

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

Tibotec Pharmaceuticals Ltd, TMC278-TiDP6-c209, Amendment III, 06-AUG-2008
A Phase III, Randomized, Double-blind Study of TMC278 25 mg q.d. versus Efavirenz 600 mg q.d. in
Combination with a Fixed Background Regimen Consisting of Tenofovir Disoproxil Fumarate and
Emtricitabine in Antiretroviral-Naïve HIV-1 Infected Subjects

INFORMED CONSENT FORM FOR DNA AND RNA RESEARCH

Your contacts for this study are:

Principal Investigator:	Pablo Tebas, MD	(215) 615-4321
Coordinator:	Joseph Quinn, RN	(215) 349-8092
Study Nurse:	Aleshia Thomas, RN	(215) 349-8092

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

READ THIS INFORMATION CAREFULLY

You have already agreed to take part in the clinical research study indicated above. With this form, you are being asked for your consent to take part in an additional part of the clinical study on DNA and RNA Research. This additional part involves testing for differences in code of genes (DNA research) and for differences in the activity of genes (RNA research). We will use these tests to improve our knowledge how the HIV virus causes the disease, how the drugs used in this study work on the virus and in the human body, and to better understand and predict the (side) effects of these drugs. Participation in the DNA and RNA Research part of the study is voluntary. You may remain in the main part of the clinical study if you would decide not to give samples for DNA and RNA research. Your decision will not affect the medical care that you receive from your study doctor or his/her staff. Before you consent to this DNA and RNA Research part of the study, please read this form. Ask your study doctor (or staff) as many questions as you need, to be sure that you understand what taking part in the DNA and RNA research will involve.

WHAT IS THE PURPOSE OF THIS PART OF THE STUDY?

DNA research

The cells of your body contain deoxyribonucleic acid, or DNA for short. The DNA in most cells of your body is the same, and does not change during life. DNA is passed down from parents to their children. It carries the code for the genes that determine your physical appearance such as the color of your hair and eyes. The DNA is specific for an individual but the DNA in most cells in the same. The DNA code can be determined in the laboratory. Subtle differences in the DNA code of our genes help explain why we all look different. It also can help explain why some people are more likely to get certain diseases, while others do not. Differences in the DNA code may also help explain why some drugs work and are safe in some people, but not in others.

The Sponsor would like to study differences in people's DNA to try improving our knowledge on how the HIV virus causes the disease, to better understand how the drugs used in this study work on the virus and in the human body, or to predict (side) effects of these drugs. Such knowledge would possibly allow the Sponsor to explain why different groups of people respond differently to its drugs, and might guide the development of safer and better drugs in the future.

RNA research

Genes in your DNA that are active produce ribonucleic acid, or RNA for short. The RNA acts as a messenger to tell your cells to produce certain features. In the laboratory RNA from your cells can be

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isolated and used to measure the activity of genes. In contrast to DNA, the amount of RNA from individual genes is different in different cells in your body, under different conditions, and may vary over time. This is very comparable to the changes over time that can be seen in many laboratory tests that are routinely performed in the hospital, such as blood cholesterol.

The study of RNA may allow scientists to identify specific genes from which the activity is influenced by certain diseases or drugs. This may help to understand how the HIV virus causes the disease, how the drugs used in this study work on the virus and in the human body, or to predict (side) effects of these drugs. Such knowledge would possibly allow the Sponsor to explain why different groups of people respond differently to its drugs, and might guide the development of safer and better drugs in the future.

WHAT AM I BEING ASKED TO DO?

You are being asked to provide a total number of 2 blood samples that can be stored and used for DNA and RNA research. These tests are not for your medical care. If you agree, small blood samples (each 2.5 mL, about a half teaspoon) will be collected during Visit 2 (baseline visit) and at Visit 8 (week 24), as scheduled in the main part of the clinical study. Blood will be drawn from a vein using a needle.

You may also decide not to agree to this part of the clinical study. Whatever your decision, it will not affect your participation in the main part of the clinical study or the usual medical care that you receive from your doctor.

WHAT WILL BE DONE WITH YOUR SAMPLE?

Part 1: DNA research

You are being asked to agree to test DNA from your blood. The DNA from your blood sample will only be used to test genes related to HIV infection or related to the activity of the drugs used in the study. At any time, you have the right to ask your study doctor for an updated list of genes that are planned to be tested or have already been tested. Following such request, the Sponsor will send an updated list to your study doctor.

Part 2: Storage of DNA Samples

You are being asked by the Sponsor to agree to the storage of your DNA sample. As scientific discoveries are made, valuable research can be done in the future on samples collected today. Therefore, the Sponsor asks your approval to store your DNA sample to allow for more research to be done in the future. If you agree, the Sponsor will remove all direct links to your identity and store your sample for up to 15 years after the clinical study is completed.

Part 3: RNA research

You are being asked to agree to extracting and testing of RNA from your blood. The RNA testing is to see for which genes the activity is changed as a consequence of the disease or the treatment with the drugs under study. The experiments might test the RNA for thousands of genes to see which ones are active. No other testing will be done on your RNA samples.

Part 4: Storage of RNA Samples

You are being asked by the Sponsor to agree to the storage of your RNA sample. As scientific discoveries are made, valuable research can be done in the future on samples collected today. Therefore, the Sponsor asks your approval to store your RNA sample to allow for more research to be

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done in the future. If you agree, the Sponsor will remove all direct links to your identity and store your sample for up to 15 years after the clinical study is completed.

HOW WILL MY IDENTITY AND RESULTS BE KEPT CONFIDENTIAL?

The Sponsor has taken several steps to keep your identity and results confidential. These are described below.

I) DOUBLE CODING OF YOUR SAMPLES

Only your study doctor will know your name and address. Only your study doctor will be able to link you to a study subject number that will be used to identify your data in the clinical study. The samples for DNA and RNA Research will not be labeled with your name, initials, or study subject number, but only with an independent sample number. This double-coded link of your sample number to your name is maintained to allow for the possibility to return your individual results. Also, it allows for the possibility to add newly collected data from the clinical study in the data analysis, which might be important for the interpretation of the results.

II) RESTRICTED ACCESS TO YOUR SAMPLES

Your samples will be stored in a secure room where only authorized staff is allowed to enter. The Sponsor will control your double-coded DNA and RNA samples. Your samples may be transferred to other companies belonging to the Tibotec-Virco group of companies or to research partners working with the Sponsor. Your samples will not be sold, loaned or given to any other independent groups for their own use. Research partners working with the Sponsor are not allowed to share these samples.

III) RESTRICTED ACCESS TO TESTING RESULTS

The Sponsor will store the testing results of the DNA and RNA Research. Your name or study subject number will not be in these records. This is to protect your privacy. The results of the DNA and RNA Research on your sample(s) may be presented in public meetings, published, or added to public databases. However, you will not be identified in any publication or presentation on the results of the research.

Only employees, research partners, or other people hired by the Sponsor who have signed a confidentiality agreement will handle your DNA and RNA test results. The double coding system makes it very difficult for these researchers to make a link back to you. Regulatory authorities (such as the FDA) and members of Institutional Review Boards may also look at your results to make sure the study is properly done. Unless the law requires it, your results will not be given to anyone else who is not listed above. Research partners working with the Sponsor may not use or share your results without permission from the Sponsor.

IV) SEPARATE STORAGE OF DNA AND RNA RESEARCH FORMS

Your study doctor will keep your signed Informed Consent Form for DNA and RNA Research, and any other form related to this DNA and RNA Research part, separate from your other medical files. Regulatory authorities (such as the FDA), members of Institutional Review Boards, study site personnel and authorized representatives of the Sponsor may review these forms. This is to make sure that the study is properly done. By signing this consent form, you are allowing this review.

If you agree to take part in DNA and RNA testing, you will be given a copy of your signed Informed Consent Form for DNA and RNA Research.

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WHAT IF I CHANGE MY MIND LATER?

Your participation is voluntary. If you change your mind and decide that you no longer want to take part in the DNA and RNA Research part, you may ask for your DNA and RNA sample to be destroyed. This can be done at any time. Therefore, you must ask your study doctor for your DNA and RNA samples to be destroyed. Your study doctor will inform the Sponsor in writing, who will then destroy the samples. Still, results from tests already done will not be erased. This is to protect the quality of the research.

Changing your mind to participate in the DNA and RNA Research part will not affect your participation to the clinical study or the usual medical care that you receive from your doctor. It will also not result in any penalty or loss of benefits to which you are entitled.

If you withdraw from the main study, you can also ask to have your DNA and RNA samples destroyed. Again, you must ask your study doctor for this. Otherwise, your sample will be kept and used according to your original consent.

WILL I GET MY DNA AND RNA RESEARCH TEST RESULTS?

The tests will be performed in a research laboratory. Results from a research laboratory may not always be exact. They cannot be used to make a diagnosis about your health. Also, research laboratories cannot give advice on health or health risks. For these reasons, the results of your DNA and RNA tests will not normally be given to you or your study doctor (or his/her staff).

However, you have the right to ask your study doctor in writing for your results. Upon request by your study doctor, the Sponsor will give your test results to your study doctor. This is possible because of the double-coding system of the samples. Your study doctor will be told to keep these results confidential and to store them separate from your other medical files. However, the Sponsor has no control over the privacy of your results after they are sent to your study doctor. The Sponsor cannot give an interpretation of the test results nor provide genetic counseling.

WHAT ARE THE BENEFITS?

You will not directly benefit from taking part in this DNA and RNA Research. This research could provide new scientific information about HIV infection or how the investigated drugs work. Although not of direct benefit for you, this new scientific information could help others in the future.

WHAT ARE THE RISKS?

There may be some pain or bruising from the needle stick used to draw the blood. Some people may faint when their blood is drawn. Very rarely, there may be an infection at the place where the needle went into the skin. Any problem that you have from drawing blood will be handled the same way as described in the main informed consent form for the study.

The research results cannot and should not be used to make a diagnosis about your health. Yet, it is possible that those results could affect you psychologically. For example, tests might reveal a higher risk for a certain disease in you or in your family members.

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WILL I BE PAID FOR TAKING PART OR FOR THE USE OF MY RESULTS?

You will not be paid for taking part in the DNA and RNA Research part of the study. You will not be paid for any use of your DNA or RNA samples, or the results or for any inventions that are made from them. If you take part, you are providing your DNA and RNA samples for use by the Sponsor, but you will not be entitled to any right of ownership in any inventions or profits that might arise from this DNA and RNA Research.

CONTACTS FOR QUESTIONS

For questions about your participation in DNA and RNA research study or a research-related injury, contact:

- Pablo Tebas, MD (215-615-4321)
- 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

This consent form contains important information, to help you decide if you wish to take part in this DNA and RNA Research part of the study. If you still have questions, please ask the study doctor (or his/her staff), before signing this form.

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CRF ID or relevant Subject ID:						

I have read the Informed Consent Form for DNA and RNA Research IC V1 10/2/07. My questions about the study procedures and possible risks have been answered. By putting my initials in the correct box below, I show whether or not I agree to the DNA and RNA Research part in the TMC278-TiDP6-209 study. I have been informed that I should not fill out this form if I do not want to take part.

I voluntarily agree that blood samples are collected and will be used for DNA and RNA research. These samples will not be labeled with my name or study subject number. These samples will only be used to perform DNA and RNA research that aims to better understand how the HIV virus causes the disease, how the drugs used in this study work on the virus and in the human body, and to better understand and predict the (side) effects of these drugs.

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I have indicated below my decision regarding the testing described in this consent form.

Part 1	I DO _____ / DO NOT _____ (initials) (initials)	Voluntarily agree that DNA testing relating to TMC 278 and/or HIV can be done on my blood sample.
Part 2	I DO _____ / DO NOT _____ (initials) (initials)	Voluntarily agree that my DNA sample can be stored. This will allow more tests to be done in the future on other genes that may be related to TMC 278 and/or HIV.
Part 3	I DO _____ / DO NOT _____ (initials) (initials)	Voluntarily agree that RNA testing relating to TMC 278 and/or HIV can be done on my blood sample.
Part 4	I DO _____ / DO NOT _____ (initials) (initials)	Voluntarily agree that my RNA sample can be stored. This will allow more tests to be done in the future on other genes that may be related to TMC 278 and/or HIV.

Printed name of subject, in full

Signature of subject

Date (day/month/year) eg: 15/June/2007

Person obtaining the informed consent:

I confirm that I have explained the nature and purpose of the DNA and RNA Research part of this study and the potential risks and benefits to the subject. The subject indicated whether he/she agreed to participate in the DNA and RNA Research part of this study.

Printed name of person obtaining the informed consent, in full

Signature of person obtaining the informed consent

Date (day/month/year)
e.g. 15/June/2007