UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title: Extracellular Microvessicles (EVs) as biomarkers of atherosclerotic disease In HIV Patients

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Why am I being asked to volunteer?

You are being invited to participate in a research study. This study involves 3 blood draws at 3 time points for Cohort 1 (naïve to HIV treatments) or a 1 time blood draw for Cohort 2 (currently taking HIV treatment). Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled.

Before you decide to participate in this research study, we ask that you read this form carefully in its entirety and that you ask as many questions as you need to fully understand the study. This form explains the procedures, potential risks and discomforts for the study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

The purpose of this study is to collect blood to measure part of cell membranes called extracellular vesicles (EVs) and immunological biomarkers in HIV positive persons just starting antiretroviral treatment or on stable therapy. EVs play a role in the inflammatory response and atherosclerosis (build up of a waxy plaque on the inside of blood vessels).

Several studies have reported a higher incidence of cardiovascular disease (CVD) events among HIV-infected patients with well-controlled viral replication than HIV-negative controls. CVD now accounts for 8% to 22% of deaths among HIV-infected patients and this percentage appears to be increasing. CVD in HIV is incompletely understood but is not completely explained by traditional risk factors (smoking, low HDL, hyperlipidemia, chronic kidney disease and hypertension). The direct effects of chronic HIV infection and effects of antiretroviral therapy may contribute as well. Dr. Mohler's laboratory has developed specialized blood tests to measure EV biomarkers to explore the association of CVD with HIV, antiretroviral therapy and traditional risk factors.

How long will I be in the study? How many other people will be in the study?

If you are in Cohort 1 you will come in for 3 visits and be on the study for about 6 months. Cohort 2 participants will have one visit only. 40 people will take part in this study. The University of Pennsylvania is the only study center.

What am I being asked to do?

This study involves collection of medical and medication history and blood for specialized immunology testing. If you agree to participate in this study, you will come to the MacGregor Clinic in the Perelman Center for Advanced Medicine for your study visits. The two tables below summarize the study visits for Cohorts 1 and 2. You will be required to come to the visits fasting, that is nothing to eat but water and required prescription medications, for 8 hours prior to your study visit.

Cohort 1: Longitudinal study in patients starting antiretroviral therapy.

	Screening/enrollment day 0	**Week 12**	**Week 24**
Informed Consent	X		
History, PE	X		
Documentation of HIV status	X		
HIV-1 RNA /CD4	X	X	X
Blood counts, chemistry and fasting lipid	X	X	X
EV measurements	X	X	X
Inflammatory markers	X	X	X
Stored specimens	X	X	X
Blood volume	45 ml	45ml	45 ml

Cohort 2: Cross sectional study in patient well controlled on ART

	Screening/enrollment day 0
Informed Consent	X
History, PE	X
Documentation of HIV status	X
HIV-1 RNA /CD4	X
Blood counts, chemistry and fasting lipid	X
EV measurements	X
Inflammatory markers	X
Stored specimens	X
Blood volume	45 mls

Results of Blood Tests

Results of HIV viral load, CD4, blood counts, chemistry and fasting lipids will be provided to your health care provider and you. Results from research tests, such as EV measurements, will not be released as these tests have not been validated for use in clinical care.

Use of Your Samples Required for this Study
Some of your blood samples will be stored and used for testing that is required for this study. No one will know just from looking at the labels of your stored samples that they came from you.

Use of Your Stored Samples
If you agree, some of your blood that is left over after all required study testing is done may be stored for future research that is not yet planned for about 2 years. These samples will be stored in locked freezers at PENN in the Infectious Disease Division and only study staff will have access to them. Stored samples are labeled with a code number and not information that can identify you. Any future research done on the samples will be approved by Penn's IRB.

What are the possible risks or discomforts?

Blood Draw:
The risks of having blood taken are discomfort, bleeding, fainting, small blood clot or swelling to the vein and area surrounding where the blood is drawn, bruising where the needle enters the skin and infection. There is also a very small chance of infection at the needle puncture site.

Risk of loss of confidentiality:
Although the risk is very low, it is possible that your personal information could be given to someone who should not have it. If that happened, you could face discrimination, stress, and embarrassment. We will take several steps to protect your personal information. All study information will be kept in locked files cabinets and data will be keyed into a computer that needs a certain code to be opened, and only the study team will know that code. Computers will be kept behind locked doors in an area only accessed by study staff.

What if new information becomes available about the study?
During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?
You are not expected to get any benefit from being in this research study. However, your participation may contribute to a better understanding of vascular health in HIV+ patients. Ultimately, the knowledge gained through this study may be useful to you and to other persons infected with HIV.

What other choices do I have if I do not participate?
If you decide not to participate in the research study, you will undergo the standard of care.

Will I be paid for being in this study?
You will be compensated $50 for each visit attended. Cohort 1 participants will be compensated $150 if all three visits are completed and Cohort 2 participants will be compensated $50 for the one time visit. Compensation will be given as cash or ClinCard (a debit card). The maximum amount of compensation for the study is $150. There is no other form of compensation available such as reimbursements for parking, tokens or child care.

In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

Will I have to pay for anything?
There will be no cost to you for participating in this study. All clinical and professional services, diagnosis and laboratory works that are part of this research will be provided at no cost to you.

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay.

Will the researchers running this study benefit financially?
This research study is designed to test the vascular health profile developed by CytoVas, LLC. The person leading this medical research study, Dr. Mohler, is an employee of the University of Pennsylvania who own equity in CytoVas LLC. and is an inventor on intellectual property licensed to CytoVas, LLC. Thus, he might benefit financially from the results of this research study. If you would like more information please ask the study coordinator.

What happens if I am injured from being in the study?
We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

When is the Study over? Can I leave the Study before it ends?
This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The study Principal Investigator has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

Electronic Medical Records and Research Results

Who can see or use my information? How will my personal information be protected?
Results of laboratory tests and clinical procedures will be placed in your medical record and may be accessible to employees of the health system that are not part of the research team. This information may also be viewed by your insurance company during routine audits. We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy.

Your personal information may be given out if required by law. As part of this study, your HIV status may be confirmed and a positive test for HIV will be generated and by law we have to report the infection to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born. This is to keep track of how many people in the U.S. have HIV infection. It is also to make sure that states get enough money from the federal government to support the medical care of people living with HIV. The Health Department does not share the names of HIV infected people with anyone else. It removes all personal identifiers, such as your name, before giving information on the number of HIV infections to the federal government.

If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. The IRB at the University of Pennsylvania will have access to the research record. All subjects will be de-identified and assigned a numerical code to track their data.

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

What information about me may be collected, used or shared with others?

- Name, address, telephone number, email address, medical record number, date of birth
- Personal medical history
- Results from any examinations, tests or procedures

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- see if the research was done right
- to evaluate and manage research functions

Who may use and share information about me?

The following individuals may use or share your information for this research study:

- The investigator for the study and the study team
- Other authorized personnel at Penn, including offices that support research operations.

Who, outside of the School of Medicine, might receive my information?

Oversight organizations

- The Office of Human Research Protections

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?
Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?
If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study.

Name of Participant (Please Print)	Signature of Participant	Date

Name of Person Obtaining Consent (Please Print)	Signature	Date

IRB Approval From: 05/02/2016to: 05/01/2017