Essai Clinique

Généré le 18 mai 2024 à partir de

Titre	Étude de phase I du topotécan à dose métronomique et pazopanib chez les enfants et adolescents avec une tumeur solide récurrente ou réfractaire incluant les tumeurs du système nerveux central
Protocole ID	IND.217 (TOPAZ)
ClinicalTrials.gov ID	NCT02303028
Type(s) de cancer	Pédiatrique divers
Phase	Phase I
Institution	CENTRE HOSPITALIER UNIVERSITAIRE SAINTE-JUSTINE
Ville	Montréal
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Statut	Actif en recrutement
But étude	This is a phase I, dose escalation study where topotecan will be administered at lower doses given more frequently on a prolonged schedule (low dose metronomic; LDM), in combination with a fixed dose of pazopanib. The maximum tolerated dose (MTD) and the recommended phase 2 dose (RP2D) will be evaluated for LDM topotecan in combination with pazopanib in children with recurrent or refractory solid tumours including CNS tumours. Pharmacokinetic and pharmacodynamic studies will be conducted to further define the exposure to and activity of LDM topotecan in combination with pazopanib.

Critères d'éligibilité	• Disease: Part 1-Relapsed or refractory solid tumours including CNS tumours; Part 2A-Neuroblastoma, Part 2B Rhabdomyosarcoma
	• Measurable or evaluable disease
	• No known curative therapy, or therapy proven to prolong survival with an acceptable QOL
	• Organ Function Criteria
	  • Peripheral ANC ≥ 1,500/µL; Plt ≥ 100,000/ and Hb ≥ 80 g/L (RBC transfusion permitted)
	  • Measured creatinine clearance or radioisotope GFR ≥ 70 mL/min/1.73 m2, OR a serum creatinine based on age/gender that meets the criteria outlined in the protocol
	  • Urinalysis negative for protein, urine protein:creatinine ratio of ≤ 1, OR a 24-hour urine protein < 1000 mg/dL
	  • <Gr.1 abnormalities of K, Ca (confirmed by ionized Ca),Mg or Ph (supplementation allowed)
	  • Total serum bilirubin ≤ 1.5xULN for age
	  • SGPT (ALT) ≤ 2.5 x ULN and SGOT (AST) ≤ 2.5 x ULN
	  • Serum albumin ≥ 20 g/L
	  • Adequate systolic ventricular function (LVSF≥ 27% or LVEF ≥ 50%)
	  • QTc measured by ECG must be < 450 msec.
	  • No history of MI, severe or unstable angina, peripheral vascular disease, or familial QTc prolongation
	  • Blood pressure ≤ 95th percentile for age, height, gender AND one of:
	  • No current anti-hypertensive therapy, OR on stable doses of no more than one anti-hypertensive medication
	  • Subjects with known history of seizures must have well-controlled seizures and not receiving enzyme-inducing anti-convulsants
	  • INR ≤ 1.2 and PTT ≤ 1.2xULN
	• Prior Therapy
	  • Myelosuppressive chemo must not have been given within 3 weeks of study enrolment (6 weeks if nitrosourea)
	  • At least 7 days must have elapsed since completion of therapy with a growth factor that supports platelet or white cell number or function. At least 14 days must have elapsed after receiving pegfilgrastim.
	  • Biologic anti-neoplastic agent (including VEGF-blocking TKI) must not have been

	administered within 7 days of study enrolment • At least 3 half lives of the monoclonal antibody must have elapsed since the last dose administered • ≥ 2 weeks must have elapsed since local palliative XRT (small port); > 13 weeks since prior total body irradiation (TBI), craniospinal XRT or > 50% radiation of pelvis; or > 6 weeks if other substantial bone marrow irradiation • ≥ 8 weeks must have elapsed since MIBG therapy for neuroblastoma • At least 60 days must have elapsed from autologous or allogeneic stem cell transplant with no signs of GVHD. • At least 28 days from major surgery and wounds must be healed. At least 7 days from open and/or core biopsy. • Ability to take liquid medication by mouth
Critères d'exclusion	• Patients with DIPG, or known CNS metastases • Pregnancy, breast feeding, or unwillingness to use effective contraception during the study • Subjects currently receiving: • Corticosteroids who haven't been on a stable or decreasing dose of corticosteroid for 7 days prior • Another investigational drug; other anti-cancer agents or radiation therapy • More than one medication for blood pressure control • Therapeutic anticoagulation, including systemic use of warfarin, heparin, or low molecular weight heparin at any dose • Aspirin, and/or ibuprofen, or other NSAIDs • Drugs metabolized through several of the specific P450 cytochrome isoforms and those receiving drugs with a known risk of torsades de pointes • Subjects who require thyroid replacement therapy are not eligible if they have not been receiving a stable replacement dose for at least 4 weeks prior to study enrolment. • Subjects who have an uncontrolled infection or serious non-healing would, ulcer or bone fracture. • Evidence of active bleeding, intratumoral haemorrhage, or bleeding diathesis, hemoptysis or any evidence of GI hemorrhage. • Major surgical procedure, laparoscopic procedure or significant traumatic injury within 28 days prior to Day 1 therapy. Open or core biopsy within 7 days prior to Day 1 of therapy. • Previous, documented hypersensitivity reactions to topotecan or pazopanib • History of abdominal fistula, GI perforation, or intra-abdominal abscess within 28 days of study enrolment.