Essai Clinique

Généré le 25 avr. 2025 à partir de

Titre	A Randomized, Open-label, Phase 3 Trial of Dato-DXd Plus Pembrolizumab vs Pembrolizumab Alone in Treatment-naïve Subjects With Advanced or Metastatic PD-L1 High (TPS ?50%) Non-small Cell Lung Cancer Without Actionable Genomic Alterations
Protocole ID	TROPION-Lung08
ClinicalTrials.gov ID	NCT05215340
Type(s) de cancer	Poumon non à petites cellules
Phase	Phase III
Type étude	Clinique
Médicament	Datopotamab deruxtecan avec pembrolizumab versus pembrolizumab en monothérapie
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	
Investigateur principal	Dr Benjamin Shieh
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Statut	Actif en recrutement
Date d'activation	30-12-2023
But étude	This study is designed to assess the efficacy and safety of datopotamab deruxtecan (Dato-DXd) in combination with pembrolizumab versus pembrolizumab alone in participants with advanced or metastatic non-small cell lung cancer (NSCLC).

Critères d'éligibilité	Participants eligible for inclusion in the study must meet all inclusion criteria within 28 days of randomization into the study.
	• Sign and date the Tissue Screening and Main Informed Consent Forms, prior to the start of any study-specific qualification procedures.
	• Adults ≥18 years or the minimum legal adult age (whichever is greater) at the time of informed consent.
	• Histologically documented NSCLC that meets all of the following criteria:
	  • Stage IIIB or IIIC disease and not candidates for surgical resection or definitive chemoradiation, or Stage IV NSCLC disease at the time of randomization (based on the American Joint Committee on Cancer, Eighth Edition). Participants with early-stage NSCLC who have relapsed should be restaged during screening to ensure their eligibility for the study.
	  • Documented negative test results for epidermal growth factor receptor (EGFR), lymphoma kinase (ALK), and proto-oncogene1 (ROS1) actionable genomic alterations based on analysis of tumor tissue.
	  • No known actionable genomic alterations in neurotrophic tyrosine receptor kinase (NTRK), proto-oncogene B-raf (BRAF), rearranged during transfection (RET), mesenchymal-epithelial transition factor (MET), or other actionable driver kinases with locally approved therapies.
	• Has provided a formalin-fixed tumor tissue sample for the measurement of trophoblast cell surface protein 2 (TROP2) protein expression and for the assessment of other exploratory biomarkers.
	• Tumor has high programmed death receptor-1 (PD-L1) expression (TPS ≥50%) as determined by PD-L1 immunohistochemistry (IHC) 22C3 pharmDx assay by central testing (minimum of 6

	slides). • Has an adequate treatment washout period before Cycle 1 Day 1. • Measurable disease based on local imaging assessment using RECIST Version 1.1. • Has left ventricular ejection fraction (LVEF) ≥50% by either an echocardiogram (ECHO) or multigated acquisition scan (MUGA) within 28 days before randomization. • Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1 at screening. • Has a life expectancy of at least 3 months. • Adequate bone marrow function within 7 days before randomization.

Critères d'exclusion	• Has received prior systemic treatment for advanced or metastatic NSCLC.
	• Has received prior treatment for NSCLC with any of the following, including in the adjuvant/neoadjuvant setting:
	  • Any agent, including an antibody-drug conjugate, containing a chemotherapeutic agent targeting topoisomerase I.
	  • TROP2-targeted therapy.
	  • Any anti-programmed death receptor-1 (PD-1), anti-PD-L1, or anti-PD-ligand 2 (L2) agent or with an agent directed to another stimulatory or co-inhibitory T-cell receptor (eg, CTLA-4, OX40, CD137).
	  • Any other immune checkpoint inhibitors. Participants who received adjuvant or neoadjuvant therapy OTHER than those listed above, are eligible if the adjuvant/neoadjuvant therapy was completed at least 6 months prior to the diagnosis of advanced/metastatic disease.
	• Has spinal cord compression or active and untreated central nervous system (CNS) metastases and/or carcinomatous meningitis. Participants with previously treated brain metastases may participate provided they are radiologically stable.
	• Has received prior radiotherapy ≤4 weeks of start of study intervention or more than 30 Gy (unit of ionizing radiation dose in the International System of Units) to the lung within 6 months of Cycle 1 Day 1.
	• History of another primary malignancy (beyond NSCLC) except for:
	  • Malignancy treated with curative intent and with no known active disease ≥3 years before the first dose of study treatment and of low potential risk for recurrence.
	  • Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease.
	  • Adequately treated carcinoma in situ without evidence of disease.
	  • Participants with a history of prostate cancer (tumor/node/metastasis stage) of Stage ≤T2cN0M0 without biochemical recurrence or progression and who in the opinion of the Investigator are not deemed to require active intervention.
	• Has a history of (non-infectious) interstitial lung disease (ILD)/pneumonitis including radiation pneumonitis that required steroids, has current ILD/pneumonitis, or where suspected ILD/pneumonitis cannot be ruled out by imaging at screening.
	• Clinically severe pulmonary compromise, as judged by the investigator, resulting from intercurrent pulmonary illnesses including, but not limited to, any underlying pulmonary disorder, or any autoimmune, connective tissue or inflammatory disorders with pulmonary involvement or prior complete pneumonectomy.
	• Uncontrolled or significant cardiovascular disease, including:
	  • Mean QT interval corrected for heart rate using Fridericia's formula (QTcF) interval >470 msec regardless of sex (based on the average of the 12-lead electrocardiogram determination at screening).
	  • Myocardial infarction within 6 months prior to randomization.
	  • Uncontrolled angina pectoris within 6 months prior to randomization.
	  • LVEF <50% by ECHO or MUGA scan within 28 days before randomization.
	  • New York Heart Association Class 2 to 4 congestive heart failure (CHF) at screening.
	  • Uncontrolled hypertension (resting systolic blood pressure >180 mmHg or diastolic blood pressure >110 mmHg) within 28 days before randomization.
	
	Participants with a history of Class 2 to 4 CHF prior to screening, must have returned to Class 1 CHF and have LVEF ≥50% (by either an ECHO or MUGA scan within 28 days before randomization) in order to be eligible.
	
	• Clinically significant corneal disease.
	• Has received a live vaccine or live-attenuated vaccine (messenger ribonucleic acid and replication-incompetent adenoviral vaccines are not considered attenuated live vaccines) within 30 days prior to the first dose of study drug. For any participant receiving an approved severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) vaccine, please follow the vaccine label and/or local guidance.
	• Active, known, or suspected autoimmune disease (has an active autoimmune disease that has required systemic treatment in the past 2 years).
	• Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosage >10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy ≤7 days prior to the first dose of study drug.
	• Has known human immunodeficiency virus (HIV) infection that is not well controlled.
	• Has an active hepatitis or uncontrolled hepatitis B or active hepatitis C infection.
	• Has an uncontrolled infection requiring IV antibiotics, antivirals, or antifungals.
	• Had an allogeneic tissue/solid organ transplant.
	• Has a history of severe hypersensitivity reactions to either the drug or inactive ingredients (including but not limited to polysorbate 80) of Dato-DXd or pembrolizumab.