Essai Clinique

Généré le 25 avr. 2024 à partir de

Titre	Étude multicentrique, ouverte, de phase IIIb à un seul groupe portant sur l'innocuité ET l'efficacité du fédratinib chez des sujets présentant un risque intermédiaire ou élevé de myélofibrose primaire, de myélofibrose post-polycythémie vraie ou de myélofibrose avec thrombocythémie post-essentielle selon le système DIPSS
Protocole ID	FEDR-MF-001 (FREEDOM)
ClinicalTrials.gov ID	NCT03755518
Type(s) de cancer	NMP : Vaquez , Thrombocythémie essentielle, Métaplasie myéloide
Phase	Phase III
Type étude	Traitement
Médicament	Fedratinib
Institution	CIUSSS DE L'EST-DE-L'ILE-DE-MONTREAL PAV. MAISONNEUVE/PAV. MARCEL-LAMOUREUX 5415 boul. de l'Assomption, Montréal, QC, H1T2M4
Ville	
Investigateur principal	Dr Lambert Busque
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Statut	Fermé
But étude	This is Single-Arm, Open-Label Efficacy and Safety Trial of Fedratinib in Subjects with DIPSS (Dynamic International Prognostic Scoring System)-Intermediate or High- Risk Primary Myelofibrosis (PMF), Post-Polycythemia Vera Myelofibrosis (post-PV MF), or Post-Essential Thrombocythemia Myelofibrosis (post-ET MF) and Previously Treated with RuxolitinibThe primary objective of the study is to evaluate the percentage of subjects with at least a 35% reduction of spleen volume and one of the secondary objectives is to evaluate the safety of fedratinib
Critères d'éligibilité	• Subject is at least 18 years of age at the time of signing the informed consent form (ICF) • Subject has an Eastern Cooperative Oncology Group (ECOG) Performance Score (PS) of 0, 1 or 2 • Subject has diagnosis of primary myelofibrosis (PMF) according to the 2016 World Health Organization (WHO) criteria, or diagnosis of post-ET or post-PV myelofibrosis according to the IWG-MRT 2007 criteria, confirmed by the most recent local pathology report • Subject has a DIPSS Risk score of Intermediate or High • Subject has a measurable splenomegaly during the screening period as demonstrated by spleen volume of ≥ 450 cm3 by MRI or CT-scan assessment or by palpable spleen measuring ≥ 5 cm below the left costal margin • Subject has been previously exposed to ruxolitinib, and must meet at least one of the following criteria (a or b) • a. Treatment with ruxolitinib for ≥ 3 months b. Treatment with ruxolitinib for ≥ 28 days complicated by any of the following: • Development of a red blood cell transfusion requirement (at least 2 units/month for 2 months) or • Grade ≥ 3 AEs of thrombocytopenia, anemia, hematoma, and/or hemorrhage while on treatment with ruxolitinib • Subject must have treatment-related toxicities from prior therapy resolved to Grade 1 or pretreatment baseline before start of last therapy prior to fedratinib treatment. • Subject must understand and voluntarily sign an ICF prior to any study-related assessments/procedures being conducted • Subject is willing and able to adhere to the study visit schedule and other protocol requirements • A female of childbearing potential (FCBP) must:

- Have two negative pregnancy tests as verified by the Investigator prior to starting study therapy. She must agree to ongoing pregnancy testing during the course of the study, and after end of study therapy. This applies even if the subject practices true abstinence* from heterosexual contact.
- Either commit to true abstinence* from heterosexual contact (which must be reviewed on a monthly basis and source documented) or agree to use, and be able to comply with acceptable effective contraception** without interruption, -14 days prior to starting investigational product, during the study therapy (including dose interruptions), and for 30 days after discontinuation of study therapy.
- Note: A female of childbearing potential (FCBP) is a female who: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy, or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (ie has had menses at any time in the preceding 24 consecutive months).
- Male subjects must:
- Practice true abstinence* (which must be reviewed on a monthly basis) or agree to use a condom during sexual contact with a pregnant female or a female of childbearing potential while participating in the study, during dose interruptions and for at least 30 days following investigational product discontinuation, or longer if required for each compound and/or by local regulations, even if he has undergone a successful vasectomy.
- True abstinence is acceptable when this is in line with the preferred and usual lifestyle of the subject. [Periodic abstinence (eg, calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception].
- Agreement to use highly effective methods of contraception that alone or in combination result in a failure rate of a Pearl index of less than 1% per year when used consistently and correctly throughout the course of the study. Such methods include: Combined (estrogen and progestogen containing) hormonal contraception: Oral; Intravaginal; Transdermal; Progestogen-only hormonal contraception associated with inhibition of ovulation: Oral; Injectable hormonal contraception; Implantable hormonal contraception; Placement of an intrauterine device; Placement of an intrauterine hormone-releasing system; Bilateral tubal occlusion; Vasectomized partner.

Critères d'exclusion

- Any of the following laboratory abnormalities:
- Platelets < 50,000/µL
- Absolute neutrophil count (ANC) < 1.0 x 109/L
- Myeloblasts ≥ 5 % in peripheral blood
- Serum creatinine clearance < 30 mL/min (as per the Modification of Diet in Renal Disease [MDRD] formula)
- Serum amylase or lipase > 1.5 x ULN (upper limit of normal)
- Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 3 x ULN
- Total bilirubin > 1.5 x ULN, subject's total bilirubin between 1.5 - 3.0 x ULN are eligible if the direct bilirubin fraction is < 25% of the total bilirubin
- Subject is pregnant or lactating female
- Subject with previous splenectomy
- Subject with previous or planned hematopoietic cell transplant
- Subject with prior history of Wernicke encephalopathy (WE)
- Subject with signs or symptoms of WE (eg, severe ataxia, ocular paralysis or cerebellar signs) without documented exclusion of WE by thiamine level and brain MRI
- Subject with thiamine deficiency, defined as thiamine levels in whole blood below normal range according to institutional standard and not corrected prior to enrollment on the study
- Subject with concomitant treatment with or use of pharmaceutical, herbal agents or food known to be strong inducers of Cytochrome P450 3A4 (CYP3A4), sensitive CYP3A4 substrates with narrow therapeutic range, sensitive Cytochrome P450 2C19 (CYP2C19) substrates with narrow therapeutic range, or sensitive Cytochrome P450 2D6 (CYP2D6) substrates with narrow therapeutic range
- Subject on any chemotherapy, immunomodulatory drug therapy (eg, thalidomide, interferon-alpha), anagrelide, immunosuppressive therapy, systemic corticosteroids > 10 mg/day prednisone or equivalent. Subjects who have had prior exposure to hydroxyurea (eg, Hydrea) in the past may be enrolled into the study as long as it has not been administered within 14 days prior to the start of fedratinib treatment
- Subject has received ruxolitinib within 14 days prior to the start of fedratinib
- Subject on treatment with myeloid growth factor (eg, granulocyte-colony stimulating factor [G-CSF]) within 14 days prior to the start of fedratinib treatment
- Subject with previous exposure to Janus kinase (JAK) inhibitor(s) other than ruxolitinib treatment
- Subject on treatment with aspirin with doses > 150 mg daily
- Subject with major surgery within 28 days before starting fedratinib treatment
- Subject with diagnosis of chronic liver disease (eg, chronic alcoholic liver disease, autoimmune hepatitis, sclerosing cholangitis, primary biliary cirrhosis, hemochromatosis, non-alcoholic steatohepatitis)
- Subject with prior malignancy other than the disease under study unless the subject has not required treatment for the malignancy for at least 3 years prior to enrollment.
- However, subject with the following history/concurrent conditions provided successfully treated may enroll: non-invasive skin cancer, in situ cervical cancer, carcinoma in situ of the breast, incidental histologic finding of prostate cancer (T1a or T1b using the tumor, nodes, metastasis [TNM] clinical staging system), or is free of disease and on hormonal treatment only

- Subject with uncontrolled congestive heart failure (New York Heart Association Classification 3 or 4)
- Subject with known human immunodeficiency virus (HIV), known active infectious Hepatitis B (HepB), and/or known active infectious Hepatitis C (HepC)
- Subject with serious active infection
- Subject with presence of any significant gastric or other disorder that would inhibit absorption of oral medication
- Subject is unable to swallow capsule
- Subject has any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from participating in the study
- Subject has any condition including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study
- Subject has any condition that confounds the ability to interpret data from the study
- Subject with participation in any study of an investigational agent (drug, biologic, device) within 30 days prior to start of fedratinib treatment