Essai Clinique

Généré le 04 mai 2024 à partir de

Titre	Étude de phase I/II évaluant le TAK-981 en association avec le rituximab chez des patients atteints d'un lymphome non hodgkinien récidivant ou réfractaire positif pour l'antigène CD20
Protocole ID	TAK-981-1501
ClinicalTrials.gov ID	NCT04074330
Type(s) de cancer	Lymphome non-hodgkinien (LNH)
Phase	Phase I-II
Stade	Récidivant/réfractaire (2ième ligne de traitement et plus)
Type étude	Traitement
Médicament	TAK-981 avec Rituximab
Institution	CENTRE HOSPITALIER DE L'UNIVERSITE DE MONTREAL
Ville	
Investigateur principal	Dr Stéphane Doucet
Coordonnateur	Adeline Hamon 514-890-8000 poste 30737
Statut	Fermé
But étude	The drug being tested in this study is called TAK-981 in combination with rituximab. The study will determine the safety, tolerability and efficacy of TAK-981 in combination with rituximab in participants with r/r CD20+ NHL. The study will include a dose escalation phase (Phase 1b) and an open label study (Phase 2).The study will enroll approximately 90 participants, approximately 34 participants in Phase 1b and approximately 56 participants in Phase 2. The phase 1b will identify the maximum tolerated dose (MTD) and/or pharmacologically active dose (PAD). In the dose escalation phase, the starting dose of TAK-981 will be 3 mg, however, a starting dose of TAK-981 that is greater than (>) 3 mg may be considered if emerging preliminary safety experience from the ongoing TAK-981-1002 single agent study supports it. The starting dose level will be escalated based on available safety, PK and pharmacodynamic data, and after any early antitumor activity is observed. Participants in the Phase 2b will be enrolled once the Phase 1b of the study is completed, and MTD and/or PAD is determined. Participants in Phase 2 will be enrolled in 2 treatment arms: indolent non-Hodgkin lymphoma (iNHL) and aggressive non-Hodgkin lymphoma (aNHL).This multi-center trial will be conducted in the United States and Canada. The overall time to participate in this study is approximately 36 months. Participants will make multiple visits to the clinic, and will attend the end of treatment (EOT) visit 30 days after receiving their last dose of drug or before the start of subsequent systemic anticancer therapy, whichever occurs first for a follow-up assessment.
Critères d'éligibilité	• Each participant must meet all the following inclusion criteria to be enrolled in the study: • CD20+ aNHL include mantle cell lymphoma (phase 1b only) and diffuse large B-cell lymphoma (DLBCL) histologies such as transformed DLBCL from low-grade lymphoma (follicular or others), DLBCL associated with small-cell infiltration in bone marrow, CD20+ B-cell lymphoma with intermediate features between DLBCL and Burkitt's lymphoma or with intermediate features between DLBCL and Hodgkin lymphoma, follicular lymphoma grade 3B, and CD20+ aggressive B-cell lymphoma unclassifiable who must have previously received rituximab, cyclophosphamide, doxorubicin (hydroxydaunorubicin), vincristine, (Oncovin) and prednisone (R-CHOP) (or equivalent anti-CD20 containing therapy) and 1 additional line of therapy in the r/r setting. • CD20+ iNHL (including follicular lymphoma of grades 1-3A and marginal zone lymphoma) refractory to rituximab or to any other anti-CD20 monoclonal antibodies, who have received at least 1 prior systemic therapy for r/r iNHL:

	• Rituximab or anti-CD20 refractoriness is defined as failure to respond to, or progression during, any previous rituximab/anti-CD20-containing regimen (monotherapy or combined with chemotherapy), or progression within 6 months of the last rituximab or anti-CD20 dose. • The minimum qualifying rituximab/anti-CD20 dose is 1 full cycle (that is, weekly*4 doses monotherapy or 1 complete dose if combined with chemotherapy). • Prior anti-CD20 antibody or cytotoxic drugs may have been administered as single agents or as components of combination therapies. Each repeated course of the same single-agent or combination is considered an independent regimen. • Must be ineligible or refused autologous or allogenic hematopoietic stem cell transplantation or Chimeric Antigen Receptor (CAR) T-cell therapy. • Eastern Cooperative Oncology Group (ECOG) performance score of less than or equal to (<=) 2. • Adequate bone marrow function per local laboratory reference range at screening as follows: • Platelet count >=75.0*10^9/L, Grade 2 thrombocytopenia (platelet count >=50.0*10^9 per liter [/L]) is allowed if it is clearly due to marrow involvement with no evidence of myelodysplastic syndrome or hypoplastic bone marrow if found. Absolute neutrophil count (ANC) >=1.0*10^9/L. Hemoglobin >=85 gram per liter (g/L) (red blood cell [RBC] transfusion allowed >=14 days before assessment). • Adequate renal and hepatic function, per local laboratory reference range at screening as follows: • Calculated creatinine clearance >=45 milliliter per minute (mL/min) using measured 24-hour creatinine clearance or calculated with modified Cockcroft-Gault formula. Participants can be enrolled based only on calculated glomerular filtration rate; however, if creatinine clearance is measured, this value must be used for inclusion. • Aspartate aminotransferase and alanine aminotransferase <=3.0*the upper limit of normal (ULN) of the institution's normal range; bilirubin <=1.5*ULN. Participants with Gilbert's syndrome may have a bilirubin level >1.5*ULN, per discussion between the investigator and the medical monitor. • Left ventricular ejection fraction (LVEF) >=40 percent (%); as measured by ECG or multiple gated acquisition scan (MUGA). • Suitable venous access for safe drug administration and the study-required PK and pharmacodynamic sampling. • Have at least 1 bidimensionally measurable lesion per Lugano Classification (>1.5 centimeter [cm] in its largest dimension) by computed tomography (CT) that has not been previously irradiated. In the phase 2 portion of the study >1 measurable lesions are required, 1 for biopsy, and 1 for response. • Willing to consent to 1 mandatory pretreatment and 1 on-treatment skin biopsy during phase 1b and 1 mandatory pretreatment and 1 on-treatment skin and tumor biopsies during phase 2. The skin biopsy entry requirement may be discontinued by the sponsor once there is enough pharmacodynamic evidence of target engagement. • Recovered to Grade 1, baseline or established as sequela, from all toxic effects of previous therapy (except alopecia, neuropathy, autoimmune endocrinopathies with stable endocrine replacement therapy, neurotoxicity [Grade 1 or 2 permitted], or bone marrow parameters [any of Grade 1, 2, permitted if directly related to bone marrow involvement]).
Critères d'exclusion	Participants meeting any of the following exclusion criteria are not to be enrolled in the study: • CNS lymphoma; active brain or leptomeningeal metastases, as indicated by positive cytology from lumbar puncture or CT scan/magnetic resonance imaging (MRI). • History of Grade >=3 infusion-related reaction (IRR) that lead to permanent discontinuation of previous rituximab treatment. • Posttransplantation lymphoproliferative disease except relapsed NHL after autologous stem cell transplantation. • Prior allogeneic hematopoietic stem-cell transplantation. • Lymphomas with leukemic expression. • Prior anticancer therapy including chemotherapy, hormonal therapy, or investigational agents within 2 weeks or within at least 5 half-lives before TAK-981 dosing (up to a maximum of 4 weeks), whichever is shorter. Low dose steroids (oral prednisone or equivalent <=20 mg per day), hormonal therapy for prostate cancer or breast cancer (in adjuvant situation), and treatment with bisphosphonates and receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitors are allowed. • Major surgery within 14 days before the first dose of study drug and not recovered fully from any complications from surgery. • Significant medical diseases or conditions, as assessed by the Investigators and Sponsor that would substantially increase the risk-benefit ratio of participating in the study. This includes but is not limited to acute myocardial infarction or unstable angina within the last 6 months, uncontrolled diabetes mellitus, significant active bacterial, viral or fungal infections, severely immunocompromised state, severe non-compensated hypertension and congestive heart failure New York Heart Association Class III or IV, ongoing symptomatic cardiac arrhythmias of >Grade 2, pulmonary embolism, or symptomatic cerebrovascular events, or any other serious cardiac condition (example, pericardial effusion or restrictive cardiomyopathy). Chronic atrial fibrillation on stable anticoagulant therapy is allowed. • Known chronic hepatitis C and/or positive serology (unless due to vaccination or passive immunization due to immunoglobulin (Ig) therapy) for chronic hepatitis B. Known Human Immunodeficiency Virus (HIV) infection. • Second malignancy within the previous 3 years, except treated basal cell or localized squamous skin carcinomas, localized prostate cancer, cervical carcinoma in situ, resected colorectal adenomatous polyps, breast cancer in situ, or other malignancy for which the participant is not

on active anticancer therapy.
- Receipt of any live vaccine (example, varicella, pneumococcus) within 4 weeks of initiation of study treatment.
- Active, uncontrolled autoimmune disease requiring >20 mg of prednisone or equivalent, cytotoxics or biologicals.
- Corticosteroid use within 1 week before the first dose of study drug, except as indicated for other medical conditions such as inhaled steroid for asthma, topical steroid use, or as premedication for administration of study drug or contrast. Participants requiring steroids at daily doses >20 mg prednisone equivalent systemic exposure daily, or those who are administered steroids for lymphoma control or white blood cell count lowering are not eligible.
- Participants with baseline prolongation of the Fridericia-corrected QT interval (example, repeated demonstration of QTc interval >480 millisecond (ms), history of congenital long QT syndrome, or torsades de pointes).
- Receiving or requiring the continued use of medications that are known to be strong or moderate inhibitors and inducers of Cytochrome P450 3A4/5b (CYP3A4/5 b) and strong P-glycoprotein (Pgp) inhibitors. To participate in this study, such participants should discontinue use of such agents for at least 2 weeks (1 week washout for CYP3A4/5 inhibitors, and 2 weeks washout if using CYP3A4/5 inducers) before receiving a dose of TAK-981.