Essai Clinique

Généré le 09 mai 2025 à partir de

Titre	A Phase 3b, Multi-center, Open-label, Treatment Optimization Study of Oral Asciminib in Patients With Chronic Myelogenous Leukemia in Chronic Phase (CML-CP) Previously Treated With 2 or More Tyrosine Kinase Inhibitors.
Protocole ID	CABL001A2302
ClinicalTrials.gov ID	NCT04948333
Type(s) de cancer	Leucémie myéloïde chronique (LMC)
Phase	Phase III
Type étude	Clinique
Médicament	Asciminib
Institution	CHU DE QUEBEC – UNIVERSITE LAVAL HOPITAL DE L'ENFANT-JESUS 1401 18e Rue, Québec, QC, G1J 1Z4
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But étude	The purpose of the study is to optimize the treatment of asciminib in patients with chronic myelogenous leukemia in chronic phase (CML-CP) previously treated with 2 or more Tyrosine Kinase Inhibitors (TKIs). Patients for this study will be identified based on warning criteria and resistance definition following European Leukemia Network (ELN) 2020 recommendations. In addition, the study will investigate the use of two different posologies. For this, patients will receive asciminib 40 mg (twice-daily) BID or of 80 mg (once daily) once daily (QD).

Critères d'éligibilité	Male or female patients with a diagnosis of CML-CP ≥ 18 years of age Patients must meet all the following laboratory values at the screening visit:
	• < 15% blasts in peripheral blood and bone marrow
	• < 30% blasts plus promyelocytes in peripheral blood and bone marrow
	• < 20% basophils in the peripheral blood
	• ≥ 50 x 109/L (≥ 50,000/mm3) platelets
	• Transient prior therapy related thrombocytopenia (< 50,000/mm3 for ≤ 30 days prior to screening) is acceptable
	• No evidence of extramedullary leukemic involvement, with the exception of hepatosplenomegaly Prior treatment with a minimum of 2 prior TKIs (i.e. imatinib, nilotinib, dasatinib, bosutinib, radotinib or ponatinib) Warning or failure (adapted from the 2020 ELN Recommendations) or intolerance to the most recent TKI therapy at the time of screening
	• Warning is defined as:
	  • Three months after the initiation of treatment: BCR-ABL1 > 10% IS
	  • Six months after the initiation of treatment: BCR-ABL1 >1-10% IS
	  • Twelve months after the initiation of treatment BCR-ABL1>0,1-1% IS
	  • At any time after the initiation of therapy BCR-ABL1 >0.1-1% IS, loss of MMR (>0.1% with 5-fold increase of BCR-ABL1 transcripts).
	• In addition, patients with failure of treatment according to the ELN 2020 recommendations will be eligible:
	  • Three months after the initiation of treatment: BCR-ABL1 > 10% IS if confirmed within 1-3 months
	  • Six months after the initiation of treatment: BCR-ABL1 >10% IS
	  • Twelve months after the initiation of treatment BCR-ABL1 >1% IS

	• At any time after the initiation of therapy BCR-ABL1 >1% IS, emergence of resistance mutations, high-risk ACA
	• Intolerance is defined as:
	  • Non-hematologic intolerance: Patients with grade 3 or 4 toxicity while on therapy, or with persistent grade 2 toxicity, unresponsive to optimal management, including dose adjustments (unless dose reduction is not considered in the best interest of the patient if response is already suboptimal)
	  • Hematologic intolerance: Patients with grade 3 or 4 toxicity (absolute neutrophil count [ANC] or platelets) while on therapy that is recurrent after dose reduction to the lowest doses recommended by manufacturer

Critères d'exclusion	Known presence of the BCR-ABL1 T315I mutation at any time prior to study entry. Known history of AP/BC Previous treatment with a hematopoietic stem-cell transplantation Patient planning to undergo allogeneic hematopoietic stem cell transplantation Cardiac or cardiac repolarization abnormality, including any of the following:
	• History of myocardial infarction (MI), angina pectoris, coronary artery bypass graft (CABG) within 6 months prior to starting study treatment
	• Clinically significant cardiac arrhythmias (e.g., ventricular tachycardia), complete left bundle branch block, high-grade AV block (e.g., bifascicular block, Mobitz type II and third degree AV block, permanent pace maker)
	• QTcF at screening ≥450 msec (male patients), ≥460 msec (female patients)
	• Long QT syndrome, family history of idiopathic sudden death or congenital long QT syndrome, or any of the following:
	  • Risk factors for Torsades de Pointes (TdP) including uncorrected hypokalemia or hypomagnesemia, history of cardiac failure, or history of clinically significant/ symptomatic bradycardia
	  • Concomitant medication(s) with a "Known risk of Torsades de Pointes" (per www.crediblemeds.org/) that cannot be discontinued or replaced 7 days prior to starting study drug by safe alternative medication.
	  • Inability to determine the QTcF interval Severe and/or uncontrolled concurrent medical disease that in the opinion of the investigator could cause unacceptable safety risks or compromise compliance with the protocol (e.g. uncontrolled diabetes, active or uncontrolled infection, pulmonary hypertension) History of acute pancreatitis within 1 year of study entry or past medical history of chronic pancreatitis History of active ongoing acute or chronic liver disease Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception during dosing and for 3 days after last dose of asciminib.
	Other Inclusion/Exclusion criteria may apply.