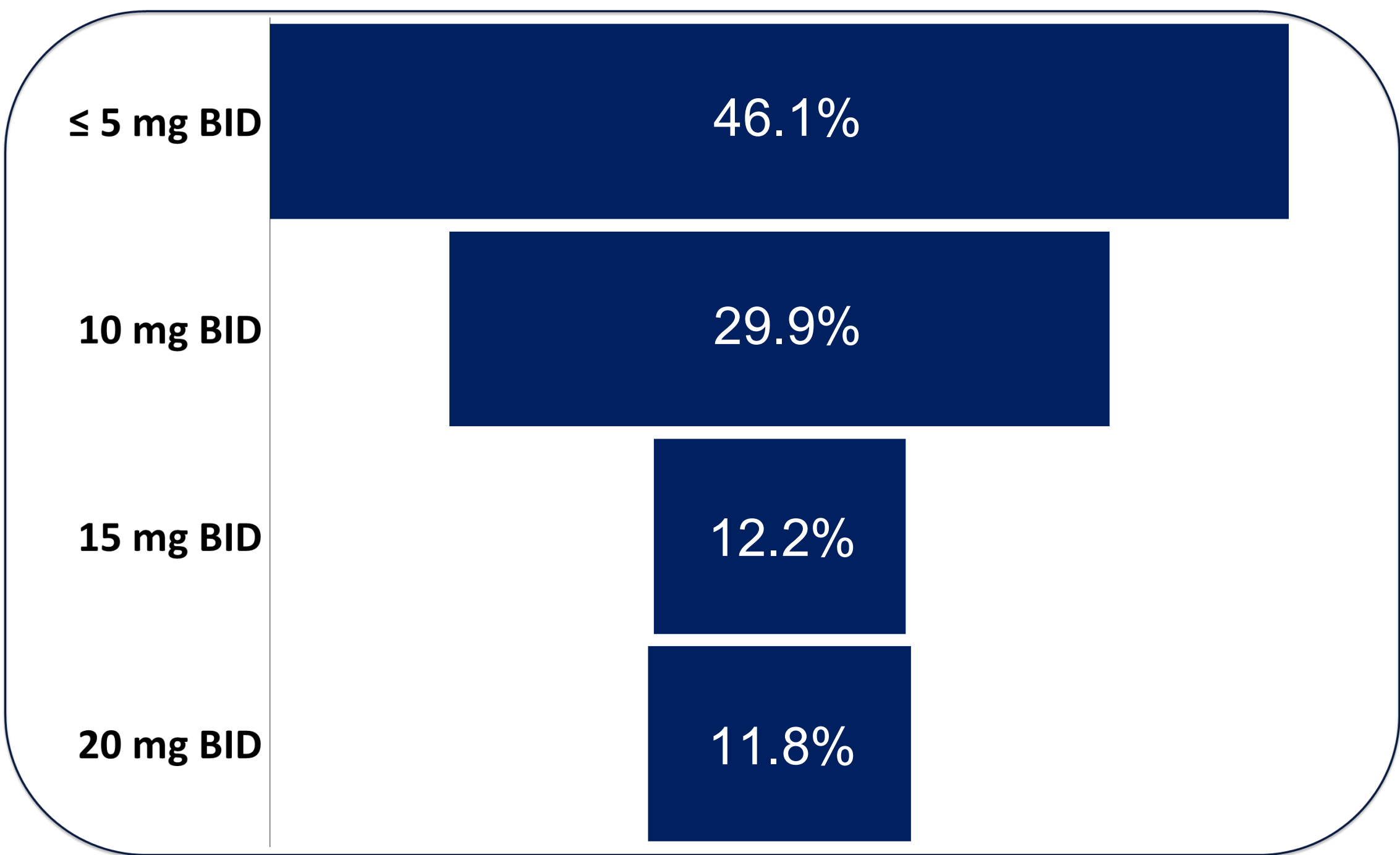
Table 1: SD, Standard Deviation; MF, myelofibrosis; PV, polycythemia vera; ET, essential thrombocythemia; RBC, red blood cells; DIPSS, Dynamic International Prognostic Scoring System. TD was defined as ≥3 units in the 12 weeks prior baseline (ref. 24).

Cytopenic phenotype defined as hemoglobin (Hb)<10 and/or platelet count (PLT)<100x10⁹/L
MF, myelofibrosis; MMB: momelotinib; RUX: ruxolitinib; RBC, red blood cells; TSS, Total Symptoms Score; HMR, high molecular risk

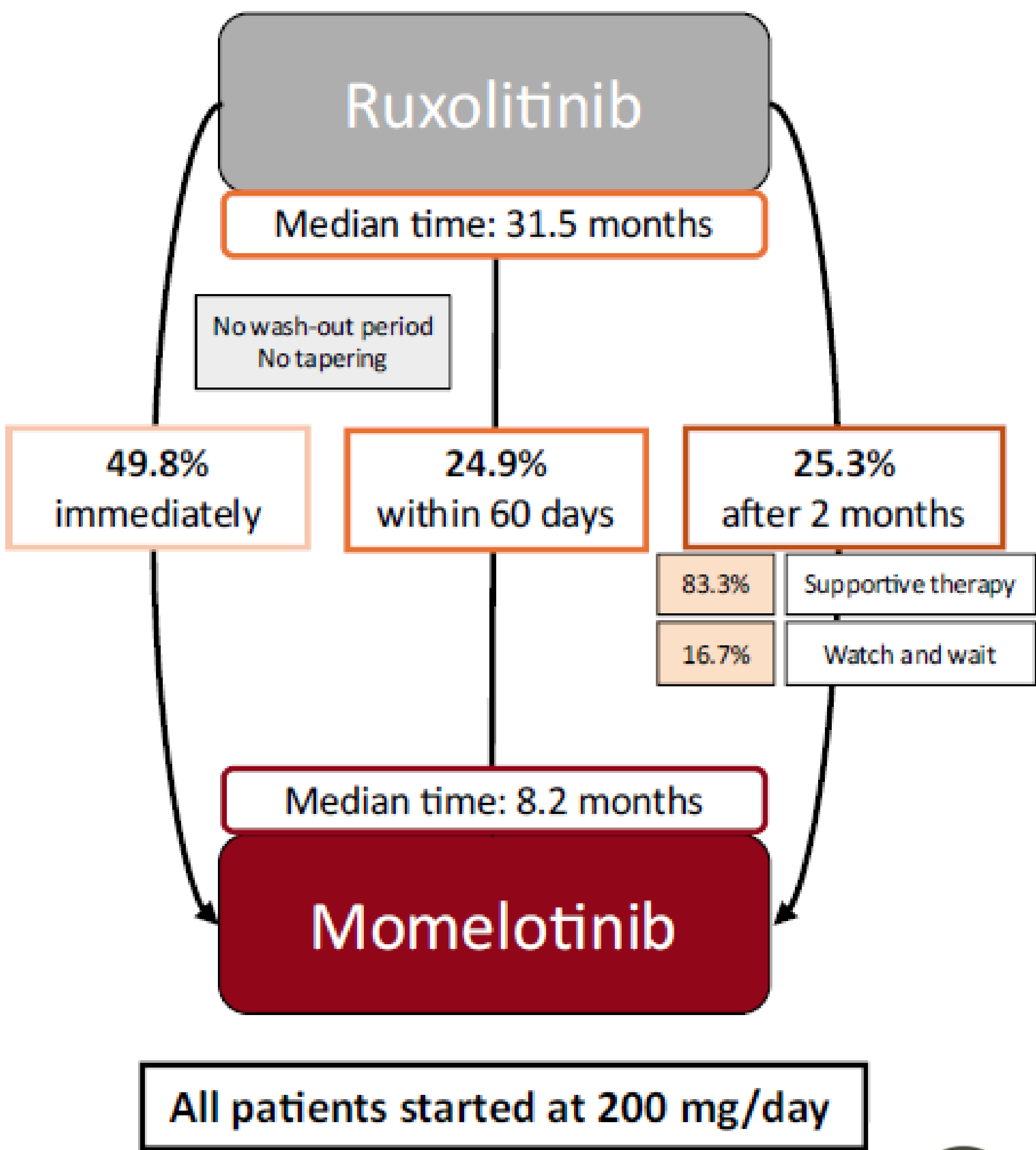


Retrospective data collection of MF patients treated with 2nd-line MMB, after RUX failure

Ruxolitinib dose at discontinuation



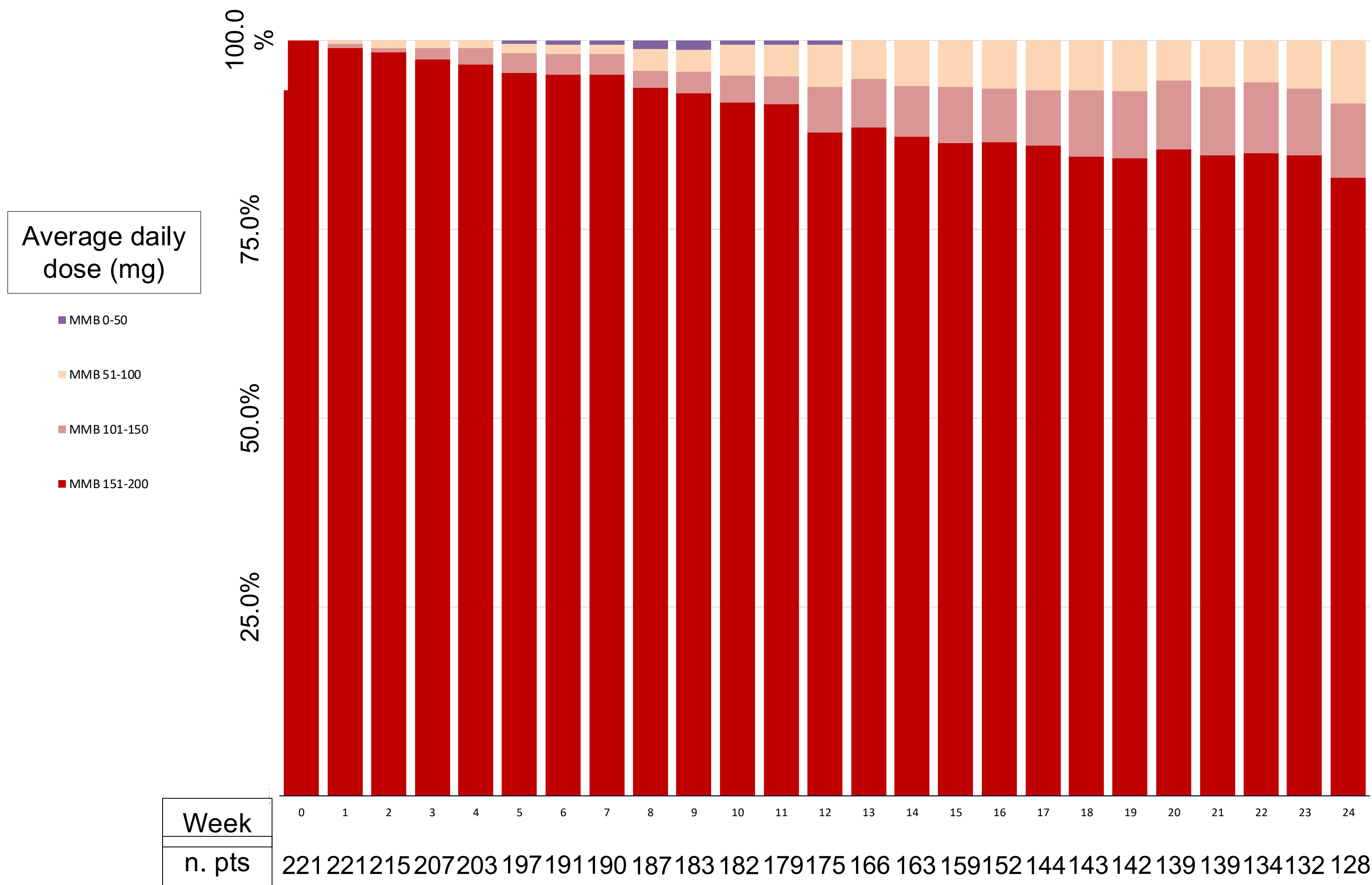
42.5%
of patients were receiving a lower dose of ruxolitinib than that recommended by the prescribing indication based on platelet count



MMB: momelotinib; RUX: ruxolitinib; BID: bis in die



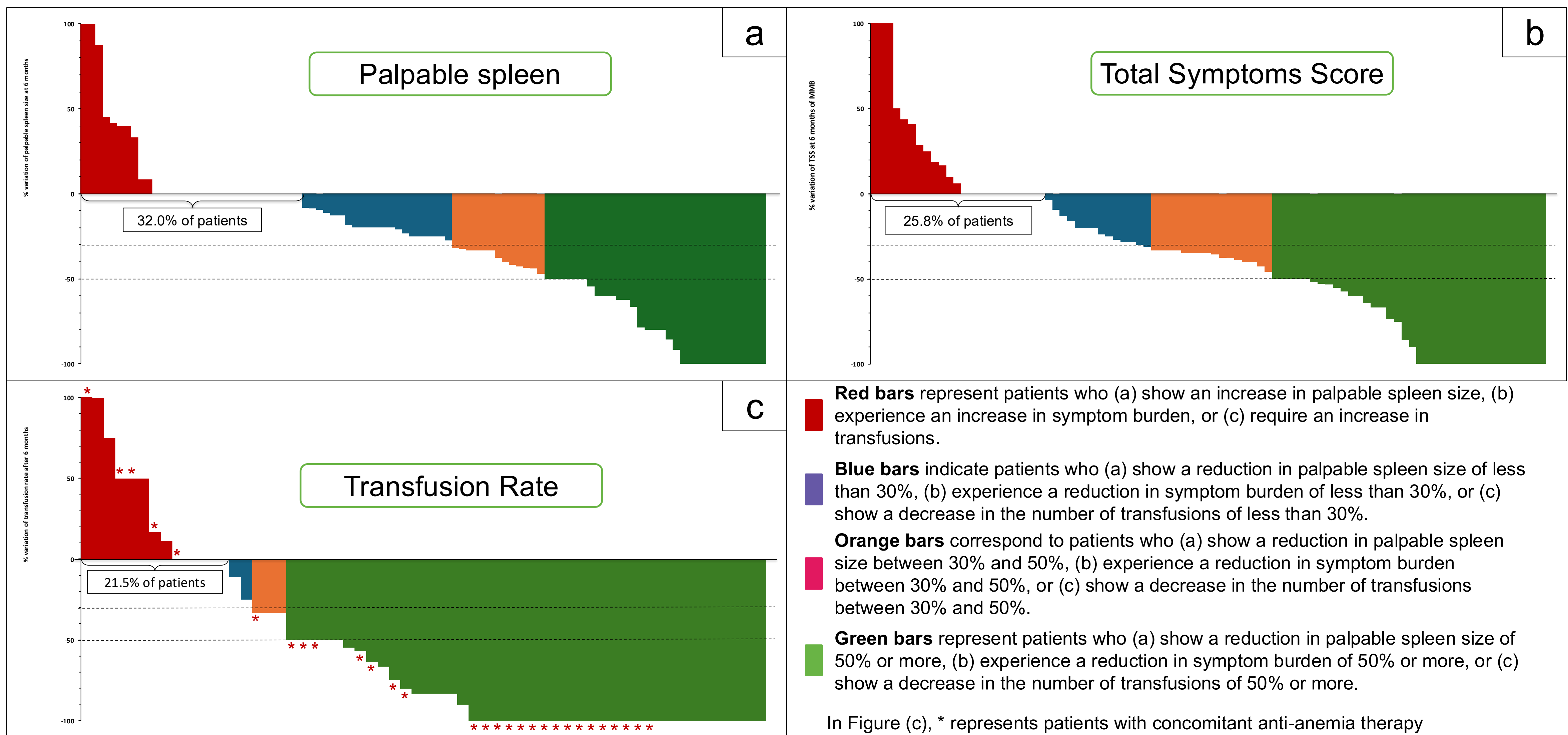
Momelotinib Dose Intensity



- All patients started MMB at full dose (200 mg daily)
- Among the evaluable patients at 6 months, 82.4% of patients maintained a full momelotinib dose throughout the first 24 weeks of therapy.
- Adverse events required transient / stable dose reductions in 28 patients (12.7%) and prompt momelotinib discontinuation in 44 patients (19.9%).
- The most common adverse event leading to discontinuation was thrombocytopenia (14, 6.3%)

MMB: momelotinib

Variations of palpable spleen, total symptoms score and transfusion rate at 6 months



Transfusion Independence with OMJJARA Regardless of Baseline Erythropoietin Levels in the Phase 3 SIMPLIFY-1 Trial

Study Design

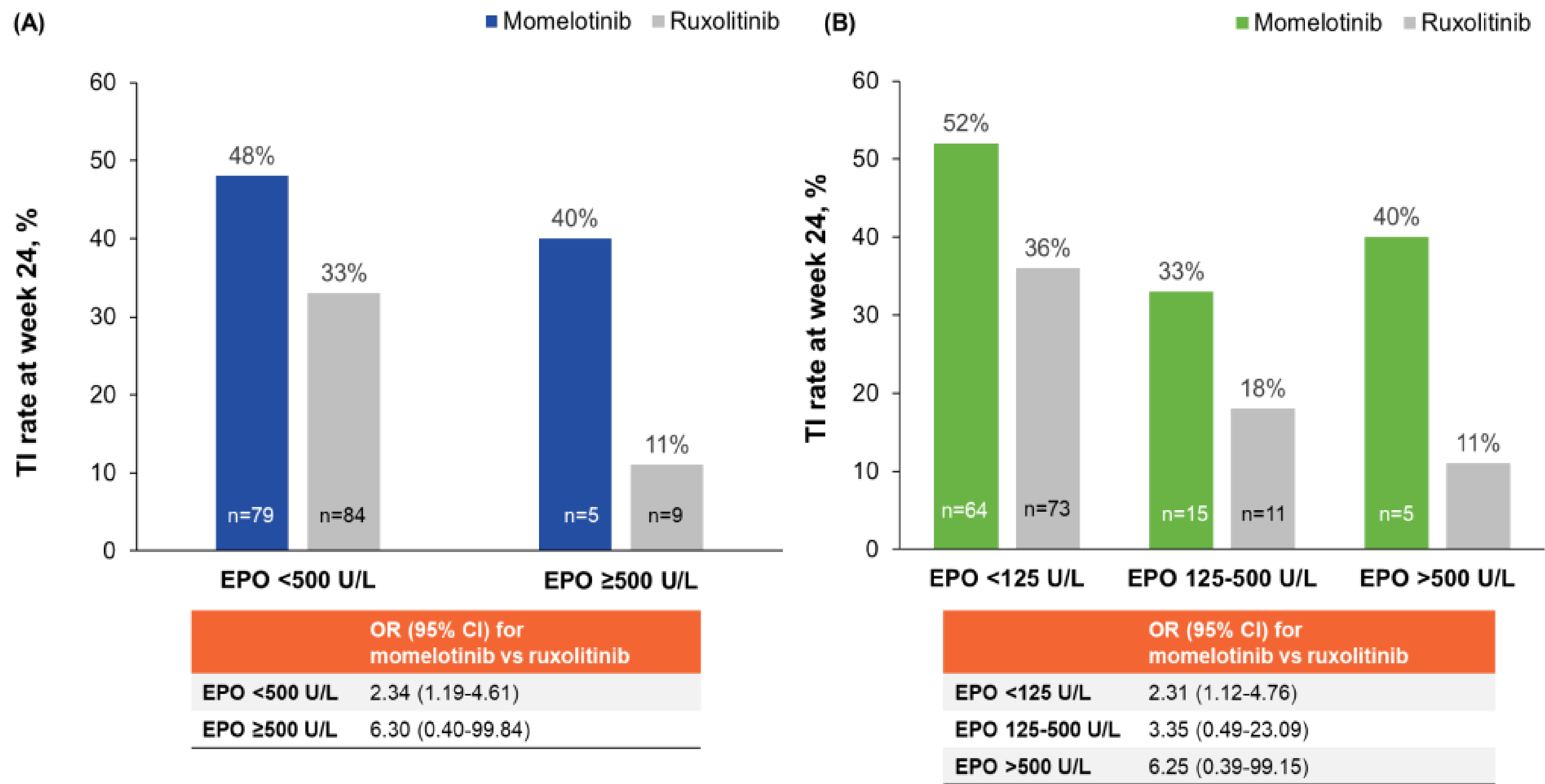
SIMPLIFY-1 (NCT01969838)
mometotinib vs ruxolitinib



- Patients from SIMPLIFY-1 were divided into EPO subgroups, defined post hoc with a 2-cohort or a 3-cohort stratification based on clinically relevant thresholds
 - Analyses were carried out in the ITT as well as populations that were anemic (Hb ≤ 10 g/dL) and *JAK2* V617F positive at baseline
- Additional analyses evaluated treatment and baseline EPO as a continuous variable using all available information from patients with confirmed *JAK2* mutational status and nonmissing EPO data

Transfusion Independence with OMJJARA Regardless of Baseline Erythropoietin Levels in the Phase 3 SIMPLIFY-1 Trial

Patients With Hb ≤10 g/dL Achieving TI Stratified by EPO Level

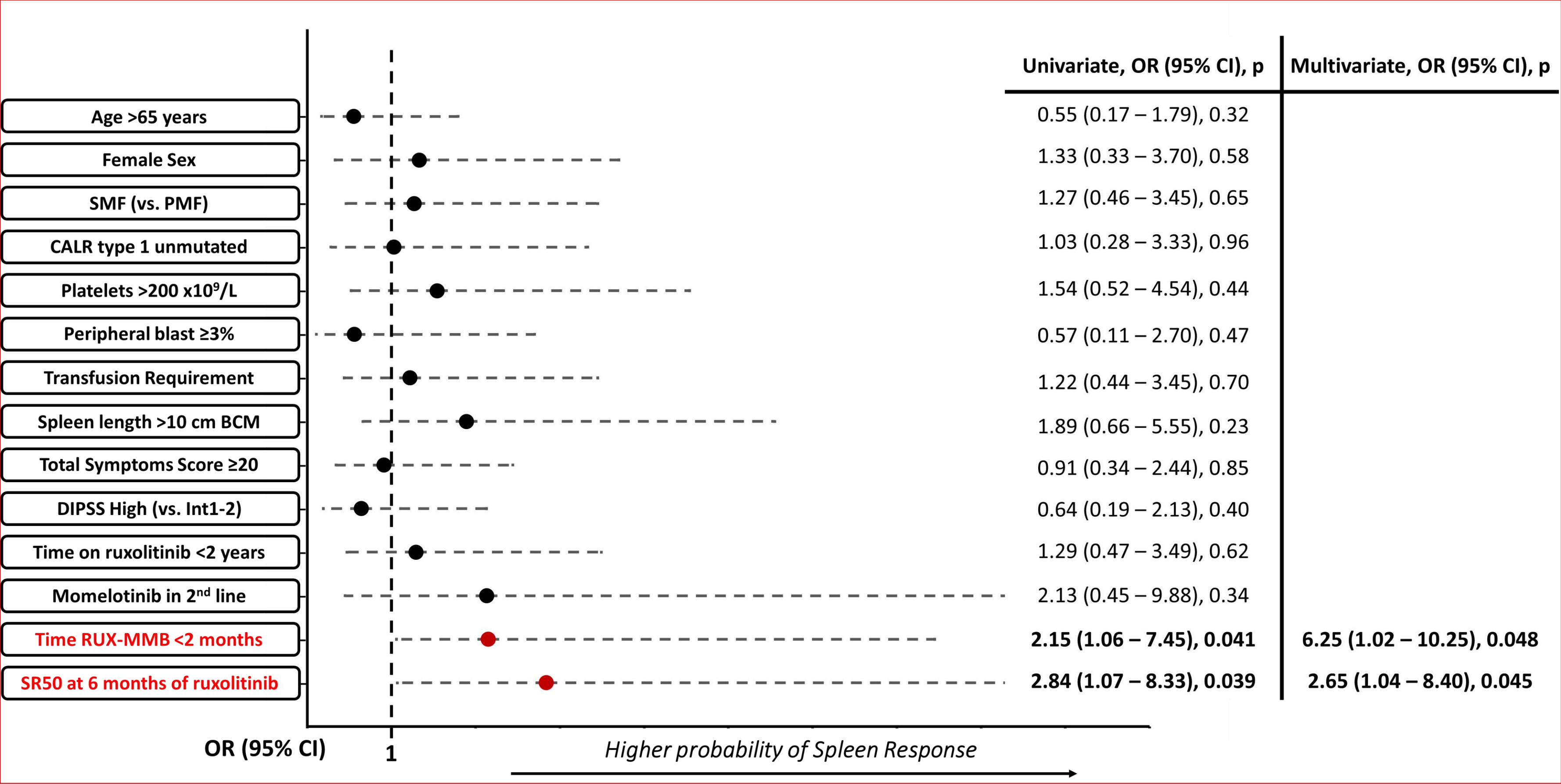


These results underscore the anemia-related benefits of OMJJARA in JAK inhibitor–naïve patients with MF, irrespective of EPO levels

EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; JAK, Janus kinase; TI, transfusion independence; ITT, intention-to-treat; OR, odds ratio; CI, confidence interval
References: 1. McLoman D, Harrison CN. *Fast Facts: Myelofibrosis*. S. Karger Publishers Ltd; 2022. 2. Bose P, Verstovsek S. *Curr Hematol Malig Rep*. 2018;13(3):164-172. 3. Crisa E, et al. *Br J Haematol*. 2018;182(5):701-704. 4. Naymagon L, Mascarenhas J. *Hemasphere*. 2017;1(1):e1.



Baseline predictors of IWG-MRT spleen response at 3 and/or 6 months

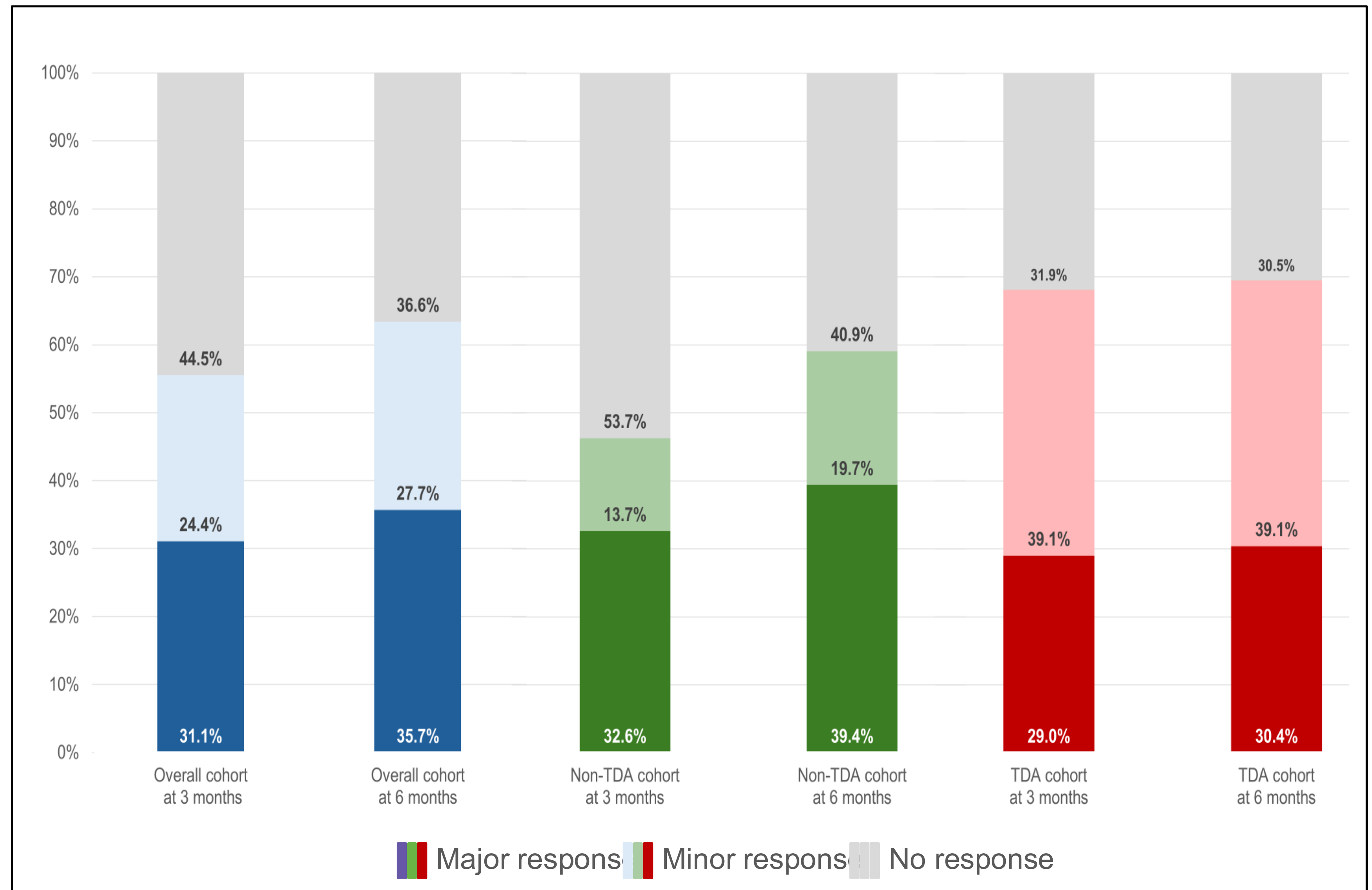


- In multivariate logistic regression, **achieving a SR50 at 6 months during prior ruxolitinib** (OR: 6.25, 95%CI: 1.02-10.25, $p=0.048$) and a **transition time between ruxolitinib and momelotinib <2 months** (OR: 2.65, 95%CI: 1.04-8.40, $p=0.045$) remained independent predictors of higher probability of achieving a IWG-MRT spleen response to momelotinib at 3 and/or 6 months

IWG-MRT: International Working Group-Myeloproliferative Neoplasms Research and Treatment; **SMF:** secondary myelofibrosis; **PMF:** primary myelofibrosis; **BCM:** below coastal margin; **DIPSS:** Dynamic International Prognostic Scoring System; **RUX:** ruxolitinib; **MMB:** momelotinib; **SR50:** spleen reduction 50%; **OR:** odds ratio; **CI:** confidence interval

Anemia Response at 3 and 6 months

- At 3 months, 55.5% of patients achieved an anemia response (major: 31.1%).
- The proportion of responders increased at 6 months (63.4%; major: 35.7%).
- In the TD cohort, the median frequency of RBC transfusions decreased from 6 to 2.5 units at 3 months and to 2 units at 6 months.
- In the non-TD group, the mean Hb level at baseline was 9.3 g/dL ($\pm$ SD: 1.1), increased to 10.3 g/dL ($\pm$ SD: 1.5) at 3 months and then remained stable at 6 months (10.4 g/dL $\pm$ SD: 1.6).
- Globally, 37.0% of evaluable patients at 6 months who required transfusions at baseline achieved complete transfusion independence between months 3 and 6.



TD: transfusion-dependent; RBC: red blood cell; SD: standard deviation; TDA: transfusion-dependent anemia

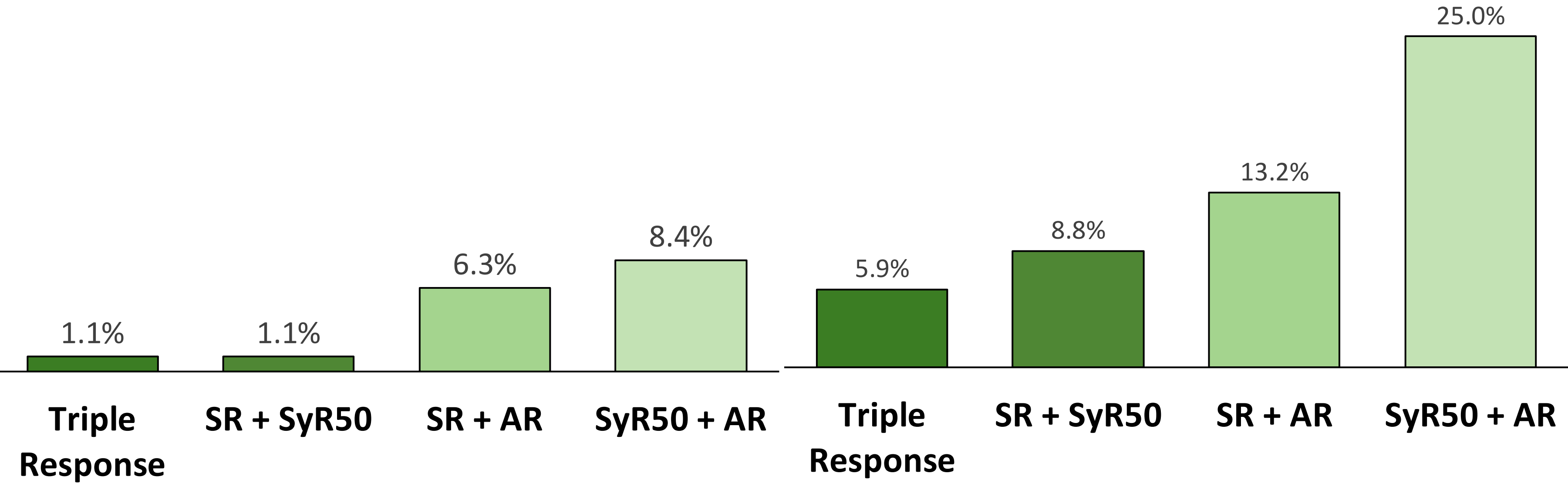
Retrospective data collection of MF patients treated with 2nd-line MMB, after RUX failure

Responders at 3 and 6 months (IWG-MRT response criteria)

At 3 months

At 6 months

Triple response increase between 3 and 6 months, primarily due to a **significant improvement in symptoms relief**



SR, Spleen Response; SyR50, TSS reduction ≥50%; AR, anemia response

Multiple response: 108 patients evaluable

Multiple response: 77 patients evaluable

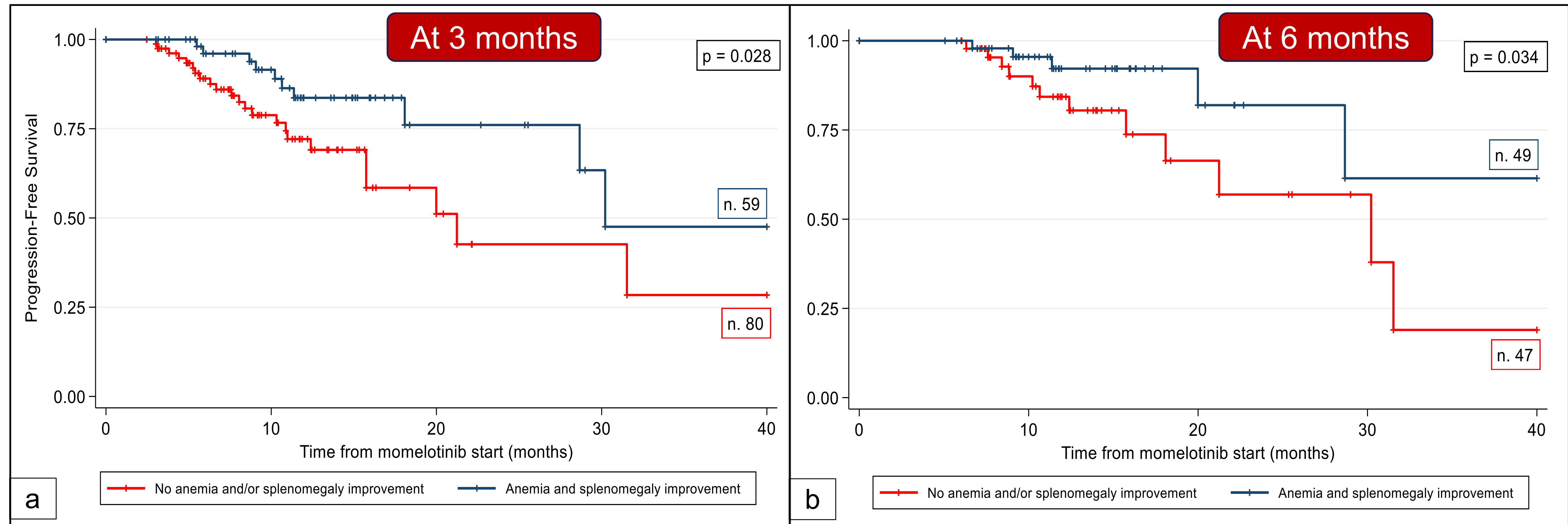
Multiple responses were evaluated in all patients with palpable splenomegaly ≥5 cm and Total Symptoms Score (TSS) >0 at baseline

IWG-MRT: International Working Group-Myeloproliferative Neoplasms Research and Treatment; **RUX:** ruxolitinib; **MMB:** momelotinib; **SR:** spleen response; **SyR50:** Total Symptom Score reduction ≥50%; **AR:** anemia response
Courtesy of speaker, manuscript already accepted for publication



Retrospective data collection of MF patients treated with 2nd-line MMB, after RUX failure

Anemia & Splenomegaly Improvement may impact PFS



- Patients showing a combined improvement in anemia and spleen size (**blue line**) demonstrate better Progression-Free Survival, including death and leukemic transformation.
 - 2-Year PFS (by improvement at 3 months): **Red**: 42.6% versus **Blue**: 76.1%
 - 2-Year PFS (by improvement at 6 months): **Red**: 56.9% versus **Blue**: 82.0%

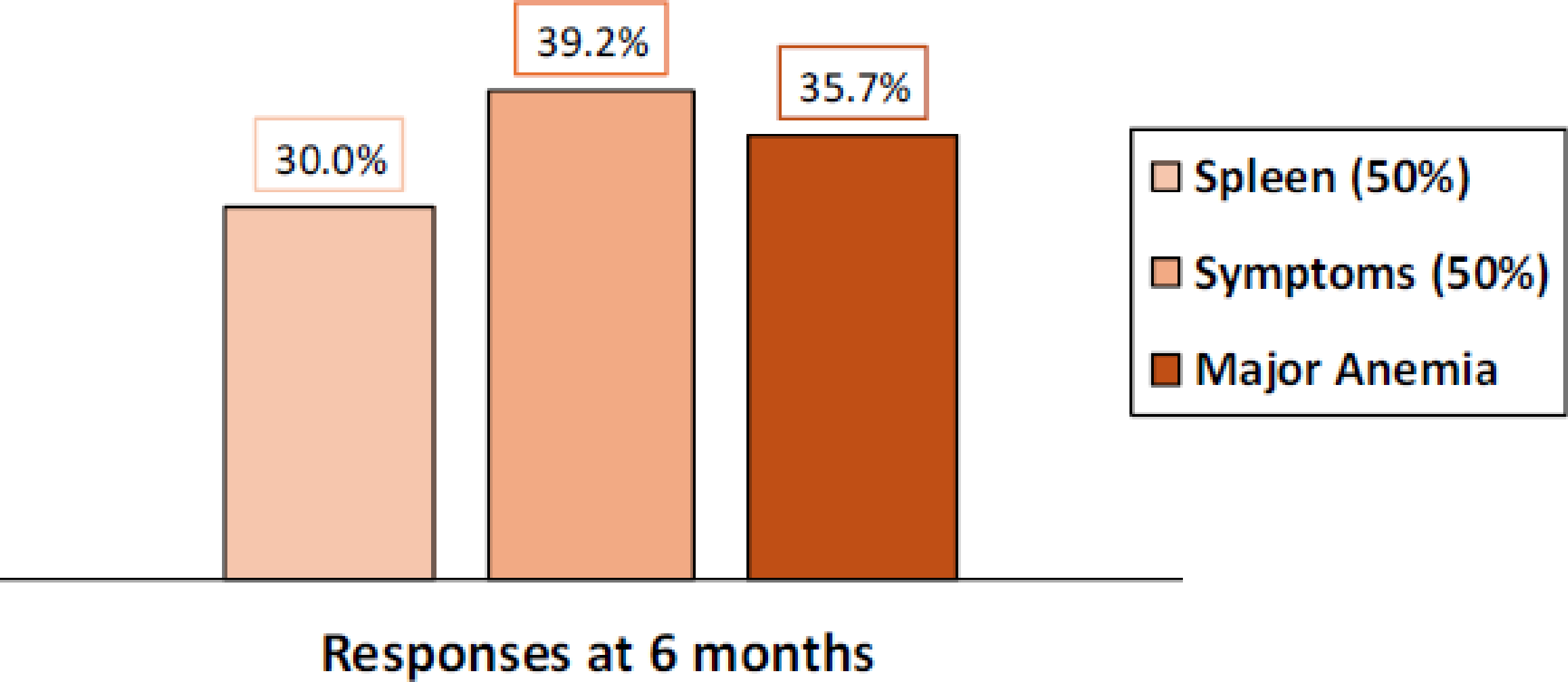
MF: myelofibrosis; MMB: momelotinib; RUX: ruxolitinib; PFS: progression-free survival
Patients were censored at transplantation in both curves



Retrospective data collection of MF patients treated with 2nd-line MMB, after RUX failure

Conclusions

Multidimensional Clinical Benefit



Predictive Patterns & Tolerability

- Shorter ruxolitinib-to-momelotinib interval → better spleen/anemia responses; prior spleen response predicted response
- Favorable safety profile: only 12.7% reduced dose; most patients maintained full-dose intensity

Outcome Relevance

- 2-year OS (60.9%) and PFS (59.0%)
- Combined spleen + anemia improvement at 3 or 6 months linked to better progression-free survival

Concluding Remarks

Unmet Need

Cytopenic MF patients represent a large group with significant unmet medical needs

Anemia as a Key Treatment Goal

- Achieving Hb >10 g/dl by week 24 associated with longer OS, regardless of baseline anemia severity
- Moderate baseline anemia: faster and more likely to reach Hb >10 g/dl vs severe anemia — do not delay treatment
- TI may contribute to long-term outcomes with momelotinib
- Anemia improvement should be a primary treatment goal

Momelotinib Efficacy in Cytopenic Pts

- Higher SVR35 rates vs ruxolitinib in patients with platelets <200,000/mcl
- Initiated at full dose even in low-platelet patients, unlike ruxolitinib
- Most responders achieved dual SVR35 + TI, confirming combined spleen and anemia benefit
- Multiple real-world studies confirmed clinical trial data

MF, Myelofibrosis; **OS**, Overall survival; **SVR35**, Spleen volume reduction 35%; **TI**, Transfusion independence



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Grazie!
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