Essai Clinique

Généré le 03 mai 2024 à partir de

Titre	Étude de phases II et III à répartition aléatoire visant à comparer l'association cédiranib et olaparib au cédiranib ou à l'olaparib en monothérapie ou à la chimiothérapie de référence chez les femmes atteintes d'un cancer de l'ovaire, d'un cancer des trompes de Fallope ou d'un cancer péritonéal primitif, récidivant et résistant ou réfractaire aux platines
Protocole ID	OVC.2 - COCOs
ClinicalTrials.gov ID	NCT02502266
Type(s) de cancer	Ovaire
Phase	Phase II
Stade	Métastatique
Type étude	Traitement
Médicament	Cediranib maleate et Olaparib
Institution	CHU DE QUEBEC – UNIVERSITE LAVAL L'HOTEL-DIEU DE QUEBEC ET CRCEO 11 Côte du Palais, Québec, QC, G1R 2J6
Ville	Québec
Investigateur principal	Dr Vincent Castonguay
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Statut	Fermé
But étude	This randomized phase II/III trial studies how well cediranib maleate and olaparib work when given together or separately, and compares them to standard chemotherapy in treating patients with ovarian, fallopian tube, or primary peritoneal cancer that has returned after receiving chemotherapy with drugs that contain platinum (platinum-resistant) or continued to grow while being treated with platinum-based chemotherapy drugs (platinum-refractory). Cediranib maleate and olaparib may stop the growth of tumor cells by blocking enzymes needed for cell growth. Drugs used in chemotherapy work in different ways to stop the growth of tumor cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. It is not yet known whether giving cediranib maleate and olaparib together may cause more damage to cancer cells when compared to either drug alone or standard chemotherapy.
Critères d'éligibilité	• Patients must have histologically or cytologically confirmed ovarian cancer, peritoneal cancer or fallopian tube cancer and must have a histological diagnosis of either serous or endometrioid cancer based on local histopathological findings; both endometrioid and serous histology should be high-grade for eligibility of non-mutation carriers; patients with clear cell, mixed epithelial, undifferentiated carcinoma, or transitional cell carcinoma histologies are also eligible, provided that the patient has a known deleterious germline BRCA1 or BRCA2 mutation identified through testing at a clinical laboratory • Patients should have recurrent platinum-resistant or- refractory disease - defined as disease that has progressed by imaging while receiving platinum or had recurrence within 6 months of the last receipt of platinum-based chemotherapy; rising CA125 only is not considered as platinum-resistant or refractory disease • Phase II study: measurable disease by RECIST 1.1 criteria; if archival tumor sample is not available tumor sample from fresh biopsy is acceptable • Phase III study: evaluable disease - defined as RECIST 1.1 measurable disease OR non-measurable disease (defined as solid and/or cystic abnormalities on radiographic imaging that do not meet RECIST 1.1 definitions for target lesions OR ascites and/or pleural effusion

	that has been pathologically demonstrated to be disease-related in the setting of a cancer antigen [CA]125 >= 2 x upper limit of normal [ULN]) • No more than 3 prior treatment regimens (including primary therapy; no more than 1 prior non-platinum based therapy in the platinum-resistant/-refractory setting); hormonal therapies used as single agents (i.e. tamoxifen, aromatase inhibitors) will not count towards this line limit • Patients may not have had a prior anti-angiogenic agent in the recurrent setting; prior use of bevacizumab in the upfront or upfront maintenance setting is allowed • Patients may not have previously received a PARP-inhibitor • Patient must have provided study specific informed consent prior to study entry • Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1 or 2 • Absolute neutrophil count >= 1,500/mcL • Platelets >= 100,000/mcL • Hemoglobin >= 10 g/dL • Total bilirubin within =< 1.5 times the upper limit of normal (ULN) institutional limits • Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase [SGOT])/alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase [SGPT]) =< 3 x institutional ULN; if intrahepatic liver metastases are present, AST and ALT must be =< 5 times institutional ULN • Creatinine =< 1.5 x the institutional ULN • Urine protein: creatinine ratio urine protein creatinine (UPC) of =< 1 OR less than or equal to 2+ proteinuria on two consecutive dipsticks taken no less than 1 week apart; UPC is the preferred test; patients with 2+ proteinuria on dipstick must also have a 24-hour urine collection demonstrating protein of =< 500 mg over 24 hours • Toxicities of prior therapy (excepting alopecia) should be resolved to less than or equal to grade 1 as per CTCAE v 4.0 • Adequately controlled blood pressure (systolic blood pressure [SBP] =< 140; diastolic blood pressure [DBP] =< 90 mmHg) on maximum of three antihypertensive medications; patients must have a BP of =< 140/90 mmHg taken in the clinic setting by a medical professional within 2 weeks prior to starting study; it is strongly recommended that patients who are on three antihypertensive medications must be actively followed by a cardiologist or a primary care physician for management of BP while on protocol; patients must be willing and able to check and record daily blood pressure readings; blood pressure cuffs will be provided to patients randomized to cediranib alone and the combination of olaparib and cediranib arms • Adequately controlled thyroid function, with no symptoms of thyroid dysfunction and thyroid-stimulating hormone (TSH) within normal limits • Able to swallow and retain oral medications and without gastrointestinal (GI) illnesses that would preclude absorption of cediranib or olaparib • Women of child-bearing potential must have a negative pregnancy test prior to study entry; women of child-bearing potential must agree to use two reliable forms of contraception (hormonal or barrier method of birth control; abstinence) prior to study entry, for the duration of study participation, and for 6 weeks after cediranib discontinuation; should a woman become pregnant or suspect she is pregnant while participating in this study, she should inform her treating physician immediately • Women of child-bearing potential must have a negative pregnancy test prior to study entry; women of child-bearing potential must agree to use must agree to use two reliable forms of contraception (hormonal or barrier method of birth control; abstinence) prior to study entry, for the duration of study participation, and for 3 months after the last dose of olaparib; should a woman become pregnant or suspect she is pregnant while participating in this study, she should inform her treating physician immediately
Critères d'exclusion	• Patients who have had chemotherapy or radiotherapy within 4 weeks (6 weeks for nitrosoureas or mitomycin C) of starting treatment or those who have not recovered from adverse events due to agents administered more than 4 weeks earlier; patients may not have had hormonal therapy within 2 weeks prior to entering the study; patients receiving raloxifene for bone health as per Food and Drug Administration (FDA) indication may remain on raloxifene absent other drug interactions • Any other investigational agents within the past 4 weeks • Prior treatment affecting the VEGF/VEGFR pathway or the angiopoietin pathway in the recurrent setting, including but not limited to thalidomide, bevacizumab, sunitinib, sorafenib, pazopanib, cediranib, nintedanib, and trebananib; bevacizumab used in the upfront setting in conjunction with chemotherapy and/or as maintenance to treat newly diagnosed disease will be allowed • Prior use of PARP-inhibitors • CA-125 only disease without Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 measurable or otherwise evaluable disease • Major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to starting cediranib • Current signs and/or symptoms of bowel obstruction or signs and/or symptoms of bowel obstruction within 3 months prior to starting study drugs • History of intra-abdominal abscess within the past 3 months • History of gastrointestinal perforation; patients with a history of abdominal fistula will be considered eligible if the fistula was surgically repaired or has healed, there has been no evidence of fistula for at least 6 months, and patient is deemed to be at low risk of recurrent fistula • Dependency on IV hydration or total parenteral nutrition (TPN) • Any concomitant or prior invasive malignancies with the following curatively treated exceptions:

- Treated limited stage basal cell or squamous cell carcinoma of the skin
- Carcinoma in situ of the breast or cervix
- Primary endometrial cancer meeting the following conditions: stage not greater than IA, grade 1 or 2, no more than superficial myometrial invasion, without vascular or lymphatic invasion; no poorly differentiated subtypes, including papillary serous/serous, clear cell, or other Federation of Gynecology and Obstetrics (FIGO) grade 3 lesions
- Prior cancer treated with a curative intent with no evidence of recurrent disease 5 years following diagnosis and judged by the investigator to be at low risk of recurrence

- Patients with untreated brain metastases, spinal cord compression, or evidence of symptomatic brain metastases or leptomeningeal disease as noted on computed tomography (CT) or magnetic resonance imaging (MRI) scans should not be included on this study, since neurologic dysfunction may confound the evaluation of neurologic and other adverse events; patients with treated brain metastases and resolution of any associated symptoms must demonstrate stable post-therapeutic imaging for at least 6 months following therapy prior to starting study drug
- Patients with any of the following:
    - History of myocardial infarction within six months
    - Unstable angina
    - Resting electrocardiogram (ECG) with clinically significant abnormal findings
    - New York Heart Association functional classification of III or IV
- If cardiac function assessment is clinically indicated or performed: left ventricular ejection fraction (LVEF) less than normal per institutional guidelines, or < 55%, if threshold for normal not otherwise specified by institutional guidelines
    - Patients with the following risk factors should have a baseline cardiac function assessment:
        - Prior treatment with anthracyclines
        - Prior treatment with trastuzumab
        - Prior central thoracic radiation therapy (RT), including RT to the heart
        - History of myocardial infarction within 6 to 12 months (Patients with history of myocardial infarction within 6 months are excluded from the study)
        - Prior history of impaired cardiac function
- History of stroke or transient ischemic attack within six months
- Clinical significant peripheral vascular disease or vascular disease (aortic aneurysm or aortic dissection)
- Evidence of coagulopathy or bleeding diathesis; therapeutic anticoagulation for prior thromboembolic events is permitted
- Evidence suggestive of myelodysplastic syndrome (MDS) or acute myelogenous leukemia (AML) on peripheral blood smear or bone marrow biopsy, if clinically indicated
    - No prior allogeneic bone marrow transplant or double umbilical cord blood transplantation (dUBCT)
- Patients may not use any complementary or alternative medicines including natural herbal products or folk remedies
- Uncontrolled intercurrent illness including, but not limited to ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia (other than atrial fibrillation with controlled ventricular rate), or psychiatric illness/social situations that would limit compliance with study requirements
- Known human immunodeficiency virus (HIV)-positive individuals are ineligible
- Participants receiving any medications or substances that are strong inhibitors or inducers of CYP3A4 are ineligible
    - Strong inhibitors and inducers of UGT/PgP should be used with caution
- Pregnant women are excluded from this study; breastfeeding should be discontinued if the mother is treated with cediranib or olaparib