Essai Clinique

Généré le 05 mai 2024 à partir de

Titre	Étude multicentrique ouverte de phase I/II visant à évaluer l'innocuité, les paramètres pharmacocinétiques et l'efficacité du CC-92480 en monothérapie et en association avec la dexaméthasone chez des sujets atteints d'un myélome multiple récidivant et réfractaire
Protocole ID	CC-92480-MM-001
ClinicalTrials.gov ID	NCT03374085
Type(s) de cancer	Myélome
Phase	Phase I-II
Stade	Récidivant/réfractaire (2ième ligne de traitement et plus)
Type étude	Clinique
Médicament	CC-92480 en monothérapie et en association avec dexaméthasone
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	
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Statut	Actif en recrutement
But étude	This is an open-label, multi-center, international, Phase 1/2 study to assess the safety, PK and efficacy of CC-92480 monotherapy and in combination with dexamethasone in subjects with relapsed and refractory multiple myeloma (RRMM). RRMM patient previously treated with at least 3 prior regimens including lenalidomide or pomalidomide, a proteasome inhibitor and a CD38 antibody will be eligible.

Critères d'éligibilité	• Subject is ≥ 18 years of age at the time of signing the informed consent form (ICF).
	• Subject must understand and voluntarily sign an ICF prior to any study-related assessments/procedures being conducted.
	• Subject is willing and able to adhere to the study visit schedule and other protocol requirements.
	• Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1 or 2.
	• Subjects must have a documented diagnosis of MM and measurable disease at enrollment. Measurable disease is defined as:
	  • M-protein quantities ≥ 0.5 g/dL by sPEP or
	  • ≥ 200 mg/24 hour urine collection by uPEP or
	  • Serum FLC levels > 100 mg/L (milligrams/liter) involved light chain and an abnormal kappa/lambda (κ/λ) ratio in subjects without measurable serum or urine M-protein or
	  • For subjects with immunoglobulin class A (IgA), myeloma whose disease can only be reliably measured by quantitative immunoglobulin measurement, a serum IgA level ≥ 0.50 g/dL.
	• All subjects must have:
	  • Received at least 3 prior anti-myeloma regimens including at least 2 consecutive cycles of lenalidomide, pomalidomide, a proteasome inhibitor, a glucocorticoid and a CD38 antibody (note: induction with or without bone marrow transplant and with or without maintenance therapy is considered one regimen).
	  • Documented disease progression on or within 60 days from the last dose of their last myeloma therapy

- Subjects who had CAR-T therapy as their last myeloma therapy are eligible as long as they have documented disease progression following CAR-T therapy.
- In addition to criteria above (a and b), subjects enrolled in Part 2 must have disease refractory to an immunomodulatory agent (lenalidomide and/or pomalidomide), a glucocorticoid, a proteasome inhibitor, and a CD38 antibody. Refractory is defined as disease that is nonresponsive on therapy (failure to achieve minimal response or development of progressive disease), or progresses within 60 days of last dose.

- Subjects must have the following laboratory values:
  - Absolute neutrophil count (ANC) ≥ 1.25 x 109/L without growth factor support for ≥ 7 days (≥ 14 days for pegfilgrastim). ANC of ≥ 1.00 x 109/L is permitted for the dose expansion cohorts (Part 2).
  - Hemoglobin (Hgb) ≥ 8 g/dL.
  - Platelets (plt) ≥ 75 x 109/L without transfusion for ≥ 7 days.
  - Corrected serum calcium ≤ 13.5 mg/dL (≤ 3.4 mmol/L).
  - Creatinine clearance (CrCl) based on Cockcroft-Gault formula ≥ 45 mL/min.
  - AST/SGOT and ALT/SGPT ≤ 3.0 x upper limit of normal (ULN).
  - Serum bilirubin ≤ 1.5 x ULN or < 3.0 mg/dL for subjects with documented Gilbert's syndrome.
  - Uric acid ≤ 7.5 mg/dL (446 µmol/L).
  - PT/INR < 1.5 x ULN and partial thromboplastin time (PTT) < 1.5 x ULN, (for subjects not receiving therapeutic anticoagulation).
- Females of childbearing potential (FCBP) must:
  - Have two negative pregnancy tests as verified by the Investigator prior to starting study therapy. She must agree to ongoing pregnancy testing during the course of the study, and after discontinuation of CC-92480. This applies even if the subject practices true abstinence* from heterosexual contact.
  - Either commit to true abstinence* from heterosexual contact (which must be reviewed on a monthly basis and source documented) or agree to use, and be able to comply with, two reliable forms of contraception as defined in the PPP and provided to the subject at the time of informed consent, without interruption, 28 days prior to starting CC-92480, during the study therapy (including during dose interruptions), and for 28 days after discontinuation of study therapy.
- Note: A female of childbearing potential (FCBP) is a female who: 1) has achieved menarche at some point and, 2) has not undergone a hysterectomy or bilateral oophorectomy, or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (ie, has had menses at any time in the preceding 24 consecutive months).
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- Male subjects must: Practice true abstinence* (which must be reviewed on a monthly basis) or agree to use of a condom during sexual contact with a pregnant female or a female of childbearing potential while participating in the study (even during dose interruptions) and for at least 3 months following CC-92480 discontinuation in accordance with the PPP provided to the subject at the time of informed consent, even if he has undergone a successful vasectomy. *True abstinence is acceptable when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (eg, calendar, ovulation, symptothermal, post-ovulation methods) and coitus interruptus (withdrawal) are not acceptable methods of contraception.
- Males must agree to refrain from donating sperm while on CC-92480 for 90 days after its discontinuation. Females must agree to refrain from donating ova while on CC-92480 for 28 days after its discontinuation.
- All subjects must agree to refrain from donating blood while on CC-92480 and for 28 days after its discontinuation.

Critères d'exclusion

- Subject has a significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from participating in the study.
- Subject has any condition including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study.
- Subject has any condition that confounds the ability to interpret data from the study.
- Subject has non-secretory multiple myeloma.
- Subject has refractory primary multiple myeloma (ie, no history of at least a minor response to a prior treatment regimen).
- Subject has plasma cell leukemia or active leptomeningeal myelomatosis.
- Subject has documented, systemic light chain amyloidosis or Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, and Skin changes (POEMS) Syndrome.
- Subject has immunoglobulin class M (IgM) myeloma.
- Part 1: Subject has a history of allogeneic bone marrow transplantation. Part 2: Subject has a history of allogeneic bone marrow transplantation within 6 months prior to first dose. Subject should not have ongoing graft-versus-host disease (GVHD) requiring systemic immunosuppression.
- Subject is undergoing dialysis.
- Subjects with peripheral neuropathy ≥ Grade 2.
- Subjects with gastrointestinal disease that may significantly alter the absorption of CC-92480.
- Subject has impaired cardiac function or clinically significant cardiac disease, including any of the following:
  - LVEF < 45% as determined by ECHO or MUGA scan at Screening.
  - Complete left bundle branch, bifascicular block or other clinically significant abnormal

electrocardiographic (ECG) finding at Screening.
    - A prolongation of QT interval on Screening ECG as defined by repeated demonstration of a QTc interval >480 milliseconds (ms) using Fridericia's QT correction formula; a history of or current risk factors for Torsades de Pointe (eg, heart failure, hypokalemia, or a family history of Long QT Syndrome); and concurrent administration of medications that prolong the QT/QTc interval.
    - Congestive heart failure (New York Heart Association Class III or IV).
    - Myocardial infarction ≤6 months prior to starting CC-92480.
    - Unstable or poorly controlled angina pectoris, including the Prinzmetal variant of angina pectoris.
- Concurrent administration of strong CYP3A modulators; concurrent administration of proton-pump inhibitors (eg, omeprazole, esomeprazole, lansoprazole, pantoprazole) ≤ 2 weeks prior to starting CC-92480.
- Subject had prior systemic myeloma treatment with an investigational anti-myeloma agent (eg, anti-PD-1, anti-PD-L1) ≤ 5 half-lives prior to starting CC-92480 (not applicable for subjects who had CAR-T as last prior regimen); subject had prior exposure to approved myeloma therapies (including therapeutic monoclonal antibodies such as anti-CD38 or anti-SLAM-7) ≤ 5 half-lives or within 4 weeks prior to starting CC-92480 whichever is shorter.
- Subject had major surgery ≤ 2 weeks prior to starting CC-92480. Note: Subjects must have recovered from any clinically significant effects of recent surgery.
- Subject is a pregnant or nursing female, or intends to become pregnant or donate ova during participation in the study.
- Subject has known human immunodeficiency virus (HIV) infection.
- Subject has known active chronic hepatitis B or C virus (HBV/HCV) infection.
- Subject has a history of concurrent second cancer requiring ongoing systemic treatment.
- Subjects has a history of prior malignancy other than MM, except if the subject has been free of disease for ≥3 years OR the subject had one of the following noninvasive malignancies treated with curative intent without known recurrence:
    - Basal or squamous cell carcinoma of the skin.
    - Carcinoma in situ of the cervix or breast.
    - Stage 1 bladder cancer.
    - Incidental histological findings of localized prostate cancer such as tumor stage 1a or 1b (T1a or T1b) using the Tumor/Node/Metastasis (TNM) classification of malignant tumors OR prostate cancer that has been treated with curative intent.
- Subject has a history of anaphylaxis to thalidomide, lenalidomide, pomalidomide or dexamethasone.
- Subject has known or suspected hypersensitivity to the excipients (excipients include silica dimethyl silylate, anhydrous colloidal silicon dioxide, mannitol, fumaric acid and stearic acid) contained in the formulation of CC-92480 or dexamethasone.
- Subject has undergone either of the following within 14 days of initiating CC-92480:
    - Plasmapheresis.
    - Radiation therapy other than local therapy for symptomatic relief of MM associated bone lesions.
- Subject has received immunosuppressive medication within 14 days prior to the first dose of CC-92480. The following are exceptions to this criterion:
    - Intranasal, inhaled, topical or local corticosteroid injections (eg, intra-articular injection).
    - Systemic corticosteroids at doses that do not exceed 10 mg/day of prednisone or the equivalent.
    - Steroids as premedication for hypersensitivity reactions (eg, computed tomography [CT] scan premedication).
- Subject is unable or unwilling to undergo protocol required venous thromboembolism (VTE) prophylaxis.