Informed Consent Form

Granulocyte-Macrophage Stimulating Factor (GM-CSF) for Mobilization of Progenitor Cells in Peripheral Arterial Disease: A Phase II Randomized Study (GPAD-3)

IRB Approval Date: November 6, 2024

NCT03304821

You Are Being Asked to Be in a Research Study

Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study you will be one of 120 people who are being studied, at Emory and elsewhere.

Why is this study being done?
This study is being done to answer the question: Does the study drug (GM-CSF) improve symptoms and blood vessel function in people with Peripheral Arterial Disease (PAD). You are being asked to be in this research study because you have PAD.

Do you have to be in the study?
It is your decision to be part of this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition. Before you make your decision, you should take time to learn about the study.

What do I have to do if I choose to participate in this study?
If you are eligible and want to be part of the study, you will participate for 9 months (11 study visits). The researchers will ask you to do the following: answer questions, have blood drawn for testing, walking tests, blood flow measurements. Some participants will be asked to have MRIs or Ultrasounds. ALL of these procedures will be paid for by the study.

How is this study going to help you?
If you are in the study, you will be helping the researchers answer the study question. Your PAD may improve while you are in the study but it may not, and it may get worse.

What are the risks or discomforts I should know about before making a decision?
The study will take time. The drug that is being tested may not work any better than regular care, and may even cause harm. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious – for this study, these include fever, chills, nausea, vomiting, diarrhea, fatigue, weakness, headache, decreased appetite, feeling of faintness, facial flushing, pain in the bones, muscles, chest, abdomen, or joints, local reaction at the site of injection and rashes, bruising, bleeding, kidney and liver dysfunction, loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are in the “What are the possible risks and discomforts?” section of this document.

Alternatives to Joining This Study
Patients with PAD can be treated with medication, lifestyle changes, angioplasty and surgery. The study doctor will discuss these with you. You do not have to be in this study to be treated for PAD.

Costs
You WILL NOT have to pay for any of the study procedures, in particular those that are not covered by your medical insurance.

The study team can help you work out how much you might have to pay. There is more information in the cost section below.

What Should I Do Next?
Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Make sure you understand which parts of the study are research and which are standard care that you would have even if you did not join the study. Take time to consider this, and talk about it with your family and friends.

Emory University and Grady Health System
Consent to be a Research Subject / HIPAA Authorization

Title: Granulocyte-Macrophage Stimulating Factor (GM-CSF) for Mobilization of Progenitor Cells in Peripheral Arterial Disease: A Phase II Randomized Study (GPAD-3)

Principal Investigator: Arshed A. Quyyumi, MD

Sponsor: National Institutes of Health, National Heart, Lung, and Blood Institute (NHLBI)

Investigator-Sponsor: Arshed A. Quyyumi, MD

Introduction
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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.

What is the purpose of this study?
The purpose of this study is to evaluate whether a drug called GM-CSF (granulocyte-macrophage colony stimulating factor or Sargramostim) improves symptoms and blood vessel function in people who have pain in their legs while walking because of blockages in the arteries of their legs from peripheral arterial disease (PAD). You should already have had a diagnosis of PAD and have symptoms related to it such as pain, aching, cramps, or fatigue in the muscles of the leg when you walk, that gets better when you rest.

Background: People who have blockages in the arteries of their legs have reduced blood flow to the muscles of their legs – especially with exercise, which causes the pain, aching, cramping or tiredness in the muscles of the legs when they walk. Some individuals are able to naturally grow new blood vessels in an attempt to form bypasses around the blockages, so that ultimately they are getting blood to the muscles of the legs – even with exercise. Often, however, these new blood vessels are inadequate in their ability to supply sufficient blood.

We now believe that stem cells made in our bone marrow contribute to the making of these new blood vessels when blockages develop. Specific types of stem cells called progenitor cells are thought to be mainly responsible for the growth of new blood vessels and repair of damaged ones.

Substances like GM-CSF stimulate the bone marrow to release stem cells. We will use one of the most commonly used drugs called GM-CSF to study if it can safely be given by injections under the skin in patients with your condition to stimulate new blood vessel growth and relieve symptoms. GM-CSF or placebo (an injection of sterile salt water) will be given to you on Mondays, Wednesdays and Fridays for three weeks. In an earlier study that enrolled 160 patients with PAD, we found GM-CSF given for up to 4 weeks was well tolerated and not associated with serious side effects. There was some improvement in symptoms and exercise capacity of the treated subjects. We are now doing a study to see if two 3-week administrations of GM-CSF at 3 month intervals will further help improve symptoms.

Currently, GM-CSF is approved for use in the following situations: 1) in cancer patients receiving chemotherapy; 2) in normal individuals to stimulate their bone marrow to release stem cells for donation, and 3) in patients who have had bone marrow transplants. It is not approved for use in patients with your condition and is therefore considered experimental.

If you agree to participate in this study, we will follow you for up to 3 years. A member of our staff will contact you by telephone at 1 year, 2 years, and 3 years after enrollment in the study to ask about your overall health.

What will I be asked to do?

We will ask you to fill out questionnaires, do blood tests, walk on the treadmill, and if you meet the selection requirements, have measurements of blood flow in the leg. You will be asked to wear a physical activity monitor similar to a Fitbit to monitor your activity during the length of the study. This technology requires regular access to either a computer with internet access or a smart phone with an active data plan. If you do not have access to either of these, you will be unable to participate in this study. We are seeking to enroll 120 patients. The study will take 9 months to complete. During this period, we request that you not change the medicines you are taking unless there is an emergency.

Schedule of Study Visits

Consent form discussions and questionnaires may be completed via Zoom video conference or phone call within one week of your scheduled study visit.

Visit 1
(Screening)

Test		Time for Test
Discuss & Sign Consent Form		45 minutes
History and Physical		30 minutes
Treadmill Test #1		20 minutes
6-Minute Walk		6 minutes
Blood Work		10 minutes
Questionnaire (San Diego)		20 minutes

Total visit time: 2- 2 1/2 hours

4 weeks of home exercise
Start medication injections for 4 weeks

Visit 2
(Randomization)

Test		Time for Test
Mini Physical Exam		10 minutes
Blood Work		10 minutes
Ankle-brachial index (ABI) before exercise		10 minutes
Treadmill Test (2 times)		20 minutes
6-Minute Walk (2 times)		6 minutes
ABI after exercise		10 minutes
Questionnaires (SF-36 & WIQ)		20 minutes

Total visit time: 2 – 2 1/2 hours

Start medication injections
Visits 3, 4, 5
(Week 1, 2, 3)
These visits may occur at the Emory research site or conducted by phone or Zoom with blood draw at a Quest Laboratory location.

Test		Time for Test
Mini Physical Exam (if needed)		10 minutes
Blood Work		10 minutes
Questionnaire (Side effects)		10 minutes

Total visit time: 1-1 ½ hours

Visit 6
(Month 3)

Test		Time for Test
Mini Physical Exam		10 minutes
Blood Work		10 minutes
Ankle-brachial index (ABI) before exercise		10 minutes
Treadmill Test (2 times)		20 minutes
6-Minute Walk (2 times)		6 minutes
ABI after exercise		10 minutes
Questionnaires (SF-36 & WIQ)		20 minutes

Total visit time: 2-2 ½ hours

Re-start medication injections
Visits 7, 8, 9
(Weeks 13, 14, 15)
These visits may occur at the Emory research site or conducted by phone or Zoom with blood draw at a Quest Laboratory location.

Test		Time for Test
Mini Physical Exam (if needed)		10 minutes
Blood Work		10 minutes
Questionnaire (Side effects)		10 minutes

Total visit time: 1-1 ½ hours

Visit 10
(Month 6)

Test		Time for Test
Mini Physical Exam		10 minutes
Blood Work		10 minutes
Ankle-brachial index (ABI) before exercise		10 minutes
Treadmill Test (2 times)		20 minutes
6-Minute Walk (2 times)		6 minutes
ABI after exercise		10 minutes
Questionnaires (SF-36 & WIQ)		20 minutes

Total visit time: 3 hours

Visit 11
(Month 9)

Test		Time for Test
Mini Physical Exam		10 minutes
Blood Work		10 minutes
Ankle-brachial index (ABI) before exercise		10 minutes
Treadmill Test (2 times)		20 minutes
6-Minute Walk (2 times)		6 minutes
ABI after exercise		10 minutes
Questionnaires (SF-36 & WIQ)		20 minutes

Total visit time: 3 hours

During the study, you will meet several people including physicians, research coordinators, and technicians. They are all familiar with the study and will be able to answer any questions that you might have.

You must not eat or drink caffeine-containing beverages for at least 4 hours before each study visit and you must also follow the instructions you will be given regarding the medications that you are taking. We will do a physical exam initially and will take about 30 minutes. A brief exam lasting 10 minutes will also be done at each of your other visits. Blood tests will be done at each visit. During visits 1, 4, 6, 9 and 10 approximately 3 tablespoons of blood will be taken with a small needle placed into a vein in your arm. At visit 2 approximately 5 tablespoons of blood will be taken. During visits 3, 5, 7, 8, and 11 we will take up to 2 tablespoons of blood. We will measure your blood count and other routine tests as well as research tests that measure progenitor cells, inflammatory markers, growth factors, and markers of immunity. Blood will also be stored for future testing. During the first 4 weeks we encourage you to walk at least three times a day until you get your usual symptoms in your leg(s). The activity will be tracked with standardized mobile pedometer provided by the study coordinator.

Treadmill Test

If you have not been on a treadmill before, the first treadmill test will serve to familiarize you with the test. Following this, you will have another treadmill tests within two weeks before starting the study. If there is a large difference in your performance in the two tests, we will do a third test. If there continues to be a large difference, we will not include you in the study. You should have no food or drink other than water with your regular medications for 4 hours before you come for the treadmill test.

Your ability to exercise can be measured using equipment that records your heart rate, blood pressure, and respiration. Electrocardiogram (ECG) electrodes are attached to your chest (the area may be shaved if necessary), a blood pressure

cuff is placed on your arm, and a pulse oximeter is placed on your finger, ear, or nose. After two or three minutes, the speed and incline on the treadmill is increased. You will be asked to inform us when discomfort first occurs in your leg and also when you want to stop. The ECG recording is performed continuously during the test, and your blood pressure and the amount of oxygen in your blood are monitored. The test will take about thirty minutes.

Before and after each treadmill test, we will measure the pulses in your feet using the Ankle Brachial Index (ABI) test. The ABI is done by taking blood pressure in each arm and in each leg. It is a routine and painless procedure. Each ABI measurement will take about ten minutes.

6-Minute Walk

For the 6-minute walk test, you will be asked to walk up and down a 100-foot hallway for up to 6 minutes to cover the maximum distance possible. The distance that you cover after 6-minutes will be recorded. While you walk, you will be asked to inform us when discomfort first occurs in your leg and you may stop walking at any time. You will also be asked to wear a small device on your finger (pulse-oximeter) to record heart rate, and will be asked to describe your fatigue and shortness of breath based on the 10 point Borg Scale, which will be provided during the test.

Foot Transcutaneous Oxygen Tension Measurements

At the beginning and again at the end of the study, before, during and after exercise, we will measure the oxygen content in the tissues of your foot with an oxygen monitor. The measurement requires that a warm electrode be placed on the top of your foot. This electrode is connected to a machine that tells us the oxygen level in the tissues of your foot. This test will be done at the same time as the treadmill test and last for the amount of time that you are able to exercise. This is an optional test that may be offered to subjects depending on the availability of the device.

Questionnaires

At the beginning of the study and at visit 2, and at 3, 6, and 9 months you will be asked to fill out two questionnaires regarding your health. These will take 15 to 30 minutes to complete. We will also ask you to complete a questionnaire regarding any side effect you may be experiencing from the treatment you are receiving. This will take 5 to 10 minutes to complete. We may ask you to complete these questionnaires via Zoom teleconference or phone call within one week of your scheduled study visit.

Study Drugs

GM-CSF injections, as stated above, will be used in this study. We will study whether this drug will stimulate your bone marrow to produce more stem/progenitor cells and send them into your bloodstream that will help grow new blood vessels in your leg(s) and relieve your symptoms. The dose of this medication will be 500 micrograms per injection. We will randomly assign you to treatment with GM-CSF or placebo injections (salt water) rather than make a conscious decision about which treatment to give you. You have a 2 in 3 chance of receiving GM-CSF. It is kind of like “drawing straws”. This will help assure that both known and unknown factors that may affect the results of the study are evenly distributed within each group. You will not be told which group you are in or if you are receiving GM-CSF or placebo.

The drug or placebo will be given by injection under the skin with a small needle in your upper arm, thigh or belly. You will be given the drug by us on the first time. You will be taught to give the drug at home for the remaining 3 weeks of treatment. You will be using these injections for 4 weeks at the beginning of the study, for 3 weeks after Visit 2 and for another 3 weeks after Visit 6.

Physical Activity Monitor

You will be given a wearable physical activity monitor (similar to a Fitbit) with instructions on how to use the device and upload data. The device will be worn on your wrist and it will record your levels of physical activity during the day and will record the number of hours you sleep each night. You will be asked to use this device for the length of the study.

The study team will have access to the data collected using this device. This technology requires regular access to either a computer with internet access or a smart phone with an active data plan.

We request that you walk every day at least three times so that you develop symptoms of pain or tightness in your legs during the first 3 weeks of the study while you receive treatment.

Follow up
We would like your permission to contact you regarding your condition in the future. We would like to contact all participants who sign a consent form, even if you do not qualify for participation in the study due to the selection requirements. This follow-up will likely consist of a questionnaire administered over the phone by a research staff member, or will be mailed to you with a stamped return envelope. We might also contact you for participation in future research studies. If you would not like to be contacted in the future for follow-up questioning or future research, please inform the research staff.

Optional MRI
Some participants may be asked to have magnetic resonance imaging (MRI) at the baseline and 1 month visits. MRI is a way of taking pictures of the body and internal organs by using radio-frequency waves and a very large magnet.

This imaging is optional and you do not have to have these tests to participate in this study. You will be asked to sign a separate consent form if you are asked to have the optional MRI.

Optional Ultrasound
Some participants may be asked to have ultrasound of arterial blood vessels in both legs during each study visit. Ultrasound is a safe, non-invasive way of taking pictures of the body and internal organs by using high frequency sound waves.

This imaging is optional and you do not have to have these tests to participate in this study.

How will my medicine be provided?
The medicine that you will take will be dispensed by the pharmacy and delivered to the principal investigator or study team member. The principal investigator or health care providers on his/her research team will provide the medicine to you. If you have questions about the medicine, you should ask the principal investigator or study nurse. You may also call the pharmacy if you have questions about the medicine. The number for the pharmacy is included on your medicine package.

Who owns my study information and samples?
If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study.

What are the possible risks and discomforts?
There may be side effects from the study drug or procedures that are not known at this time.
The most common risks and discomforts expected in this study are listed below.

Drug: GM-CSF (Sargramostim)
When given for two weeks, GM-CSF has been shown to be safe in patients being treated for a variety of cancers, receiving bone marrow transplants, for low blood counts, and in healthy people donating their blood for bone marrow transplant. It also appears to have been well tolerated in a small number of patients with blocked heart arteries.

The following side effects are common (occurring in greater than 30%) for patients taking GM-CSF: fever; chills; nausea; vomiting; diarrhea; fatigue; weakness; headache; decreased appetite; feeling of faintness; facial flushing; pain in the bones, muscles, chest, abdomen, or joints; local reaction at the site of injection and rashes. There have also been reports of low blood pressure, a low level of oxygen in the blood, transient loss of consciousness, and difficulty in breathing after the first injection of GM-CSF. These signs may or may not recur with additional injections of GM-CSF.

The following side effects are less common (occurring in about 10-29%) for patients receiving GM-CSF: kidney and liver dysfunction. Patients with prior heart, lung, kidney, or liver problems may have worsening of their symptoms following administration of GM-SCF. Increases in certain white blood cells (eosinophilia) or other blood component abnormalities may occur.

Rare side effects (occurring in less than 1%) for patients taking GM-CSF include fluid accumulation or worsening of pre-existing fluid accumulation in the extremities, in the lungs, and around the heart which may result in breathing problems or heart failure. Rarely, patients have developed acute allergic reactions. There may be other side effects that could occur.

Pregnant or nursing women and women of childbearing potential and fertile men not using an effective method of birth control are not permitted to participate in this study because the effects of the study drug on fertility or the risks of the study drug to an unborn or newborn child are unknown. If you are a woman who could become pregnant, you will agree to notify your physician immediately if you suspect or know you are pregnant while on the study. If you are still receiving study drug, you will be withdrawn from the study.

Additionally, due to the investigational nature of this study, there may be risks associated with the study drug that are currently unknown.

Blood tests or administration of drug by injection under the skin may cause local pain, bleeding, bruising, and rarely, infection.

Exercise
The study is designed to minimize the risks to you. Patients who are exercised on a treadmill can get a musculoskeletal injury (like a sprained ankle) and rarely, can have a cardiovascular complication. The initial screening is done to make sure this risk is as small as possible. There is a 1 in 10,000 risk of heart attack, blackout, or death. The exercise tests will always be supervised by a physician.

Blood Tests
There may be slight discomfort from the needle as it enters the skin and a small bruise may occur. This will resolve in a few days. There are no long-term side effects. If during the routine tests we discover any abnormalities, we will inform you and your physician. The research tests are not hazardous and at present do not alter the way you are treated by your physicians.

Physical Activity Monitor
This device does not pose any medical risk and does not diagnose any medical conditions or illnesses. Wearing the activity monitor may cause minimal discomfort.

As with any test or procedure, there may be risks or side effects that occur that are unexpected.

If you are a woman: to protect against possible side effects of the study drug, women who are pregnant or nursing a child may not take part in this study. If you become pregnant, there may be risks to you, the embryo, or fetus. These risks are not yet known. If you are a woman of childbearing ability, you and the study doctor must agree on a method of birth control or abstinence to use throughout the study. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

If you are a man: the effect of the study drug on sperm is not known. To protect against possible side effects, if you are a man you should not get a sexual partner pregnant while taking the study drug. You and the study doctor should agree on a method of birth control to use throughout the study.

If you will be taking the study drug home, keep it out of the reach of children or anyone else who may not be able to read or understand the label. Do not let anyone else take the study drug besides you.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Will I benefit directly from the study?

This study is not designed to benefit you directly. Your PAD may improve while you are in this study but it may not, and it may even get worse. This study is designed to learn more about whether or not GM-CSF improves symptoms and blood vessel function in people with PAD. The study results may be used to help others in the future.

Will I be compensated for my time and effort?

You will get $25 for completing study visits 1-10 and any unscheduled visits and $50 for the final study visit, to compensate you for your time and effort. If you do not finish the study, we will compensate you only for the visits you have completed. You will get $300 total, if you complete all study visits. You may be asked to fill out a tax form, including your Social Security or Taxpayer Identification Number, in order to be reimbursed, depending on the amount and method of payment. Some payment methods involve mail coming to your house, which may be seen by others in your household. You can decline payment if you are concerned about confidentiality, or you can talk to the study team to see if there are other payment options.

What are my other options?

If you decide not to enter this study, there is care available to you outside of this research study.
Patients with PAD can be treated with medication, lifestyle changes, angioplasty and surgery. The study doctor will discuss these with you. You do not have to be in this study to be treated for PAD.

Taking part in this study, however, may make you unable to participate in some other research studies, if they exclude people who have taken certain treatments. You should discuss this with the researchers if you have concerns. You may wish to research other study options at websites like clinicaltrials.gov and ResearchMatch.org.

How will you protect my private information that you collect in this study?

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Certificate of Confidentiality

There is a Certificate of Confidentiality from the National Institutes of Health for this Study. The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know that you are in this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases,
- Giving law officials information about abuse of a child, elderly person or disabled person.
- Giving out information to prevent harm to you or others.

Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Storing and Sharing your Information

De-identified data from this study (data that has been stripped of all information that can identify you), including your de-identified genetic information, may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Your data and specimens from this study may be useful for other research being done by investigators at Emory or elsewhere. To help further science, we may provide your de-identified data and/or specimens to other researchers. If we do, we will not include any information that could identify you. If your data or specimens are labeled with your study ID, we will not allow the other investigators to link that ID to your identifiable information.

We will use your sample and data only for research. We will not sell them. However, the results of this research might someday lead to the development of products (such as a commercial cell line, a medical or genetic test, a drug, or other commercial product) that could be sold by a company. You will not receive money from the sale of any such product.

In general, we will not give you any individual results from the study of the samples you give us. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

How is my Genetic Information Protected? What are the Risks?

The Genetic Information Nondiscrimination Act (GINA) is a federal law that generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that GINA does **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, and does not apply to employers with less than 15 employees.

In addition to GINA, the State of Georgia has laws that prohibit insurers from using genetic testing information for any non-treatment purpose. However, like GINA, this state law protection has exclusions: life insurance policies, disability income policies, accidental death or dismemberment policies, Medicare supplement policies, long-term care insurance policies, credit insurance policies, specified disease policies, hospital indemnity policies, blanket accident and sickness policies, franchise policies issued on an insurance policy written as a part of workers' compensation equivalent coverage, or other similar limited accident and sickness policies.

Privilege
In the State of Georgia, in some circumstances your genetic information has may have special legal protections called "privilege." This means that the information cannot be used as evidence in a court. By allowing us to use and disclose your genetic information for this research study along with other information about you that genetic information used in the research may no longer have that legal protection. Other protections described in this form will still apply. There are also other confidentiality protections for research data in general under Georgia state law.

Medical Record
If you have been an Emory, Saint Joseph's and Grady Health System patient before, then you already have an Emory, Saint Joseph's, and Grady Health System medical record. If you have never been an Emory, Saint Joseph's and Grady Health System patient, you do not have one. An Emory, Saint Joseph's and Grady Health System medical record will be made for you if an Emory and Grady Health System provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory, Saint Joseph's and Grady Health System medical record you have now or any time during the study.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record. For this study, those items include: blood tests, blood flow measurements, MRI.

Tests and procedures done at non-Emory, Saint Joseph's and Grady Health System places may not become part of your Emory, Saint Joseph's and Grady Health System medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury
If you believe you have become ill or injured from this research, you should contact Dr. Quyyumi at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

If you get ill or injured from being in the study, Emory, Saint Joseph's and Grady Health System will help you to get medical treatment. Neither Emory, Grady Health System nor the sponsor will pay for your medical treatment. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurance does not pay, then you will have to pay these costs.

Emory, Saint Joseph's, Grady Health System and the sponsor have not, however, set aside any money to pay you if you are injured as a result of being in this study or to pay for this medical treatment. For Emory, Saint Joseph's and Grady

Health System, the only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory and Grady Health System employee. "Negligence" is the failure to follow a standard duty of care. You do not give up any legal rights you may have by being in this study, including any right to bring a claim for negligence.

Costs
There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities. If the study procedures result in any medical complications that would not fall under "injury" as discussed above, the cost of treatment for those complications may be charged to you or your insurance.

Withdrawal from the Study
You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done, specifically:

- Blood Tests
- Physical Exam

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

These are the expected reasons why the researchers may stop your participation:

- Severe reaction to study drug
- Worsening of existing health condition
- Pregnancy

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the main study and for any optional studies in which you may choose to participate.

Main Study

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places

that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information. We will use and disclose your PHI for the administration and payment of any costs relating to subject injury from the study.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory, Saint Joseph's and Grady Health System may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- National Institutes of Health, National Heart, Lung and Blood Institute (NHLBI) is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The research team and the Sponsor may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory, Saint Joseph's and Grady Health System offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Grady Research Oversight Committee, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Other researchers and centers that are a part of this study.
    - Government agencies that regulate the research including: Office for Human Research Protections; Food and Drug Administration.
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization

Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at: Dr. Arshed Quyyumi [redacted]

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the main study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. The Sponsor, and people and companies working with the Sponsor on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information
Contact Afif Martini at [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory University Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

If you are a patient receiving care from the Grady Health System and have a question about your rights, you may contact the Office of Research Administration at research@gmh.edu.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in this research study, and any optional studies you initialed above. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____

Name of Subject

_____ _____

Signature of Subject (18 or older and able to consent) **Date** **Time**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____ _____

Name of Person Conducting Informed Consent Discussion **Date/Time when IC discussion took place**

_____ _____

Signature of Person Conducting Informed Consent Discussion **Date/Time when IC was signed**

Emory University
Addendum to Consent to be a Research Subject / HIPAA Authorization

Title: **Granulocyte-Macrophage Stimulating Factor (GM-CSF) for Mobilization of Progenitor Cells in Peripheral Arterial Disease: A Phase II Randomized Study (GPAD-3)**

Principal Investigator: Arshed A. Quyyumi, MD

Sponsor: National Institutes of Health, National Heart, Lung, and Blood Institute (NHLBI)

Investigator-Sponsor: Arshed A. Quyyumi, MD

This consent addendum provides information about appointment and dosing reminders which you can receive while participating in this study.

APPOINTMENT AND DOSING REMINDERS
To help you remember study appointments and your dosing schedule, a reminder system will be made available to you. This will allow you to receive a welcome message, dosing reminder, educational/motivational, appreciation, and appointment messages on your mobile phone, your email or by telephone. All reminders/messages are optional.

You may indicate below that you would like to receive these reminders/messages by completing this consent form and providing your contact information below. If you indicate that you would not like to receive reminders/messages at this time, you will be given directions on how to receive these reminders/messages and you can register on-line or by phone.

How are you protecting the privacy of my information?
The reminder/message system will only contain your Subject ID and preferred method of contact (mobile, email or telephone). No other personal information will be included. This information will not be released to anyone other than the company operating the service. This company will not release this information to anyone else and they will not contact you other than to send you the reminders/messages.

Please provide your preferred contact information and initial your choice below. If you have any questions, please don't hesitate to ask your study coordinator. If you choose to receive your reminders/messages via text messaging, standard text message rates may apply. **If you participate in the reminders/messaging program you may be responsible for text messaging charges depending on your mobile network provider.**

Mobile Phone number (including area code): _____

Or Email Address: _____

Or Telephone Number (including area code): _____

If at any time the contact information provided above changes, you are responsible for notifying the study coordinator of the change to avoid a disruption in receiving reminders/messages.

Request to Receive Reminders (Please initial one option)

_____ I would like to receive dosing reminders only.

_____ I would like to receive, dosing reminder, educational/motivational, appreciation, and appointment messages.

_____ I would NOT like to receive dosing reminder, educational/motivational, appreciation, and appointment messages.

You can change your mind about receiving the reminders/messages. If you agree to receive the messages initially you can opt-out at any time. If you have chosen to not receive the reminder messages you will be able to start receiving them if you decide to. Please discuss any changes with the study site.

SIGNATURES:
I have read and understand the information in this addendum to the informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I have been given enough time to decide whether or not I want to participate in the reminder/messaging program. I do not give up any of my legal rights by signing this consent document.

I have been told that I will receive a signed and dated copy of this document.

_____
Printed name of study participant

_____ _____
Signature of study participant Date of signature

Emory University
Consent to Optional Storage of Data/Specimens for Future Research

Title: **Optional Storage of Data/Specimens for Future Research**

Principal Investigator: Arshed A. Quyyumi, MD

Storing and Sharing your Information
Your de-identified samples, genomic data and health information will be stored and shared with other researchers for future research. The samples and information will be available for any future research question, such as research to understand what causes certain diseases (for example heart disease, cancer, or psychiatric disorders), development of new scientific methods, or the study of where different groups of people may have come from.

Your individual genomic data and health information will be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database will agree not to attempt to identify you.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the main study and for any optional studies in which you may choose to participate.

PHI That Will be Used/Disclosed for Optional Study:
The PHI that we will use and/or disclose (share) for the optional storage and future research use of your PHI includes: samples, genomic data, and health information.

Purposes for which your PHI will be Used/Disclosed for Optional Study:
We will use and disclose your PHI for the conduct and oversight of the optional storage and future research use of your PHI.

Authorization for This Use of PHI is Required to Participate in Optional Study, but Not in Main Study:
You do not have to authorize the use and disclosure of your PHI. If you do not authorize the use and disclosure of your PHI for the optional study, then you may not participate in the optional research study. You can still be in the main research study even if you don't participate in the optional study.

People Who Will Use/Disclose Your PHI for Optional Study:
The following people and groups will use and disclose your PHI in connection with the storage and future research of your PHI. The same people and groups who will use and disclose your PHI for the Main Study will also do so in connection with the optional research study/storage of PHI for future research. In addition, the following people and groups may also use and disclose your PHI for the Optional Study:

- Future researchers

Expiration of Your Authorization
If you agree to the optional storage of data and specimens for future research, your PHI will be used indefinitely.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Dr. Arshed Quyyumi
[redacted]

Consent and HIPAA Authorization for Optional Storage of Data/Specimens for Future Research:
Please initial below if you opt to participate in and authorize use and disclosure of your PHI in the optional storage of data and specimens for future research previously described:

Optional Storage of Data/Specimens for Future Research _____Initials

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____
Signature of Subject (18 or older and able to consent) **Date** **Time**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____ _____
Name of Person Conducting Informed Consent Discussion **Date/Time when IC discussion took place**

_____ _____
Signature of Person Conducting Informed Consent Discussion **Date/Time when IC was signed**