# Essai Clinique

Généré le 04 mai 2024 à partir de

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| Titre | Étude de phase III à double insu et à répartition aléatoire sur la chimiothérapie avec ou sans pembrolizumab suivie d'un traitement d'entretien par l'olaparib ou un placebo dans le traitement de première intention du cancer de l'ovaire épithélial (COE) au stade avancé sans mutation du gène BRCA |
| Protocole ID | MK-7339-001 |
| ClinicalTrials.gov ID | NCT03740165 |
| Type(s) de cancer | Ovaire |
| Phase | Phase III |
| Type étude | Traitement |
| Médicament | Chimiothérapie avec ou sans pembrolizumab suivi d'Olaparib en maintien |
| Institution | CENTRE UNIVERSITAIRE DE SANTE MCGILL<br>H SITE GLEN<br>1001 boul. Décarie , Montréal, QC, H4A 3J1 |
| Ville | |
| Investigateur principal | Dre Lucy Gilbert |
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| Statut | Fermé |
| But étude | The purpose of this study is to assess the efficacy and safety of treatment with carboplatin/paclitaxel PLUS pembrolizumab (MK-3475) and maintenance olaparib (MK-7339) in women with epithelial ovarian cancer (EOC), fallopian tube cancer, or primary peritoneal cancer. The primary study hypotheses are that the combination of pembrolizumab plus carboplatin/paclitaxel followed by continued pembrolizumab and maintenance olaparib is superior to carboplatin/paclitaxel alone with respect to Progression Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) and/or Overall Survival (OS), and that the combination of pembrolizumab plus carboplatin/paclitaxel followed by continued pembrolizumab is superior to carboplatin/paclitaxel alone with respect to PFS per RECIST 1.1 and/or OS. |
| Critères d'éligibilité | • Has histologically confirmed International Federation of Gynecology and Obstetrics (FIGO) Stage III or Stage IV EOC (high-grade predominantly serous, endometrioid, carcinosarcoma, mixed mullerian with high-grade serous component, clear cell, or low-grade serous OC), primary peritoneal cancer, or fallopian tube cancer<br>• Has just completed primary debulking surgery or is eligible for primary or interval debulking surgery<br>• Is a candidate for carboplatin and paclitaxel chemotherapy, to be administered in the adjuvant or neoadjuvant setting<br>• Candidates for neoadjuvant chemotherapy, has a cancer antigen 125 (CA-125) (kilounits/L):carcinoembryonic antigen (CEA; ng/mL) ratio greater than or equal to 25<br>• Is able to provide a newly obtained core or excisional biopsy of a tumor lesion for prospective testing of BRCA1/2 and Programmed Cell Death-Ligand 1 (PD-L1) tumor markers status prior to randomization<br>• Has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, as assessed within 7 days prior to initiating chemotherapy in the lead-in period and within 7 days prior to randomization<br>• Is not pregnant, not breastfeeding, and 1 of the following conditions applies: a.) Not a woman of childbearing potential (WOCBP) OR b.) A WOCBP who agrees to follow contraceptive guidance during the treatment period and for at least 120 days following the last dose of pembrolizumab (or pembrolizumab placebo) and olaparib (or olaparib placebo) and at least 210 days following |

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| | the last dose of chemotherapy or bevacizumab (if administered)<br>• Has adequate organ function |
| Critères d'exclusion | • Has mucinous, germ cell, or borderline tumor of the ovary<br>• Has a known or suspected deleterious mutation (germline or somatic) in either BRCA1 or BRCA2<br>• Has a history of non-infectious pneumonitis that required treatment with steroids or currently has pneumonitis<br>• Has either myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML) or has features suggestive of MDS/AML<br>• Has a known additional malignancy that is progressing or has required active treatment in the last 3 years Note: Participants with basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or carcinoma in situ (e.g. ductal carcinoma in situ, cervical carcinoma in situ) that has undergone potentially curative therapy are not excluded.<br>• Has ongoing Grade 3 or Grade 4 toxicity, excluding alopecia, following chemotherapy administered during the lead-in period<br>• Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis<br>• Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (dosing >10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior to randomization<br>• Has an active autoimmune disease that has required systemic treatment in the past 2 years (i.e., with use of disease modifying agents, corticosteroids or immunosuppressive drugs) Note: Replacement therapy (e.g. thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.<br>• Has a known history of active tuberculosis (TB; Bacillus Tuberculosis)<br>• Has an active infection requiring systemic therapy<br>• Has received colony-stimulating factors (eg, granulocyte colony stimulating factor [G-CSF], granulocyte macrophage colony-stimulating factor [GM-CSF] or recombinant erythropoietin) within 4 weeks prior to receiving chemotherapy during the lead-in period<br>• Is considered to be of poor medical risk due to a serious, uncontrolled medical disorder, non-malignant systemic disease or active, uncontrolled infection<br>• Has had surgery to treat borderline tumors, early stage EOC, or fallopian tube cancer <6 months prior to screening<br>• Has a known history of human immunodeficiency virus (HIV) infection<br>• Has a known history of hepatitis B virus (HBV) or known active hepatitis C virus (HCV) infection<br>• Is either unable to swallow orally administered medication or has a gastrointestinal (GI) disorder affecting absorption (e.g. gastrectomy, partial bowel obstruction, malabsorption)<br>• Has uncontrolled hypertension, defined as defined as systolic >140 mm Hg or diastolic >90 mm Hg documented by 2 blood pressure readings taken at least 1 hour apart. Note: This applies to participants who will receive bevacizumab. Use of antihypertensive medications to control blood pressure is allowed.<br>• Has current, clinically relevant bowel obstruction (including sub-occlusive disease), abdominal fistula or GI perforation, related to underlying EOC (for participants receiving bevacizumab)<br>• Has a history of hemorrhage, hemoptysis or active GI bleeding within 6 months prior to randomization (for participants receiving bevacizumab)<br>• Is a WOCBP who has a positive urine pregnancy test within 72 hours before the first dose of chemotherapy in the lead-in period and within 72 hours prior to randomization, is pregnant or breastfeeding, or is expecting to conceive children within the projected duration of the study, starting with screening through 120 days following the last dose of pembrolizumab (or pembrolizumab placebo) and olaparib (or olaparib placebo) and at least 210 days following the last dose of chemotherapy or bevacizumab (if administered)<br>• Has received prior treatment for advanced or metastatic OC, including radiation or systemic anti-cancer therapy (e.g. chemotherapy, hormonal therapy, immunotherapy, investigational therapy)<br>• Has received prior therapy with an anti-Programmed Cell Death-1 (anti-PD-1), anti-PD-L1, or anti-PD-L2 agent or with an agent directed to another stimulatory or co-inhibitory T-cell receptor (e.g. cytotoxic T lymphocyte antigen-4 [CTLA-4], OX 40, CD137)<br>• Has received prior therapy with either olaparib or any other poly(adenosine-ribose) polymerase (PARP) inhibitor<br>• Has intraperitoneal chemotherapy planned or has been administered as first-line therapy<br>• Has received a live vaccine within 30 days prior to the first dose of study treatment<br>• Has severe hypersensitivity (≥Grade 3) to pembrolizumab, olaparib, carboplatin, paclitaxel or bevacizumab (if using) and/or any of their excipients<br>• Is currently receiving either strong (e.g. itraconazole, telithromycin, clarithromycin, protease inhibitors boosted with ritonavir or cobicistat, indinavir, saquinavir, nelfinavir, boceprevir, telaprevir) or moderate (eg, ciprofloxacin, erythromycin, diltiazem, fluconazole, verapamil) inhibitors of cytochrome P450 (CYP)3A4 that cannot be discontinued for the duration of the study<br>• Is currently receiving either strong (e.g. phenobarbital, enzalutamide, phenytoin, rifampicin, rifabutin, rifapentine, carbamazepine, nevirapine, and St John's Wort) or moderate (e.g. bosentan, efavirenz, modafinil) inducers of CYP3A4 that cannot be discontinued for the duration of the study<br>• Has received whole blood transfusions in the last 120 days prior to randomization<br>• Is currently participating or has participated in a study of an investigational agent or has used an investigational device within 4 weeks of the first dose of study treatment<br>• Has resting electrocardiogram (ECG) indicating uncontrolled, potentially reversible cardiac conditions or participant has congenital long QT syndrome |

- Has had an allogenic tissue/solid organ transplant, has received previous allogenic bone-marrow transplant, or has received double umbilical cord transplantation
- Either has had major surgery within 2 weeks of randomization or has not recovered from any effects of any major surgery