

IRB Approval
From: 5/22/2009
To: 2/11/2010

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

A5260s, Version 1.0, 11/24/08; Letter of Amendment #1, 3/31/09:

Cardiovascular, Anthropometric, and Skeletal Effects of Antiretroviral Therapy (ART) Initiation with Emtricitabine/Tenofovir Disoproxil Fumarate (FTC/TDF) plus Atazanavir/ Ritonavir (ATV/r), Darunavir/Ritonavir (DRV/r), or Raltegravir (RAL): Metabolic Substudy of A5257

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

If you are seen at the Hospital of the University of Pennsylvania [HUP], your contacts are:

Principal Investigator:	Pablo Tebas, MD	(215) 349-8092
Coordinator:	Joseph Quinn, RN	(215) 349-8092
Study Nurse:	Kathryn Maffei, RN	(215) 349-8092
	Aleshia Thomas, RN	(215) 349-8092
	Wayne Wagner, RN	(215) 349-8092
	Larisa Zifchak, RN	(215) 349-8092

24 Hour Emergency Number (215) 662-6059 Ask for the Immunodeficiency Program Doctor on call

Introduction:

You are being asked to take part in this research substudy because you are taking raltegravir, darunavir, or atazanavir as part of the treatment for your HIV infection on the main study A5257. This study is sponsored by the National Institutes of Health (NIH). The doctor in charge of this study at this site is Pablo Tebas, MD. Before you decide if you want to be a part of this study, we want you to know about the substudy.

This is a consent form. It gives you information about this substudy. The substudy staff will talk with you about this information. You are free to ask questions about this substudy at any time. If you agree to take part in this substudy, you will be asked to sign this consent form. You will get a copy to keep.

Why Is This Substudy Being Done?

The purpose of this substudy is to learn about the metabolic changes in participants receiving one of the three treatment regimens given in A5257 as their first antiretroviral regimen. The metabolic changes we will be measuring are in body fat, bone, the blood vessels, blood sugar, cholesterol, and kidney function.

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

If you agree to participate in this substudy and sign this consent form, there are several procedures that you will be asked to undergo which are described below. You will be asked to come in for visits at Entry and at Weeks 4, 24, 48, 96, and 144. All visits will last about 1-2 hours and will occur at the same time as your main study visits.

At all visits, you will be asked to come in fasting (no food or drink except water, decaffeinated black coffee without sugar, and your prescription drugs for the 8 hours just before the visit). You will also be asked not to use any tobacco products for at least 8 hours prior to coming in for each visit. If you are not fasting you will be asked to come back fasting within 4 days to repeat some blood tests. A physical exam will be completed including measuring your blood pressure and pulse. For women capable of having children, a urine pregnancy test will be completed. You must notify the research staff if you are pregnant, think you may be pregnant, or if you are trying to become

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pregnant. You will have about 4 tablespoons of blood drawn to test for various substances in your blood related to cholesterol, blood sugar, and other metabolic and immunologic changes. Some of your blood will be processed, stored (with usual protectors of identity), and tested for fat levels and special proteins in your blood at the end of the study. You will be asked to give a urine specimen which will be stored (with usual protectors of identity) for future tests. You will not receive the test results of the substudy procedures.

At most visits you will be asked to complete a questionnaire regarding your level of activity.

Special Tests

You will have a special test done called a carotid intima-media thickness (CIMT) test. This test measures the thickness of the carotid artery in your neck by using sound waves (ultrasound) to take a picture. For this test you will have to lie quietly on your back for about 20 minutes. This test will be done twice at Entry, and once at Weeks 48, 96, and 144.

You will have an ultrasound test of an artery in your right lower arm. This test is called a brachial artery flow mediated dilatation (FMD). Brachial artery FMD is a painless 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. A blood pressure cuff will be applied to your lower arm and inflated for approximately 5 minutes. After release of the cuff, a repeat ultrasound test of the artery in your arm will be obtained. This test will be done at Entry and Weeks 4, 24, and 48. If you are 1 of the first 5 participants to have this test done at your imaging site, at week 24 you will have the tests done twice.

You will have an abdominal computed tomography (CT) scan. A CT scan is a special kind of x-ray that takes pictures of the inside of the body using a small amount of radiation. Intravenous dye is not administered. You will be asked to lie quietly while your body is moved inside a large machine and the x-ray is taken. The CT scan takes about 15 minutes. This test will be done at Entry and Weeks 48 and 96.

You will have a whole body fat and bone mineral density dual-energy x-ray absorptiometry (DXA) scan. A DXA 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 DXA scan, you will lie very still on a table for about 15 minutes. The machine will then take the x-rays. This test will be done at Entry and Week 96.

You will not receive the results of the special tests except the DXA scan which will be available at the end of the substudy.

Premature Discontinuation of Substudy A5260s

If you decide to discontinue your participation in this substudy, you may continue in the main study A5257. If you discontinue study drugs in the main study, you may continue in the substudy. If you discontinue your participation in the main study, you will be removed from this substudy as well. If you decide to discontinue your participation in the substudy, you will be asked to return to the clinic for additional evaluations. This visit will last about 1-2 hours. You will have most or all of the tests described above at this visit.

If you are a woman and become pregnant while on the substudy, you must immediately notify the study staff. You will be taken off of the substudy and will not have anymore substudy evaluations performed.

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Other

Some of your blood that is leftover after all required substudy testing is done may be stored (with usual protectors of identity) and used for ACTG-approved HIV-related research. Storage of leftover blood is not a requirement to participate in the substudy and you may withdraw your approval for the storage of your leftover blood, at anytime. These samples may be held for an indefinite length of time. We cannot ensure that you will be told of the results of the research done on these samples. Please indicate and initial below whether you approve the use of your leftover blood.

_____ YES

_____ NO

How Many People Will Take Part in This SubStudy?

About 330 people will take part in this study. About 10 people are expected to participate at the University of Pennsylvania.

How Long Will I Be in This SubStudy?

You will be in this substudy for about 3 years.

What Are The Risks Of The SubStudy?

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 of the Carotid Intima-Media Thickness (CIMT) test

The CIMT test does not pose any risk to you. The test uses sound waves and does not expose you to x-rays or radiation of any kind. You will have to lie quietly on your back for about 20 minutes, which may be uncomfortable.

Risks for the Brachial Artery Flow Mediated Dilatation (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 (less than a blood draw) because the blood pressure cuff is applied tightly to your arm.

Risks of Radiation (from CT and DXA scans)

This research study involves exposure to radiation from the CT and DXA scans. 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 machines will not cause any physical discomfort other than from having to lie still on the table for the duration of the test.

Risks of Fasting

Some individuals find fasting and not smoking or consuming caffeine to be bothersome. It may make some individuals feel anxious, irritable, or hungry. Patients who are required to take their

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morning medications with food should wait until after the visit has been completed to take their medications.

Are There Benefits to Taking Part in This SubStudy?

There is no direct benefit to you from being in this substudy. Knowledge from this substudy may help others with HIV infection in the future.

What Are the Costs To Me?

Taking part in this substudy may lead to added costs to you and your insurance company. In some cases it is possible that your insurance company will not pay for these costs because you are taking part in a research study.

Will I Receive Any Payment?

You will be compensated for participation in the substudy and the amount will be determined by which tests are conducted at the substudy visit. Compensation will be \$25 for the CIMT, \$25 for the brachial artery FMD, and \$25 for the abdominal CT and \$25 for the DXA. No more than three of these tests are performed at each visit, so depending on the visit you may receive compensation of \$25 to \$75.

Participants should be aware that a maximum of \$99 can be provided as cash at a particular study visit. If the compensation amount goes over that limit, then the compensation will be provided as a check which needs to go through the University's accounting system and may take 6-8 weeks to arrive. So you may be able to receive compensation for your main study visit, but the additional compensation for the substudy participation may need to be provided as a check.

OTHER

All other information that is contained in the main study (A5257) consent you signed, applies to this substudy consent as well.

CONSENT

When you sign this form, you are agreeing to take part in this research substudy. 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.

Name of Subject (Please Print)

Signature of Subject

Date

Name of Person Obtaining Consent (PRINT)

Signature

Date