

Informed Consent to Participate in Research



Your Name: _____

Study Title: A Multi-center Phase II Trial Randomizing Novel Approaches for Graft-versus-Host Disease Prevention Compared to Contemporary Controls

Protocol: BMT CTN 1203

Principal Investigator: *Insert local PI information*

Sponsor: The National Institutes of Health (NIH) is sponsoring this study by providing financial support through the Blood and Marrow Transplant Clinical Trials Network (BMT CTN).

1. Introduction

We invite you to join this clinical trial, also known as a research study. We are doing this study because we want to compare three new combinations of medications to see which is better at preventing Graft-versus-Host Disease (GVHD). You are being asked to join this study because:

1. You have a disease that can be treated by a peripheral blood stem cell transplant; and
2. Your doctor plans on using a reduced-intensity conditioning regimen for your transplant.

This study will take at least two (2) years and will include 270 participants – 90 participants in each of three (3) treatment groups.

This Consent Form will tell you about the purpose of the study, the possible risks and benefits, other options available to you, and your rights as a participant in the study.

Everyone who takes part in research at [*insert facility name*] should know that:

- Being in any research study is voluntary.
- You may or may not benefit from being in the study. Knowledge we gain from this study may benefit others.

- If you join the study, you can quit the study at any time.
- If you decide to quit the study, it will not affect your care at [insert name of facility or institution].
- Please ask the study staff questions about anything that you do not understand, or if you would like to have more information.
- You can ask questions now or any time during the study.
- Please take the time you need to talk about the study with your doctor, study staff, and your family and friends. It is your decision to be in the study. If you decide to join, please sign and date the end of the Consent Form.

You and your doctor will discuss other treatment choices if you do not want to participate in this study.

2. Study Background

The National Institutes of Health (NIH), through the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), are providing staff support and money for this research study. The BMT CTN and the NIH will make decisions about how to manage the study.

A stem cell transplant is a standard therapy for blood cancers such as acute and chronic leukemias, lymphoma and myelodysplastic disorders. A common problem that may occur after a stem cell transplant is a condition known as GVHD. The word “graft” refers to the donor blood cells that you will receive during your transplant. The word “host” refers to the person (in this case, you) receiving the cells. GVHD is a complication where the donor graft attacks and damages some of your (the transplant recipient's) tissues.

- GVHD can cause skin rash, intestinal problems such as nausea, vomiting, or diarrhea,
- It may also damage your liver and cause hepatitis or jaundice.
- GVHD may also increase your risks of infection.

3. Study Purpose

We are inviting you to take part in this study because you have a cancer of the blood or lymph glands and a stem cell transplant is a treatment option.

The purpose of this study is to compare three combinations of medications to see whether one or more of them are better than the current standard of care (Tacrolimus/Methotrexate) to prevent GVHD. These combinations of medication in this study are:

Treatment Group A: Tacrolimus, methotrexate and bortezomib

Treatment Group B: Tacrolimus, methotrexate and maraviroc

Treatment Group C: Tacrolimus, mycophenolate mofetil and cyclophosphamide

Doctors want to know which combination (A, B or C) is better, or if they give the same results. The current standard of care for preventing GVHD is Tacrolimus/Methotrexate. This combination is not available on this study. The study will help doctors make choices about medications to prevent GVHD for future transplant patients.

4. Right to Ask Questions and/or Withdraw

You have the right to ask questions about the study at any time. If you have questions about your rights as a participant or you want to leave the study, please contact:

[insert contact info]

Being in this study is voluntary. You can choose not to be in this study or leave this study at any time. If you choose not to take part or leave this study, it will not affect your regular medical care in any way.

Your study doctor and study staff will be available to answer any questions that you may have about taking part in or leaving this study.

5. Study Treatment and Tests

We will check your health before you start treatment, while you receive treatment, and for one year after transplant.

Before You Begin the Study

Before you begin the study, you will need to have several exams, tests or procedures to find out if you can be in the study. All patients participating in this study need to have a matched donor. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. These include:

- Medical history
- Physical examination, including height and weight
- Blood and urine tests
- Heart function tests, including EKG and ejection fraction
- Lung (pulmonary) function tests
- Tests to evaluate your cancer, including a bone marrow aspirate/biopsy if you have acute leukemia, chronic myelogenous leukemia or myelodysplastic syndrome, and imaging studies if you have lymphoma.
- Chest X-ray or chest CT
- A pregnancy test if you are a woman able to have children. If you are pregnant, you will not be able to take part in this study.

- *Optional* blood samples for future research (see Section 19: Blood Samples for Future Research).

Study Participation

If you decide to join the study, your participation will last for **1 year** after your transplant. We will ask you to sign this Consent Form and you will get a copy of the signed form to keep.

Before the Transplant

Before your transplant, your doctor will choose from one of several conditioning regimens. The conditioning regimen prepares your body for transplant. It uses treatments such as chemotherapy and radiation to destroy the cancer cells and the cells that make up your immune system. Your doctor will decide which conditioning regimen you will receive before you are assigned to one of the three (3) treatment groups.

Randomization

We will use a computer to randomly assign you to 1 of 3 treatment groups. You will have an equal chance of being placed in 1 of the 3 groups. Neither you nor your doctor or study investigator will have any control over which treatment group you will be assigned.

During Your Transplant

The treatments that are used to prevent GVHD either start before or after the infusion of stem cells. These treatments are a combination of immune suppressing drugs and a standard component of the transplant.

The 3 treatment groups being included in this study are outlined below:

Treatment Group A: Tacrolimus, methotrexate and bortezomib

- Tacrolimus will be given daily per institutional standards, as a pill by mouth or by intravenous infusion (through your vein), beginning three (3) days before your transplant. The amount of drug given will slowly be decreased over time and eventually stopped. This process occurs over several months.
- Methotrexate will be given by intravenous infusion (through your vein) on four (4) different days (1, 3, 6 and 11) after your transplant.
- Bortezomib will be given by intravenous push (3-5 second shot in your vein) on three (3) different days (1, 4 and 7) after your transplant.

Treatment Group B: Tacrolimus, methotrexate and maraviroc group

- Tacrolimus will be given daily per institutional standards, as a pill by mouth or by intravenous infusion (through your vein), beginning three (3) days before your transplant. The amount of drug given will slowly be decreased over time and eventually stopped. This process occurs over several months.
- Methotrexate will be given by intravenous infusion (through your vein) on four (4) different days (1, 3, 6 and 11) after your transplant.

- Maraviroc will be given as a pill by mouth twice a day, beginning three (3) days before your transplant and will continue for 30 days after your transplant.

Treatment Group C: Tacrolimus, mycophenolate mofetil and cyclophosphamide group

- Tacrolimus will be given daily per institutional standards, as a pill by mouth or by intravenous infusion (through your vein), beginning on day five (5) after your transplant. The amount of drug given will slowly be decreased over time and eventually stopped. This process occurs over several months.
- Mycophenolate mofetil will be given daily by intravenous infusion (through your vein) or as a pill by mouth three times a day, beginning on Day 5 after your transplant, and will continue for 30 days. Your doctor may decide to continue this drug if active GVHD is present.
- Cyclophosphamide will be given by intravenous infusion (through your vein), over 1-2 hours, on Day 3 and Day 4 after your transplant.

Peripheral Blood Stem Cell Transplant

On your transplant day, the stem cells will be given to you through your catheter, like a blood transfusion. The cells will travel to your bone marrow where they will start to make healthy, new blood cells after several weeks.

Health Evaluations After the Transplant

We will test (evaluate) your health during the study. These tests and how often they are scheduled are standard care for patients receiving an allogeneic transplant. They would be done even if you were not part of this study. You will be watched closely for any signs and symptoms of GVHD.

- Physical exam to assess toxicities, and infections weekly until Day 63 and then at Days 100, 120, 150, 180, 270 and 365.
- Physical exam to assess GVHD weekly starting Day 7 until Day 63 and then at Days 100, 120, 150, 180, 270 and 365.
- Routine blood tests (cell counts, liver and kidney function) weekly until Day 63 and then at Days 100, 180, 270 and 365.
- Blood or bone marrow tests to find the amount of donor cells in your body on Days 28 and 100. This is also called *chimerism*.
- Disease evaluation tests to see how much cancer you have after treatment on Days 100, 180 and 365.
- Lung (pulmonary) function tests on Day 365.
- *Optional* blood samples for future research on Days 35, 100, 180 and 365 (see Section 19: Blood Samples for Future Research).

6. Risks and Discomforts

You will have side effects while on the study. Side effects can range from mild to serious.

The risks and discomforts of participating in this study will be similar to what you may have with stem cell transplant if you do not participate in this study, but you might do better or worse than on standard transplant treatment. Your health care team may give you medicines to help lessen side effects such as feeling sick to your stomach (nausea). In some cases, side effects can be long lasting or may never go away.

Risks and Toxicities Related to Medications

All immune suppressive drugs, except for bortezomib and maraviroc, are commonly used in allogeneic hematopoietic cell transplantation.

Table 1- Risks and Side Effects

Likely	What it means: This type of side effect is expected to occur in more than 20% of patients. This means that 21 or more patients out of 100 might get this side effect.
Less Likely	What it means: This type of side effect is expected to occur in 20% of patients or fewer. This means that 20 patients or fewer out of 100 might get this side effect.
Rare, but Serious	What it means: This type of side effect does not occur very often – in fewer than 2% of patients – but is serious when it occurs. This means that 1 or 2 patients (or fewer) out of 100 might get this side effect.

Bortezomib (Velcade®)

Likely	Less Likely	Rare, but Serious
<ul style="list-style-type: none"> ▪ Anemia ▪ Decreased platelet count with increased risk of bleeding ▪ Feeling weak, tired and generally uncomfortable ▪ Fever, with shaking chills ▪ Anorexia – loss of appetite ▪ Constipation ▪ Diarrhea ▪ Nausea ▪ Vomiting ▪ Abdominal pain 	<ul style="list-style-type: none"> • Decreased white blood cell count with risk of infection • Difficulty sleeping • Skin rash with itching and redness • Low blood pressure • Changes in heart beat that can cause you to feel light-headed, dizzy, faint, short of breath, or have chest pain • Heartburn, dyspepsia • Bleeding (GI, pulmonary/upper respiratory) • Blood in the urine 	<ul style="list-style-type: none"> • Coughing up blood • Syndrome associated with high blood pressure characterized by headache, confusion, seizures, and vision loss associated with imaging findings • Hepatitis and liver failure • Inflammation of the intestines, stomach, or pancreas • Inflammation and fluid build-up in and around the lungs

Likely	Less Likely	Rare, but Serious
<ul style="list-style-type: none"> ▪ Painful feelings or numbness and tingling in hands and feet 	<ul style="list-style-type: none"> • Pneumonia and bronchitis • Confusion • Anxiety • Painful sores of the mouth and/or throat • Changes in the way things taste • Abnormal liver tests • Blurred vision • Inflammation of the eye • Aches and pains in muscles, joints and the bone in the arms and legs • Muscle weakness • Cough • Shortness of breath • Headache • Nose bleeds • Changes in blood sugar • Lowered amount of potassium and sodium in your blood • Increase in the amount of calcium in your blood • Flu-like symptoms such as chills, sore throat, runny nose and sinus and throat infections • Swelling or fluid build-up in the arms and legs, feeling dizzy and weight gain • Herpes virus such as shingles • New or worsening heart failure • Infections of the bladder, sinuses, throat, stomach and intestines and skin • Fungal infections in the mouth and throat • Life-threatening infections in the blood 	<ul style="list-style-type: none"> • Inflammation of the layers surrounding your heart or collection of fluid around the heart • Loss of hearing • Bleeding in the brain • Loss of some to all vision in one or both eyes • Encephalopathy or brain dysfunction that can lead to death • Allergic reactions that may include skin swelling and/or swelling of the face or throat and could be severe or life-threatening • Severe, life-threatening or deadly rash with skin peeling and mouth sores • Pain, redness, swelling and infection in the area of the skin where bortezomib is injected • Pain in the mouth and throat when swallowing • Intestinal obstruction • Fast death of cancer cells that may let toxin into the blood and injure organs, such as the kidneys • Severe muscle weakness and paralysis

Cyclophosphamide (Cytosan®)

Likely	Less Likely	Rare, but Serious
<ul style="list-style-type: none"> ▪ Decreased white blood cell count with increased risk of infection ▪ Temporary hair loss ▪ Nausea ▪ Vomiting ▪ Loss of appetite ▪ Sores in mouth or on lips ▪ Diarrhea ▪ Stopping of menstrual periods in women ▪ Decreased sperm production in men ▪ Decreased platelet count (mild) with increased risk of bleeding 	<ul style="list-style-type: none"> ▪ Anemia ▪ Temporary tiredness ▪ Damage to the fetus if you become pregnant while taking drug ▪ Abdominal pain ▪ Skin rash ▪ Bleeding in the bladder 	<ul style="list-style-type: none"> ▪ Scarring of lung tissue, with cough and shortness of breath ▪ Severe heart muscle injury and death at very high doses ▪ New (secondary) cancers

Maraviroc (Selzentry®)

Likely	Less Likely	Rare, but Serious
<ul style="list-style-type: none"> ▪ Fever, cough and flu-like symptoms ▪ Rash and redness of the skin ▪ Upper respiratory infections 	<ul style="list-style-type: none"> ▪ Fever ▪ Dizziness ▪ Insomnia ▪ Anxiety ▪ Depression ▪ Itching ▪ Benign skin tumors ▪ High blood pressure ▪ Decrease appetite ▪ Constipation ▪ Low white blood counts with increase risk of infections ▪ Joint pain ▪ Excessive sweating ▪ Nerve damage causing numbness, tingling, burning ▪ Muscle pain ▪ Bladder irritation ▪ Acne ▪ Abnormal liver tests ▪ Herpes infections ▪ Eye infections/inflammation ▪ Breathing abnormalities ▪ Genital warts ▪ Abnormal growth or change of fat in the body 	<ul style="list-style-type: none"> ▪ Loss of consciousness (fainting) ▪ Rash affecting the whole body ▪ Allergic reactions associated with liver damage and jaundice

Methotrexate

Likely	Less Likely	Rare, but Serious
<ul style="list-style-type: none"> ▪ Decreased white blood cell count with increased risk of infection. ▪ Fatigue ▪ Infections 	<ul style="list-style-type: none"> ▪ Nausea/Vomiting ▪ Irritation or sores in the lining of the throat or mouth ▪ Diarrhea ▪ Abdominal discomfort ▪ Fever ▪ Chills ▪ Anemia ▪ Abnormal liver tests ▪ Kidney failure 	<ul style="list-style-type: none"> ▪ Dizziness ▪ Scarring of the lungs

Mycophenolate Mofetil (MMF, Cellcept®)

Likely	Less Likely	Rare, but Serious
<ul style="list-style-type: none"> ▪ Miscarriage ▪ Birth defects ▪ Diarrhea ▪ Damage to unborn baby ▪ Limited effectiveness of birth control ▪ Stomach pain ▪ Upset stomach ▪ Nausea/Vomiting ▪ Headache ▪ Tremors ▪ Low white blood cell count with increased risk of infection ▪ Increased blood cholesterols ▪ Decreased platelet count with increased risk of bleeding ▪ Swelling of the hands, feet, ankles, or lower legs 	<ul style="list-style-type: none"> ▪ Anemia ▪ Rash ▪ Difficulty falling asleep or staying asleep ▪ Dizziness 	<ul style="list-style-type: none"> ▪ Difficulty breathing ▪ Unusual bruising ▪ Fast heartbeat ▪ Excessive tiredness ▪ Weakness ▪ Blood in stool ▪ Bloody vomit ▪ Change in vision ▪ Encephalopathy or brain dysfunction that can lead to death ▪ New (secondary) cancers

Tacrolimus (FK506, Prograf®)

Likely	Less Likely	Rare, but Serious
<ul style="list-style-type: none"> ▪ Kidney problems ▪ Loss of magnesium, calcium, potassium ▪ High blood pressure ▪ Tremors ▪ Increases in cholesterol and triglyceride ▪ Decreased platelet count with increased risk of bleeding ▪ Infections 	<ul style="list-style-type: none"> ▪ Nausea ▪ Vomiting ▪ Liver problems ▪ Changes in how clearly one can think ▪ Insomnia ▪ Unwanted hair growth ▪ Confusion 	<ul style="list-style-type: none"> ▪ Seizures ▪ Changes in vision ▪ Dizziness ▪ Red blood cell destruction

It is very important that you do not eat grapefruit or drink grapefruit juice while taking Tacrolimus. Grapefruit has an ingredient called bergamottin, which can affect some of the treatment drugs used in this study. Common soft drinks that have bergamottin are *Fresca*, *Squirt*, and *Sunny Delight*.

Risks and Toxicities Related to Transplant

The following problems may occur as a result of stem cell transplantation. These risks may occur whether a transplant was done as part of the study or not:

Slow recovery of blood counts. The red blood cells, white blood cells, and platelets can be slow to recover after blood or marrow transplant. Until your blood counts recover, you will need blood and platelet transfusions, and will be at risk for bleeding and infections. To speed the recovery of the white cells as much as possible you may receive Filgrastim.

Graft failure. The stem cells (the “graft”) may fail to grow inside your body. Past experience suggests that there can be up to a 10-15% chance of graft failure. If graft failure occurs, this may result in low blood counts for a long period of time. If your counts do not recover, you may need to receive a second transplant. Graft failure can be fatal.

Graft-Versus-Host Disease (GVHD). GVHD results from cells in the graft recognizing your body as foreign and attacking it. In most cases, GVHD can be successfully treated. Sometimes GVHD is severe or difficult to treat and may lead to death. You will be watched closely for this complication and given drugs to prevent and/or treat it.

Acute GVHD may produce skin rash, nausea, vomiting, diarrhea, abdominal pain, abnormalities of liver function, and an increased risk of infection. Chronic GVHD may produce skin rashes, hair loss, thickened dry skin, dry eyes, dry mouth, liver disease, weight loss, diarrhea, and an increased

risk of infection. To confirm the diagnosis of acute or chronic GVHD, you may be asked to have a biopsy (a small sample of your tissue to look at under the microscope) of your skin, gut, or, rarely, your liver.

Other complications. Other complications may include:

- a. Damage to the vital organs in your body.** The transplant could cause problems in any body organ such as the heart, lungs, liver, gut, kidneys and bladder, or brain. The kidneys and the liver are most likely to be damaged. Some patients will experience serious lung problems from infections or the chemotherapy and radiation.
- b. Serious infections.** Full and complete recovery of your immune system may take many months. During this time, there is an increased risk of infections. You will be prescribed certain drugs to reduce the chance of those infections. However, these treatments do not always work. If you have an infection, you may have to stay in the hospital longer or be re-hospitalized after transplant. Although most infections can be successfully treated, some infections may result in death.
- c. Relapse of disease or a new blood cancer.** Your leukemia or lymphoma may come back even if the transplant is initially successful. In rare cases, a new blood cancer may develop from the donor cells. Cyclophosphamide can cause damage to blood cells, which may result in a blood cancer such as myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). The blood cancer usually develops 2-10 years after treatment, or 6 years on average. The risk of developing a new blood cancer after allogeneic blood or marrow transplant is probably less than 2%. If cancer develops in your donor's blood cells, you may require additional treatment with chemotherapy or another blood or marrow transplant.
- d. Risk to the unborn.** The treatments in this study have not been proven to be safe at any stage of pregnancy. Therefore, if you are pregnant or nursing, you are not eligible for this study. Women who can become pregnant must use effective birth control while receiving chemotherapy, TBI, and drugs to prevent GVHD, and for 1 year after transplant. Effective birth control is defined as the following:
 1. Refraining from all acts of vaginal sex (abstinence)
 2. Consistent use of birth control pills
 3. Injectable birth control methods (Depo-Provera, Norplant)
 4. Tubal sterilization or male partner who has undergone a vasectomy
 5. Placement of an IUD (intrauterine device)
 6. Use of a diaphragm with contraceptive jelly and/or condoms with contraceptive foam every time you have sex.

Reproductive Risks

The drugs used in this research study may damage your reproductive organs, affect your ability to have children or possibly cause birth defects if you take them while you are pregnant. It is important that a woman is not pregnant or breast-feeding and does not become pregnant during the course of the study.

It is important that both women who can become pregnant and their male partners use birth control for 1 year after transplantation while on this study.

If you are a woman and can become pregnant, you will need to take a pregnancy test before you start the study. You should discuss ways to prevent pregnancy while you are in the study. Women who have gone through puberty may find that their menstrual cycle becomes irregular or stops permanently. This does not mean that you cannot become pregnant. You must still use an effective method of birth control during your transplant and continue until you are finished with your GVHD prevention treatment.

If you are a man, your body may not be able to produce sperm (become sterile). You should talk with your doctor about banking your sperm before having a transplant.

Please check with your doctor to understand more about these risks.

Additional Information about Bortezomib (Velcade®)

- The effect of Velcade® on reproduction and its safety in pregnancy are unknown. If you are a woman capable of becoming pregnant [anyone who has not undergone a hysterectomy (removal of the womb), has not had both ovaries removed or has not been post-menopausal (stopped menstrual periods) for more than 24 months in a row], you must have a negative pregnancy test before beginning treatment. In addition, you must not be breastfeeding a baby during this study.
- If you think that you have become pregnant or may have fathered a child while taking part in this study you must tell the study doctor immediately. The study doctor will advise you of the possible risks to your unborn baby and discuss options for managing the pregnancy with you. You should also notify the doctor managing your pregnancy that the mother/father received a study drug called Velcade®.
- If you are a woman and you become pregnant during your participation in this study, your treatment with Velcade® will be stopped and you may be withdrawn from some of the study procedures but not from follow-up by your study doctor. The study doctor will ask for your permission to stay in contact with you throughout the length of the pregnancy.
- If you are a man and your partner becomes pregnant, the study doctor will ask for your partner's permission to collect information about her pregnancy and the health of the baby.
- Laboratory tests show that Velcade® may damage DNA. Based on this information, it is possible that Velcade® may cause infertility in men and women.

Additional Information about MMF

- MMF could be damaging to an unborn baby if you are pregnant or become pregnant while receiving the drug.
- MMF can make birth control pills less effective and increase your chances of becoming pregnant while you are taking it.
- If you could become pregnant, you must use 2 effective forms of birth control for 4 weeks before starting MMF, during treatment, and for one year after transplantation.

If you think you might be pregnant or could be become pregnant prior to enrollment, you should not join this study.

Unforeseen Risks

New risks might appear at any time during the study. These risks might be different from what is listed in this Consent Form. We will promptly tell you about new information that may affect your decision to take part in the study. We may learn new things about reduced-intensity transplants that might make you want to stop being in the study. We will let you know if this happens and you can decide if you want to continue in the study.

Other Treatments or Medications

Some medicines react with each other, and it is important that you tell the study doctor or staff about any other drugs, treatments, or medicines you are taking. This includes non-prescription medications, vitamins and herbal treatments.

It is also important that you tell the study staff about any changes to these medications during your participation in the study.

For more information about risks and side effects, ask your study doctor.

7. Alternative Treatments

Participation in this study is optional. If you choose not to take part, you may still receive an allogeneic transplant to treat your disease. The treatment and evaluations you would receive could be very similar to what would receive if you join this study.

Your study doctor will talk with you about your options. If you decide not to participate in this study, your medical care will not be affected in any way.

Your other choices may include:

- Treatment with other drugs, radiation, or a combination of drugs and radiation without a transplant.
- An allogeneic blood or marrow transplant that is not part of the study, or another type of transplant
- Participation in another clinical trial, if available (check with your doctor)

- No treatment for your blood cancer at this time
- Comfort care

Every treatment option has benefits and risks. Talk with your doctor about your treatment choices before you decide if you will take part in this study.

8. Possible Benefits

Taking part in this study may or may not make your health better. The information from this study will help doctors learn more about medications used to prevent GVHD.

9. New Information Available During the Study

During this research study, the study doctors may learn about new information about the study drugs or the risks and benefits of the study. If this happens, they will tell you about the new information. The new information may mean that you can no longer participate in the study, or that you may not want to continue in the study.

If this happens, the study doctor will stop your participation in the study and will offer you all available care to suit your needs and medical conditions.

10. Privacy, Confidentiality and Use of Information

Your confidentiality is one of our main concerns. We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. All your medical and demographic (such as race and ethnicity, gender and household income) information will be kept private and confidential. *(Name of Transplant Center)* and the organizations listed below will not disclose your participation by any means of communication to any person or organization, except by your written request, or permission, or unless required by federal, state or local laws, or regulatory agencies.

Individuals authorized by the organizations below will have access to your research and medical information. They may use this information for inspections or audits to study the outcomes of your treatment, or for required reporting to regulatory authorities (such as to the FDA for serious adverse events). In agreeing to participate, you consent to such inspections and to the copying of parts of your records, if required by these organizations.

- The National Institutes of Health (NIH), which include the National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI)
- The Center for International Blood and Marrow Transplant Research (CIBMTR)
- The National Marrow Donor Program (NMDP)

- The Food and Drug Administration (FDA)
- Data and Coordinating Center of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN DCC)
- Millennium Pharmaceuticals, Inc., supplier of bortezomib

We will not identify you by name in any publications or reports that come from these organizations or groups.

Information that does not include personally identifiable information about this clinical trial has been or will be submitted, at the appropriate and required time, to the government-operated clinical trial registry data bank, which contains registration, results, and other information about registered clinical trials.

This data bank can be accessed by you and the general public at www.ClinicalTrials.gov. Federal law requires clinical trial information for certain clinical trials to be submitted to the data bank.

11. Ending Your Participation

Being in this study is voluntary. You can choose to not be in this study, or leave this study at any time. If you choose not to take part or leave this study, your regular medical care will not be affected in any way. Tell your doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

The study doctor or the study sponsor may stop the study at any time, and we may ask you to leave the study. We may ask you to leave the study if you do not follow directions or if you suffer from side effects of the treatment. If we ask you to leave the study, the reasons will be discussed with you. Possible reasons to end your participation in this study include:

- You do not meet the study requirements.
- You need a medical treatment not allowed in this study.
- The study doctor decides that it would be harmful to you to stay in the study.
- You are having serious side effects.
- You become pregnant.
- You cannot keep appointments or take study drugs as directed.
- The study is stopped for any reason.

If you decide to leave this study after taking the study treatment, or are asked to leave by your doctor for medical reason, you will need to come back to the doctor's office for tests for your safety. Even if you leave the study, the information collected from your participation will be included in the study evaluation, unless you specifically ask that it not be included.

12. Physical Injury as a Result of Participation

It is important that you tell your doctor, _____ [investigator's name(s)] or study staff if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ [telephone number].

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

In case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

13. Compensation or Payment

You will not be paid for your participation in the research study. You will not get compensation or reimbursement for any extra expenses (travel, meals, etc.) you may have through your participation on this trial. Your participation in this research study may contribute to the development of commercial products from which Millennium Pharmaceuticals, Inc. (manufacturer of bortezomib) or others, may derive an economic benefit. You will have no rights to any patents or discoveries arising from this research, and you will receive no economic benefit.

14. Costs and Reimbursements

Most of the visits for this research study are standard medical care for patients undergoing allogeneic transplants and will be billed to your insurance company. You and/or your health plan/insurance company will need to pay for some or all of the costs of standard treatment in this study

The drug bortezomib is being provided by the manufacturer (Millennium Pharmaceuticals, Inc.), free of charge. The drug maraviroc is being provided by the study, free of charge.

You or your insurance will not be charged for optional blood samples for research on this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

15. Ethical Review

The ethical aspects of this research study have been reviewed and approved by [name of IRB].

16. For More Information

If you need more information about this study, or if you have problems while you are participating in this study, you can contact the study doctor or his/her staff. They can be reached at the telephone numbers listed here:

[Insert name and contact details]

17. Contact Someone about Your Rights

If you wish to speak to someone not directly involved in the study, or if you have any complaints about any aspect of the project, the way it is being conducted or any questions about your rights as a research participant, then you may contact:

[Insert appropriate contact details]

For questions about your rights while taking part in this study, call the _____ *[name of center]* Institutional Review Board (a group of people who review the research to protect your rights) at _____ *(telephone number)*.

18. Blood Samples for Research (*Optional*)

This section of the informed consent form is about future research studies that will be done using blood samples from people who are taking part in the main study described above. You may give small blood samples for these future research studies if you want to. You can still be a part of the main study even if you say “no” to giving blood samples for future research studies. You can say "yes" or "no" to giving blood samples for future research studies. Please mark your choice at the end of this section.

We would like to have five (5) small blood samples for future research. If you agree, these samples will be drawn before you begin the conditioning regimen for your transplant (3 teaspoons or 16 mL), and at 4 different times after your transplant: on Days 35, 100, 180 and 365 (10 teaspoons or 40 mL each). These samples will be kept and may be used in research to learn more about immune reconstitution, GVHD, cancer and other diseases. Usually the blood can be drawn from a vein in your arm at the same time as other blood collections. When the samples are given to investigators for research, no information about your name, address, phone number or other information that will let the researcher know who you are will be provided.

The samples collected for research purposes will be sent to the BMT CTN Repository. The samples will be labeled with unique codes that do not contain information that could identify you. A link to this code does exist. The link is stored at the Data and Coordinating Center for the Blood and Marrow Transplant Clinical Trials Network (BMT CTN DCC). The staff at the Repository where your sample is being stored does not have a link to this code. Your research samples will continue to be stored at the BMT CTN Repository until they are used up for approved research.

Genome-Wide Association Studies:

DNA from your stored blood samples might be used in genome-wide association (GWA) studies for a future project either done or supported by the National Institutes of Health (NIH). Genome-wide association studies are a way for scientists to find genes that have a role in human disease or treatment. Each study can look at hundreds of thousands of genetic changes at the same time.

If your coded samples are used in such a study, the researcher is required to add your test results and sample information into a public research database. This public database is called the NIH Genotype and Phenotype Database and it is managed by the National Center for Biotechnology Information (NCBI). The NCBI will never have any information that would identify you, or link you to your information or research samples, although the results of genetic studies could theoretically include identifying information about you.

Genetic Information Nondiscrimination Act:

A new federal law (2009), called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and employers of 15 or more persons to discriminate against you based on your genetic information. Health insurance companies and group health plans may not request your genetic information that we get from this research. This means that they must not use your genetic information when making decisions regarding insurability. Be aware that this new federal law will not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Things to Think About:

- The choice to let us have blood samples for future research is up to you. No matter what you decide to do, it will not affect your care.
- If you decide now that your blood can be kept for research, you can change your mind at any time. Just contact your study doctor and let him or her know that you do not want us to use your blood sample. Then any blood that remains will no longer be used for research.
- In the future, people who do research on these blood samples may need to know more about your health. While the study doctor or others involved in running this study may give the researchers reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.
- Sometimes blood is used for genetic research (about diseases that are passed on in families). Even if your blood is used for this kind of research, the results will not be put in your health records.
- Your blood will be used only for research and will not be sold. The research done with your blood may help to develop new products in the future.

- Reports about research done with your blood will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Benefits:

The research that may be done with your blood is not designed specifically to help you. The benefits of research using blood include learning more about what causes GVHD, cancer and other diseases, how to prevent them, and how to treat them.

Risks:

There is a small risk of an infection or fainting from the blood draw.

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice:

Please read each sentence below and think about your choice. After reading each sentence, please indicate your choice below. If you have any questions, please talk to your doctor or nurse, or call our research review board at _____.

No matter what you decide to do, it will not affect your care.

Health Insurance Portability and Accountability Act 1 (HIPAA1) Authorization to use and disclose individual health information for research purposes**A. Purpose:**

As a research participant, I authorize the Principal Investigators and the researcher's staff to use and disclose my individual health information for the purpose of conducting the research study:

A Multi-Center Phase II Trial Randomizing Novel Approaches for Graft-versus-Host Disease Prevention Compared to Contemporary Controls

B. Individual Health Information to be Used or Disclosed:

My individual health information that may be used or disclosed to do this research includes:

- Demographic information (for example: date of birth, sex, weight)
- Medical history (for example: diagnosis, complications with prior treatment)
- Findings from physical exams
- Laboratory test results obtained at the time of work up and after transplant (for example: blood tests, biopsy results)

C. Parties Who May Disclose My Individual Health Information:

The researcher and the researcher's staff may collect my individual health information from: *[List hospitals, clinics or providers from which health care information can be requested]*

D. Parties Who May Receive or Use My Individual Health Information:

The individual health information disclosed by parties listed in item c and information disclosed by me during the course of the research may be received and used by the following parties:

Principal Investigators and the researchers' staff

Dr. Javier Bolaños-Meade, Co-Principal Investigator

Dr. John Koreth, Co-Principal Investigator

Dr. Ran Reshef, Co-Principal Investigator

Study Sponsors

- National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI), both of the National Institutes of Health (NIH),
- Blood and Marrow Transplant Clinical Trials Network (BMT CTN), Data and Coordinating Center

¹ HIPAA is the Health Insurance Portability and Accountability Act of 1996, a federal law related to privacy of health information

Other organizations

- U.S. government agencies that are responsible for overseeing research such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP)
- U.S. government agencies that are responsible for overseeing public health concerns such as the Centers for Disease Control (CDC) and federal, state and local health departments.
- Millennium Pharmaceuticals, Inc., supplier of bortezomib

E. Right to Refuse to Sign this Authorization:

I do not have to sign this Authorization. If I decide not to sign the Authorization, I will not be allowed to participate in this study or receive any treatment related to research that is provided through the study.

My decision not to sign this authorization will not affect any other treatment, payment, or enrollment in health plans or eligibility for benefits.

F. Right to Revoke:

I can change my mind and withdraw this authorization at any time by sending a written notice to the Principal Investigator to inform the researcher of my decision.

If I withdraw this authorization, the researcher may only use and disclose the protected health information already collected for this research study. No further health information about me will be collected by or disclosed to the researcher for this study.

G. Potential for Re-disclosure:

My individual health information disclosed under this authorization may be subject to re-disclosure outside the research study and no longer protected.

Examples include potential disclosures for law enforcement purposes, mandated reporting or abuse or neglect, judicial proceedings, health oversight activities and public health measures.

H. This authorization does not have an expiration date.

I have read and understood this Consent Form. The nature and purpose of the research study has been explained to me.

- I have had the chance to ask questions, and understand the answers I have been given. I understand that I may ask questions at any time during the study.
- I freely agree to be a participant in the study.
- I understand that I may not directly benefit from taking part in the study.
- I understand that, while information gained during the study may be published, I will not be identified and my personal results will stay confidential.
- I have had the chance to discuss my participation in this research study with a family member or friend.
- I understand that I can leave this study at any time, and doing so will not affect my current care or prevent me from receiving future treatment.
- I understand that I will be given a copy of this signed consent form.

Participant Name _____ Date _____

Signature _____ Date _____

I certify that I have provided a verbal explanation of the details of the research study, including the procedures and risks. I believe the participant has understood the information provided.

Name of Counseling Physician _____ Date _____

Signature of Counseling Physician _____ Date _____