SENTRY (XPORT-MF-034): A Global, Multicenter, Double-blind, Phase 1/3 Study of Selinexor in Combination with Ruxolitinib in JAKi Treatment-naïve Patients with Myelofibrosis (NCT04562389)

BACKGROUND

- Myelofibrosis (MF) is a heterogenous, progressive, and fatal disease.[1] Underlying biological hallmarks include aberrant blood and bone marrow differentiation, cytokine production and inflammation, bone marrow fibrosis, and extramedullary hematopoiesis.[1,2]
- An urgent need persists for therapies, beyond Janus kinase inhibitors (JAKi), with rapid, effective, and durable responses that address underlying drivers of MF, due to limited responses as well as the lack of evidence of disease modification, treatments for patients with cytopenic MF, and improved outcomes.[2,3]
- Selinexor, an oral exportin 1 (XPO1) inhibitor with pro-apoptotic and anti-inflammatory properties that may impact both Janus kinase (JAK) and non-JAK pathways, is undergoing investigation for treatment of MF.[4,5]

STUDY DESIGN

- Based on the Phase 1 results, the combination of selinexor and ruxolitinib is being evaluated in a double-blind, randomized, placebo-controlled Phase 3 study.[6,7]
- 306 JAKi-naïve patients with MF are expected to be enrolled in a 2:1 ratio to receive selinexor + ruxolitinib or placebo + ruxolitinib.[6,7]

SELECT STUDY OBJECTIVES

- To evaluate the efficacy (SVR35 and TSS50 at Week 24) of selinexor + ruxolitinib vs placebo + ruxolitinib in JAKi-naïve patients with MF[6,7]
- To evaluate anemia response in JAKi-naïve patients with MF receiving selinexor + ruxolitinib compared to placebo + ruxolitinib[6,7]
- To evaluate safety of selinexor + ruxolitinib compared to placebo + ruxolitinib in patients with MF[5,6]

CONTACT

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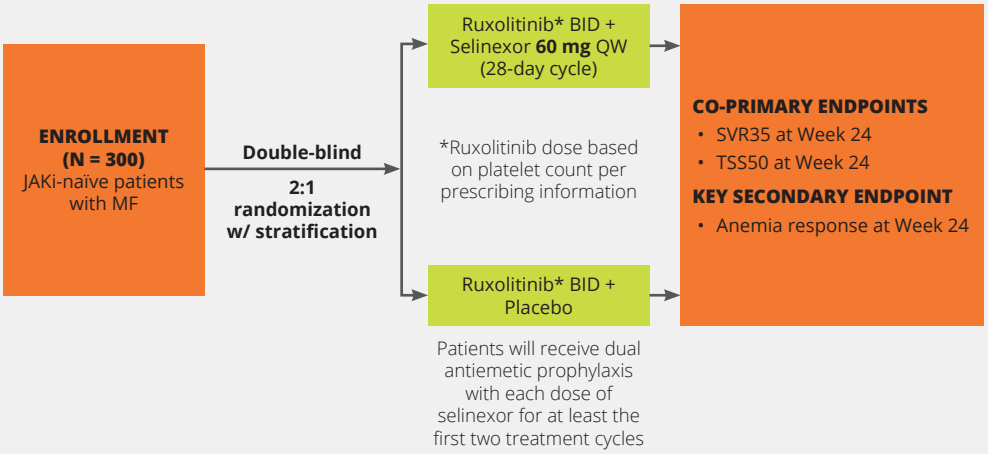
Scan here for more information on ClinicalTrials.gov

PHASE 3 TRIAL DESIGN

Study Status: Actively Recruiting



Randomization stratified by:

- Dynamic International Prognostic Scoring System (DIPSS) risk category intermediate -1 vs. intermediate -2 or high-risk
- Spleen volume < 1800 cm^3 vs. ≥ 1800 cm^3 by MRI/CT scan
- Baseline platelet counts 100–200 × 10^9/L vs. > 200 × 10^9/L

SELECT INCLUSION CRITERIA[6,7]

- ≥ 18 years of age
- A diagnosis of primary MF or post-ET or post-(PV) MF
- Measurable splenomegaly as demonstrated by spleen volume of ≥ 450 cm^3 by MRI or CT scan
- DIPSS risk category of intermediate-1, or intermediate-2, or high-risk
- Active symptoms of MF as determined by presence of at least 2 symptoms with a score ≥ 3 or total score of ≥ 10 at screening using the MFSAF v4.0
- Participant currently not eligible for stem cell transplantation
- ECOG PS ≤ 2
- Platelet count ≥ 100 × 10^9/L
- CrCl > 15 mL/min

SELECT EXCLUSION CRITERIA[6,7]

- More than 10% blasts in peripheral blood or bone marrow (accelerated or blast phase)
- Previous treatment with JAKi for MF
- Previous treatment with selinexor or other XPO1 inhibitors
- Impairment of GI function or GI disease that could significantly alter the absorption of selinexor

BID, twice a day; CrCl, creatinine clearance; CT, computer topography; DIPSS, Dynamic International Prognostic Scoring System; ECOG PS, Eastern Cooperative Oncology Group Performance Status; GI, gastrointestinal; JAK, Janus kinase; JAKi, Janus kinase inhibitor; MF, myelofibrosis; MFSAF, Myelofibrosis Symptom Assessment Form; MRI, magnetic resonance imaging; PV, polycythemia vera; QW, once a week; SVR35, spleen volume reduction ≥ 35%; TSS50, Proportion of patients with total symptom score reduction of ≥ 50%; XPO1, exportin-1.

1. Tefferi A. *Am J Hematol*. 2023;98(5):801–21. **2.** O'Sullivan JM, Harrison CN. *Clin Adv Hematol Oncol*. 2018;16(2):121–31. **3.** Levavi H, et al. *Clin Adv Hematol Oncol*. 2022;20(7):456–67. **4.** Kashyap T, et al. *Oncotarget*. 2016;7(48):78883–95. **5.** Maloof M, et al. Poster presented at: the 15th International Congress for Myeloproliferative Neoplasms (MPN); November 2–3, 2023; Brooklyn, NY. **6.** Karyopharm Therapeutics Inc. Clinical Study Protocol Version 4.0. XPORT-MF-034. **7.** ClinicalTrials.gov. NCT04562389. https://clinicaltrials.gov/ct2/show/NCT04562389. Accessed April 9, 2024.