SUMMARY OF CHANGES

A Phase I Study of Stem Cell Gene Therapy for HIV Mediated by Lentivector Transduced, Pre-Selected CD34+ Cells

Version 9.0

NCI Protocol #: AMC-097
Local Protocol #: AMC-097

NCI Version Date: 07FEB2022
Protocol Date: 07FEB2022

I. Scientific and Substantive Changes

#	Section	Description of Change
1.	How long will I be in this study	During years 3-15, participants will be contacted by a person from the clinic rather than a person from the protocol team to collect information about their health.
2.	During the Study	The conditioning regimen prior to transplant has been revised to indicate that agents proven that have the same effects as rituximab (biosimilars) may be used instead of ritixumab for participants with B cell lymphoma. Participants will be informed of whether they will receive rituximab or a similar agent. In addition, the duration that each chemotherapy agent will be given has been removed. Both of these changes are because instiutions are permitted to administer conditioning regimens in accordance to their local guidelines and for consistency with the protocol. In addition, allowing administration of agents similar to ritiumab will give participating centers an alternative option for treatment if there is a supply shortage of rituximab.
3.	Use of HIV-1 Medications During the Study Risk Considerations related to COVID-19 Attachment 2	Additional information on the effects and risks of stopping HIV medications have been added. In addition recommendations and requirements to help reduce these risks have been added. Participants will be informed that HIV levels will increase while immune function may decrease and that it may take over 4-6 weeks for these levels to return to baseline, increasing the risk of developing symptoms. Additional risks include: • Symptoms similar to those experienced upon initial HIV infection • Inflammation / heart problems • Resistence to HIV medications, increased risk of spreading HIV • Increased risk of infection of another strain of HIV

#	Section	Description of Change
		• Risks related to COVID-19 have been added. Participants will be counseled on the risks of stopping HIV medications, and if sexually active, advised to use condoms and to refer their partners for HIV testing and post-exposure treatment. Participants will now be required to be tested for COVID-19 before stopping HIV medications. In addition, participants will restart their HIV medications if they development symptoms believed to be related to increased levels of HIV, have been exposed to HIV infection, or become pregnant. A calendar was added in Attachment 2 that outlines required assessment required after stopping and restarting HIV medications.
4.	Use of HIV-1 Medications During the Study Attachment 2	The duration that HIV medications may be stopped post transplant has been updated from 12 weeks to until the onset of criterion for resumption to allow for additional assessment on the survival of the anti-HIV gene. This is considered a safe duration as participants will be closely monitored and HIV medications will be restarted if symptoms develop.
5.	Use of HIV-1 Medications During the Study	Requirements during the conditioning regimen were revised to indicate that HIV medication may be held and that participants will be informed by their study doctor whether holding HIV medications is necessary. This change is consistent with the protocol requirements.
6.	Optional Sample Collections Attachment 2	The consent has been revised to include information on the SCOPE study being conducted by University of Califnornia San Franscico. The SCOPE study includes optional GI biopsies at the same timepoints as the optional GI biopsies in this study. Participants that join this study and the SCOPE study at the same time and consent to optional studies may have biopsy results from the SCOPE study used for this study. This will minimize the number of biopsies taken for participants planning to participate in both studies and that consent to optional GI biopsies. GI biopsies were added to the study calendar to clarify timepoints and collection.
7.	How long will I be in this study Optional Bone Marrow Biospies Optional Sample	Optional bone marrow collections have been added for research to study the effects of the vector on participants' genetics and immune system. Participants that consent to optional bone marrow biopsies will have about 2 tablespoons (20mL) of bone marrow collected at 3, months, 12 months, and at study discontinuation. Risks of participating in optional bone marrow collection include discomfort, pain, bleeding, scarring or infection at the site of the aspirate/biopsy and chance of allergic reaction to the numbing medicine.

#	Section	Description of Change
	Collections What is Involved? Risks of bone marrow biopsies Samples for Future Research Studies Attachment 2	
8.	How long will I be in this study Optional Blood Sample Collections Optional Sample Collections What is Involved? Risk of blood collections Samples for Future Research Studies Attachment 2	Optional blood sample collections have been added to monitor HIV levels and the vector. Participants that consent to optional blood collections will have about 3 tablespoons (30mL) of blood collected every 12 months for years 3-15 on study. Risks of bloow draws include pain, a bruise or lump at the point where the blood is taken, redness and swelling of the vein and infection, and a rare risk of fainting.
9.	Attachment 2	Required bone marrow biopsies to assess disease for staging were added for consistency with the protocol

II. Administrative and Editorial Changes

#	Section	Description of Change
10.	Global	The protocol version was changed to 9.0 and the date to 07FEB2022
11.	Attachment 2	Optional GI biopsy collections were added to attachment 2 for consistency with the optional study collections sections of the consent form.

AMC-097 MODEL INFORMED CONSENT FORM

Study Title for Study Participants: **Stem Cell Gene Therapy for HIV-1 in AIDS Lymphoma Participants**

Official Study Title for Internet Search on **http://www.ClinicalTrials.gov: A Phase I Study of Stem Cell Gene Therapy for HIV Mediated by Lentivector Transduced, Pre-selected CD34+ Cells**

A Clinical Trial of the AIDS Malignancy Consortium (AMC)

INTRODUCTION

You are being asked if you want to take part in a research study. The main goal of a research study is to learn things to help participants in the future. No one can guarantee that a research study will help you.

Participating in research is voluntary. You have the right to know about the procedures, risks, and benefits of the research study. To participate in this study, you will need to give your written consent by signing this form. Please take your time to make your decision and discuss it with your family, friends, and caregivers.

This study is being led by Mehrdad Abedi, MD from the Department of Hematology/Oncology at the University of California Davis, with AIDS Malignancy Consortium (AMC) sites at medical centers across the U.S.

WHAT IS THE USUAL APPROACH TO TREAT MY LYMPHOMA?

You are being asked to take part in this study because you have human immunodeficiency virus (HIV) infection and a type of blood cancer called lymphoma. You have already been treated with chemotherapy and your disease is now growing. People who are not in a study are usually treated with an autologous peripheral blood stem cell transplant with high dose chemotherapy (for example BEAM, described below). An autologous peripheral blood stem cell transplant is when your own stem cells are collected from your blood, frozen, and then given back to you after you receive high dose chemotherapy. This transplant with high dose chemotherapy is intended to prevent your disease from coming back in the future.

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study, you have other choices. For example:

- You may choose to have the usual approach described above.
- You may choose to take part in a different study, if one is available.
- You may choose not to be treated for cancer, but you may want to receive comfort care to relieve symptoms. Comfort care, or palliative care, helps reduce pain, tiredness, appetite problems, and other issues caused by your disease. It does not treat the disease directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to test the safety of combining the autologous stem cell therapy with gene therapy to treat your lymphoma. For gene therapy, researchers in a laboratory will add small

stretches of DNA called “anti-HIV genes” into your stem cells to make the gene therapy product used in this study. The type of anti-HIV genes and therapy in this study might make your immune cells more resistant to HIV.

The goal of the study is to develop an immune system that can actively prevent new immune cells from getting infected with HIV, while the older cells die due to HIV. This new immune system might be able to fight the spread of HIV even without HIV medications.

The gene therapy product in combination with your clinically indicated stem cell transplant in this study is considered experimental, because it has not been used in human clinical trials in the setting of an autologous transplant, and has not been approved by the Food and Drug Administration (FDA) for treatment of HIV. A similar gene therapy product has been used in other human clinical trials with stem cell therapy. Up to 18 people will take part in this study.

WHAT ARE THE STUDY GROUPS?

Study participants will get increasing amounts of stem cells with anti-HIV genes with autologous stem cell transplant.

- The first group of study participants will receive equal amounts of the stem cells with anti-HIV genes and stem cells without anti-HIV genes.
- If gene therapy does not cause serious side effects, it will be given to the second group of study participants. The second group will receive more stem cells with anti-HIV genes and fewer stem cells without anti-HIV genes.
- If the second group does not have serious side effects, the third group of participants will receive only stem cells with anti-HIV genes.
- If there are issues with cells engrafting in the third group of participants, a fourth group will receive only stem cells with anti-HIV genes, but at a higher amount than the third group received.

If you are among the participants that receive only stem cells with anti-HIV-1 genes, some of the stem cells without anti-HIV genes will be stored and will only be used as a safety back up if you need them. This means that the backup cells would be used if the stem cells with the anti-HIV genes do not allow for recovery of your blood cells quickly enough.

HOW LONG WILL I BE IN THIS STUDY?

You will receive a one-time infusion of stem cells with anti-HIV genes. The infusion goes into your vein like a blood transfusion over less than an hour. This is called an autologous transplant.

You will have clinic visits to follow up on your transplant on this clinical trial for two years after your stem cell transplant. However, we would like to keep track of your medical condition for at least 15 years and maybe for the rest of your life. Additionally, every 12 months for years 3-15 we will request optional lab studies to monitor your HIV levels and to see how the vector is working in your body. A member of the research team at the clinic will contact you by phone or mail once a year for a short conversation and to ask if any new changes have occurred in your health.

Keeping in touch with you and checking on your condition every year helps us look at the long-term effects of the study and the process of transplantation in general. Many transplant centers include this type of long-term follow-up as part of their regular medical care.

WHAT EXTRA TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra exams, tests, and/or procedures that you will need to have if you take part in this study.

Before You Begin the Study:

Your study doctor will review your past medical history to determine if you are eligible to participate. If you are eligible, you will have an opportunity to ask questions and review the study completely. If you agree to participate, you will sign the consent form. You will also be required to have certain tests performed prior to the start of the study to make sure you are eligible for this study. Most of these tests are standard of care for autologous transplant.

You will have:

- A review of your HIV status, which includes asking questions about behaviors related to risk factors for HIV,
- A physical examination,
- A chest x-ray,
- Pregnancy test for females who could become pregnant,
- An EKG (basic heart test),
- An echocardiogram (heart ultrasound) that assesses the heart function and heart valves,
- A pulmonary function test to determine how well your lungs are working and how well you are breathing,
- Blood tests (several tablespoons will be taken from a vein in your arm).

If you recently had any of these tests, your doctor may decide it is not necessary to repeat them.

You may be required to have:

- A cardiac stress test that assess heart function when you are exercising for about 20 minutes,
- An imaging scan of your body called CT scan, to look at the location and size of your cancer and any possible source for infection,
- A bone scan if clinically indicated, and/or a bone marrow biopsy.

During the Study:

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, you will be admitted to the hospital as an inpatient only to give you the experimental stem cell therapy. If you experience sudden side effects or your lymphoma worsens during the study, an additional blood sample (about two tablespoons) may be drawn to study the causes.

The three parts of the experimental stem cell therapy include:

Part 1: Taking Blood for Stem Cells

To collect your stem cells, you will get standard drugs to move stem cells from your bone marrow into your blood. This process is called stem cell mobilization. The treatment required for stem cell mobilization is called the mobilization regimen. This is a standard of care

procedure for all patients undergoing autologous transplant. Your transplant doctor will discuss the procedure with you.

After the stem cells are in your blood, you will have a procedure called leukopheresis. This is where your blood is run through a machine to collect the stem cells. Leukopheresis will take about 4 hours for most people. You will have this procedure to collect stem cells each day until there are enough stem cells for a safe transplant.

The stem cells that are collected will be split into two parts:

- The first part will be used for stem cells with the anti-HIV genes. In a very clean laboratory, the anti-HIV genes will be put into your stem cells. Once the anti-HIV genes are in the stem cells, they will be frozen and stored until you are ready to receive them.
- The second part of the stem cells will just be frozen and stored without the anti-HIV genes in them.

Part 2: Conditioning Regimen

Starting six days before your stem cell transplant, you will get a high dose chemotherapy conditioning regimen called BEAM or R-BEAM through a vein in your arm to kill the lymphoma cells in your body. BEAM and R-BEAM are a mixture of several chemotherapy drugs that stop the growth of cancer cells. These chemotherapy drugs are widely used to treat lymphoma and for stem cell transplants. The name of the chemotherapy drugs in BEAM and R-BEAM regimens are:

- BCNU (also called carmustine)
- Etoposide (also called VP-16)
- Ara-C (also called cytarabine)
- Melphalan
- If you have a type of lymphoma called B cell lymphoma, you may receive rituximab or a drug proven to have the same effect. Rituximab or similar drug will be given before the transplant, and again after the transplant on day 21 and day 28. The study doctor will let you know if you will be given rituximab or a biological similar agent.

Part 3: Reinfusion of Stem Cells (Transplantation)

One day after BEAM conditioning regimen is complete, the frozen stem cells that were previously collected from you will be thawed and re-infused into your veins through a catheter in your arm.

As mentioned before, depending on the study group you are in, you may receive only anti-HIV gene treated stem cells, or a combination of anti-HIV gene treated stem cells and stem cells without anti-HIV genes. The stem cells with or without anti-HIV genes are supposed to travel to your bone marrow where they will begin making healthy, new blood cells. This step is necessary because the high doses of chemotherapy given to you during the conditioning regimen will not only destroy lymphoma cells, but also healthy cells in your bone marrow. Until the new stem cells begin producing healthy blood cells, you will be at an increased risk of excessive bleeding or developing an infection.

You will stay in the hospital for about 3 to 4 weeks until your blood counts recover. The duration of hospital stay can be longer if any complication occurs or if your blood counts do not recover on time and you require additional stem cell infusion. During your transplant and

for about 6 months after transplant you will receive antibiotics to prevent some specific infections that can occur after transplant. Your transplant doctor will prescribe those medications for you based on the hospital's guidelines.

Use of HIV-1 Medications During the Study

You are expected to take your anti-HIV medications during this study except for two occasions:

1. The anti-HIV medications you are currently taking may be stopped during BEAM chemotherapy, and may be held immediately after that if you cannot tolerate taking oral medicines because of the side effects of BEAM chemotherapy. The anti-HIV medications will be resumed as soon as you are able to tolerate taking pills. The study doctor will let you know if any of your anti-HIV medications need to be stopped. In addition, some antiretroviral therapies may have effects on the bone marrow during its recovery (e.g., zidovudine) or may interact with BEAM chemotherapy causing side effects. The study doctor will let you know if any of your anti-HIV medications need to be changed.
2. At a minimum of 6 months after transplant and only when we document that your immune system has recovered from the transplant, you will be asked if you would agree to stop all anti-HIV medications until you meet criteria for resuming your medications. This is to give an opportunity for the immune cells that have anti-HIV genes in them to increase in number; the cells that do not have anti-HIV genes will be eliminated. We will check your level of HIV-1 in the blood and its impact on your blood cells and your general health weekly.Your doctor will restart your anti-HIV medications if you or your doctor decides this is necessary, or you feel uncomfortable at any time. The decision to stop the anti-HIV medications during that time is voluntary and will not affect your follow up in this study. Even if the approach works, your virus is expected to come back (rebound) for several weeks before it comes under control. If the regimen works, the viral rebound will be temporary, meaning that it should go up and then down, but this is not guaranteed. Different participants might have different "patterns" of rebound – quick versus slow, high levels versus low levels, short versus prolonged. During this time, the study doctor will monitor you very carefully. Your capacity to transmit HIV will increase during this time, particularly when the virus rebounds, so we will ask you to protect your sexual partner(s). The study doctor will give you information on HIV testing sites and HIV prevention programs and will counsel you about risks related to stopping your HIV medications.

If you choose to pause your HIV medications, you will be asked to get tested for the virus that causes COVID-19. If the test is positive, we will ask you to stay on your HIV medicines until you recover. During the period when you pause taking your HIV medications, if you experience COVID-19 symptoms you will be asked to get tested for the virus that causes COVID-19. If you test positive, you will need to resume your HIV medications.

The follow-up study visits will be in an outpatient clinic. Your study doctor or a nurse will see you in the clinic to assess your health status. You will be requested to have blood tests on a periodic basis after you finish receiving the experimental treatment. These blood tests include:

- About three and a half tablespoons of blood will be taken from a vein in your arm for the blood tests to test the status of your health, and
- Approximately 4 large tablespoons of blood (60 mL) will be taken from a vein in your arm at

several time points for studies of your immune system, genetic studies of the effect of introduced gene in your blood cells and HIV-1 studies.

Optional Intestinal Biopsies

With your consent, we will collect optional biopsies from your upper intestine to see if combining the autologous stem cell therapy with gene therapy works to treat your lymphoma. More information about this optional study will be explained to you in the Additional Studies Section of this consent.

Optional Blood Tests:

With your consent, we will ask you have to have blood tests to monitor the levels of HIV in your blood. More information about this optional study will be explained to you in the Additional Studies Section of this consent.

Optional Bone Marrow Biopises

With your consent, we will collect optional bone marrow biospies to study the effects of the introduced gene on your genetics and immune systems. You can find more information about this optional study in the Additional Studies Section of this consent.

A study calendar that shows how often these exams, tests, and procedures will be done is attached.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

You may have side effects while on this study. Everyone taking part in the study will be watched carefully for any side effects. However, the study doctor may not know or be able to predict all the side effects or risks. Side effects may be mild or very serious. The study doctors may give you medicines to help lessen side effects. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death. You should talk to the study doctor about any side effects that you have while taking part in the study.

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss.
- The study approach may not be better, and could possibly be worse, than the usual approach for your cancer.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.

The study doctor may adjust the study drugs to try to reduce side effects. The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

The side effects associated with this study can be divided into side effects associated with autologous transplant that is the standard of care for the treatment of your lymphoma, and the side effect associated with gene therapy that is specific to your participation in this clinical trial.

Potential Side Effects with Autologous Transplant with BEAM Chemotherapy Include (But Not Limited To):

COMMON, SOME MAY BE SERIOUS In 100 people receiving BEAM, more than 20 and up to 100 may have:
• Low blood counts • Nausea/vomiting • Mouth sores • Sores in esophagus • Abdominal pain/diarrhea • Difficulty eating • Hair loss • Fatigue

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving BEAM, from 4 to 20 may have:
• Liver problems • Lung problems • Low blood pressure • High levels of uric acid • Skin rash • Chills

RARE, AND SERIOUS In 100 people receiving BEAM, 3 or fewer may have:
• Liver failure • Severe lung problems • Severe allergic reactions • Second cancers, including Myelodysplastic Syndromes (MDS) and leukemia • Life-threatening infection • Disease of the peripheral nervous system • Sterility

Potential Side Effects with Gene Therapy Include (But Not Limited To):

As with any procedure, new adverse effects resulting in injury may be discovered. However, a similar gene therapy clinical trial for HIV-1 with a similar product given to five previous participants in a different institution was well tolerated. In the laboratory, no side effects have been seen. However, the potential side effects are:

- Failure of the stem cells to "take" and thrive in the bone marrow after infusion (this is known as engraftment). Back up stem cells will be saved if you are in the third group, and can be given to you if this happens.
- Gene therapy could theoretically cause leukemia. This has not been seen with this gene therapy model in the laboratory in extensive testing and in limited human studies with a similar vector. Four instances of leukemia were reported in children who participated in an experimental gene therapy study conducted in France, not under the jurisdiction of the U.S. Food and Drug Administration (FDA). In that study, children were treated by gene therapy for a serious genetic disease.
- Allergic Reactions: Proteins made from large amounts of non-human (protein) can sometimes lead to future allergic reactions. There is a small amount of a modified protein in the modified cells for which there is a small chance of allergic reaction, but it is unlikely to be harmful to you even if it occurs. If an allergic reaction occurs, it is more likely that the modified cells will be destroyed. After you receive the stem cells, your blood will be tested for any reaction that could affect the use of these agents in the future, but this reaction would not be directly harmful to you. This reaction is estimated to happen in about 4 out of 100 people.
- Reproductive Risks: You should not get pregnant, breastfeed, or father a baby during stem cell transplant and for the first 3 months after the day of stem cell transplant. The stem cells with anti-HIV genes used in this study could be very damaging to an unborn baby.

  If you are a woman of childbearing age, you can only be admitted to the study if:

a) you are not breast feeding;

b) you are not pregnant (as determined by a pre-study blood test for pregnancy);

c) you have been surgically sterilized or are using effective birth control.

Since the effects of the proposed treatments on a fetus are unknown, any woman who becomes pregnant while on this study must immediately let the study doctor know and will be removed from the study. Another method of treatment will be suggested.

If you are a male participant, you must practice effective birth control. You must immediately let the study doctor know if your partner becomes pregnant, and advise your partner to contact her physician.

Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

- Unknown Risks: The experimental treatments may have side effects that no one knows about yet. In addition, there may be problems of gene therapy that are unexpected but which may occur. The special virus ("retroviral vector") that is used to modify your cells does not have the genes needed to reproduce itself, but it is possible in the future that it could combine with other genes in your body, or that it could activate an unknown virus in your body, to result in a known or unknown medical problem or disease, including the possibility of another cancer.

For more information about risks and side effects of the gene therapy transplant, ask your study doctor.

Potential Side Effects with Stem Cell Infusion Unrelated to the Gene Therapy

COMMON, SOME MAY BE SERIOUS In 100 people receiving Gene Therapy, more than 20 and up to 100 may have:
• Low blood pressure • Lightheadedness • Fainting • Fever • Decrease in oxygen in the blood

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Gene Therapy, from 4 to 20 may have:
• Rapid heart rate • Chills • Allergic reactions

RARE, AND SERIOUS In 100 people receiving Gene Therapy, 3 or fewer may have:
• Bronchospasm (asthma like symptoms) • Second cancers, including leukemia

Additionally, while the cells are infused you may experience a garlic-like taste and a scratchy throat sensation. This is caused by the chemical used to preserve the cells and is usually a mild and temporary discomfort.

Risk of Antiviral Therapy Withdrawal: Your doctor will ask if you would agree to stop taking your anti-HIV medications on at least two occasions as discussed above.

Each time you stop your anti-HIV medications, there is a potential risk that HIV-1 infection become reactivated and suppress your immune system and make you susceptible to severe and potentially life threatening infections. The study doctors, including your HIV-1 doctor, will closely watch your immune system and will restart your anti-HIV medications if HIV viral reactivation and suppression of immune system reaches certain levels. However, restarting the anti-HIV medications may not completely stop the risk of complications.

Your HIV viral load will increase several days to weeks after you stop your HIV medications. The viral load might increase to very high levels. If this happens, your CD4+ T cell counts will likely drop. It is important to realize that, in this study, the doctors will monitor you very closely and will restart your HIV medications as soon as it is clear that the viral load or T cell count puts you at high risk of developing any new clinical problems. Your viral load and immune function might take over 4-6 weeks to return back to levels comparable to where they were when you entered the study.

When your HIV medications are stopped, you might have symptoms similar to when you first were infected with HIV, such as fever, rash, swollen glands, headache, sore throat, nausea, or vomiting. Other serious inflammation related symptoms, like increased buildup of plaque on artery walls which could possibly result in future heart attacks could happen. If you develop these symptoms, the study team will examine you and may restart your HIV medications if they believe the symptoms are due to increased HIV levels.

Resistance to your HIV medications might occur once viral loads become detectable. However, because the study doctor will stop all of your HIV medications the same time, the risk of developing resistance to your HIV medications is lower.

While you are off your HIV medications, you are at increased risk of transmitting HIV to sexual partners. You may also be at increased risk of becoming infected with a different HIV strain (called "superinfection"). Therefore, you should use male or female condoms at all times after HIV medications are stopped. If you feel you may have exposed someone to HIV, you should immediately refer them for testing and post-exposure prophylaxis (PEP). You should also seriously consider referring your HIV- negative sexual partner(s) for pre-exposure prophylaxis (PrEP) if you will be sexually active during the treatment interruption period. If you feel you have been exposed to HIV while off your HIV medications you may restart your medication this is recommended by your primary care provider.

If you are a woman and become pregnant while not taking your HIV medications, the study team will ask you to restart your medications immediately because there is a chance that you could transmit HIV to your developing baby.

Considerations related to COVID-19

There are additional risks of participation in this study due to the SARS-CoV-2 pandemic. SARS-CoV-2 is the virus that causes COVID-19, which is an illness that affects each person differently. Some people have no symptoms at all, and some people have very severe symptoms that require hospitalization, oxygen, or support with a breathing machine. COVID-19 is a potentially deadly illness.

The effects of COVID-19 in people with HIV are not fully known. It is currently thought that people with HIV on HIV medications are at similar risk of getting severe COVID-19 as people without HIV. The risk in people with HIV who are not taking HIV medications is unknown, but may very well be higher. This is important during the portion of the study when you will be asked to pause your HIV medications. If you choose to pause your HIV medications, you will be asked to get tested for the virus that causes COVID-19. If the test is positive, we will ask you to stay on your HIV medicines until you recover. Once you pause your HIV medications, you will be offered testing periodically or if you develop symptoms. If a test for the virus that causes COVID-19 returns positive, you may be asked to restart HIV medications.

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

You may not personally benefit from participating in this study. This study may help us learn things that may help people in the future.

CAN I STOP TAKING PART IN THIS STUDY?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your samples or your medical information to the organization running the study. If you decide you no longer want your samples to be used, any sample that remains will be destroyed and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

WHAT ARE MY RIGHTS IN THIS STUDY?

Taking part in this study is your choice. No matter what decision you make, and even if your

decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

The gene modified anti-HIV stem cells will be supplied at no charge while you take part in this study. The cost of getting a regular stem cell transplant as a standard of care for your disease is not paid by the study sponsor, so you or your insurance company may have to pay for this usually before transplant.

You and/or your health plan/insurance company will need to pay for all the other costs of taking care of your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in the mandatory part of this study. For the optional intestinal biopsy (upper endoscopy), a fee of $300 for each procedure completed will be paid to you.

WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS STUDY?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will **not** offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

WHO WILL SEE MY MEDICAL INFORMATION?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The AIDS Malignancy Consortium (AMC)
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.

- The Food and Drug Administration and the National Cancer Institute in the U.S.
- The drug manufacturers supporting the study (University of California Davis and University of Indiana).

WHERE CAN I GET MORE INFORMATION?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

ADDITIONAL STUDIES SECTION

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records, but you or your study doctor will know the results if requested.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

Optional Sample Collections for Laboratory Studies and Donation of Leftover Tissue Samples to the Aids and Cancer Specimen Resource (ACSR)

Researchers are trying to learn more about cancer, HIV/AIDS, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part in this study, the study doctor for the main study would like to collect these specimen types:

- **Optional intestinal biopsy:** To obtain important information about the efficacy of this study, we would like to ask you to provide a biopsy sample from your upper intestine. Your doctor will discuss this with you 6 months after the transplant, or when your CD4 count is greater than 300 cells/ mm^3. The endoscopy would be repeated 2 months after the first biopsy. **If you agree to the intestinal biopsy 6 months and 8 months after the transplant, you will be asked to sign a separate consent at that time before those procedures.** Our study partner at The University of California San Francisco is conducting a cohort study called SCOPE. There is also optional intestinal biopsies in this study. If you chose to coenroll in the SCOPE study, we will use their intestinal biopsy results for both studies. SCOPE is a separate study and requires a separate consent form. Participation in SCOPE is not a requirement of this study. If you agree to participate, you will be asked to sign a separate SCOPE consent form. We will give you the contact information for the SCOPE team if you are interested in learning more.
- **Optional bone marrow biopsies (for participants that do not have bone marrow involvement at baseline):** If you agree to participate in the optional portion of the study, we will request a research bone marrow biopsy or aspirate performed for research studies at 3 months, 12 months after your stem cell infusion, and when you discontinue the study. These studies would normally be standard of care if there is lymphoma in your bone marrow. These samples will be used to monitor the effects of the introduced gene on your genetic and immune systems.
- **Optional blood collections:** If you choose to take part in this study we will request optional lab studies every 12 months for years 3-15 to monitor your HIV levels and to see how the vector is working in your body.
- **Donation of left over study specimens to the ACSR for all study participants:** If you choose to take part in this clinical trial, the researchers would like to collect unused blood and biopsy tissue left over after the study is done. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking." The Biobank is being run by the **AIDS and Cancer Specimen Resource** and is supported by the National Cancer Institute.

What is Involved?

If you agree to take part, here is what will happen next:

1) **Optional intestinal biopsy:** An endoscopy will be performed to obtain small GI tissue samples. An endoscope (a small flexible tube) will be inserted into your stomach and a small tissue sample will be collected from your upper intestine using forceps. We will attempt to collect 24 very small tissue samples during each endoscopy session from you.
2) **Optional bone marrow biopsies:** About 2 tablespoons (20mL) of your bone marrow will be collected. A bone marrow biopsy is performed using a hollow needle to remove a small sample of bone marrow. Before the biopsy, a local anesthetic is used to numb the area where the needle will be inserted.
3) **Optional blood sample collections:** We will ask you to have about 3 tablespoons (30 mL) of blood collected. You will be seated in the lab or clinic and blood will be drawn by putting a needle into a vein in your arm.
4) **Donation of left over study specimens to the ACSR for all study participants:** Your sample and some related health information will be stored in the ACSR Biobank, along with samples

and information from other people who take part. The samples will be kept until they are used up. Information from your medical record may be updated after the study is over.

Qualified researchers can submit a request to use the materials stored in the ACSR. A science committee at the ACSR will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.

Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.

Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

Optional bone marrow biopsies, intestinal biopsy, and blood samples collected may be stored for up to 15 years to address research questions related to the treatment or the disease under study.

What are the Possible Risks?

Risks of Participating in the Optional Intestinal Biopsy (Upper Endoscopy)

1) Endoscopy risks: The upper endoscopy is being performed as a part of a research project. The risks of endoscopy are remote, however, there can be pain, gagging, bleeding, infection, perforation (a hole through the bowel wall can occur) and rarely, death can occur.
2) Sedation risks: The risks of intravenous sedation (putting someone to sleep) include bleeding, bruising, pain, infection from intravenous catheter, low blood pressure, decreased breathing, and allergic reaction to the medicine.
3) Allergic reaction risks: Symptoms of allergic reaction may vary from individual to individual but often consists of generalized rash (red skin), itchiness, and a feeling of being excited or anxious.
4) Very rarely swelling of the throat and/or difficulty breathing can accompany these symptoms. Occasionally (rare), midazolam (also called versed, a drug used for sedation) may cause a state of over excitement. The risks for small bowl biopsy are perforation and bleeding. These events have occurred in some patients though not with these physicians. These risks will be explained to you again by in detail prior to the endoscopy procedure by the gastroenterologist.
5) Reproductive risks: You should not become pregnant or father a baby if having an upper endoscopy because the drugs used during the procedure can affect an unborn baby. Women should not breastfeed a baby if having an upper endoscopy. It is important to understand that you need to use birth control. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

Risks of Participating in the Optional Bone Marrow Biopsies:

The procedure may cause discomfort, pain, bleeding, scarring or infection at the site of the aspirate/biopsy. There is also a small chance that you could have an allergic reaction to the numbing medicine. After your skin heals, you may have a small scar where we took the sample.

Risks of Participating in Optional Blood Sample Collections

The risks of taking blood include pain, a bruise or lump at the point where the blood is taken, redness and swelling of the vein and infection, and a rare risk of fainting.

Risks of Donation of Left Over Study Specimens to the ACSR

1) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
2) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
3) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

How Will Information About Me be Kept Private?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. The ACSR and AMC staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom the ACSR and the AMC send your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

What are the Possible Benefits?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are There any Costs or Payments?

There are no additional costs to you or your insurance for these optional studies. You will not be paid for taking part in the mandatory part of this study. For the optional intestinal biopsy (upper endoscopy), a fee of $300 for each procedure completed will be paid to you. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I Change My Mind?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

What if I Have More Questions?

If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial)*, at _____ *(insert telephone number of study doctor for main trial)*.

Please circle your answer to show whether or not you would like to take part in each option:

Samples for Future Research Studies:

I agree to have an optional intestinal biopsy and/or have biopsy results from the SCOPE study used for this study as described above.

☐ YES ☐ NO Participant Initials: ____

I agree to have to have bone marrow biopsies as described above

☐ YES ☐ NO Participant Initials: ____

I agree to have blood samples collected as described above.

☐ YES ☐ NO Participant Initials: ____

My samples and related information may be donated to ACSR Biobank for use in future health research.

☐ YES ☐ NO Participant Initials: ____

I agree to have my samples undergo genetic testing to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.

☐ YES ☐ NO Participant Initials: ____

This is the end of the section about optional studies

MY SIGNATURE AGREEING TO TAKE PART IN THE MAIN STUDY

I have read the consent form or had it read to me and understand the information above. I have discussed it with the study doctor and my questions have been answered I understand that I will be given a signed and dated copy of this consent form. I agree to take part in the main study and any additional studies where I circled 'yes.' My signature below indicates that I understand my rights and want to take part in this study as a research participant.

Participant's signature: _____

Date of signature: _____

Signature of person(s) conducting the informed consent discussion: _____

Date of signature: _____

ATTACHMENT 1: AMC CERTIFICATE OF CONFIDENTIALITY STATEMENT

The NIH has given the AMC a Certificate of Confidentiality. The Certificate does not mean that the NIH or the U.S. Government recommend that you take part in this study. This Certificate helps us keep your health information private.

Your records for this study will have information that may identify you. This Certificate lets us turn down legal demands for your study records. We can use the Certificate to turn down demands for records from a U.S. court. The Certificate can be used in any federal, state, or local legal matters. We will use the Certificate to turn down any demands for your study records. The cases where we cannot use the Certificate are explained below.

We cannot use the Certificate to turn down a demand from the U.S. Government for study records. This applies to audits or reviews of the AMC. This also applies to study records that we have to report to the FDA.

The Certificate does not stop you or your family members from sharing your health information. It does not stop you from talking about taking part in this study. You may give written permission for an insurer, employer, or other person to get copies of your study records. If you give permission, we cannot use the Certificate to say no to a request for your study records.

ATTACHMENT 2: STUDY CALENDAR

Prior to study enrollment and treatment, the following tests will be performed:

Required Studies/Testing	Within 8 weeks prior to enrollment (stem cell collection)	Within 1 week prior to admission for transplant	On the day of admission for transplant before start of chemotherapy
Medical history and physical examination	X	X	X
Infectious disease tests	X		
Chest X ray	X	X	
Heart strip	X		
Imaging for staging of your disease	X		
Lung function test	X		
Kidney function blood tests	X		
Bone marrow biopsy	X		
Tests for HIV-1	X	X	
Heart tests	X		
Review of your diagnosis slides	X		
Tests of your immune systems	X	X	X
Future research blood sample		X	
Pregnancy test for females of childbearing potential	X		X

After you receive your stem cell transplant, you will have the following tests and follow up visits:

Study Assessments/ Testing Post Transplant	Weeks after-HCT					Months After-HCT												Years After-HCT
	1	2	3	4	6	2	3	4	6	8	10	12	14	16,	18	20	22	24	3-15, once a year
Blood count	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
History and physical exam	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Imaging for staging of your disease							X		X			X						X	
Required bone marrow if you have bone							X					X							X

Study Assessments/ Testing Post Transplant	Weeks after-HCT					Months After-HCT													Years After-HCT
	1	2	3	4	6	2	3	4	6	8	10	12	14	16,	18	20	22	24	3-15, once a year
marrow involvement (for staging your disease)																			
Optional bone marrow biopsy (for research)							X					X							X
Optional GI biospy									X	X									
Tests of your immune system				X		X	X	X	X	X	X	X			X			X	X*
Tests for HIV-1 activity							X		X	X	X	X		X		X		X	X*
Genetic testing				X		X		X	X	X	X	X			X			X	X*
Telephone contact with you or your health care provider for the follow up of HIV status and development of any other cancer																			X

Most of the tests above involve standard medical care. Standard care is what is normally done to prevent, diagnose, or treat a certain condition or illness. Other parts of this study, namely administration of stem cells with anti-HIV gene in them is investigational. Furthermore, the follow up visits and test for assessment of the side effects and the evaluation of your immune system will be a part of the study, and out of the standard of care boundaries, and the follow up blood work may involve that are being tested for a certain condition or illness.

Assessments if you stop taking your HIV medicaitons:

Assessments	Within 1 Week prior to stopping HIV medications	After stopping your HIV medications (for about 12 weeks or more)	After you resume taking your HIV medications			
		Weekly	When you start	W4	W8	W24

			your HIV medications			
COVID Testing	X					
Stop taking ART medication		X				
Clinical Assessment		X	X	X	X	X
Tests on your immune system		X	X	X	X	X
HIV studies		X	X	X	X	X
Blood samples collected for research			X	X	X	X
Couseling about not taking your HIV medications	X	X				