Essai Clinique

Généré le 18 mai 2024 à partir de

Titre	A Phase 1/2 First in Human Study of the Menin-MLL(KMT2A) Inhibitor KO-539 in Patients With Relapsed or Refractory Acute Myeloid Leukemia
Protocole ID	KO-MEN-001
ClinicalTrials.gov ID	NCT04067336
Type(s) de cancer	Leucémie myéloïde aiguë (LMA)
Phase	Phase I-II
Type étude	Clinique
Médicament	ziftomenib
Institution	CHU DE QUEBEC – UNIVERSITE LAVAL HOPITAL DE L'ENFANT-JESUS 1401 18e Rue, Québec, QC, G1J 1Z4
Ville	
Investigateur principal	Dr Frédéric Barabé
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Statut	Actif en recrutement
Date d'activation	30-10-2023
But étude	This first-in-human dose-escalation and dose-validation/expansion study will assess ziftomenib, a menin-MLL(KMT2A) inhibitor, in patients with relapsed or refractory acute myeloid leukemia (AML) as part of Phase 1. In Phase 2, assessment of ziftomenib will continue in patients with NPM1-m AML.

Critères d'éligibilité	Patients with refractory or relapsed AML defined as the reappearance of ≥ 5% blasts in the bone marrow and who have also failed or are ineligible for any approved standard of care therapies, including HSCT.
	• Phase 1b:
	  • Patients with a documented lysine[K]-specific methyltransferase 2-rearrangement (KMT2A-r), or
	  • Patients with a documented nucleophosmin 1 mutation (NPM1-m)
	• Phase 2: a. Patients with a documented nucleophosmin 1 mutation (NPM1-m)
	• ≥ 18 years of age.
	• Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2, and a life expectancy of at least 2 months.
	• Adequate liver and kidney function according to protocol requirements.
	• Peripheral white blood cell (WBC) counts ≤ 30,000/µL. Patients may receive hydroxyurea to control and maintain white blood cell count prior to enrollment.
	• Women of childbearing potential must be willing to use a highly effective method of contraception throughout the study and for at least 180 days after the last dose of study treatment.
	• Males with female partners of childbearing potential must agree to use a highly effective method of contraception throughout the study and for at least 90 days after the last dose of study treatment.

Critères d'exclusion	• Diagnosis of acute promyelocytic leukemia. • Diagnosis of chronic myelogenous leukemia in blast crisis. • Donor lymphocyte infusion < 30 days prior to study entry. • Clinically active central nervous system (CNS) leukemia. • Undergone HSCT and have not had adequate hematologic recovery. • Receiving immunosuppressive therapy post HSCT within 2 weeks of Cycle 1 Day 1. • Grade ≥ 2 active graft-versus-host disease (GVHD), moderate or severe limited chronic GVHD, or extensive chronic GVHD of any severity. • Received chemotherapy immunotherapy, radiotherapy, or any ancillary therapy that is considered to be investigational (i.e., used for non-approved indications(s) and in the context of a research investigation) < 14 days prior to the first dose of ziftomenib or within 5 drug half-lives prior to the first dose of study drug. • Not recovered to < Grade 2 (National Cancer Institute Common Terminology Criteria for Adverse Events v5.0) from all acute toxicities or deemed back to a stable baseline. • Treatment with concomitant drugs that are strong inhibitors or inducers of cytochrome P450-isozyme 3A4 (CYP3A4) with the exception of antibiotics, antifungals, and antivirals that are used as standard of care or to prevent or treat infections and other such drugs that are considered absolutely essential for the care of the patient. • Detectable viral load for human immunodeficiency virus, hepatitis C, or hepatitis B surface antigen indicative of active infection. Patients with controlled disease will not be excluded from study enrollment. • Pre-existing disorder predisposing the patient to a serious or life-threatening infection (e.g. cystic fibrosis, congenital or acquired immunodeficiency, bleeding disorder, or cytopenias not related to AML). • Active uncontrolled acute or chronic systemic fungal, bacterial, viral, or other infection. • Significant cardiovascular disease including unstable angina pectoris, uncontrolled hypertension or arrhythmia, history of cerebrovascular accident including transient ischemic attack within the past 6 months, congestive heart failure (NYHA Class III or IV) related to primary cardiac disease, ischemic or severe valvular heart disease, or a myocardial infarction within 6 months prior to the first dose of study treatment. • Mean QTcF >480 ms on triplicate ECG. • Major surgery within 4 weeks prior to the first dose of study treatment. • Women who are pregnant or lactating. All female patients with reproductive potential must have a negative serum pregnancy test within 72 hours prior to starting treatment.