Essai Clinique

Généré le 12 mai 2025 à partir de

Titre	A Phase 1b/2, First-in-Human, Dose Escalation and Expansion Study of XMT-1536 In Patients With Solid Tumors Likely to Express NaPi2b
Protocole ID	XMT-1536-1
ClinicalTrials.gov ID	NCT03319628
Type(s) de cancer	Ovaire Poumon non à petites cellules
Phase	Phase I-II
Type étude	Clinique
Médicament	XMT-1536
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL H SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
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Statut	Fermé
Date d'activation	20-07-2022
But étude	First-in-human, Phase 1b/2 safety study of the antibody-drug conjugate (ADC) XMT-1536 (upifitamab rilsodotin) administered as an intravenous infusion once every four weeks. Patients with tumor types likely to express NaPi2b were enrolled in dose escalation. Patients with platinum-resistant ovarian cancer and non-small cell lung cancer (adenocarcinoma subtype) are being enrolled in the expansion segment of this study. Patients with platinum-resistant, high-grade serous ovarian cancer are being enrolled in the UPLIFT segment of this study. In addition to safety assessments, the pharmacokinetics of the drug will be assessed along with ADC activity. A QTc sub-study has been added for the UPLIFT cohort for a sub-set of sites.

Critères d'éligibilité	**General Inclusion Criteria (for Dose Escalation, Expansion, and UPLIFT):**
	• ECOG performance status 0 or 1
	• Measurable disease as per RECIST, version 1.1
	• Resolution of all acute toxic effects of prior therapy or surgical procedures to ≤Grade 1 (except alopecia, stable immune-related toxicity such as hypothyroidism on hormone replacement, adrenal insufficiency on ≤10 mg daily prednisone [or equivalent], chronic Grade 2 peripheral sensory neuropathy after prior taxane therapy).
	• Cardiac left ventricular ejection fraction (LVEF) ≥50% or ≥ the institution's lower limit of normal by either Echo or MUGA scan
	• Adequate organ function as defined by the following criteria:
	  • Absolute neutrophil count (ANC) ≥1500 cells/mm3
	  • Platelet count ≥100,000/mm3
	  • Hemoglobin ≥9 g/dL
	  • In patients not on anticoagulation therapy: INR, activated partial thromboplastin time (aPTT), and prothrombin time (PT) all within 1.2 times the institution's upper limit of normal (ULN). Patients on anticoagulation therapy are allowed if their relevant laboratory values are within the therapeutic window.
	  • Estimated glomerular filtration rate (GFR) ≥45 mL/min
	  • Total bilirubin ≤ULN

- Patients with asymptomatic elevations in unconjugated bilirubin due to Gilbert syndrome or stable chronic hemolytic anemia (e.g., hereditary spherocytosis, sickle cell disease, thalassemia intermedia) may be eligible after discussion with the Sponsor Medical Monitor.
- Aspartate aminotransferase (AST or SGOT) and alanine aminotransferase (ALT or SGPT) ≤1.5 times the institutional ULN.
- Albumin ≥3.0 g/dL
- Able to provide informed consent.

Ovarian Cancer Inclusion Criteria for UPLIFT:

- Histological diagnosis of high grade serous ovarian cancer, which includes fallopian tube, or primary peritoneal cancer, that is metastatic or recurrent.
- Platinum-resistant disease
  - Patients who have only had 1 line of platinum-based therapy must have received at least 4 cycles of platinum, must have had a response [complete response/remission (CR) or partial response/remission (PR)], and then progressed between 3 months and ≤ 6 months after the date of the last dose of platinum
  - Patients who have received 2 to 4 lines of prior therapy must have received at least 4 cycles of platinum and then progressed within 6 months after the date of the last dose of platinum
- One to 4 prior lines of systemic therapy for ovarian cancer a. Prior treatment with bevacizumab is required for patients with 1 to 2 prior lines of therapy
- Patients must be willing to provide an archival tumor tissue block or slides or if not available, undergo procedure to obtain a new tumor biopsy using a low-risk, medically routine procedure

Ovarian Cancer Inclusion Criteria for QTc sub-study: Note: patients must meet all UPLIFT cohort inclusion criteria in order to participate in the QTc sub-study• Study patient has agreed to remain in the clinic for the additional QTc related study activities on the Day 1 of Cycle 1 and Cycle 3.

Critères d'exclusion

General Exclusion Criteria (for Dose Escalation, Expansion, and UPLIFT) :

- Major surgery within 28 days of starting study treatment, systemic anti-cancer therapy within the lesser of 28 days or 5 half-lives of the prior therapy before starting study treatment, or recent radiation therapy with unresolved toxicity or within a time window of potential toxicity.
- Patients with untreated CNS metastases (including new and progressive brain metastases), history of leptomeningeal metastasis or carcinomatous meningitis.
- Current known active infection with HIV, hepatitis B virus, or hepatitis C virus.
- Prior history of liver disease such as liver cirrhosis, hepatic fibrosis
- Current severe, uncontrolled systemic disease (e.g., clinically significant cardiovascular, pulmonary, or metabolic disease) or intercurrent illness that could interfere with per-protocol evaluations.
- Current use of either constant or intermittent supplementary oxygen therapy.
- History of suspected pneumonitis or interstitial lung disease.
- Pregnant or nursing women.
- History of other malignancy within the last 2 years, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, or other malignancy with a similar expected curative outcome.
- Active corneal disease, or history of corneal disease within 12 months prior to enrollment
- Use of strong CYP450 inhibitors
- Oxygen saturation on room air <93%

Ovarian Cancer Exclusion Criteria for UPLIFT:

- Low-grade, clear cell, endometrioid, mucinous, carcinosarcoma, germ-cell, mixed histology, or stromal tumors
- Prior treatment with mirvetuximab soravtansine or another ADC containing an antitubulin payload
- Primary platinum-resistant disease, defined by a lack of response or by progression within 3 months after completing front-line, platinum-containing therapy.
- Participation in DES or EXP segments of this study

Ovarian Cancer Exclusion Criteria for QTc sub-study:

- Use of strong CYP3A4 inducers.
- Uncontrolled cardiac arrhythmias, for example, atrial fibrillation with a ventricular response at rest > 100 beats per minute. left bundle branch block (LBBB)
- Known abnormality of any cardiac valve (either stenosis or regurgitation) that is greater than moderate in severity.
- Subjects not in sinus rhythm at screening with HR >45- <100
- Any ECG abnormality that can interfere with the measurement of the QT interval