Essai Clinique

Généré le 29 avr. 2024 à partir de

Titre	Étude de phase II à répartition aléatoire portant sur l'administration de cisplatine combinée à la radiothérapie versus durvalumab combinée à la radiothérapie suivie d'un traitement adjuvant par durvalumab versus durvalumab combinée à la radiothérapie suivie d'un traitement adjuvant par trémélimumab et durvalumab dans le cadre du traitement du carcinome épidermoïde oropharyngé avancé locorégional positif pour le VPH à risque intermédiaire
Protocole ID	HN.9
ClinicalTrials.gov ID	NCT03410615
Type(s) de cancer	ORL
Phase	Phase II
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	Montréal
Investigateur principal	Dr Nathaniel Bouganim
Coordonnateur	Stéphanie Mackenzie 514-934-1934 poste 34095
Statut	Fermé
But étude	Sometimes, cancer patients receive an initial treatment, followed by additional treatment to lower the chance of cancer coming back. The standard or usual treatment for this type of disease is initially having radiation therapy at the same time as chemotherapy (with a drug called cisplatin), with no additional therapy afterwards. This study is looking at whether a type of drug called durvalumab can be used with radiation during the initial treatment, (instead of cisplatin) and also afterwards as additional therapy. Durvalumab is an immunotherapy drug . It has been tested in many different types of cancers. Durvalumab works by allowing the immune system to detect the cancer and reactivate the immune response. This may help to slow down the growth of cancer or may cause cancer cells to die. Durvalumab has been shown to shrink tumours in animals. It has been studied in more than 5000 people, approved for use in other cancers and seems promising. This clinical trial will also test another type of immunotherapy drug called tremelimumab, which would also be given as additional treatment. Tremelimumab works in a different way to durvalumab to enhance the immune system reaction against cancer cells and may improve the effect of durvalumab. Tremelimumab may also help slow the growth of the cancer cells or may cause cancer cells to die. It has been shown to shrink tumours in animals. Tremelimumab has been studied in over 1200 people, approved for use in other cancers and seems promising. As of February 2019, tremelimumab will no longer be tested with new participants joining the study.
Critères d'éligibilité	• Histologically and/or cytologically confirmed (primary lesion or regional lymph nodes) squamous cell carcinoma of the oropharynx (OSCC) which is locoregionally advanced, intermediate risk and non-metastatic (M0) as defined by the following (UICC/AJCC 8th Edition staging) • T1-2 N1 (smokers); • T3 N0-N1 (smokers); • T1-3 N2 (any smoking hx). • Human papillomavirus (HPV)-related as determined by positive p16 immunohistochemical staining on any tumour specimens. Positive p16 expression is defined as strong and diffuse nuclear and cytoplasmic staining in 70% or more of the tumour cells. Local testing is acceptable; testing will not be done centrally in real-time. • Must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 (see Appendix I) and a body weight of > 30 kg. • The following radiological investigations must be done within 8 weeks of randomization: • CT or MRI of the head and neck (with PET-CT as indicated); • CT chest or x-ray, other radiology tests as clinically indicated. • Women/men of childbearing potential must have agreed to use a highly effective contraceptive

	method. • Patient must consent to provision of, and investigator(s) must confirm adequacy, of non-cytology tissue samples and confirm access to and agree to submit within 4 weeks of randomization to the CCTG Central Tumour Bank, a representative formalin fixed paraffin block of non-cytology tumour tissue in order that the specific correlative mark assays may be conducted. • Patient must consent to provision of samples of blood, saliva and oropharyngeal swab in order that the specific correlative marker assays may be conducted • Patient is able (i.e. sufficiently fluent) and willing to complete the quality of life and health economics questionnaires in the languages provided. • Patients must be accessible for treatment and follow-up. Patients registered on this trial must be treated and followed at the participating centre • In accordance with CCTG policy, protocol treatment (cisplatin/RT or durvalumab) is to begin within 1 week of randomization. • The patient is not receiving anti-cancer therapy in a concurrent clinical study testing new treatments or treatment strategies and the patient agrees not to participate in other clinical studies during their participation in this trial while on study treatment. • Adequate normal organ and marrow function as defined below (must be done within 14 days prior to randomization): Absolute neutrophils - ≥ 1.5 x 10^9/L; Platelets ≥100 x 10^9; Hemoglobin ≥90 g/L; Bilirubin ≤ 1.5 x UNL; AST and ALT ≤2.5 x UNL; Creatine clearance ≥ 60 mL/min. • Patient consent must be appropriately obtained in accordance with applicable local and regulatory requirements • Patients must be assessed by a radiation oncologist and medical oncologist and deemed suitable for study participation
Critères d'exclusion	• Patients with a history of other malignancies, except: adequately treated non-melanoma skin cancer, curatively treated in-situ cancer of the cervix, or other solid tumours curatively treated with no evidence of disease for ≥ 5 years. • Current history of other non-OSCC malignancies of the head and neck. • Any previous treatment with a PD1 or PD-L1 inhibitor, including durvalumab, or an anti-CTLA4, including tremelimumab. • Any previous cisplatin or carboplatin chemotherapy. • Any previous induction chemotherapy for current SCCHN. • Any previous surgical treatment of the current cancer (except for a diagnostic biopsy) and no major surgery within 28 days prior to randomization. • Any previous radiation to the head and neck region that would result in overlap of fields for the current study. • Peripheral neuropathy ≥ grade 2 (CTCAE v4.0). • Hearing loss/tinnitus ≥ grade 3 (CTCAE v4.0). • History of allergic or hypersensitivity reactions to any study drug or their excipients. • Mean QT interval corrected for heart rate using Fridericia's formula (QTcF) ≥ 470 msec in screening ECG measured using standard institutional method or history of familial long QT syndrome. • History of primary immunodeficiency, history of allogenic organ transplant that requires therapeutic immunosuppression and the use of immunosuppressive agents within 28 days of randomization* or a prior history of severe (grade 3 or 4) immune mediated toxicity from other immune therapy or grade ≥ 3 infusion reaction • Current or prior use of immunosuppressive medication within 28 days of study entry, with the exceptions of intranasal and inhaled corticosteroids or systemic chronic corticosteroids at physiological doses, which are not to exceed 10 mg/day of prednisone, or an equivalent corticosteroid. Corticosteroids used on study for anti-emetic purpose are allowed. Corticosteroids as premedication for hypersensitivity reactions (e.g. computed tomography [CT] scan premedication) are allowed. • Active or prior documented autoimmune or inflammatory disorders (including inflammatory bowel disease (e.g. colitis or Crohn's disease), diverticulitis with the exception of diverticulosis, celiac disease (controlled by diet alone) or other serious gastrointestinal chronic conditions associated with diarrhea), systemic lupus erythematosus, Sarcoidosis syndrome, or Wegener syndrome (granulomatosis with polyangiitis), rheumatoid arthritis, hypophysitis, uveitis, etc., within the past 3 years prior to the start of treatment. The following are exceptions to this criterion: • Patients with vitiligo or alopecia; • Patients with Grave's disease, vitiligo or psoriasis not requiring systemic treatment (within the last 2 years); • Patients with hypothyroidism (e.g. following Hashimoto syndrome) stable on hormone replacement; • Any chronic skin condition that does not require systemic therapy. • Patients with active or uncontrolled intercurrent illness including, but not limited to: • cardiac dysfunction (symptomatic congestive heart failure, uncontrolled hypertension, unstable angina pectoris, cardiac arrhythmia); • active peptic ulcer disease or gastritis; • active bleeding diatheses; • psychiatric illness/social situations that would limit compliance with study requirements or compromise the ability of the subject to give written informed consent; • known history of previous clinical diagnosis of tuberculosis; • known human immunodeficiency virus infection (positive HIV 1/2 antibodies); • known active hepatitis B infection (positive HBV surface antigen (HBsAg). Patients with a past

or resolved HBV infection (defined as presence of hepatitis B core antibody (anti-HBc) and absence of HBsAg) are eligible;
- known active hepatitis C infection. Patients positive for hepatitis C (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA.
- History of interstitial lung disease e.g. pneumonitis or pulmonary fibrosis or evidence of interstitial lung disease on baseline CT scan.
- Receipt of live attenuated vaccination (examples include, but are not limited to, vaccines for measles, mumps, and rubella, live attenuated influenza vaccine (nasal), chicken pox vaccine, oral polio vaccine, rotavirus vaccine, yellow fever vaccine, BCG vaccine, typhoid vaccine and typhus vaccine) within 30 days prior to randomization.
- Pregnant or lactating women
- Any active disease condition which would render the protocol treatment dangerous or impair the ability of the patient to receive protocol therapy.
- Any condition (e.g. psychological, geographical, etc.) that does not permit compliance with the protocol