Essai Clinique

Généré le 13 mai 2025 à partir de

Titre	A Randomized, Open-Label, Phase 3 Study Evaluating Efficacy and Safety of Navitoclax in Combination With Ruxolitinib Versus Best Available Therapy in Subjects With Relapsed/Refractory Myelofibrosis
Protocole ID	TRANSFORM-2
ClinicalTrials.gov ID	NCT04468984
Type(s) de cancer	NMP : Vaquez , Thrombocythémie essentielle, Métaplasie myéloide
Phase	Phase III
Stade	Récidivant/réfractaire (2ième ligne de traitement et plus)
Type étude	Clinique
Médicament	Navitoclax en association avec le ruxolitinib
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But étude	Myelofibrosis (MF) is a bone marrow illness that affects blood-forming tissues in the body. MF disturbs the body's normal production of blood cells, causing extensive scarring in the bone marrow. This leads to severe anemia, weakness, fatigue, and an enlarged spleen. The purpose of this study is to assess safety and change in spleen volume when navitoclax is given in combination with ruxolitinib, as compared to best available therapy, for adult participants with MF. Navitoclax is an investigational drug (not yet approved) being developed for the treatment of MF. The study has 2 arms - A and B. In Arm A, participants will receive navitoclax in combination with ruxolitinib. In Arm B, participants will receive the best available therapy (BAT) for MF. Adult participants with a diagnosis of relapsed/refractory (R/R) MF will be enrolled. Approximately 330 participants will be enrolled in approximately 210 sites across the world. In Arm A, participants will receive oral navitoclax tablet once daily with oral ruxolitinib tablet twice daily. In Arm B, participants will receive the BAT as identified by the investigator. Treatment will continue until clinical benefit is not seen, participants cannot tolerate the study drugs, or participants withdraw consent. The approximate treatment duration is about 3 years. There may be higher treatment burden for participants in this trial compared to their standard of care. Participants will attend regular visits during the study at a hospital or clinic. The effect of treatment will be checked by medical assessments, blood and bone marrow tests, checking for side effects, and completing questionnaires.
Critères d'éligibilité	• Must be able to complete the Myelofibrosis Symptom Assessment Form (MFSAF) v4.0 on at least 4 out of 7 days prior to randomization.-- Has at least 2 symptoms with a score >= 3 or a total score of >= 12, as measured by the MFSAF v4.0. • Documented diagnosis of primary myelofibrosis (MF) as defined by the World Health Organization (WHO) classification, post polycythemia vera (PPV)-MF, or post essential thrombocytopenia (PET)-MF . • Classified as intermediate-2 or high-risk MF, as defined by the Dynamic International Prognostic Scoring System Plus (DIPSS+). • Must currently be on treatment or have received prior treatment with a single Janus Kinase 2 (JAK2) inhibitor, ruxolitinib, and meet one of the following criteria (in addition to the minimum splenomegaly and symptom burden also required for eligibility):

	• Treatment with ruxolitinib for >= 24 weeks that was stopped due to lack of spleen response (refractory), or loss of spleen response or symptom control after a previous response (relapsed), or was continued despite relapsed/refractory status.
	• Treatment with ruxolitinib for < 24 weeks with documented disease progression while on therapy as defined by any of the following:
	  • Appearance of new splenomegaly that is palpable to at least 5 cm below the left costal margin (LCM) in participants with no evidence of splenomegaly prior to the initiation of ruxolitinib.
	  • A >= 100% increase in the palpable distance below the LCM in participants with measurable spleen distance 5 to 10 centimeters (cm) prior to the initiation of ruxolitinib.
	  • A >= 50% increase in the palpable distance below the LCM in participants with measurable spleen distance > 10 cm prior to the initiation of ruxolitinib.
	  • A spleen volume increase of >= 25% (as assessed by Magnetic Resonance Imaging [MRI] or Computed Tomography [CT] scan) in participants with a spleen volume assessment prior to the initiation of ruxolitinib.
	• Prior or current treatment with ruxolitinib for >= 28 days with intolerance defined as new RBC transfusion requirement (at least 2 units/month for 2 months) while receiving a total daily ruxolitinib dose of >= 30 mg but unable to reduce dose further due to lack of efficacy.
	• Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2.
	• Splenomegaly defined as palpable spleen measurement >= 5 cm below left costal margin or spleen volume >= 450 cm3 as assessed centrally by MRI or CT scan.
	• Baseline platelet count >= 100 × 10^9/L.

Critères d'exclusion	• Received prior treatment with a BH3-mimetic compound, bromodomain and extra-terminal (BET) inhibitor, or prior use of > 1 JAK2 inhibitor or stem cell transplant. • Eligible for allogeneic stem cell transplantation at the time of study entry. • Receiving medication that interferes with coagulation or platelet function within 3 days prior to the first dose of study drug or during the study treatment period except for low dose aspirin (up to 100 mg daily) and low molecular weight heparin (LMWH). • Receiving anticancer therapy for an active malignancy or MF including chemotherapy, radiation therapy, hormonal therapy within 30 days prior to first dose of study drug, and during the study treatment period (other than any overlapping therapy as part of the selected BAT).