Essai Clinique

Généré le 05 mai 2024 à partir de

Titre	A Phase 3 Randomized, Open Label, Multicenter Study of Isatuximab (SAR650984) in Combination With Lenalidomide and Dexamethasone Versus Lenalidomide and Dexamethasone in Patients With High-risk Smoldering Multiple Myeloma
Protocole ID	ITHACA
ClinicalTrials.gov ID	NCT04270409
Type(s) de cancer	Myélome
Phase	Phase III
Type étude	Clinique
Médicament	Isatuximab en association avec lénalidomide et dexaméthasone versus lénalidomide et dexaméthasone
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 Richard Leblanc
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Statut	Actif en recrutement
But étude	• Safety run-in: To confirm the recommended dose of isatuximab when combined with lenalidomide and dexamethasone in participants with high-risk smoldering multiple myeloma (SMM) • Randomized Phase 3: To demonstrate the clinical benefit of isatuximab in combination with lenalidomide and dexamethasone in the prolongation of progression-free survival when compared to lenalidomide and dexamethasone in participants with high-risk SMM • Study duration is expected to be approximately 10 years, including a 28-day screening period, followed by an up to 36-month treatment period, and a follow-up period of approximately 7 years.
Critères d'éligibilité	• Participant must be at least 18 years of age inclusive or older • Participants who are diagnosed within 5 years with SMM (per International Myeloma Working Group [IMWG] criteria), defined as serum M-protein ≥30 g/L or urinary M-protein ≥500 mg per 24 hour or both, and/or clonal bone marrow plasma cells (BMPCs) 10% to <60%, and absence of myeloma defining events or other related conditions and with high-risk SMM • Eastern Cooperative Oncology Group (ECOG) Performance Status 0 or 1 or 2 • Capable of giving voluntary written informed consent • Absolute neutrophil count (ANC) ≥1000/µL (1 × 109/L) • Platelets ≥50,000/µL (50 × 109/L) • Total bilirubin ≤3 mg/dL (except Gilbert syndrome, in which direct bilirubin should be ≤5 mg/dL) • Alanine aminotransferase ≤3× upper limit of normal (ULN), aspartate aminotransferase ≤ 3 × ULN

Critères d'exclusion

- Evidence of any of the following calcium, renal failure, anemia, bone lesions (CRAB) criteria or Myeloma Defining Events (SLiM CRAB) detailed below (attributable to the participants SMM involvement):
    - Increased calcium levels: Corrected serum calcium >1 mg/dL above the ULN or >11 mg/dL
    - Renal insufficiency: Determined by glomerular filtration rate (GFR) <40 mL/min/1.73 m² (Modification of Diet in Renal Disease [MDRD] Formula) or serum creatinine >2 mg/dL
    - Anemia (hemoglobin 2 g/dL below lower limit of normal or <10 g/dL or both) transfusion support or concurrent treatment with erythropoietin stimulating agents is not permitted
    - ≥ 1 bone lytic lesion of ≥5mm in size
    - BMPCs ≥60%
    - Serum involved/uninvolved FLC ratio ≥100
    - Whole body magnetic resonance imaging (WB-MRI) or positron emission tomography-computed tomography (PET-CT) with more than 1 focal lesion (≥5 mm in diameter by MRI)
- Primary systemic and localized amyloid light-chain (immunoglobulin light chain) amyloidosis, monoclonal gammopathy of undetermined significance (MGUS), standard risk smoldering myeloma, soft tissue plasmacytoma, symptomatic myeloma
- Uncontrolled infection within 28 days prior to randomization in Phase 3 or first study intervention administration in safety run-in
- Clinically significant cardiac disease, including:
    - Myocardial infarction within 6 months with left ventricular dysfunction or uncontrolled ischemic cardiac disease before Cycle 1 Day 1, or unstable or uncontrolled disease/condition related to or affecting cardiac function (eg, unstable angina, congestive heart failure, New York Heart Association Class III-IV)
    - Uncontrolled cardiac arrhythmia (Grade 2 or higher by NCI-CTCAE Version 5.0) or clinically significant electrocardiogram (ECG) abnormalities
- Known acquired immunodeficiency syndrome (AIDS)-related illness or known human immunodeficiency virus (HIV) disease requiring antiviral treatment or active hepatitis A (defined as positive hepatitis A antigen or positive IgM). HIV serology at screening will be tested for German participants and any other country where required as per local regulations and serology hepatitis B and C at screening will be tested for all participants
    - Uncontrolled or active HBV infection: Patients with positive HBsAg and/or HBV DNA

Of note: Patient can be eligible if anti-HBc IgG positive (with or without positive anti-HBs) but HBsAg and HBV DNA are negative. If anti-HBV therapy in relation with prior infection was started before initiation of IMP, the anti-HBV therapy and monitoring should continue throughout the study-treatment period.Patients with negative HBsAg and positive HBV DNA observed during screening period will be evaluated by a specialist for start of anti-viral treatment: study treatment could be proposed if HBV DNA becomes negative and all the other study criteria are still met.Active HCV infection: positive HCV RNA and negative anti-HCVOf note: Patients with antiviral therapy for HCV started before initiation of IMP and positive HCV antibodies are eligible. The antiviral therapy for HCV should continue throughout the treatment period until seroconversion.Patients with positive anti-HCV and undetectable HCV RNA without antiviral therapy for HCV are eligible

- Malabsorption syndrome or any condition that can significantly impact the absorption of lenalidomide
- Any of the following within 3 months prior to randomization (or first study intervention administration in safety run-in cohort): treatment resistant peptic ulcer disease, erosive esophagitis or gastritis, infectious or inflammatory bowel disease, diverticulitis, pulmonary embolism, or other uncontrolled thromboembolic event
- Received treatment (eg surgery, radiotherapy, medication) for a malignancy within 3 years of randomization (or first study intervention administration in safety run-in cohort)
- Prior exposure to approved or investigational treatments for SMM or MM (including but not limited to conventional chemotherapies, immunomodulatory imid drugs, or Proteasome inhibitors); concurrent use of bisphosphonates or receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor denosumab is not permitted; however, prior bisphosphonates or once-a-year intravenous bisphosphonate given for the treatment of osteoporosis is permitted
- Ongoing treatment with corticosteroids with a dose >10 mg prednisone or equivalent per day at the time of randomization (or first study intervention administration in safety run-in cohort)
- Women of childbearing potential or male participant with women of childbearing potential who do not agree to use a highly effective method of birth control
- Vaccination with a live vaccine 4 weeks before the start of the study drug. Seasonal flu vaccines that do not contain live virus are permitted

The above information is not intended to contain all considerations relevant to a patient's potential participation in a clinical trial.