UPMC HEALTH SYSTEM

University of Pittsburgh HIV/AIDS Program

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CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE: A Phase I/II Pilot Study of Dipyridamole as a Modulator of Immune Activation and Systemic Inflammation in HIV-1-Infected Subjects on Antiretroviral Therapy – DAIDS-ES ID 11987, Final Version 2.0 [05 Feb 2015]

Short Title: Dipyridamole for Immune Activation in HIV

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QUESTIONS ABOUT THE STUDY: If you have any questions about your rights as a research participant or wish to talk to someone other than the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668. If you have any questions about the study, concerns or complaints, you can contact the co-principal investigators, Dr. Bernard Macatangay or Dr. Sharon Riddler, or a co-investigator at the number above or call the UPMC Presbyterian operator at (412) 647-2345 and ask to page Dr. Macatangay, Riddler, or McMahon.

INTRODUCTION: You are being asked to participate in the research study named above because you are infected with the human immunodeficiency virus (HIV), the virus that causes acquired immunodeficiency syndrome (AIDS), and are currently taking anti-HIV medications.

Is my participation in this research study voluntary?
Before you decide whether to join the study, we would like to explain the purpose of the study, the risks and benefits to you, and what is expected of you. This consent form gives information about the study that will be discussed with you. Once you understand the study, and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep. Before you learn about the study, it is important that you know the following:

- Your participation is voluntary. You do not have to take part in any of the tests or procedures in the study.
- You may decide not to take part in the study, or you may decide to leave the study at any time without losing your regular medical care. Whether or not you provide your consent to participate in this study will have no effect on your current or future relationship with the University of Pittsburgh, on your current or future medical care at a UPMC hospital or affiliated health care provider, on your current or future relationship with a health care insurance provider, or on your participation in other studies conducted by the NIH.

Your physician may also be involved as an investigator in this research study. Before agreeing to participate, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your physician.

Why is this study being done?
Since HIV-infected individuals started taking anti-HIV medications, illnesses from AIDS have decreased, but other serious diseases have increased. Researchers think this may be caused by an increase in activity of the immune system that fights infection, leading to inflammation. Inflammation is a normal body reaction to any infection. However, if inflammation lasts a long time, like in HIV infection, it may lead to complications such as heart disease, cancer, liver disease, and problems with thinking. Many HIV researchers are studying the harmful effects of this prolonged immune system activity and inflammation and possible ways to prevent these complications.

A drug called dipyridamole is approved by the Food and Drug Administration (FDA) under the trade name Persantine® for use with other drugs to reduce the risk of blood clots after heart valve replacement. Laboratory studies have shown that dipyridamole also lowers the level of immune system activity and inflammation measured in the blood.

The main purpose of this research study is to see how dipyridamole affects blood tests to measure immune system activity and inflammation and to look at the safety and tolerability of dipyridamole in people infected with HIV. This use of dipyridamole is investigational, or not approved by the FDA; however, the dose to be used in this study, 100mg four times a day, is the dose approved by the FDA.

How will the drug be used in this study?
If you are eligible to participate in this study, you will be randomly assigned as if by the toss of a coin to one of two study drug groups: Group A or Group B.

- Group A will receive dipyridamole for 24 weeks.
- Group B will receive a placebo for 12 weeks then dipyridamole for 12 weeks. The placebo looks the same as dipyridamole but does not contain any active drug.

You have an equal chance of being in either group; however, this is a "double-blind" study which means that you may not choose which group you are in and that you, your doctor, and the clinic staff will not know whether you are taking dipyridamole or the placebo.

Both dipyridamole and placebo will be provided by this study. Your anti-HIV medications will not be provided by this study; you will need to continue to obtain them through your HIV care doctor or provider.

How many people will take part in this study?
Up to 50 men and women 18 years of age and older will participate in this study at the University of Pittsburgh.

How long will I be in this study?
You will participate in this study for about 9 months, up to 2 months for screening then about 7 months on study, unless you choose to or have to come off study early.

What do I have to do if I am in the study?

- You will have 10 study visits at Screening, Pre-Entry, Entry/Week 0 then Weeks 4, 8, 12, 16, 20, 24, and 28 in the AIDS Clinical Trials Unit (ACTU) clinic on the 7th floor of the Falk Medical Building. Each study visit will take about 1-2 hours, depending on the procedures scheduled for that visit. It may be necessary for you to make additional unscheduled visit(s) during your participation in this study to have any of the study procedures listed below repeated in the event of unforeseen or unanticipated abnormal results; difficulties in sample shipping, processing, or testing; and/or if you experience any changes in your physical condition as determined by the study doctor. At Week 2 and Week 14, the study nurse will talk to you on the telephone to determine if you are having any problems with the study medications.
- At Entry/Week 0 and Weeks 4, 12, and 24, you will be asked to fast (no food or liquid other than plain water), not exercise, and not smoke for at least 8 hours before each visit, otherwise the visit will be rescheduled. You will have a special study procedure called Brachial Artery Flow Mediated Dilation (FMD) in the University of Pittsburgh Ultrasound Research Lab (URL). This test is painless and will take about 30 minutes. First, a picture will be taken of an artery in your lower right arm using sound waves (ultrasound), and the thickness of the artery will be measured. Next, a blood pressure cuff will be applied to your lower arm, inflated for about 5 minutes and then released. The ultrasound will be repeated, and the thickness of the artery will be measured again. You will not receive the results of any of these tests. You may be asked to return for a repeat FMD test if any of these pictures are not of good quality. At Weeks 4, 12, or 24, you may also be asked to have a second FMD test so that the URL can verify how well they can repeat a test on the same participant. This will strictly be voluntary; therefore if you are unable to stay longer for your visits you will be under no obligation to participate in this double testing.
- If you are entering this study under Version 2.0, at Entry/Week 0 and Weeks 4, 12, and 24, you will have a spirometry test performed if it is safe for you to do so. This is a measurement of the amount of air that you can inhale (breathe in) and exhale (blow out) from your lungs. This test will be performed in the research clinic by the study nurse or other study staff. If you use an inhaled bronchodilator to help with breathing, you will be asked to not use any short-acting products such as albuterol (Proventil, Ventolin) for at least 4 hours before the test and long-acting products such as salmeterol (Serevent, Advair) or formoterol (Foradil) for at least 12 hours before the test. For this test, you will be asked to take a breath in as far as you can and then blow it out as fast and hard as possible into the device that measures the amount of air. You will be asked to do this several times (between 3 and 8). Then you will have 4 puffs of albuterol, a medication that helps to relax or open up the bronchioles (breathing tubes) of your lungs. You will then be asked to repeat the spirometry as above.

- During your participation in this study, you must not take medicines that increase the risk of bleeding such as heparin, Lovenox®, warfarin (Coumadin®), or Plavix® and will be advised to avoid any herbal medication or supplements that may increase the risk of bleeding such as ginkgo, ginger, fish oil omega-3 fatty acids more than 3grams daily, green tea more than 5 cups daily, or niacin more than 100mg daily. In addition, you must not take aspirin or any non-steroidal anti-inflammatory drugs, such as ibuprofen (Motrin®, Advil®) or naproxen (Naprosyn®, Aleve®), for more than 3 days in a row. Study staff will discuss this with you. You may be asked to consent to some additional procedures called the "Rectal Tissue Subset". About 20 participants will be asked to enroll in this Subset, and the procedures are described in another consent form that you will be asked to read and sign if you are interested in participating. You are not required to participate in the Subset in order to participate in this study.

What procedures will be performed for research purposes?
The procedures performed in this study are done for research purposes. The study investigators will review the results of all of these procedures, and these results will become part of your research record. During the study, you will be given the results of most labs, evaluations, and procedures as soon as they are available except as noted below. You will not receive the results of any future study-related tests, such as tests of the immune system and inflammation.

Screening Procedures to determine if you are eligible to take part in this research study will be done at the Screening and Pre-Entry Visits.

Screening Visit: At this visit, which will take place within 60 days before Entry, you will be asked to read and sign this consent form before you have any study procedures or evaluations. Then,
- Your HIV infection status will be confirmed by past results in your medical records. If these results are not available, another HIV test will be done.
- You will be asked questions about your medical and medication history and have a complete physical exam including height, weight, and vital signs (temperature by mouth, pulse, blood pressure, breathing)
- If you are a woman who is able to become pregnant, a blood or urine pregnancy test will be done. This test must be negative. You cannot take part in this study if you are pregnant or breastfeeding.
- You will have about 2 tablespoons (27ml) of blood drawn for safety to check the health of your blood, liver, and kidneys; to measure your viral load (amount of HIV in your blood) and CD4+/CD8+ cell counts (types of white blood cells that fight infection); and to test for hepatitis B and C.

Pre-Entry Visit: At this visit, which will take place at least 24 hours after Screening and within 14 days before Entry, you will:
- Be asked about any medications you are currently taking and have taken in the past.
- Have a brief physical exam including weight and vital signs.
- Have about 8 tablespoons (120ml) of blood drawn for storage for future study-related tests.

Study Procedures If all of the Screening and Pre-Entry tests show that you meet the eligibility requirements and qualify to take part in this study, you will undergo the following study procedures to determine the effectiveness of the study drug and to monitor your health during the study. These procedures are listed in the table below then explained in more detail.

Evaluation or Procedure	*Entry Week 0*	*Week 2*	*Week 4*	*Week 8*	*Week 12*	*Week 14*	*Week 16*	*Week 20*	*Week 24*	*Final Week 28♦*	*Early Disc**
Fasting before visit	√		√		√				√		√
Brief physical exam	√		√	√	√		√	√	√	√	√
Blood draw for:											
Safety tests	√		√		√		√		√		√
Lipids (fats)	√				√				√		√
HIV viral load	√				√				√		√
CD4+/CD8+ cell counts	√				√				√		√
Study drug level			√	√	√		√	√	√		√
Blood Storage	√		√		√		√		√	√	√
Urine for storage	√		√		√		√		√		√
Pregnancy test	√		√	√	√		√	√	√	√	√
Brachial artery FMD	√		√		√				√		√
Spirometry	√		√		√				√		
Study drug administration	√		√	√	√		√	√	√		
Study drug adherence	√		√		√		√		√		
Telephone call with study nurse		√				√					
Total Blood Drawn [T=tablespoon]	10 T (149ml)	none	8½ T (130ml)	1/3 T (5ml)	10 T (154ml)	none	8½ T (130ml)	1/3 T (5ml)	10 T (154ml)	8 T (120ml)	10 T (154ml)

Fasting before visit: At Entry/Week 0 and Weeks 4, 12, and 24, you will be asked to fast (no food or liquid other than plain water and prescription medications), not exercise, and not smoke for at least 8 hours before each visit, otherwise the visit will be rescheduled.

Brief physical exam: Vital signs will be taken, your weight will be measured, and you will be asked about any changes in your medications since your last visit

Blood draw for:

Safety tests: To check the health of your blood and/or liver and kidneys

Lipids (fats): To measure cholesterol and triglycerides in your blood

HIV viral load: To measure the amount of HIV in your blood

CD4+/CD8+ cell counts: To measure these types of white blood cells that fight infection

Study drug level: To measure the amount of study drug in your blood

Blood for Storage: For future study-related tests.

Urine for storage: Urine will be collected and stored for future study-related tests.

Pregnancy Test: If you are a woman who is able to become pregnant, you will have a blood or urine pregnancy test. This test must be negative.

Brachial Artery FMD: Performed in the URL as described above

Spirometry (Lung function): Performed in the clinic as described above

Study drug administration: Beginning at Entry/Week 0, you will be given enough study drug to last until at least your next study visit and instructed to take one (1) capsule by mouth four times daily with or without food through Week 24. **Study drug adherence:** You will be asked to bring in the bottle of study drug so that the number of capsules can be counted. You will also be asked how you are doing with taking the study drug.

♦**Final Week 28:** Following the Week 28 visit, you will have completed the study.
*** Early Discontinuation:** If you stop taking the study drug or leave the study before Week 24.

During your participation in this study, you may have a total of about 2 pints (33 ounces or 994ml) of blood drawn.

Is there any other information that I need to know?
During this study, about 8 tablespoons (120ml) blood and urine collected at Entry/Week 0; Weeks 4, 12, 16, 24, and 28; and, if applicable, at Early Discontinuation will be stored locally for future study-related tests, such as tests of the immune system and inflammation.

In addition, if you consent, any biological samples (blood and/or urine) left over after all the study tests are done may be stored for possible future unspecified research, including HIV-related research. You do not have to agree to have these samples stored for future testing in order to participate in this study and will be asked to initial a separate line on the Voluntary Consent page of this consent form for the storage and testing of this samples. These samples will be labeled with a unique identifier (such as your participant identification number) and stored locally under the sole control of the investigators. These samples may be stored indefinitely, and the exact time at which these samples will be analyzed has not been determined. You will not receive the results of any future studies as the testing done on these samples may be experimental, and the information collected may not apply to your medical care. If these samples are provided to secondary investigators, all participant identifiers will be removed. If you do not agree to have your samples stored for possible future research, then your samples will be destroyed at the end of this study. If you withdraw consent from having your samples stored for future unspecified research, then your samples will be destroyed if you specifically request so.

What are the possible risks, side effects and discomforts of the study?
As with any research study, there may be adverse events or side effects that are currently unknown and it is possible that certain of these unknown risks could be permanent, serious, or life-threatening.

The drug used in this study may have side effects, some of which are listed below. Please note that this list may be incomplete and does not include all the side effects seen with this drug, such as a previously unknown allergic reaction causing a rash*, swelling, and trouble breathing. This list includes the more serious or common side effects with a known or possible relationship. If you have questions concerning the additional study drug side effects, please ask the medical staff at your site.

* Any rash should immediately be brought to the attention of your study doctor, no matter how long you have been receiving study drug.

You will be monitored for signs or symptoms of any of these side effects throughout this study.

There is a risk of serious and/or life-threatening side effects when non-study medications are taken with the study drug. For your safety, you must tell the study doctor or nurse about all medications (which includes over-the-counter medications, herbal products and dietary supplements) you are taking before you start the study and also before starting any new medications while on the study. Also, you must tell the study doctor or nurse before enrolling in any other clinical trials while on this study.

Risks of Dipyridamole (Persantine®): The following serious side effects have rarely been associated with use of dipyridamole:

- Chest pain (angina)
- Liver problems causing yellowing of the skin or eyes and dark urine

- Severe allergic reaction (rash, itching, swelling of the face, tongue or throat, trouble breathing)
- Unusual bleeding or bruising
- Weakness on one side of the body
- Pounding or rapid heartbeat
- Muscle or bone pain
- Alopecia (hair loss)
- Cholelithiasis (gallbladder stones)
- Hypotension (low blood pressure)

Possible common side effects of dipyridamole include:

- Dizziness
- Headache
- Rash
- Malaise (fatigue)
- Flushing
- Abdominal distress
- Nausea
- Vomiting
- Diarrhea

Risks of Placebo for Dipyridamole: There are no risks from receiving the placebo as it does not contain any active drug.

Risks of Brachial Artery Flow-Mediated Dilation (FMD): Brachial artery FMD is a painless imaging test that has no known short or long-term risks. The test uses sound waves and does not expose you to x-rays or radiation of any kind. The test may be mildly uncomfortable because the blood pressure cuff is applied tightly to your arm.

Risks of Spirometry: Spirometry is a routine test and involves a very low level of risk. Common risks of spirometry include a sensation of shortness of breath, cough, faintness or a feeling of light-headedness. These sensations subside rather quickly after completing the testing. All lung function tests will be performed sitting down so as to protect against injury from falling. Albuterol is a well-tolerated bronchodilator to be inhaled during the breathing tests. Common side effects of albuterol include heart palpitations, increased heart rate, chest pain, shakiness, nervousness, headache, dizziness, sore throat, and runny nose. Rarely, albuterol may cause an allergic reaction.

Risks of Drawing Blood: Occasionally there is swelling in the area where the needle enters the body and a rare risk of fainting, infection, or blood clots. Common risks of drawing blood include lightheadedness, discomfort, or bleeding or bruising at the spot where blood is drawn.

Risks of Fasting Before Study Visits: You may find fasting to be bothersome, and you may feel anxious, irritable, or hungry.

Are there risks related to pregnancy?

Pregnant and breastfeeding women are excluded from study participation. The effects of the study medication on a pregnant woman, unborn baby, or breastfeeding infant are not known. If you are a woman who is able to become pregnant, you must have a negative blood or urine pregnancy test at Screening, at Entry before starting the study medication, every 4 weeks during the study, and at any other time that you think you might be pregnant during study participation.

If you are a woman who is able to become pregnant, it is important that you not become pregnant while participating in this research study. Avoiding sexual activity is the only certain method to prevent pregnancy. If you are having sex that could lead to pregnancy, you must use at least one method of birth control that you

discuss with the study staff while receiving study drug and for 4 weeks after stopping study drug. You may choose one of the birth control methods listed below:

- Condoms (male or female) with or without a spermicidal agent. Condoms are recommended because their appropriate use is the only contraception method effective for preventing HIV transmission.
- Diaphragm or cervical cap with spermicide
- Intrauterine device (IUD)
- Hormone-based contraceptive

If you choose to be sexually active during this study, you must accept the risk that pregnancy could still result, exposing you to potential loss of pregnancy as well as other unknown effects on the developing fetus.
If you think that you may be pregnant at any time while you are participating in this study, tell your study doctor or coordinator right away. You will be given a pregnancy test. If the pregnancy test is positive, you must immediately stop taking the study medication. You will be asked to return to the clinic for an Early Discontinuation Visit to have blood drawn for safety tests and then taken off study. You will be asked if the study staff can contact you by phone monthly until your pregnancy has ended to see how you, and your baby, are doing.

Your pregnancy will be reported to an international database that collects information about pregnancies in women taking anti-HIV drugs: the Antiretroviral Pregnancy Registry, www.apregistry.com Phone: (800) 258-4263; Fax: (800) 800-1052. This report will not use your name or other information that could be used to identify you.

What are the possible benefits from taking part in this research study?
There is currently no known benefit of taking dipyridamole in HIV infection. Information learned from this study may help others who have HIV.

What treatments or procedures are available if I decide not to take part in this research study?
Alternatives to your participation in this study include using other prescription drugs available to you as prescribed by your primary care doctor, using investigational drugs through another clinical trial if you qualify, or using no drugs. Please talk to your doctor about these and other choices available to you. Your doctor will explain the risks and benefits of these choices.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
You will be promptly notified if any new information, either good or bad, develops during the course of this study and which may cause you to change your mind about continuing to participate. At the end of the study, the study staff will tell you when study results may be available and how to learn about them.

Will I or my insurance provider be charged for the costs of any procedures performed as part of this research study?
All of the services you will receive in this research study are being done only because you are participating in this study. You will not be charged for the study drug, dipyridamole or placebo, or any of the research activities [clinic visits, procedures, laboratory tests, brachial artery FMD tests] that are administered to you during this study. If you think that you or your health insurance has been charged, please contact a member of the research team and the UPMC billing office that sent the bill.

Taking part in this study may lead to added costs to you and/or your insurer. In some cases, it is possible that your insurer company will not pay for these costs because you are taking parting in a research study. You and/or your insurer will be billed for any routine care services that are provided. You will be responsible for any applicable copays, coinsurances, and deductibles.

Will I be compensated if I take part in this research study?
Beginning with the Screening Visit, you will be reimbursed $25 to $100 for parking and travel-related expenses for each scheduled study visit depending on the distance traveled from your residence to the clinic. In addition, you will receive $50 for each brachial artery FMD at Entry/Week 0, Week 4, Week 12, and Week 24. If you have a second brachial artery FMD at Weeks 4, 12, or 24, you will receive an extra $25. Finally, if you have a spirometry test at Entry/Week 0 and Weeks 4, 12, and 24, you will receive an additional $10. You will not otherwise be paid for participating in this study.

Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the Accounting Office. If the total reimbursement for your participation in research is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income.

Your biological samples may lead, in the future, to new inventions or products. If the investigators are able to develop new products from the research use of your biological samples, there are currently no plans to share with you any money or other rewards that may result from the development of these new products.

Who will pay if I am injured as a result of taking part in this research study?
If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation either through this institution or the National Institutes of Health (NIH). You will not, however, be giving up any of your legal rights by signing this consent form.

What about privacy and confidentiality?
There is a possibility that if your participation in this HIV research study or if the results of the research studies involving your biologic samples were to become generally known this information could impact future insurability, employability, or reproduction plans, or have a negative impact on family relationships, and/or result in stigmatization. To minimize this risk, any information about you obtained from this research will be kept as confidential (private) as possible. . Pennsylvania state law requires the reporting of positive HIV test results to the Allegheny County Health Department with your name and contact information. All information will be handled in compliance with the Pennsylvania law on HIV-related confidential information. All records related to your involvement in this research study will be stored in a secure, double-locked area at the AIDS Clinical Trials Unit (ACTU) that is accessible only by members of the research team. Your identity on these records will be indicated by your participant identification number rather than by your name, and the information linking your participant identification number with your identity will be kept separate from the research records.

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

Will this research study involve the use or disclosure of my identifiable information?
This research study will involve the recording of current and/or future identifiable medical information from your hospital and/or other health care provider records. This research study will also result in identifiable information that will be placed into your medical records held at the University of Pittsburgh HIV/AIDS Clinical Research Site or, with your written permission, by your primary health care provider. The identifiable information that will be recorded includes results of study-required laboratory tests, adverse event information related to the study drug, and/or hospitalizations or illnesses related or unrelated to HIV infection.

You will be asked to initial a separate line on the Voluntary Consent page of this consent form to have your biological samples (blood, urine, etc.) obtained for routine study tests (red and white blood cell counts, liver and kidney tests, etc. and, if applicable, HIV tests) labeled with identifiers (your first and last name, date of birth, gender, and medical record number) before being sent to QUEST Diagnostics, Inc. for study testing so that the results can be entered into your electronic medical record by QUEST for viewing by your primary healthcare provider(s).. You do not have to consent to this labeling in order to participate in this study, and you may withdraw consent at any time. Your samples will then be labeled with your participant study identification number. With your written permission, your test results will be sent directly to your primary healthcare provider(s) by the research team. Any biological samples stored for future study testing will still be labeled with a unique identifier, such as your participant identification number, as explained above in the Other Information section.

Who will have access to identifiable information related to my participation in this research study?
In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical record information) related to your participation in this research study:

- University of Pittsburgh Research Conduct and Compliance Office
- The sponsors of this research study, the National Institutes of Health (NIH)/National Institute of Allergy and Infectious Diseases (NIAID)
- Representatives of the US Federal Government, including the Office for Human Research Protections (OHRP) and/or contractors of the NIH
- Authorized representatives of QUEST Diagnostics, Inc. will have access to your identifiable information (your first and last name, date of birth, gender, and medical record number) for the purpose of analyzing your biological samples obtained for this research study. The results will be electronically entered into your medical record; therefore, authorized representatives of QUEST Diagnostics, Inc. will not have access to any additional information contained within your electronic medical record. Also, QUEST Diagnostics, Inc. has a Notice of Privacy Practices that prohibits disclosure of your identifiable information for other purposes without your written permission.

The investigators involved in the conduct of this research study may receive funding from the sponsor to perform the research procedures and to provide the sponsor with identifiable research and medical record information related to your participation in the study.

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical record information) related to your participation in this research study for a minimum of 7 years and for as long as it may take to complete this research study.

You are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider.

May I withdraw, at a future date, my consent for participation in this research study?
You can, at any time withdraw from this research study. You can also withdraw your authorization for us to use your identifiable medical information for the purposes described above. This means that you will also be withdrawn from further participation in this research study. Any identifiable research or medical information obtained as part of this study prior to the date that you withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw from this research study, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form. Your decision to withdraw from this study will have no effect on your current or future relationship with the University of Pittsburgh, on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

If I agree to participate in this research study, can I be removed from the study without my consent?
It is possible that you may be removed from the research study without your consent by the investigators in the event of the reasons listed below:

- You are not able to take the study medication as required by the study
- You are not able to attend the study visits as required by the study
- The study investigator or your doctor thinks the study is no longer in your best interest
- The University of Pittsburgh Institutional Data and Safety Monitoring Board (IDSMB) recommends that the study be stopped early. (The IDSMB is a group of experts who monitor the study.)
- The study is cancelled

It is possible that you may be taken off the study medication without your consent by the investigators if:

- You need a treatment that you may not take while on the study
- You take a non-steroidal anti-inflammatory drug for more than 3 days in a row
- Continuing the study drug may be harmful to you
- You stop study drug for 7 days in a row
- You become pregnant or are breastfeeding
- You request to stop study medication

If you decide to withdraw from study participation or are withdrawn from study participation without your consent, or if you must permanently stop the study medication before Week 24, you may be asked to return for a final study visit. After this visit, you will be removed from this study with no further study evaluations required.
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VOLUNTARY CONSENT: The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation. By signing this form I agree to participate in this research study. A copy of this consent form will be given to me.

Please indicate if you consent to have any remaining biological samples left over after all the study tests are done stored without identifiers for use in future research that is not part of this study, including HIV-related research. You do not have to agree to have these samples stored for future testing in order to participate in this study. You may change your mind at any time and your samples will be destroyed.

YES, I consent (initial & date) _____ NO, I do not consent (initial & date) _____

Please indicate if you consent to have your biological samples obtained for routine study tests labeled with your first and last name, date of birth, gender, and medical record number before being sent to QUEST Diagnostics, Inc. for study testing so that the results can be entered into your electronic medical record by QUEST for viewing by your primary healthcare provider(s).

YES, I consent (initial & date) _____ NO, I do not consent (initial & date) _____

_____	_____	_____
Participant's Printed Name	Participant's Signature	Date & time

CERTIFICATION OF INFORMED CONSENT: I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____
Printed Name of Person Obtaining Consent	Role in Research Study
_____	_____
Signature of Person Obtaining Consent	Date & time