Essai Clinique

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Titre	Étude de phase III randomisée avec le Sorafenib versus la radiothérapie stéréotaxique suivie du Sorafenib dans le cancer hépatocellulaire
Protocole ID	RTOG 1112
ClinicalTrials.gov ID	NCT01730937
Type(s) de cancer	Foie
Phase	Phase III
Type étude	Traitement
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	Montréal
Investigateur principal	Dr Neil Kopek
Coordonnateur	Tatiana Carvalho 514-934-1934 poste 43698
Statut	Fermé
Date d'activation	16-07-2018
But étude	This randomized phase III trial studies sorafenib tosylate and stereotactic body radiation therapy to see how well they work compared to sorafenib tosylate alone in treating patients with liver cancer. Sorafenib tosylate may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. Stereotactic body radiation therapy may be able to send the radiation dose directly to the tumor and cause less damage to normal tissue. Giving sorafenib tosylate together with stereotactic body radiation therapy may kill more tumor cells.
Critères d'éligibilité	• Patients must have a diagnosis of HCC by at least one criterion listed below within 360 days prior to study entry: • Pathologically (histologically or cytologically) proven diagnosis of HCC,(biopsies are recommended, and are to be submitted for research evaluation if patients consent) • At least one solid liver lesion or vascular tumor thrombosis (involving portal vein, inferior vena cava [IVC] and/or hepatic vein) > 1 cm with arterial enhancement and delayed washout on multi-phasic computerized tomography (CT) or magnetic resonance imaging (MRI) in the setting of cirrhosis or chronic hepatitis B or C without cirrhosis. • For patients whose CURRENT disease is vascular only: enhancing vascular thrombosis (involving portal vein, IVC and/or hepatic vein) demonstrating early arterial enhancement and delayed washout on multi-phasic CT or MRI in a patient with known HCC (diagnosed previously) using the above criteria. • Measureable hepatic disease and/or presence of vascular tumor thrombosis (involving portal vein, IVC and/or hepatic vein) which may not be measureable as per Response Evaluation Criteria in Solid Tumors (RECIST) on liver CT or MRI, within 28 days of registration • Appropriate for protocol entry based upon the following minimum diagnostic workup: • History/physical examination including examination for encephalopathy, ascites, weight, height, and blood pressure within 14 days prior to study entry • Assessment by radiation oncologist and medical oncologist or hepatologist who specializes in treatment of HCC within 28 days prior to study entry • Pre-randomization Scan (REQUIRED for All Patients): CT scan chest/abdomen/pelvis with multiphasic liver CT scan within 28 days prior to study entry; if CT contrast is contraindicated, CT chest without contrast and MRI of abdomen and pelvis is permitted • Zubrod performance status 0-2 within 28 days prior to study entry • Absolute neutrophil count (ANC) >= 1,500 cells/mm^3

	• Platelets >= 70,000 cells/mm^3 • Hemoglobin >= 8.0 g/dl (note: the use of transfusion or other intervention to achieve hemoglobin [Hgb] >= 8.0 g/dl is acceptable) • Total bilirubin < 2 mg/dL • Prothrombin time/international normalized ratio (INR) < 1.7 • Albumin >= 28 g/L • Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) < 6 times upper limit of normal (ULN) • Serum creatinine =< 1.5 x ULN or creatinine clearance >= 60 mL/min • Barcelona Clinic Liver Cancer (BCLC) stage: intermediate (B) or advanced (C) within 14 days prior to study entry • Child-Pugh score A within 14 days prior to study entry • Women of childbearing potential and male participants must agree to practice adequate contraception while on study and for at least 6 months following the last dose of radiation therapy (RT) and for at least 28 days following the last dose of sorafenib (whichever is later) • Unsuitable for resection or transplant or radiofrequency ablation (RFA) • Unsuitable for or refractory to transarterial hepatic chemo-embolization (TACE) or drug eluting beads (DEB) for any of the following reasons, as described by Raoul et al (2011): • Technical contraindications: arteriovenous fistula, including transjugular intrahepatic portosystemic shunt (TIPS), surgical portosystemic shunt, spontaneous portosystemic shunt or hepatofugal portal vein flow • Severe reduction in portal vein flow: due to tumor portal vein, IVC or atrial invasion or bland portal vein occlusion • Medical contraindications including congestive heart failure, angina, severe peripheral vascular disease • Presence of extrahepatic disease • No response post TACE (or DEB) x 2 or progressive HCC despite TACE; prior TACE or DEB is allowed but must be > 28 days from study entry • Serious toxicity following prior TACE (or DEB); prior TACE or DEB must be > 28 days from study entry • Other medical comorbidities making TACE (or DEB) unsafe and/or risky (e.g. combination of relative contraindications including age > 80 years, tumor > 10 cm, > 50% replacement of the liver by HCC, extensive multinodular bilobar HCC, biliary drainage) • Patients treated with prior surgery are eligible for this study if they otherwise meet eligibility criteria • Patient must be able to provide study-specific informed consent prior to study entry
Critères d'exclusion	• Prior invasive malignancy (except non-melanomatous skin cancer) unless disease free for a minimum of 2 years (note that carcinoma in situ of the breast, oral cavity, or cervix are all permissible) • Prior sorafenib use; note that prior chemotherapy for HCC or a different cancer is allowable • Prior radiotherapy to the region of the liver that would result in overlap of radiation therapy fields • Prior selective internal radiotherapy/hepatic arterial yttrium therapy, at any time • Severe, active co-morbidity, defined as follows: • Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months before registration • Transmural myocardial infarction within the last 6 months prior to study entry • Unstable ventricular arrhythmia within the last 6 months prior to study entry • Acute bacterial or fungal infection requiring intravenous antibiotics within 28 days prior to study entry • Hepatic insufficiency resulting in clinical jaundice, encephalopathy and/or variceal bleed within 60 days prior to study entry • Bleeding within 60 days prior to study entry due to any cause, requiring transfusion • Thrombolytic therapy within 28 days prior to study entry. Subcutaneous heparin is permitted. • Known bleeding or clotting disorder • Uncontrolled psychotic disorder • 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 • Any one hepatocellular carcinoma > 15 cm • Total maximal sum of hepatocellular carcinomas or a single conglomerate HCC > 20 cm • More than 5 discrete intrahepatic parenchymal foci of HCC • Direct tumor extension into the stomach, duodenum, small bowel or large bowel • Measureable common or main branch biliary duct involvement with HCC • Extrahepatic metastases or malignant nodes (that enhance with typical features of HCC) > 2.0 cm, in sum of maximal diameters (e.g. presence of one 2.4 cm metastatic lymph node or two 1.2 cm lung lesions); note that benign non-enhancing periportal lymphadenopathy is not unusual in the presence of hepatitis and is permitted, even if the sum of enlarged nodes is > 2.0 cm • Use of regular phenytoin, carbamazepine, hypericum perforatum (also known as St. John's wort) or rifampin • Use of combination anti-retroviral therapy for human immunodeficiency virus (HIV), as these agents may modulate cytochrome P450 isozymes