Medical Affairs

BY COR2ED

MYELOFIBROSIS: UNMET NEEDS AND NEW DIRECTIONS

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AUGUST 2026

ACKNOWLEDGEMENT AND DISCLOSURES

- This programme has been sponsored by Menarini Stemline and is intended for healthcare professionals only

Expert disclosures:

- Prof. Francesco Passamonti has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies:
  - Advisory board: AbbVie, Bristol Myers Squibb/Celgene, GSK, Keros, Menarini Stemline, Novartis, Sumitomo
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EDUCATIONAL OBJECTIVES

- Identify current unmet clinical needs in the treatment of myelofibrosis
- Evaluate how genomic profiling enhances clinical models to guide risk-adapted care
- Assess the role of VAF reduction, cytokines, blasts, and BMF in tracking disease modification
- Explore how emerging combination therapies aim to prolong survival beyond basic symptom control

BMF, bone marrow fibrosis; VAF, variant allele frequency

CLINICAL TAKEAWAYS

- **Beyond Symptom Control:** current treatments leave significant gaps; novel approaches must move beyond symptom control to alter the underlying disease course
- **Genomic Profiles Enhance Prognosis:** adding mutational data to established clinical parameters could provide a useful layer of insight for guiding risk-adapted care
- **VAF and Biomarkers Indicate Response:** reducing VAF appears to be a strong marker of disease modification, while biological markers (cytokines, blasts, and BMF) often correlate closely with treatment outcomes
- **Combinations Hold Future Potential:** Emerging combination therapies could reshape MF management by targeting multiple disease pathways, improving outcomes

BMF, bone marrow fibrosis; VAF, variant allele frequency

WHAT ARE TODAY'S UNMET NEEDS IN MF?

THE FOUR HALLMARK SYMPTOMS OF MF

Constitutional symptoms: fatigue, night sweats, weight loss, fever, itching and thought to be caused by cytokines

Splenomegaly: caused by splenic extramedullary hematopoiesis, spleen size increases by ~10x normal (2500 cm^3 vs. 200 cm^3)

Cytopenias: anemia, frequently multifactorial, appears in ~35–38% of patients at the time of diagnosis

Bone marrow fibrosis: central feature of MF, with progressive reticulin and potentially collagen deposition in the bone marrow

Myelofibrosis poses progression risks: AML, infections, and cardiovascular disease

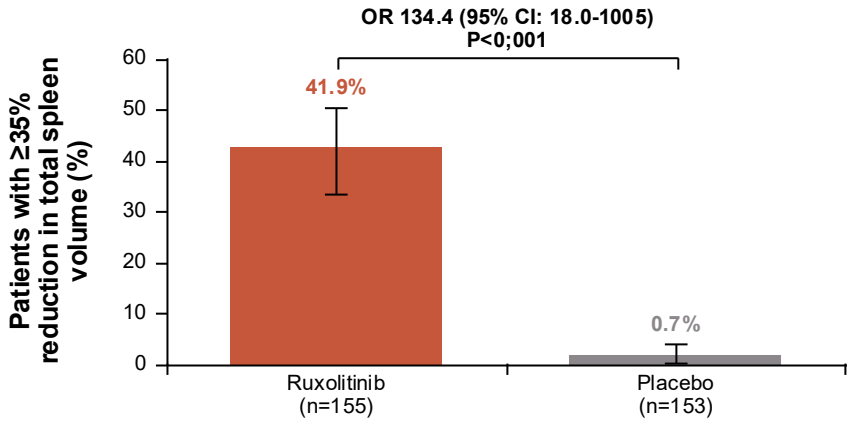
AML, acute myeloid leukemia; MF, myelofibrosis

Koschmieder S, et al. Leukemia. 2024;38:1831-8; 2. Mehta J, et al. Leuk Lymphoma. 2014;55(3):595-600; 3. Mughal TI, et al. Int J Gen Med. 2014;7:89-101; 4. Passamonti F, et al. Crit Rev Hematol. 2022;180:103862; 5. Song MK, et al. Int J Mol Sci. 2018;19(3):898; 6. Verstovsek S, et al. N Engl J Med. 2012;366:799-807; 7. Zahr AA, et al. Haematologica. 2016;101:660-71

NOT ALL PATIENTS RESPOND TO JAK INHIBITOR MONOTHERAPY

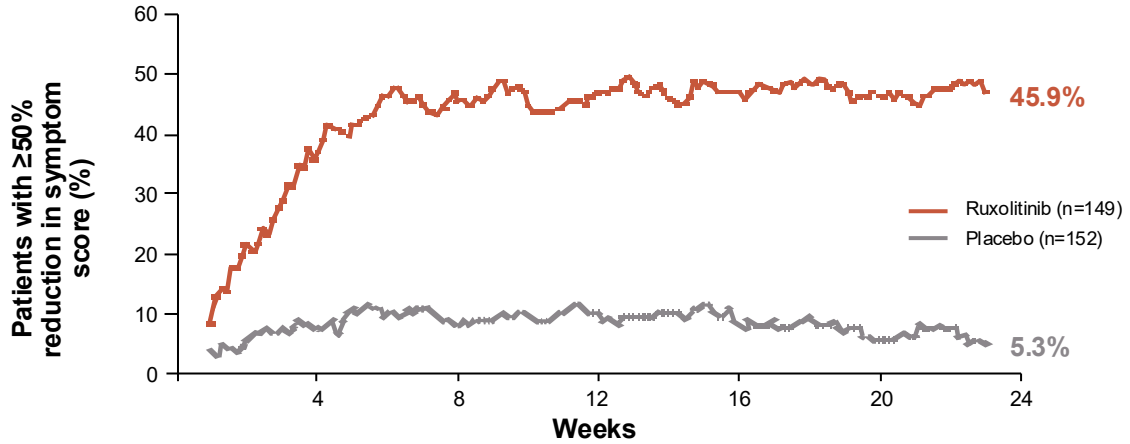
COMFORT-I: Spleen and symptom response at 24 weeks[1]

Spleen response



Adapted from Verstovsek S, et al. 2012

Symptom response



Adapted from Verstovsek S, et al. 2012

The primary endpoint of SVR35 at Week 24 was met. Ruxolitinib, compared with placebo, provided **significant clinical benefits** in patients with MF by reducing spleen size and ameliorating debilitating MF-related symptoms[1]

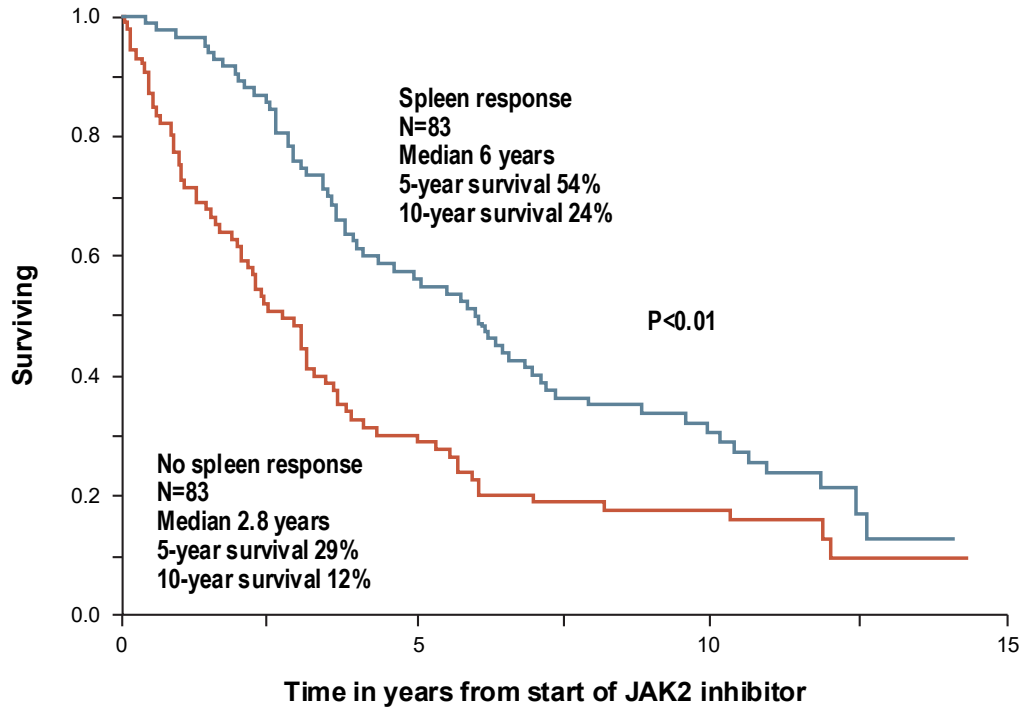
- With current JAK inhibitor monotherapy:
  - Responses lack rapidity and durability[2]
  - 50 to 70% discontinue JAK inhibitors within 3 to 5 years due to loss of response and disease progression[2]

CI, confidence interval; MF, myelofibrosis; OR, odds ratio; RUX, ruxolitinib; SVR35, spleen volume response rate of ≥35%

1. Verstovsek S, et al. N Engl J Med. 2012;366(9):799-807; 2. Mascarenhas J, et al. Future Oncol. 2023;19(11):763-73;

DOES A RESPONSE TO JAK INHIBITORS CORRELATE WITH SURVIVAL?

Correlation between spleen response and survival in patients treated with any JAK inhibitor



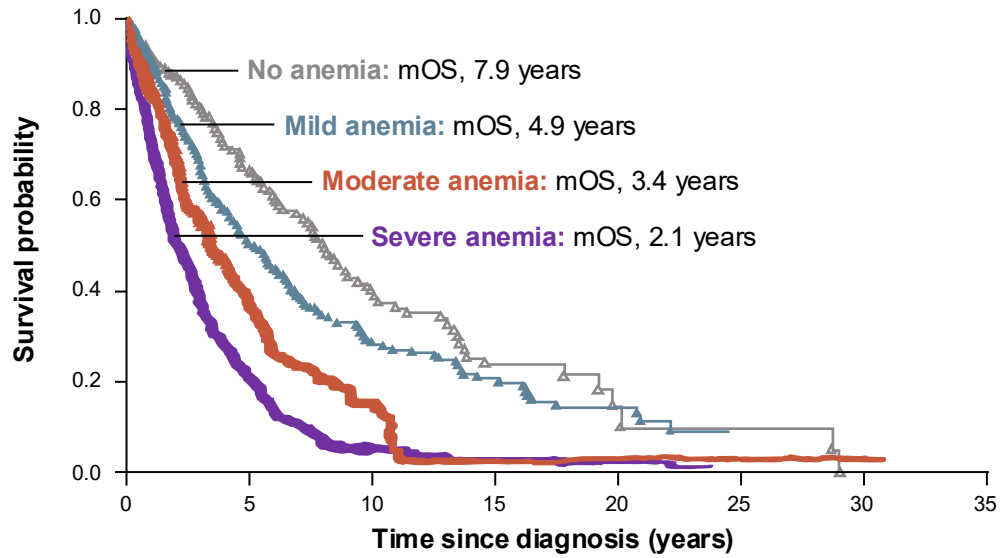
- JAK inhibitor *spleen* response seems to correlate with overall survival
- Evidence is unclear on whether *TSS* response also correlates with OS

JAKi, janus kinase inhibitor; OS, overall survival; TSS, total symptom score

Gangat, N, et al. Blood Cancer J. 2023;13(1):3; Kosiorek HE, et al. Br J Haematol. 2022;198(6):1065-8

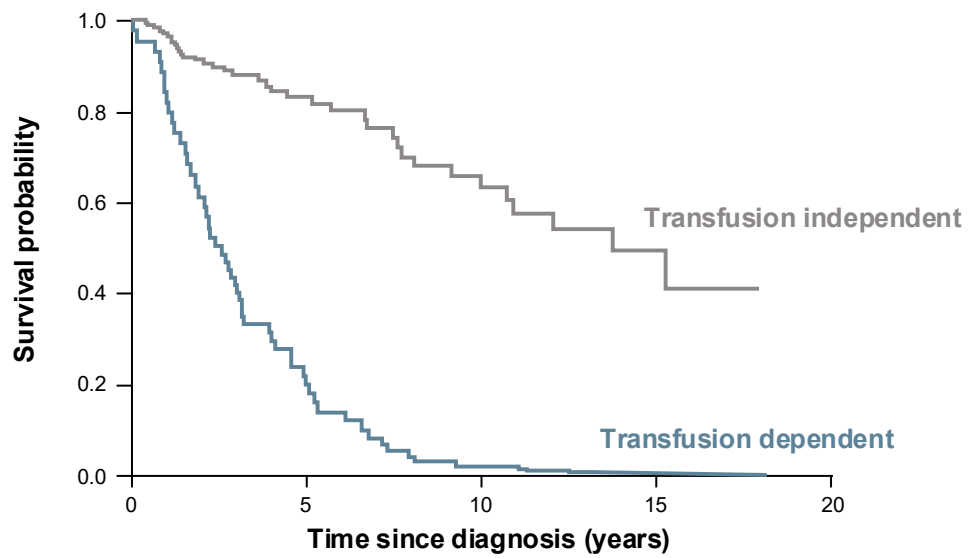
CYTOPENIA IN MF REMAINS A CHALLENGE

OS by anemia severity[1]



Adapted from Nicolosi M, et al.[1]

OS by transfusion status[2]



Adapted from Elena C, et al.[2]

- MF related anemia and TD are associated with poor overall survival
- Anemia symptoms may worsen in patients with MF and lead to transfusion dependence[1,2]
- Treatment-emergent cytopenias, particularly anemia, necessitate supportive interventions (transfusions, ESAs, growth factors)[3,4]

MF, myelofibrosis; mOS, median overall survival; OS, overall survival; TD, transfusion dependance,

1. Nicolosi M, et al. Leukemia. 2018;32(5):1254-8; 2. Elena C, et al. Hematologica. 2011;96(1):167-70; 3. Verstovsek S, et al. N Engl J Med. 2012;366:799-807;
4. Harrison C, et al. Leukemia. 2016;30:1701-7

WHAT ARE POSSIBLE NEW DIRECTIONS IN MF TREATMENT ?

IMPROVING RISK MODELS WITH GENOMIC PROFILING

- Clinical parameters alone don't capture full disease biology
- Genomic/mutational profiling adds independent prognostic value

Mutation profiles define PMF survival

Driver mutations

	CALR	*MPL*	*JAK2*	*Triple negative*
Median survival, years[1,2]	15.9-17.7	9.1-9.9	5.9-9.2	2.3-3.2

Worsening progression

'High molecular risk' mutations[3,4]

Patients harbouring one or more mutations in *ASXL1*, *EZH2*, *SRSF2*, and *IDH1/IDH2* are considered to constitute a high molecular risk category[3]

High molecular risk mutations:
ASXL1, EZH2, SRSF2, and IDH1/IDH2[3]

Worse prognosis in patients with ≥2 high molecular risk mutations[4]

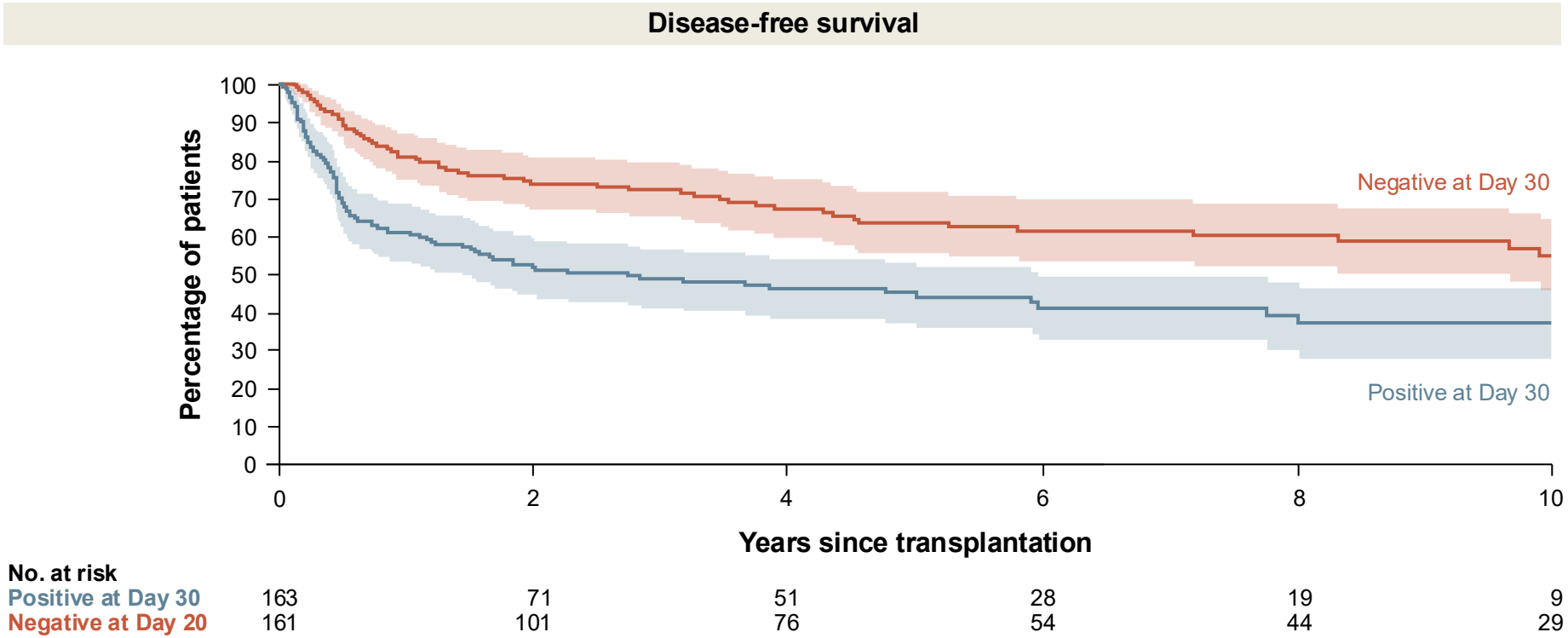
U2AF1[5] and TP53[6] status further refine prognosis beyond driver mutation and HMR status alone

GIPSS, Genetically Inspired Prognostic Scoring System; MIPSS70, Mutation-enhanced International Prognostic Scoring System; OS, overall survival; PMF, primary myelofibrosis

1. Rumi E, et al. Blood. 2014;124:1062-9; 2. Tefferi A, et al. Blood. 2014;124:2507-13; 3. Vannucchi AM, et al. Leukemia. 2013;27:1861-9;
4. Guglielmelli P, et al. Leukemia. 2014;28:1804-10; 5. Tefferi A, et al. Leukemia. 2018;32(10):2274-8; 6. Rolles B, et al. Leukemia. 2026;40:773-782

VAF REDUCTION APPEARS TO BE A MARKER OF TRUE MF DISEASE MODIFICATION

SCT and the impact of clone abrogation



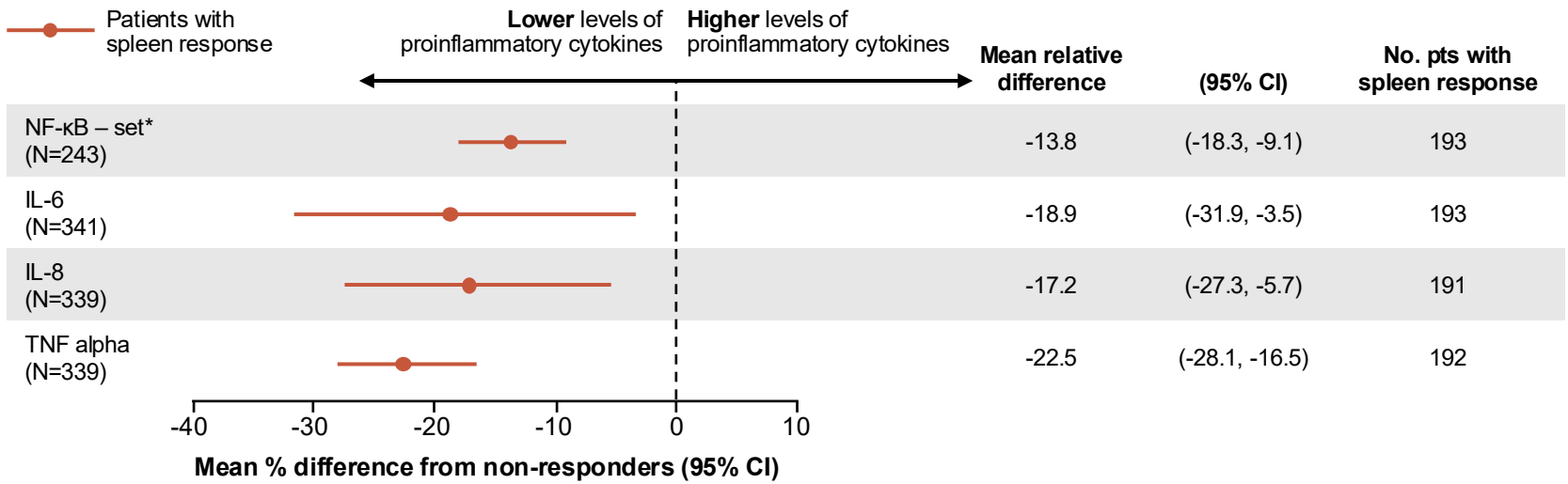
Day 30 mutation clearance is predictive of improved disease-free and overall survival – irrespective of driver mutation type

SCT, stem call transplantation

Gagelmann N, et al. N Engl J Med. 2025;392:150-60

BIOLOGICAL MARKERS: CYTOKINES, BLASTS, AND BMF

Mean relative difference in cytokine changes from BL at Week 24 in patients with SR vs. without SR in MANIFEST-2



Spleen responders showed lower proinflammatory cytokines, independent of treatment

- Cytokines, BMF grading as well as PB blasts appear biologically central to MF, correlating well with outcomes

*NF-KB set included B2M, CRP, CD40-L, hepcidin, IL-6, IL-12p40, MIP-1 beta, MPIF-1, RANTES, TNFR2, TNF, VCAM-1

BL, baseline; BMF, bone marrow fibrosis; CI, confidence interval; IL, interleukin; NF-KB, nuclear factor kappa B; PB: peripheral blood; SR, spleen response; TNF, tumour necrosis factor

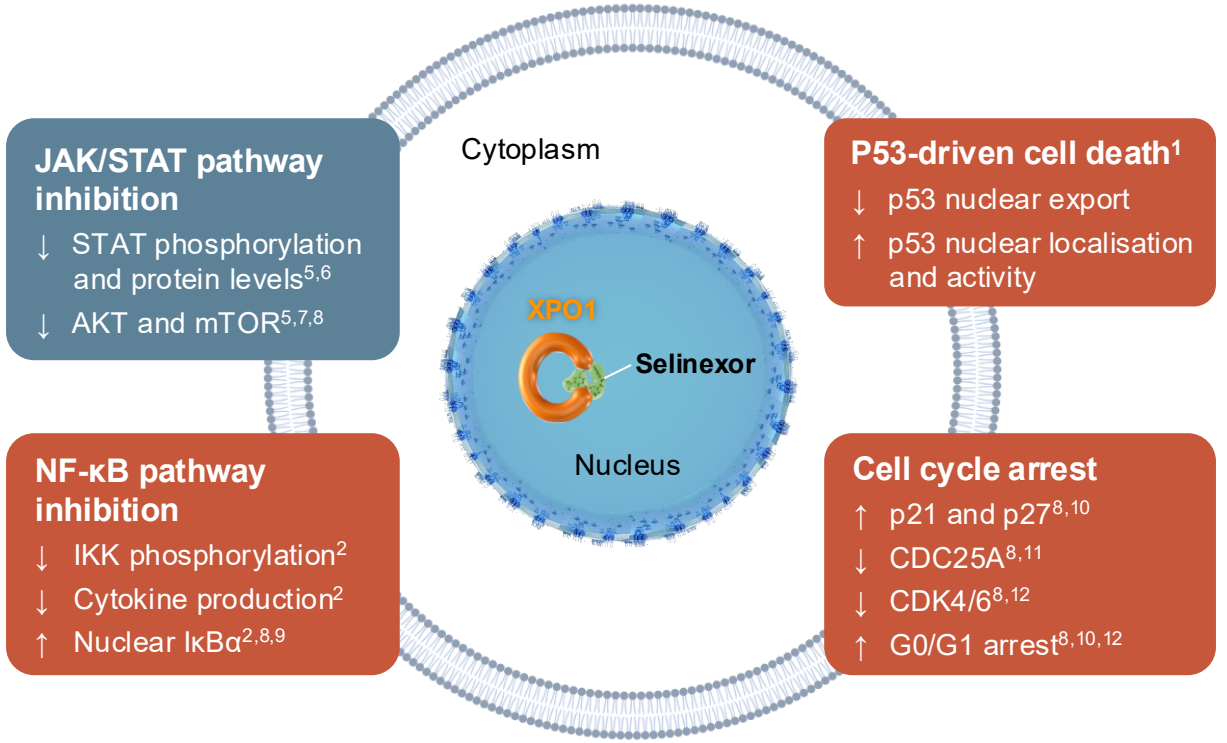
Guglielmelli P, et al. Blood. 2017;129:3227-3236; Masarova L, et al. Cancer. 2020;126:4322-4331; Mora B, et al. Am J Hematol. 2020;95:E1-E3; Rampal RK, et al. Nat Med. 2025;31:1531-1538

IS COMBINATION THERAPY THE FUTURE OF MF TREATMENT? RATIONALE FOR XPO1 INHIBITION

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]



AKT, protein kinase B; CD, cluster of differentiation; IkBa, inhibitor of nuclear factor kappa-B kinase subunit alpha; IKK, IKB kinase complex; *JAK2*, Janus kinase 2; JAK/STAT, Janus kinase/signal transducer and activator of transcription; MF, myelofibrosis; mTOR, mammalian target of rapamycin; NF-KB, nuclear factor KB; STAT, signal transducer and activator of transcription; XPO1, exportin 1

1. Yan D, et al. Clin Cancer Res. 2019;25:2323-35; 2. Kashyap T, et al. Oncotarget. 2016;7:78883-95; 3. Lu M, et al. Presented at ASH 2023; Abstract 1792; 4. Maloof M, et al. Presented at 15th International Congress for MPNs 2023; Abstract #123; 5. Walker CJ, et al. Blood. 2013;122:3034-44; 6. Cheng Y, et al. Mol Cancer Ther. 2014;13:675-86; 7. Argueta C, et al. Oncotarget. 2018;9;25529-44; 8. Gandhi UH, et al. Clin Lymphoma Myeloma Leuk. 2018;18:335-45; 9. Turner JG, et al. Oncotarget. 2016;7:78896-909; 10. Gravina GL, et al. BMC Cancer. 2015;15:941; 11. Garg M, et al. Oncotarget. 2017;8:7521-32; 12. Tan M, et al. Am J Physiol Renal Physiol. 2014;307:F1179-86

IS COMBINATION THERAPY THE FUTURE OF MF TREATMENT? MF ONGOING PHASE 3 TRIALS

- **SENTRY:** a double-blind, placebo-controlled, phase 3 study of selinexor + ruxolitinib vs. placebo plus ruxolitinib in patients with intermediate-risk or higher, JAKi-naïve MF
- **MANIFEST-3:** a phase 3, randomised, double-blind, active-controlled study of pelabresib plus ruxolitinib vs. placebo plus ruxolitinib in JAKi-naïve patients with MF
- **POIESIS:** a randomised, double-blind, phase 3 add-on trial of navtemadlin plus ruxolitinib vs. placebo plus ruxolitinib in JAKi-naïve patients with MF who have a suboptimal response to ruxolitinib

JAKi,, janus kinase inhibitor; MF, myelofibrosis

Rampal R, et al. Presented at ASH 2025; Oral presentation for Abstract 910; ClinicalTrials.gov. NCT06479135. Available at https://clinicaltrials.gov/studv/NCT06479135. Accessed March 5. 2026; Vachani P. et al. Presented at ASH 2024: Poster presentation 1808; Harrison C, et al. Abstract LB5002, EHA 2026

MYELOFIBROSIS CLINICAL TRIAL HIGHLIGHTS FROM EHA 2026

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AUGUST 2026

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EDUCATIONAL OBJECTIVES

- Explore the latest EHA 2026 myelofibrosis clinical trial data and potential implications for patient management

CLINICAL TAKEAWAYS

- **Pelabresib:** pelabresib seems to safely improve splenomegaly, symptoms, and bone marrow fibrosis in difficult-to-treat myelofibrosis, either as monotherapy post-failure or added to ruxolitinib in phase 2 trials
- **Selinexor:** selinexor plus ruxolitinib phase 3 SENTRY results show rapid, deep spleen volume reductions that predict overall survival, potentially making it the first regimen to demonstrate a survival benefit
- **Luspatercept:** luspatercept might soon help to reduce transfusion dependence for myelofibrosis patients treated with Janus kinase (JAK) inhibitors
- **Momelotinib:** immediate, washout-free transition from ruxolitinib to momelotinib seems feasible without worry of discontinuation syndrome
- **INCA033989:** INCA033989 early trial shows disease-modifying potential in calreticulin (CALR)-mutated myelofibrosis failing JAK inhibitors, improving symptoms and anemia, and reducing mutant allele frequency
- **AJ1-11095:** The type II JAK2 inhibitor AJ1-11095 overcomes standard resistance in pretreated myelofibrosis, effectively reducing spleen volume, symptoms, and mutant clone size

Pelabresib

Evaluation of pelabresib (PELA) as add-on therapy to ruxolitinib (RUX) in myelofibrosis (MF) patients: results from arm 2 of the open-label, phase 2 MANIFEST study

Kremyanskaya M, et al. Abstract PF894, EHA 2026

Pelabresib monotherapy in myelofibrosis after Janus kinase inhibitor failure: results from arm 1 of the open-label, phase 2 MANIFEST study

Talpaz M, et al. Abstract PS1987, EHA 2026

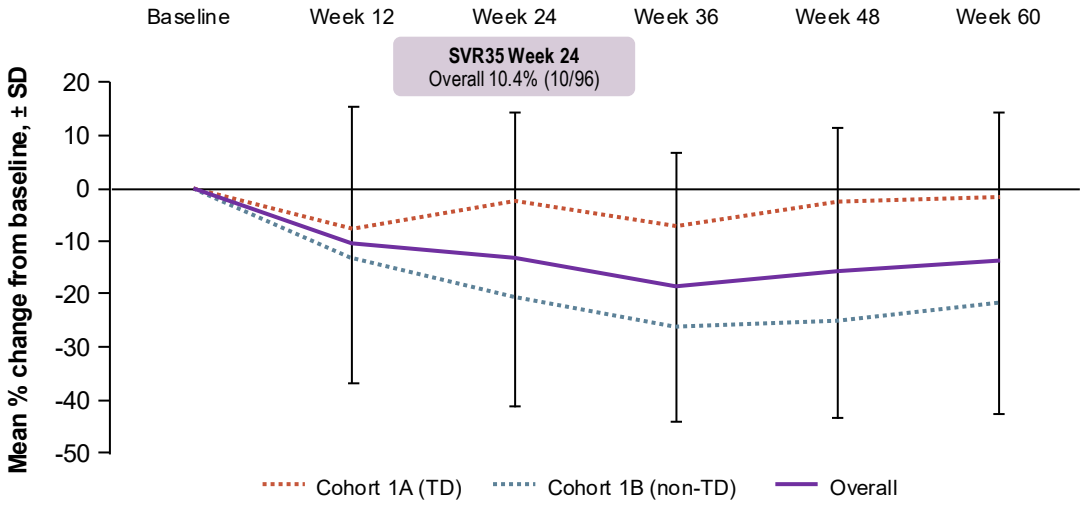
MANIFEST PHASE 2 TRIAL

MANIFEST Arm 1 evaluated the safety, tolerability and clinical activity of **pelabresib monotherapy** in 100 heavily pre-treated patients with MF who were JAKi relapsed/refractory, intolerant or ineligible[1]

MANIFEST Arm 2 evaluated the **addition of pelabresib to ongoing ruxolitinib (prior median treatment duration: 30.2 months)** in 87 patients whose disease was inadequately controlled by ruxolitinib alone[2]

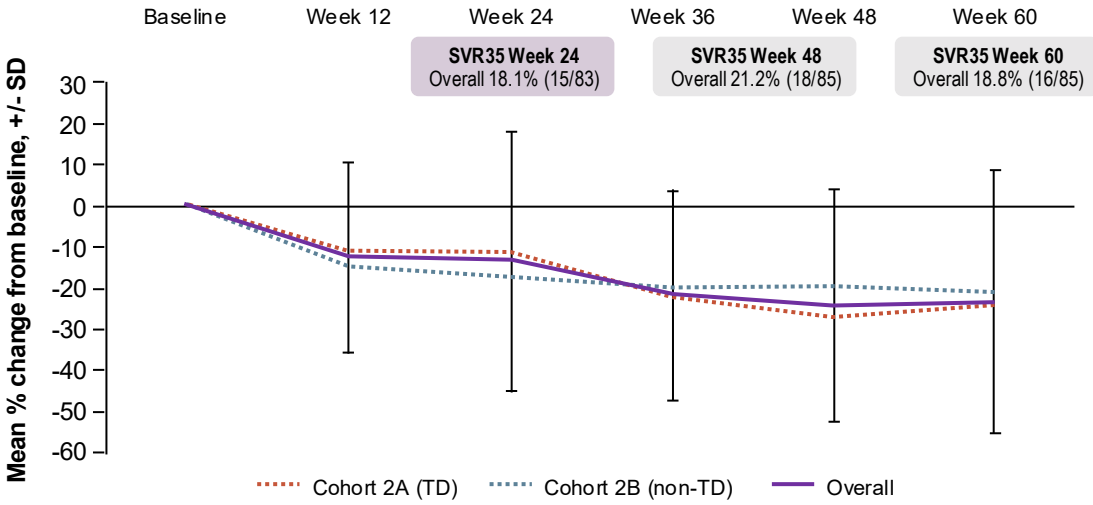
SVR35 at Week 24 and change in spleen volume over time

Arm 1: Pelabresib monotherapy led to deep and durable spleen responses in non-TD patients



SVR35 at Week 24, TD: 0% (n=0/44), and non-TD: 19.2% (n=10/52)

Arm 2: Pelabresib added to ruxolitinib led to deep and durable spleen responses



SVR35 at Week 24, TD: 16.4% (9/55), and non-TD: 21.4% (6/28)

Pelabresib, in both monotherapy and in addition to ruxolitinib, demonstrated meaningful clinical benefit through splenic response

JAKi, Janus kinase inhibitor; MF, myelofibrosis; SD, standard deviation; SVR35, spleen volume reduction of ≥35%; TD, transfusion dependent

1. Talpaz M, et al. Poster ID #PS1987; presented at EHA 2026; 2. Kremyanskaya M, et al. Poster ID #PF894; presented at EHA 2026

MANIFEST PHASE 2 TRIAL

MANIFEST Arm 1 (pelabresib monotherapy)[1]

Symptom burden
- TSS50 at Week 24: **TD, 15.6%; non-TD: 34.7%**

Anemia response and transfusion independence
- Among TD patients, **25.6%** converted from TD to TI

BMF
- BMF improvements by ≥1 grade in **33.3%** patients at Week 24 and **32.3%** patients at Week 48

Safety
- Most TEAEs were Grade ≤2
- Most common Grade ≥3 TEAEs: Thrombocytopenia (23%), anemia (24%), and pneumonia (8%)

MANIFEST Arm 2 (pelabresib + ruxolitinib)[2]

Symptom burden
- TSS50 at Week 24: **TD, 36.2%; non-TD: 40.7%**

Anemia response and transfusion independence
- Among TD patients, **26.1%** converted from TD to TI

BMF
- BMF improvements by ≥1 grade in **31.3%** patients at Week 24 and **37.1%** patients at Week 48

Safety
- Most TEAEs were Grade ≤2
- Most common Grade ≥3 TEAEs: Thrombocytopenia (39%), anemia (23%), and pneumonia (9%)

Improvements in anemia and bone marrow pathology in both monotherapy and in addition to ruxolitinib suggest that pelabresib may have disease-modifying activity

BMF, bone marrow fibrosis; JAKi, Janus kinase inhibitor; TD, transfusion dependent; TEAE, treatment-emergent adverse event; TI, transfusion independent; TSS50, ≥ 50% reduction in total symptom score

1. Talpaz M et al. Poster ID #PS1987, presented at EHA 2026; 2. Kremyanskaya M, et al. Poster ID #PF894, presented at EHA 2026

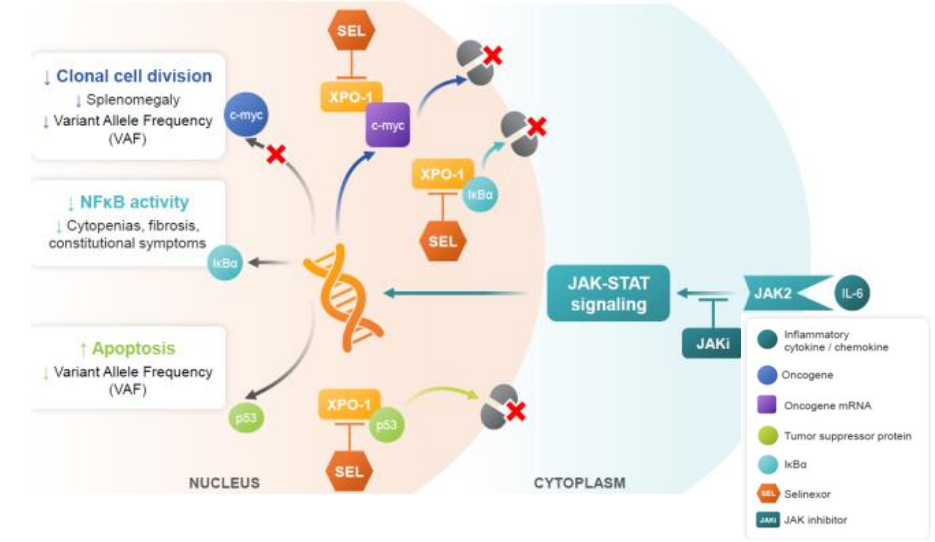
Selinexor

Selinexor plus ruxolitinib in Janus kinase inhibitor–naïve myelofibrosis: phase 3 SENTRY trial

Harrison C, et al. Abstract LB5002, EHA 2026

SENTRY PHASE 3 TRIAL: SELINEXOR MOA AND STUDY DESIGN

Dual targeting of JAK–STAT signalling and XPO1-mediated nuclear export enhances depth of response and may improve disease control



- In MF, JAK/STAT activation drives malignant clone proliferation, splenomegaly and disease-related symptoms; however, the importance of XPO1 activity for MPN cell survival is less known
- Dual targeting of JAK/STAT signalling and XPO1-mediated nuclear export may enhance the depth of treatment response and improve disease control

- SENTRY is an ongoing global, double-blind, placebo-controlled, phase 3 study
- Aim: To investigate the efficacy and safety of selinexor + ruxolitinib vs. ruxolitinib monotherapy in patients with intermediate-risk or higher, JAKi-naïve MF

Interim data at Week 24 are presented here, Data cut off: 20 February 2026

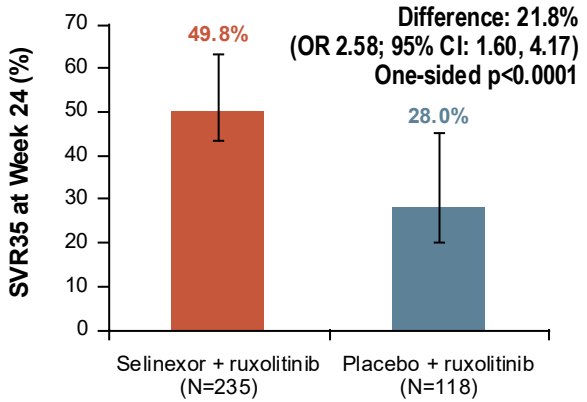
JAK, Janus kinase; MF, myelofibrosis; MOA, mechanism of action; MPN, myeloproliferative neoplasm; STAT, signal transducer and activator of transcription; XPO1, exportin-1

Mascarenhas D, et al. Presented at ASCO 2026; oral presentation; 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. Walker CJ, et al. Blood. 2013;122(17):3034-3044. 4. Cheng Y, et al. Mol Cancer Ther. 2014;13(3):675-686. 5. Argueta C, et al. Oncotarget. 2018;9(39):25529-25544.

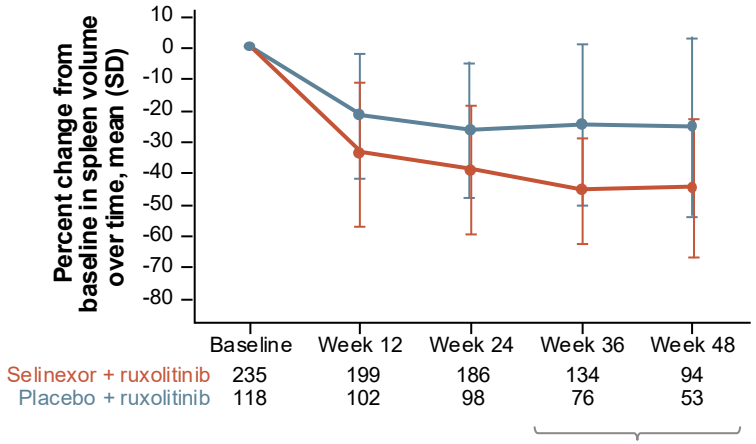
SENTRY PHASE 3 TRIAL: RESULTS (1/2)

Results

SVR35 at Week 24 (co-primary endpoint)

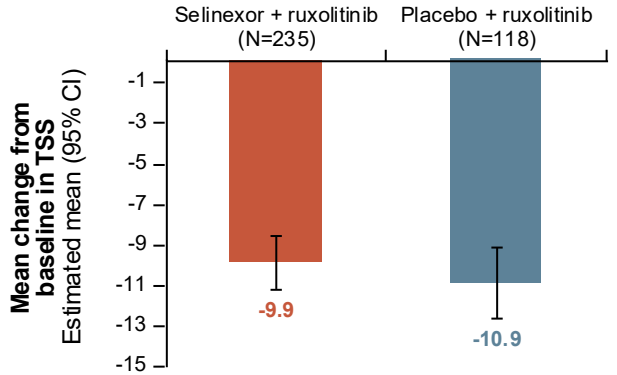


Change in spleen volume from baseline over time[a]



Not all patients have been followed beyond Week 24

Change in absolute TSS from baseline at Week 24 (co-primary endpoint)



A significantly higher proportion of **patients achieved rapid, deep and sustained SVR35 with selinexor + ruxolitinib** vs. ruxolitinib alone

Meaningful reductions in absolute TSS from baseline were seen in both treatment arms

Data cut off: 20 February 2026

[a] Not all patients had reached Week 36 and Week 48 timepoints

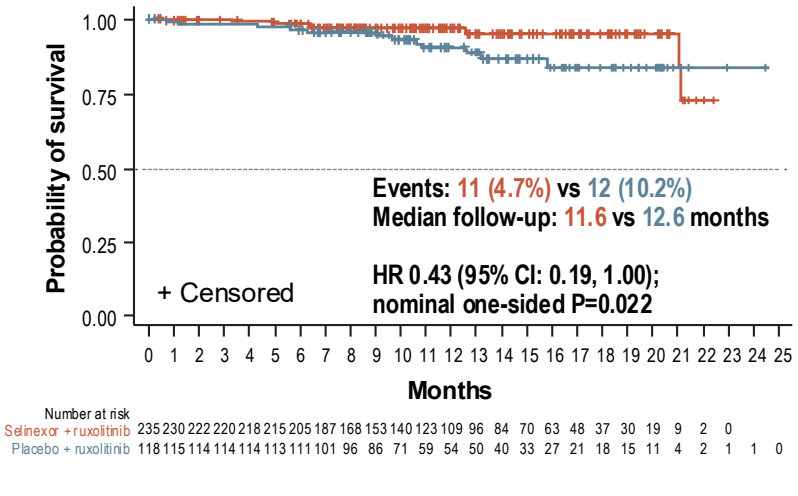
CI, confidence interval; JAKi, Janus kinase inhibitor; MF, myelofibrosis; OR, odds ratio; SD, standard deviation; SVR35, spleen volume reduction ≥35%; TSS, total symptom score

Harrison C, et al. Presented at EHA 2026; oral presentation

SENTRY PHASE 3 TRIAL: RESULTS (2/2)

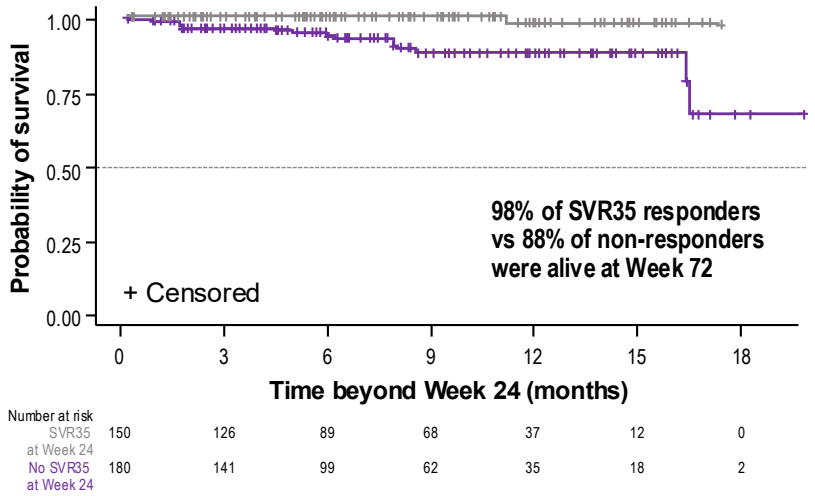
Results

OS



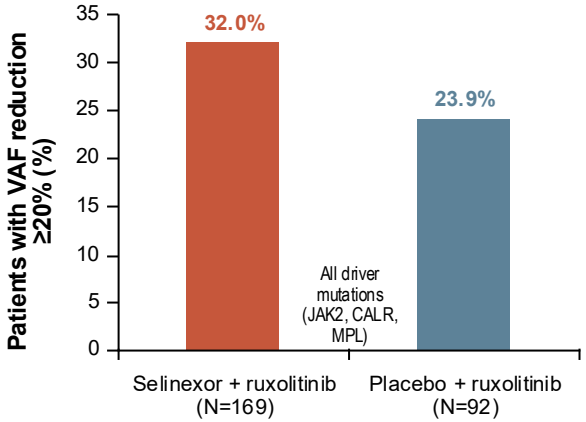
OS favoured selinexor + ruxolitinib vs. ruxolitinib alone; however, data are immature

OS: SVR35 responders vs. non-responders



SVR35 at Week 24 was predictive of OS, irrespective of treatment

VAF reduction ≥20% at Week 24



Higher rates of ≥20% VAF reduction were seen with selinexor + ruxolitinib vs. ruxolitinib alone

Data cut off: 20 February 2026.

CALR, calreticulin; CI, confidence interval; HR, hazard ratio; JAK2, Janus kinase 2; JAKi, Janus kinase inhibitor; MF, myelofibrosis; MPL, myeloproliferative leukemia virus oncogene; OS, overall survival; SVR35, spleen volume reduction of ≥35%; VAF, variant allele frequency

Harrison C, et al. Presented at EHA 2026; oral presentation

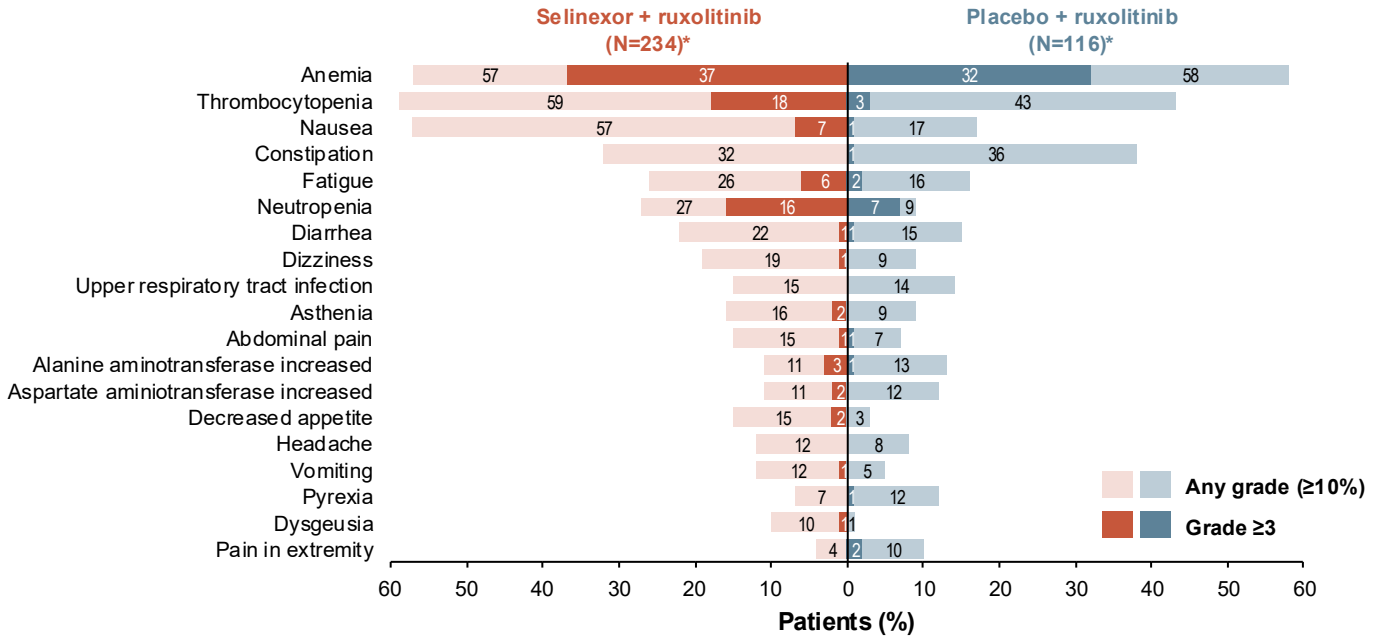
SENTRY PHASE 3 TRIAL: SAFETY

Results

- **AEs were manageable** and consistent with the known safety profiles of both agents

Overall safety profile

TEAEs, n (%)	Selinexor + ruxolitinib (N=234[a])	Ruxolitinib (N=116[a])
Any grade	232 (99.1)	113 (97.4)
Grade ≥3	164 (70.1)	58 (50.0)
Serious TEAEs	63 (26.9)	28 (24.1)
Leading to treatment discontinuation	34 (14.5)	10 (8.6)
Leading to death	2 (0.9)	3 (2.6)



- Transformation to **acute myeloid leukemia was rare** and rates were equivalent between arms (1.7%)

Findings from the SENTRY study suggest the potential of selinexor + ruxolitinib as a novel treatment approach for JAKi-naïve MF

Data cut off: 20 February 2026

[a] Analysis excluded three patients that did not receive treatment (selinexor + ruxolitinib, n=1; ruxolitinib, n=2)

AE, adverse event; JAKi, Janus kinase inhibitor; MF, myelofibrosis; TEAE, treatment-emergent adverse event

Harrison C, et al. Presented at EHA 2026; oral presentation

Luspatercept

Efficacy and safety of luspatercept in patients with myelofibrosis on Janus kinase inhibitors who require red blood cell transfusions: primary analysis of the phase 3 INDEPENDENCE trial

Passamonti F, et al. Abstract S215, EHA 2026

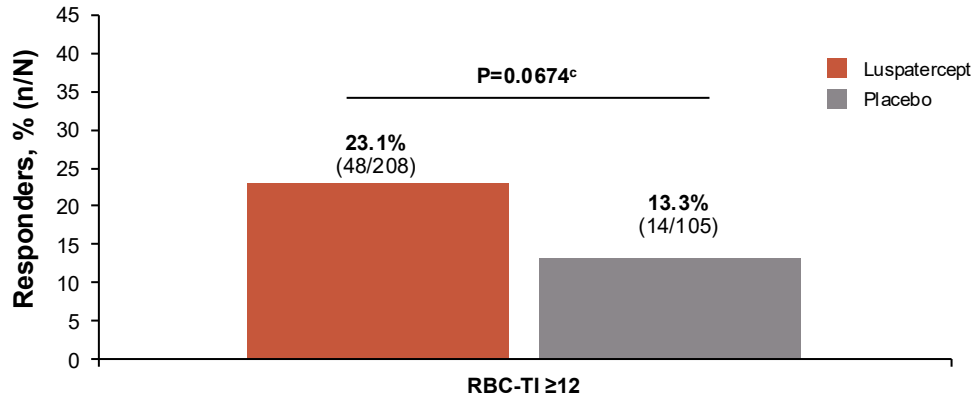
INDEPENDENCE PHASE 3 TRIAL

- Luspatercept vs placebo in a phase 3, double-blind, randomised patients on concurrent JAKi (N=313)
- Primary endpoint: RBC-TI for ≥12 consecutive weeks starting within the first 24 weeks

Results

RBC-TI ≥12[a] (primary endpoint; ITT population[b])

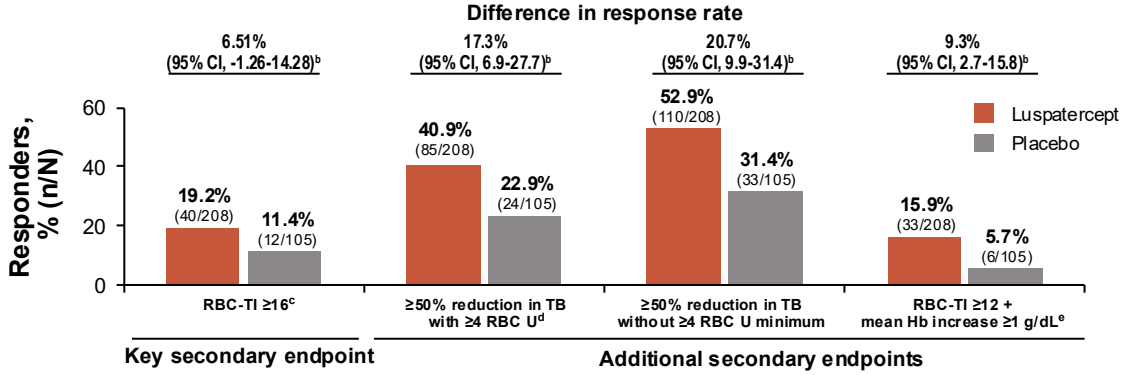
Approximately 1 in 4 patients with advanced MF treated with luspatercept in combination with JAKi therapy achieved RBC-TI ≥12



[a] Any consecutive 12-week or longer period of transfusion independence starting between the first dose and no later than the end of Week 24; [b] Defined as all randomised patients, regardless of whether the patient received the study treatment; [c] CMH method of weighting using stratification factors per CRF and Sato for variance estimate. p value from CMH method: the prespecified significance threshold for the final analysis was p<0.044 to account for alpha spending during the interim analysis

Secondary efficacy endpoints (ITT population[a])

Luspatercept demonstrated consistent clinical benefit vs placebo across all prespecified secondary efficacy endpoints



[a] Defined as all randomised patients, regardless of whether the patient received the study treatment; [b] CMH method of weighting using stratification factors per CRF and Sato for variance estimate; [c] Any consecutive 16-week or longer period of transfusion independence starting between the first dose and no later than the end of Week 24; [d] Defined as the proportion of patients who reduced their TB by ≥50% (and by ≥4 U) from baseline over any consecutive 12-week period or longer, starting within the first 24 weeks; [e] Defined as the proportion of patients achieving a mean Hb increase ≥1 g/dL from baseline over any consecutive 12-week period or longer in absence of RBC transfusions, starting within the first 24 weeks

- The luspatercept safety profile was manageable and consistent with that expected in advanced MF
- Results support luspatercept as a clinically meaningful treatment for MF-associated anemia, a setting where effective therapies remain a critical unmet need

Data cutoff date: May 26, 2025. Median (range) follow-up was 13.6 (0.4-48.9) months for luspatercept and 13.8 (0.3-45.4) months for placebo

CI, confidence interval; CMH, Cochran-Mantel-Haenszel; CRF, cast report form; Hb, hemoglobin; ITT, intent to treat; JAKi, Januskinase inhibitor; MF, myelofibrosis; RBC, red blood cell; TB, transfusion burden; TI, transfusion independence; U, units

Passamonti FC, et al. Presented at EHA 2026; oral presentation

Momelotinib

Characterisation of symptoms after immediate transition from ruxolitinib to momelotinib in patients with myelofibrosis: post hoc analyses of the phase 3 SIMPLIFY-1 and SIMPLIFY-2 trials

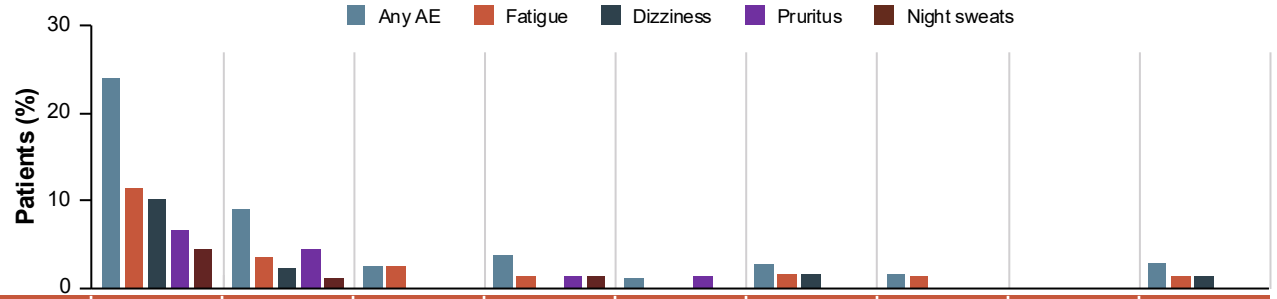
Vachhani P, et al. Abstract PS2001, EHA 2026

SIMPLIFY-1 AND SIMPLIFY-2 PHASE 2 TRIALS: POST HOC ANALYSES

- Discontinuation of ruxolitinib in MF patients carries a risk of ruxolitinib discontinuation syndrome (RDS)
- This post hoc analysis of the SIMPLIFY trials addressed gaps in safety knowledge regarding RDS during a direct switch from ruxolitinib to momelotinib

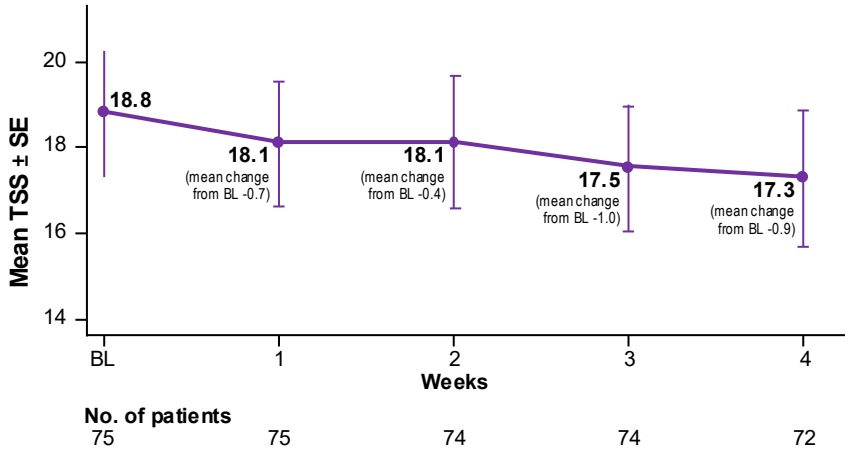
Results

Incidence over time of AEs resembling MF symptoms post crossover in SIMPLIFY-1



Weeks	1-2 (n=88)	3-4 (n=88)	5-6 (n=84)	7-8 (n=79)	9-10 (n=76)	11-12 (n=73)	13-14 (n=72)	15-16 (n=72)	17-18 (n=71)
Overall, n (%)	21 (23.9)	8 (9.1)	2 (2.4)	3 (3.8)	1 (1.3)	2 (2.7)	1 (1.4)	0	2 (2.8)
Fatigue	10 (11.4)	3 (3.4)	2 (2.4)	1 (1.3)	0	1 (1.4)	1 (1.4)	0	1 (1.4)
Dizziness	9 (10.2)	2 (2.3)	0	0	0	1 (1.4)	0	0	1 (1.4)
Pruritus	6 (6.8)	4 (4.5)	0	1 (1.3)	1 (1.3)	0	0	0	0
Night sweats	4 (4.5)	1 (1.1)	0	1 (1.3)	0	0	0	0	0

Mean TSS (± SE) during weeks 1-4 in patients receiving ≥12 weeks of ruxolitinib prior to momelotinib in SIMPLIFY-2



- Immediate transition from ruxolitinib to momelotinib appears to be well tolerated, with no evidence of severe or acute symptom relapses, and infrequent, low-grade and transient symptoms reported primarily in the first few weeks post crossover
- Safety findings from SIMPLIFY-1 aligned with individual symptom data in SIMPLIFY-2, showing early symptom improvement or stabilisation post crossover with minimal worsening

AE, adverse event; BL, baseline; MF, myelofibrosis; SE, standard error; TSS, total symptom score

Vachhani P, et al. Abstract PS2001, EHA 2026; poster

INCA033989

Mutant calreticulin–specific monoclonal antibody, INCA033989, is well tolerated and achieves robust spleen, anemia, and molecular responses in patients with myelofibrosis

Harrison C, et al. Abstract S216, EHA 2026

INCA033989 PHASE 1 TRIAL (1/2)

- Mutations in exon 9 of the calreticulin gene (mut*CALR*) occur in ~25–35% of MF patients
- Novel MoA: Mutant calreticulin-specific IgG1 monoclonal antibody
- Aim: Evaluate safety and efficacy of INCA033989 as monotherapy or in combination with ruxolitinib
  - MF monotherapy: patients intolerant to, relapsed/refractory after ≥12 weeks, or ineligible for JAKi
  - MF combination: patients with suboptimal ruxolitinib response after ≥12 weeks

Summary of Treatment-Emergent Adverse Events (TEAEs)

n (%)	Monotherapy N=83	Combination N=21
Any TEAE	76 (91.6)	21 (100.0)
Treatment related	48 (57.8)	14 (66.7)
Grade ≥3	22 (26.5)	14 (66.7)
Serious	7 (8.4)	6 (28.6)
Fatal	0	0
Discontinuation due to TEAEs	2 (2.4)	3 (14.3)
Dose reduction due to TEAEs	2 (2.4)	2 (9.5)
Infusion interruption due to TEAEs	5 (6.0)	1 (4.8)
Dose delay due to TEAEs	17 (20.5)	9 (42.9)

- No dose relationship with TEAEs was observed
- Most frequent grade ≥3 TEAEs were cytopenias, usually occurring in patients with pre-existing cytopenias

Demographics and Disease Characteristics

Variable	Monotherapy (N=83)		Combination (N=21)
	Monotherapy JAKi R/R/I (N=62)	Monotherapy JAKi Ineligible (N=21)	
CALR exon 9 mutation type, n (%)			
Type 1	37 (59.7)	11 (52.4)	13 (61.9)
Non-Type 1	25 (40.3)	10 (47.6)	8 (38.1)
Median duration of INCA033989 exposure (range), days	233 (1, 889)	345 (17, 815)	335.0 (137, 593)
Median baseline ruxolitinib daily dose (range), mg	N/A	N/A	40 (10, 50)
Median *CALR* VAF (range)	37 (30, 73)	36 (24, 53)	39 (30, 85)

CALR, calreticulin; IgG, immunoglobulin; JAKi, Janus kinase inhibitor; MF, myelofibrosis; MoA: Mechanism of Action; N/A, not applicable; R/R/I, relapses/refractory/intolerant; VAF, variant allele frequency

Harrison C, et al. Abstract S216, EHA 2026; oral presentation

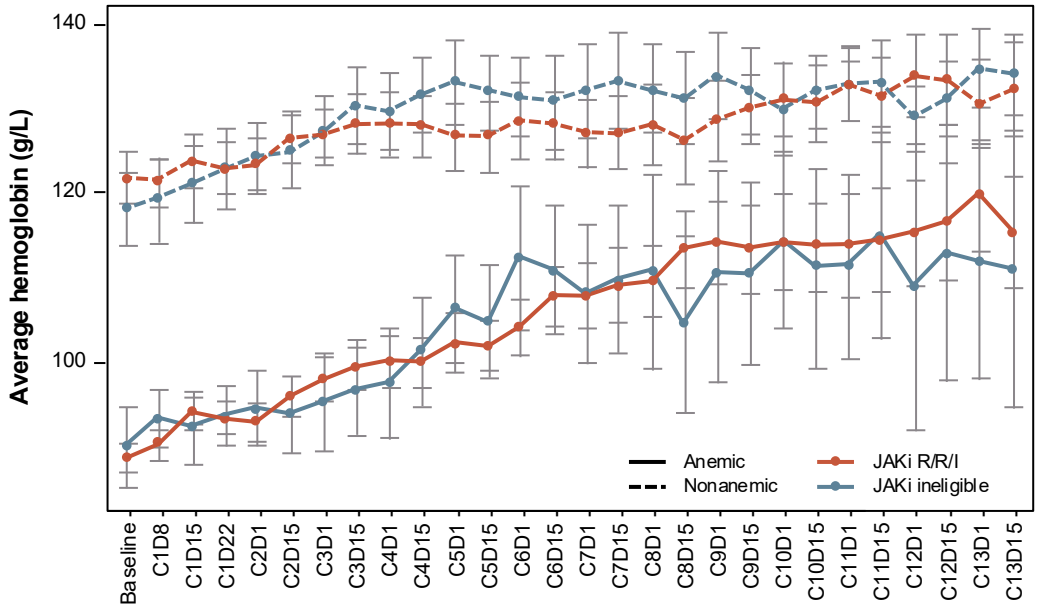
INCA033989 PHASE 1 TRIAL (2/2)

Summary of Efficacy Endpoints

Endpoint	Response Rate
SVR25	55% (38/69)
SVR35 (Best SVR)	39% (27/69)
TSS Reduction (≥50%)	53% (37/70)
mut*CALR* PBMCs Reduction (≥25%)	81% (21/26) – (62% (13/21) Type 1; 38% (8/21) non-Type 1)
Whole Blood mut*CALR* VAF Reduction	89% – (35/39 Type 1; 23/26 non-Type 1)
MR25 (Best Molecular Response)	12%

- Overall, 84% of patients remain on INCA033989 monotherapy and 76% of patients remain on INCA033989 + ruxolitinib

Mean hemoglobin by anemic status (monotherapy; n=83)



Anemia response:

- 60% (24/40) of evaluable anemic patients
- 63% (31/49) JAKi R/R/I and 55% (11/20) JAKi ineligible patients
- 35% (6/17) of evaluable anemic patients in combination with ruxolitinib

C, Cycle, D, Day; JAKi, Janus kinase inhibitor; MR25, molecular response of 25% reduction mut*CALR* VAF; mut*CALR*, mutations of calreticulin; PBMC, peripheral blood mononuclear cell; R/R/I, relapses/refractory/intolerant; SVR25/35, spleen volume reduction of ≥25%/35%; TSS, total symptom score; VAF, variant allele frequency

Harrison C, et al. Abstract S216, EHA 2026; poster

AJ1-11095

Results of AJX-101, a phase 1 clinical trial of the type II JAK2 inhibitor AJ1-11095, in patients with myelofibrosis who have been failed by a type I JAK2 inhibitor

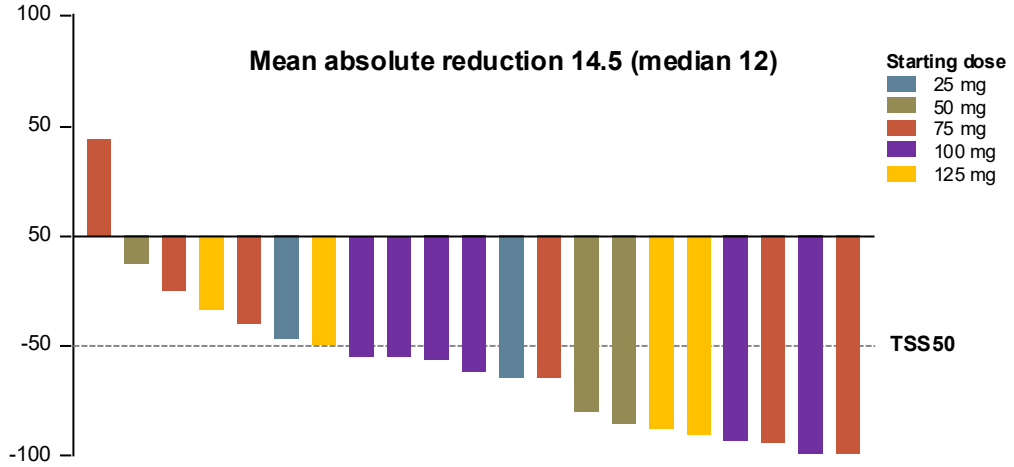
Mascarenhas J, et al. Abstract S218, EHA 2026

AJX-101 PHASE 1 TRIAL

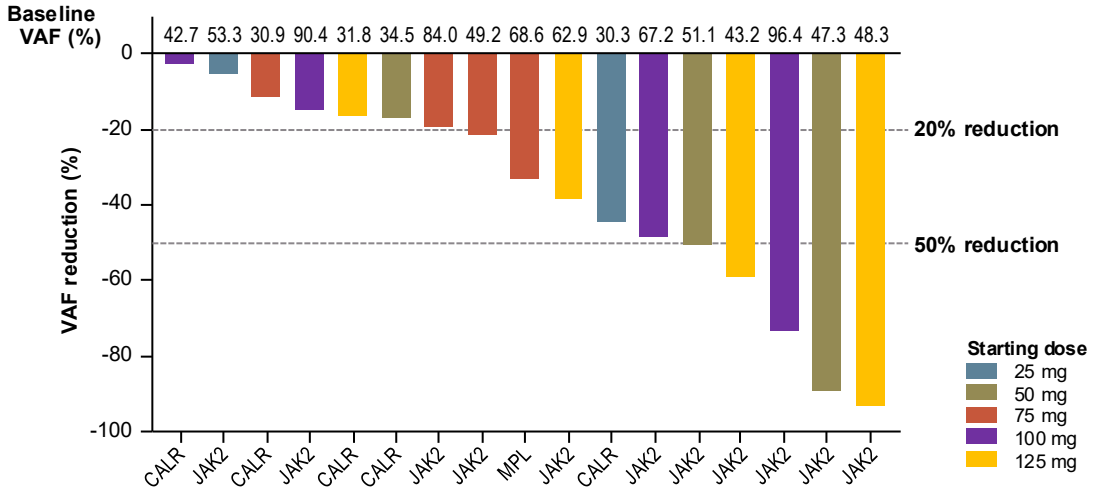
- Phase 1 clinical trial of the first-in-class Type II JAK2 inhibitor AJ1-11095
- Patients with myelofibrosis (N=23) who have been failed by a Type I JAK2 inhibitor
- Primary endpoints of safety & tolerability, with secondary endpoints of PK, SVR and TSS

Results

MFSAF v4.0 Total Symptom Score Change (Week 24)



Best relative VAF reduction to date for patients for whom Cycle 7 (week 24) data are available



- High rates of TSS50 observed with AJ1-11095 therapy, with improvements observed in all 7 domains of MFSAF v4.0
- Most patients (21/23; 91%)) showed VAF reduction, with week-24 data (n=17) demonstrating ≥20% and ≥50% relative reductions in 59% and 35% of patients, respectively
- Most common AE was on-target anemia, which has been manageable with dose adjustment

AE, adverse event; CALR, calreticulin; JAK2, Janus kinase 2; MFSAF, Myelofibrosis Symptom Assessment Form; MPL, myeloproliferative leukemia virus oncogene; PK, pharmacokinetics; SVR, spleen volume reduction; TSS(50), (≥50% reduction in) total symptom score; VAF, variant allele frequency

Mascarenhas J, et al. Abstract S218, EHA 2026

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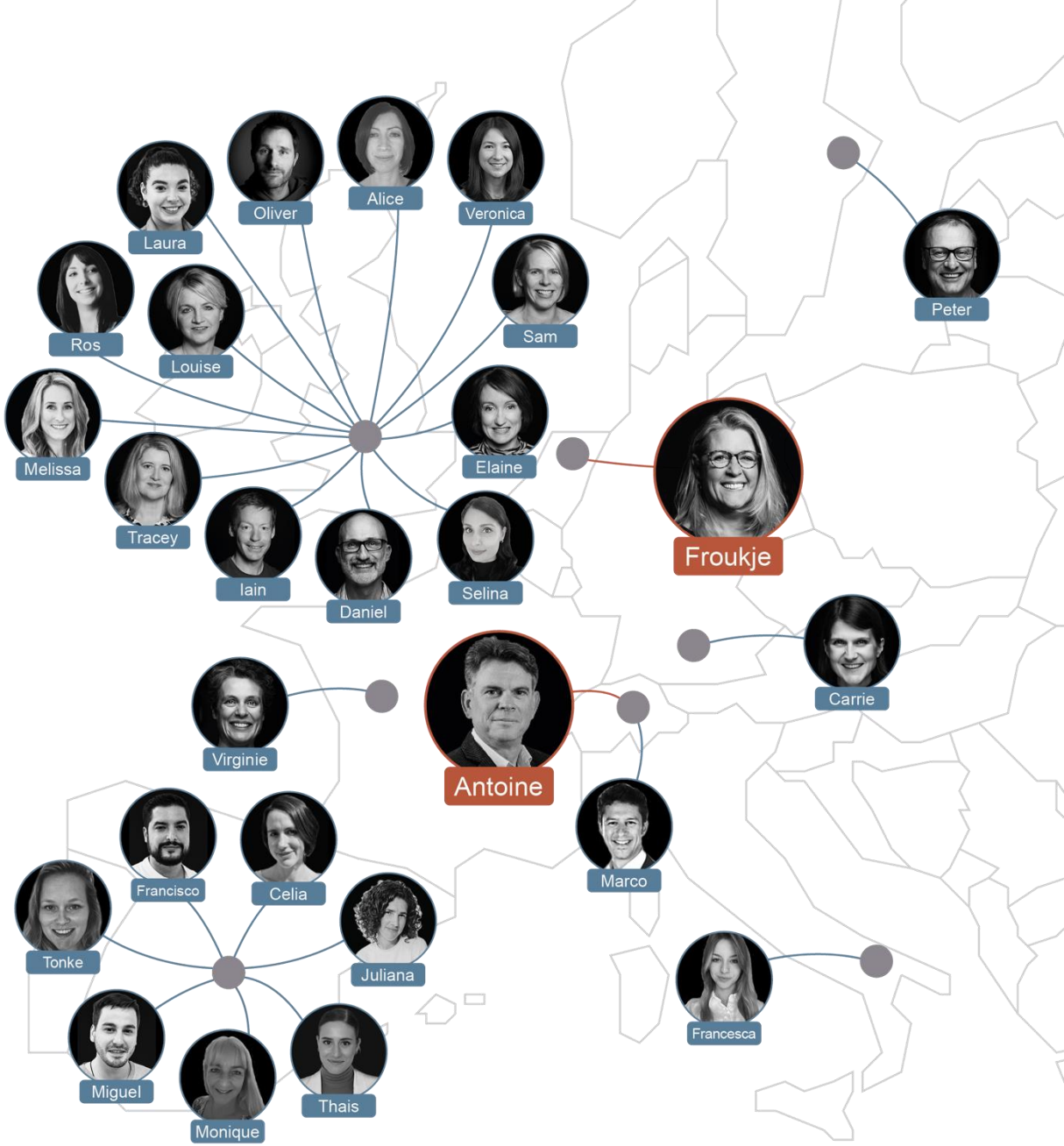

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