Essai Clinique

Généré le 05 mai 2024 à partir de

Titre	Essai de phase II sur l'inhibition périopératoire de PD-L1 par l'avélumab et le schéma docétaxel, cisplatine et 5-fluorouracile (DCF) dans le traitement de l'adénocarcinome œsophagogastrique localement avancé résécable
Protocole ID	MS100070_0073
ClinicalTrials.gov ID	NCT03288350
Type(s) de cancer	Oesophage
Phase	Phase II
Stade	Localement avancé
Type étude	Traitement
Médicament	Avelumab et Docétaxel, Cisplatine et 5-Fluorouracil
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	
Investigateur principal	Dr Thierry Alcindor
Coordonnateur	Charlotte Abbou 514-934-1934
Statut	Fermé
But étude	This is a single-center, single-arm, open-label, Simon 2-stage, phase II trial in up to 55 patients with a potentially resectable, histologically-proven, adenocarcinoma or poorly differentiated carcinoma of the stomach, esophagogastric junction (EGJ), or lower third of the esophagus. Patients will receive neoadjuvant therapy consisting of 4 cycles of avelumab added to the modified chemotherapy regimen of docetaxel, cisplatin, 5- fluorouracil. Following surgery, pathologic response will be assessed. Patients will then receive adjuvant therapy consisting of 4 cycles of mDCF + avelumab. Patients will be followed to assess two-year disease-free survival rate. The primary objective of this study is to assess the effect on pathologic complete response rate (pCR) of adding avelumab to an mDCF regimen. The secondary objectives of this study are to determine the safety of adding avelumab to an mDCF regimen and assess its effect on two-year disease-free survival.
Critères d'éligibilité	• Signed, informed consent; • Age 18 years or older; • Histological diagnosis of adenocarcinoma or poorly differentiated carcinoma of the stomach, esophagogastric junction (EGJ), or lower third of the esophagus; • The tumour must be deemed by the team to be potentially resectable. This includes imaging studies (detailed below) to clinically stage the tumor and rule out the presence of metastatic disease, and includes a preoperative laparoscopic evaluation for gastric tumors only; • Stage IB (TINI only), II, IHA, IIIB; • Life expectancy greater than 3 months; • ECOG performance status of 0-1; • Neutrophils ~ 1500/µL; • Platelet count~ 100,000/µL; • Hemoglobin~ 9 g/dL; • Total bilirubin level :S 1.5 x the upper limit of normal (ULN) range unless consistent with Gilbert's syndrome (normal direct bilirubin); • AST and ALT :S 2.5 x ULN; • If serum creatinine above upper limit of normal (ULN), creatinine clearance ~ 60 ml/min as

	determined by 24-h creatinine clearance or Cockcroft-Gault formula; • Negative pregnancy test for women of child-bearing potential; and • Highly effective contraception for both male and female subjects throughout the study and for at least 60 days after last avelumab treatment administration if the risk of conception exists.
Critères d'exclusion	• Current or prior use of immunosuppressive medication, including corticosteroids, within 7 days prior to registration EXCEPT for the following: • intranasal, intra-ocular, inhaled, topical steroids, or local steroid injection (e.g., intraarticular injection); • Systemic corticosteroids at physiologic doses :S 10 mg/day of prednisone or equivalent; • Steroids as premedication for hypersensitivity reactions (e.g., CT scan premedication); • Active autoimmune disease that might deteriorate when receiving an immuno-stimulatory agent. However, patients with diabetes type I, vitiligo, psoriasis, hypo- or hyperthyroid disease not requiring immunosuppressive treatment are eligible; • Prior organ transplantation, including allogeneic stem cell transplantation; • Squamous-cell carcinoma diagnosis; • Significant acute or chronic active infections requiring systemic therapy, including, among others: • Known history of testing positive test for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS); • Positive test for HBV surface antigen and I or confirmatory HCV RNA (if anti-HCV antibody tested positive); • Vaccination with live vaccines within 4 weeks of the first dose of avelumab and while on trial; • Known severe hypersensitivity reactions to monoclonal antibodies (Grade 2: 3 NCI CTCAE v 4.03) or to any component in avelumab's formulation, any history of anaphylaxis, or uncontrolled asthma (that is, 3 or more features of partially controlled asthma); • Known severe hypersensitivity reaction to cisplatin, docetaxel, 5-FU or drugs formulated with polysorbate; • Clinically significant (i.e., active) cardiovascular disease: cerebral vascular accident/stroke (< 6 months prior to enrollment), myocardial infarction(< 6 months prior to enrollment), unstable angina, congestive heart failure (2: New York Heart Association Classification Class II), or serious cardiac arrhythmia requiring medication; • Persisting toxicity related to prior therapy (NCI CTCAE v. 4.03 Grade> 1); however, alopecia, sensory neuropathy Grade :S 2, or other Grade :S 2 not constituting a safety risk based on investigator's judgment are acceptable; • Other severe acute or chronic medical conditions including colitis, inflammatory bowel disease, pneumonitis, pulmonary fibrosis or psychiatric conditions including recent (within the past year) or active suicidal ideation or behavior; or laboratory abnormalities that may increase the risk associated with study participation or study treatment administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the patient inappropriate for entry into this study; • Known alcohol or drug abuse; • Prior systemic therapy for gastric cancer; • Prior exposure to antibodies directed at PD-1, PD-L 1, CTLA 4 antigens; • Pre-existing medical conditions precluding treatment, including any contraindication for major surgery; • Pregnancy or lactating mothers. Women of childbearing age must use contraception during and for 3 months following treatment; • ECOG performance status of 2 or higher; • Significant hearing impairment, as judged by the need for or use of a hearing aid. If there is any uncertainty regarding the degree of hearing impairment, an audiogram will be done. If the audiogram is grossly normal or shows only minor hearing impairment (i.e. not requiring hearing aid), the patient may be enrolled; • Unwillingness to undergo investigations and/or treatment as outlined on the study; or • Participation to another trial where an investigational drug is being used. • History of another malignancy requiring treatment within the last 3 years. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin treated curatively and in-situ cervical cancer.