**A Phase 2 Study to Evaluate the Efficacy and Safety of Selinexor Monotherapy in Patients With JAK-Inhibitor-Naïve Myelofibrosis and Moderate Thrombocytopenia (XPORT-MF-044)**

**INTRODUCTION**

Myelofibrosis (MF) is a heterogenous, progressive, and fatal disease. Underlying biological hallmarks include aberrant blood and bone marrow differentiation, cytokine production and inflammation, bone marrow fibrosis, and extramedullary hematopoiesis. Thrombocytosis is common in patients with MF and associated with poor outcomes. Suboptimal dosing of JAK inhibitors (JAKi) leading to suboptimal symptom and/or spleen volume reduction. Unmet need for effective non-JAKi treatments for patients with MF and moderate thrombocytosis.

**RATIONALE**

Selinexor: Oral exportin 1 (XPO1) inhibitor with pro-apoptotic and anti-inflammatory properties that may impact both Janus kinase (JAK) and non-JAK pathways, underlying investigation for treatment of MF. Findings from the Phase 1 analysis: Splenomegaly with improvement in spleen volume at Week 24 in JAKi-naive patients with MF was observed. The most common adverse events were nausea (75%), fatigue (58%), anemia (54%), and thrombocytopenia (25%). Suboptimal dosing of JAKi in patients with thrombocytopenia leads to suboptimal symptom and/or spleen volume reduction.

**STUDY DESIGN**

XPORT-MF-044 (NCT05980806)

A two-arm, sequential, multicenter, open-label, Phase 2 study with optional expansion arms.

- **Primary Endpoint:** Spleen volume reduction ≥35% (SVR35) at Week 24
- **Secondary Endpoints:** Safety, TSS50 at Week 24, Anemia response at Week 24, Overall survival, Duration of response, Exploratory Endpoints: Pharmacokinetics/pharmacodynamics, Bone marrow fibrosis (BMF), Changes in variant allele frequency (VAF), Duration of response

**ENDPOINTS**

- **Primary Endpoint:** Spleen volume reduction ≥35% (SVR35) at Week 24
- **Secondary Endpoints:** Safety, TSS50 at Week 24, Anemia response at Week 24, Overall survival, Duration of response, Exploratory Endpoints: Pharmacokinetics/pharmacodynamics, Bone marrow fibrosis (BMF), Changes in variant allele frequency (VAF), Duration of response

**STUDY INFORMATION**

- **Participating locations:** Belgium, France, Germany, Greece, Hungary, Italy, Netherlands, Poland, Romania, South Korea, Spain, Taiwan, United Kingdom, USA

- **To learn more about other ongoing clinical studies of selinexor in MF:** XPORT-MF-044 Phase 2 study is currently open for enrollment. Study contact: clinicaltrials@karyopharm.com. Thank you to the patients, caregivers, and study investigators.

**Abbreviations:** BMF = bone marrow fibrosis; BMPP = bone marrow paraxial fibrosis; C1D1 = Cycle 1, Day 1; CT = computed tomography; DIPSS = Dynamic International Prognostic Scoring System; ECOG = Eastern Cooperative Oncology Group; GI = gastrointestinal; INT = intermediate; JAK = Janus kinase; JAKi = Janus kinase inhibitor; MF = myelofibrosis; MFSI = Myelofibrosis Symptom Assessment Questionnaire; MRI = magnetic resonance imaging; n = number of patients; SD = standard deviation; TSS = total symptom score; TSS50 = total symptom score reduction of 50% from baseline; VAF = variant allele frequency; XPO1 = exportin 1.

**References:**


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