Essai Clinique

Généré le 04 mai 2024 à partir de

Titre	A Modular Phase I/II, Open-label, Multicentre Study to Assess AZD4573 in Novel Combinations With Anti-cancer Agents in Patients With Advanced Haematological Malignancies
Protocole ID	D8230C00002
ClinicalTrials.gov ID	NCT04630756
Type(s) de cancer	Lymphome non-hodgkinien (LNH)
Phase	Phase I-II
Stade	Maladie avancée ou métastatique
Type étude	Clinique
Médicament	AZD4573 et acalabrutinib
Institution	CHU DE QUEBEC – UNIVERSITE LAVAL L'HOTEL-DIEU DE QUEBEC ET CRCEO 11 Côte du Palais, Québec, QC, G1R 2J6
Ville	
Investigateur principal	Dr Olivier Dumas
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Statut	Fermé
But étude	This is a modular, multicentre, open-label, non-randomised, Phase I/II, dose-setting and expansion study including an intra-participants dose ramp up. AZD4573 will be administered intravenously, in novel combinations with anti-cancer agents, to participants with relapsed/refractory (r/r) haematological malignancies.
Critères d'éligibilité	**Core** • Participant must be ≥ 18 years of age at the time of signing the informed consent. • Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 2. • Must have received at least one prior line of therapy for the treatment of current disease and a clinical study is the best option for next treatment based on prior response and/or tolerability. • Documented active disease requiring treatment that is r/r defined as: Recurrence of disease after response to at least one prior line(s) of therapy or Progressive disease after completion of or on the treatment regimen preceding entry into the study or Disease that did not achieve an objective response (CR or PR). • Adequate haematological function. • Adequate organ function at Screening. • Uric acid level < upper limit of normal (ULN). **Module 1** - Participants with histologically confirmed, r/r DLBCL, or r/r MZL, for whom a clinical study is the best option for next treatment based on response and/or tolerability to prior lines of therapy.**PART A** • Patients with r/r DLBCL, including subtypes such as DLBCL not otherwise specified [NOS], high-grade B cell lymphoma [HGBCL], primary mediastinal large B-cell lymphoma [PMBCL], or large B cell lymphoma transformed from indolent B-cell lymphomas (including but not limited to Richter Syndrome, transformed Follicular Lymphoma, transformed MZL), or r/r MZL,: patients with r/r MZL are eligible as well. In case fresh tumor biopsy is not available, archival tumor samples are acceptable, if done with 24 months **PART B** • Patients with r/r de novo r/r DLBCL only, fresh tumor biopsy, done at screening or within 60 days before planned 1st dosing, unless there was any anticancer treatment given after tumor biopsy, but prior initiated study treatment.

- Presence of radiographically measurable lymphadenopathy or extranodal lymphoid malignancy.
- Participants must have failed at least two prior therapies for the treatment of current disease. Patients shall not be eligible for curative treatment options, and have no standard therapy available.
- Adequate haematologic function at screening: No growth factor support within 14 days prior to the date of the screening laboratory assessment; No transfusions within 7 days prior to the date of the screening laboratory assessment.
- Optional tumour biopsy on study: Participants are also encouraged to consent to and undergo an optional tumour biopsy at disease progression to support correlative biomarker studies.
- All participants must be willing and able to provide mandatory baseline bone marrow biopsy/aspirate.

Module 2 - Patients with histologically confirmed r/r MCL for whom a clinical study is the best option (in the opinion of the investigator) for next treatment based on response and/or tolerability to prior lines of therapy.**PART A**

- Patients with r/r MCL:
    - Diagnosis must be confirmed by biopsy and be immunohistologically characterised.
    - Tumour tissue must also be available for sending to AstraZeneca for pathology testing.
- Presence of radiographically measurable lymphadenopathy or extranodal lymphoid malignancy
- Patients must have failed at least one prior therapy for the treatment of current disease and not be eligible for curative treatment options.
- Adequate haematologic function at screening: No growth factor support within 14 days prior to the date of the screening laboratory assessment; No transfusions within 7 days prior to the date of the screening laboratory assessment.
- Optional tumour biopsy on study: Participants are also encouraged to consent to and undergo an optional tumour biopsy at disease progression to support correlative biomarker studies.
- All participants must be willing and able to provide mandatory baseline bone marrow biopsy/aspirate.

Critères d'exclusion

Core

- Participants with non-secretory myeloma.
- With the exception of alopecia and neutropenia, any unresolved non-haematological toxicities from prior therapy greater than Common Terminology Criteria for Adverse Events (CTCAE) Grade 1 at the time of starting study treatment.
- Presence of, or history of, central nervous system (CNS) lymphoma, leptomeningeal disease, or spinal cord compression.
- History of prior non-haematological malignancy except for the following: Malignancy treated with curative intent and with no evidence of active disease for >1 year before Screening and felt to be at low risk for recurrence by treating physician; Adequately treated lentigo maligna melanoma without evidence of disease or adequately controlled non-melanomatous skin cancer; Adequately treated carcinoma in situ without current evidence of disease.
- Any evidence of severe or uncontrolled systemic disease (eg, severe hepatic impairment, interstitial lung disease), or current unstable or uncompensated respiratory or cardiac conditions, or uncontrolled hypertension, history of, or active, bleeding diatheses or uncontrolled active systemic fungal, bacterial, viral, or other infection, or IV anti infective treatment within two weeks before first dose of study drug.
- Known history of infection with human immunodeficiency virus (HIV).
- Serologic status reflecting active hepatitis B or C infection.
- Any of the following cardiac criteria: Resting QT interval corrected using Fridericia's formula (QTcF) ≥ 470 msec obtained from a single electrocardiogram (ECG); any clinically important abnormalities in rhythm (except for participants with a pacemaker in place), conduction or morphology of resting ECG); any factors that increase the risk of QTc prolongation or risk of arrhythmic events such as heart failure, congenital long QT syndrome, family history of long QT syndrome or unexplained sudden death under 40 years of age. Concomitant medications known to prolong QTc should be used with caution and cannot be used starting with the first dose of study drug and through the DLT-assessment period (Part A) or during the scheduled ECG assessments.
- History of severe allergic or anaphylactic reactions to BH3 mimetics or history of hypersensitivity to active or inactive excipients of study treatment.
- Documented confirmation and ongoing treatment of adrenal gland insufficiency or pancreatitis.
- History, within the previous 6 months prior to first dose, of: coronary artery bypass graft; angioplasty; vascular stent; myocardial infarction; angina pectoris; congestive heart failure (New York Heart Association Class ≥ 2); ventricular arrhythmias requiring continuous therapy; atrial fibrillation, which is judged as uncontrolled by the treating physician; haemorrhagic or thrombotic stroke, including transient ischaemic attacks or any other CNS bleeding.

Module 1

- Prior Bruton's tyrosine kinase (BTK) inhibitor treatments for patients with r/r DLBCL. Prior BTK inhibitor treatment is allowed in patients with r/r MZL
- Current refractory nausea and vomiting, malabsorption syndrome, disease significantly affecting gastrointestinal function, stomach resection, extensive small bowel resection that is likely to affect absorption, symptomatic inflammatory bowel disease, bowel obstruction, or gastric restrictions and bariatric surgery.
- Prior use of standard anti-lymphoma therapy or radiation therapy within 14 days of receiving

the first dose of study treatment.
- Requires treatment with strong CYP3A inhibitors or inducers.
- Requires treatment with proton-pump inhibitors. Participants receiving proton-pump inhibitors who switch to H2-receptor antagonists or antacids are eligible for enrolment to this study.
- Serologic status reflecting active hepatitis B or C infection.
- Active Cytomegalovirus (CMV) infection.
- Requires or receiving therapeutic anticoagulants, with the exception of short-acting heparins, within 7 days of first dose of study treatment.
- Participants on dual antiplatelet and therapeutic anticoagulant therapy.
- Requires or receiving anticoagulation with warfarin or equivalent vitamin K antagonists.
- History of or ongoing confirmed progressive multifocal leukoencephalopathy

Module 2

- Current refractory nausea and vomiting, malabsorption syndrome, disease significantly affecting gastrointestinal function, stomach resection, extensive small bowel resection that is likely to affect absorption, symptomatic inflammatory bowel disease, partial or complete bowel obstruction, or gastric restrictions and bariatric surgery.
- Prior use of standard anti-lymphoma therapy or radiation therapy within 14 days of receiving the first dose of study treatment.
- Requires or receiving anticoagulation with warfarin or equivalent vitamin K antagonists.
- Requires treatment with strong CYP3A inhibitors or inducers.
- Requires treatment with proton-pump inhibitors. Participants receiving proton-pump inhibitors who switch to H2-receptor antagonists or antacids are eligible for enrolment to this study.
- Serologic status reflecting active hepatitis B or C infection.
- Active CMV infection.
- Requires or receiving therapeutic anticoagulants, with the exception of short-acting heparins, within 7 days of first dose of study treatment.
- Participants on dual antiplatelet and therapeutic anticoagulant therapy.
- History of or ongoing confirmed progressive multifocal leukoencephalopathy