Essai Clinique

Généré le 18 mai 2024 à partir de

Titre	Étude d'augmentation et d'expansion de la dose de phase I/II sans insu évaluant l'innocuité, la tolérabilité et l'activité clinique du conjugué anticorps-médicament GSK2857916 administré en association avec le schéma lénalidomide plus dexaméthasone (groupe A) ou le schéma bortézomib plus dexaméthasone (groupe B) chez des participants atteints d'un myélome multiple récidivant ou réfractaire
Protocole ID	DREAMM-6
ClinicalTrials.gov ID	NCT03544281
Type(s) de cancer	Myélome
Phase	Phase I-II
Stade	Récidivant/réfractaire (2ième ligne de traitement et plus)
Type étude	Traitement
Médicament	GSK2857916 en association avec Lénalidomide + Dexaméthasone (Bras A), ou Bortézomib + Dexaméthasone (Bras B)
Institution	CIUSSS DE L'EST-DE-L'ILE-DE-MONTREAL PAV. MAISONNEUVE/PAV. MARCEL-LAMOUREUX 5415 boul. de l'Assomption, Montréal, QC, H1T2M4
Ville	
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Statut	Fermé
But étude	This study will evaluate the safety and tolerability profile of belantamab mafodotin when administered in combination with approved regimens of either Lenalidomide Plus Dexamethasone [Len/Dex (Arm A)] or Bortezomib Plus Dexamethasone [Bor/Dex (Arm B)] in participants with RRMM, i.e., those who have relapsed or who are refractory to at least 1 line of approved therapy. Part 1 of the study will be a dose escalation phase to evaluate the safety and tolerability of up to 3 dose levels and up to 2 dosing schedules of belantamab mafodotin in combination with the two standard of care (SoC) regimens. Part 2 will further evaluate the safety and preliminary clinical activity of belantamab mafodotin at selected dose levels and dosing schedules in combination with Len/Dex or Bor/Dex. A total of 152 evaluable participants will be enrolled in the study with up to 27 in Part 1 and up to 125 in Part 2. Participants receiving treatment Arm A, may continue combination treatment until the occurrence of progressive disease (PD), intolerable adverse events (AEs), consent withdrawal, death or end of study. The participants receiving treatment Arm B, may continue combination treatment for a total of up to 8 cycles. After 8 cycles of combination therapy, the participants will continue treatment with belantamab mafodotin, as a monotherapy until the occurrence of PD, intolerable AEs, consent withdrawal, death or end of study.
Critères d'éligibilité	• Capable of giving signed informed consent. • Male or female, 18 years or older (at the time consent is obtained). • Have confirmed diagnosis of Multiple Myeloma (MM) as defined by the IMWG. • Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1 for Arm A and 0 to 2 for Arm B. • Have undergone stem cell transplant (SCT), or are considered transplant ineligible. • Have been previously treated with at least 1 prior line of MM therapy, and must have documented disease progression during or after their most recent therapy. • Must have at least ONE aspect of measurable disease, defined as one the following: Urine

	M-protein excretion >=200 milligram (mg)/24 hours, or; Serum M-protein concentration >=0.5 gram (g)/deciliter (dL) (>=5.0 g/Liter), or; Serum free light chain (FLC) assay: involved FLC level >=10 mg/dL (>=100 mg/L) and an abnormal serum FLC ratio (<0.26 or >1.65). • Participants with a history of autologous SCT, are eligible for study participation provided the following eligibility criteria are met: Autologous SCT was >100 days prior to study enrollment; No active bacterial, viral, or fungal infection(s) present; Participant meets the remainder of the eligibility criteria. • All prior treatment-related toxicities (defined by National Cancer Institute Common Toxicity Criteria for Adverse Events [NCI-CTCAE], Version 4.03, 2010) must be Grade <= 1 at the time of enrollment, except for alopecia. Participants with Grade 2 neuropathy can be enrolled into Len/Dex treatment arm, but not into Bor/Dex treatment arm. • Adequate organ system functions as defined by the laboratory assessments. • The contraceptions used by female participants be consistent with local regulations, regarding methods of contraception for those participating in clinical studies. A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies: is not a woman of child bearing potential (WOCBP) or Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of <1% per year), preferably with low user dependency, during the intervention period and for at least 4 months after the last dose of belantamab mafodotin and agrees not to donate eggs (ova, oocytes) for the purpose of reproduction during this period. The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy. WOCBP Participants Assigned to Arm A: • Due to lenalidomide being a thalidomide analogue with risk for embryo-fetal toxicity and prescribed under a pregnancy prevention/controlled distribution program, WOCBP participants will be eligible if they commit either to abstain continuously from heterosexual sexual intercourse or to use two methods of reliable birth control (one method that is highly effective; beginning 4 weeks prior to initiating treatment with lenalidomide, during therapy, during dose interruptions and continuing for 4 weeks following discontinuation of lenalidomide treatment. Thereafter, WOCBP participants must use a contraceptive method that is highly effective (with a failure rate of <1% per year) for a further 3 months, and agree not to donate eggs (ova, oocytes) for the purpose of reproduction during this period: Two negative pregnancy tests must be obtained prior to initiating lenalidomide therapy. The first test should be performed within 10-14 days and the second test within 24 hours prior to prescribing lenalidomide therapy. WOCBP Participants Assigned to Arm B • WOCBP assigned to Arm B must have a negative highly sensitive serum pregnancy test within 72 hours of dosing on C1D1 and agree to use effective contraception during the study and for 4 months after the last dose of belantamab mafodotin or 7 months from the last dose of bortezomib, whichever is longer. • Male participants using contraception should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies. • Male participants are eligible to participate if they agree to the following: Arm A: from the time of first dose of study until 6 months after the last dose of belantamab mafodotin 4 weeks after the last dose of lenalidomide, whichever is longer, to allow for clearance of any altered spermArm B: from the time of first dose of study until 6 months after the last dose of belantamab mafodotin or 4 months from the last dose of bortezomib (whichever is the longer) to allow for clearance of any altered sperm. • Male participants must agree to refrain from donating sperm and either be abstinent from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long term and persistent basis) and agree to remain abstinent OR Must agree to use contraception/barrier as detailed below. • Agree to use a male condom even if they have undergone a successful vasectomy and female partner to use an additional highly effective contraceptive method with a failure rate of <1% per year when having sexual intercourse. Male participants should also use a condom with pregnant females. If the female partner of the male participant is pregnant at the time of enrollment, or becomes pregnant during the trial, the male participant must agree to remain abstinent (if it is consistent with their preferred and usual lifestyle) or use a male condom.
Critères d'exclusion	• Systemic anti-myeloma therapy (including systemic steroids) within <=14 days, or plasmapheresis within 7 days prior to the first dose of study drug. • Use of an investigational drug within 14 days or five half-lives (whichever is longer) preceding the first dose of study drug. • Prior treatment with a monoclonal antibody within 30 days of receiving the first dose of study drugs. • Prior allogenic stem cell transplant. Note: Participants who have undergone syngeneic transplant will be allowed only if they have no history and no currently active, graft versus host disease (GvHD). • Evidence of active mucosal or internal bleeding. • Any major surgery within the last four weeks. • Presence of active renal condition (infection, requirement for dialysis or any other condition that could affect participant's safety). Participants with isolated proteinuria resulting from MM are eligible, provided they fulfill criteria.

- Any serious and/or unstable pre-existing medical, psychiatric disorder or other conditions (including lab abnormalities) that could interfere with participant's safety, obtaining informed consent or compliance to the study procedures.
- Current active liver or biliary disease (with the exception of Gilbert's syndrome or asymptomatic gallstones, or otherwise stable chronic liver disease per investigator's assessment).
- Participants with invasive malignancies other than multiple myeloma are excluded, unless the second malignancy has been considered medically stable for at least 2 years. The participant must not be receiving active therapy, other than hormonal therapy for this disease. Note: Participants with curatively treated non-melanoma skin cancer are allowed without a 2-year restriction.
- Evidence of cardiovascular risk including any of the following: Evidence of current clinically significant uncontrolled arrhythmias, including clinically significant ECG abnormalities including 2nd degree (Type II) or 3rd degree atrioventricular (AV) block; History of myocardial infarction, acute coronary syndromes (including unstable angina), coronary angioplasty, or stenting or bypass grafting within 3 months of Screening; Class III or IV heart failure as defined by the New York Heart Association functional classification system; Uncontrolled hypertension.
- Known immediate or delayed hypersensitivity reaction or idiosyncratic reaction to drugs chemically related to belantamab mafodotin, or any of the components of the study treatment.
- Pregnant or lactating female.
- Active infection requiring treatment.
- Known Human immunodeficiency virus (HIV) infection.
- Presence of hepatitis B surface antigen (HBsAg), or hepatitis B core antibody (HBcAb at Screening or within 3 months prior to first dose of study treatment).
- Current corneal disease except for mild punctuate keratopathy.
- Positive hepatitis C antibody test result or positive hepatitis C Ribonucleic acid (RNA) test result at Screening or within 3 months prior to first dose of study treatment.
- Current corneal disease except for mild punctute keratopathy.
- Participants Assigned to Treatment A (belantamab mafodotin plus Len/Dex): Participants unable to tolerate antithrombotic prophylaxis must be excluded; Discontinuation of prior treatment with lenalidomide due to intolerable AEs.
- Participants Assigned to Treatment B (belantamab mafodotin plus Bor/Dex): Unacceptable AEs from previous bortezomib treatment; Ongoing Grade 2 or higher peripheral neuropathy or neuropathic pain from previous bortezomib treatment; Intolerance or contraindications to anti-viral prophylaxis.