Essai Clinique

Généré le 05 mai 2024 à partir de

Titre	Essai de phase II à répartition aléatoire évaluant le traitement trimodal avec ou sans traitement adjuvant par durvalumab pour traiter les patients atteints d'un cancer de la vessie à envahissement musculaire.
Protocole ID	BL13
ClinicalTrials.gov ID	NCT03768570
Type(s) de cancer	Vessie/urothélial
Phase	Phase II
Stade	Métastatique
Type étude	Traitement
Médicament	Durvalumab
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	Montréal
Investigateur principal	Dr Wassim Kassouf
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Statut	Fermé
But étude	This study is looking at whether a type of immunotherapy drug called durvalumab can be safely administered after initial treatment received by a patient. Durvalumab has been tested in many different types of cancers. Durvalumab works by allowing the immune system to detect cancer and reactivate the immune response. This may help to slow down the growth of cancer or may cause cancer cells to die. It is unclear if the addition of durvalumab is beneficial in patients with bladder cancer who have completed surgery, radiotherapy and chemotherapy.
Critères d'éligibilité	• Histologic diagnosis of urothelial carcinoma of the bladder. Patients with mixed histology and focal differentiation are eligible but patients with pure small cell histology will be excluded. • Stage T2-T4a N0M0 at time of diagnosis based on trans-urethral resection of bladder tumour, imaging, and/or bimanual examination under anesthesia. • CT scan of the chest/abdomen/pelvis within 8 weeks from enrollment, showing no evidence of metastatic disease. • Patients must be ≥ 18 years of age. • Patients must have a life expectancy greater than 6 months. • Patients must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 and a body weight of > 30kg. • Patients must have adequate hematologic reserve: Platelet count ≥ 75 x 10^9/L, Absolute neutrophils ≥ 1.0 x 10^9/L. Anemia will be corrected to minimum hemoglobin of 90 g/L with red cell transfusions, if necessary. • Patients must have an estimated creatinine clearance (Cockcroft-Gault Equation) ≥ 30 ml/min. • Patients must have adequate liver function with a bilirubin ≤ 1.5 ULN (if confirmed Gilbert's, eligible providing bilirubin ≤ 3 x UNL) and AST/ALT (SGOT/SGPT) < 2.5 x the upper normal limit. • All patients must have a tumour block from their primary tumour available and consent to release the block/cores/cut slides for correlative analyses (and the centre/pathologist must have agreed to the submission of the specimen(s). • Patients have completed prior trimodality therapy (TMT) consisting of surgery, chemotherapy and radiation therapy treatment prior to enrollment. Patient should start treatment within 42

	days after completion of TMT. • Patients have completed transurethral resection prior to study enrollment. • Patient may have completed up to 4 cycles of cisplatin-based neo-adjuvant chemotherapy. Adjuvant chemotherapy is not permitted. Patients will have received cisplatin, given intravenously during the radiation therapy. OR Patients may have received fluorouracil and mitomycin given intravenously once weekly or gemcitabine as an alternative to cisplatin during radiotherapy. • The following are radiotherapy guidelines for patients treated on study. Patients will be treated to radical treatment doses using IMRT, VMAT or 4 field conformal techniques. Planning will be based on CT planning. IGRT is recommended during the radiotherapy treatment. Recognizing differences in usual radiotherapy doses used in the various participating countries and centres the following would be acceptable doses in this study. The bladder CTV will include the whole empty bladder and any extravesical extension. PTV expansion will be a minimum of 0.75 cm right, left and inferiorly, 1.5 cm Anteriorly and superiorly and 1 cm posteriorly. These minimum expansions are with Cone beam verification. For patients undergoing RT without image-guided verification 1.5 cm expansion in all directions is recommended. Acceptable doses for this study include: • Bladder only: 64-66 Gy in 32-33 fractions over 6.5 weeks; 50-55 Gy in 20 fractions over 4 weeks • Pelvis and bladder: 45-46 Gy to pelvic nodes + 17-20 Gy bladder boost in 33-35 fractions over 6.5-7 wks [Note: minimal nodal dose (if used) is 44 Gy in 32f or 40 Gy in 20f] • Patients receiving concurrent bladder boost: pelvis dose 40 Gy and bladder dose 50 Gy given in 20 fractions over 4 weeks. Adaptive radiotherapy techniques would be acceptable. • Patient is able (i.e. sufficiently fluent) and willing to complete the quality of life questionnaires in either English or French. • Patient consent must be appropriately obtained in accordance with applicable local and regulatory requirements. Each patient must sign a consent form prior to enrollment in the trial to document their willingness to participate. • Patients must be accessible for treatment and follow up. Patients registered on this trial must be treated and followed at the participating centre. This implies there must be reasonable geographical limits placed on patients being considered for this trial. • In accordance with CCTG policy, protocol treatment is to begin within 2 working days of patient enrollment. • Women/men of childbearing potential must have agreed to use a highly effective contraceptive method during and for 3 months following treatment. • Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.
Critères d'exclusion	• Pre-existing medical conditions precluding treatment. • Pregnancy or lactating mothers. • Received prior therapy with an anti-programmed cell death protein 1 (anti-PD-1), anti-PD-L1, including durvalumab anti-programmed cell death-ligand 2 (anti-PD-L2), anti-CD137 (4-1BB ligand, a member of the Tumour Necrosis Factor Receptor [TNFR] family), or anti-Cytotoxic T-lymphocyte-associated antigen-4 (anti-CTLA-4) antibody (including ipilimumab or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways). • 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 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 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.
- Peripheral neuropathy ≥ grade 2 (CTCAE v5.0).
- 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 interstitial lung disease e.g. pneumonitis or pulmonary fibrosis or evidence of interstitial lung disease on baseline CT scan.
- 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.
- Live attenuated vaccination administered within 30 days prior to randomization.