Essai Clinique

Généré le 21 mai 2024 à partir de

Titre	A Phase III Trial of Gleostine® (Lomustine)-Temozolomide Combination Therapy Versus Standard Temozolomide in Patients With Methylated MGMT Promoter Glioblastoma
Protocole ID	NRG-BN011
ClinicalTrials.gov ID	NCT05095376
Type(s) de cancer	Cerveau (SNC)
Phase	Phase III
Type étude	Clinique
Médicament	Lomustine-Temozolomide versus Temozolomide seul
Institution	CENTRE HOSPITALIER DE L'UNIVERSITE DE MONTREAL
Ville	
Investigateur principal	Dr Jean-Paul Bahary
Coordonnateur	Mom Phat 514-890-8000 poste 11171
Statut	Actif en recrutement
Date d'activation	08-12-2023
But étude	This phase III trial compares the effect of adding lomustine to temozolomide and radiation therapy versus temozolomide and radiation therapy alone in shrinking or stabilizing newly diagnosed MGMT methylated glioblastoma. Chemotherapy drugs, such as lomustine and temozolomide, work in different ways to stop the growth of tumor cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. Radiation therapy uses high energy photons to kill tumor cells and shrink tumors. Adding lomustine to usual treatment of temozolomide and radiation therapy may help shrink and stabilize glioblastoma
Critères d'éligibilité	**STEP 1 REGISTRATION** • No known IDH mutation. (If tested before step 1 registration, patients known to have IDH mutation in the tumor on local or other testing are ineligible and should not be registered) • Availability of formalin-fixed paraffin-embedded (FFPE) tumor tissue block and hematoxylin and eosin (H&E) stained slide to be sent for central pathology review for confirmation of histology and MGMT promoter methylation status. Note that tissue for central pathology review and central MGMT assessment must be received by the NYU Center for Biospecimen Research and Development (CBRD) on or before postoperative calendar day 30. If tissue cannot be received by postoperative calendar day 30, then patients may NOT enroll on this trial as central pathology review will not be complete in time for the patient to start treatment no later than 8 weeks following surgery. Results of central pathology review and central MGMT analysis will generally be conveyed to NRG Oncology within 10 business days of receipt of tissue. Note: In the event of an additional tumor resection(s), tissue must be received within 30 days of the most recent resection and the latest resection must have been performed within 30 days after the initial resection. Surgical resection is required; stereotactic biopsy alone is not allowed because it will not provide sufficient tissue for MGMT analysis • Contrast-enhanced brain MRI after surgery • Willing to use highly effective method of contraception for participants of childbearing potential (participants who may become pregnant or who may impregnate a partner) during therapy and for 6 months after completing treatment; this inclusion is necessary because the treatment in this study may be significantly teratogenic • The patient or a legally authorized representative must provide study-specific informed consent prior to study entry and, for patients treated in the United States (U.S.), authorization permitting

release of personal health information

STEP 2 REGISTRATION

- Histopathologically proven diagnosis of glioblastoma (or gliosarcoma as a subtype of glioblastoma) confirmed by central pathology review
- MGMT promoter with methylation confirmed by central pathology review (See Section 10 for details). Note: Patients with tissue that is insufficient or inadequate for analysis, fails MGMT testing, or has indeterminate or unmethylated MGMT promoter are excluded.
- IDH mutation testing by at least one method (such as immunohistochemistry for IDH1 R132H) must be performed as part of standard of care and no mutation must be found (i.e IDH wildtype). (If a mutation is identified then the patient will be ineligible and must be registered as ineligible at Step 2.)
- History/physical examination within 28 days prior to Step 2 registration
- Karnofsky performance status (KPS) >= 70 within 28 days prior to Step 2 registration
- Neurologic function assessment within 28 days prior to Step 2 registration
- Age 18-70 years

Adequate hematologic, renal, and hepatic function within 14 days prior to STEP 2 REGISTRATION defined as follows:

- Hemoglobin >= 10 g/dl (Note: the use of transfusion or other intervention to achieve hemoglobin (Hgb) >= 10.0 g/dl is acceptable)
- Leukocytes >= 2,000/mm^3
- Absolute neutrophil count >= 1,500/mm^3
- Platelets >= 100,000/mm^3
- Total bilirubin =< 1.5 x institutional/lab upper limit of normal (ULN)
- Aspartate aminotransferase (AST) (serum glutamic-oxaloacetic transaminase [SGOT]) =< 2.5 x ULN
- Alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase [SGPT]) =< 2.5 x ULN
- Serum creatinine =< 1.5 x ULN OR creatinine clearance (CrCl) >= 50 mL/min (if using the Cockcroft-Gault formula
- For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated
    - Note: Known positive test for hepatitis B virus surface antigen (HBV sAg) indicating acute or chronic infection would make the patient ineligible unless the viral load becomes undetectable on suppressive therapy. Patients who are immune to hepatitis B (anti-hepatitis B surface antibody positive) are eligible (e.g. patients immunized against hepatitis B)
- For patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load
    - Note: Known positive test for hepatitis C virus ribonucleic acid (HCV ribonucleic acid [RNA]) indicating acute or chronic infection would make the patient ineligible unless the viral load becomes undetectable on suppressive therapy
- Known human immunodeficiency virus (HIV) infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months prior to step 2 registration are eligible for this trial. Testing is not required for entry into protocol
- Negative serum or urine pregnancy test (in persons of childbearing potential) within 14 days prior to Step 2 registration
    - Childbearing potential is defined as any person who has experienced menarche and who has not undergone surgical sterilization (hysterectomy or bilateral oophorectomy) or who is not postmenopausal

Critères d'exclusion

STEP 2 REGISTRATION

- Prior therapy for tumor, except for resection or prior laser interstitial thermal therapy (LITT). For example, prior chemotherapy, immunotherapy, or targeted therapy for GBM or lower grade glioma is disallowed (including but not limited to temozolomide, lomustine, bevacizumab, any viral therapy, ipilimumab or other CTLA-4 antibody, PD-1 antibody, CD-137 agonist, CD40 antibody, PDL-1 or 2 antibody, vaccine therapy, polio or similar viral injection as treatment for the tumor, and/or any other antibody or drug specifically targeting T-cell co-stimulation or immune checkpoint pathways) as is Gliadel wafer, radiotherapy, radiosurgery, vaccine or other immunotherapy, brachytherapy, or convection enhanced delivery
    - Note: 5-aminolevulinic acid (ALA)-mediated fluorescent guided resection (FGR) photodynamic therapy (PDT) or fluorescein administered prior to/during surgery to aid resection is not exclusionary and is not considered a chemotherapy or intracerebral agent. Prior laser interstitial thermal therapy (LITT) is allowed.
- Current or planned treatment with any other investigational agents for the study cancer
- Definitive clinical or radiologic evidence of metastatic disease outside the brain
- Prior invasive malignancy (except non-melanomatous skin cancer, cervical cancer in situ and melanoma in situ) unless disease free for a minimum of 2 years
- Prior radiotherapy to the head or neck that would result in overlap of radiation therapy fields
- Pregnancy and individuals unwilling to discontinue nursing due to the potential teratogenic effects and potential risk for adverse events in nursing infants
- History of allergic reactions attributed to compounds of similar chemical or biologic composition to temozolomide or lomustine

- History of pulmonary fibrosis
- Uncontrolled intercurrent illness including, but not limited to:
    - Ongoing or active infection requiring IV antibiotics, IV antiviral, or IV antifungal treatment
    - Symptomatic congestive heart failure, defined as New York Heart Association Functional Classification III/IV (Note: Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification)
    - Unstable angina pectoris within 6 months prior to Step 2 registration
    - Uncontrolled cardiac arrhythmia
    - Psychiatric illness/social situations that would limit compliance with study requirements
- No evidence of diffuse leptomeningeal disease that requires whole brain irradiation.