Essai Clinique

Généré le 14 mai 2024 à partir de

Titre	A Phase 3, Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial of Selinexor in Maintenance Therapy After Systemic Therapy for Patients With p53 Wild-Type, Advanced or Recurrent Endometrial Carcinoma
Protocole ID	XPORT-EC-042
ClinicalTrials.gov ID	NCT05611931
Type(s) de cancer	Endomètre
Phase	Phase III
Type étude	Clinique
Médicament	Selinexor
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	
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Statut	Actif en recrutement
Date d'activation	22-11-2023
But étude	The purpose of this study is to evaluate the efficacy and safety of selinexor as a maintenance treatment in patients with p53 wt endometrial carcinoma (EC), who have achieved a partial response (PR) or complete response (CR) (per Response Evaluation Criteria in Solid Tumors version 1.1 [RECIST v 1.1]) after completing at least 12 weeks of platinum-based therapy. A total of 220 participants will be enrolled in the study and randomized in a 1:1 ratio to maintenance therapy with either selinexor or placebo.
Critères d'éligibilité	• At least 18 years of age at the time of signing informed consent. • Histologically confirmed EC including: endometrioid, serous, undifferentiated, and carcinosarcoma. • TP53 wt assessed by next generation sequencing (NGS), evaluated by a central vendor. • Completed a single line, at least 12 weeks of platinum-based therapy (not including adjuvant or neoadjuvant therapy for Stage I-III disease) and achieved confirmed partial or complete response (PR or CR) by imaging, according to RECIST version 1.1. The participants should have received treatment for: Primary Stage IV disease, defined as: • had a primary or later debulking surgery during first-line platinum-based therapy with R0 resection (R0 resection indicates a macroscopic complete resection of all visible tumor) and achieved CR after at least 12 weeks platinum-based therapy, OR • had a primary or later debulking surgery during first-line platinum-based therapy with R1 resection (R1 resection indicates incomplete removal of all macroscopic disease) and achieved PR or CR after at least 12 weeks platinum-based chemotherapy, OR • had no surgery and achieved PR or CR after at least 12 weeks platinum-based chemotherapy OR At first relapse (i.e., relapse after primary therapy including surgery and/or chemotherapy and/or immunotherapy for Stage I-IV disease), defined as: • had Stage I - III disease at diagnosis and received, at initial diagnosis, adjuvant chemotherapy and relapsed later. Participants should have PR or CR after at least 12 weeks of

	platinum-based chemotherapy compared with the start of this chemotherapy at the time of relapse,
	• had Stage I-III disease at diagnosis and did not receive adjuvant chemotherapy at initial diagnosis and relapsed later. Participants should have PR or CR after at least 12 weeks of platinum-based chemotherapy compared with the start of this chemotherapy at the time of relapse, OR
	• had Stage IV disease at diagnosis and received initially chemotherapy with or without surgery and relapsed later. At the time of relapse, participants should have PR or CR after at least 12 weeks of platinum-based chemotherapy compared with the start of this chemotherapy at the time of relapse.
	  • Previous treatment with anti-programmed cell death protein 1(PD-1) or anti-programmed death-ligand 1(PD-L1) monoclonal antibody and concomitant biologic agents (e.g., bevacizumab, trastuzumab) is allowed.
	  • Must be able to initiate study drug 3 to 8 weeks after completion of their final dose of chemotherapy.
	  • Eastern Cooperative Oncology Group (ECOG) performance status of 0-1.
	  • Participants must have adequate bone marrow function and organ function within 2 weeks before starting study drug as defined by the following laboratory criteria:
	• Hepatic function: total bilirubin up to less than (<) 3*upper limit of normal (ULN); alanine aminotransferase (ALT) and aspartate aminotransferase (AST) less than or equal to (<=) 2.5*ULN in participants without liver metastasis. For participants with known liver involvement of their tumor: AST and ALT (<=) 5*ULN
	• Hematopoietic function within 1 week: Absolute neutrophil count (ANC) greater than or equal to (>=) 1.5*10^9/liter (L); platelet count >= 100*10^9/L; hemoglobin >= 9.0 gram per deciliter (g/dL) per local laboratory results
	• Renal function: estimated creatinine clearance (CrCl) of >= 20 milliliter per minute (mL/min), calculated using the standard local formula, as applicable- In the opinion of the Investigator, the participant must:
	• Have a life expectancy of at least 12 weeks, and
	• Be fit to receive investigational therapy
	  • Premenopausal females of childbearing potential must have a negative pregnancy test (serum β-human chorionic gonadotropin test) prior to the first dose of study drug. Female participants of childbearing potential must agree to use highly effective methods of contraception throughout the study and for 90 days following the last dose of study drug.
	  • Written informed consent signed in accordance with federal, local, and institutional guidelines prior to the first screening procedure.

Critères d'exclusion	• Participants meeting any of the following exclusion criteria are not eligible to enroll in this study: • Has any uterine sarcomas (carcinosarcomas - not excluded), clear cell or small cell carcinoma with neuroendocrine differentiation • Received a blood or platelet transfusion during the 2 weeks prior to Cycle 1 Day 1 (C1D1). Participants' hemoglobin must be assessed within 2 weeks of screening and at least 1 week post transfusion • Concurrent systemic steroid therapy higher than physiologic dose (> 10 milligram per day [mg/day] of prednisone or equivalent). Systemic steroid therapy as pre-medication for taxane is allowed • Insufficient time since or not recovered from procedures or anti-cancer therapy, defined as: • Not recovered from major surgery <= 28 days prior to Day 1 dosing. Minor procedures, such as biopsies, dental work, or placement of a port or intravenous (IV) line for infusion are permitted • Having ongoing clinically significant anti-cancer therapy-related toxicities CTCAE Grade > 1, with the exception of alopecia. In specific cases, participants whose toxicity has stabilized or with Grade 2 non-hematologic toxicities can be allowed following documented approval by the Sponsor's Medical Monitor • Palliative radiotherapy within 14 days of the intended C1D1. Palliative radiotherapy may be permitted for symptomatic control of pain from bone metastases, provided that the radiotherapy does not involve target lesions, and the reason for the radiotherapy does not reflect evidence of disease progression. • Any gastrointestinal dysfunctions that could interfere with the absorption of selinexor (e.g., bowel obstruction, inability to swallow tablets, malabsorption syndrome, unresolved nausea, vomiting, diarrhea CTCAE v 5.0 > grade 1). • Participants unable to tolerate two forms of antiemetics for at least 2 cycles will not be eligible for the trial. • Active, ongoing or uncontrolled active infection requiring parenteral antibiotics, antivirals, or antifungals within 1 week of screening. • Serious psychiatric or medical condition that could interfere with participation in the study or in the opinion of the Investigator would make study involvement unreasonably hazardous. • Previous treatment with an XPO1 inhibitor. • Stable disease or PD on the post-chemotherapy scan or clinical evidence of progression prior to randomization. • Participants who received any systemic anticancer therapy including investigational agents <= 3 weeks (or <= 5 half-lives of the drug [whichever is shorter]) prior to C1D1. • Major injuries or surgery within 14 days prior to C1D1 and/or planned major surgery during the on-treatment study period. • Other malignant disease with disease-free <= 3 years except: curatively treated carcinoma in situ of the cervix, basal cell carcinoma of the skin, or ductal carcinoma in situ (DCIS) of the breast.

- History of allergic reactions attributed to compounds of similar chemical or biologic composition to selinexor, or other agents used in the study.
- Active brain metastases (e.g., stable for < 8 weeks, no adequate previous treatment with radiotherapy and/or surgery, symptomatic, requiring treatment with anti-convulsant therapy. Corticoid therapy is allowed if administered as stable dose for at least 1 month before randomization).
- Females who are pregnant or lactating.
- Any other life-threatening illness, active medical condition, organ system dysfunction, or serious active psychiatric issue which, in the Investigator's opinion, could compromise the participant's safety or the participant's ability to remain compliant with study procedures.