Essai Clinique

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Titre	A Randomized, Double-Blind, Phase 3 Study of Pemetrexed + Platinum Chemotherapy With or Without Pembrolizumab (MK-3475) in TKI-resistant EGFR-mutated Tumors in Metastatic Non-squamous Non-small Cell Lung Cancer (NSCLC) Participants
Protocole ID	MK-3475-789/KEYNOTE-789
ClinicalTrials.gov ID	NCT03515837
Type(s) de cancer	Poumon non à petites cellules
Phase	Phase III
Stade	Métastatique
Type étude	Traitement
Médicament	Pemetrexed + chimiothérapie à base de platine avec ou sans Pembrolizumab
Institution	CIUSSS DU CENTRE-OUEST-DE-L'ILE-DE-MONTREAL HOPITAL GENERAL JUIF SIR MORTIMER B.DAVIS 3755 rue de la Côte Ste. Catherine, Montréal, QC, H3T 1E2
Ville	Montréal
Investigateur principal	Dr Jason Agulnik
Coordonnateur	Heather Gregory 514-340-8222 poste 24596
Statut	Fermé
But étude	The purpose of this study is to evaluate the efficacy and safety of pemetrexed plus platinum chemotherapy (carboplatin or cisplatin) with or without pembrolizumab (MK-3475; KEYTRUDA®) in the treatment of adults with the following types of tyrosine kinase inhibitor (TKI)-resistant, epidermal growth factor receptor (EGFR)-mutated, metastatic non-squamous non-small cell lung cancer (NSCLC) tumors: 1) TKI-failures (including osimertinib [TAGRISSO®] failure) with T790M-negative mutation tumors, 2) T790M-positive mutation tumors with prior exposure to osimertinib, and 3) first-line osimertinib failure regardless of T790M mutation status. The primary study hypotheses are that the combination of pembrolizumab plus chemotherapy has superior efficacy compared to saline placebo plus chemotherapy in terms of: 1) Progression-free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) based on blinded independent central review, and 2) Overall Survival (OS). This study will be considered to have met its success criteria if the combination of pembrolizumab plus chemotherapy is superior to saline placebo plus chemotherapy in terms of PFS or OS.
Critères d'éligibilité	• Histologically or cytologically confirmed diagnosis of Stage IV non-squamous NSCLC. • Documentation of tumor activating EGFR mutation, specifically either DEL19 or L858R. • Investigator-determined radiographic disease progression per RECIST 1.1 after treatment with an EGFR TKI therapy: a) Participants previously treated with 1st or 2nd generation EGFR TKI (e.g. erlotinib/afatinib/gefitinib) are required to have confirmed documented absence of EGFR T790M mutation; b) Participants with confirmed acquired T790M mutation after 1st or 2nd generation EGFR TKI (e.g. erlotinib/afatinib/gefitinib) are required to have osimertinib TKI treatment failure prior to enrollment; c) Participants previously failed osimertinib TKI treatment as 1st line therapy are eligible regardless of their EGFR T790M mutation status. Note: TKI washout period for all participants is 1 week or 2 half-lives after last treatment dose, whichever is longer. TKI washout should be completed prior to first dose of study treatment. • Measurable disease per RECIST 1.1 as assessed by the local site investigator/radiology. • Provided archival tumor tissue sample or newly obtained (no anti-neoplastic therapy since biopsy) core or excisional biopsy of a tumor lesion not previously irradiated. • Life expectancy of at least 3 months.

	• Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 within 7 days prior to the first dose of study treatment but before randomization. • Male participants must agree to use contraception during the treatment period and for at least 120 days after the last dose of pembrolizumab and up to 180 days after last dose of chemotherapeutic agents. • Female participants must not be pregnant, not breastfeeding, and must agree to use contraception during the treatment period and for at least 120 days after the last dose of pembrolizumab and up to 180 days after the last dose of chemotherapeutic agents. • Adequate organ function.
Critères d'exclusion	• Predominantly squamous cell histology NSCLC. Mixed tumors will be categorized by the predominant cell type; if small cell elements are present, the participant is ineligible. • Symptomatic ascites or pleural effusion. A participant who is clinically stable following treatment for these conditions (including therapeutic thoraco- or paracentesis) is eligible. • Received prior therapy with an anti-programmed cell death protein-1 (anti-PD-1), anti-programmed cell death-ligand 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-associated protein-4 [CTLA-4], OX-40, CD137). • Received prior systemic cytotoxic chemotherapy or investigational agent(s), excluding EGFR TKIs, for metastatic NSCLC. [Notes: 1) Prior treatment with chemotherapy and/or radiation as part of neoadjuvant/adjuvant therapy is allowed as long as therapy was completed at least 6 months prior to the diagnosis of metastatic NSCLC. 2) If participant received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study treatment. 3) Prior exposure to traditional medicine(s) is allowed as long as therapy was discontinued at least 4 weeks prior to the first dose of study treatment.] • Received prior radiotherapy within 2 weeks of start of study treatment or has received lung radiation therapy of >30 Gray (Gy) within 6 months before the first dose of study treatment. Participants must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had radiation pneumonitis. A 1-week washout is permitted for palliative radiation (≤2 weeks of radiotherapy) to non-central nervous system (CNS) disease. • Received a live vaccine within 30 days prior to the first dose of study treatment. • Currently participating in or has participated in a study of an investigational agent or has used an investigational device within 4 weeks prior to the first dose of study treatment. • Diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior the first dose of study treatment. • Known additional malignancy that is progressing or has required active treatment within the past 5 years. (Note: Participants with basal cell carcinoma of the skin, squamous cell carcinoma of the skin, superficial bladder cancer, or carcinoma in situ (e.g. breast carcinoma, cervical cancer in situ) that have undergone potentially curative therapy are not excluded.) • Known active untreated CNS metastases and/or carcinomatous meningitis. • Severe hypersensitivity (≥ Grade 3) to pembrolizumab and/or any of its excipients. • Known sensitivity to any component of cisplatin, carboplatin, or pemetrexed. • Active autoimmune disease that has required systemic treatment in past 2 years. • History of (non-infectious) pneumonitis that required steroids or has current pneumonitis. • Active infection requiring systemic therapy. • Known history of human immunodeficiency virus (HIV) infection. • Known history of Hepatitis B or known active Hepatitis C virus. • Known history of active tuberculosis (TB; Bacillus tuberculosis) • Pregnant, breastfeeding or expecting to conceive or father children within the projected duration of the study, starting with the screening visit through 120 days after the last dose of pembrolizumab and up to 180 days after the last dose of chemotherapeutic agents.