Poster# MPN-752

Selinexor Plus Ruxolitinib in JAK Inhibitor–naïve Myelofibrosis: Phase 3 SENTRY Trial

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Introduction

- Myelofibrosis (MF) is a hematologic malignancy characterized by aberrant proliferation of myeloid progenitor cells, resulting in progressive bone marrow fibrosis, splenomegaly, and substantial symptom burden[1,2]
- Despite therapeutic advances, MF remains associated with substantial morbidity and reduced survival[1,3]
- Ruxolitinib, the current standard of care, reduces splenomegaly and improves symptoms; however, responses may be suboptimal or not durable,[4-7] highlighting the need for therapies that extend beyond JAK-STAT pathway inhibition and improve long-term outcomes
- Selinexor is an oral, selective inhibitor of XPO1 under investigation for the treatment of MF[8]
- XPO1 inhibition promotes nuclear retention and activation of tumor suppressor proteins, modulates multiple oncogenic pathways, and induces apoptosis of malignant cells[9-13]

Methods

- This global, double-blind, randomized, active-controlled, Phase 3 study evaluated the efficacy and safety of selinexor + ruxolitinib compared with ruxolitinib alone in patients with JAKi–naïve MF[14]

Study Design

Study population

JAKi-naïve patients with MF
(Primary or post-ET/PV)
- Spleen volume ≥ 450 cm³
- DIPSS Int-1 or Int-2/High risk
- Symptomatic (MFSAF v4.0): average symptom score ≥ 5 or TSS ≥ 12
- Platelet count ≥ 100 × 10⁹/L

R 2:1

Double-blind treatment

Selinexor 60 mg PO QW (28-day cycle) + ruxolitinib* BID

Dual anti-emetics for nausea prophylaxis required for first 2 cycles

Placebo + ruxolitinib* BID

Co-primary endpoints

SVR35 at Week 24†,‡
+
Absolute change in **TSS** from baseline at Week 24†,§

Stratification
- DIPSS risk: Int-1 vs Int-2 or high risk
- Spleen volume: < 1800 cm³ vs ≥ 1800 cm³ by MRI/CT scan
- Baseline platelet counts: 100–200 × 10⁹/L vs > 200 × 10⁹/L

Select secondary endpoints
- **OS**
- **Safety**

Statistical analysis plan
- Sequential testing of co-primary endpoints (1-sided α = 0.025)
  - Stratified CMH for SVR35
  - MMRM for TSS

*Ruxolitinib dose based on platelet count per prescribing information; †Both endpoints are powered at > 80%; ‡SVR35 was analyzed using a stratified CMH test according to randomization stratification factors. ORs with 95% CIs and 1-sided P-value are reported; §TSS measured by the MFSAF v4.0 (excluding fatigue) analyzed using a MMRM that included treatment group, visit, baseline score, and stratification factors. Longitudinal least-squares adjusted means with 95% CIs and 1-sided P-value are reported.
SENTRY: XPORT-MF-034 (NCT04562389)

Results

- Data cutoff: February 20, 2026
- The study opened for enrollment in June 2023; the first patient was randomized on December 29, 2023, and the last patient was enrolled on September 9, 2025

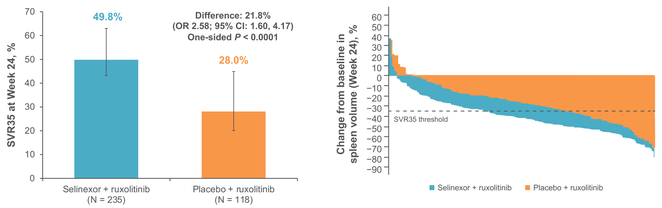
Demographics and Baseline Disease Characteristics

Characteristic	Selinexor + ruxolitinib (N = 235)	Placebo + ruxolitinib (N = 118)
Age, years		
Median (range)	66 (20–86)	67 (33–87)
Sex, n (%)		
Male	142 (60.4)	61 (51.7)
MF subtype, n (%)		
Primary MF	119 (50.6)	60 (50.8)
Post-PV MF	56 (23.8)	26 (22.0)
Post-ET MF	59 (25.1)	32 (27.1)
DIPSS, n (%)*		
Intermediate-1	134 (57.0)	64 (54.2)
Intermediate-2	83 (35.3)	41 (34.7)
High risk	18 (7.7)	13 (11.0)
Time since MF diagnosis, months		
Median (range)	3.1 (0.3–316.9)	4.4 (0.3–270.2)
Hemoglobin level, g/dL		
Median (range)	11.4 (6.4–18.3)	11.4 (6.7–17.2)
Platelet count, 10⁹/L		
Median (range)	325 (67–1313)	324 (101–2001)
Peripheral blasts, %		
Median (range)	0.0 (0.0–9.0)	0.0 (0.0–15.0)
Red blood cell transfusion, n (%)		
Dependent at baseline	14 (6.0)	8 (6.8)

Characteristic	Selinexor + ruxolitinib (N = 235)	Placebo + ruxolitinib (N = 118)
Molecular profile, n (%)		
JAK2	155 (66.0)	81 (68.6)
CALR	57 (24.3)	21 (17.8)
MPL	13 (5.5)	8 (6.8)
High–molecular risk mutations†	75 (31.9)	45 (38.1)
Other‡	10 (4.3)	8 (6.8)
Bone marrow fibrosis Grade, n (%)§		
Grade 0	5 (2.1)	3 (2.5)
Grade 1	31 (13.2)	11 (9.3)
Grade 2	111 (47.2)	54 (45.8)
Grade 3	76 (32.3)	43 (36.4)
Missing	12 (5.1)	7 (5.9)
ECOG performance status, n (%)‖		
0	101 (43.0)	52 (44.1)
1	124 (52.8)	61 (51.7)
2	10 (4.3)	5 (4.2)
Spleen volume, cm³		
Median (range)	1385 (450–9210)	1448 (464–7929)
Mean ± SD	1636 ± 1020	1651 ± 1038
TSS (excluding fatigue)		
Median (range)	21.7 (2.1–53.9)	19.6 (3.0–58.3)
Mean ± SD	22.7 ± 11.9	22.2 ± 13.0

*DIPSS comprises four risk categories: low, intermediate-1, intermediate-2, and high risk; †High molecular risk genes include *ASXL1, EZH2, IDH1, IDH2, SRSF2, U2AF1*; ‡Other included multiple driver mutations, triple negative, and missing; §Bone marrow was centrally evaluated; ‖ECOG performance status scores range from 0 to 5, with higher scores indicating greater disability.

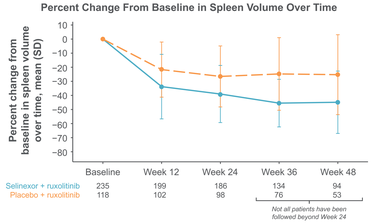
Significantly Higher SVR35 at Week 24 With Selinexor + Ruxolitinib vs Ruxolitinib Alone



*CMH test stratified by randomization factors.
Placebo arm scaled 2:1 to compensate for randomization ratio.

Rapid, Deep, and Sustained Spleen Volume Reduction With Selinexor + Ruxolitinib vs Ruxolitinib Alone

Percent Change From Baseline in Spleen Volume Over Time



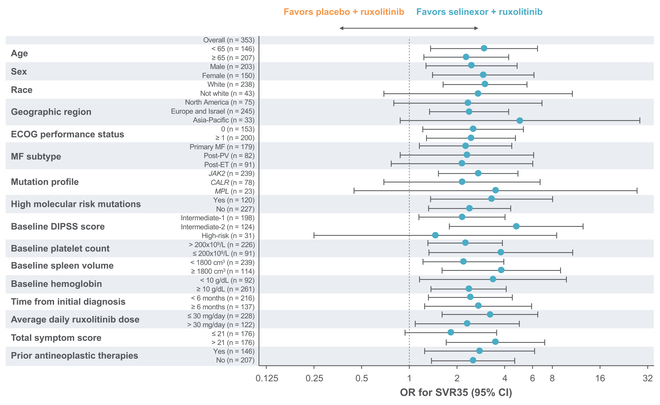
SVR35 Rates Over Time

SVR35*	Selinexor + ruxolitinib (N = 235)	Placebo + ruxolitinib (N = 118)
Week 12, n (%)	116 (49.4)	24 (20.3)
Week 24, n (%)	117 (49.8)	33 (28.0)
Week 36, n/n‡1 (%)	97/207 (46.9)	23/100 (23.0)
At any time, n (%)	159 (67.7)	53 (44.9)
	OR 2.59 (95% CI: 1.64, 4.10) Nominal P < 0.0001	

*SVR35 at any time defined as proportion of patients with SVR35 to any post-baseline assessment regardless of visit window before any new anti-MF therapy or disease progression; ‡n1 = number of patients who completed spleen assessment or discontinued the study prior to the specific timepoint.

- Mean AbsTSS change at week 24 was −9.9 vs −10.9 for selinexor + ruxolitinib vs ruxolitinib; adjusted mean difference 0.97 (95% CI: −1.07, 3.02; *P* = 0.825)

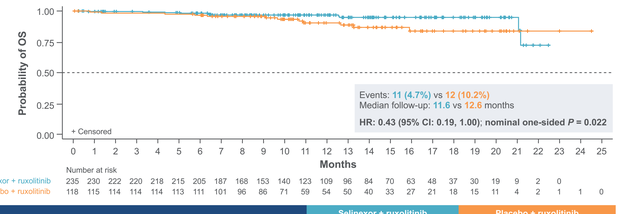
Consistent SVR35 Benefit Observed Across Prespecified Subgroups



Selinexor Maintained Spleen Responses Despite Reduced Ruxolitinib Dosing

Selinexor + Ruxolitinib Improved SVR35 Compared With Ruxolitinib Alone Regardless of Baseline Spleen Volume

Meaningful OS With Selinexor + Ruxolitinib vs Ruxolitinib Alone



Deaths	Selinexor + ruxolitinib (N = 235)	Placebo + ruxolitinib (N = 118)
Primary cause of death, n (%)		
Disease progression	3 (1.3)	3 (2.5)
AE	3 (1.3)	5 (4.2)
Other/Unknown	5 (2.1)	4 (3.4)

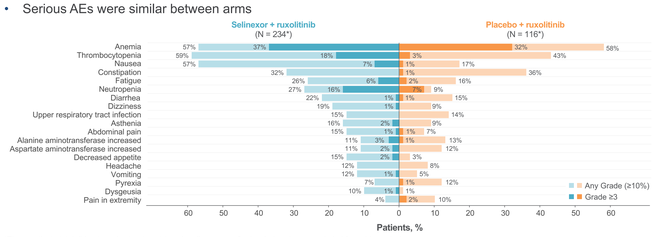
OS defined as the duration from date of randomization to date of death due to any cause. Follow-up time based on reverse Kaplan-Meier method by swapping the censoring status. OS analysis stratified by the randomization stratification factors. HR based on Cox Proportional Hazards model with Efron's method of handling ties.

Achievement of SVR35, Regardless of Timing, Predicted Subsequent Survival

Hazard ratio, 95% CI, and *P*-value are from Cox Proportional Hazards model with time-dependent SVR35 response covariate using the ITT principles. Patients were included in the with/without SVR35 response groups based on when they achieved SVR35.

Overall Safety Summary

- TEAEs occurred in 99.1% vs 97.4% for selinexor + ruxolitinib vs ruxolitinib (grade ≥3: 70.1% vs 50.0%)
  - Discontinuation rates were 14.5% vs 8.6%
- TEAEs leading to death occurred in 0.9% vs 2.6%
- Confirmed leukemic transformation was 1.7% in both arms
- Safety profile was manageable and consistent with known profiles of both agents
- Serious AEs were similar between arms



*Three patients total did not receive treatment (n = 1, selinexor; n = 2, placebo) and were excluded from this analysis.

Conclusions

- Selinexor + ruxolitinib achieved rapid, deep, and sustained spleen volume reduction vs ruxolitinib alone, with consistent benefit across subgroups
- Meaningful OS was observed, with spleen volume reduction associated with improved OS
- Safety profile was manageable and consistent with known profile of both agents
- Selinexor + ruxolitinib represents a novel treatment approach in JAKi–naïve MF

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Abbreviations: AbsTSS, absolute mean change in total symptom score; AE, adverse event; BID, twice daily; CALR, calreticulin; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; CT, computed tomography; DIPSS, Dynamic International Prognostic Scoring System; ECOG, Eastern Cooperative Oncology Group; ET; essential thrombocythemia; HR, hazard ratio; Int, intermediate; ITT, intention-to-treat; JAK, Janus kinase; JAK2, Janus kinase 2; JAKi, JAK inhibitor; MF, myelofibrosis; MFSAF, Myelofibrosis Symptom Assessment Form; MMRM, mixed-effects model for repeated measures; MPL, myeloproliferative leukemia protein; MRI, magnetic resonance imaging; OR, odds ratio; OS, overall survival; PO, orally; PV, polycythemia vera; QW, once weekly; R, randomization; SD, standard deviation; STAT, signal transducer and activator of transcription; SVR35, spleen volume reduction of at least 35%; TEAE, treatment-emergent adverse event; TSS, total symptom score; XPO1, exportin 1.

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