Essai Clinique

Généré le 05 mai 2024 à partir de

Titre	A First-In-Human, Open-Label, Multicenter Study of VOR33 in Patients With Acute Myeloid Leukemia Who Are at High-Risk for Leukemia Relapse Following Hematopoietic Cell Transplantation
Protocole ID	VBP101
ClinicalTrials.gov ID	NCT04849910
Type(s) de cancer	Leucémie myéloïde aiguë (LMA)
Phase	Phase I-II
Type étude	Clinique
Médicament	VOR33
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	Actif en recrutement
Date d'activation	13-06-2022
But étude	This is a Phase 1/2a, multicenter, open-label, first-in-human (FIH) study of VOR33 in participants with AML who are undergoing human leukocyte antigen (HLA)-matched allogeneic hematopoietic cell transplant (HCT). High risk acute myeloid leukemia (AML) frequently relapses despite hematopoietic stem cell transplant (HCT). Post-HCT targeted therapy to reduce relapse is limited by toxicity to the engrafted cells. VOR33, an allogeneic CRISPR/Cas9 genome-edited hematopoietic stem and progenitor cell (HSPC) therapy product, lacking the CD33 protein, is being investigated for participants with CD33+ AML at high risk for relapse after HCT to allow post-HCT targeting of residual CD33+ acute AML cells using Mylotarg™ without toxicity to engrafted VOR33 cells. Participants will undergo a myeloablative HCT with matched related or unrelated donor CD34+-selected hematopoietic stem and progenitor cells (HSPCs) engineered to remove CD33 expression (VOR33 product). Mylotarg™ will be given after engraftment for up to 4 cycles. The primary endpoint assessing safety of VOR33 will be the incidence of successful engraftment at 28 days. Part 1 of this study will evaluate the safety of escalating Mylotarg™ dose levels to determine the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D). Part 2 will expand the number of participants to evaluate the Mylotarg™ RP2D.

Critères d'éligibilité	• Must be ≥18 and ≤70 years of age.
	• Must have confirmed diagnosis of AML in first or second complete remission (CR1 or CR2) or have bone marrow blasts ≤10% without circulating blasts.
	• AML sample from the patient must have evidence of CD33 expression (>0%)
	• AML must have intermediate or high-risk disease-related genetics and the presence of minimal residual disease (MRD). Subjects in CR2 or with persistent morphologic blasts; may have favorable disease-related genetics.
	• Candidate for HLA-matched allogeneic HCT using a myeloablative conditioning regimen.
	• Must have a related or unrelated stem cell donor that is a 10/10 match for HLA-A, -B, -C, -DRB1 and -DQB1.
	• Must have adequate performance status and organ function as defined below:
	  • Performance Status: Karnofsky score of ≥70.
	  • Cardiac: left ventricular ejection fraction (LVEF) ≥50%
	  • Pulmonary: diffusing capacity of lung for carbon monoxide (DLCO), forced vital capacity

	(FVC), and forced expiratory volume in one second (FEV1) ≥66%. • Renal: estimated glomerular filtration rate (GFR) >60 mL/min • Hepatic: total bilirubin <1.5 × ULN, or if ≥1.5 × ULN direct bilirubin <ULN and ALT/AST <1.5 × ULN (per institutional criteria).
Critères d'exclusion	• Prior autologous or allogeneic stem cell transplantation. • Presence of the following disease-related genetics: t(15; 17)(q22; q21), or t(9; 22)(q34; q11), or other evidence of acute promyelocytic leukemia or chronic myeloid leukemia. • Prior treatment with Mylotarg™ (gemtuzumab ozogamicin). • Active central nervous system (CNS) leukemia or history of other active malignancy(ies). • Patients diagnosed with Gilbert's syndrome. • Uncontrolled bacterial, viral, or fungal infections; or known human immunodeficiency virus (HIV), Hepatitis B, or Hepatitis C infection.