Essai Clinique

Généré le 26 avr. 2024 à partir de

Titre	A Phase III Randomized, Placebo-Controlled Study of Pembrolizumab in Addition to Paclitaxel and Carboplatin for Measurable Stage III or IVA, Stage IVB or Recurrent Endometrial Cancer
Protocole ID	ENC.1
ClinicalTrials.gov ID	NCT03914612
Type(s) de cancer	Endomètre
Phase	Phase III
Stade	Récidivant/réfractaire (2ième ligne de traitement et plus)
Type étude	Clinique
Médicament	Pembrolizumab avec Paclitaxel et Carboplatine
Institution	CISSS DE LAVAL HOPITAL DE LA CITE-DE-LA-SANTE 1755 boul. René-Laennec, Laval, QC, H7M 3L9
Ville	
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Statut	Actif en recrutement
But étude	This phase III trial studies how well the combination of pembrolizumab, paclitaxel and carboplatin works compared with paclitaxel and carboplatin alone in treating patients with endometrial cancer that is stage III or IV, or has come back (recurrent). Immunotherapy with monoclonal antibodies, such as pembrolizumab, may help the body's immune system attack the cancer, and may interfere with the ability of tumor cells to grow and spread. Paclitaxel and carboplatin are chemotherapy drugs used as part of the usual treatment approach for this type of cancer. This study aims to assess if adding immunotherapy to these drugs is better or worse than the usual approach for treatment of this cancer.

Critères d'éligibilité	• Measurable stage III, measurable stage IVA, stage IVB (with or without measurable disease) or recurrent (with or without measurable disease) endometrial cancer.
	• Pathology report showing results of institutional MMR IHC testing. (This requirement does not apply to sites in Japan.).
	• Histologic confirmation of the original primary tumor is required (submission of pathology report(s) is required). Patients with the following histologic types are eligible: Endometrioid adenocarcinoma, serous adenocarcinoma, dedifferentiated/undifferentiated carcinoma, clear cell adenocarcinoma, mixed epithelial carcinoma, adenocarcinoma not otherwise specified (N.O.S.).
	• Submission of tumor specimens for centralized MMR IHC testing is required after Step 1 and before Step 2 registration.
	• In patients with measurable disease, lesions will be defined and monitored by RECIST version (v) 1.1. Measurable disease is defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded). Each lesion must be >= 10 mm when measured by computed tomography (CT) or magnetic resonance imaging (MRI). Lymph nodes must be >= 15 mm in short axis when measured by CT or MRI.
	• Patients may have received
	  • NO prior chemotherapy for treatment of endometrial cancer OR
	  • Prior adjuvant chemotherapy (e.g., paclitaxel/carboplatin alone or as a component of concurrent chemotherapy and radiation therapy [with or without cisplatin]) provided adjuvant chemotherapy was completed >= 12 months prior to STEP 2 registration.

- Patients may have received prior radiation therapy for treatment of endometrial cancer. Prior radiation therapy may have included pelvic radiation therapy, extended field pelvic/para aortic radiation therapy, intravaginal brachytherapy and/or palliative radiation therapy. All radiation therapy must be completed at least 4 weeks prior to STEP 2 registration.
- Patients may have received prior hormonal therapy for treatment of endometrial cancer. All hormonal therapy must be discontinued at least three weeks prior to STEP 2 registration.
- Performance status of 0, 1 or 2.
- Platelets >= 100,000/mcl.
- Absolute neutrophil count (ANC) >= 1,500/mcl.
- Creatinine =< 1.5 x institutional/laboratory upper limit of normal (ULN).
- Total serum bilirubin level =< 1.5 x upper limit of normal (ULN) (patients with known Gilbert's disease who have bilirubin level =< 3 x ULN may be enrolled).
- Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) =< 3 x ULN.
- Thyroid stimulating hormone (TSH) within normal limits (TSH < ULN allowed in euthyroid patients on thyroid replacement therapy).
- Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of Step 2 registration are eligible for this trial.
- For patients of child bearing potential: negative urine or serum pregnancy test. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test is required.
- Administration of study drugs (pembrolizumab, paclitaxel, carboplatin) may have an adverse effect on pregnancy and poses a risk to the human fetus, including embryo-lethality. Women of childbearing potential (WOCBP) must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) from at least 14 days prior to Step 2 registration (for oral contraceptives), during treatment, and for 120 days after the last dose of study medication. Should a woman become pregnant or suspect she is pregnant while she is participating in this study, she should inform her treating physician immediately. Patients will be considered of nonreproductive potential if they are either:
    - Postmenopausal (defined as at least 12 months with no menses without an alternative medical cause; in women < 45 years of age, a high follicle stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy. In the absence of 12 months of amenorrhea, a single FSH measurement is insufficient); OR
    - Have a hysterectomy and/or bilateral oophorectomy, bilateral salpingectomy or bilateral tubal ligation/occlusion, at least 6 weeks prior to Step 2 registration; OR
    - Have a congenital or acquired condition that prevents childbearing.
- Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.
- The patient or a legally authorized representative must provide study-specific informed consent prior to study entry and, for patients treated in the United States (U.S.), authorization permitting release of personal health information.

Critères d'exclusion

- Patients with prior treatment with anti-PD-1, anti-PD-L1 or anti-CTLA-4 therapeutic antibody or other similar agents.
- Patients who have a history of a severe hypersensitivity reaction to monoclonal antibody or pembrolizumab (MK-3475) and/or its excipients; and/or a severe hypersensitivity reaction to paclitaxel and/or carboplatin
- Patients who are currently participating and receiving cancer-directed study therapy or have participated in a study of an investigational agent and received cancer-directed study therapy within 4 weeks prior to Step 2 registration.
- Patients who have a diagnosis of immunodeficiency or are receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to Step 2 registration.
    - Patients who have received steroids as CT scan contrast premedication may be enrolled.
    - The use of inhaled or topical corticosteroids is allowed.
    - The use of mineralocorticoids (e.g., fludrocortisone) for patients with orthostatic hypotension or adrenocortical insufficiency is allowed.
    - The use of physiologic doses of corticosteroids may be approved after consultation with the study chair.
- Patients with treated brain metastases are eligible if follow-up brain imaging after central nervous system (CNS)-directed therapy shows no evidence of progression, and they have been off steroids for at least 4 weeks prior to Step 2 registration and remain clinically stable.
- Patients with active autoimmune disease or history of autoimmune disease that might recur, which may affect vital organ function or require immune suppressive treatment including systemic corticosteroids. This includes, but is not limited to, patients with a history of immune related neurologic disease, multiple sclerosis, autoimmune (demyelinating) neuropathy, Guillain-Barre syndrome, myasthenia gravis; systemic autoimmune disease such as systemic lupus erythematosus (SLE), connective tissue diseases, scleroderma, inflammatory bowel disease (IBD), Crohn's, ulcerative colitis, hepatitis; and patients with a history of toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome, or phospholipid syndrome because of the risk of recurrence or exacerbation of disease.
- Patients with vitiligo, endocrine deficiencies including type I diabetes mellitus, thyroiditis managed with replacement hormones including physiologic corticosteroids are eligible.
- Patients with rheumatoid arthritis and other arthropathies, Sjogren's syndrome and psoriasis controlled with topical medication and patients with positive serology, such as antinuclear antibodies (ANA), anti-thyroid antibodies should be evaluated for the presence of target organ

involvement and potential need for systemic treatment but should otherwise be eligible.
- Patients who have a history of (non-infectious) pneumonitis that required steroids, or current pneumonitis.
- Uncontrolled intercurrent illness including, but not limited to: ongoing or active infection (except for uncomplicated urinary tract infection), interstitial lung disease or active, non-infectious pneumonitis, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
- Known clinically significant liver disease, including active viral, alcoholic, or other hepatitis; and cirrhosis.
    - For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.
    - Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load.
- Pregnant or lactating patients.