UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

CID 0910 Version 2.0, dated March 30, 2010; LOA#1, 3/2/11: A Cross-Sectional Assessment of Markers Inflammation, Coagulation and Endothelial Function Among Patients Receiving Nucleoside Reverse Transcriptase Inhibitors – The NICE Study

Sponsor: The University of North Carolina at Chapel Hill

Funding Source: GlaxoSmithKline (GSK)

CONSENT TO PARTICIPATE IN A RESEARCH STUDY AND RESEARCH SUBJECT HIPAA AUTHORIZATION

Your contacts for this study at the Hospital of the University of Pennsylvania [HUP] are:

Principal Investigator:	Pablo Tebas, MD	(215) 349-8092
Coordinator:	Joseph Quinn, RN, BSN	(215) 349-8092
Study Nurse:	Aleshia Thomas, RN, BSN	(215) 349-8092
Research Assistants:	Emily Stumm, BS	(215) 349-8092
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24 Hour Emergency Number (215) 662-6059 Ask for the Immunodeficiency Program Doctor on call

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Introduction:

You are being invited to participate in a research study. 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 can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this 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. You will get a copy to keep.

Why Is This Study Being Done?

You are being asked to be in the study because you are HIV positive and 18 years of age or older and meet one of the following criteria:

- have previously been receiving abacavir or tenofovir on a clinical trial as a part of your initial HIV treatment for at least 6 months but did not start taking these drugs before 2003.
- have received zidovudine as part of an initial treatment for HIV infection, whether during a clinical trial or routine HIV care, for at least 6 months and are still receiving zidovudine at the time you enter this study.

The first purpose of this research study is to better understand the inflammation (response by the body to disease and injury) that occurs in patients with HIV on different antiretroviral medications. Inflammation in blood vessels is known to happen in lots of different medical conditions including heart disease, kidney disease, and HIV and can put someone at a higher risk for complications like strokes or heart attacks. One of the objectives of this study is to determine if there is a difference in the degree of inflammation depending on what antiretroviral medication an individual is taking. This will be done by testing your blood for inflammatory markers and doing a brachial artery flow mediated vasodilation (FMD) test. This is an ultrasound test of an artery in your right lower arm. Brachial artery FMD is a test that involves bouncing sound beams off an artery in your arm so it can be seen on a TV screen and measurements may be made.

The second purpose is to find out if patients taking certain antiretroviral medications have differences in how their bodies process phosphate. Phosphate is an electrolyte found in the body that is important for kidney and bone health. Some people with HIV lose phosphate in their urine, but we don't know if this is related to antiretroviral therapy or not. If someone loses too much phosphate in their urine, their bones can become weak and put them at higher risk for fractures. We will be testing for phosphate in the urine and compare it to phosphate in the blood, and we will do a bone mineral density dual-energy x-ray absorptiometry (DEXA) scan of the hip and back to measure how strong your bones are. A DEXA scan is a special kind of x-ray using a small amount of radiation, allowing the doctor to see parts of the body better than a regular x-ray. There are other things that can change how a person's body processes phosphate like vitamin D deficiency or hyperparathyroidism so we will be testing for these as well. Hyperparathyroidism is having more than the usual amount of parathyroid hormone in the body. Parathyroid hormone is produced by the parathyroid glands that control the amount of calcium in the blood and within the bones.

Are There Any Reasons You Should Not Be In This Study?

You should not be in this study if:

- you are a female who is pregnant or planning to become pregnant
- you have been on any combination of abacavir (Ziagen), tenofovir (Viread), or zidovudine (Retrovir or also known as ZDV or azidothymidine, AZT) at any point in your HIV treatment

How Many People Will Take Part in This Study?

A total of approximately 170 people at approximately 10 institutions will take part in this study, including approximately 17 people from the University of Pennsylvania.

How Long Will I Be In This Study?

Only one visit is required for this study. This study visit will last approximately 3-4 hours.

What Do I Have To Do If I Am In This Study?

If you agree to participate in this study and sign this consent form, there are several procedures that you will be asked to undergo which are described below.

You will have a complete medical history and medication history. We will measure your height and weight and take your temperature, pulse, and blood pressure.

You will be asked to come in fasting (no food or drink except plain water, and your prescription drugs for the 8 hours just before the visit) for some of the blood work and for the brachial artery FMD test that you will have done.

You will be asked not to do any vigorous (intense) exercise and not to have any caffeine or use any tobacco or cigarettes or over-the-counter drugs that may relax or constrict your blood vessels (e.g., decongestants) for at least 8 hours before you have the brachial artery FMD test.

If you are taking medications that are required to be taken with food, please bring those medications with you to the study visit. You will be allowed to take those medications with food after you complete the study visit.

We will collect blood and urine samples from you. You will have about 3-4 teaspoons of blood drawn. There is a blood test that can help determine if someone has a higher risk of having a bad reaction to Abacavir. If you have never had this blood test done as part of your HIV care, then we will do this test, which will require us to draw about one teaspoon of blood. In this case, you would have a total of about 4 teaspoons of blood drawn. However, if you have already had this blood test done as part of your HIV care, then you would only have a total of about 3 teaspoons of blood drawn. You will also be asked to give a urine sample. This urine sample is only going to be tested for certain electrolytes that are markers of bone health.

Stored Serum Samples

We would like to store some of your left over serum (blood) samples collected at your study visit for possible future use for investigations related to this study and for possible future research. You will be asked to sign a separate consent form for stored specimens, where you will choose whether or not to allow future genetic testing to be performed on these left over blood samples.

Special Tests

You will have an ultrasound test of an artery in your right lower arm. This test is called a brachial artery flow mediated vasodilation (FMD). Brachial artery FMD is a test that involves bouncing sound beams off an artery in your arm so it can be seen on a TV screen and measurements may be made. It takes about 20 minutes, and you will have a baseline measurement taken. Then a blood pressure cuff will be applied to your lower arm and inflated for approximately 5 minutes. You may experience some discomfort from the application of the blood pressure cuff. After release of the cuff, a repeat ultrasound test of the artery in your arm will be obtained for a second measurement. This test is being done for research only and the results will not be provided to you.

You will have a bone mineral density dual-energy x-ray absorptiometry (DEXA) scan of the hip and back. A DEXA scan is a special kind of x-ray using a small amount of radiation, allowing the doctor to see parts of the body better than a regular x-ray. During the DEXA scan, you will lie very still on a table for about 15 minutes. The machine will then take the x-rays. The results of the DEXA scan will be given to you or your provider.

What Are The Risks Of The Study?

Risks of Drawing Blood

Taking blood may cause discomfort, bleeding, and bruising where the blood is drawn.
Occasionally, there is swelling in the area where the needle enters the body and there is a small risk of infection. There is also a risk of lightheadedness, fainting, and blood clots.

Risks for the Brachial Artery Flow Mediated Vasodilation (FMD)

Brachial artery FMD is an 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 uncomfortable (less than a blood draw) because the blood pressure cuff is applied tightly to your arm.

Risks of Radiation (from DEXA scan)

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This research study involves exposure to radiation from one DEXA scan. Therefore, you will receive a radiation dose. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.

The scanning machine will not cause any physical discomfort other than from having to lie still on the table for the duration of the test.

If you are a woman who is able to get pregnant, you will have a pregnancy test within 7 days prior to your DEXA scan. This pregnancy test will be paid for by the study.

Risks of Fasting

Some individuals find fasting to be bothersome. It may make some individuals feel anxious, irritable, or hungry. Subjects who are required to take their morning medications with food should wait until after the study visit has been completed to take their medications.

In addition, there may be uncommon or previously unknown risks that might occur. You should report any problems to the researchers.

If you are a woman and you are planning to get pregnant, you should not be in the study.

Are There Benefits to Taking Part in This Study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study. The knowledge gained from this study may benefit others with HIV infection.

What If We Learn About New Findings Or Information During The Study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How Will Your Privacy Be Protected?

No subjects will be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, University of Pennsylvania will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University of Pennsylvania, the University of North Carolina at Chapel Hill, research sponsors, or government agencies for purposes such as quality control or safety.

A copy of this consent form will go in to your medical record. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study.

HIPAA AUTHORIZATION

The authorization part of the consent gives more detailed information about how your personal health information may be used and disclosed by the University of Pennsylvania Health System

(UPHS), the School of Medicine and the individual Principal Investigator, subject to University of Pennsylvania procedures.

What information about me may be collected, used or shared with others?
The following information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Name, address, telephone number, date of birth
- Medical Record Number
- Personal and family medical history
- Current and past medications or therapies
- Information from questionnaires administered in the study
- Results of tests and procedures you will undergo during this research study
- Social Security Number

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
- to see if the research was done right.

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

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

Individuals or organizations responsible for administering the study:

- Pharmaceutical Companies: GlaxoSmithKline, the funding source of the study.
- University of North Carolina at Chapel Hill: As the sponsor of the study, data for this study will be recorded, keyed into a central database and submitted to the University of North Carolina. The data will be cleaned and analyzed and then published by investigators.

Regulatory and safety oversight organizations

- The Office of Human Research Protections
- The Study Monitoring Committee

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.

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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. 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.

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

By signing this document you are permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

What Happens If I Am Injured?
All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill and the University of Pennsylvania have not set aside funds to pay you for any such reactions or injuries, or for the related medical care. However, by signing this form, you do not give up any of your legal rights.

What If You Want To Stop Before Your Part In The Study Is Complete?
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will You Receive Anything For Being In This Study?
You will be receiving $75 for taking part in this study.

Please note that if you receive more than $600.00 compensation in one year for participation in research studies at the University of Pennsylvania, you must provide a Individual Tax Identification number or Social Security Number for tax purposes.

Will It Cost You Anything To Be In This Study?
It will not cost you anything in addition to what you will be billed for your routine medical care to be in this study. All study specific tests and visits will be paid for by the study.

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Who Is Sponsoring This Study?

This research is funded by GlaxoSmithKline (GSK). The sponsor, the University of North Carolina at Chapel Hill (UNC-CH), is providing money from GSK or other support to the University of Pennsylvania to help conduct this study. In addition, Dr. David Wohl, the principal investigator of the study, receives money from GlaxoSmithKline for work that is not part of this study. These activities may include consulting, service on advisory boards, giving speeches, or writing reports. The researchers do not, however, have a direct financial interest with GlaxoSmithKline or in the final results of the study.

A committee at the University of North Carolina at Chapel Hill has reviewed these financial arrangements. They concluded that the possible financial benefit to the persons involved in the research is not likely to affect your safety and/or the scientific quality of the study.

What Do I Do If I Have Questions Or Problems?

For questions about this study or a research-related injury, contact:

- Pablo Tebas, MD (215-349-8092)
- Clinical Trials Unit (215 349-8092)

For questions about your rights as a research subject, contact:

- Director of Regulatory Affairs at the University of Pennsylvania by phoning (215) 898-2614

CONSENT

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 Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you. You will also be given the University of Pennsylvania Health System and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your health information.

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Signature of Research Subject Date

_____

Printed Name of Research Subject

_____ _____

Signature of Research Team Member Obtaining Consent Date

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Printed Name of Research Team Member Obtaining Consent