


Titre	Metformine avec témozolomide néo-adjuvant et radiothérapie accélérée hypofractionnée à marge minimale suivis de témozolomide adjuvant auprès de patients atteints de glioblastome multiforme
Protocole ID	MUHC ID: 4315 (M-HARTT STUDY)
ClinicalTrials.gov ID	NCT02780024
Type(s) de cancer	Cerveau (SNC)
Phase	Phase II
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Statut	Actif en recrutement
But étude	<p>Glioblastoma Multiforme is one of the most common, and unfortunately one of the most aggressive brain tumors in adults with most of the patients recurring and dying of the disease with a median survival of 16 months from diagnosis. Current treatment for patients with newly diagnosed Glioblastoma Multiforme (GBM) is safe maximal surgical resection followed by concomitant conventional Radiotherapy (RT) delivered in 6 weeks + Temozolomide (TMZ) followed by TMZ for 6 to 12 cycles. Recent scientific research has shown that Metformin, a common drug used to treat diabetes mellitus, may improve the results of the treatment in patients with a variety of cancers, such as breast, colon, and prostate cancer. Metformin is an attractive and safe medication to be used in this group of patients because of its very low toxicity. Our center the investigators have been using TMZ for 2 weeks prior to a short course (4 weeks) of RT which equivalent to the standard RT of 6 weeks. Temozolomide is used 2 weeks before RT + TMZ, and this is followed by the 6 to 12 cycles of TMZ. Our results are quiet encouraging with a median survival of 20 months, and acceptable toxicity.</p>
Critères d'éligibilité	<ul style="list-style-type: none">• Age: 18 years or older• Histological confirmation of supra-tentorial GBM• KPS > 60• Neurological function 0 or 1• Adequate bone marrow as defined below:• Absolute neutrophil count (ANC) ≥ 1500 cells/mm³. Platelets ≥ 100,000 cells/mm³ Hemoglobin ≥ 10 g/dl.• Adequate renal function, as defined below:• Creatinine clearance of >60 ml/min/1.73m² (using the Cockcroft Gault equation for eGFR) within 14 days prior to study registration• Adequate hepatic function, as defined below:• Bilirubin of 1.7 to 18.9 umol/L within 14 days prior to study registration• ALT ≤ 3 x normal range within 14 days prior to study registration• Neo-adjuvant TMZ and Metformin to start within 4 weeks of surgery• Concomitant TMZ and Metformin and accelerated Hypofractionated EBRT to start at least 2 weeks after adjuvant TMZ starting date, and no later than five weeks from surgery.• Surgical diagnosis/intervention may include: partial or near total resection• Patients must have recovered from the effects of surgery, postoperative infection and other complications before study registration.• A diagnostic contrast-enhanced MRI or CT scan of the brain must be performed preoperatively and postoperatively. The postoperative scan must be done within 28 days prior to the initiation of neo-adjuvant TMZ. Preoperative and postoperative scans must be the same type. Patients unable to undergo MR imaging can be enrolled provided pre- and post-operative contrast-enhanced CT scans are obtained and are of sufficient quality.

- History/physical examination, including neurologic exam within 14 days prior to study registration.
- Documentation of steroid doses within 14 days prior to study registration and stable or decreasing steroid dose within 5 days prior to registration.
- For females of child-bearing potential, negative serum pregnancy test within 72 hours prior to starting TMZ and Metformin. Women of childbearing potential and male participants must practice adequate contraception.
- Adequate tissue specimen for MGMT status analysis.
- Able to sign an informed study-specific consent

Critères d'exclusion

- Diabetic patients both type I and type II.
- No tissue provided for MGMT promoter methylation status determination.
- Margin of contrast-enhanced residual mass closer than 15 mm from the optic chiasm or optic nerves.
- Prior invasive malignancy (except for non-melanoma skin cancer) unless disease free for ≥ 3 years
- Recurrent or multifocal GBM.
- Prior chemotherapy or radio-sensitizers for cancers of the head and neck region; prior chemotherapy for a different cancer is allowable.
- Severe, active co-morbidity, defined as follows:
- Acute or chronic renal failure.
- Unstable angina and/or congestive heart failure requiring hospitalization
- Transmural myocardial infarction within the last 6 months
- Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration.
- Chronic Obstructive Pulmonary Disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of registration
- Acquired Immune Deficiency Syndrome (AIDS) based upon current CDC definition.
- Major medical illnesses or psychiatric impairments that in the investigator's opinion will prevent administration or completion of protocol therapy.
- Pregnancy or women of childbearing potential and men who are sexually active and not willing/able to use medically acceptable forms of contraception; this exclusion is necessary because the treatment involved in this study may be significantly teratogenic.
- Pregnant or lactating women, due to possible adverse effects on the developing foetus or infant due to study drug.
- Prior allergic reaction to Temozolomide or Metformin.
- Patients treated on any other therapeutic clinical protocols within 30 days prior to study entry or during participation in the study