Cover Page

Consent Form

Acute Microvascular Changes with LDL Apheresis

NCT02388633

Date June 5, 2019

CO1450

OREGON HEALTH&SCIENCE UNIVERSITY

IRB#: 11381

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

Clinical Research Consent Summary

TITLE: Assessment of Changes in Tissue Perfusion after Plasma LDL Apheresis

PRINCIPAL INVESTIGATOR:	Jonathan Lindner, MD	503-494-8750
	Melinda Wu, MD	503-494-4772
	Brian Davidson, MD	503-494-4772
	Todd Belcik, BS, RCS, RDCS	503-494-4772
	Sergio Fazio, MD, PhD	503-494-8750
	P. Barton Duell, MD	503-494-3273

1. You are being asked to join a research study. You do not have to join the study. Even if you decide to join now, you can change your mind later.The purpose of this study is to learn more about elevated cholesterol levels (severe hypercholesterolemia)
2. In this study, we will use an imaging procedure called contrast-enhanced ultrasound (CEU) using a contrast agent called Definity (perflutren lipid microsphere). Contrast enhanced ultrasound will be called “CEU” throughout this form. We want to learn:
    a. If this technique provides a valuable way to assess blood flow differences when cholesterol levels are severely elevated, compared to when they are at normal levels after plasma LDL apheresis.
    b. Whether we can detect blood markers in the blood that can affect blood flow.
3. We are studying whether or not differences in blood flow can be detected before and after plasma LDL apheresis by CEU.
4. The study procedure and contrast agent have been approved by the Food and Drug Administration (FDA) to visualize the heart chambers more clearly during ultrasound imaging, but not blood flow in the heart or skeletal muscles.
5. The study procedure will be performed once before plasma LDL apheresis and once immediately after (total of 2 visits to the clinic) plasma LDL apheresis. Definity, the contrast agent, is given through an intravenous line (IV).
6. If you join the study, you will have the procedure performed 2 times during the same plasma apheresis session.

7. If necessary, we may request blood to be drawn before and after another apheresis session separate from the session that imaging will be taking place.
8. There are risks involved in participating in the study.

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Clinical Research Consent and Authorization Form

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PRINCIPAL INVESTIGATOR:	Jonathan Lindner, MD	503-494-8750
CO-INVESTIGATORS:	Melinda Wu, MD	503-494-4772
	Brian Davidson, MD	503-494-4772
	Todd Belcik, BS, RCS, RDCS	503-494-4772
	Sergio Fazio, MD, PhD	503-494-8750
	P. Barton Duell, MD	503 494-8750

PURPOSE:

You have been invited to be in this research study because you have very high levels of cholesterol (severe hypercholesterolemia). Your physician has scheduled you to have a procedure called apheresis to remove the extra cholesterol in your blood.

The purpose of this study is to learn if imaging blood flow in your heart muscle and in the muscle of your arms (perfusion imaging) can provide valuable information as to whether or not extremely high levels of cholesterol cause blood flow changes. In this study, we will use an imaging procedure called contrast-enhanced ultrasound (CEU) using a contrast agent called Definity (perflutren lipid microsphere).

The study procedure may provide a more detailed evaluation of the effects of high cholesterol levels in the blood and can potentially lead to better assessment of the benefits of anti-cholesterol therapies in the future.

Right now, this study procedure is not approved for the evaluation of blood flow in patients with high cholesterol in the United States because we do not know enough about it.

This study requires 1 visit to the clinic and will take less than 1 day to complete for most subjects. For some subjects, we may request that blood be taken on another apheresis session without the CEU imaging technique.

CO1450 We will enroll up to 12 subjects with severe hypercholesterolemia and the study will be conducted at OHSU only.

PROCEDURES:

- Women who can become pregnant will have a urine sample collected for a pregnancy test before this study, and will be excluded if pregnant.
- We will ask you about your medical history and the medications you take regularly.

- A physical examination involving blood pressure measurement, looking into your eyes, listening to your chest, evaluating your nerve function and evaluating muscle strength will be performed.
- An ultrasound scan of your heart will be performed. This procedure involves placing an ultrasound probe on the outside of your chest. This procedure is painless. We will first examine the size and function of your heart. If there is evidence of significant unrecognized heart disease on the ultrasound, then we will contact your physician if you give us permission to do so.
- You will have an intravenous (IV) line inserted into a small vein in your hand or arm.
- A blood sample (about 1 tablespoon) will be taken from you to determine your cholesterol levels and specific blood markers of inflammation.
- Ultrasound imaging of your arm blood vessels will be performed before and after inflation of a blood pressure cuff on your arm for 3 minutes to examine your vessel's ability to widen and narrow.
- Ultrasound imaging of your heart muscle will then be performed during the administration of Definity, which is an ultrasound contrast agent that will be given through the IV. This agent is composed of tiny microbubbles smaller than the size of a red blood cell. These bubbles stay inside the blood vessels and go where the red blood cells go. This contrast agent allows us to evaluate blood flow. Definity has been approved for use in humans during ultrasound of the heart cavity and has been shown to be safe for that use. It has not been approved for obtaining images of flow in the heart muscle or muscles such as those in the arm. The dose of Definity has been approved for use in humans by the Food and Drug Administration.
- After this, we will perform ultrasound imaging of one of your forearm muscles during the infusion. Then we will have you perform 3 minutes of hand-grip exercises by squeezing a stress-ball. This exercise portion of the procedure will not be performed if you are unable to exercise using this method.
- During the imaging studies, we will measure your blood oxygen levels by putting a small device on the finger or ear. Blood pressure measurements will be recorded by placing a cuff on your upper arm. We will also your monitor heart rate during the whole study by an electrocardiogram (ECG) by placing several small patches (electrodes) on your chest.
- You will be asked how you are feeling during and after the administration of the Definity microbubbles.
- You will have apheresis catheter or other catheter placed as per your regular planned apheresis procedure to treat your hypertriglyceridemia. You will then undergo your scheduled apheresis procedure.
- After your apheresis procedure, we will perform a second study similar to the first (Definity microbubble imaging of the heart muscle, and the forearm muscle before and during exercise). This second study will allow us to determine if there are changes in your blood flow and if they are related to levels of triglycerides in the blood.
- After imaging is completed, we will continue to monitor your heart rate, blood pressure, oxygen levels, and ECG every few minutes for 15 minutes, or longer if you are having any discomfort. We will also remove the small IV in your arm/hand.
- At a future time point, we may take additional blood (about 1 tablespoon) before and after a scheduled apheresis session

We expect this testing will take a total of 2-3 hours total.

Initial Study (all participants)		
	Before Apheresis	After Apheresis
Consent Discussion, Screening tests and medical history	X	
Blood draw (about 1 tablespoon)	X	X
Ultrasound imaging procedures	X	X
Total time	2 hours	1 hour

Subsequent Study for Blood Draw (select participants)		
	Before Apheresis	After Apheresis
Consent Discussion	X	
Blood draw (about 1 tablespoon)	X	X
Total time	15 min	15 min

Each blood draw will be no more than 20 milliliters (about 1 tablespoon).

If you have any questions, concerns, or complaints regarding this study now or in the future, contact Jonathan Lindner, MD (503) 494-8750.

The results of these studies will not be made available to you because the research is still in an early phase and the reliability of the results is unknown.

If we discover new information that is important for your health care, either in this study or the future, you will be asked whether you wish to receive the results. You may be required to have the test repeated in a clinical laboratory. You would be responsible for all costs associated with having the test repeated and visiting a doctor discuss the results.

RISKS AND DISCOMFORTS:

- A potential side effect of Definity is temporary back pain. If this happens then let us know and the procedure will be stopped. The back pain will go away in a few minutes. An allergic reaction to ultrasound contrast agents is unlikely (1 in 10,000 for all agents, less than this for Definity), but possible. Symptoms of an allergic reaction include: rash, itching, swelling, severe dizziness and trouble breathing. If this occurs, then the procedure will be stopped. You may not have symptoms for some of these side effects, but you will be monitored by the investigator to check for any changes throughout the study.
- We will draw blood from the blood vessels in your arm. You may feel some pain when your blood is drawn. There is a small chance the needle will cause bleeding, a bruise, an infection, or fainting.

BENEFITS:
You will not personally benefit from being in this study. However, by serving as a subject, you may help us learn how to benefit patients in the future.

ALTERNATIVES:
You may choose not to be in this study. The care you receive at OHSU will not be affected in any way by your decision.

CONFIDENTIALITY
We will take steps to keep your personal information confidential, but we cannot guarantee total privacy. All data/medical records will be coded with a unique identifier.

We will create and collect health information about you as described in the Purpose and Procedures sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The Office for Human Research Protections, a federal agency that oversees research involving humans
- The Food and Drug Administration

Those listed above may also be permitted to review and copy your records, including your medical records.

We may also share your information with other researchers, who may use it for future research studies.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

Data from this study may be shared with other investigators for future research studies. All identifying information about you will be removed from the samples before they are released to any other investigators.

We may continue to use and disclose your information as described above indefinitely.

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

COMMERCIAL DEVELOPMENT:
Samples and information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

COSTS:
There will be no cost to you or your insurance company to participate in this study.

LIABILITY: If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact Jonathan Lindner, MD (503) 494-8750.

If you are injured or harmed by the study procedures or Definity, you will be treated. OHSU does not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.

If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

PARTICIPATION:
This research is being overseen by an Institutional Review Board ("IRB"). You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by 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 more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study. Some parts of the study are optional. You can choose not to participate in some or all of the optional parts but still participate in the rest of the study.

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. You can choose to withdraw from some or all of the optional parts of this study without withdrawing from the whole study. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study or change which parts of the study you are participating in.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Jonathan Lindner, MD
Cardiology UHN-62
3181 SW Sam Jackson Park Rd
Portland, OR 97239
(503) 494-8750

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

The samples and information we will collect from you will not be stored with your name or any other identifier. Therefore, there will not be a way for us to identify and destroy your materials if you decide in the future that you do not wish to participate in this research.

You may be removed from the study if the investigator stops the study or you develop serious side effects.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

Your health care provider may be one of the investigators of this research study and, as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

Subject Printed Name	Subject Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Complete if the participant is not fluent in English and an interpreter was used to obtain consent. Participants who do not read or understand English must not sign this full consent form, but instead sign the short form translated into their native language. This form should be signed by the investigator and interpreter only.

Print name of interpreter: _____

Signature of interpreter: _____ Date: _____

An oral translation of this document was administered to the subject in _____ (state language) by an individual proficient in English and _____ (state language).

See the attached short form for documentation.