Essai Clinique

Généré le 18 mai 2024 à partir de

Titre	A Phase 1/2 Study of the Oral TRK Inhibitor LOXO-101 (Larotrectinib) in Pediatric Patients With Advanced Solid or Primary Central Nervous System Tumors
Protocole ID	LOXO-TRK-15003
ClinicalTrials.gov ID	NCT02637687
Type(s) de cancer	Pédiatrique divers
Phase	Phase I-II
Type étude	Traitement
Médicament	Larotrectinib
Institution	CENTRE HOSPITALIER UNIVERSITAIRE SAINTE-JUSTINE
Ville	Montréal
Investigateur principal	Dr Sébastien Perreault
Coordonnateur	Annie La Haye 514 345-4931 poste 6325
Statut	Actif en recrutement
But étude	This is a multicenter, open label, Phase 1/2 study in pediatric patients with advanced solid or primary CNS tumors. LOXO?101 (larotrectinib) will be administered orally (PO) twice daily (BID), with the dose adjusted by body surface area (BSA).
Critères d'éligibilité	• Pediatric patients ≥ 1 day old on Cycle 1 Day 1 (C1D1) • Phase 1: Birth through 21 years of age at C1D1 with a locally advanced or metastatic solid tumor or primary CNS tumor that has relapsed, progressed or was nonresponsive to available therapies and for which no standard or available systemic curative therapy exists, or infants from birth and older with a diagnosis of malignancy and with a documented NTRK fusion that has progressed or was nonresponsive to available therapies, and for which no standard or available curative therapy exists, or patients with locally advanced infantile fibrosarcoma who would require, in the opinion of the Investigator, disfiguring surgery or limb amputation to achieve a complete surgical resection. The Phase I dose escalation cohorts are closed to enrollment. In addition to the above stated Inclusion Criteria, patients eligible for enrollment into this cohort must have a malignancy with a documented NTRK gene fusion with the exception of patients with infantile fibrosarcoma, congenital mesoblastic nephroma or secretory breast cancer. Patients with infantile fibrosarcoma, congenital mesoblastic nephroma or secretory breast cancer may enroll into this cohort with documentation of an ETV6 rearrangement by FISH or RT-PCR or a documented NTRK fusion by NGS. • Phase 2 only: Infants from birth and older at C1D1 with a locally advanced or metastatic infantile fibrosarcoma, patients with locally advanced infantile fibrosarcoma who would require, in the opinion of the Investigator, disfiguring surgery or limb amputation to achieve a complete surgical resection or birth through 21 years of age at C1D1 with a locally advanced or metastatic solid tumor or primary CNS tumor that has relapsed, progressed or was nonresponsive to available therapies and for which no standard or available systemic curative therapy exists with a documented NTRK gene fusion (or in the case of infantile fibrosarcoma, congenital medoblastic nephroma or secretory breast cancer with documented ETV6 rearrangement by FISH or RT-PCR or a documented NTRK fusion by NGS) (identified through molecular assays as routinely performed at CLIA or other similarly-certified laboratories) or (including Expansion Phase) potential patients older than 21 years of age with a tumor diagnosis with histology typical of a pediatric patient and an NTRK fusion may be considered for enrollment following discussion between the local site Investigator and the Sponsor's Medical Monitor. Patients with NTRK-fusion positive benign tumors are also eligible. • Karnofsky (those 16 years old or older) or Lansky (those younger than 16 years) performance

	score of at least 50 • Adequate hematologic function: Absolute neutrophil count (ANC) ≥ 1.0 109/L, platelet count ≥ 100.0 109/L and hemoglobin ≥ 8.0 g/dL (patients with bone marrow involvement will not be evaluable for hematologic DLT and can enroll with ANC ≥ 0.75 109/L, platelet count ≥ 50.0 109/L and hemoglobin ≥ 8.0 g/dL) • Adequate hepatic function: Bilirubin (sum of conjugated + unconjugated) ≤ 2.5 upper limit of normal (ULN) for age (patients with documented Gilbert's Disease may be enrolled with Sponsor approval). • Adequate renal function: Estimated glomerular filtration rate ≥ 30 mL/minute using the Cockroft-Gault formula or: a serum creatinine based on age/gender as outlined in the protocol • Requirement of highly effective birth control methods with a failure rate of less than 1% per year for male subjects. Also defined sexual abstinence as a birth control method per CTFG guidelines.
Critères d'exclusion	• Investigational agent, anticancer therapy, or major surgery within 14 days (2 weeks) prior to C1D1 • Clinically significant active cardiovascular disease or history of prolonged QT interval corrected for heart rate (QTc) • Current treatment with a strong cytochrome P450 (CYP) 3A4 inhibitor or inducer (EIAEDs and dexamethasone for CNS tumors or metastases, on a stable dose, are allowed) • Phase 2 Only: Prior progression while receiving approved or investigational tyrosine kinase inhibitors targeting TRK, including entrectinib, crizotinib and lestaurtanib. Patients who received a TRK inhibitor for less than 28 days of treatment and discontinued because of intolerance remain eligible.