Clinical research protocols

The various clinical studies on multiple myeloma open to recruitment at Hôpital Maisonneuve-Rosemont are presented on this page. These studies exclude forthcoming studies and ongoing studies closed to recruitment. The display of these various clinical studies is a tool to promote patient participation in clinical studies. Once again, improving the outcome of patients with multiple myeloma does not happen by chance; it is the result of research, which includes patient participation in clinical research!

First Line: Eligible for transplant

A phase II, open-label study of Bortezomib following nonmyeloablative allogeneic stem cell transplant in patients with high-risk multiple myeloma
HMR-MM-001
Research nurse Nathalie Lachapelle 514-252-3400 ext 4471

Inclusion Criteria :

- Age 18 to 65 years, inclusively.
- Newly diagnosed multiple myeloma patients (based on IMWG criteria) with measurable disease at diagnosis, based on presence of any of the following:
    - Serum intact immunoglobulin ≥ 10 g/L;
    - Bence-Jones proteinuria ≥ 200 mg/day;
    - Serum free light chain (sFLC) assay ≥ 100 mg/L (difference between involved and uninvolved FLC

levels) and an abnormal sFLC ratio.

- High-risk patients presenting any of the following:
    - ISS III;
    - del(17p13), t(4;14) with ISS II or III, t(14;16), t(14;20) and chromosome 1 abnormalities by FISH;
        - At this time, there is no international consensus on the threshold to consider these cytogenetic abnormalities as significant. For this study, we will consider arbitrarily a percentage ≥ 10% as significant.
    - PCL, defined as an absolute blood plasma cell count > 2×10^9/L and the presence of > 20% plasma cells among peripheral blood white cells;
    - Patients ≤ 50 years, regardless of cytogenetics or ISS stage.
- Having received a Bortezomib-containing regimen (VTD, CyBorD, VRD or PAD [in patients with PCL]) for a minimum of 4 cycles with ≥ partial response.
- Received high-dose Melphalan ≥ 140 mg/m^2 followed by autologous stem cell transplantation.
- Available HLA-identical sibling donor or 8/8 allele matched (HLA-A, -B, -C, -DR) MUD.

Exclusion Criteria

- Failure to achieve at least a partial response with a Bortezomib-based induction therapy.
- Progressive disease any time before NMA allogeneic transplant.
- Having received tandem autologous stem cell transplantation.
- Having received maintenance or consolidation therapy with Bortezomib after ASCT.
    - However, one common characteristic of high-risk

myeloma is short duration of response and early relapse after standard treatment. If delays to allogeneic transplant are expected because of complications or donor assessment, Lenalidomide at 10 mg die for a maximum of three months will be allowed after ASCT (initiated after day +90) and discontinued at least 14 days before the start of the conditioning regimen.

- Karnofsky score < 70% or comorbidity index HCT-CI > 3.
- Bilirubin > 2 x upper limit of normal (ULN) unless felt to be related to Gilbert's disease or hemolysis; AST and ALT > 2.5 x ULN; alkaline phosphatase > 5 x ULN.
- Peripheral neuropathies or neuropathic pain ≥ grade II.
- Poor organ function defined as either:
    - Diffusing capacity of the lung for carbon monoxide corrected for hemoglobin using Dinakara method (DLCOc) < 50%; forced expiratory volume in 1 second < 50%; forced vital capacity < 50%;
    - Left ventricular ejection fraction (LVEF) < 40% evaluated by echocardiogram or multi-gated acquisition scan (MUGA); uncontrolled arrhythmia; symptomatic cardiac disease;
    - Creatinine clearance < 60 mL/minute;
    - Liver cirrhosis.
- Patients with non secretory disease or non measurable disease in serum or urine at time of diagnosis.
- Known hypersensitivity to boron, mannitol or Bortezomib.
- Active infection with any of the following viruses: HIV, HTLV-1 or 2, hepatitis B (defined as HBsAg positivity) or hepatitis C (defined as anti-HCV positivity or HCV-RNA positivity).
- Presence of another malignancy with an expected survival estimated < 75% at 5 years (complete resection of basal cell carcinoma or squamous cell carcinoma, complete

resection of a ductal carcinoma in situ, presence of lobular carcinoma in situ, complete resection of carcinoma in situ of the cervix, or an in situ or low-risk prostate cancer after curative therapy are not exclusion criteria).

- Positive beta-human chorionic gonadotropin (β-hCG) pregnancy test, to be performed in all women of childbearing potential at screening and baseline. Female study participants who are surgically sterile (hysterectomy) or who have been postmenopausal for at least 12 consecutive months are automatically eligible for this criterion.
- Study participants not agreeing to remain abstinent or to practice double-barrier forms of birth control from trial screening through 90 days from the last dose of Bortezomib.
- Women who are lactating.
- Women of childbearing potential who are planning to become pregnant while enrolled in this study up to 30 days after the last Bortezomib injection.
- Participation in a trial with an investigational agent within 30 days prior to entry in the study.
- Inability to provide written informed consent prior to initiation of any study-related procedures, and inability, in the opinion of investigators, to comply with all requirements of the study.
- Estimated probability to survive less than 6 months after allogeneic transplant.
- Suspicion of cardiac amyloidosis.
- Current history of drug and/or alcohol abuse.
- Any abnormal condition or laboratory result that is considered by investigators capableof altering patient’s condition, compliance or study outcome.
- Any patient who, in the opinion of investigators, should not participate in this study.

A Phase II Study of Busulfan & Melphalan as Conditioning Regimen for Autologous Stem Cell Transplantation in Patients Who Received Bortezomib based induction for Newly Diagnosed Multiple Myeloma Followed by Lenalidomide Maintenance until Progression

NCT01702831

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Inclusion Criteria

- Age 18 to 75 years, inclusive.
- Study participants must have a diagnosis of multiple myeloma and are eligible for the planned ASCT.
- Untreated bone marrow sample was shipped to Princess Margaret Hosipital for MRD assay.
- Must have been treated with a velcade-based induction regimen. No limit to the number of cycles of induction.
- Study participants in whom the minimum stem cell dose of 2.0 x 106 CD34+ cells/kg has been collected.
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2.
- Negative beta-human chorionic gonadotropin (β-HCG) pregnancy test in all women of child-bearing potential (WOCBP).
- Study participants who are surgically sterile (ie, have undergone orchidectomy or hysterectomy); female study participants who have been postmenopausal for at least 12 consecutive months; or study participants who agree to

remain abstinent or to practice double-barrier forms of birth control from trial
screening through 30 days (for females) and 90 days (for males) from the last dose of the study drugs. If employing birth control, two of the following precautions must be used: vasectomy, tubal ligation, vaginal diaphragm, intrauterine device (IUD), birth control pill, birth control implant, condom, or sponge with spermicide.

- Ability to provide written informed consent prior to initiation of any study-related procedures, and ability, in the opinion of the Principal Investigator, to comply with all requirements of the study.

Exclusion Criteria

- Study participants with any of the following will be excluded from participation in the study:
- Myeloma progression at any time since starting initial therapy for myeloma.
- Prior treatment history of ASCT for any medical reason.
- Prior treatment history of high-dose chemotherapy with stem cell rescue for any medical reason, not limited to myeloma treatment.
- Prior treatment with busulfan or gemtuzumab ozogamicin for any reason.
- Systemic amyloidosis.
- Left ventricular ejection fraction (LVEF) < 45% as measured by either multi-gated acquisition scan (MUGA) or echocardiogram (ECHO) performed within 75 days prior to day of busulfan dose. If cyclophosphamide was used for stem cell harvest, an
- ECHO or MUGA must be done after the stem cell collection and prior to enrollment to confirm adequate cardiac function.
- Uncontrolled arrhythmia or symptomatic cardiac disease at

the time of screening.

- Symptomatic pulmonary disease, based on Forced Expiratory Volume in 1 Second (FEV1), Forced Vital Capacity (FVC) or Diffusing Capacity of the Lung for
- Carbon Monoxide (DLCO) < 50% of predicted (corrected for hemoglobin) measured within 75 days prior to day of busulfan dose.
- Aspartate transaminase (AST)/alanine transaminase (ALT) ≥ 3 x the upper limit of normal (ULN).
- History of elevated total serum bilirubin >2 mg/dL that had been caused by previous chemotherapy at any point, or total bilirubin > 2.0 mg/dL at the time of screening with the exception of Gilbert’s disease.
- Hepatic synthetic dysfunction evidenced by prolongation of the prothrombin time as
- International Normalized Ratio (INR) ≥ 2.0 at the time of screening.
- Any previous history of fulminant liver failure, cirrhosis, alcoholic hepatitis, esophageal varices, hepatic encephalopathy, ascites related to portal hypertension, bacterial or fungal liver abscess, biliary obstruction, and symptomatic biliary disease.
- Prior total body irradiation therapy, or radiation therapy directly applied to the liver.
- Patients with a known history of hepatitis B or hepatitis C should be on appropriate anti-viral therapy. Even so, these cases must be discussed with the sponsor and approval obtained prior to screening.
- Known history of or current HIV infection, or active hepatitis B or c infection or any uncontrolled active infection of any kind at the time busulfan administration.
- Serum creatinine >177 umol/L at the time of screening.
- Women who are pregnant or lactating.
- Current or history of drug and/or alcohol abuse.

- Use of other investigational therapies within 30 days of enrollment in this study.
- Clinically significant abnormality in medical history or upon examination that might interfere with the outcomes of the study in the opinion of the investigator.
- Any patient, who in the opinion of the investigator, should not participate in this study.

First line: Non-eligible for transplant

A phase III study of Lenalidomide and low-dose Dexamethasone with or without Pembrolizumab (MK-3475) in Newly Diagnosed and Treatment-Naïve Multiple Myeloma (KEYNOTE 185)

NCT02579863

Research nurse Nathalie Lachapelle 514-252-3400 ext 4471

Inclusion Criteria :

- Confirmed diagnosis of active multiple myeloma and measurable disease.
- Ineligible to receive treatment with auto-SCT due to age (≥65 years old) or any significant coexisting medical condition (cardiac, renal, pulmonary or hepatic dysfunction), likely to have a negative impact on tolerability of auto-SCT. Participants <65 years of age who refuse auto-SCT are not eligible for this study.
- Eastern Cooperative Oncology Group (ECOG) Performance

Status of 0 or 1.

- Female participants of childbearing potential must have 2 negative urine pregnancy tests (with a sensitivity of at least 25 Milli-international units/Milliliter) within 10 to 14 days and within 24 hours prior to receiving study medication.
- Female participants of childbearing potential must agree to use adequate contraception 28 days prior to study start, continuing throughout the study, and for up to 28 days after the last dose of lenalidomide (or 120 days after the last dose of pembrolizumab).
- Male participants of childbearing potential must agree to use adequate contraception from the first dose of study medication, continuing throughout the study, and for up to 28 days after the last dose of lenalidomide (or 120 days after the last dose of pembrolizumab)

Exclusion Criteria

- Has undergone prior allogeneic hematopoetic stem cell transplantation within the last 5 years.
- Has peripheral neuropathy ≥ Grade 2.
- Has a known additional malignancy that is progressing or requires active treatment within the last 5 years (except for basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ cervical cancer that has undergone potentially curative therapy).
- Has history of non-infectious pneumonitis that required steroids or current pneumonitis
- Has received prior therapy with an anti-programmed cell death 1 receptor (anti-PD-1), anti-programmed death-ligand 1 (anti-PD-L1), anti-PD-L2, anti-CD137, or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody (including ipilimumab or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint

pathways).
- Has a known Human Immunodeficiency Virus (HIV), or a known, active Hepatitis B (HBV), or a known, active Hepatitis C (HCV) infection.
- Is unable or unwilling to undergo thromboembolic prophylaxis including, as clinically indicated, aspirin, Coumadin (warfarin) or low-molecular weight heparin.
- Has lactose intolerance.
- Has an invasive fungal infection.

Refractory or relapsed Multiple Myeloma

A phase III study of Pomalidomide and low dose Dexamethasone with or without Pembrolizumab (MK3475) in refractory or relapsed and refractory Multiple Myeloma (rrMM). (KEYNOTE 183)
NCT02576977
Research nurse Nathalie Lachapelle 514-252-3400 ext 4471

Inclusion Criteria

- Has a confirmed diagnosis of active multiple myeloma and measurable disease
- Must have undergone prior treatment with ≥2 treatment lines of anti-myeloma therapy and must have failed last line of treatment (refractory to last line of treatment)
- Prior anti-myeloma treatments must have included an immunomodulatory drug (IMiD) AND proteasome inhibitor

alone or in combination and participant must have failed therapy with an IMiD OR proteasome inhibitor
- Has performance status of 0 or 1 on the Eastern Cooperative Oncology Group (ECOG) Performance Scale
- Female participants of childbearing potential must have 2 negative urine human chorionic gonadotropin tests within 10 to 14 days and within 24 hours prior to receiving study medication
- Female participants of childbearing potential and male participants must agree to use adequate contraception 28 days prior to study start and continuing for up to 28 days after the last dose of pomalidomide (or 120 days after the last dose of pembrolizumab)

Exclusion Criteria

- Has had prior anti-myeloma therapy within 2 weeks prior to study start and has not recovered (i.e., ≤ Grade 1 or at Baseline) from adverse events due to a previously administered agent
- Has undergone prior allogeneic hematopoetic stem cell transplantation within the last 5 years. (Participants who have had a transplant greater than 5 years ago are eligible as long as there are no symptoms of Graft versus Host Disease [GVHD]).
- Has received autologous stem cell transplant (auto-SCT) within 12 weeks before the first infusion or is planning for or is eligible for auto-SCT
- Has received previous therapy with pomalidomide
- Has peripheral neuropathy ≥ Grade 2
- Has a known additional malignancy that is progressing or requires active treatment within the last 5 years (except for basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ cervical cancer that has undergone potentially curative therapy)

- Has a history of (non-infectious) pneumonitis that required steroids or current pneumonitis
- Has received prior therapy with an anti-programmed cell death 1 receptor (anti-PD-1), antiprogrammed death-ligand 1 (anti-PD-L1), anti-PD-L2, anti-CD137, or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody (including ipilimumab or any other antibody or drug specifically targeting T-cell costimulation or checkpoint pathways)
- Is pregnant or breast-feeding

A phase 1b/2 study of Selinexor (KPT-330) in combination with backbone treatments for relapsed/refractory Multiple Myeloma NCT02343042

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Inclusion Criteria

- Histologically confirmed diagnosis, measurable disease and evidence of disease progression of MM, as described below.
- Symptomatic MM, based on IMWG guidelines. Patients must have measurable disease as defined by at least one of the following:
    - Serum M-protein ≥ 0.5 g/dL by serum electrophoresis (SPEP) or, for IgA myeloma, by quantitative IgA
    - Urinary M-protein excretion at least 200 mg/24 hours
    - Serum FLC ≥ 100 mg/L, provided that FLC ratio is abnormal
    - If serum protein electrophoresis is felt to be unreliable for routine M-protein measurement, then quantitative Ig levels by nephelometry or

turbidometry are acceptable.

- Any non-hematological toxicities (except for peripheral neuropathy as described in exclusion criterion #22) that patients experienced from treatments in previous clinical studies must have resolved to ≤ Grade 2 by Cycle 1 Day 1.
- Adequate hepatic function within 21 days prior to C1 D1:
- Adequate renal function within 21 days prior to C1 D1:
- Adequate hematopoietic function within 21 days prior to C1 D1:
- SdP (Arm 1) Only: Relapsed and refractory MM with:
    - Documented evidence of PD after achieving at least SD for ≥ 1 cycle during a previous MM regimen (i.e., relapsed MM)
    - ≤ 25% response (i.e., patients never achieved ≥ MR) or PD during or within 60 days from the end of the most recent MM regimen (i.e., refractory MM)
    - Previously undergone ≥ 2 cycles of lenalidomide and a proteasome inhibitor (in separate therapeutic regimens [not for maintenance] or in combination)
- SdB (Arm 2) Only: Relapsed or refractory MM with:
    - Documented evidence of relapse after ≥ 1 previous line of therapy
    - Not refractory to bortezomib in their most recent line of therapy
- SdL (Arm 3) Only:
    - Patients who received ≥ 1 prior therapeutic regimen (prior lenalidomide is allowed as long as patient was not refractory to prior lenalidomide)

Exclusion Criteria

- Smoldering MM.
- MM that does not express M-protein or FLC (i.e., non-secretory MM is excluded), and quantitative immunoglobulin levels cannot be used instead

- Documented active systemic amyloid light chain amyloidosis
- Active MM involving the central nervous system (CNS)
- Active plasma cell leukemia
- Blood (or blood product) transfusions and blood growth factors within 7 days of C1 D1 only for patients enrolling into the Expansion Phase
- Radiation, chemotherapy, or immunotherapy or any other anticancer therapy ≤ 2 weeks prior to C1 D1, and radio-immunotherapy within 6 weeks prior to C1 D1. Patients on long-term glucocorticoids during Screening, including use for spinal cord compression, do not require a washout period. Prior radiation is permitted for treatment of fractures or to prevent fractures as well as for pain management
- Treatment with an investigational anti-cancer therapy within 3 weeks prior to C1 D1
- Prior autologous stem cell transplantation < 1 month, or allogeneic stem cell transplantation < 3 months prior to C1 D1
- Active graft versus host disease after allogeneic stem cell transplantation
- A life expectancy of < 3 months
- Major surgery within 4 weeks prior to C1 D1
- Active, unstable cardiovascular function:
    - Symptomatic ischemia, or
    - Uncontrolled clinically-significant conduction abnormalities (e.g., patients with ventricular tachycardia on antiarrhythmics are excluded; patients with 1st degree atrioventricular (AV) block or asymptomatic left anterior fascicular block/right bundle branch block (LAFB/RBBB) will not be excluded), or
    - Congestive heart failure (CHF) of New York Heart Association (NYHA) Class ≥ 3, or

    - Myocardial infarction (MI) within 3 months prior to C1 D1
    - Ejection fraction (EF) < 50% at screening
- Uncontrolled active hypertension
- Uncontrolled active infection requiring parenteral antibiotics, antivirals, or antifungals within one week prior to first dose
- Known active hepatitis A, B or C
- Known HIV infection or HIV seropositivity
- Prior history of malignancies: cancer treated with curative intent > 5 years before study enrollment and without evidence of recurrence will be allowed. Cancer treated with curative intent < 5 years previously will not be allowed unless approved by the medical monitor. Exceptions include:
    - Resected basal or squamous cell carcinoma of the skin
    - Carcinoma in situ of the cervix
- Any active gastrointestinal dysfunction that prevents the patient from swallowing tablets, or interferes with absorption of study treatment
- Currently pregnant or breastfeeding
- A serious psychiatric or medical condition which, in the opinion of the investigator, could interfere with treatment
- Hypersensitivity to any of the treatments for the Arm in which the patient is enrolled
- In the SdB (Arm 2)only:
    - Prior history of neuropathy Grade > 2, or Grade 2 neuropathy with pain at screening (within 21 days prior to C1 D1)

An Open Label, Randomized Phase 2 Trial of Pomalidomide/Dexamethasone With or Without Elotuzumab in relapsed and refractory Multiple Myeloma
NCT02654132
Research nurse Nathalie Lachapelle 514-252-3400 ext 4471

Inclusion Criteria

- ≥ 2 prior lines of therapy which must have included at least 2 consecutive cycles of lenalidomide and a proteosome inhibitor alone or in combination
- Documented refractory or relapsed and refractory multiple myeloma
- Refractory to proteosome inhibitor and lenalidomide, and to last treatment
- Relapsed and refractory patients must have achieved at least a partial response to previous treatment with proteosome inhibitor or lenalidomide, or both, but progressed within 6 months, and were refractory to their last treatment
- Measurable disease at screening
- Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2

Exclusion Criteria

- Active plasma cell leukemia
- Prior treatment with pomalidomide
- Unable to tolerate thromboembolic prophylaxis while on the study
- Prior autologous stem cell transplant within 12 weeks

- Known Human Immunodeficiency Virus (HIV) infection or active hepatitis A, B, or C

Other types of studies including evaluation of support treatments

None

Patient referral

To refer a patient to us for a clinical study, please contact Nathalie Lachapelle, nurse and research coordinator, at 514-252-3400, ext. 4471.

For multiple myeloma studies in other centers in Quebec, please refer to the GEOQ site.