Essai Clinique

Généré le 19 mai 2024 à partir de

Titre	A Multi-Center, Open-Label, Single-Arm Phase II Trial of Bendamustine, Rituximab and the Second Generation BTK Inhibitor Acalabrutinib in Previously Untreated Waldenstrom's Macroglobulinemia
Protocole ID	BRAWM
ClinicalTrials.gov ID	NCT04624906
Type(s) de cancer	Lymphome non-hodgkinien (LNH)
Phase	Phase II
Type étude	Clinique
Médicament	Bendamustine, Rituximab et Acalabrutinib
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	
Investigateur principal	Dr Chaim Shustik Dr Michael Sebag
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Statut	Actif en recrutement
But étude	This is a multi-centre, open label, single-arm, phase II clinical trial in untreated patients with Waldenstrom's Macroglobulinemia. Symptomatic, previously untreated patients will receive SOC bendamustine and rituximab for 6 28-day cycles. Bendamustine will be given intravenously at 90 mg/m2 on days 1 and 2 of each cycle. Rituximab will be given on day 1 of each cycle (375 mg/m2 intravenously for the first cycle and 1400 mg subcutaneously OR 375 mg/m2 intravenously for subsequent cycles (as per institutional procedures)). Concomitantly, participants will receive 100 mg of the investigational product, Acalabrutinib, orally for 1 year (365 days) at 100 mg BID.
Critères d'éligibilité	• Have biopsy proven Waldenstrom's macroglobulinemia (biopsy from within 3 months (+/- 7 days) prior to Day 1). • Have not received any systemic treatment for the disease (plasmapheresis, involved field radiation or corticosteroids are allowed (as premedication or for contrast enhanced studies)). • Be willing and able to provide written informed consent for the trial. • Male or female greater than 18 years of age on day of signing informed consent and of any racial or ethnic group. • Have at least one measurable site of disease based on Cheson Criteria using standard CT imaging or a quantifiable IgM paraprotein that is two times the upper limit of normal. • Have symptomatic or impending symptomatic disease or evidence of hematologic or biochemical compromise related to the lymphoma. • Pathology sample must be available for molecular testing or otherwise be willing to provide tissue from a core biopsy prior to starting treatment. • Have a performance status of 0-1 on the ECOG Performance Scale. • Demonstrate adequate organ function as defined in Table 2 below. Adequate organ function should be confirmed within 48 hours prior to enrollment. Patients with abnormal liver enzymes of up to 5 times the upper limit of normal and/or reduced glomerular filtration rate (GFR) or estimated glomerular filtration rate (eGRF) of ≥ 30 mL/min/1.73 m2can be considered for enrolment. • A life expectancy > 6 months. • Female subject of childbearing potential should have a negative serum pregnancy test within 72 hours prior to receiving the first dose of study medication (day 0).

	• Female subjects of childbearing potential should be willing to use 2 highly effective methods of birth control or be surgically sterile, or abstain from heterosexual activity for the course of the study until 2 days post-last dose of acalabrutinib, 4 weeks post-last dose of bendamustine, and 12 months post-last dose of rituximab. Subjects of childbearing potential are those who have not been surgically sterilized or have not been free from menses for > 1 year. • Male subjects should agree to use a highly-effective method of contraception starting with the first dose of study therapy until 2 days post-last dose of acalabrutinib, 6 months post-last dose of bendamustine, and 12 months post-last dose of rituximab. study medication. • Ability to comply with protocol requirements.
Critères d'exclusion	• Previous systemic therapy for WM (other than described in the inclusion criteria). • Is currently participating and receiving study therapy or has participated in a study of an investigational agent and received study therapy or used an investigational device within 21 days of the first dose of treatment (SD0). • Patient is being planned for consolidative autologous stem cell transplant (ASCT). • Is on warfarin anti-coagulation or a proton pump inhibitor. • Has clinically significant cardiovascular disease such as uncontrolled or symptomatic arrhythmias, congestive heart failure, or myocardial infarction within 6 months of screening, or any Class 3 or 4 cardiac diseases as defined by the New York Heart Association Functional Classification, or corrected QT interval (QTc) > 480 msec at screening. Subjects with controlled, asymptomatic atrial fibrillation during screening can enroll on study. • Has difficult to control hypertension. • Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 35 days prior to the first dose of trial treatment (SD0), except that used as pre-medication for chemotherapy or contrast-enhanced studies are eligible. Subjects may be on physiologic doses of replacement prednisone or equivalent doses of corticosteroid (<10 mg daily). • Has a known history of active TB (Bacillus Tuberculosis). • Has a known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin or squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer. • Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate provided they are stable (without evidence of progression by imaging for at least four weeks prior to the first dose of trial treatment and any neurologic symptoms have returned to baseline), have no evidence of new or enlarging brain metastases, and are not using steroids for their CNS disease for at least 35 days prior to trial treatment. • Has history of active autoimmune disease that has required systemic immune suppressive treatment in the past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (eg., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is allowed. • Has known history of, or any evidence of active, non-infectious pneumonitis that has required treatment in the last five years. • Thyroiditis within the past 5 years. • Has an active infection requiring systemic therapy. Note: Subjects completing a course of antibiotic for acute infection 7 days prior to SD0 and who do not experience a recurrence of symptoms or fever are eligible. • Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the subject's participation for the full duration of the trial, or is not in the best interest of the subject to participate, in the opinion of the treating investigator. • Has known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial. • Is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the trial, starting with screening visit to 120 days post completion of study • Has a known history of Human Immunodeficiency Virus (HIV) (HIV 1/2 antibodies). • Has known active Hepatitis B (e.g., HBsAg reactive) or Hepatitis C (e.g., Hepatitis C Virus (HCV) RNA [qualitative] is detected). Evidence of Hepatitis B surface antigen or Hepatitis B DNA are exclusion criteria. Participants with positive hepatitis B core antibody (HBcAb) can be enrolled only if confirmatory negative Hepatitis B Virus (HBV) DNA levels is obtained by polymerase chain reaction (PCR) AND the patient is on Hepatitis B prophylaxis before the first dose of study drug. • Serious intercurrent chronic or acute illness, such as hepatic disease, or other illness considered by the investigator as an unwarranted high risk for an investigational product.