Essai Clinique

Généré le 04 mai 2024 à partir de

Titre	A Phase 3, Randomized, Open-Label Study Evaluating the Safety and Efficacy of Magrolimab in Combination With Azacitidine Versus Physician's Choice of Venetoclax in Combination With Azacitidine or Intensive Chemotherapy in Previously Untreated Patients With TP53 Mutant Acute Myeloid Leukemia
Protocole ID	ENHANCE-2
ClinicalTrials.gov ID	NCT04778397
Type(s) de cancer	Leucémie myéloïde aiguë (LMA)
Phase	Phase III
Type étude	Clinique
Médicament	Magrolimab en association avec l'azacitidine versus une thérapie au choix du clinicien soit vénétoclax en association avec azacitidine ou une chimiothérapie intensive
Institution	CIUSSS DE L'EST-DE-L'ILE-DE-MONTREAL PAV. MAISONNEUVE/PAV. MARCEL-LAMOUREUX 5415 boul. de l'Assomption, Montréal, QC, H1T2M4
Ville	
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Statut	Fermé
Date d'activation	07-02-2023
But étude	The primary objective of this study is to compare the efficacy of magrolimab + azacitidine versus venetoclax + azacitidine in adults with previously untreated TP53 mutant acute myeloid leukemia (AML) who are appropriate for non-intensive therapy as measured by overall survival (OS).
Critères d'éligibilité	• Individuals with confirmation of AML by World Health Organization criteria, previously untreated for AML, and who have presence of at least 1 TP53 gene mutation that is not benign or likely benign based on evaluation by either central laboratory or an approved local laboratory (after central review of the bone marrow TP53 mitigation next-generation sequencing test results) (individuals with biallelic 17p deletions, loss of both 17p alleles, are eligible based on locally evaluated cytogenetics/karyotype/fluorescence in situ hybridization (FISH) report) • Individuals with white blood cell (WBC) count ≤ 20×10^3/microliter (µL) prior to randomization. If the individual's WBC is > 20×10^3/µL prior to randomization, the individual can be enrolled, assuming all other eligibility criteria are met. However, the WBC should be ≤ 20×10^3/µL prior to the first dose of study treatment and prior to each magrolimab dose the first 4 weeks (if the individual is randomized to the experimental arm) Note: Individuals can be treated with hydroxyurea and/or leukapheresis throughout the study or prior to randomization to reduce the WBC to ≤ 20×10^3/µL to enable eligibility for study drug dosing. • The hemoglobin must be ≥ 9 grams per deciliter (g/dL) prior to initial dose of study treatment Notes:Transfusions are allowed to meet hemoglobin eligibility • Individual has provided informed consent • Individual is willing and able to comply with clinic visits and procedure outlined in the study protocol • Individuals must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2, except for individuals less than 75 years of age and appropriate for non-intensive treatment. For these individuals, the ECOG performance status score may be 0 to 3 • Individuals must have adequate renal function as demonstrated by a creatinine clearance ≥ 30

	milliliters per minute calculated by the Cockcroft Gault formula • Adequate cardiac function as demonstrated by: • Lack of symptomatic congestive heart failure and clinically significant cardiac arrhythmias and ischemic heart disease • LVEF > 50% for individuals appropriate for intensive therapy • Adequate liver function as demonstrated by: • Aspartate aminotransferase ≤ 3.0 × upper limit of normal (ULN) • Alanine aminotransferase ≤ 3.0 × ULN • Total bilirubin ≤ 1.5 × ULN, or primary unconjugated bilirubin ≤ 3.0 × ULN if individual has a documented history of Gilbert's syndrome or genetic equivalent • Pretreatment blood cross-match completed • Males and females of childbearing potential who engage in heterosexual intercourse must agree to use protocol-specified method(s) of contraception • Individuals must be willing to consent to mandatory pretreatment and ontreatment bone marrow biopsies (aspirate and trephines).
Critères d'exclusion	• Positive serum pregnancy test • Breastfeeding female • Known hypersensitivity to any of the study drugs, the metabolites, or formulation excipient • Prior treatment with any of the following: • Cluster of differentiation 47 (CD47) or signal regulatory protein alpha (SIRPα)-targeting agents • Antileukemic therapy for the treatment of AML (excluding hydroxyurea), hypomethylating agent (HMA), low dose cytarabine and/or venetoclax Note: Individuals with prior myelodysplastic syndrome (MDS) who have not received prior HMAs or chemotherapeutic agents for MDS are allowed on study. Other prior MDS therapies including, but not limited to, lenalidomide, erythroid stimulating agents, or similar RBC-direct therapies, are allowed. Localized non-central nervous system (CNS) radiotherapy, erythroid and/or myeloid growth factors, hormonal therapy with luteinizing hormone-releasing hormone agonists for prostate cancer, hormonal therapy or maintenance for breast cancer, and treatment with bisphosphonates and receptor activator of nuclear factor kappa-B ligand inhibitors are also not criteria for exclusion. • Individuals who are appropriate for intensive treatment but who have been previously treated with maximum cumulative doses of idarubicin and/or other anthracyclines and anthracenediones will be excluded. • Individuals receiving any live vaccine within 4 weeks prior to initiation of study treatments. • For individuals appropriate for intensive therapy, individuals treated with trastuzumab within 7 months prior to initiation of study treatments. • Current participation in another interventional clinical study • Known inherited or acquired bleeding disorders • Individuals appropriate for non-intensive therapy, who have received treatment with strong and/or moderate cytochrome P450 enzyme 3A (CYP3A) inducers within 7 days prior to the initiation of study treatments • Individuals appropriate for non-intensive therapy who have consumed grapefruit, grapefruit products, Seville oranges (including marmalade containing Seville oranges) or starfruit within 3 days prior to the initiation of study treatment • Individuals appropriate for non-intensive therapy who have malabsorption syndrome or other conditions that preclude enteral route of administration • Clinical suspicion of active CNS involvement with AML • Individuals who have acute promyelocytic leukemia • Significant disease or medical conditions, as assessed by the Investigator and Sponsor, that would substantially increase the risk-benefit ratio of participating in the study. This includes, but is not limited to, acute myocardial infarction within the last 6 months, unstable angina, uncontrolled diabetes mellitus, significant active infections, and congestive heart failure New York Heart Association Class III-IV • Second malignancy, except MDS, treated basal cell or localized squamous skin carcinomas, localized prostate cancer, or other malignancies for which individuals are not on active anti-cancer therapies and have had no evidence of active malignancy for at least ≥ 1 year Note: Individuals on maintenance therapy alone who have no evidence of active malignancy for at least ≥ 1 year are eligible. • Known active or chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection or human immunodeficiency virus (HIV) infection in medical history • Active HBV, and/or active HCV, and/or HIV following testing at screening: • Individuals who test positive for hepatitis B surface antigen (HBsAg). Individuals who test positive for hepatitis B core antibody (anti-HBc) will require HBV deoxyribose nucleic acid (DNA) by quantitative polymerase chain reaction (PCR) for confirmation of active disease • Individuals who test positive for HCV antibody. These individuals will require HCV ribose nucleic acid (RNA) quantitative PCR for confirmation of active disease • Individuals who test positive for HIV antibody • Individuals not currently receiving antiviral therapy and who have an undetectable viral load in the prior 3 months may be eligible for the study.