A Study to Evaluate Safety and Efficacy of Selinexor Versus Treatment of Physician's Choice in Participants With Previously Treated Myelofibrosis

Status: Recruiting

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

• A diagnosis of primary MF or post-essential thrombocythemia (ET) or post-polycythemia (PV) MF according to the 2016 World Health Organization (WHO) classification of myeloproliferative neoplasms (MPN), confirmed by the most recent local pathology report.

• Previous treatment with JAK inhibitors for at least 6 months.

• Measurable splenomegaly during the screening period as demonstrated by spleen volume of ≥450 centimeter cube (cm^3) by magnetic resonance imaging (MRI) or computerized tomography (CT) scan.

• Relapsed, Refractory or Intolerant to JAK inhibitors as defined as meeting one of the criteria below:

• less than (<) 35% spleen volume reduction by MRI or CT-scan (from baseline) or

• <50% decrease in spleen size by palpation (from baseline) or an increase of at least 3 cm with the spleen at least 5 cm below the left costal margin or

• Spleen volume increase greater than (>) 25% from nadir or a return to within 10% of baseline after any initial response or

• Treatment with JAK inhibitor was complicated by development of red blood cells (RBC) transfusion requirement (2 units per month for 2 month); or grade 3 thrombocytopenia, anemia, hematoma/hemorrhage; or grade 2 non-hematologic toxicity while on JAK inhibitors

• Participants ≥18 years of age.

• Eastern Cooperative Oncology Group (ECOG) less than or equal to (≤) 2.

• Platelet count ≥75*10^9 per liter (/L).

• Absolute neutrophil count (ANC) ≥1.5*10^9/L.

• Serum direct bilirubin ≤1.5*upper limit of normal (ULN); aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤2.5*ULN.

• Calculated creatinine clearance (CrCl) >15 milliliter (mL)/minute (min) based on the Cockcroft and Gault formula.

• Participants with active hepatitis B virus (HBV) are eligible if antiviral therapy for hepatitis B has been given for >8 weeks and viral load is <100 International Units (IU)/mL.

• Participants with untreated hepatitis C virus (HCV) are eligible if there is a documentation of negative viral load per institutional standard.

• Participants with history of human immunodeficiency virus (HIV) are eligible if they have cluster of differentiation 4 (CD4)+ T-cell counts ≥350 cells/microliter (mcL), negative viral load per institutional standard, and no history of acquired immunodeficiency syndrome (AIDS)-defining opportunistic infections in the last year.

• Female participants of childbearing potential must have a negative serum pregnancy test at screening and agree to use highly effective methods of contraception throughout the study and for at least 90 days after the last dose of selinexor, or for the duration as stated on the label (SmPC/USPI) for those on the comparator drug (physician's choice arm). Childbearing potential excludes: Age >50 years and naturally amenorrhoeic for >1 year, or previous bilateral salpingo-oophorectomy, or hysterectomy.

• Male participants who are sexually active must use highly effective methods of contraception throughout the study and for at least 90 days after the last dose of selinexor, or for the duration as stated on the label (SmPC/USPI) for those on the comparator drug (physician's choice arm). Male participants must agree not to donate sperm during the study treatment period.

• Participants must sign written informed consent in accordance with federal, local and institutional guidelines.

Exclusion Criteria:

• >5% blasts in peripheral blood or >10% blasts in bone marrow (i.e., accelerated phase).

• Previous treatment with selinexor or other exportin 1 (XPO1) inhibitors.

• Use of any standard or experimental anti-MF therapy <21 days prior to Cycle 1 Day 1 (hydroxyurea or growth factors are allowed).

• Impairment of gastrointestinal (GI) function or GI disease that could significantly alter the absorption of selinexor (Example: vomiting, or diarrhea that is Common Terminology Criteria for Adverse Events (CTCAE) grade >1).

• Received strong cytochrome P450 3A (CYP3A) inhibitors ≤7 days prior to selinexor dosing or strong CYP3A inducers ≤14 days prior to selinexor dosing.

• Major surgery <28 days prior to cycle 1 day 1 (C1D1).

• Uncontrolled (ie, clinically unstable) infection requiring parenteral antibiotics, antivirals, or antifungals within 7 days prior to first dose of study treatment; however, prophylactic use of these agents is acceptable (including parenteral).

• Any life-threatening illness, medical condition, or organ system dysfunction which, in the Investigator's opinion, could compromise the participants safety, prevent the participant from giving informed consent, or being compliant with the study procedures.

• Female participants who are pregnant or lactating.

• Participants with contraindications to use of selinexor or all the drugs intended to be used in the comparative treatment arm.

Conditions & Interventions

Interventions:

Drug: Selinexor, Other: Physician's Choice Treatment

Conditions:

Myelofibrosis

Keywords:

Myelofibrosis, Selinexor, Total Symptom Score, Spleen Volume Reduction, Anemia response, TSS50, SVR35, SVR25, KPT-330, JAK1, JAK2, XPOVIO, SINE, XPORT-MF-035, Karyopharm

More Information

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