Essai Clinique

Généré le 18 mai 2024 à partir de

Titre	A Single-Arm, Open-Label Pharmacokinetic, Safety, and Efficacy Study of ASTX727 in Combination With Venetoclax in Adult Patients With Acute Myeloid Leukemia
Protocole ID	ASTX727-07
ClinicalTrials.gov ID	NCT04657081
Type(s) de cancer	Leucémie myéloïde aiguë (LMA)
Phase	Phase I-II
Type étude	Clinique
Médicament	ASTX727 en association avec venetoclax
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Ville	
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Statut	Actif en recrutement
Date d'activation	11-10-2023
But étude	The Phase 1 portion of this study is a single-arm, open-label, multicenter, non-randomized interventional study to evaluate the pharmacokinetic (PK) interaction, safety, and efficacy of ASTX727 when given in combination with venetoclax for the treatment of newly diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. The primary purpose of the study is to rule out drug-drug interactions between ASTX727 and venetoclax combination therapy by evaluating area under the curve (AUC) and maximum plasma concentration (Cmax) exposure. The Phase 2 portion of the study is to assess the efficacy of ASTX727 and venetoclax when given in combination and to evaluate potential PK interactions. Phase 2 will follow the same overall study design as Phase 1 and has two parts, Part A and Part B.
Critères d'éligibilité	• Participant must be 18 years of age or older. • Histological confirmation of newly diagnosed AML by World Health Organization (WHO) 2016 criteria. • Projected life expectancy of at least 3 months. • Participants must be considered ineligible for intensive induction chemotherapy defined by the following: a) Age 75 years or older, or b) Age 18 to 74 years with at least one of the following comorbidities: i) Severe cardiac disorder (eg, congestive heart failure requiring treatment, ejection fraction ≤50%, or chronic stable angina), ii) Severe pulmonary disorder (eg, diffusing lung capacity for carbon monoxide DLCO ≤65% or forced expiratory volume in 1 second [FEV1] ≤65%), iii) Creatinine clearance ≥30 mL/min to <45 mL/min, iv) Moderate hepatic impairment with total bilirubin >1.5 to ≤3.0 × upper limit of normal (ULN), v) Phase 1: Eastern Cooperative Oncology Group (ECOG) Performance Status of 2 (participants with ECOG ≥3 are not eligible); Phase 2, Parts A and B: ECOG Performance Status of 2 or 3 (participants with ECOG 4 are not eligible). • Phase 1: ECOG Performance Status of 0-2; Phase 2, Parts A and B: ECOG 0-3. • Women of child-bearing potential (according to recommendations of the Clinical Trial Facilitation Group [CTFG]) must not be pregnant or breastfeeding and must have a negative pregnancy test at screening.

	• Participants and their partners with reproductive potential must agree to use a highly effective contraceptive measure during the study and for 3 months after the last dose of study treatment, including refraining from sperm donation. Effective contraception includes methods such as oral contraceptives or double-barrier method (eg, use of a condom AND diaphragm, with spermicide). • Capable of giving legally effective informed consent, which includes compliance with the requirements and restrictions listed in the informed consent form and protocol, and willing to participate in the study.
Critères d'exclusion	• History of myeloproliferative neoplasm including myelofibrosis, essential thrombocythemia, polycythemia vera, chronic myeloid leukemia with or without BCR-ABL1 translocation and AML with BCR-ABL1 translocation. • The following karyotype abnormalities: t(8;21), inv(16) or t(15;17), or other acute promyelocytic leukemia variants that remain sensitive to all-trans retinoic acid (ATRA) therapy. • Known active central nervous system involvement from AML. • Known human immunodeficiency virus (HIV) infection (due to potential drug-drug interactions between antiretroviral medications and venetoclax). Human immunodeficiency virus testing will be performed at Screening, only if indicated per local guidelines or institutional standards. • Known active hepatitis B or C infection (detectable viral load). Hepatitis B or C testing will be performed at Screening, only if indicated per local guidelines or institutional standards. • Severe hepatic impairment defined as: bilirubin >1.5×upper limit of normal (ULN) for participants ≥75 years or >3×ULN for participants <75 years; or aspartate aminotransferase (AST)/serum glutamic oxaloacetic transaminase (SGOT) or alanine aminotransferase (ALT)/serum glutamic pyruvic transaminase (SGPT) >3×ULN (unless considered to be due to leukemic organ involvement). • Severe renal impairment defined as: calculated creatinine clearance or glomerular filtration rate <30 mL/min. • A malabsorption syndrome or other condition that precludes enteral route of administration. • Cardiovascular disability status of New York Heart Association Class >2. Class 2 is defined as cardiac disease in which patients are comfortable at rest but ordinary physical activity results in fatigue, palpitations, dyspnea, or anginal pain. • Chronic respiratory disease that requires continuous oxygen, or significant history of renal, neurologic, psychiatric, endocrinologic, metabolic, immunologic, hepatic, cardiovascular disease, any other medical condition or known hypersensitivity to any of the study medications that in the opinion of the investigator would adversely affect his/her participating in this study. • Clinically significant uncontrolled systemic infection requiring therapy (viral, bacterial, or fungal). • History of other malignancies prior to study entry, with the exception of adequately treated in situ carcinoma of the breast or cervix uteri; localized basal cell carcinoma or squamous cell carcinoma of the skin; previous malignancy confined and surgically resected (or adequately treated and controlled with other modalities); and any early stage malignancy for which no definitive therapy is required. • White blood cell (WBC) count >25,000/μL (Hydroxyurea treatment is permitted to meet this criterion). • Treatment with the following: a) A hypomethylating agent (azacitidine or decitabine), or venetoclax including prior treatment for myelodysplastic syndrome (MDS), b) Chimeric Antigen Receptor (CAR)-T cell therapy, c) Investigational therapies for MDS or AML. • Participants who cannot discontinue concomitant prophylactic antifungal therapy with CYP3A inhibitor activity or other concomitant medications with moderate or strong CYP3A inhibitor activity ≥7 days or 5 half-lives, whichever is greater, prior to cycle 1 day 1 (C1D1). • Participants who cannot discontinue concomitant drugs that are strong CYP3A or P-gp inhibitors ≥7 days or 5 half-lives, whichever is greater, prior to C1D1. • Participants who cannot avoid concomitant drugs known as moderate or strong CYP3A inducers. • Current participation in another research study requiring interventions such as drug therapy or study procedures. • Known or suspected hypersensitivity to decitabine, cedazuridine, venetoclax, or any of their excipients. • Known significant mental illness or other condition such as active alcohol or other substance abuse or addiction that, in the opinion of the investigator, predisposes the participant to high risk of noncompliance with the protocol. • Participants who consume grapefruit, grapefruit products, Seville oranges (including marmalade containing Seville oranges) or starfruit ≤7 days prior to C1D1.