Essai Clinique

Généré le 05 mai 2024 à partir de

Titre	Étude de phase III évaluant BBI-608 en association avec le 5-fluorouracile, la leucovorine et l'irinotécan (FOLFIRI) chez des patients adultes atteints d'un cancer colorectal (CCR) métastatique déjà traité
Protocole ID	CANSTEM303C
ClinicalTrials.gov ID	NCT02753127
Type(s) de cancer	Côlon et rectum
Phase	Phase III
Stade	Maladie avancée ou métastatique
Type étude	Traitement
Médicament	napabucasin
Institution	CIUSSS DE L'OUEST-DE-L'ILE-DE-MONTREAL CENTRE HOSPITALIER DE ST. MARY 3830 av. Lacombe, Montréal, QC, H3T 1M5
Ville	Montréal
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Statut	Fermé
Date d'activation	05-12-2017
But étude	To assess the effect of napabucasin plus biweekly FOLFIRI versus biweekly FOLFIRI on the Overall Survival of patients with previously treated metastatic colorectal cancer.
Critères d'éligibilité	• Written, signed consent for trial participation must be obtained from the patient appropriately in accordance with applicable ICH guidelines and local and regulatory requirements prior to the performance of any study specific procedure. • Must have histologically confirmed advanced CRC that is metastatic. • Must have failed treatment with one regimen containing a fluoropyrimidine, oxaliplatin and bevacizumab for metastatic disease. All patients must have received a minimum of 6 weeks of the first-line regimen that included bevacizumab, oxaliplatin and a fluoropyrimidine in the same cycle. Treatment failure is defined as radiologic progression during or < 6 months after the last dose of first-line therapy. • FOLFIRI therapy is appropriate for the patient and is recommended by the Investigator. • Imaging investigations including CT/MRI of chest/abdomen/pelvis or other scans as necessary to document all sites of disease performed within 21 days prior to randomization. Patients with either measurable disease or non-measurable evaluable disease are eligible. • Must have an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1. • Must be ≥ 18 years of age. • For male or female patient of child producing potential: Must agree to use contraception or take measures to avoid pregnancy during the study and for 180 days for female and male patients, of the final FOLFIRI dose. Patients who receive single agent napabucasin without FOLFIRI must agree to use contraception or take measures to avoid pregnancy during the study and for 30 days for female patients and 90 days for male patients, of the final napabucasin dose. • Women of child bearing potential (WOCBP) must have a negative serum or urine pregnancy test within 5 days prior to randomization. The minimum sensitivity of the pregnancy test must be 25 IU/L or equivalent units of HCG.

- Must have alanine transaminase (ALT) ≤ 3 × institutional upper limit of normal (ULN) [≤ 5 × ULN in presence of liver metastases] within 14 days prior to randomization.
- Must have hemoglobin (Hgb) ≥ 9.0 g/dL within 14 days prior to randomization. Must not have required transfusion of red blood cells within 1 week of baseline Hgb assessment.
- Must have total bilirubin ≤ 1.5 × institutional ULN [≤ 2.0 x ULN in presence of liver metastases] within 14 days prior to randomization.
- Must have creatinine ≤ 1.5 × institutional ULN or Creatinine Clearance > 50 ml/min (as calculated by the Cockcroft-Gault equation) within 14 days prior to randomization.
- Must have absolute neutrophil count ≥ 1.5 x 10^9/L within 14 days prior to randomization.
- Must have platelet count ≥ 100 x 10^9/L within 14 days prior to randomization. Must not have required transfusion of platelets within 1 week of baseline platelet assessment.
- Other baseline laboratory evaluations, listed in Section 6.0, must be done within 14 days prior to randomization.
- Patient must consent to provision of, and Investigator(s) must confirm access to and agree to submit a representative formalin fixed paraffin block of tumor tissue in order that the specific correlative marker assays may be conducted. Submission of the tissue does not have to occur prior to randomization. Where local center regulations prohibit submission of blocks of tumor tissue, two 2 mm cores of tumor from the block and 10-30 unstained slides of whole sections of representative tumor tissue are preferred. Where two 2 mm cores of tumor from the block are unavailable, 10-30 unstained slides of whole sections of representative tumor tissue alone are acceptable. Where no previously resected or biopsied tumor tissue exists or is available, on the approval of the Sponsor/designated CRO, the patient may still be considered eligible for the study.
- Patient must consent to provision of a sample of blood in order that the specific correlative marker assays may be conducted.
- Patients must be accessible for treatment and follow-up. Patients registered on this trial must receive protocol treatment and be followed at the participating center. This implies there must be reasonable geographical limits placed on patients being considered for this trial. Investigators must ensure that the patients randomized on this trial will be available for complete documentation of the treatment, response assessment, adverse events, and follow-up.
- Protocol treatment is to begin within 2 calendar days of patient randomization.
- The patient is not receiving therapy in a concurrent clinical study and the patient agrees not to participate in other interventional clinical studies during their participation in this trial while on study treatment. Patients participating in surveys or observational studies are eligible to participate in this study.

Critères d'exclusion

- Anti-cancer chemotherapy or biologic therapy if administered prior to the first planned dose of study medication (napabucasin or FOLFIRI) within period of time equivalent to the usual cycle length of the regimen. An exception is made for oral fluoropyrimidines (e.g. capecitabine, S-1), where a minimum of 10 days since last dose must be observed prior to the first planned dose of study medication. Standard dose of bevacizumab (5 mg/kg) may be administered prior to FOLFIRI infusion, per Investigator decision, for as long as permanent decision to include or exclude bevacizumab is made prior to patient randomization. Radiotherapy, immunotherapy (including immunotherapy administered for non-malignant disease neoplastic treatment purposes), or investigational agents within four weeks of first planned dose of napabucasin, with the exception of a single dose of radiation up to 8 Gy (equal to 800 RAD) with palliative intent for pain control up to 14 days before randomization.
- More than one prior chemotherapy regimen administered in the metastatic setting.
- Major surgery within 4 weeks prior to randomization.
- Patients with any known brain or leptomeningeal metastases are excluded, even if treated.
- Women who are pregnant or breastfeeding. Women should not breastfeed while taking study treatment and for 4 weeks after the last dose of napabucasin or while undergoing treatment with FOLFIRI and for 180 days after the last dose of FOLFIRI.
- Gastrointestinal disorder(s) which, in the opinion of the Qualified/Principal Investigator, would significantly impede the absorption of an oral agent (e.g. active Crohn's disease, ulcerative colitis, extensive gastric and small intestine resection).
- Unable or unwilling to swallow napabucasin capsules daily.
- Prior treatment with napabucasin.
- Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, clinically significant non-healing or healing wounds, symptomatic congestive heart failure, unstable angina pectoris, clinically significant cardiac arrhythmia, significant pulmonary disease (shortness of breath at rest or mild exertion), uncontrolled infection or psychiatric illness/social situations that would limit compliance with study requirements.
- Known hypersensitivity to 5-fluorouracil/leucovorin
- Known dihydropyrimidine dehydrogenase (DPD) deficiency
- Known hypersensitivity to irinotecan
- Abnormal glucuronidation of bilirubin, known Gilbert's syndrome
- Patients with QTc interval > 470 milliseconds
- For patients to be treated with a regimen containing bevacizumab:
    - History of cardiac disease: congestive heart failure (CHF) > New York Heart Association (NYHA) Class II; active coronary artery disease, myocardial infarction within 6 months prior to study entry; unevaluated new onset angina within 3 months or unstable angina (angina symptoms at rest) or cardiac arrhythmias requiring anti-arrhythmic therapy (beta blockers or digoxin are permitted).
    - Current uncontrolled hypertension (systolic blood pressure [BP] > 150 mmHg or diastolic pressure > 90 mmHg despite optimal medical management) as well as prior

history of hypertensive crisis or hypertensive encephalopathy.
    - History of arterial thrombotic or embolic events (within 6 months prior to study entry)
    - Significant vascular disease (e.g., aortic aneurysm, aortic dissection, symptomatic peripheral vascular disease)
    - Evidence of bleeding diathesis or clinically significant coagulopathy
    - Major surgical procedure (including open biopsy, significant traumatic injury, etc.) within 28 days, or anticipation of the need for major surgical procedure during the course of the study as well as minor surgical procedure (excluding placement of a vascular access device or bone marrow biopsy) within 7 days prior to study enrollment
    - Proteinuria at screening as demonstrated by urinalysis with proteinuria ≥ 2+ (patients discovered to have ≥2+ proteinuria on dipstick urinalysis at baseline should undergo a 24 hour urine collection and must demonstrate ≤ 1g of protein in 24 hours to be eligible).
    - History of abdominal fistula, gastrointestinal perforation, peptic ulcer, or intra-abdominal abscess within 6 months
    - Ongoing serious, non-healing wound, ulcer, or bone fracture
    - Known hypersensitivity to any component of bevacizumab
    - History of reversible posterior leukoencephalopathy syndrome (RPLS)
- Patients with a history of other malignancies except: adequately treated non-melanoma skin cancer, curatively treated in-situ cancer of the cervix, or other solid tumors curatively treated with no evidence of disease for > 3 years.
- Any active disease condition which would render the protocol treatment dangerous or impair the ability of the patient to receive protocol therapy.
- Any condition (e.g. psychological, geographical, etc.) that does not permit compliance with the protocol.