Essai Clinique

Généré le 02 mai 2024 à partir de

Titre	Étude de phase III internationale, multicentrique, à double insu et à répartition aléatoire comparant l'efficacité du zolbétuximab en association avec le protocole mFOLFOX6 à celle d'un placebo en association avec le protocole mFOLFOX6 comme traitement de première intention chez des sujets atteints d'un adénocarcinome de l'estomac ou de la jonction gastro-œsophagienne positif pour la protéine claudine (CLDN) 18,2 et négatif pour le récepteur HER2, localement avancé, non résécable ou métastatique
Protocole ID	8951-CL-0301
ClinicalTrials.gov ID	NCT03504397
Type(s) de cancer	Oesophage
Phase	Phase III
Stade	Stade localement avancé
Type étude	Traitement
Médicament	Zolbetuximab + mFOLFOX6 vs placebo + mFOLFOX6
Institution	CIUSSS DE L'OUEST-DE-L'ILE-DE-MONTREAL CENTRE HOSPITALIER DE ST. MARY 3830 av. Lacombe, Montréal, QC, H3T 1M5
Ville	
Investigateur principal	Dr Richard Dalfen
Coordonnateur	Natalia Gonzalez-Cardenas 514-345-3511 poste 5507
Statut	Fermé
But étude	A study of zolbetuximab (IMAB362) plus mFOLFOX6 versus placebo plus mFOLFOX6 in subjects with Claudin 18.2 positive, HER2-negative, locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinomaWhy is this study being done? SPOTLIGHT is a new clinical study for adult patients who have any of:advanced unresectable gastric or GEJ cancer metastatic gastric or GEJ cancer These types of cancers have a unique set of proteins (called Claudin 18.2). We may be able to use a treatment that targets the proteins to kill the cancer cells. For patients with one of the types of cancer listed above, mFOLFOX6 (a combination of three chemotherapies known as Oxaliplatin, Leucovorin, and Fluorouracil) is a current treatment option. This study is testing an experimental medicine called zolbetuximab (IMAB362). Zolbetuximab attaches itself to Claudin 18.2 on the cancer cells causing cancer cell death.Patients will be assigned to one of two groups by chance and given either:zolbetuximab with mFOLFOX6; or a placebo with mFOLFOX6 A placebo is a treatment that looks like the experimental medicine, but contains no medicine. The goal of the study is to find out if zolbetuximab with mFOLFOX6 helps patients to live longer by stopping the cancer from getting worse.
Critères d'éligibilité	• Female subject eligible to participate if she is not pregnant (negative serum pregnancy test at screening; female subjects with elevated serum beta human chorionic gonadotropin and a demonstrated non-pregnant status through additional testing are eligible) and at least one of the following conditions applies: • Not a woman of child-bearing potential (WOCBP) OR • WOCBP who agrees to follow the contraceptive guidance throughout the treatment period and for at least 6 months after the final study drug administration • Female subject must agree not to breastfeed starting at screening and throughout the study period, and for 6 months after the final study drug administration.

	• Female subject must agree not to donate ova starting at screening and throughout the study period, and for 6 months after the final study drug administration. • A sexually active male subject with a female partner(s) who is of child-bearing potential must agree to use contraception during the treatment period and for at least 6 months after the final study drug administration. • Male subject must agree not to donate sperm starting at screening and throughout the study period, and for 6 months after the final study drug administration. • Male subject with a pregnant or breastfeeding partner(s) must agree to remain abstinent or use a condom for the duration of the pregnancy or time partner is breastfeeding throughout the study period and for 6 months after the final study drug administration. • Subject has histologically confirmed diagnosis of Gastric or GEJ adenocarcinoma. • Subject has radiologically confirmed locally advanced unresectable or metastatic disease within 28 days prior to randomization. • Subject has radiologically evaluable disease (measurable and/or non-measurable disease according to RECIST 1.1), per local assessment, ≤ 28 days prior to randomization. For subjects with only 1 evaluable lesion and prior radiotherapy ≤ 3 months before randomization, the lesion must either be outside the field of prior radiotherapy or have documented progression following radiation therapy. • Subject's tumor expresses CLDN18.2 in ≥ 75% of tumor cells demonstrating moderate to strong membranous staining as determined by central immunohistochemistry (IHC) testing. • Subject has a HER2-Negative tumor as determined by local or central testing on a gastric or GEJ tumor specimen. • Subject has ECOG performance status 0 to 1. • Subject has predicted life expectancy ≥ 12 weeks. • Subject must meet all of the following criteria based on the centrally or locally analyzed laboratory tests collected within 14 days prior to randomization. In case of multiple laboratory data within this period, the most recent data should be used to determine eligibility. • Hemoglobin (Hgb) ≥ 9 g/dL. Subjects requiring transfusions are eligible if they have a post-transfusion Hgb ≥ 9 g/dL. • Absolute neutrophil count (ANC) ≥ 1.5 x 10^9/L • Platelets ≥ 100 x 10^9/L • Albumin ≥ 2.5 g/dL • Total bilirubin ≤ 1.5 x upper limit of normal (ULN) without liver metastases (or < 3.0 x ULN if liver metastases are present) • Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 2.5 x ULN without liver metastases (or ≤ 5 x ULN if liver metastases are present) • Estimated creatinine clearance ≥ 30 mL/min • Prothrombin time (PT)/international normalized ratio (INR) and partial thromboplastin time (PTT) ≤ 1.5 x ULN (except for subjects receiving anticoagulation therapy)
Critères d'exclusion	• Subject has received prior systemic chemotherapy for locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma. However, subject may have received either neo-adjuvant or adjuvant chemotherapy as long as it was completed at least 6 months prior to randomization. Subject may have received treatment with herbal medications that have known antitumor activity > 28 days prior to randomization. • Subject has received radiotherapy for locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma ≤ 14 days prior to randomization and has not recovered from any related toxicity. • Subject has received systemic immunosuppressive therapy, including systemic corticosteroids within 14 days prior to randomization. Subjects using a physiologic replacement dose of hydrocortisone or its equivalent (defined as up to 30 mg per day of hydrocortisone or up to 10 mg per day of prednisone), receiving a single dose of systemic corticosteroids or receiving systemic corticosteroids as premedication for radiologic imaging contrast use are allowed. • Subject has received other investigational agents or devices within 28 days prior to randomization. • Subject has prior severe allergic reaction or intolerance to known ingredients of zolbetuximab or other monoclonal antibodies, including humanized or chimeric antibodies. • Subject has known immediate or delayed hypersensitivity, intolerance or contraindication to any component of study treatment. • Subject has prior severe allergic reaction or intolerance to any component of mFOLFOX6. • Subject has known dihydropyrimidine dehydrogenase deficiency. • Subject has a complete gastric outlet syndrome or a partial gastric outlet syndrome with persistent/recurrent vomiting. • Subject has significant gastric bleeding and/or untreated gastric ulcers that would exclude the subject from participation. • Subject has a known history of a positive test for human immunodeficiency virus (HIV) infection or known active hepatitis B (positive hepatitis B surface antigen (HBs Ag)) or C infection. NOTE: Screening for these infections should be conducted per local requirements. • For subjects who are negative for HBs Ag, but hepatitis B core antibody (HBc Ab) positive, an HB deoxyribonucleic acid (DNA) test will be performed and if positive, the subject will be excluded. • Subjects with positive hepatitis C virus (HCV) serology, but negative HCV ribonucleic acid (RNA) test are eligible. • Subjects treated for HCV with undetectable viral load results are eligible. • Subject has an active autoimmune disease that has required systemic treatment within the past 3 months prior to randomization.

- Subject has active infection requiring systemic therapy that has not completely resolved within 7 days prior to randomization.
- Subject has significant cardiovascular disease, including any of the following:
- Congestive heart failure (defined as New York Heart Association Class III or IV), myocardial infarction, unstable angina, coronary angioplasty, stenting, coronary artery bypass graft, cerebrovascular accident (CVA) or hypertensive crisis within 6 months prior to randomization.
- History of clinically significant ventricular arrhythmias (i.e., sustained ventricular tachycardia, ventricular fibrillation or Torsades de Pointes)
- QTc interval > 450 msec for male subjects; QTc interval > 470 msec for female subjects
- History or family history of congenital long QT syndrome
- Cardiac arrhythmias requiring anti-arrhythmic medications (Subject with rate controlled atrial fibrillation for > 1 month prior to randomization are eligible).
- Subject has a history of central nervous system metastases and/or carcinomatous meningitis from gastric/GEJ cancer.
- Subject has known peripheral sensory neuropathy > Grade 1 unless the absence of deep tendon reflexes is the sole neurological abnormality.
- Subject has had a major surgical procedure ≤ 28 days prior to randomization.
- Subject is without complete recovery from a major surgical procedure ≤ 14 days prior to randomization.
- Subject has psychiatric illness or social situations that would preclude study compliance.
- Subject has another malignancy for which treatment is required.
- Subject has any concurrent disease, infection or comorbid condition that interferes with the ability of the subject to participate in the study, which places the subject at undue risk or complicates the interpretation of data.