Essai Clinique

Généré le 03 mai 2024 à partir de

Titre	Essai ouvert et multicentrique de phase II portant sur l'administration intratumorale de pIL-12 avec électroporation en association avec du pembrolizumab intraveineux à des patients atteints d'un mélanome de stade III ou IV qui progresse pendant le traitement par le pembrolizumab ou le nivolumab
Protocole ID	PISCES
ClinicalTrials.gov ID	NCT03132675
Type(s) de cancer	Mélanome
Phase	Phase II
Type étude	Traitement
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
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But étude	This will be a Phase 2 study of intratumoral tavokinogene telseplasmid (tavo; pIL-12) Electroporation (EP) plus IV pembrolizumab. Eligible patients will be those with pathological diagnosis of unresectable or metastatic melanoma who are progressing or have progressed on pembrolizumab or nivolumab.
Critères d'éligibilité	• Pathologically documented unresectable melanoma, AJCC Stage III or IV. Subjects must have histological or cytological confirmed diagnosis of unresectable melanoma with progressive locally advanced or metastatic disease. • Subjects must be refractory to anti-PD-1 monoclonal antibodies (pembrolizumab or nivolumab either as monotherapy or in combination with other approved checkpoint inhibitors or targeted therapies according to their approved label) and subjects must meet all of the following criteria: • Received at least 4 doses of anti-PD1 mAb (minimum dose of 2 mg/kg or fixed dose of 200 mg given Q3W for pembrolizumab; minimum dose of 240 mg given Q2W for nivolumab in monotherapy; minimum dose of 1 mg/kg given Q3W for nivolumab in combination with ipilimumab) • Progressive disease after anti-PD1 mAb will be defined according to RECIST v1.1. • Documented disease progression within 24 weeks of the last dose of anti-PD1 mAb. • Resolution/improvement of anti-PD1 mAb-related AEs • No history of common toxicity criteria adverse events (CTCAE) Grade 4 irAEs from anti-PD1 mAb. • No history of CTCAE Grade 3 requiring steroid treatment (>10 mg/day prednisone or equivalent dose) for >12 weeks or CTCAE Grade 2 pneumonitis regardless of steroid treatment. • Minimum of 4 weeks (washout period) from the last dose of anti PD1 mAb. • Prior treatment with an approved BRAF inhibitor if BRAF V600 mutation-positive. • Age ≥ 18 years of age on day of signing informed consent. • Has a performance status of 0 or 1 on the ECOG Performance Scale. • Have measurable disease based on RECIST v1.1, with at least one anatomically distinct lesion. Lesion or lesions must meet all the following baseline criteria: • Accessible for electroporation, • Must be accurately measured in at least one dimension (longest diameter in the plane of measurement is to be recorded) • Demonstrate adequate organ function as defined below. All screening laboratories should be performed within 10 days of treatment initiation.System Laboratory Value Hematological Absolute neutrophil count (ANC) ≥1.5 × 109/L Platelets ≥100 × 109/L Hemoglobin ≥9 g/dL or ≥5.6 mmol/L* Renal Creatinine OR ≤1.5 × the upper limit of normal (ULN) OR Measured or

	calculated** creatinine clearance (CrCl) Glomerular filtration rate (GFR) can also be used instead of creatinine or CrCl ≥ 30 mL/min for patient with creatinine levels >1.5 × institutional ULN Hepatic Total bilirubin ≤1.5 × ULN OR direct bilirubin ≤ULN for patients with total bilirubin levels > 1.5× ULN Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤2.5 × ULN OR ≤5 × ULN for patients with liver metastases Coagulation International Normalized Ratio (INR) or Prothrombin Time (PT) ≤1.5 × ULN unless patient is receiving anticoagulant therapy as long as PT or PTT is within therapeutic range of intended use of anticoagulants Activated Partial Thromboplastin Time (aPTT) ≤1.5 × ULN unless patient is receiving anticoagulant therapy as long as PT or PTT is within therapeutic range of intended use of anticoagulants Criteria must be met without erythropoietin dependency and without packed red blood cell (pRBC) transfusion within last 2 weeks** Creatinine clearance should be calculated per institutional standard. • Women of childbearing potential must have negative serum or urine pregnancy test within 72 hours prior to receiving the first study drug administration. • For women of childbearing potential, must be willing to use an adequate method of contraception from 30 days prior to the first study drug administration and 120 days following last day study drug administration. Spermicide alone is not considered sufficient in Canada and will not be accepted. • Male patients must be surgically sterile, or must agree to use adequate method of contraception during the study and at least 120 days following the last day of study drug administration. • Able and willing to provide written informed consent and to follow study instructions.
Critères d'exclusion	• Subject has disease that is suitable for local therapy administered with curative intent. • Subject with a diagnosis of uveal melanoma. • Subject has a known additional malignancy that is progressing or requires active treatment within the past 3 years. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer. • Clinically active CNS metastases or non-measurable bone-only metastases. Subjects with previously treated brain metastases may participate provided they are radiologically stable, i.e., without evidence of progression for at least 4 weeks by repeat imaging, clinically stable and without requirement of steroid treatment for at least 14 days prior to first dose of study drug. • Greater than 3 visceral sites of metastases. Liver lesions must meet RECIST v1.1 criteria for SD for at least 1 month prior to enrolment. • Subjects with electronic pacemakers or defibrillators. • Subjects who have a known history of Human Immunodeficiency Virus (HIV) (HIV 1/2 antibodies). • Subjects who have known active Hepatitis B (defined as HBsAg reactive) or Hepatitis C virus infection (defined as HCV RNA [qualitative] is detected) • Subject has a 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 to the first dose of study drug. The use of physiologic doses of corticosteroids may be approved after consultation with the Sponsor. • Subjects who have received a live-virus vaccination within 30 days of the first dose of treatment. Seasonal flu vaccines that do not contain live virus are permitted. • Subject has severe hypersensitivity (≥Grade 3) to pembrolizumab and/or any of its excipients. • Subject who have received transfusion of blood products (including platelets or red blood cells) or administration of colony stimulating factors (including G-CSF, GM-CSF or recombinant erythropoietin) within 4 weeks prior to study Cycle 1, Day 1 (baseline). • Subject has a history of (non-infectious) pneumonitis that required steroids or current pneumonitis. • Subject has a history of interstitial lung disease. • Subject has an active infection requiring systemic therapy. • Subject has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the subject's participation for the full duration of the study, or is not in the best interest of the subject to participate, in the opinion of the treating Investigator. • Subject has not recovered (i.e., ≤ Grade 1 or at baseline) from adverse events due to a previously administered agent. • Participation in another clinical study of an investigational agent or has used an investigational device within 30 days of screening. • Subjects who have had any targeted small molecule therapy or any immunotherapy after their confirmed progression on anti-PD-1 therapy. • Subject has known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the study. • Subjects who are pregnant or 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 study treatment.