# Essai Clinique

Généré le 19 avr. 2024 à partir de

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| Titre | Une étude de phase II portant sur la chimioradiothérapie au carboplatine intra-artériel dans le traitement du glioblastome récidivant. |
| Protocole ID | 2018-2452 |
| ClinicalTrials.gov ID | NCT03672721 |
| Type(s) de cancer | Cerveau (SNC) |
| Phase | Phase II |
| Stade | Récidive |
| Type étude | Traitement |
| Médicament | Carboplatine |
| Institution | CIUSSS DE L'ESTRIE – CENTRE HOSP. UNIV. DE SHERBROOKE<br>HOPITAL FLEURIMONT<br>3001 12e Avenue Nord, Sherbrooke, QC, J1H 5N4 |
| Ville | Sherbrooke |
| Investigateur principal | Dr David Fortin |
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| Statut | Actif en recrutement |
| But étude | Treatment of glioblastoma involves an optimal surgery, followed by a combination of radiation and temozolomide chemotherapy. Progression-free survival (PFS) with this treatment is only 6.9 months and relapse is the norm. The rationale behind the fact that limited chemotherapy agents are available in the treatment of malignant gliomas is related to the blood-brain barrier (BBB), which limits drug entry to the brain. Intraarterial (IA) chemotherapy allows to circumvent this. Using IA delivery of carboplatin, the investigators have observed responses in 70% of patients for a median PFS of 5 months. Median survival from study entry was 11 months, whereas the overall survival 23 months. How can we improve on this? By coupling radiation with a chemotherapeutic which is also a potent radiosensitizer such as carboplatin.Study design: In this phase I/II trial, patients will be treated at recurrence; a surgery will be performed for cytoreduction and to obtain tumor sample, followed with a combination of re-irradiation and IA carboplatin chemotherapy. A careful escalation scheme from 1.5Gy/fraction up to 3.5Gy/fraction will allow the investigators to determine the optimal re-irradiation dose (10 fractions of radiation over 2 weeks). Toxicity will be assessed according to the NCIC common toxicity criteria. Combined with radiation, patients will receive 2 treatments of IA carboplatin, 400 mg/m2, 4 hours prior to the first and the sixth radiation fraction. IA treatments will then be continued on a monthly basis, up to a total of 12 months, or until progression.Outcome measurements: Tumor response will be evaluated using the RANO criteria by magnetic resonance imaging monthly. The investigators will also acquire a sequence that enables the measurement of cerebral blood flow, cerebral blood volume and blood vessel permeability that are all relevant to understand the delivery of therapeutics to the CNS. Primary outcome will be OS and PFS. Secondary outcome will be QOL, neurocognition, and carboplatin delivery.In vitro intracellular carboplatin accumulation: Tumor samples from re-operation will be be analyzed for intracellular Pt concentration by ICP-MS. The amount of Pt bound to DNA will be measured. The level of apoptosis will be determined for each of the sample.Putting together these data will allow to correlate clinical and radiological response to QOL, NC (MOCA), and to delivery surrogates for the IA infusion and intracellular penetration of carboplatin. |

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| Critères d'éligibilité | • Histological diagnosis of glioblastoma multiforme<br>• Radiological progression on an MRI scan, according to the RANO criteria, in the context of a known glioblastoma multiforme, already treated with the Stupp protocol of combined radiotherapy-Temozolomide, and progressing. This implies a measurable disease on MRI.<br>• Prior radiotherapy and temozolomide, as per the Stupp protocol, no sooner than 4 weeks, is permitted.<br>• 18 of age and over<br>• Performance status: Karnofsky 60-100%<br>• Haematopoietic parameters at enrolment:<br>• Platelet counts > 100,000/mm^3<br>• Hemoglobin > 8 g/dL<br>• Absolute neutrophil count > 1,500/mm^3<br>• No impaired bone marrow function<br>• Hepatic parameters at enrolment:<br>• Bilirubin ≤ 2 times normal value<br>• AST and ALT ≤ 2 times upper limit of normal (ULN) Alkaline phosphatase ≤ 2 times ULN (unless attributed to tumor)<br>• No impaired hepatic function<br>• Renal parameters at enrollment:<br>• No impaired renal function<br>• Creatinine no greater than 1.5 fold of the normal value<br>• Creatinine clearance > 30 ml/min.<br>• Normal ECG<br>• Written informed consent obtained<br>• Patient should be either sterile or else use a contraceptive strategy (for at least 2 months prior to study accrual). |
| Critères d'exclusion | • Presence of a severe psychiatric or medical condition that would interfere with treatment administration or study enrolment.<br>• Presence of an active auto-immune disease.<br>• Occurrence of another malignancy within the past 5 years except curatively treated basal cell or squamous cell skin cancer or carcinoma in situ of the cervix<br>• Pregnancy (as objectivated by a positive b-HCG) or actively nursing<br>• Presence of an uncontrolled systemic infection |