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POSTER ABSTRACTS

634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

A Global, Phase 3, Randomized, Double-Blind Study to Evaluate Safety and Efficacy of Selinexor, an XPO-1 Inhibitor, in Combination with Ruxolitinib in JAK Inhibitor-Naïve Myelofibrosis (XPORT-MF-034)

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Background and Significance: Myelofibrosis (MF) is a myeloproliferative neoplasm that commonly harbors somatic gene driver mutations in Janus kinase 2 (*JAK2*), calreticulin (*CALR*), and myeloproliferative leukemia virus (*MPL*) genes. Selinexor is an investigational oral XPO1 inhibitor that may inhibit MF-relevant pathways including STAT, extracellular signal-regulated kinase (ERK), protein kinase B (AKT) and p53. Furthermore, *in vivo* preclinical studies have shown potential synergy between selinexor and ruxolitinib treatment. The Phase 3 trial was initiated based on data from the Phase 1 portion of XPORT-MF-034 evaluating the combination of selinexor and ruxolitinib in JAKi-naïve patients with MF. Previously we reported that the combination of selinexor and ruxolitinib was generally tolerable and manageable and that the 60 mg selinexor dose cohort showed 71% and 79% of the intent-to-treat (ITT) population achieving a ≥35% reduction in spleen volume from baseline (SVR35) at Week 12 and Week 24, respectively; SVR35 rates were consistent across subgroups, including gender and regardless of ruxolitinib starting dose. Robust symptom improvement was also observed with 58% of the ITT achieving a ≥50% reduction in total symptom score from baseline (TSS50) at Week 24 (Ali et *al.*, ASCO 2023; Ali et *al.*, AACR 2023). These data provided strong support to further evaluate selinexor (60 mg) and ruxolitinib in patients with JAKi-naïve MF.
Study Design and Methods: The XPORT-MF-034 (NCT04562389) trial includes a global, Phase 3 randomized, double-blind, placebo-controlled study designed to evaluate the combination of 60 mg selinexor and ruxolitinib. Patients will be randomized 2:1 to receive oral selinexor 60 mg or placebo once weekly (28-day cycle) and twice daily ruxolitinib. Select eligibility criteria include patients ≥18 years of age, with a spleen volume of ≥450 cm ^{3} by MRI or CT, dynamic international prognostic scoring system (DIPSS) of intermediate-1, 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, currently not eligible for stem cell transplantation, ECOG PS ≤2, platelet count ≥100 x 10 ^{9}/L, and creatinine clearance >15mL/min. Patients will be excluded if more than 10% blasts are present in peripheral blood or bone marrow; received previous treatment with JAK inhibitors for MF, or previous treatment with selinexor or other XPO1 inhibitors. The co-primary study endpoints are SVR35 at Week 24 as measured by MRI or CT scan and TSS50 at Week 24 as measured by the Myelofibrosis Symptom Assessment Form (MFSAF) V4.0. The key secondary endpoint is anemia response as per the International Working Group Myeloproliferative Neoplasms Research and Treatment and European Leukemia Network (IWG-MRT and ELN) criteria at Week 24.
Results: TheXPORT-MF-034 Phase 3 trial is currently open for enrollment; a total of 306 JAKi-naïve MF patients will be enrolled and the study was initiated on June 28, 2023.

Disclosures Maher: *Sobi (Doptelet):* Speakers Bureau; *Bristol Myers Squibb:* Membership on an entity's Board of Directors or advisory committees. **Rampal:** *Galecto:* Consultancy; *CTI BioPharma Corp:* Consultancy; *Celgene-BMS:* Consultancy; *Morphosys/Constellation:* Consultancy; *Sumitomo:* Consultancy; *Zentalis:* Consultancy; *Servier:* Consultancy; *Kartos:* Consultancy; *Incyte:* Research Funding; *Karyopharm:* Consultancy; *Zentalis:* Research Funding; *Dainippon:* Consultancy; *Pharmaessentia:*

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Figure. Phase 3 Trial Design

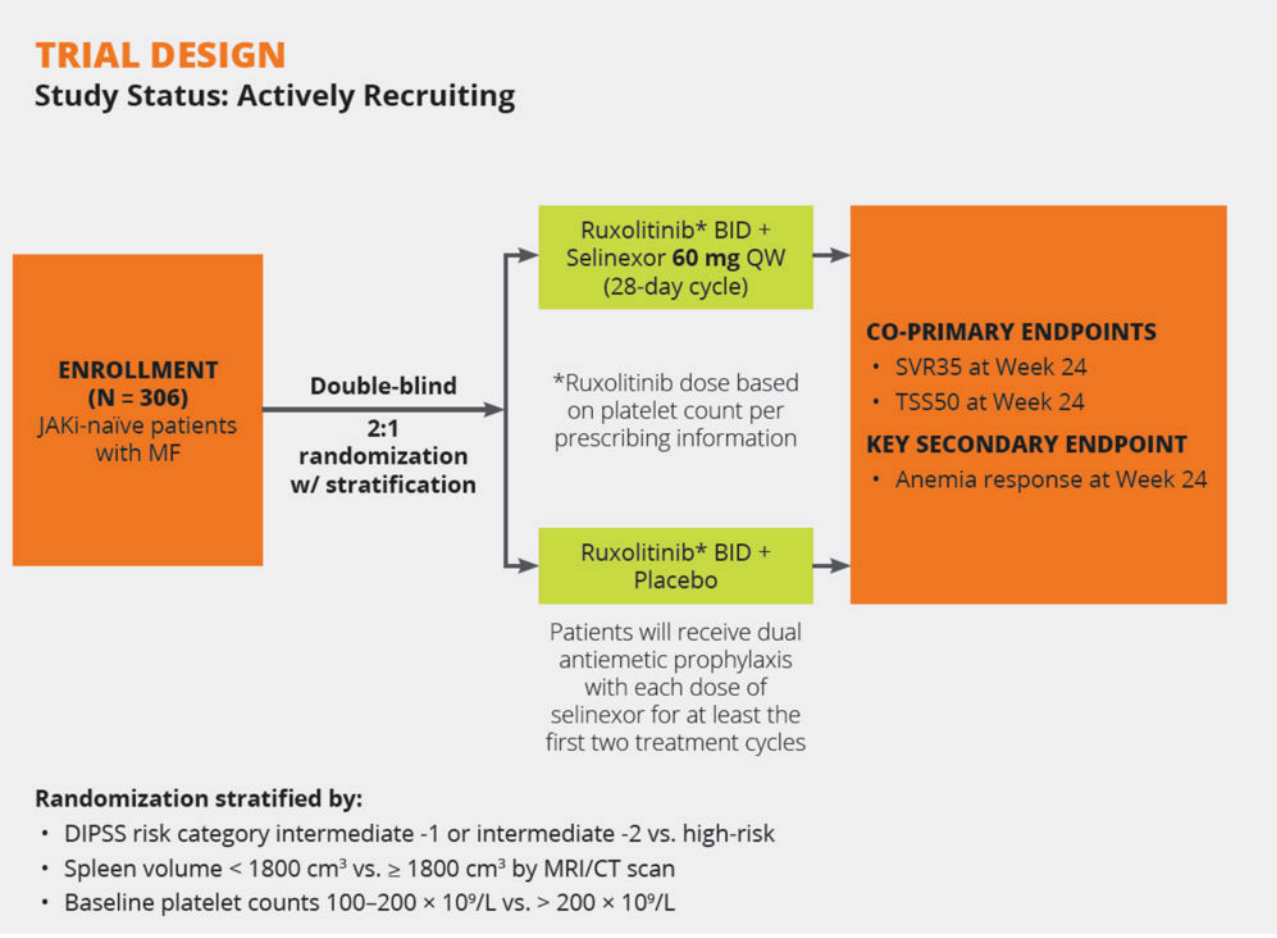

Figure 1

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