Essai Clinique

Généré le 03 mai 2024 à partir de

Titre	A Phase 2A Multi Centre, Open Label, Pilot Study Of Pembrolizumab Added to The Standard First-Line Therapy Of Cyclophosphamide, Bortezomib And Dexamethasone (CyBorD) In Newly Diagnosed Multiple Myeloma Patients Not Eligible For Autologous Stem Cell Transplantation
Protocole ID	CMRG 006
ClinicalTrials.gov ID	NCT04258683
Type(s) de cancer	Myélome
Phase	Phase II
Type étude	Clinique
Médicament	Pembrolizumab avec CyBorD
Institution	CIUSSS DE L'ESTRIE – CENTRE HOSP. UNIV. DE SHERBROOKE H HOPITAL FLEURIMONT 3001 12e Avenue Nord, Sherbrooke, QC, J1H 5N4
Ville	
Investigateur principal	Dr Michel Pavic
Coordonnateur	Anick Champoux 819-346-1110 poste 12811
Statut	Fermé
But étude	This is a phase 2A multi-centre, open label, pilot study of pembrolizumab added to the standard first-line therapy of cyclophosphamide, bortezomib and dexamethasone (CyBorD) in newly diagnosed patients with multiple myeloma that are not eligible for autologous stem cell transplantation.

Critères d'éligibilité	• Must be able to understand and voluntarily sign an informed consent form (ICF).
	• Must be ≥ 18 years of age at the time of signing the ICF.
	• Newly diagnosed multiple myeloma (according to the IMWG diagnostic criteria) receiving standard of care CyBorD treatment and have not achieved at least VGPR or progressed after 2 cycles of treatment.
	• Must have measurable disease according to the IMWG criteria as defined below:
	  • Serum M-protein ≥ 5 g/l
	  • Urine M-protein ≥ 200 mg/24 h
	  • Serum free light chains (FLC) assay: Involved FLC level ≥ 100 mg/l and an abnormal serum free light chain ratio (< 0.26 or > 1.65)
	• Must have Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2.
	• Must not be eligible for consolidation with high dose chemotherapy and autologous stem cell transplantation (ASCT).
	• Must not have any known congenital or acquired immune suppression.
	• Must have negative serology for HIV, HBV and HCV.
	• Male subject must agree to use contraception as detailed in Appendix 3 of this protocol during the treatment period and for at least 120 days after the last dose of study treatment and refrain from donating sperm during this period.
	• Female subject is eligible to participate if she is not pregnant (see Appendix 3 of protocol), not breastfeeding, and at least one of the following conditions applies:
	  • Not a woman of childbearing potential (WOCBP) as defined in Appendix 3 of protocol OR
	  • A WOCBP who agrees to follow the contraceptive guidance in Appendix 3 of protocol during the treatment period and for at least 30 days after the last dose of study treatment.
	• Must have adequate organ function as defined below. Specimens must be collected within 10 days prior to the start of study treatment.
	  • Absolute neutrophil count (ANC) ≥1500/µL
	  • Platelets ≥100 000/µL

- Hemoglobin ≥9.0 g/dL or ≥5.6 mmol/La
- Creatinine OR Measured or calculated creatinine clearance (GFR can also be used in place of creatinine or CrCl) ≤1.5 × ULN OR≥30 mL/min for subject with creatinine levels >1.5 × institutional ULN
- Total bilirubin ≤1.5 ×ULN OR direct bilirubin ≤ULN for subjects with total bilirubin levels >1.5 × ULN
- AST (SGOT) and ALT (SGPT) ≤2.5 × ULN (≤5 × ULN for subjects with liver metastases)
- International normalized ratio (INR) OR prothrombin time (PT) Activated partial thromboplastin time (aPTT) ≤1.5 × ULN unless subject is receiving anticoagulant therapy as long as PT or aPTT is within therapeutic range of intended use of anticoagulants

Critères d'exclusion

- Prior exposure to Pembrolizumab (or other anti-PD-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., CTLA-4, OX 40, CD137)).
- Known allergies, hypersensitivity to mannitol, corticosteroids, monoclonal antibodies or human proteins, or their excipients (refer to the Pembrolizumab IB), or known sensitivity to mammalian-derived products
- History of prior allogeneic stem cell transplantation or solid organ transplantation that requires immunosuppressive therapy.
- History of prior autologous peripheral stem cell transplantation or bone marrow transplantation for any indication.
- Subject who is 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. Subjects who have entered the follow-up phase of an investigational study may participate as long as it has been 4 weeks after the last dose of the previous investigational agent.
- Myeloma with known CNS involvement, plasma cell leukemia or amyloidosis.
- Chemotherapy or other anti-myeloma therapy other than three or less cycles of CyBorD. Prior bisphosphonates or other bone consolidation therapy is acceptable either if it was given for myeloma or for any other indication.
- Known congenital or acquired immune deficiency or ongoing chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immune suppressive therapy within 7 days prior to the first dose of study drug for any indication, excluding Dexamethasone or steroids given as part of myeloma treatment.
- Has a history of (non-infectious) pneumonitis that required steroids or has current pneumonitis.
- Known chronic obstructive pulmonary disease (COPD), defined as a FEV1 <50% predicted value.
- Known moderate or severe persistent asthma within the last 2 years, or currently has uncontrolled asthma of any classification.
- History of or current uncontrolled cardiovascular disease including:
    - Unstable angina, myocardial infarction, or known congestive heart failure Class III/IV (Appendix 5 of protocol) within the preceding 12 months.
    - Transient ischemic attack within the preceding 3 months, pulmonary embolism within the preceding 2 months.
    - Any of the following: sustained ventricular tachycardia, ventricular fibrillation, Torsades de Pointes, cardiac arrest, Mobitz II second degree heart block or third-degree heart block; known presence of dilated, hypertrophic, or restrictive cardiomyopathy.
    - QTc prolongation as confirmed by ECG assessment at screening (QTc >470 milliseconds).
- Has an active infection requiring systemic therapy.
- Has received a live vaccine within 30 days prior to the first dose of study drug. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette-Guérin (BCG), and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (eg, FluMist®) are live attenuated vaccines and are not allowed.
- Has received prior radiotherapy within 2 weeks of start of study treatment. Subjects must have recovered from all radiation-related toxicities
- Prior history of malignancies, other than MM, unless the subject has been free of the disease for 3 years or longer. Exceptions include the following:
    - Basal or squamous cell carcinoma of the skin.
    - Carcinoma in situ of the cervix or breast
    - Adenocarcinoma of the prostate (TNM stage of T1a or T1b)
- Women who are pregnant, breastfeeding or planning to become pregnant while enrolled in this study, or within 90 days after the last dose of study medications. Male subject who plans to father a child while enrolled in this study, or within 120 days after the last dose of study medications.
- Has known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the study.
- Has a history or current evidence of any condition (i.e. uncontrolled diabetes, active or uncontrolled infection, acute diffuse pulmonary disease, pericardial disease, uncontrolled thyroid dysfunction), therapy or laboratory abnormality that might confound the results of the study, 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.