Essai Clinique

Généré le 05 mai 2024 à partir de

Titre	A Phase IB/II Multi-Arm Study With Venetoclax in Combination With Cobimetinib and Venetoclax in Combination With Idasanutlin in Patients Aged >/= 60 Years With Relapsed or Refractory Acute Myeloid Leukemia Who Are Not Eligible for Cytotoxic Therapy
Protocole ID	GH29914
ClinicalTrials.gov ID	NCT02670044
Type(s) de cancer	Leucémie myéloïde aiguë (LMA)
Phase	Phase I-II
Institution	CIUSSS DU CENTRE-OUEST-DE-L'ILE-DE-MONTREAL HOPITAL GENERAL JUIF SIR MORTIMER B.DAVIS 3755 rue de la Côte Ste. Catherine, Montréal, QC, H3T 1E2
Ville	Montréal
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Statut	Fermé
But étude	The primary objective for this study is to assess the safety and tolerability as well as preliminary efficacy of venetoclax in combination with cobimetinib, and venetoclax in combination with idasanutlin in patients >/= 60 years of age with relapsed or refractory acute myeloid leukemia (R/R) AML who are not eligible for cytotoxic therapy.
Critères d'éligibilité	• Age >/= 60 years • Histological confirmation of relapsed or refractory AML after prior anti-leukemic therapy by WHO Classification • Not eligible for cytotoxic therapies • Ineligible for allogeneic stem cell transplant • Life expectancy of at least 12 weeks • Eastern Cooperative Oncology Group (ECOG) Performance Status 0-2 • Adequate liver and renal function
Critères d'exclusion	• Patients with acute promyelocytic leukemia (French-American-British [FAB] class M3 AML) • Known active central nervous system (CNS) involvement with AML at study entry • Prior exposure to Bcl-2 inhibitors, murine double minute 2 (MDM2) antagonists or prior exposure to experimental treatment targeting Raf, mitogen-activated protein kinase (MEK), or the mitogen-activated protein kinase (MAPK) RAS/RAF/MEK/ERK MAPK pathway • Positive for hepatitis C virus (HCV), hepatitis B surface antigen (HBsAg) and known history of HIV, malignancy, active infection and cardiovascular diseases (CVs) • Received strong cytochrome (CYP) 3A inhibitors, moderate CYP3A inhibitors, strong CYP3A inducers and moderate CYP3A inducers within 7 days prior to initiation of study treatment • History of symptomatic Clostridium difficile infection within 1 month prior to dosing • Additional phase specific exclusion criteria: • Phase Ib Dose Escalation Arm A (Venetoclax and Cobimetinib) • History or evidence of retinal pathology on ophthalmologic examination that is considered a risk factor for neurosensory retinal detachment/central serous chorioretinopathy (CSCR), retinal vein occlusion (RVO), or neovascular macular degeneration • Left ventricular ejection fraction (LVEF) below institutional lower limit of normal (LLN) or below 50%, whichever is lower • Phase Ib Dose-Escalation Arm B (Venetoclax and Idasanutlin): • Received the following within 7 days prior to the initiation of study treatment: • Strong CYP2C8 inhibitors or CYP2C8 substrates • OATP1B1/3 substrates • Received the following within 14 days prior to the initiation of study treatment:

- * Strong CYP2C8 inducers
- Received hormonal therapy (apart from luteinizing hormone releasing hormone agonist/antagonist for prostate cancer and hormone replacement therapy) within 2 weeks prior to the first dose of study treatment
- History of liver cirrhosis by radiologic, clinical or laboratory data, or biopsy despite normal liver function tests
- Phase II Expansion Arm A and Arm B:
- Received the following within 7 days prior to the initiation of study treatment:
- Strong CYP2C8 inhibitors or CYP2C8 substrates
- OATP1B1/3 substrates
- Received the following within 14 days prior to the initiation of study treatment: * Strong CYP2C8 inducers
- History or evidence of retinal pathology on ophthalmologic examination that is considered a risk factor for neurosensory retinal detachment/CSCR, RVO, or neovascular macular degeneration
- LVEF below institutional LLN or below 50%, whichever is lower
- Received hormonal therapy (apart from luteinizing hormone releasing hormone agonist/antagonist for prostate cancer and hormone replacement therapy) within 2 weeks prior to the first dose of study treatment
- History of liver cirrhosis by radiologic, clinical or laboratory data, or biopsy despite normal liver function tests