Essai Clinique

Généré le 24 avr. 2024 à partir de

Titre	Étude de phase 3 à répartition aléatoire, à double insu et contrôlée par placebo portant sur le régorafénib dans le cancer gastro-œsophagien avancé réfractaire (AGOC)
Protocole ID	INTEGRATEII
ClinicalTrials.gov ID	NCT02773524
Type(s) de cancer	Estomac
Phase	Phase III
Stade	Maladie réfractaire
Type étude	Traitement
Médicament	Regorafenib
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	
Investigateur principal	Dr Thierry Alcindor
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Statut	Fermé
But étude	Purpose: The purpose of this Phase III study is to determine if regorafenib improves overall survival in patients with Advanced Gastro-Oesophageal Carcinoma. Who is it for: You may be eligible to join this study if you are aged 18 years or above and have been diagnosed with advanced (metastatic or locally recurrent) Gastro-Oesophageal Carcinoma which has not responded to a minimum of 2 and a maximum of 3 lines of prior anti-cancer therapyTrial Details: Participants will be randomly (by chance) allocated to one of two groups: regorafenib or placebo in 2:1 ratio respectively and will not be aware of their group allocation. Regorafenib or matching placebo will be self-administered by participants orally once daily on days 1-21 of each 28 days cycle. Treatment will continue until disease progression or prohibitive toxicity. Participants will be followed up every 2-4 weeks in order to evaluate their progress on the study.
Critères d'éligibilité	• Adults (18 years or over) with metastatic or locally recurrent gastro-oesophageal cancer which: Note: Neoadjuvant or adjuvant chemotherapy or chemoradiotherapy will be considered as first line treatment where people have relapsed or progressed within 6 months of completing treatment; Radiosensitising chemotherapy given solely for this purpose concurrent with palliative radiation will not be considered as a line of treatment. Ramucirumab monotherapy, or immunotherapy with a checkpoint inhibitor, will be considered a line of treatment. • has arisen in any primary gastro-oesophageal site (oesophago-gastric junction (GOJ) or stomach); and • is of adenocarcinoma or undifferentiated carcinoma histology , and • is evaluable according to Response Evaluation Criteria in Solid Tumours (RECIST Version 1.1) by computed tomography (CT) scan performed within 21 days prior to randomisation. A lesion in a previously irradiated area is eligible to be considered as measurable disease as long as there is objective evidence of progression of the lesion prior to study enrolment; and • has failed or been intolerant to a minimum of 2 and a maximum of 3 lines of prior anti-cancer therapy for recurrent/metastatic disease which must have included at least one platinum agent and one fluoropyrimidine analogue. • Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1. • Ability to swallow oral medication.

	• Adequate bone marrow function (Platelets ≥100x109/L; Absolute Neutrophil Count (ANC) ≥1.5x109/L and Haemoglobin ≥ 9.0g/dL). • Adequate renal function (Creatinine clearance >50 ml/min) based on either the Cockcroft-Gault formula (Appendix 2), 24-hour urine or Glomerular Filtration Rate (GFR) scan; and serum creatinine ≤1.5 x Upper Limit of Normal (ULN). • Adequate liver function (Serum total bilirubin ≤1.5 x ULN, and INR ≤ 1.5 x ULN, and Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP) ≤2.5 x ULN (≤ 5 x ULN for participants with liver metastases)). Participants being treated with an anti-coagulant, such as warfarin or heparin, will be allowed to participate provided that no prior evidence of an underlying abnormality in these parameters exists. • Adequate cardiac function (Left Ventricular Ejection Fraction (LVEF) ≥ 50% or above the lower limit of normal (LLN) for the Institution (whichever is lower). Cardiac function should be assessed within 3 months prior to randomisation, but after completion of any anthracycline-containing chemotherapy. • Willing and able to comply with all study requirements, including treatment, timing, and/or nature of required assessments and follow-up. • Study treatment both planned and able to start within 7 days after randomisation (note: subjects randomised on a Friday should commence treatment no earlier than the following Monday). • Signed, written informed consent.
Critères d'exclusion	• Known allergy to the investigational product drug class or excipients in the regorafenib. • Poorly-controlled hypertension (systolic blood pressure >140mmHg or diastolic pressure> 90mmHg despite optimal medical management). • Participants with known, uncontrolled malabsorption syndromes. • Any prior anti-VEGF targeted therapy using small molecule VEGF TKIs (e.g. apatinib). Prior anti-VEGF targeted monoclonal antibody therapies (e.g. bevacizumab and ramucirumab) are permitted. • Treatment with any previous drug therapy within 3 weeks prior to randomization. This includes any investigational therapy. • Use of biological response modifiers, such as granulocyte colony stimulating factor (G-CSF), within 3 weeks prior to randomisation. • Concurrent treatment with strong CYP3A4 inhibitors or inducers. • Palliative radiotherapy, unless more than 14 days have elapsed between completion of radiation and the date of registration, and adverse events resulting from radiation have resolved to< Grade 2 according to CTCAE V4.03. • Major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to randomization. • Arterial thrombotic or ischaemic events, such as cerebrovascular accident, within 6 months prior to randomization. • Venous thrombotic events and pulmonary embolism within 3 months prior to randomization. • Any haemorrhage or bleeding event ≥ Grade 3 according to CTCAE v4.03 within 4 weeks prior to randomization. • Non-healing wound, ulcer, or bone fracture. • Interstitial lung disease with ongoing signs and symptoms. • Clinical hyperthyroidism or hypothyroidism. Note: non-clinically significant abnormal TFTs (abnormal TSH and abnormal T3 and/or abnormal T4) considered to be due to sick euthyroid syndrome is allowed. • Persistent proteinuria of ≥ Grade 3 according to CTCAE v4.03 (equivalent to > 3.5g of protein over 24 hours, measured on either a random specimen or 24 hour collection). • Uncontrolled metastatic disease to the central nervous system. To be eligible, CNS metastases should have been treated with surgery and/or radiotherapy and the patient should have been receiving a stable dose of steroids for at least 2 weeks prior to randomization, with no deterioration in neurological symptoms during this time. • History of another malignancy within 2 years prior to randomization. Participants with the following are eligible for this study: • curatively treated cervical carcinoma in situ, • non-melanomatous carcinoma of the skin, • superficial bladder tumours (T1a [Non-invasive tumour], and Tis[Carcinoma in situ]), • treated thyroid papillary cancer • Any significant active infection, including chronic active hepatitis B, hepatitis C, or HIV. Testing for these is not mandatory unless clinically indicated. Participants with known Hepatitis B/C infection will be allowed to participate providing evidence of viral suppression has been documented and the patient remains on appropriate anti-viral therapy. • Serious medical or psychiatric condition(s) that might limit the ability of the patient to comply with the protocol. • Pregnancy, lactation, or inadequate contraception. Women must be post-menopausal infertile, or use a reliable means of contraception. Women of childbearing potential must have a negative pregnancy test done within 7 days prior to randomization. Men must have been surgically sterilized or use a barrier method of contraception.