

UNIVERSITY OF PENNSYLVANIA

A5001, version 3.0, 3/24/06, Letter of Amendment #1, 12/26/08:
ADULT AIDS CLINICAL TRIALS GROUP LONGITUDINAL LINKED RANDOMIZED TRIALS (ALLRT)

INFORMED CONSENT

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

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

INFORMED CONSENT

You are being asked to take part in the research study named above, because you are infected with the human immunodeficiency virus (HIV), the virus that causes AIDS. This is a long-term follow-up study of subjects who are HIV infected and are being treated or have been treated in selected clinical trials conducted by the Adult AIDS Clinical Trials Group (AACTG). The study doctor and nurse who oversee your care on the main study will also be your care providers on this trial. Before you can decide whether to take part in this study, we want to explain the purpose of the study, how it may help you, any risks to you, and what is expected of you.

YOUR PARTICIPATION IS VOLUNTARY

This consent form gives you information about the study, which 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 your participation is entirely voluntary and you may decide not to take part or to withdraw from the study at any time without losing the benefits of your routine medical care. You may continue on the main AACTG study and withdraw from this study as well.

PURPOSE OF STUDY

This study is being done to learn how the body responds to HIV infection and its treatment over several years. Examples of things the study will look at include:

- What combinations of drugs work best over several years;
- What factors determine the amount of blood cells (T cells) that help fight infection and HIV;
- If the order in which combinations of drugs are given affects outcome;
- What kinds of side effects and illnesses occur during long-term (4 or more years) treatment of HIV infection;
- How many people experience these side effects and illnesses; and
- How people with very low or undetectable levels of virus in their blood (viral load) for a long time compare with those whose viral load is higher.

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The study will enroll about 6100 subjects nationwide; about 250 people are expected to enroll at PENN. They will have different stages of HIV infection. The study will last through 2013. You will be asked to stay on the study through 2013.

PROCEDURES

To enroll in this study, you must either be in an AACTG treatment trial or you must have been in one within the last 8 weeks. This is called a parent study. The parent study must provide (or have provided) anti-HIV therapy or a strategy for managing anti-HIV therapy that is assigned by chance (as if by a flip of a coin). You will be asked to continue follow-up as long as the ALLRT (Adult Longitudinal Linked Randomized Trials) study lasts. You will be followed on the ALLRT study even if your treatment on the other or future AACTG study (or studies) ends. The ALLRT study does not provide any therapy.

Because this study is looking at long-term effects of HIV and its treatment, the ALLRT study team will need to see the results of tests done and information collected on the parent study and any other AACTG study in which you will enroll during your participation in the ALLRT study. The ALLRT study team will also need to see the results of tests done and information collected from AACTG studies other than the parent study if these were collected within 8 weeks before enrolling in the parent study and are needed for the ALLRT study. Tests you have on the parent study that are also required for the ALLRT will only be done once and will not be repeated for the ALLRT study. Information from the parent study, other AACTG studies, and the ALLRT study will not have your name on it. Your information will be identified by a number to protect your privacy. It is important that you understand that when you sign this informed consent, you are also giving the team permission to look at these other records. When you are not on a parent study, you will undergo all the tests that are part of the ALLRT study, and information may need to be obtained from your clinic records. Information collected from your clinic records will also be kept confidential and identified by a number to protect your privacy.

Entry

At entry, your medical history, what medications you have taken to treat HIV infection or to treat or prevent other infections and cancers that commonly occur in HIV-infected people, whether you have had the hepatitis B vaccine, and laboratory results will be obtained from your parent study records. You will also be asked for your family's history of heart disease, and your own history of heart disease or stroke, diabetes, and smoking. You will be asked about how you are feeling.

Unless done as part of a clinic visit for a parent study, you will have a routine physical examination with measurements of your height and weight. You will have your hip, waist, and arm measured to learn about changes in body shape. You will be asked to fill out a short questionnaire about how you feel, how you take your medicine, and what kinds of medical care you have used. It will take about 15 minutes to complete.

You will also be asked to have a neurologic exam to test the way you think through or understand information and to test how your nerves are working. Some of these tests are paper and pencil tests. The neurologic exam will take about 20-30 minutes to complete. These tests are being done to find out if any of the anti-HIV treatments you are receiving are associated with changes over the long-term in how you think through or understand new information or in how your nerves work.

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If you are a woman, you will be asked about your menstrual periods and, unless you have had a pelvic exam and Pap smear in the last 6 months, you will be asked to have them at this visit. You do not have to have the pelvic exam and Pap smear to be on the study.

The entire ALLRT study visit will take about 1-2 hours.

You will have between 1 and 5 tablespoons of blood drawn for this study in addition to what is drawn for the parent study. The amount of blood drawn will vary depending upon what parent study you are on. The blood will be used for routine tests, to measure your viral load and your T cells, and to store for future testing. Unless you have had a blood test that showed a previous or current infection with hepatitis A, B, and/or C viruses (three types of viruses that can cause liver inflammation or abnormal liver function), these tests will be done and the results will be provided to you. When you are not on a parent protocol and viral load and/or T-cell count is measured on the ALLRT, the results will be provided to you. You will be asked to give a urine sample for tests to see how your kidneys are working. You will be asked to come to the clinic fasting (to not eat or drink anything other than water for 8 hours before you come to the clinic) to have your blood drawn, but you do not have to be fasting if this is too difficult. However, if the blood tests that check for diabetes or fats in the blood are not normal, you will need to fast overnight and come back to the clinic to have your blood checked again.

Some of your blood that is left over after all required study testing is done may be stored (with the usual protectors of identity) and used for ACTG-approved HIV-related research in the future. You will need to sign a consent form for ACTG5128 and give your permission for your blood to be stored and tested. Some of your blood will be stored (with the usual protectors of identity) and used for immunologic and virologic testing that is required for this study. Some of these tests will look at your HIV, at whether your HIV is sensitive to anti-HIV drugs, and at how your immune system functions, including your T cells and other immune cells. The tests may also look at anti-HIV drug levels in your blood. The tests may also look at changes to the virus' genes that may affect your health and some types of genes that you may carry that could affect how your immune system responds to HIV. Examples of the gene tests that might be studied include ones called "chemokine receptor genes" and "HLA" genes. These genes have been linked with the ability of the immune system to keep HIV disease from becoming worse or with the development of some side effects or toxicities of some medications.

Whether or not you are on a parent study and have blood drawn on that study for tests, you must agree to have your blood drawn for additional tests that are required for the entry visit on the ALLRT study. You also have to agree to let the team see the results from the parent study and other co-enrolled AACTG studies, and you must allow a clinical exam to check your health.

On Study

On-study visits will be timed from when you begin your parent study. You will be asked to come back to the clinic every 16 weeks (about 3 times a year). If you are on a parent AACTG clinical trial, these visits will be at the same time, if possible. Information or tests required by the ALLRT study that are also required on the parent study will be done only once. If you are not on another AACTG clinical trial, you will be asked about your health since the last visit and any treatment you have taken for your HIV infection or to prevent or treat related problems. Most of the same blood tests and measurements that are done at entry will be repeated at each ALLRT study visit. The neurologic exam, the body measurements, questionnaire, and urine test will be done about once a year. If you are a woman, you will have the pelvic exam and Pap smear, and be asked about your menstrual periods, about once a year

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(women can refuse the pelvic exam and Pap smear and still participate in the ALLRT study). Viral load and T cells will be measured only twice a year. The hepatitis tests, if needed, will be done about every two years. In the first year of the study, you may be asked to complete these evaluations more than once a year to coordinate the time points with your parent study. The amount of blood drawn will depend on whether you are on a parent study but will be between 1 and 5 tablespoons.

In order to remain enrolled in the ALLRT study after you have completed the ALLRT entry evaluations, you must agree to:

- Have blood drawn specifically for the ALLRT study at least once a year;
- Allow the team to see the results from your parent study, other AACTG studies, and information from your medical records that collect data needed for the ALLRT study;
- Have clinical evaluations including medical history updates at least once a year.

Early or Permanent Discontinuation

If you want to leave the study before it is over or when the study ends, you will be asked to return to the clinic for a final evaluation. This evaluation will include all the tests and measurements that were done during your study participation.

RISKS and/or DISCOMFORTS

Risks of Blood Draws

Taking blood may cause some discomfort, bleeding, bruising, and/or swelling where the needle enters the body, and in rare cases it may result in fainting. There is a small risk of infection.

Risks of a Pelvic Exam

The risks of a pelvic exam and Pap smear are some pain and discomfort, and sometimes light bleeding. There is a slight risk of infection.

PREGNANCY

If you become pregnant you may still participate in the ALLRT study. If you are on a parent study, you will need to follow the guidelines of the parent study. However, you may still participate in the ALLRT even if you must leave the parent study.

BENEFITS

There is no guarantee of a direct benefit to you from being in this study. However, taking part in this study will provide information about T cell counts and viral load that may help you and your doctor manage your HIV infection. Knowledge gained from this study may in the future help others who suffer from the HIV infection.

NEW FINDINGS

You will be told of any new information learned during the course of the study that might cause you to change your mind about staying in the study. At the end of the study, you will be told when study results may be available and how to learn about them.

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REASONS WHY YOU MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT:

You may be removed from the study without your consent for the following reasons:

- the investigator decides that continuing in the study would be harmful to you;
- you are unable to keep appointments as instructed;
- the study is canceled by the National Institute of Allergy and Infectious Diseases (NIAID); the ACTG, or the site's Institutional Review Board (IRB). (An IRB is a committee that watches over the safety and rights of research subjects.)
- other administrative reasons.

ALTERNATIVES TO PARTICIPATION

You may choose not to participate in this study at any time. You may enroll in other clinical studies.

COSTS TO YOU

There will be no cost to you for any of the tests that you have as part of the ALLRT study.

COMPENSATION

For your time and inconvenience and to cover the cost of transportation or parking, day care, meals, you will be compensated \$30.00 for each ALLRT visit you complete.

CONFIDENTIALITY

Every attempt will be made by investigators to maintain all information collected in this study strictly confidential, except as may be required by court order or by law. Authorized representatives of the sponsor (ACTG), the University of Pennsylvania, as well as the Food and Drug Administration (FDA), will have access to and may copy, both your medical records and records from your participation in this study. This access is necessary to insure the accuracy of the findings and your safety and welfare. If any publication or presentation results from this research, you will not be identified by name.

RESEARCH-RELATED INJURY

If you are injured as a result of being in this study, you will be given immediate treatment for your injuries. In the event of any physical injury resulting from the research procedures, medical treatment will be provided without cost to you. There is no program for compensation either through this institution or the National Institutes of Health (NIH) or the University of Pennsylvania. You will not be giving up any of your legal rights by signing this consent form.

PROBLEMS OR QUESTIONS

If you ever have questions about this study or in case of research related injury, you should contact one of the investigators listed on the first page of this form, for concerns regarding your rights as a volunteer, you should contact the Director of Regulatory Affairs at the University of Pennsylvania at (215) 898-2614.

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AGREEMENT

You have read and understand the above sections of the consent form. You have been given the opportunity to ask questions and they have been answered satisfactorily. You have received a copy of this consent form. You agree to participate in this study.

Participant's signature

Participant's Printed Name

Date/Time

Person Obtaining Consent's Signature

Person Obtaining Consent's PRINTED

Date