Essai Clinique

Généré le 30 avr. 2024 à partir de

Titre	A Randomized, Open-label, Controlled, Phase 2 Study of Pevonedistat, Venetoclax, and Azacitidine Versus Venetoclax Plus Azacitidine in Adults With Newly Diagnosed Acute Myeloid Leukemia Who Are Unfit for Intensive Chemotherapy
Protocole ID	PEVENAZA
ClinicalTrials.gov ID	NCT04266795
Type(s) de cancer	Leucémie myéloïde aiguë (LMA)
Phase	Phase II
Type étude	Clinique
Médicament	Pevonedistat, Venetoclax, et Azacitidine versus Venetoclax + Azacitidine
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Ville	
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Statut	Fermé
But étude	The purpose of this study is to determine whether the combination of pevonedistat + venetoclax + azacitidine improves event-free survival (EFS) compared with venetoclax + azacitidine in patients with newly diagnosed acute myeloid leukemia (AML) who are unfit for intensive chemotherapy.

Critères d'éligibilité	• Has morphologically confirmed diagnosis of AML (World Health Organization [WHO] criteria 2008). Participants may have newly diagnosed primary de novo AML or secondary AML (sAML), defined as AML after myelodysplastic syndromes (MDS) or myeloproliferative neoplasm (MPN), or therapy-related AML (t-AML) following cytotoxic therapy, and/or radiotherapy for a malignant or nonmalignant disease.
	• Is unfit for treatment with a standard Ara-C and anthracycline induction regimen due to age or co-morbidities defined by 1 of the following:
	  • ≥75 years of age. OR
	  • ≥18 to <75 years of age with at least one of the following:
	• Eastern Cooperative Oncology Group (ECOG) performance status of 2 or 3.
	• Severe cardiac disorder (e.g., congestive heart failure requiring treatment, ejection fraction ≤50%, or chronic stable angina).
	• Severe pulmonary disorder (e.g., carbon monoxide lung diffusion capacity ≤65% or forced expiratory volume in 1 second ≤65%).
	• Creatinine clearance (CrCl) <45 mL/min (but ≥30 mL/min as part of general eligibility criteria).
	• Hepatic disorder with total bilirubin >1.5 times the upper limit of the normal range (ULN).
	• Has clinical laboratory values within the following parameters (repeat within 3 days before the first dose of study drug if laboratory values used for randomization were obtained more than 3 days before the first dose of study drug):
	  • Total bilirubin ≤1.5 times the ULN except in participants with Gilbert's syndrome. Participants with Gilbert's syndrome may enroll with direct bilirubin ≤3 times the ULN of the direct bilirubin. Elevated indirect bilirubin due to posttransfusion hemolysis is allowed.
	  • Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤3.0 times the ULN.
	  • Creatinine clearance (CrCl) ≥30 mL/min (calculated by the Modification of Diet in Renal Disease [MDRD] Study equation).
	  • Albumin >2.7 g/dL.

	• WBC count <25 × 10^9/L. Participants who are cytoreduced with leukapheresis or with hydroxyurea may be enrolled if they meet the eligibility criteria before starting therapy.

Critères d'exclusion	• Has history of MPN with BCR-ABL1 translocation or AML with BCR-ABL1 translocation.
	• Has genetic diagnosis of acute promyelocytic leukemia.
	• Is eligible for intensive chemotherapy and/or allogeneic stem cell transplantation.
	• Has extramedullary AML without evidence of bone marrow involvement.
	• Had prior treatment with hypomethylating agents for AML (hypomethylating agent treatment for prior MDS is not exclusionary).
	• Has clinical evidence of or history of central nervous system involvement by AML.
	• Had diagnosed or treated for another malignancy (except for adequately treated carcinoma in situ of any organ or nonmelanoma skin cancer) within 1 year before randomization or previously diagnosed with another malignancy and have any evidence of residual disease that may compromise the administration of pevonedistat, venetoclax or azacitidine. Prior MDS is also allowed, but the participant cannot have received treatment for MDS within 14 days before first dose of any study drug.
	• Has a WBC count ≥25 × 10^9/L
	• Has uncontrolled human immunodeficiency virus (HIV) infection. Note: Known HIV positive participants who meet the following criteria will be considered eligible:
	  • Cluster difference 4 (CD4) count >350 cells/mm^3.
	  • Undetectable viral load.
	  • Maintained on modern therapeutic regimens utilizing non-cytochrome P (CYP)-interactive agents.
	  • No history of acquired immune deficiency syndrome (AIDS)-defining opportunistic infections.
	• Participant is known to be positive for hepatitis B or C infection, with the exception of those with an undetectable viral load within 3 months (hepatitis B or C testing is not required for eligibility assessment).
	• Has hepatic cirrhosis.
	• Has uncontrolled coagulopathy or bleeding disorder.
	• Has high blood pressure which cannot be controlled by standard treatments.
	• Has prolonged rate QTc interval ≥500 msec, calculated according to institutional guidelines.
	• Has left ventricular ejection fraction (LVEF) <40%, based on echocardiogram or multigated acquisition (MUGA) scan at screening (data to be available within last 3 months of screening).
	• As infection is a common feature of AML, participants with active infection are permitted to enroll provided that the infection is under control and no signs of systemic inflammatory response beyond low grade fever that makes participant clinically unstable in the opinion of the investigator. Participants with uncontrolled infection shall not be enrolled until infection is treated and brought under control.