

## UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

Tibotec Pharmaceuticals Ltd, TMC278-TiDP6-c209, Version 6-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 (ECHO TRIAL)

CONSENT FORM TO PARTICIPATE IN

A substudy of TMC278-TiDP6-c209 to Evaluate the Effects of Long-Term TMC278 25 mg q.d. and efavirenz Therapy on Body Fat and Bone Mineral Density

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

INTRODUCTION:

You have been asked to participate in a research study with a new study drug called TMC278, which is in development for the treatment of patients who are infected with the HIV-1 virus. In humans, this virus may lead to acquired immune deficiency syndrome (AIDS).

With this form, you are being asked for your consent to take part in an additional part of the clinical study that assesses changes in body fat distribution (amount of fat tissue in trunk, arm and legs) and bone density (meaning how weak or strong the bone is). This is done by a procedure called DEXA-scan. DEXA stands for Dual Energy X-Ray Absorptiometry (low energy x-ray). DEXA-scan is increasingly being used to measure body composition in terms of fat and fat-free mass. It can be used to perform whole-body scans in order to determine the bone and soft tissue composition of the whole body and specific regions such as arms, legs, and trunk. DEXA-scan measures the amount of low energy x-rays that are absorbed by the tissues in your body. Two x-ray energies allow the machine to tell the difference between bone and soft tissue, giving a very accurate estimation of the fat distribution and how dense or strong your bones are.

This consent form contains important information to help you to decide whether or not it is in your best interest to participate in this sub-study. Before you agree to take part in this study, please read this consent form carefully and ask as many questions as you need in order to be sure you understand the study procedures, including possible risks and benefits. If you have questions that are not properly explained or answered in this consent form, someone of the research staff will be available to give you more information.

DESCRIPTION AND PURPOSE OF THE STUDY

At this study center, a sub-study (TMC278-TiDP6-C209subDEXA) is being conducted in addition to the main study TMC278-TiDP6-C209, which is described in a separate Consent Form. The aim of this sub-study is to obtain more detailed information regarding the changes in body fat distribution and bone density. One of the known side effects of long-term antiretroviral treatment is the loss of limb fat. This is particularly the case with protease inhibitors, one class of antiretroviral drugs, but also with efavirenz (EFV), which is being used as comparator in the main study. The results will provide valuable additional information to the results of the main research study.

A total of about 186 subjects who enroll in the main study TMC278-TiDP6-C209 will participate in this sub-study.

TMC278-c209, 06-Aug-2008: Consent form for DEXA Substudy**STUDY PROCEDURES**

You are only eligible for this sub-study if you are enrolled in the main trial TMC278-TiDP6-C209.

This study will last 2 years (96 weeks) and will include having a total of 3 DEXA-scans taken at the following TMC278-TiDP6-C209 visits:

- Visit 2 (baseline) The first scan (baseline scan) will be performed after you successfully completed all screening procedures and prior to the first intake of study medication.
- Visit 11 (Week 48)
- Visit 15 (Week 96)
- If you decide to stop your participation in the main trial before Week 96 but after you have received 64 weeks of treatment you will be asked to complete a final scan.

In exceptional cases it is possible you will be asked to return for a retest DEXA-scan. This can occur when your study doctor is informed that due to technical reasons, the quality of the data is not good for analysis.

For the DEXA-scan, you will be asked to lie without moving on a table, and you will be able to breathe normally throughout the procedure. You will not feel any discomfort during the procedure. A thin, invisible beam of 2 low-dose x-rays passes through your body and is measured by a detector. The scan will take about 20 minutes to perform.

**WILL I GET MY DEXA-SCAN TEST RESULTS?**

Your images will be sent to a central facility identified by the sponsor where they will be reviewed to ensure they are a good quality image. A good quality image means that all of your anatomy is included and that the image is clear and not blurry because you may have moved while the image was taken. Your images will not identify you by name, the same code provided by the sponsor for the main study will be used here to link your images to the procedures you have had done in the main study. Your study doctor will be provided with your results.

**POTENTIAL BENEFITS**

By participating in this substudy you will not have any direct benefit, but we hope the information collected in this substudy will benefit others in the future.

**RISKS**

This research study involves exposure to radiation from DEXA scans and 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.

Even though the x-ray dose from the DEXA-scan is very low, please inform the operator before your test if there is any chance that you might be pregnant, although pregnancy is not allowed in the main study.

TMC278-c209, 06-Aug-2008: Consent form for DEXA Substudy**Reproductive Risks**

You may not take part in this sub-study if you are pregnant, or think that you may be pregnant. If you are pregnant there may be risks to you and the baby that are not known at this time. Women who can get pregnant will be tested for pregnancy during the main study. For more details on the methods of birth control, please check the informed consent of the main study.

**ALTERNATIVES**

The alternative is not to participate in the sub study and just participate in the main study.

**STUDY-RELATED INJURY**

If you have a medical emergency during the study you should go to the nearest emergency room. You may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek therapies outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

In the event that you are hurt or injured as a result of participation in this research study, please contact the investigator listed on page one of this form.

In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise offered from the University of Pennsylvania.

The sponsor will pay for any immediate care and/or treatment beyond what is covered by your health insurance. This agreement to provide free medical treatment does not include treatment for any injury/illness that is not the result of research. No financial compensation other than medical treatment of the injury will be provided.

**COSTS/PAYMENTS**

There will be no cost to you for the 3 DEXA scans.

To compensate you for the additional time for the DEXA scans, you will receive \$25 each time you have a scan. Thus, if you have all the DEXA scans required (3), the maximum compensation you will receive \$75. This compensation is in addition to what is received from the main study. If the study nurse asks you to return for a repeat scan because your first scan was not readable, you will be compensated \$25 for that visit as well.

The investigator/institution will receive a reasonable financial compensation for conducting this study.

**YOUR RIGHTS**

You have the right to ask any questions concerning the potential and/or known hazards of this study at any time. Should you as a result of the participation in this study, be harmed in any way, you will receive appropriate medical treatment.

TMC278-c209, 06-Aug-2008: Consent form for DEXA Substudy

If additional information becomes available during the study that might affect your willingness to continue in this study, you or your legally acceptable representative will be informed in a timely manner.

**CONFIDENTIALITY**

Your signature on this form will give permission for the study staff to collect and use information that can identify you as stated in the main Participant Informed Consent Form and HIPAA Authorization.

All data collected in this sub-study will be handled in the same manner as the data collected in the main study as stated in the main Participant Informed Consent Form and HIPAA.

You are free to withdraw your consent to participate in TMC278-TiDP6-C209subDEXA at any time for any reason. If you withdraw your consent for the sub-study, you may still participate in the main study, TMC278-TiDP6-C209.

All other information described in the Participant Informed Consent for the main study applies to this sub-study.

**QUESTIONS OR PROBLEMS**

For questions about this 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

**CONSENT**

You have read and understood the attached DEXA substudy consent Form (IC V6 14 OCT 2008) and you want to take part in this DEXA-scan sub-study of TMC278 under protocol TMC278-TiDP6-C209SubDEXA.

You were given a copy of this signed and dated Informed Consent Form. You have received an explanation of the nature, purpose, duration and foreseeable effects of this study and of what you will be expected to do. The possible risks and benefits of this study and the alternative therapies available for your illness have been explained to you. You were given enough time and opportunity to inquire about the study and all your questions were answered to your satisfaction.

You have been told that you are free to withdraw from the sub-study at any time for any reason.

You agree that results of the sub-study will be handled in the same manner as in the main study.

You give permission for the study staff to collect and use information that can identify me as stated in the main Participant Informed Consent Form.

You voluntarily consent to participate in this sub-study.

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*IRB Approval*  
From: 11/04/2008  
To: 08/19/2009

TMC278-c209, 06-Aug-2008: Consent form for DEXA Substudy

You have been informed about the risks for women of child bearing potential.

\_\_\_\_\_  
*Subject's Signature*

\_\_\_\_/\_\_\_\_/\_\_\_\_\_  
*Date (DD/MMM/YYYY)*

For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

_____ Authorized subject representative [print]	_____ Authorized subject representative Signature	_____ Date
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Provide a brief description of above person authority to serve as the subject's authorized representative.

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I confirm that I have explained the nature, purpose and foreseeable effects of the study to the subject (and, if applicable) whose name is printed above. The subject consented to participate by his/her personally dated signature.

\_\_\_\_\_  
*Informed Consent Provider's Signature*

\_\_\_\_/\_\_\_\_/\_\_\_\_\_  
*Date (DD/MMM/YYYY)*

\_\_\_\_\_  
*Informed Consent Provider's Name in printing*