Essai Clinique

Généré le 18 avr. 2024 à partir de

Titre	Phase 2 Study of an Immunotherapeutic Vaccine, DPX-Survivac With Low Dose Cyclophosphamide Administered With Pembrolizumab in Patients With Persistent or Recurrent/Refractory Diffuse Large B-Cell Lymphoma (DLBCL)
Protocole ID	SPiReL
ClinicalTrials.gov ID	NCT03349450
Type(s) de cancer	Lymphome non-hodgkinien (LNH)
Phase	Phase II
Type étude	Traitement
Médicament	DPX-Survivac
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL H SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	Montréal
Investigateur principal	Dr Pierre Laneuville
Coordonnateur	Lorena Iglesias 514-934-1934 poste 34907
Statut	Fermé
But étude	This is a Phase 2 non-randomized, open label, uncontrolled, efficacy and safety study. Study participants will receive two priming doses of 0.5mL of DPX-Survivac 21 days apart and up to six 0.1ml booster vaccinations every two months with low dose metronomic oral cyclophosphamide (50 mg BID) for one year or until disease progression, whichever occurs first. Pembrolizumab 200 mg will be administered every 3 weeks for up to one year or until disease progression, whichever occurs first.
Critères d'éligibilité	• Subjects with histologically proven recurrent DLBCL. Subjects may have recurrence after primary, secondary or tertiary treatment regimens for DLBCL. • Subjects with recurrence at least 90 days post aggressive first line combination chemotherapy (e.g. RCHOP, Hyper-CVAD or other aggressive "curative" combination), autologous stem cell transplantation (ASCT), or aggressive second line combination therapy are eligible. • Patients with partial response or measurable disease after first line therapy (who are not candidates for ASCT) or after second or third line therapy without disease progression may also be eligible. • Patients with recurrence any time after non-aggressive combination or single agent therapy with or without Rituximab (ie. CVP, CHL or, VP16) for first, second or third line disease are eligible. • Patients may have evidence of transformed lymphoma with past history of indolent lymphoma provided current biopsy shows DLBCL. • Patients with double hit or high grade lymphomas including Burkitts lymphoma and High Grade B-Cell lymphoma unclassifiable (with features intermediate between Burkitts and diffuse large B cell lymphoma are eligible. • Be willing and able to provide written informed consent/assent for the trial. • Male or female ≥ 18 years of age on day of signing informed consent • Have at least one measurable site of disease based on Cheson Criteria using standard CT imaging. • Be willing to provide tissue from a newly obtained (up to 3 month prior to Day 0) biopsy of a tumour lesion. If this is not available, the patient must be willing to undergo a core biopsy prior to starting treatment. They must also be willing to provide an on-treatment biopsy. • Have a performance status of 0-1 on the ECOG Performance Scale. • Demonstrate adequate organ function confirmed 48 hours prior to enrollment. • Previous localized surgery, radiotherapy, chemotherapy, and immunotherapy more than 21

	days prior to SD0. Cyclophosphamide, up to 100 mg/day, may be administered until SD-1 for subjects already receiving as a single agent therapy. • Subjects must have evidence of survivin expression in pre-treatment tumour sample (> 10% of tumour cells stained). • A life expectancy > 6 months. • Female subject of childbearing potential should have a negative urine or serum pregnancy within 72 hours prior to receiving the first dose of study medication • Ability to comply with protocol requirements
Critères d'exclusion	• Is currently participating and receiving study therapy or has participated in a study of an investigational agent and received study therapy or used an investigational device within 21 days of the first dose of treatment (SD0). • Patients eligible for possible curative therapies such as ASCT. • LDH greater than 5 times the upper limit of normal. • Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 35 days prior to the first dose of trial treatment (SD0), except that used as pre-medication for chemotherapy or contrast-enhanced studies are eligible. Subjects may be on physiologic doses of replacement prednisone or equivalent doses of corticosteroid (<10 mg daily). • Has a known history of active TB (Bacillus Tuberculosis) • Hypersensitivity to Pembrolizumab or any of its excipients. • Has had a prior anti-cancer monoclonal antibody (mAb) within 21 days prior to study Day 0 or who has not recovered (i.e., ≤ Grade 1) from adverse events due to agents administered more than 21 days earlier. • Has had prior chemotherapy, targeted small molecule therapy, or radiation therapy within 21 days prior to study Day 0 • Has a known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin or squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer. • Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis. • Progressive CNS lymphoma requiring treatment within 35 days prior to SD0. • Has history of active autoimmune disease that has required systemic treatment in the past 2 years. Replacement therapy (eg., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment. • Has known history of, or any evidence of active, non-infectious pneumonitis. • Thyroiditis within the past 5 years. • Has an active infection requiring systemic therapy. Note: Subjects completing a course of antibiotic for acute infection 7 days prior to SD0 and who do not experience a recurrence of symptoms or fever are eligible. • Presence of a serious acute infection or chronic infection • Other serious intercurrent chronic or acute illness • Is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the trial, starting with screening visit to 120 days post completion of study • Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent. • Has a known history of Human Immunodeficiency Virus (HIV) (HIV 1/2 antibodies). • Has known active Hepatitis B (e.g., HBsAg reactive) or Hepatitis C (e.g., HCV RNA [qualitative] is detected). Evidence of Hepatitis B surface antigen without transaminitis is allowed provided patient is treated with anti-viral therapy (Heptovir or Tenofovir) • Patients who have received prior survivin based vaccines. • Acute or chronic skin disorders that will interfere with subcutaneous injection of the vaccine or subsequent assessment of potential skin reactions. • Serious intercurrent chronic or acute illness, such as cardiac disease (New York Heart Association class III or IV), hepatic disease, or other illness considered by the investigator as an unwarranted high risk for an investigational product. • Allergies to any vaccine, that after discussion with the medical monitor are serious enough to warrant exclusion from this study. • Received a live vaccine within 30 days of planned start of study therapy. Note: Seasonal influenza vaccines for injection are generally inactivated flu vaccines and are allowed; however intranasal influenza vaccines (e.g., Flu-Mist®) are live attenuated vaccines, and are not allowed