Informed Consent to Participate in Research

Your Name: _____

Study Title: Allogeneic Hematopoietic Cell Transplant for Hematological Cancers and Myelodysplastic Syndromes in HIV-Infected Individuals

Protocol: BMT CTN #0903 (AMC 080)

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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 find out how well allogeneic marrow transplant (a marrow transplant using cells from someone other than the patient) treats specific blood cancers in people with HIV (human immunodeficiency virus).

This study will take at least two (2) years and will include 15 participants.

This Consent Form will tell you about the purpose of the study, its 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. 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.

This study will look at the risks and benefits of allogeneic transplant for people with specific kinds of blood cancers and HIV infection.

Blood Cancer and Transplant

For people with a blood cancer, the main treatment choices include chemotherapy, radiation therapy, immunotherapy, and a transplant using cells that can make blood. The blood-making cells are most often collected from bone marrow and the bloodstream. These cells are called **hematopoietic cells** and transplant using these kinds of cells is called **hematopoietic cell transplant**, or **HCT**. These treatments may be used alone or used in combination. For some people with a blood cancer, a HCT transplant may offer the best chance to be free of signs of disease for a long time (long-term remission).

This clinical trial will study how well allogeneic transplant works as a treatment for people who have a blood cancer and HIV. An allogeneic transplant uses blood-making cells from a family member or an unrelated donor to remove and replace the abnormal blood cells in the patient.

An allogeneic transplant is a common treatment for patients with a blood cancer that has either returned (relapsed) or does not respond well to other treatments (refractory), or is known to be likely to return (high risk). The blood cancers we will include in this study are: acute myeloid or lymphocytic leukemia (AML or ALL), myelodysplastic syndrome (MDS), Hodgkin lymphoma and non-Hodgkin lymphoma.

Conditioning Regimen

We will use a combination of chemotherapy and in some cases radiation as a treatment to destroy cancer cells and help donor cells start to grow in your bone marrow. Depending on the combination used, each treatment (or "conditioning regimen") can have a different intensity or strength.

- High intensity treatment uses a combination of chemotherapy that uses strong or higher amounts of drugs and sometimes radiation. This is also called "myeloablative conditioning".
- Reduced intensity treatment uses a combination of chemotherapy, using less strong or lower amounts of drugs and sometimes radiation. This is also called "reduced intensity conditioning".

Both kinds of treatments are used by blood and marrow transplant doctors around the world and are not experimental. You and your doctor will decide which conditioning regimen intensity is the best choice for you. This study will help us to better understand how to use these treatments in people with HIV who have an allogeneic transplant to treat their blood cancer.

If you volunteer to join this study, the treating physician at the center will assign you to have either a high intensity or a reduced intensity treatment before you receive the blood stem cells or bone marrow from your donor.

3. Purpose

The main purpose of this study is to learn how well allogeneic transplant treats blood cancers in people with HIV. We invite you to participate in this study because you have HIV and a blood cancer.

4. Right to Ask Questions

You have the right to ask questions about **t**he 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]

5. Procedures

Before you join the study, we will evaluate your general health, medical history, and your current medications.

Study Participation

Your study participation will last for **2 years** after your transplant.

Follow-up tests for your transplant (described below) will last as long as you need care.

We would like to keep track of your medical condition for the rest of your life. We would contact you and the doctor who gives your regular medical care by phone or mail once a year. Following up with you every year helps us learn about the long-term effects of the study and transplant. Many transplant centers include this type of long-term follow-up as part of their regular medical care.

Before You Start Your Treatment

You will need to have health evaluations before you start treatment, while you receive your treatment, and for several years after you finish your treatment. These tests are standard care for patients with blood cancer and would happen even if you were not part of this study. It will be up to your study doctor to decide what tests you need and when.

If you decide to join, we will ask you to sign this Consent Form, and you will get a copy of the signed form to keep.

You will have several tests to find out if you can be in the study. The tests include:

- Medical history
- Physical examination, including height and weight
- Blood and urine tests
- Heart function tests, including a MUGA or an electrocardiogram (ECG)

- Lung (pulmonary) function tests
- Tests to evaluate your blood cancer including a bone marrow biopsy/aspirate
- If you have lymphoma, you will also have PET (positron-emission tomography) and/or CT (computed tomography) scans
- A blood 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.

During The Study

- **Study Evaluations**
  We will evaluate your health at specific points during your participation. These tests and how often they are scheduled are standard care for patients receiving an allogeneic transplant and would be done even if you were not part of this study.
- **Research Study Evaluations**
  Researchers are trying to learn more about HIV and the effect of HCT on HIV. Much of this research is done using blood samples. As a result, blood samples will be collected from you during the study to help researchers learn more about the effect of HCT on your HIV.
  - In patients that do not have any detectable HIV using standard tests, 30 mL (about 6 teaspoons) of blood will be drawn at two times before your HCT and at 100 days, 6 months, 12 months and 24 months after your HCT. Another 180 mL (about 36 teaspoons) of blood will also be drawn before your HCT and 13 months after your HCT if necessary. This blood will be used to look closer at any HIV that may still be present in your body.
  - In all patients, 10 mL (about 2 teaspoons) of blood will be drawn at two times before your HCT and at 1 week, 2 weeks and 100 days after your HCT. Another 37 mL (about 7 teaspoons) will be drawn at 8 weeks, 6 months and 12 months after your HCT. This blood will be used to look at how your immune system is responding to the treatment.
- **Antiretroviral Therapy**
  Your antiretroviral therapy (your HIV therapy) will be reviewed. An outside review committee will look at your therapy and discuss with your doctor the best way to adjust your therapy throughout your HCT. Your doctor may or may not adjust your therapy depending on what is best for you.
- **Conditioning Regimen (Chemotherapy)**
  The conditioning regimen is a combination of chemotherapy and/or radiation given to patients before the donor cells are infused. This treatment allows donor cells to start growing (or "engraft") in your bone marrow. The conditioning regimen also helps to destroy remaining cancer cells that might not be found in tests.

Several chemotherapy drugs can be used as part of the conditioning treatment. The choice and amount of drugs or radiation determines the treatment intensity (strength). Common drug combinations used in allogeneic transplant include:

1) Busulfan and fludarabine
2) Fludarabine and melphalan
3) Radiation and cyclophosphamide (**Cytoxan)**

Allogeneic transplantation kills cancer through the conditioning regimen and through the immune cells from the donor that might recognize cancer cells and destroy them. Conditioning regimens with high intensity are also known as myeloablative conditioning regimens. High intensity treatments work very well to destroy remaining cancer cells because they use very high amounts chemotherapy or radiation. High intensity treatments can also have more side effects during and after transplant.

Using a lower or "reduced" intensity treatment before transplant can have fewer serious problems from the chemotherapy drugs. While the cancer killing effects may also be lower, studies show that immune cells given during the transplant can help destroy remaining cancer cells. Allogeneic transplants with reduced intensity conditioning (RIC) regimens are often used for people who cannot have high doses of chemotherapy drugs or radiation because of their age or other medical problems.

Your doctor will decide which type of conditioning treatment is the best choice for you, depending on the kind of blood cancer you have and your overall health. The table below lists the 4 conditioning regimens that will be used in this study.

TABLE B-1: CONDITIONING REGIMENS

Reduced Intensity Treatments	
A	Fludarabine + Busulfan (Flu/Bu)
B	Fludarabine + Melphalan (Flu/Mel)

High Intensity Treatments	
C	Busulfan + Fludarabine (Bu/Flu)
D	Cyclophosphamide + Total Body Irradiation (Cy/TBI)

- **Reinfusion of Stem Cells (Transplant)**
  We will use your intravenous catheter or central line to give you the blood or bone marrow stem cells that were collected before your transplant. The cells will travel to your bone marrow where they will start to make healthy, new blood cells after several weeks.

6. Alternative Treatments

Participation in this study is optional. If you choose not to participate you may still receive an allogeneic transplant for treatment of your disease. It is possible that the treatment and the evaluations you would receive could very similar to what would be if you were enrolled in this clinical trial.

Your study doctor will talk with you about your options. If you decide not to participate in this research 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 hematopoietic cell 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.

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.

7. Risks and Discomforts

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

The risks and discomforts in participating in this study will be similar to what you may have with a blood or bone marrow cell transplant if you do not participate in this trial. There are differences in side effects from medications based on the strength of your conditioning regimen. Myeloablative regimens often cause more side effects early after transplant compared to reduced intensity regimens. Other complications from transplants, such as graft-versus-host disease (GVHD) and infections happen equally in patients who have either type of regimen.

Your health care team will give you medicines to help lower side effects such as feeling sick to your stomach (nausea). In some cases, side effects can be long lasting or may never go away.

A. <u>Side Effects of Allogeneic Transplant</u>

Short term (days to weeks): During the transplant, you will have a higher risk of infection and bleeding from low blood counts. There is also the risk that your blood counts will not recover even though we gave you donated blood stem cells. This risk is rare, but it can happen. After your transplant, you have a higher risk of infections. This is because the new immune system needs time to learn again how to best fight some infections and because you will need to take medicines that lower immunity to reduce the risk of graft-versus-host disease (GVHD). See below for more information about GVHD.

Long term (years): If you have an allogeneic transplant, you will have a higher risk of developing cancers that are caused by the chemotherapy given as part of the transplant or to treat the blood cancer before your transplant. These secondary cancers can be of any type, including blood cancers such as leukemia. Your HIV infection also gives you a higher risk for some cancers, so the true risk for allogeneic transplant for HIV-associated cancers is not yet known.

B. Risks Related to Medications or Radiation Used in Conditioning Regimens

All chemotherapy and radiation treatments used as conditioning regimens in this study are commonly used in allogeneic hematopoietic cell transplantation. The side effects may vary, based on the dose that is given. This applies to busulfan, which is used in different amounts for myeloablative and reduced intensity regimens.

TABLE B-2 – ADVERSE EVENTS

	Likely Side Effects (May happen in 20% of patients or more)	**Less Likely** (May happen in less than 20% of patients)	**Rare** (May happen in less than 2% of patients)
Busulfan (Bu)	Abdominal discomfort Constipation Diarrhea Dizziness Fluid retention Headache Heartburn Insomnia Lack of appetite Mouth sores Nausea and vomiting Running nose Skin rashes Irregular or no menstrual cycles Tachycardia	Cough Hepatic Veno-occlusive disease High blood pressure High magnesium and phosphorus levels in the blood High sugar levels in the blood Infertility Low blood pressure Seizures	Cataracts Lung fibrosis

	Likely Side Effects (May happen in 20% of patients or more)	**Less Likely** (May happen in less than 20% of patients)	**Rare** (May happen in less than 2% of patients)
Cyclophosphamide (Cy)	Damage to male (testes) and female (ovaries) sex glands Diarrhea Fluid retention Hair loss Infertility Irregular or no menstrual cycles Loss of appetite Nausea, Vomiting Suppression of the immune system	Bleeding in the bladder Inflammation of the heart muscle (heart failure) Shortness of breath	Allergic reaction Lung fibrosis Serious skin rashes
Fludarabine (Flu)	Diarrhea Mouth sores Nausea and vomiting Suppression of the immune system	Fever Numbness in the extremities Sleepiness Visual changes Weakness	Coma Cough Inflammation of the lung Interstitial Pneumonia Skin rash
Melphalan (Mel)	Constipation Diarrhea Hair loss Mucositis Nausea and vomiting	Heart rhythm abnormalities Hepatitis Kidney failure	Allergic reaction Interstitial Pneumonia Seizure Lung fibrosis
Total Body Irradiation (TBI)	Fatigue Hair loss Infertility Loss of appetite Mouth sores Nausea and vomiting	Cataracts Inflammation of the parotid glands Skin pigmentation (reversible) Stunned Growth	Lung fibrosis Second cancers

C. Risks Related to the Medication Used to Help Prevent Graft-versus-Host Disease (GVHD)

Graft-versus-Host Disease (GVHD) is a medical condition that can become very serious and may cause death. GVHD is a common development after allogeneic stem cell transplant. It happens when the donor cells attack and damage your organ tissues after transplant. GVHD can cause:

- **Skin problems** including rashes, sores or blisters

- **Feeling sick** to your stomach (nausea),
- **Throwing up** (vomiting),
- **Abdominal pain**
- **Diarrhea**
- **Liver damage** or jaundice (yellowing of the skin or eyes)
- **There are other side effects that may be seen**
- **GVHD may be bad enough to cause death**

The most common forms of GVHD are relatively mild. Other forms of GVHD can be chronic and last well past your transplant date. GVHD can be very hard to predict. You will be monitored closely for this condition.

We will give you medications to try and prevent GVHD. These medications are usually started around the time you receive the donor cells and can continue many months after the transplant. These medications do not completely prevent GVHD and more medications might be needed if you do develop GVHD.

Your doctor will decide which GVHD prevention treatment you will receive. This choice is not part of this research study and your doctor will decide on the medications based on what is routinely used in this institution as part of allogeneic transplants. Below is a list of commonly used medications to prevent GVHD. Your doctor may choose to use other medications than what is listed here.

- **Tacrolimus:** This medication is used to try to prevent GVHD. The immediate side effects you may experience include nausea (feeling sick to your stomach) or vomiting (throwing up) when the medications are given orally. Other side effects you may experience include high blood pressure (hypertension), shaking of the hands (tremor), increased hair growth and possibly an effect on mental function.

  If you have these effects, they generally go away if your doctor lowers the amount of medication you take. A few patients have had a seizure while on this medication.

  Your liver or kidneys might not work as well as they did before. If this happens, your doctor may lower the amount of drug you take or stop giving the drug completely. The effect on kidneys seems to increase when other medications, which might cause kidney problems, are given at the same time, especially antibiotics. Occasionally, the kidney damage caused may require the use of an artificial kidney machine (hemodialysis).

  Some patients given tacrolimus develop diabetes and must take insulin while taking tacrolimus.

Rarely, patients receiving tacrolimus may develop low platelets and kidney problems that require stopping the tacrolimus, which can increase the risk of GVHD. This condition, called TTP/HUS Syndrome, can also be life-threatening.

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

- **Sirolimus:** This medication is used to try to prevent GVHD. The immediate side effects you may experience include fast heart rate, pain during breathing, shortness of breath, chest pain, nausea or vomiting. Other side effects you may experience include pale skin, easy bruising, fever, chills, body aches, night sweats, swelling in your face, stomach, hands or feet, pain or burning when you urinate, headache or skin rash. If you experience these effects, they generally go away when the dose of the medication is decreased.

  Sirolimus may increase your risk of developing lymphoma or other forms of cancer. Talk with your doctor about your specific cancer risk.

  Rarely, patients receiving sirolimus may develop low platelets and kidney problems that require stopping the sirolimus, which can increase the risk of GVHD. This condition, called TTP/HUS Syndrome, can also be life-threatening.

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

- **Mycophenolate Mofetil:** MMF is a potent immunosuppressive drug that blocks the growth of the immune cells that can cause GVHD. Side-effects you might experience include nausea and vomiting, diarrhea, infection, low blood counts, serious injury to your gut (digestive tract) including bloody stools and vomit, secondary cancers, such as lymphoproliferative disease or lymphoma, serious infections of the brain, risk to an unborn child, or Progressive Multifocal Leukoencephalopathy (PML).

- **Cyclophosphamide:** This is a chemotherapy drug that works by slowing or stopping cell growth. Side-effects you might experience include nausea and vomiting, bone marrow suppression, stomach ache, diarrhea, darkening of the skin or nails, hair loss (alopecia) or thinning of hair, changes in color and texture of the hair, and feeling tired. Blood in your urine (hemorrhagic cystitis) is a common complication. Although it is used to treat cancer, it may increase your risk of developing another kind of cancer, sometimes months to years after treatment.

- **Methotrexate:** This is also a medication used to try to prevent GVHD. Methotrexate causes damage to cells, and therefore can affect many different tissues of your body. It may cause or can worsen the mouth sores or inflammation of the mouth which you may have already developed from the procedures and medications used to prepare you for the transplant. Methotrexate may slow down the recovery of blood cells after transplantation. Methotrexate can cause kidney damage. If your kidneys are already damaged for other reasons, it can worsen kidney function. If kidney damage does occur, the methotrexate dose may be reduced or the medication may not be given at all.

- **Tacrolimus and Methotrexate:** These medications interfere with the body's defense system (the immune system). This may cause you to have more infections (especially viral infections and pneumonia) for several months after transplant.

D. Risks Related to the Transplant Procedure

The following risks are part of the transplant process and not connected to any one medication or the transplanted donor cells.

- **Bleeding:** Platelets help your blood to clot. Your platelets will be low until the new bone marrow grows and, as a result, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but more serious, life-threatening bleeding in the lungs and brain can occur if the platelet count remains low. Usually, there is success in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets and may be at serious risk for bleeding.

- **Veno-Occlusive Disease (VOD):** This can occur as a result of high dose chemotherapy, radiation therapy and/or medications used to prevent GVHD. VOD causes severe damage to the liver. Symptoms include jaundice (yellowing of the skin and eyes), weight gain, and extra fluid build-up in the abdominal cavity and other parts of the body. It can often be managed successfully, and completely resolve. However, complications can arise that may be fatal.

- **Mouth Sores and Diarrhea:** The large doses of chemotherapy and radiation cause irritation in the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. If you have severe mouth sores you will be given medicine to help control the pain. If your mouth sores are severe you may not be able to eat normally until the sores are healed. Mouth sores get better when the white blood count starts to rise, and engraftment occurs.

- **Capillary Leak Syndrome:** This may occur as a result of chemotherapy and radiation therapy. The blood vessels may become 'leaky' and fluid enters the abdominal cavity, lungs, and other tissues. You may gain water weight and not go to the bathroom as often as you normally do. Capillary leak syndrome can be difficult to manage if extra fluid enters the lungs and causes difficulty breathing, and can be life-threatening. You may die if there is continued fluid collection in the lungs.

- **Unexpected Organ Damage and Other Side Effects:** It is possible you may experience unexpected, life-threatening heart, lung, kidney, or liver damage as a result of the transplant. Occasionally, the high doses of chemotherapy and radiation cause severe lung damage that cannot always be treated. If this happens, you may need to use oxygen or even a respirator. The lung damage may get worse and be life-threatening. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal.
- **Late Effects:** You may experience side effects that occur several months to many years after your transplant. You may experience poor function of the thyroid gland, requiring you to take thyroid medication. As a result of radiation, cataracts may occur earlier in life compared to a person who had not had a transplant. If you develop cataracts (cloudiness in the eyes) they may require treatment. It is rare, but your kidneys could be affected, causing anemia (low red blood cell count) or high blood pressure. There is also a risk you may develop a second cancer as a result of the chemotherapy, radiation and/or underlying disease. If secondary cancers occur they generally do not occur until 10 to 15 years after the transplant. The long-term effects upon heart, lung, and brain are unknown.
- **Fluid Build-up:** You will receive intravenous fluids during the transplant process and your body may have trouble eliminating this fluid.

E Additional Side Effects for People with HIV

Most of the risks in this Consent Form can happen to all patients undergoing transplant, but some, such as risk of infection or organ damage, may be different in patients with HIV. There is a risk that a temporary stop to antiretroviral treatment could lead to HIV resistance to the medications you are taking.

Your HIV viral load will be monitored by your doctor and if HIV resistance were to develop, alternate antiretroviral therapy may be needed.

Many of the medications used for HIV will react with important medications to reduce the complications of the transplant (HCT). These reactions may require frequent blood checks to make sure the amount of medications in the blood are correct. It is possible those medications interactions will result in complications.

F Infections

You will need to take several antibiotics to prevent infection. You will also be watched carefully for any infections while you are being treated for HIV related Leukemia or Lymphoma. Tell your doctors right away if you get a fever, chills, cough or any other symptoms that might be a sign of an infection. Infections may be bad enough to cause death.

G Reproductive Risks

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 have the potential of becoming pregnant must use some form of effective birth control while receiving chemotherapy and GVHD prophylaxis. Effective birth control is defined as the following:

1) Refraining from all acts of vaginal intercourse (ABSTINENCE)
2) Consistent use of birth control pills
3) Injected birth control methods (Depro-Provera, Norplant)
4) Tubal sterilization or male partner who has undergone a vasectomy
5) Placement of an IUD (intrauterine device)
6) Use, with every act of intercourse, of a diaphragm with contraceptive jelly and/or condoms with contraceptive foam.

Sterility and future childbearing potential for men and women: Chemotherapy and/or irradiation may affect your ability to have children. Male patients may become sterile (unable to produce sperm) and should discuss with their doctor regarding sperm banking prior to transplantation. Female patients who have attained puberty may find that their menstrual cycle becomes irregular or stops permanently. However, this DOES NOT MEAN THAT YOU CANNOT BECOME PREGNANT, and you must use some effective method of birth control during transplant and afterwards until you are off GVHD prophylaxis. Damage to reproductive tissue may result in infertility (inability to have children). It is not known if the damage could result in birth defects.
You should discuss risks and options in detail with your doctor before entering this study.

H Unforeseen Risks

New risks might appear at any time during the study that are different from the risks listed in this Consent Form. We will promptly tell you of any new information that may affect your decision to participate.

I 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.

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 transplant as a treatment for people with a blood cancer and HIV. This information could help future people with HIV who may need a transplant.

9. New Information Available During the Study

During this research study, the study doctors may learn about new information about the study drug 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.

We may give out your personal information if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Information about your transplant from your original medical records may be seen or sent to national and international transplant registries, including:

- The Center for International Blood and Marrow Transplant Research (CIBMTR)
- The National Marrow Donor Program (NMDP)
- The Food and Drug Administration (FDA)
- The National Institutes of Health (NIH), which include the National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI)
- Data and Coordinating Center of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN)
- Other authorized study organizations.

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. This includes standard care for your blood cancer and HIV. 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.

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.

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. Further 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. Independent Contact

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. CCR5 Donor Screening

Human Immunodeficiency Virus (HIV) uses a protein called CCR5 as a way to get inside of cells. A few people are naturally able to block HIV infection because their body does not make the CCR5 protein. As a result, HIV does not have a way to enter their cells and cause an infection.

Proteins are in every cell in our body and help keep the blood, skin and other parts of our bodies healthy. Every protein is made by a specific kind of gene. Every person has 2 copies of the gene that makes the CCR5 protein. One copy is from their mother and the other copy is from their father. Some people have changes to their genes that make the CCR5 protein. Another word for changes to a gene is mutation. Changes to the CCR5 gene means the body can't make the CCR5 protein. People who have 2 copies of the CCR5 gene mutation are called CCR5delta32homozygotes and they are naturally able to block HIV infection.

Very few people in the world have mutations to both copies of their CCR5 gene. If you are Caucasian with a family background from northern Europe, the chance is about 1 out of 100 people in finding a matched donor with 2 copies of the CCR5 gene mutation. If you do not have a northern European background, the chance is very, very small that you would find a donor who has 2 copies of the CCR5 gene mutation.

In one case, a person with 2 copies of the CCR5 gene mutation donated their blood-making cells for a transplant in a patient who had HIV and a blood cancer. Now the patient does not have any signs of HIV and does not need drugs to treat his HIV. We do not know if this will happen again, even if a donor has the CCR5 gene mutation

Besides the possible benefit of blocking HIV infection, some risks may come with a donor who has the CCR5 mutations. Research has shown that people with 2 copies of the CCR5 gene mutation may not fight off infections from West Nile virus (WNV) very well. WNV spreads through mosquito bites. Serious cases of WNV can cause a brain infection.

In addition to doing the standard tests to make sure a donor is a good match for you, we will also test possible donors to see if they have the CCR5 gene mutations. This testing will not slow down our search for your donor. We will let you know if we find a donor and if that donor has

the CCR5 mutations. At that point, you and your doctor will need to decide if you want to use a donor with or without the CCR5 mutations.

♦ ♦

Blood Samples for Research (optional)

Please note: 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 one small (4 teaspoons or 17 mL) blood sample for future research. If you agree, this sample will be obtained pre-transplant. It will be kept and may be used in research to learn more about HIV, cancer and other diseases. Usually the blood can be drawn from your central venous catheter at the time of the other blood collections. If this is not possible, it will be taken from a vein. When the sample is 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 AIDS and Cancer Specimen Resource 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). 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 ACSR Repository until they are used up for approved research.

DNA from your stored blood and tissue samples and your health information 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 identify genes involved in human disease. This method searches the genome for small genetic changes that are more common in people with a particular disease than in people without the disease. Each study can look at hundreds of thousands of genetic changes at the same time. Researchers use data from this type of study to find genes that may add to a person's risk of developing a certain disease. If your coded genetic and clinical information is used in such a study, the researcher is required to add the DNA test results and non-identifying 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.

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.

The research that may be done with your blood is not designed specifically to help you. It might help people who have HIV, cancer and other diseases 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.

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.

Benefits: The benefits of research using blood include learning more about what causes HIV, cancer and other diseases, how to prevent them, and how to treat them.

Risks: 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.

Statement of Consent

The purpose of storing blood samples, the procedures involved, and the risks and benefits have been explained to me. I have asked all the questions I have at this time and I have been told whom to contact if I have more questions. I have been told that I will be given a signed copy of this consent form to keep.

I understand that I do not have to allow the use of my blood and for research. If I decide to not let you store research samples now or in the future, it will not affect my medical care in any way.

I voluntarily agree that a blood sample may be collected and that my blood and related information can be stored indefinitely by the BMT CTN and/or AIDS and Cancer Specimen Resource Repository for research to learn about, prevent, or treat health problems. I also understand that my DNA and health information may or may not be used in genome-wide association studies.

- ❑ I do agree to give a blood sample for research.
- ❑ I do not agree to give a blood sample for research.

______________________________________ ___________
Signature Date

♦ ♦

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:

Allogeneic Hematopoietic Cell Transplant for Hematological Cancers and Myelodysplastic Syndromes in HIV-Infected Individuals

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:

<u>Principal Investigator and the researcher's staff</u>

Dr. Joseph Alvarnas, Co-Principal Investigator

Dr. Richard Ambinder, Co-Principal Investigator

<u>Study Sponsors</u>

- 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

- 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.

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, t he 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

Pediatric Assent to Participate in Research

Study Title: Allogeneic Hematopoietic Cell Transplant for Hematological Cancers and Myelodysplastic Syndromes in HIV-Infected Individuals

Protocol: BMT CTN 0903 (AMC 080)

A. Why am I here?

We are inviting you to join our study because you have HIV (human immunodeficiency virus) and you need a transplant to treat your blood cancer.

B. Why are you doing this study?

We are doing this study because we want to learn how well hematopoietic cell transplant treats blood cancers in people like you who have HIV. The kind of transplant we would do for you would use blood or bone marrow from another person who matches you. This is called an allogeneic transplant.

This form gives you information to help you decide if you want to be in this study. You should read this form and ask any questions you have before agreeing to be in the study. It is up to you to decide if you want to be in the study.

C. What will happen to me?

Before enrolling on study:
Your doctor will check to see if you have a type matched donor for your transplant. You will have several tests to see if it is okay for you to be on this study.

Before the transplant:
You will have several tests done to check your organ function. These tests will check your heart, lungs, and brain. Most of these tests are X-rays or scans, questions, or blood tests. The doctors will look at the results of all these tests to make sure that it is okay for you to have a transplant.

You will also need to have several tests for research. We will ask if we can take some blood from you up to 4 times (10-47 mL or about 2-13 teaspoons) with a very small needle. Eight weeks before your transplant, we will also ask to take more blood from you (about 36 teaspoons) only if the HIV in your body does not show up in a standard test.

Preparation for the transplant:
Before the transplant, you will need to receive medicines so that your body can accept the new bone marrow cells. This is called a 'conditioning regimen.'

You will receive chemotherapy medicine before your transplant. Chemotherapy is a combination of strong drugs that work to destroy your cancer cells and get your body ready for transplant.

Post-transplant follow-up and care:
After the transplant you will continue to get medicines to help the donor cells grow. These drugs will also help lower the chance of getting graft-versus-host disease (GVHD). GVHD is a complication that happens when the donor's cells attack your body. You will receive one or more medicines to prevent GVHD. You will continue to receive these drugs for at least six months after the transplant.

You will be in the hospital for about four weeks after your transplant. You will be allowed to go home from the hospital when your doctor feels it is safe. After you go home you will need to return to visit your doctors so they can check your recovery. Your doctors will need to check your blood and bone marrow after the transplant to make sure the new blood cells are growing in your body. Your doctors will also do blood tests and other tests to make sure your organs are working well.

This study will last for 2 years and we will watch you carefully for side effects, fevers, infections and other problems.

You will also need to have several tests for research. We will take some blood from you up to 7 times (about 2-14 teaspoons each time) with a very small needle. Also, 13 months after your transplant, we will ask to take more blood from you (about 36 teaspoons) only if the HIV in your body still does not show up in a standard test.

Optional Test for Future Research

Between 1 and 3 weeks prior to your transplant, we will ask your permission to take some more blood (about 6 teaspoons of blood) from you to use for future research.

You don't have to be in this research. If you don't want to give blood samples for future research you can still be in the other parts of the study. Your care will not be changed if you decide not to give these blood samples for research purposes. Please mark your choice below (check only one box):

❑ I do agree to give a blood sample for research.

❑ I do not agree to give a blood sample for research.

D. Will it hurt?

When you have your blood taken with a needle, it may feel like a pinch. It will hurt for a minute and sometimes the place where the needle went might be red and sore. You might get a little bruise where the blood was taken but it goes away in a few days.

E. What are the risks of being in this study?

The drugs may cause a skin rash, hair loss, nausea and vomiting, diarrhea and infections. Your blood counts will fall and you may get fevers, infections or start bleeding. You may also get mouth sores. These are temporary and you will feel better as your new bone marrow grows.

Since you will not be able to fight infections while your new bone marrow is growing back, you may need to get antibiotics. You may also need to get blood transfusions since your new bone marrow will not be making new blood cells right away.

Even with medicines to prevent it, you may get GVHD. This can cause skin rash, vomiting, diarrhea, stomach pain, lung and liver problems, swelling of the hands and feet, dry eyes, stiff joints, and tiredness. These problems are usually mild but can become very serious and prolonged. Medicines are given to prevent GVHD during and after transplant. If GVHD occurs even after taking these medicines, other medicines will need to be started and hospital stays may be necessary. The medicines used to treat GVHD also have side effects. They can cause tiredness, depression, sleep problems and mood swings. They can also make you get severe infections very easily. Your doctors will do their best to make you feel better and keep you safe. Often this may require many hospital stays. However, it is important to understand that there is a small risk (about a 1 in 10 chance) that you may die as a result of one or more of the complications of unrelated donor transplantation.

F. Will the study help me?

You may or may not benefit from taking part in this study.

G. What if I have questions?

You can ask us any questions that you have about the study. If you forget to ask a question and think of it later, you can call me [*insert office number*]. You can also ask your question the next time you see me.

You can call the study office at any time to ask questions about the study.

H. Do I have to be in this study?

It is up to you if you want to participate in this research study. If you don't want to be in the study, you can tell us and your parent or guardian. Your doctor will not be upset or angry if you don't want to join. You can say yes now and change your mind at any time. If you leave the study you can still get medical care from your doctor and transplant center. You will be told about new information or changes in the study that may affect your health or your willingness to continue in the study.

I. Can the doctor who is the Principal Investigator withdraw me from this study?

You can be taken off the study (with or without your consent) for any of the following reasons:

- You need a medical treatment not allowed in this study
- The investigator decides that continuing in the study would be harmful to you
- You become pregnant and the study participation could be harmful to the fetus
- The study is cancelled by the Food and Drug Administration (FDA) or the National Institutes of Health (NIH)

J. Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

You will receive a copy of this form. If you need more information about this study, ask the study doctor.

****

Minor's Assent

I have read the information in this consent form and have had the study explained to me. My questions have been answered to my satisfaction. I agree to participate in the study.

_____ _____
Signature of Minor Date

_____ _____
Print Name of Minor *Age of Minor*

Certification of Counseling Healthcare Professional
I certify that the nature and purpose, the potential benefits, and possible risks associated with participation in this study have been explained to the above individual and that any questions about this information have been answered.

_____ _____
Counseling Healthcare Professional Date