Permission to Take Part in a Human Research Study

TITLE OF STUDY:	A Phase I/II, Randomized, Double Blind, Pilot trial to evaluate the Safety and Efficacy of ***A***llogeneic Mesenchymal Human Stem ***C***ell infusion therapy for ***E***ndothelial Dy***S***functi***O***n in diabetic subjects with Symptomatic ***I***schemic ***H***eart ***D***isease. (ACESO-IHD Study)
PRINCIPAL INVESTIGATORS:	**Nikolaos Spilias, MD** Department of Medicine, Interventional Cardiology Assistant Professor, Cardiovascular Division University of Miami Miller School of Medicine NCT04776239
PHONE NUMBER:	(305) 243-7589
EMAIL ADDRESS:	nspilias@med.miami.edu
STUDY-RELATED PHONE CONTACT:	ISCI Clinical Research Coordinators (305) 243 – 7444 (Office) ISCIStudyInfo@miami.edu

READ THE FOLLOWING CAREFULLY

This consent form has important information to help you decide if you wish to take part in this study. If you have any questions that have not been answered, please ask the study doctor or one of his/her research study personnel before signing this form.

KEY INFORMATION ABOUT THIS RESEARCH STUDY

You are asked to take part in a research study being done at the University of Miami, Miller School of Medicine - Interdisciplinary Stem Cell Institute (ISCI). The purpose of this research is is to study the safety of giving stem cells to patients with diabetes and heart disease who have recently had a Cardiac Catheterization. Cell-based therapy is an investigational procedure that has not been approved by the U.S. Food and Drug Administration (FDA).

You are asked to be in this study because you have been diagnosed with type 2 diabetes and had a recent procedure on your heart.

Your participation in this research will involve 7 visits and will last about 1 year. We expect about 30 people at the University of Miami will participate in this research. If you are a student, your decision not to participate or to withdraw from the study will not affect your grades or other academic standings at the University of Miami. If you are an employee of the University of Miami, your decision not to participate or to withdraw from the study will not affect your employment at the University of Miami System.

You will be asked to have blood tests, a physical exam, and other procedures for screening evaluation. Participants who qualify for the study will receive an infusion of either stem cells or a placebo and will be followed for one year.

Almost all research studies involve some risk. These risks/discomforts are described in detail later in this document.

Here are some reasons you may want to participate in this research: Because there is not much known about the effects in patients with your condition, this study may help us find better ways to treat diabetic mellitus subjects with cardiovascular disease in the future.

Here are some reasons you may not want to participate in this research: This study compares the effects of stem cells vs. placebo, meaning that there is a 50% chance of being randomly assigned to receive a placebo infusion.

Stem cells are a type of blood cell made by the bone marrow (spongy tissue inside our bones).

Stem cells can grow into many different types of cells. The stem cells (hMSCs) given to you in this study will be taken from a human donor's bone marrow. hMSCs have been used in other studies and have been shown to be generally well tolerated in humans.

Participation in this study is voluntary. You do not have to take part if you do not want to, and you can leave the study at any time. Whatever you decide, you will not be penalized or lose benefits.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions you need to help decide whether or not to join this study.

What if I have Questions?
If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at (305) 243–7444 or email ISCIStudyInfo@miami.edu

This research has been reviewed and approved by an Institutional Review Board ("IRB"). The Human Subject Research Office (HSRO) provides administrative support to the University of Miami's IRBs.

Please call the HSRO at 305-243-3195 if:

- The research team has not answered your questions, concerns, or complaints.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

How is being in this study different from my regular health care?
If you take part in this study, the main difference between your regular care and the study is the research infusion procedure. Being in this study will not impact your other medical care.

What happens if I say yes, I want to be in this research?
If you agree to participate in this study, you will be asked to return to the clinic to complete the procedures listed in the following table:

Study Visit	Procedures to be Performed	
Screening Visit *Within 7 days before or after cardiac catheterization. 4-6 hours approximately*	• Sign Informed Consent Form • Full Medical History and Physical Exam • Vital Signs • 12-Lead ECG • Review Medications • Eligibility for Enrollment • Standard-of-care coronary angiography	• Blood Collection • Urinalysis • Serum Pregnancy Test *If you are a female who has not gone through menopause* • Viral Serology: CMV, HIV, and Hepatitis Blood Tests
Baseline Visit *0-30 days after cardiac catheterization. 3-5 hours approximately*	• Physical Exam • Vital Signs • 12-Lead ECG • Review Medications • Randomization	• Blood Collection • Brachial Ultrasound • Questionnaires • Review adverse events
Day 0	• Physical Exam	• Post-Procedural Care

(Infusion) *0-30 days after cardiac catheterization 6-8 hours approximately*	• Vital Signs • 12-Lead ECG • Review Medications • Investigational Product Infusion *Will be prepared 2-3 hours before your infusion.*	• Blood Collection • Serum Pregnancy Test *If you are a female who has not gone through menopause* • Review adverse events • Genetic Testing
Week 2 (Post-Infusion) *±5 days 1-3 hours approximately*	• Physical Exam • Vital Signs • Review Medications • Brachial Ultrasound	• Blood Collection • Questionnaires • Review adverse events
Month 1 (Post-Infusion) *±2 weeks 3-5 hours approximately*	• Physical Exam • Vital Signs • 12-Lead ECG • Review Medications • Brachial Ultrasound	• Blood Collection • Questionnaires • Review adverse events
Month 3 (Post-Infusion) *±2 weeks 3-5 hours approximately*	• Physical Exam • Vital Signs • 12-Lead ECG • Review Medications • Brachial Ultrasound	• Blood Collection • Urinalysis • Review adverse events • Questionnaires • *(Optional)* Bone Marrow Collection
Month 6 (Post-Infusion) *±2 weeks 3-5 hours approximately*	• Physical Exam • Vital Signs • 12-Lead ECG • Review Medications • Coronary Angiogram	• Blood Collection • Urinalysis • Review adverse events • Questionnaires • Genetic Testing • Brachial Ultrasound
Month 12 (Post-Infusion) *±2 weeks 1-3 hours approximately*	• Physical Exam • Vital Signs • 12-Lead ECG • Review Medications • Review adverse events	

The treatment you get will be chosen by chance, like flipping a coin. Neither you, nor the study doctor will choose what study treatment you get. You will have an equal chance of being given either treatment. Neither you nor the study doctor will know which treatment you are getting, but in emergencies, the study doctor can quickly find out your treatment.

If you are unable to come to the site for specified visits, alternative methods for assessments (e.g., phone contact, virtual visit, alternative location for assessments, including local labs or imaging centers) could be implemented when necessary.

Screening Visit

A study doctor will check you during this visit to see if you qualify for this study. We will not have you complete any tests until you have signed this consent form. At this visit we will have you complete a physical exam, or we will use the physical exam performed by your treating physician. We will also look at your medical history and ask you if you want to take part in the study.

We will also collect information about you, such as your age, gender, past medical history, body weight, blood pressure, pulse, and blood tests taken at the outpatient clinic.

On the day of your Screening appointment, we will draw a blood sample from a vein in your arm (about 2 Tablespoons) for testing in the laboratory. A trained individual will draw your blood. We may ask you to not eat or drink anything for 8 hours prior to the blood test. The tests will measure certain chemicals (electrolytes) and count your blood cells. The Study Team will also request a urine sample of about 4 tablespoons (60ml).

We will also be testing to see if you are infected with Cytomegalovirus (CMV), HIV (the virus that causes AIDS), and hepatitis (liver) viruses. The blood test used to check for CMV prior to receiving the investigational product will be used to select the allogeneic MSC product that will be given. For the HIV testing, we will ask you to sign a separate section of this consent form. If you have HIV, or have active hepatitis, you will not be eligible to be in this study.

If you are a female of childbearing potential, we will do a pregnancy test (a blood test). If you are pregnant, you will not be eligible to be in this study.

You will have some tests of your heart function at this screening visit. First, we will do a 12-Lead electrocardiogram (ECG). In order to do this test, a trained expert will apply pads to certain areas of your body. The ECG will provide a picture of the electrical workings of the heart. It takes about 5 minutes to complete. This visit may take about 4 – 6 hours to complete.

Baseline Visit

After all screening exams are completed and it has been determined that you are still eligible for the study, you will be enrolled on the study. This visit will happen within one month after Cardiac Catheterization. At this visit, a study doctor will check to see how you are doing. They will also ask you questions about your condition and feelings. At this time, you will also be placed into either treatment Group 1 or 2 to receive allogeneic hMSCs or placebo. You will be assigned to a

group by chance (like flipping a coin). You will have an equal chance of being placed in either group.

Treatment Group 1: Allogeneic MSCs Fifteen (15) participants will receive an infusion of 100 million allogeneic hMSCs.	**Treatment Group 2:** Placebo Fifteen (15) participants will receive placebo infusion

An ultrasound of the right arm will measure the function of the deep blood vessel of the arm (also known as your brachial artery). This will be done in a non-invasive way. All ultrasound measurements of the brachial artery function will be done in the morning. This will be done in a quiet, dark room and at controlled temperatures between 68°F and 78.8°F. You will need to fast overnight for at least 10 hours (water is permitted) for this exam. Your right arm will be kept from moving and will be put in a comfortable extended position. This will allow the ultrasound scanning of the brachial artery 5–10 cm above your elbow. You will have a gel like water substance applied to your arm and a transducer will be passed over your skin, which is a camera used to take pictures of the blood vessels in your arm, will be used to complete the ultrasound scanning. The ultrasound scanning will then be followed by inflation of a manual blood pressure cuff to 40–50 mmHg above systolic pressure for 5 minutes. Then the cuff will be deflated, and pictures of the brachial artery diameter will be taken and recorded for 3 minutes. This exam is easy to perform and is not painful. It is done while you are lying down and resting.

5 tubes of blood for a total of 50 milliliters, which is about 3 tablespoons, will be drawn at this visit. Blood samples will be used to see the stem cells that can make new blood vessels. The blood will be examined using a microscope. A culture assay will be taken to count specific forms of stem cells. Part of the blood (the serum, without the cells) will be frozen and levels of inflammatory hormones will be looked at after the study ends.

You will be asked to complete the following questionnaires the baseline visit and several additional times during the study. The time it takes to complete these forms will vary. Although the study team would like you to complete the entire form, you may choose not to answer a question for whatever reason. The study team will use the results to assess your health and quality of life.

Seattle Angina Questionnaire: The SAQ is a 7-item self-administered questionnaire. The questionnaire will ask you about limitations due to coronary artery disease (CAD). It should take about fifteen (15) minutes to complete.

EQ-5D (EuroQol) Questionnaire: The EQ-5D (EuroQol) Questionnaire is a 5-item self-administered questionnaire. The questionnaire will ask you about your mobility, self-care, how good or bad you feel your health is today. It should take about fifteen (15) minutes to complete.

SF-36 (Short Form) Questionnaire: The SF-36 (Short-Form) Questionnaire is an 11-item self-administered questionnaire. The questionnaire will ask you questions about your health, such as how your health is to a year ago and how it affects your day-to-day activities. It should take about thirty (30) minutes to complete.

Male Participants will complete an IIEF Questionnaire: The IIEF (International Index for Erectile Function) Questionnaire is a 15-item self-administered questionnaire. The questionnaire will ask you about your sexual activities and should take about thirty (30) minutes to complete.

Female Participants will complete a SQOL Questionnaire: The SQOL (Sexual Quality of Life) Questionnaire is a 15-item self-administered questionnaire. The questionnaire will ask you about your sexual activities and should take about thirty (30) minutes to complete.

Day 0 - Infusion

This visit will happen within one month after cardiac catheterization. On Day 0 you will be admitted to the hospital for a peripheral intravenous infusion of the investigational product (stem cells or placebo). You will be requested to not eat or drink anything for at least 8 hours prior to the infusion.

The product will be prepared for infusion by the Interdisciplinary Stem Cell Institute at the University of Miami approximately with 2 – 3 hours prior to the scheduled peripheral intravenous infusion procedure on Day 0.

You will have blood (about 2 Tablespoons) and urine samples taken as well as 12-Lead ECG performed at the time of arrival to the site. Prior to the procedure, Hydrocortisone and Benadryl (Diphenhydramine) will be given to you at least 30 minutes before the procedure. During the procedure, a very small IV catheter (hollow tube), will be placed into your vein using a small needle. Once the catheter is in place, the Study Doctor will start the infusion with the investigational product. The process will take approximately 25 to 40 minutes. The Study Doctor and other trained technicians and nurses will carry out the procedure at the University of Miami Hospital.

You will be awake and able to follow instructions during the infusion. No additional medications will be given unless deemed medically necessary by the Investigator.

You may feel some discomfort at the site where the catheter is inserted. Local anesthesia will be used to numb the site, so the only sensation should be pressure. You may experience some discomfort from having to remain still for a long time.

After the procedure, the catheter is removed. You might feel a firm pressure at the insertion site. This is done to prevent bleeding. The Study Team and hospital staff will take your vital signs frequently for a couple of hours after the procedure.

Post-Intervention Visits

You will then return for 4 additional follow-up visits after your infusion, which will take place at 1, 3, 6, and 12 months after the infusion visit. At each visit we will review any adverse events (side effects) you may be experiencing. You will also have the tests/assessments listed in the table found earlier in this consent form.

Does this Study Involve Genetic or Genomic Research?

This study also involves genetic testing. Genes control how your body grows and changes, and how your body reacts to certain things. Genes are what we get from our parents that help make our bodies what they are. For example, eye and hair color depend on the genes we received from our parents. Genes are made up of DNA (deoxyribonucleic acid), which can be collected from blood, saliva, or other tissue samples. We want to find out how genes work in diabetes & heart disease. *We will not tell you what we find out about your genes*. For example, we might find out that you have a certain kind of gene. We may know that if people have this gene, they sometimes get a certain disease or do not respond to treatment. You could have a gene that makes it more likely that you will have a health problem. However, that does not mean you will get that health problem. You should ask the study team or a genetic counselor if you have any questions about genetic research.

We will not include your name or other identifying information on the blood that came from you. We will apply a random code to this sample. We will link the code to your identity, but we will keep the link in a separate place. We will keep your blood until it is all used up. We will also keep the information we learn about your DNA indefinitely. If you want to remove your blood from this study, contact the study doctor or study team and let them know. If the link to your identity has not been destroyed, we will find your sample and destroy it. We cannot remove the information we learned about your DNA.

We may share the information we learn about your DNA with other researchers so they can use it to learn more about heart disease. But we will not include any information that directly identifies you.

Even though your name will not be connected with the tissue or blood sample, other information about you might still be connected. Examples of this information may be your race, ethnicity, or parts of your medical history. This information may be important to scientists studying genes. The information they discover may be important for research or for public health.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for completing follow-up visits and communicating with the research team.

What happens if I want to leave the study?

Your participation in this study is voluntary. You may refuse to participate, or withdraw from the study at any time, without penalty or loss of benefits to which you are otherwise entitled.

If you leave the research, we will keep the information about you and the samples (blood, urine, saliva, or other samples) we obtained from you. If you decide to leave the study, contact the study team so the study doctor can work with you to create a plan. If you leave the research, we will keep the information about you that we obtained or created. Tell the study team if you want us to destroy the blood and other tissue samples that we collected while you were in the study. If the blood and other samples are not linked to your identity, the study team cannot destroy them.

If you leave the research, we would like to keep checking on your health. We will ask if we can review your medical record and collect data about your medical care in the future. If you agree to allow us to keep collecting data after you stop being in the study, this new data will be handled the same as the other research data.

Can I be removed from the research without my OK?

The researchers may take you out of the study, even if you want to continue, if:

- The doctor believes that participation in the study is no longer in your best interest.
- New information about the study treatment or other treatments become available.
- You are unable to follow the study rules or you no longer meet the requirements to be in the study.
- The study is cancelled.

What are my other choices if I do not take part in this study?

You do not have to be in this research study to get care for your **medical conditions,** if you decide not to take part in this study, you have other choices. For example*:* You may choose to take part in a different study if one is available. These options may have risks. Discuss the possible risks and benefits with your study doctor.

Is there any way being in this study could be bad for me?
There is always a risk to your privacy when you share information about yourself. However, the information that we collect from you in this study will be kept confidential, and there are practices in place to protect your personal information. Other possible risks include the following:

Blood draw risks: Drawing blood may cause temporary pain from the needle stick, bruising or swelling at the site, and rarely, infection or fainting.

Electrocardiogram ECG: This is a painless test that records the heart's electrical activity. The test involves attaching soft, sticky patches to the skin of your chest, arms and legs. After the test is done and the sticky patches are removed, you may have some skin irritation in the location where the patches were placed, but this typically goes away on its own

Psychological risks: Some of the questions the researchers ask you may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you can skip it and go to the next question.

Brachial Ultrasound: The ultrasound imaging of the brachial artery may cause a feeling of tightness in the arm below the transducer for a few minutes.

Infusion Catheter: Part of this study involves having a catheter (thin tube) inserted into one of your blood vessels. There may be slight discomfort during the inserting of the catheters into the vein or artery. Occasionally, a bruise or small lump may form at the point of insertion of the catheter. A small amount of bleeding may occur around the catheter site. Rarely, a local infection may occur around the catheter site.

Drowsiness: Before being given the study therapy, patients are first given two medicines to prevent allergic reaction. These medicines are Benadryl and Hydrocortisone. Because Benadryl may cause drowsiness in some patients, you should not operate heavy machinery, (such as driving a car) after the procedure, as instructed by your doctor.

Allergic reaction: As with any drug or biologic, it is possible that you could experience an allergic reaction to Allogeneic Human Mesenchymal Stem Cell (MSCs). Previous animal and human studies in which MSCs were injected into study participants have reported few complications. However, there are possible risks of this procedure. Although extremely rare, these risks include itching, skin rash, shortness of breath, breathing fast, fast heart rate, low blood pressure, or palpitations.

It is possible when receiving allogeneic mesenchymal cells that your body might react and reject the cell therapy treatment given to you during this trial. Human clinical research studies with allogeneic mesenchymal cells given to subjects have provided evidence against rejection due to graft versus host disease (GVHD), which is where the immune cells in the bone marrow stem cell product recognize the recipient as "foreign" and start an immunologic attack.

GVHD can be mild, moderate or severe - even life threatening. Its symptoms can include:

- Rashes, which include burning and redness, that erupt on the palms or soles and may spread to the trunk and eventually to the entire body
- Blistering, causing the exposed skin surface to flake off in severe cases
- Nausea, vomiting, abdominal cramps, diarrhea and loss of appetite, which can indicate that the gastrointestinal (digestive) tract is affected.
- Jaundice, or a yellowing of the skin, which can indicate that your liver is damaged.
- Excessive dryness of the mouth and throat, leading to ulcers
- Dryness of the lungs, vagina and other surfaces

GVHD can be acute or chronic. Its severity depends on the differences in tissue type between patient and donor. The older the patient, the more frequent and serious the reaction may be.

Pregnancy: This clinical research may involve unknown risks to unborn children; therefore, you must practice medically accepted methods of birth control while you are on this study.

Contraception Requirements for Women

We do not know the effects of this investigational therapy on babies before they are born, or on nursing children.

If you are pregnant or breastfeeding, you cannot take part in this study.

If you think you may be pregnant, you should not volunteer for this study.

If you are able to become pregnant, you must have a pregnancy test before you begin the study. You must not get pregnant or breastfeed while you are in this study.

If you are a woman who can become pregnant, you must take measures to avoid becoming pregnant while you are in this study.

The following are acceptable measures to avoid becoming pregnant:

- Abstinence (not having sexual relations with a person of the opposite sex)
- Implantable hormone (e.g. Norplant)
- Intrauterine Device (IUD)
- Male partner has had a vasectomy
- Female sterilization
- Hormonal injection
- Oral contraceptives
- GnRH Agonists (zoladex, triptorelin, leuprolide)-these agents are only effective if they have been in continuous use for at least 3 months

You must use contraception before starting study treatment unless you abstain from sexual intercourse. You must use contraception during study treatment and for at least 3 months after stopping study treatment.

Contraception Requirements for Men
We do not know the effects of this investigational therapy on embryo/fetus if your sexual partner is pregnant or becomes pregnant while you are in this study. If your partner is a woman of child-bearing potential, you and your partner must either practice total abstinence or use effective contraception while participating in this study. One of the following forms of contraception should be used by you or your partner:

- Abstinence (not having sexual relations with a person of the opposite sex)
- Implantable hormone (e.g. Norplant)
- Intrauterine Device (IUD)
- Vasectomy
- Female sterilization
- Hormonal injection
- Oral contraceptives

You must use contraception during study treatment and for at least 3 months after stopping study treatment. You should also refrain from donating semen during therapy and for 3months after stopping the therapy.

If your partner becomes pregnant or suspects becoming pregnant during study treatment or within three months after completing study treatment, you must inform the Study Doctor immediately. Your Study Doctor may want to follow the pregnancy and may ask your partner to sign a consent form so they can collect information about the outcome of the pregnancy.

Unknown Risks: The investigational treatment may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

You have the right to ask any questions about the potential and/or known hazards of this study at any time. You will be asked to tell the study doctor about any possible side affects you might have at any time during the study.

Will being in this study help me in any way?
Because there is not much known about the effects of human mesenchymal stem cells in humans, we do not know if you will benefit from taking part in this study. Your condition may become worse despite receiving this experimental treatment. However, your participation in the study may benefit other people with similar symptoms. This study is not a substitute for your regular medical care. You should continue to see your regular medical providers.

What if new information becomes available?
We will tell you if we have any new information that may affect your willingness to stay in the study

Will being in this study cost me anything?
The study drug will be provided free of charge during this study. Tests and procedures that are done only for the study will not be billed to you or your insurance company.

You or your health insurance plan may have to pay for medical costs associated with taking part in this study. If you have insurance, your insurance company may or may not pay for these costs. If you do not have insurance, or if your insurance company refuses to pay, you will have to pay. You should discuss any questions you have about costs with the study doctor or study team.

There will be no cost to you for the lab tests, diagnostic imaging, and clinic visits that are done for research purposes only and are not part of your regular care.

You will have to pay for basic expenses like any childcare, food, parking, or transportation related to study activities.

Will I be paid or receive anything for being in this study?
We will pay you $25 for completing follow-up visits at Month 1, Month 3, Month 6, & Month 12. If you agree to be in the Bone Marrow Biopsy sub-study, you will get an extra $100. If you undergo the repeat cardiac catheterization you will get an extra $50. Payment will be given at the end of

each visit with either a gift card, check, or cash. If you complete all the study visits and assessments, you will receive $250 for being in this study.

You may be asked for your social security number for payment purposes. It will not be used for any other purpose without your permission. If you receive $600 or more during a calendar year from the University for participating in research, you may receive a 1099 for tax reporting purposes. Reimbursements for travel and other expenses are not included in this amount.

Your information and samples may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

The University of Miami may retain, preserve, or dispose of these specimens and may use these specimens for research which may result in commercial applications. You will not receive money for donating blood, urine or tissue samples nor will you receive money from any future proceeds as a result of this research project.

What happens if I am injured or get sick because of this study?
If you are hurt or get sick as a result of being in this study, treatment will be available in most cases. If you have insurance, your insurance company may or may not pay for these costs. If you do not have insurance, or if your insurance company refuses to pay, you will be expected to pay. Funds to compensate you for pain, expenses, lost wages, and other damages caused by injury are not available. This policy does not prevent you from trying to obtain payment through the legal system.

What conflict of interest issues may be related to this research?
Any investigator who has a conflict of interest with the study must have the conflict reviewed by a properly constituted Conflict of Interest Committee with the Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All investigators will follow the University of Miami's conflict of interest policy.

Dr. Joshua Hare has disclosed that he has a personal interest related to this study.

Dr. Hare is the Chief Scientific Officer, a compensated consultant and advisory board member for Longeveron and holds equity in Longeveron. Dr. Hare is also the co-inventor of intellectual property licensed to Longeveron.

The University of Miami is an equity owner in Longeveron, which has licensed intellectual property from the University of Miami.

Please ask any questions to assure yourself that this relationship has not overly influenced the conduct of this research study. If you require further information, please contact the study doctor or HRSO at 305-243-3195 to ask questions or discuss concerns.

What happens to the information collected for the research?
We will do our best to limit the use or disclosure of your personal information, including information from this research study and from your medical records, to people who have a need to review this information. Records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available.

If the results of the trial are published, your identity will remain confidential.

We cannot promise complete confidentiality. Some organizations may be required to inspect and copy your information including the IRB and other University of Miami representatives responsible for the management or oversight of this study.

We have strict rules to protect your personal information and protected health information (PHI). We will limit who has access to your name, address, phone number, and other information that can identify you. We will remove identifiable information from the data we collect about you. After we remove all of the identifiers, we will place a code on the information. The code will be linked to your identity, but the link will be kept in a location that is separate from your study data. We will maintain your study data on encrypted computers and access to the information will be limited to only members of the research team who need the access to properly conduct the study.

We may publish and present what we learn from this study, but none of this information will identify you directly without your permission.

We may use the data and samples we collect from you for future research studies. We may also provide the data and samples to another researcher for future research. We will remove information that can identify you if we use or share the data and samples for future research. Once identifiers have been removed, we will not ask for your consent for the use or sharing of your data or specimens for future research.

The following is a list of individuals who may access your records:

- Members of the research team

- Offices and committees responsible for the oversight of research
- Personnel who schedule or perform medical tests or procedures, handle accounting and billing, or do other tasks related to this study
- U.S. Office for Human Research Protections
- The U.S. Food and Drug Administration (FDA)

The study doctor and research team may publish the results of this research. However, they will keep your name and other identifying information confidential.

For this study, we must access and share information about you that is sensitive. This information includes information about your HIV status, hepatitis B, hepatitis C, and sexually transmitted diseases.

The investigator and his/her collaborators will consider your records confidential as permitted by law. The study sponsor, Food and Drug Administration (FDA) and Department of Health and Human Services (DHHS) may review your records and the results of your HIV test. Authorized University of Miami employees or other agents who will be bound by the same provisions of confidentiality may also review your records for audit purposes. By law, we must report all positive HIV test results to the Florida Department of Health with information identifying you if you test positive.

Anonymous testing for the HIV virus is available at other locations throughout Dade County. You can visit the following site, which lists the confidential and anonymous testing sites: http://miamidade.floridahealth.gov/programs-and-services/infectious-disease-services/hiv-aids-services/counseling-testing-sites.html"

If we test you for HIV, hepatitis and some sexually transmitted diseases, we will need to report positive results to the health department. By signing this consent document, you are agreeing to this use, access and disclosure of your sensitive information.

If you are, or have been, a patient at a University of Miami facility, you will have a University of Miami electronic medical record to which we will add the research information to improve access to information important to your medical care. Your electronic medical record will show that you are in a research study and a copy of this signed consent form will be included. To provide as complete a record as possible, some or all of your study-related research information may also be placed in your electronic medical record. This specifically includes investigational drugs, devices, biologics, or anything else that may, separately or together with other substances or activities, interfere with your clinical treatment or place you at greater risk of harm. Other information from

the research study may be included as well. Including this information in the electronic medical record system is intended only to give information to caregivers providing treatment for you while you are on this study.

This information will be available to University of Miami doctors, nurses and other authorized staff who may not be part of the research team but who are involved in providing you medical care, or who are otherwise allowed to access your information. The confidentiality of the results and other documents in your electronic medical record will be governed by laws, such as HIPAA, that concern medical records. We suggest that you tell any non-University of Miami doctors that you are in a research study and that more information may be made available to them at your request. The research team may use your information to notify you of appointments, send you appointment reminders, or schedule additional appointments.

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access.

Federal law provides additional protections of your medical records and related health information. These protections are described in the second part of this document, University of Miami HIPAA Authorization for Research.

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.

This research is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. The researchers with this CoC may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding. For example, the information collected in this research cannot be used as evidence in a proceeding unless you consent to this use. Information, documents, or biospecimens protected by this CoC cannot be disclosed to anyone else who is not connected with the research, except:

- To a federal agency sponsoring this research when information is needed for auditing or program evaluations;
- To meet the requirements of the U.S. FDA;
- If a federal, state or local law requires disclosure such as a requirement to report a communicable disease;

- If information about you must be disclosed to prevent serious harm to yourself or others;
- If you consent to the disclosure, including for your medical treatment, to an insurer or employer to obtain information about you; or
- If it is used for other scientific research, as allowed by federal regulations protecting research subjects.
- To University of Miami doctors, nurses and other authorized staff who may not be part of the research team but who are involved in providing you medical care and other health care operations.

This CoC also does not prevent you or a family member from voluntarily releasing information about yourself and your involvement in this research. If you want your research information released to any other person not connected with the research, you must provide written consent to allow the researchers to release it.

The CoC will not be used to prevent disclosure for any purpose you have consented to in this informed consent document. Any information disclosed pursuant to your authorization may no longer be protected by the Certificate of Confidentiality.

Will I receive any results from this research?
Some tests done on your samples will be only for research and have no clear meaning for or impact on health care. Sometimes the tests are done on samples that are not linked to your identity. If the results of these tests may seem to be of impact to your health and the research team is able to identify you, the researchers will attempt to contact you to let you know the results.

If study team gives your genetic tests results to you, it may be because they think you could have a health risk. They may advise you to have the test re-done by a certified lab to check the results. If this happens, then you may want to ask your own doctor if you should have the test redone. You may also want to get genetic counseling. The research will not pay for those extra services

Will information or leftover specimens be used for other research?
Information collected about you and biospecimens collected from you will be used for this research and may also be used for other research studies here at the University of Miami. We may also share the information and specimens with other institutions for research. Before using the information and specimens for other research, the study team will remove information that identifies you so the individuals performing the research will not know who the information and specimens came from. We will not ask for additional consent from you to use your information and specimens for the additional research.

Are there any optional parts of the study?
This part of the consent form is about additional optional parts of the study that you can choose to take part in. Things to know about the optional part of this study:

- It is optional. You can still take part in the main study even if you say "no" to this part of the study.
- This part of the study will not help you directly. We hope the results from these optional parts of the study will help us understand how cell therapy works inside the body.
- We will not tell you the results of these optional parts of the study, and we will not put the results in your medical records.
- Taking part in the optional parts of the study will not cost you anything. You will have to pay for basic expenses like any childcare, food, parking, or transportation needed for optional study assessments.

Purpose: Detailed molecular and functional assessment of bone marrow aspirate.
Description: Bone Marrow biopsy collected at 3 months post-infusion.
Why participate? Help to understand how cell therapy works inside the body.
Why not participate? Invasive Medical Procedure.

A separate Informed Consent Form (ICF) will be provided during the month 3 visit for participants who are considering participation in this sub-study.

May we contact you by e-mail?
We are requesting your email address so we can so we can contact you if necessary to coordinate follow up visits and other important information related to this study. Email is generally not a secure way to communicate about your health, as there are many ways for unauthorized users to access email. You should avoid sending sensitive, detailed personal information by email. Email should also not be used to convey information of an urgent nature. If you need to talk to someone immediately, please contact the research coordinators office at (305) 243-7444. You do not have to provide your email address to participate in this study. Please initial one of the lines below.

_____ Yes, may use email to contact me for this study. My email address is: _____

_____ No, I do not want to be contacted by email.

PARTICIPANT'S STATEMENT/SIGNATURE

- *I have read this form and the research study has been explained to me.*
- *I have been given the chance to ask questions, and my questions have been answered. If I have more questions, I have been told who to call.*
- *I agree to be in the research study described above.*
- *I will receive a copy of this consent form after I sign it.*

_____ _____

Signature of Participant Date

_____

Printed Name of Participant

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent

WITNESS STATEMENT/SIGNATURE

- *As an impartial third party, I witnessed the entire consent discussion.*
- *I attest that the above-named participant received a verbal and written description of the study.*
- *This individual had sufficient time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participate in this study.*

_____ _____

Witness Signature Date

_____

Printed Name of Witness

PART 2: UNIVERSITY OF MIAMI RESEARCH AUTHORIZATION

What is the purpose of this part of the form?
State and federal privacy laws protect the use and disclosure of your Protected Health Information "PHI". Under these laws, your health care providers generally cannot disclose your health information for the research listed above unless you give your permission. You will use this form to give your permission. By signing this form, you authorize the University of Miami, the Principal Investigator and his/her/their/its collaborators and staff to obtain, use and disclose your health information, as described below. These people and institutions are called "Providers" in this form.

What Protected Health Information will be used or shared?
You are authorizing the use and sharing of all of the information collected or created during this research as described in the first part of this document, including information in your medical records that is relevant to this research study. Information that may be relevant includes:

- Your past medical history,
- Medical information from your primary care physician,
- All other medical information relating to your participation in the study listed at the top of this document

Who may receive my Protected Health Information?
The Providers may use and share your health information with:

- The Principal Investigator and his/her research staff
- Representatives of government agencies that have oversight of the study or who the law permits to access the information such as the U.S. Food and Drug Administration, the Department of Health and Human Services, and the Florida Department of Health
- Groups that collaborate and sponsor research (Cooperative Groups)
- Institutional Review Boards (groups of people who oversee research)
- Other persons who watch over the safety, effectiveness, and conduct of research
- The Sponsor of the research, its agents, monitors, and contractors
- Other participating researchers; and
- Independent data and safety monitoring boards

Authorized staff such as doctors and nurses who are taking care of your but are not involved in this research may be aware that you are participating in a research study and may have access to research information about you. If the study is related to your medical care, any study-related information may be placed in your permanent hospital, clinic, or physician's office records.

Why will my Protected Health Information be used and disclosed?

- Researchers (those individuals in charge of the study) and research team members will use your information to conduct the research study described in this informed consent document and other activities related to the research, such as evaluating the safety of the study.
- The research sponsor and its authorized representatives, business partners, clinical research organizations and affiliates will use your information for the purposes described in this informed consent document and for other activities related to the research, such as assessing the safety or effectiveness of the drug, device or treatment being studied, improving designs of future studies or obtaining approval for new drugs, devices or health care products.
- The University of Miami's clinical trial organizations will use your information to review and support clinical trials at the University.
- Other University of Miami offices involved in regulatory compliance, including the Institutional Review Board (IRB), Offices of General Counsel, and Compliance may use your information to ensure the research is performed correctly.
- U.S. government agencies, such as the Food and Drug Administration and the Office for Human Research Protections, government agencies from other countries, and others who are authorized by law may use your information to review or oversee this research or to see if a new drug, device or other health care product should be approved for marketing.

What other information should I know?

1. Once your information has been disclosed to a third party, the federal privacy law may no longer protect the information from further disclosure.
2. You do not have to sign this Authorization, but if you do not sign it, you may not participate in the research and receive the research treatment; however, your right to other medical treatment will not be affected.
3. You may change your mind and revoke (take back) this Authorization at any time and for any reason. To revoke this Authorization, you must write to the study doctor or to the Human Subjects Research Office at 1400 NW 10th AVE, Suite 1200A, Miami FL 33136.
4. If you revoke this Authorization, you will not be able to continue taking part in the research. Also, even if you revoke this authorization, the institutions and people listed above will continue to use and disclose the personal information they have already collected if the information is needed to protect the reliability of the research.
5. While the research is in progress, you will not be allowed to see your health information that is created or collected by the institutions and people listed above. After the research is finished, you may see your health information.

6. This Authorization does not have an expiration date. There is no set date at which your information will be destroyed or no longer used because the research will need to analyze the information for many years and it is not possible to know when they will complete the analysis.
7. You will be given a copy of this authorization after you sign it.

_____ _____

Signature of participant or participant's legal representative Date

_____ _____

Printed name of participant Printed name of legal representative (if applicable)

_____

Representative's relationship to the participant

Part 3. INFORMED CONSENT: BLOOD TESTING FOR HUMAN IMMUNODEFICIENCY VIRUS

PURPOSE

You are volunteering for a clinical research study for which there is this separate consent form. For this study, we will take a sample of your blood to find out if you carry the HIV virus which is the virus that causes AIDS. If you do not want your blood tested, you may refuse to be in this study and no further research testing will be done to you.

PROCEDURE

For the HIV test, blood will be taken from a vein in your arm. Before and after the blood is tested, you will be counseled and you will be given information on HIV testing, AIDS, and the transmission of HIV infection. We will also explain the test, its limitations, and the meaning of the test's results. If the test for HIV is positive, we will give you information on where to find medical and support services, on the importance of notifying partners who may have been exposed, and on preventing transmission of HIV. If the test is negative, we will give you information, as appropriate, on preventing the transmission of HIV.

A positive test for HIV is over 99% correct since at least one extra test is conducted to confirm the result. A negative test for HIV may mean that you have not been infected with HIV or that you may be infected but not enough time has passed between exposure to the virus and the test. After being exposed to HIV, it may take from three to six months or longer before the HIV can be detected.

RISKS

The risks of blood drawing include: temporary discomfort and/or bruising at the site of puncture, fainting, infection or the formation of a small clot or swelling to the vein and surrounding area.

If the blood test is positive for HIV infection, there is the possibility of emotional distress. There is also a possibility that your status in your workplace or other social organizations will be impacted if you or others with knowledge of your HIV infection disclose this information.

BENEFITS

There is no direct benefit for your participation in this study. However, knowing that you are HIV positive may allow you to seek medical treatment and to learn healthy behaviors. Any treatment would be your own responsibility. You will be advised how to obtain further information about HIV and its consequences.
If you test positive for HIV, another benefit is that you will learn how to prevent the spread of HIV and help anyone you may have exposed or been exposed to.

CONFIDENTIALITY

The investigator and his/her collaborators will consider your records confidential as permitted by law. The Food and Drug Administration (FDA) and Department of Health and Human Services (DHHS) may review your records. Authorized University of Miami employees or other agents who will be bound by the same

provisions of confidentiality may also review your records for audit purposes. By law, we must report all positive HIV test results to the Florida Department of Health with information identifying you if you test positive. Your records and results will not identify you in any publication without your permission.

Anonymous testing for the HIV virus is available at other locations throughout Dade County. You can visit the following site, which lists the confidential and anonymous testing sites: http://miamidade.floridahealth.gov/programs-and-services/infectious-disease-services/hiv-aids-services/counseling-testing-sites.html

COSTS

You will not have to pay for the HIV test performed in this study.

RIGHT TO WITHDRAW

Participation in this research is voluntary. You may refuse to participate or withdraw from this study at any time. If you withdraw from the study, it will not affect future medical care you seek at the University of Miami. You may ask any questions concerning this study. If you have any questions about your rights as a research subject, you may contact the Human Subject Research Office at (305) 243-3195.

VOLUNTARY CONSENT

I agree that a sample of my blood may be taken and tested to determine the presence in my body of the HIV virus that causes AIDS.

I have been told the potential uses of the HIV test, its limitations, the meaning of the test's results, and the procedures to be followed. I have also been told about the voluntary nature of the test, my right to withdraw consent to the testing process at any time prior to the HIV test, and my right to confidentiality to the extent provided by law. The procedure for drawing a blood sample and its risks have also been explained to me.

I have been given a copy of this informed consent document.

Investigator's Name: _____

Telephone Day/Night: _____

Subject Printed Name: _____

Subject Signature: _____ **Date:** _____

Person Obtaining Consent Printed Name: _____

Person Obtaining Consent Signature: _____ **Date:** _____