Essai Clinique

Généré le 04 mai 2024 à partir de

Titre	Étude de phase III à répartition aléatoire sur le nivolumab (Opdivo) en association avec AVD ou sur le brentuximab védotine (Acdetris) en association avec AVD chez des patients (âgés de 12 ans et plus) atteints d'un lymphome de Hodgkin classique de stade avancé, nouvellement diagnostiqué
Protocole ID	HDC.1
ClinicalTrials.gov ID	NCT03907488
Type(s) de cancer	Hodgkin (Maladie de)
Phase	Phase III
Stade	Maladie avancée ou métastatique
Type étude	Clinique
Médicament	Nivolumab + AVD ou brentuximab védotine + AVD
Institution	CENTRE HOSPITALIER UNIVERSITAIRE SAINTE-JUSTINE
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But étude	Cet essai de phase III vise à comparer des médicaments utilisés en immunothérapie (nivolumab et brentuximab védotine), administrés en association avec une polychimiothérapie dans le traitement de patients atteints d'un lymphome de Hodgkin classique de stade III ou IV nouvellement diagnostiqué. L'immunothérapie au moyen d'anticorps monoclonaux, comme le nivolumab, peut aider le système immunitaire de l'organisme à attaquer le cancer et peut entraver la capacité des cellules tumorales à croître et à se propager. Le brentuximab védotine est composé d'un anticorps monoclonal, le brentuximab, lié à un agent toxique appelé védotine. Le brentuximab se fixe de manière ciblée aux cellules cancéreuses et libère la védotine pour détruire ces cellules. Les médicaments de chimiothérapie, comme la doxorubicine, la vinblastine et la dacarbazine, agissent de différentes manières pour arrêter la croissance des cellules cancéreuses, soit en tuant les cellules, soit en les empêchant de se diviser ou de se propager. L'ajout de nivolumab ou de brentuximab védotine à la polychimiothérapie pourrait faire régresser le cancer ou prolonger la période avant la réapparition des symptômes de la maladie.
Critères d'éligibilité	• All patients must have histologically confirmed newly diagnosed, previously untreated stage III or IV classical Hodgkin lymphoma (nodular sclerosing, mixed cellularity, lymphocyte-rich, or lymphocyte-depleted, or not otherwise specified [NOS]). Nodular lymphocyte predominant Hodgkin lymphoma is not eligible. • Patients must have bidimensionally measurable disease (at least one lesion with longest diameter >= 1.5 cm) documented on the Lymphoma Baseline Tumor Assessment Form in Rave. • Patients must have a whole body or limited whole body PET-CT scan performed within 42 days prior to registration. (A contrast-enhanced [diagnostic] CT, MRI or MR-PET is acceptable in event that PET-CT is contra-indicated, however if it is later possible to administer a PET-CT, then PET-CT is strongly preferred for the interim scan (after cycle 2) (if performed) and the EOT assessment. Otherwise, if PET-CT is not subsequently possible, then the same modality as baseline must be used throughout the trial.) NOTE: All images from PET-CT, CT, MRI or MR-PET scans performed as standard of care to assess disease (within 42 days prior to registration) must be submitted and associated radiology reports must be submitted. • Patients must not have received any prior chemotherapy, radiation, or antibody-based treatment for classical Hodgkin lymphoma. Steroid pre-treatment is permitted.

- Patients must not have had prior solid organ transplant.
- Patients must not have had prior allogeneic stem cell transplantation.
- Patients must not have received a live vaccine within 30 days prior to planned day 1 of protocol therapy (e.g. measles, mumps, rubella, varicella, yellow fever, rabies, Bacillus Calmette-Guerin [BCG], oral polio vaccine, and oral typhoid).
- At registration, investigator must declare intent-to-treat with residual PET radiation therapy (residual PET RT- RPRT) to be administered after patient completes 6 cycles of therapy if, after end of treatment, the patient meets criteria specified for receiving RT). Patients will be stratified by investigator's intent-to-treat with residual PET RT.
    - All pediatric patients (< 18 years of age) will be considered intent-to-treat with Residual PET RT at time of registration.
- Patients must have a performance status corresponding to Zubrod scores of 0, 1 or 2. Use Lansky for patients =< 17 years of age. *The conversion of the Lansky to Eastern Cooperative Oncology Group (ECOG) scales is intended for National Cancer Institute (NCI) reporting purposes only.
- Adults (age 18 or older): Creatinine clearance >= 30 mL/min, as estimated by the Cockcroft and Gault formula. The creatinine value used in the calculation must have been obtained within 28 days prior to registration. Estimated creatinine clearance is based on actual body weight.

Pediatric Patients (age 12-17), the following must have been obtained within 14 days prior to registration:

- Measured or calculated creatinine clearance or radioisotope glomerular filtration rate (GFR) >= 70 ml/min/1.73 m^2, or
- Serum creatinine =< 1.5 x institutional upper limit of normal (IULN), or a serum creatinine (SCr) based on age/gender as follows:
    - Age < 13 maximum serum creatinine: Male 1.2 mg/dL; Female 1.2 mg/dL
    - Age 13 to < 16 maximum serum creatinine: Male 1.5 mg/dL; Female 1.4 mg/dL
    - Age 16-17 maximum serum creatinine: Male 1.7 mg/dL; Female 1.4 mg/dL
        - Total bilirubin =< 2 x IULN (must be documented within 28 days prior to registration for adults [age 18 or older]; must be documented within 14 days prior to registration for pediatric patients [age 12-17]).
- Unless due to Gilbert's disease, lymphomatous involvement of liver or vanishing bile duct syndrome
    - Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) =< 3 x IULN (must be documented within 28 days prior to registration for adults [age 18 or older]; must be documented within 14 days prior to registration for pediatric patients [age 12-17]).
- Unless due to Gilbert's disease, lymphomatous involvement of liver or vanishing bile duct syndrome
    - Patients must have an echocardiogram (ECHO), multigated acquisition (MUGA), or functional cardiac imaging scan with a left ventricular ejection (LVEF) fraction >= 50% or a shortening fraction of >= 27%. For all patients, the ECHO, MUGA, or functional cardiac imaging scan must be performed within 42 days prior to registration.
    - Patients with known human immunodeficiency virus (HIV) infection must be receiving anti-retroviral therapy and have an undetectable or unquantifiable viral load at their most recent viral load test within 6 months prior to registration.
    - Patients must not have known active hepatitis B (HBV) or hepatitis C virus (HCV) at date of registration. Patients with previously treated HBV or HCV that have an undetectable viral load within 6 months prior to registration and no residual hepatic impairment are eligible.
    - Patients must not have any known central nervous system lymphoma.
    - Patients must not have a history of or active interstitial pneumonitis or interstitial lung disease.
    - Patients must not have had a diagnosis of inherited or acquired immunodeficiency.
    - Patients must not have any known uncontrolled intercurrent illness including, but not limited to symptomatic congestive heart failure, unstable angina pectoris, hemodynamically unstable cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
    - Patients must not have a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalents) or other immunosuppressive medications within 14 days prior to registration. Inhaled or topical steroids, and adrenal replacement doses > 10 mg daily prednisone equivalents are permitted in the absence of active autoimmune disease. Steroid use for the control of Hodgkin lymphoma symptoms is allowable, but must be discontinued prior to cycle 1, day 1.
    - Patients with peripheral neuropathy must have < grade 2 at date of registration.
    - Patients must not have active autoimmune disease that has required systemic treatment in past 2 years (i.e., with use of disease modifying agents, immunosuppressive drugs, or corticosteroids with doses higher than prednisone 10 mg or equivalent). Autoimmune diseases include but are not limited to autoimmune hepatitis, inflammatory bowel disease (including ulcerative colitis and Crohn's disease), as well as symptomatic disease (e.g.: rheumatoid arthritis, systemic progressive sclerosis [scleroderma], systemic lupus erythematosus, autoimmune vasculitis [e.g., Wegener's granulomatosis]); central nervous system (CNS) or motor neuropathy considered of autoimmune origin (e.g., Guillain-Barre syndrome and myasthenia gravis, multiple sclerosis or glomerulonephritis). Vitiligo, alopecia, hypothyroidism on stable doses of thyroid replacement therapy, psoriasis not requiring systemic therapy within the past 2 years are permitted.

	• No second prior malignancy is allowed except for adequately treated basal (or squamous cell) skin cancer, any in situ cancer or other cancer for which the patient has been disease free for two years. • Females of childbearing potential must not be pregnant or nursing, and have a negative pregnancy test within 28 days prior to registration. Women/men of reproductive potential must have agreed to use an effective contraceptive method while receiving study drug and for women until 6 months after receiving the last dose of study drug or, for men, until 7 months after receiving the last dose of study drug. A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures. • Patients must have one formalin-fixed paraffin embedded (FFPE) diagnostic tumor block or at least 1 diagnostic, 4-5 micron, hematoxylin and eosin (H&E) slide collected prior to registration and available for submission. • Patients must be offered participation in banking for planned translational medicine and future research. With patient consent, any residuals from the mandatory tissue submission will also be banked for future research. • Patients who can complete Patient-Reported Outcome instruments in English, Spanish, or French must complete the PROMIS Fatigue, the FACT/GOG-Ntx, and the PROMIS Global prior to registration. • Patients who can complete Patient-Reported Outcome instruments in English, Spanish, or French must also agree to complete the PROMIS Fatigue, the FACT/GOG-Ntx, the PROMIS Global, and the PRO-CTCAE (or Ped PRO-CTCAE) at the scheduled on-study assessment timepoints. • Patients must be informed of the investigational nature of this study and all patients and/or their parents or legal guardians (for patients < 18 years of age) must sign and give informed consent and assent (where appropriate) in accordance with institutional and federal guidelines. For participants with impaired decision-making capabilities, legally authorized representatives may sign and give informed consent on behalf of study participants in accordance with applicable federal, local, and Central Institutional Review Board Initiative (CIRB) regulations. • Note: As a part of the Oncology Patient Enrollment Network (OPEN) registration process the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.
Critères d'exclusion	