UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

Gilead Sciences, Inc
GS-US-264-0110, Amendment 2.0, 5-APR-2011

A Phase 3B, Randomized, Open-label Study to Evaluate the Safety and Efficacy of a Single Tablet Regimen of Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate Compared with a Single Tablet Regimen of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate in HIV 1 Infected, Antiretroviral Treatment-Naïve Adults

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:

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Principal Investigator:	Pablo Tebas, MD	(215) 349-8092
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24 Hour Emergency Number (215) 662-6059 Ask for the Immunodeficiency Program Doctor on call

NEW INFORMATION

This is to provide updated information on one of the possible risks, disease reporting and electronic medical records on this study.

One of the risks stated in the consent form (Other section on page 12) that you have signed is the possibility of viral rebound (increases in HIV-1 levels after having previous results of lowered HIV-1 levels). If you are taking FTC/RPV/TDF STR, and your HIV-1 level when you entered the study was greater than 100,000 copies/mL, then you may have a greater chance of viral rebound occurring.

You will be asked to sign the last page of this consent form to indicate that you have been told about the above information and agree to continue to participate in this study.

INTRODUCTION

You have been asked to volunteer for a clinical research study involving an experimental combination medication, i.e., one pill containing one experimental medication [Rilpivirine (RPV)] and two medications that are approved by the United States Food and Drug Administration (FDA) for the treatment of HIV-1 infection. An experimental drug means that the FDA has not approved it for use for treatment of HIV infection. The two FDA approved medications that are included in the experimental combination tablet are Emtriva® (emtricitabine) and will be referred to in this informed consent form as FTC, and Viread® (tenofovir DF) which will be referred to as TDF. The experimental combination medication will be referred to as FTC/RPV/TDF single tablet regimen (STR) or study drug.

This research study is supported by money from Gilead Sciences. In addition, the person leading this research study receives extra money from other pharmaceutical companies for work that is not a part of this study. These activities may include consulting, advisory boards, giving speeches or writing reports. If you would like more information, please ask the researchers or the study coordinator.

This consent form may contain words you do not understand. Please ask the study doctor or study staff to explain any words or information you do not clearly understand before agreeing to volunteer for this clinical research study.

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

GS 0110: Naive Study FTC/RPV/TDF STR Compared with Atripla

YOUR RIGHTS

This consent form tells you about the study. Your study doctor or study staff will go over this with you and answer any questions you may have regarding this study. If you agree to volunteer, you will be asked to sign and date this consent form. You will be given a copy of the signed and dated consent form to keep.

No one can force you to take part in this study. Even if you agree to participate now, you are free to change your mind. You may stop at any time without penalty or loss of benefits which you would otherwise have.

Before you agree to volunteer, you must understand the purpose of the study, how your participation may help you, any potential risks to you, and what is expected of you during the study.

PURPOSE OF THE STUDY

With an estimated 33.2 million people in the world infected with the virus, HIV is a major medical problem.

The purpose of this study is to see if the combination pill FTC/RPV/TDF is safe and effective in reducing levels of HIV-1 in the blood of subjects who are treatment-naïve (those who have not received any antiretroviral medication). You have been asked to participate in this study because you have HIV and you are treatment-naïve. If you have previously (ever) taken, or are currently taking any antiretroviral medication (medications that fight retroviruses like HIV or hepatitis), you will not be allowed in the study.

The safety and effectiveness of FTC/RPV/TDF will be compared with that of Atripla®, a combination medication containing efavirenz, FTC, and TDF. Atripla® has been approved by the FDA for the treatment of HIV. An approved dose of Atripla® is being used in this study.

The safety and how well these single tablet regimens are tolerated will be determined based on vital signs, physical exams, laboratory tests and questionnaires about your HIV symptoms, HIV treatment, Quality of Life and any problems you might experience during the study.

DESIGN OF THE STUDY

If you agree to participate, you will be one of 700 subjects recruited from about 170 study sites in North America, Europe and Australia. About 7-10 persons are expected to enroll in this study at the University of Pennsylvania.

This is an open-label study, which means that you and your study doctor will know whether you are receiving FTC/RPV/TDF STR or Atripla®. This is a randomized (by chance, like a flip of a coin) study and you will be selected to receive one of the two study treatments listed below:

Study Treatment Arm 1: Single tablet regimen of FTC 200 mg/RPV 25 mg/TDF 300 mg

Study Treatment Arm 2: Single tablet regimen of EFV 600 mg/FTC 200 mg/TDF 300mg (Atripla®)

Once you are confirmed to be eligible to participate in the study, and you state that you want to take part in the study, you will be assigned a subject number.

The randomization for this study is in a 1:1 ratio, which means that your chance of being assigned to Study Treatment Arm 1 is equal to your chance of being assigned to Study Treatment Arm 2. You and your study doctor will know which study treatment arm you are assigned to.

All of your study drug (FTC/RPV/TDF or Atripla®) will be supplied by Gilead Sciences, Inc. (GSI), the Sponsor of this study. FTC/RPV/TDF STR and Atripla® must be stored at room temperature; your study doctor or study nurse will review the proper storage of study drug used in this study with you. It is very important that you take your study drug every day as instructed by the study doctor. **FTC/RPV/TDF STR must be taken once a day at the same time every day with a meal, consisting of approximately 500 kcal. Atripla® should be taken once every day on an empty stomach and preferably at bedtime.**

Examples of a meal consisting of approximately 500 kcal include:

- Yogurt, banana, plain bagel, cream cheese (2 tbsp)
- Eggs (2), bacon or sausage (3), hash browns, orange juice (approx. 1 cup/230 ml)
- Spaghetti with meat sauce (approx. 10 oz/280 g), breadsticks or slices of bread (2)
- Hamburger and French fried potatoes
- Pizza (2 slices), can or bottle of non-diet lemonade/cola/soda (approx. 12 oz/ 330 ml)
- Roast chicken/beef/pork with potatoes/rice, vegetables
- Grilled sausages (2) with bread

DURATION OF THE STUDY

The screening period (the time between the Screening visit and Baseline visit) may last up to 35 days. The screening period may be extended to up to 42 days after the Screening Visit if a certain screening test called a genotype needs to be repeated. You will be treated with the study drug for a minimum of 96 weeks (22 months). During this time, you will be required to visit the clinic at least 15 times. If you are in a country where FTC/RPV/TDF STR is not commercially available following 96 weeks on-study, you will continue to take FTC/RPV/TDF STR and attend visits every 12 weeks until FTC/RPV/TDF STR becomes commercially available or until Gilead Sciences chooses to stop the development of the FTC/RPV/TDF STR

STUDY PROCEDURES

Screening

To help the study doctor determine your eligibility and safety to participate in this study, you need to be seen at the study center within 35 days before the study starts. After you sign the informed consent form and receive a copy of the informed consent form, you will have several screening procedures done. Note that all of the procedures listed below may not be performed if at any point during the evaluation you fail eligibility. These procedures will include:

- An interview about your medical history, including any illnesses or health problems, your history of HIV-1 disease-related events, and prior medications within 30 days.
- Vital signs (blood pressure, temperature, respiratory rate, and heart rate).
- A complete physical examination, weight, and height.
- A urine sample for laboratory tests.

- If you are a female able to become pregnant, a blood pregnancy test will be required. If the blood pregnancy test is positive, you will not be eligible to participate in the study.
- If you are a female and are post-menopausal, a blood test will be required to confirm your post-menopausal status.
- About 21 mL (about 4 teaspoons) (5 mL = 1 teaspoon) of blood will be taken for general health screening tests and tests related to your HIV, such as chemistry, complete blood count, CD4+ (white blood cell that fights infection) cell count, tests for hepatitis B virus, hepatitis C virus, and to measure the amount of HIV-1 in your blood.
- About 6 mL (about 1 teaspoon) of blood will be drawn for an HIV-1 genotype test. Genotype testing is a technique that finds changes or "mutations" in certain regions of the HIV-1 gene. Some mutations can prevent certain anti-HIV drugs or drug regimens from reducing the level of HIV-1 in your blood. When this occurs, the HIV-1 has become "resistant" to that drug and possibly other similar drugs. Your screening time may be extended to 42 days if your study doctor requires you to repeat the genotype test.
- A 12-lead ECG (electrocardiogram) to check the functioning of your heart.
- Questions regarding any change in your health (illness or health problems) and whether you have taken any new medications since you signed this informed consent form.

The study doctor will review all of your medical information and findings from your Screening visit (including medical history, medications, clinical laboratory results, physical exam, etc.) and other entry criteria, as required by the study protocol, to determine if you are eligible to participate in this study.

Restrictions During the Study

- You will be told not to eat or drink anything except water for at least 8 hours before your blood is drawn at the Baseline Visit, Weeks 24, 48, 72, and 96.

- You must check with the study doctor before taking any medication or health supplements for the length of the study.

- You must agree to use contraception and not become pregnant while on this study. Please see the PREGNANCY section on page 11 of this consent for more details.

Baseline/Day 1

You will be asked to come back to the study center within 35 days after the Screening visit for the "Baseline" (Day 1) visit. The following procedures will occur during this visit:

- You will be asked whether there has been any change in your health (illness or health problems) and whether you have taken any new medications since your last visit.
- Vital signs (blood pressure, temperature, respiratory rate, and heart rate).
- Read and complete a questionnaire regarding your quality of life, as well as a questionnaire regarding your HIV symptoms.
- A complete physical examination and weight.
- A urine sample for laboratory tests. If you are a female able to become pregnant, a urine pregnancy test will be required. If the urine pregnancy test is positive, you will not be dispensed study drug at this visit. You will have a blood pregnancy test to confirm the result of the urine pregnancy test. If the blood test is positive, you will not be allowed to participate in this study.

- About 21 mL (about 4 teaspoons) of blood will be taken for testing of chemistry, complete blood count, CD4+ cell count and to determine HIV-1 levels in your blood.
- Tests on blood being drawn at this visit will be used to measure changes in the amount of sugar and fats in your blood. About 4 mL (about 1 teaspoon) of blood will be taken for this test. It is important that your blood is drawn for this sample in the morning prior to eating (in a fasting state). If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state. "Fasting" means that you will not eat or drink anything except water for at least 8 hours before your blood is drawn.
- About 17 mL (about 3.5 teaspoons) of blood will be collected to determine the amount of study drug in certain types of your blood cells called peripheral blood mononuclear cells (PBMCs).
- About 10 mL (about 2 teaspoons) of blood will be collected and stored to allow the possibility of conducting clinical tests at a later date (for example, to check whether the HIV in your blood can develop resistance to this anti-HIV study drug).
- You will be counseled regarding the importance of taking all medications as directed.
- You will receive a 4-week supply of study drug at this visit.

Week 4 to Post Week 96

You will be asked to return to the clinic for study visits at Weeks 4, 8, 12, 16, 24, 32, 40, 48, 60, 72, 84, and 96. After the Week 96 visit, you will be asked to either complete a 30-day follow-up visit or continue coming in for study visits every 12 weeks until FTC/RPV/TDF STR is commercially available in your country. The following procedures will occur during these visits:

- You will be asked whether there has been any change in your health (illness or health problems) and whether you have taken any new medications since your last visit.
- Vital signs (blood pressure, temperature, respiratory rate, and heart rate).
- Read and complete questionnaires regarding your HIV symptoms and study treatment adherence.
- Read and complete questionnaires about your HIV study treatment satisfaction and quality of life (Weeks 24, 48, 72, and 96).
- A physical examination and weight (a complete physical examination will be performed at Weeks 24, 48, 72, and 96; a symptom-directed physical examination may be performed at all other visits as needed).
- A urine sample for laboratory tests.
- If you are a female able to become pregnant, a urine pregnancy test will be required. If the urine pregnancy test is positive, you will be given a blood pregnancy test to confirm the results. If the blood pregnancy test is positive, you will be discontinued from the study.
- About 18 mL (about 4 teaspoons) of blood will be taken for testing of chemistry, complete blood count, CD4+ cell count, and to determine HIV-1 levels in your blood.
- Tests on blood being drawn at Weeks 24, 48, 72, and 96 to measure changes in the amount of sugar and fats in your blood. About 4 mL (about 1 teaspoon) of blood will be taken for this test. It is important that your blood is drawn for this sample in the morning prior to eating (in a fasting state). If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state.
- A 12-lead ECG (electrocardiogram) to check the functioning of your heart at Weeks 48 and 96.
- About 10 mL (about 2 teaspoons) of blood will be collected and stored to allow the possibility of conducting clinical tests at a later date (for example, to check whether the HIV in your blood can develop resistance to this anti-HIV study drug).

- About 17 mL (about 3.5 teaspoons) of blood will be collected to determine the amount of study drug in certain types of your blood cells called peripheral blood mononuclear cells (PBMCs) (weeks 24, 48, and 96).
- If you do not appear to be responding properly to the study drug, you will be required to return to the clinic for an unscheduled or scheduled visit to confirm whether or not you are truly failing your study treatment. Approximately 12 mL (about 2 ½ teaspoons) of blood will be drawn during this visit to measure the amount of HIV-1 in your blood and for genotype/phenotype testing. Phenotype testing is a technique used to determine whether a mutation in the HIV-1 gene changes how anti-HIV drugs affect the HIV-1 virus. The study doctor will then decide whether or not a change to your study treatment regimen is required.
- You will receive a 4-week supply of study drug at Weeks 4, 8 and 12 visits. You will receive an 8-week supply of study drug beginning at the Week 16 visit and continuing every 8 weeks until the Week 40 visit. Starting at week 48 you will receive a 12-week supply of study drug until week 96. If you are continuing on the study after Week 96 because FTC/RPV/TDF STR is not yet commercially available in your country, you will receive a 12-week supply of study drug at each visit.
    - **If you are taking FTC/RPV/TDF, your study drug must be taken <u>with a meal, consisting of approximately 500 kcal</u>.**
    - **If you are taking Atripla®, your study drug must be taken at bedtime <u>on an empty stomach</u>.**
- You will be counseled regarding the importance of taking all study drugs.
- You will be required to bring your used and unused FTC/RPV/TDF STR or Atripla® drug bottles back to the clinic at each visit. The study drug (number of tablets) will be counted. You will be asked about any missed doses since your last visit.

SUMMARY TABLE FOR ON STUDY EVALUTIONS

	4	8	12	16	24	32	40	48	60	72	84	96
Clinical assessment, including vital signs and symptom evaluation	x	x	x	x	x	x	x	x	x	x	x	x
Complete physical exam					x			x		x		x
HIV symptoms and Adherence Questionnaire	x	x	x	x	x	x	x	x	x	x	x	x
Study treatment satisfaction and Quality of Life Questionnaire					x			x		x		x
Urinalysis; Urine Pregnancy test females	x	x	x	x	x	x	x	x	x	x	x	x
Blood tests (chemistry, complete blood count, CD4, VL)	x	x	x	x	x	x	x	x	x	x	x	x
Fasting blood tests for sugar and fats					x			x		x		x
ECG								x				x
Blood for storage for future tests	x	x	x	x	x	x	x	x	x	x	x	x
Blood to test for levels of study drug					x			x				x
Dispensing of Medication; pill counts and adherence counseling	x	x	x	x	x	x	x	x	x	x	x	x

<u>Early Study Drug Discontinuation Visit</u>

If you discontinue study drug at any time before the study is complete, you will be asked to return to the study center within 72 hours of stopping study drug. You will be asked to continue attending the scheduled study visits through the Week 96 visit. Procedures at this visit will include:

- You will be asked whether there has been any change in your health (illness or health problems) and whether you have taken any new medications since your last visit.
- Vital signs (blood pressure, temperature, respiratory rate, and heart rate).
- Read and complete a questionnaire about your HIV symptoms, study treatment satisfaction, quality of life, and study treatment adherence.
- A complete physical examination and weight.
- A urine sample for laboratory tests.
- If you are a female able to become pregnant, a urine pregnancy test will be required. If the urine pregnancy test is positive, you will be given a blood pregnancy test to confirm the results.
- About 18 mL (about 4 teaspoons) of blood will be taken for testing of chemistry, complete blood count, CD4+ cell count, and to determine HIV-1 levels in your blood.
- A 12-lead ECG (electrocardiogram) to check the functioning of your heart.
- About 10 mL (about 2 teaspoons) of blood will be collected and stored to allow the possibility of conducting clinical tests at a later date (for example, to check whether the HIV in your blood can develop resistance to this anti-HIV study drug).
- About 17 mL (about 3.5 teaspoons) of blood will be collected to determine the amount of study drug in certain types of your blood cells called peripheral blood mononuclear cells (PBMCs).
- You will be required to bring your used and unused study drug bottles back to the clinic.

30-Day Follow-Up visit

You should return for an Early Study Drug Discontinuation visit or a 30-Day Follow-Up visit at the clinic in the following cases:

- If you permanently discontinue study drug prior to Week 96 and refuse to continue in the study through the Week 96 visit.
- If you complete the study through Week 96 and FTC/RPV/TDF STR is commercially available in the US.

- You will **not** be asked to return for a 30-Day Follow-Up visit after the completion of study drug in the following cases: If you continue to attend regularly scheduled study visits after you discontinue study drug.
- If you complete the study through Week 96 and FTC/RPV/TDF STR is **not** commercially available in the US. You will be asked to continue in the study until FTC/RPV/TDF STR becomes commercially available or until Gilead Sciences elects to terminate clinical development of the FTC/RPV/TDF STR.

Procedures at this visit will include:

- You will be asked whether there have been any changes in your health (illness or health problems) and whether you have taken any new medications since your last visit.
- A symptom-directed physical examination and weight.
- Vital signs (blood pressure, temperature, respiratory rate, and heart rate).
- A urine sample for laboratory tests.

- If you are a female able to become pregnant, a urine pregnancy test will be required. If the urine pregnancy test is positive, you will have a blood pregnancy test to confirm the result.
- About 18 mL (about 4 teaspoons) of blood will be taken for chemistry, complete blood count, CD4+ cell count, and to determine HIV-1 levels in your blood.

STORAGE and FUTURE USE OF BLOOD SAMPLES

A portion of your blood sample drawn (including the cells contained within it) at some visits will be frozen and stored. These stored blood samples may be used by the Sponsor or its research partners for HIV-1 genotyping/phenotyping assays or their development, for retesting the amount of HIV-1 in your blood, for measurement of antiviral study drug levels in the blood, for future testing to learn more about how the study drug has worked against HIV-1 or clinical laboratory testing to provide additional clinical data. No human genetic testing will be performed without your expressed consent. At the conclusion of this study, these samples may be retained in storage by Gilead Sciences, Inc. for a period up to 10 years.

Genotype testing detects changes or "mutations" in certain genetic regions of the HIV-1 virus. Phenotype testing is used to determine whether a mutation in an HIV-1 gene changes how anti-HIV drugs affect the HIV-1 virus. Some mutations can prevent certain anti-HIV drugs or drug regimens from reducing the level of HIV-1 in your blood. When this occurs, the HIV-1 has become "resistant" to that drug and possibly other similar drugs.

RISKS AND BENEFITS

The medications (FTC, TDF) given in this study are part of a combination tablet, it is important to know that you should not take any of the individual components in addition to the combination tablet.

FTC/RPV/TDF

FTC/RPV/TDF is a fixed-dose single tablet regimen containing three medications: rilpivirine (RPV), Emtriva® (FTC), and Viread® (TDF).

To date, 99 healthy subjects have been dosed with the FTC/RPV/TDF STR in three Phase 1 clinical studies.

Side effects on the individual components of FTC/RPV/TDF are described below:

RPV

The safety assessment is based on 1,368 subjects in the controlled trials TMC278-C209 and TMC278-C215 in antiretroviral treatment-naïve HIV-1 infected adult subjects. Of these subjects, 686 received RPV 25 mg once daily in combination with other antiretroviral medicinal products.

Common adverse events reported were depression (3.5%), unable to sleep (2.9%), headache (2.6%), increase of liver enzymes that may affect your liver function (2.5%), rash (2.2%), abnormal dreams (1.5%), stomach pain (1.3%), feeling tired (1.3%), problems with sleep (1.2%), decreased appetite (1.2%), and nausea (1.2%). Additionally, other uncommon adverse events reported were vomiting (0.9%), dizziness (0.7%), drowsiness (0.6%), depressed mood (0.4%), and stomach discomfort (0.4%). One subject (0.1%) receiving rilpivirine experienced mild immune reconstitution syndrome. This is a condition that can happen in some patients with advanced HIV infection (AIDS) who start anti-HIV treatment. Even though your HIV comes under control, an infection that you previously had might return or you may

develop a new disease. This is linked to improvements in your immune system. Fever and swollen lymph nodes are some of the signs and symptoms.
Call your study doctor right away if you notice any signs or symptoms of an infection after starting study medication.

Fat Redistribution
Combination antiretroviral therapy has been associated with redistribution of body fat (lipodystrophy) in HIV infected patients, including fat loss that can occur in the arms, legs, or face (sunken cheeks), fat deposits that can show up in the stomach, the back of the neck (a "buffalo hump"), the breast (in both men and women), and other areas. Additionally, metabolic changes can include increases in blood fats (cholesterol and triglycerides) or lactic acid and insulin resistance. Too much lactic acid and insulin resistance can cause serious health problems leading to lactic acidosis and diabetes.

FTC
The most common side effects seen in patients treated with FTC in combination with other anti-HIV drugs are: headache, diarrhea, nausea, and rash, which were generally mild. Other common side effects with FTC include dizziness, changes in skin color primarily on the palms and/or soles, weakness, difficulty sleeping, abnormal dreams, pain, vomiting, stomach pain, problems with digestion resulting in gastrointestinal discomfort after meals, increased triglycerides (fatty acid), increased bilirubin in the blood, increased glucose in the blood, allergic reaction, hives, adverse effects on the function of the liver and pancreas, and low white blood cell count. A reduction in your white blood cell count can make you more prone to infection. You may also experience increased creatine kinase in the blood. If creatine kinase is increased, you may experience muscle pain and weakness.

Additionally, cases of lactic acidosis (high levels of lactic acid in the blood), liver problems with enlargement of the liver and fat in the liver, including fatal cases, were reported in HIV-infected patients treated with anti-HIV agents similar to FTC. The symptoms of lactic acidosis include: weakness, unexpected and uncommon abdominal pain, nausea and vomiting. Symptoms of liver problems include; yellowing of the skin or whites of the eyes, dark urine, light-colored bowel movements, loss of appetite, nausea and lower abdominal pain. If you notice any of these symptoms, please request medical assistance immediately.

Please talk to your study doctor for more details on side effects or refer to the FTC package insert for additional information.

TDF
TDF has been studied in approximately 12,000 HIV-infected adults for as long as 204 weeks in some patients. Common potential side effects identified in patients who received at least one dose of tenofovir DF 300 mg include diarrhea, nausea, vomiting, flatulence (intestinal gas), and dizziness. Those side effects were often mild or moderate in severity, and did not lead to discontinuation of TDF.

In addition to side effects reported from clinical trials the following side effects have also been indentified after TDF was approved in HIV-infected patients treated with combination therapy that has included TDF and other anti-HIV drugs: weakness, abdominal pain, allergic reaction including potentially serious swelling of the face, lips, and/or tongue, with or without rash, pancreatitis (inflammation of the pancreas), high levels of amylase in the blood, shortness of breath, rash, abnormalities of tests that measure hepatic (liver) function and hepatitis (inflammation of liver).

Cases of lactic acidosis (high levels of lactic acid in the blood), liver problems with enlargement of the liver and fat in the liver, including fatal cases, were reported in HIV-infected patients treated with anti-retroviral agents similar to TDF. The symptoms of lactic acidosis include: weakness, unexpected and uncommon abdominal pain, nausea and vomiting. Symptoms of liver problems include yellowing of the skin or whites of the eyes, dark urine, light colored bowel movements, loss of appetite, nausea and lower abdominal pain. If you notice any of these symptoms, please request medical assistance immediately.

Cases of kidney damage have been reported in patients taking TDF who already have circulatory disease or specific kidney disease, and patients who, while receiving tenofovir DF, were also taking medications that may cause damage to the kidneys. Kidney damage has also been reported in patients without any of these factors. For example, some patients have had damage to the structure and function of the kidneys, which may lead to muscle abnormalities, muscular weakness, destruction of muscle tissue, bone pain and fractures due to softening of bones, and low potassium and phosphate in the blood. In addition, death of kidney tissue, continuous or sudden kidney failure, abnormal kidney function, inflammation of the kidneys, protein in the urine, excessive urination, nephrogenic diabetes insipidus (excretion of urine resulting in dehydration and thirst), and increased creatinine in the blood have also been reported in patients taking TDF.

Bone toxicity, including a decrease in bone mineral density, was seen in animals following treatment with TDF. Decreases in bone mineral density have been seen in humans. These types of changes may increase the risk of bone fractures, although this has not been seen in human studies.

Because these events have been reported voluntarily from a population of unknown size, estimates of frequency cannot be made.

If you are infected with hepatitis B virus (HBV), there is a possibility of an unexpected worsening of hepatitis B if you stop taking TDF.

Please talk to your study doctor for more details on side effects or refer to the TDF package insert for additional information.

FTC/TDF
Please refer to the FTC and TDF side effects described above for side effects associated with Truvada®, a combination medication containing FTC and TDF.

Atripla®
Please refer to the FTC and TDF side effects described above for side effects associated with Atripla®, a combination medication containing FTC and TDF.

EFV
The most common side effect reported in clinical trials of EFV was rash. Rashes usually go away without any change in treatment. In a small number of patients, rash may be serious. If you develop a rash, call your study doctor right away. Other side effects including insomnia, abnormal dreams, trouble concentrating, dizziness, headache, and drowsiness, and are commonly reported during the first weeks of therapy with EFV.

Dosing at bedtime may improve the tolerability of these symptoms, which are likely to improve with continued therapy. Tell your study doctor right away if any of these side effects continue or if they

bother you. It is possible that these symptoms may be more severe if efavirenz is used with alcohol or mood altering (street) drugs. If you are dizzy, have trouble concentrating, or are drowsy, avoid activities that may be dangerous, such as driving or operating machinery. Other common side effects include anxiety, depression, diarrhea, nausea, vomiting, tiredness, stupor, and changes in thinking. A small number of patients may experience strange thoughts or angry behavior while taking efavirenz. Some patients have thoughts of suicide, and a few have actually committed suicide. These problems may occur more often in patients who have had mental illness. Tell the study doctor if you have thoughts of hurting or killing yourself.

Other uncommon side effects include hypersensitivity (allergic reaction), emotional lability (mood swings), sense of elation, hallucination, manic reactions, paranoid reactions, confusion, agitation, amnesia (memory loss), ataxia (unsteadiness when walking), abnormal coordination, vertigo (sensation of spinning), and hepatitis.

Other side effects that have been reported with the use of EFV include psychosis (mental illness), delusion, neurosis, tremor, convulsions, blurred vision, tinnitus (buzzing in ears), inflammation of the pancreas, abdominal pain, liver failure, photosensitivity (increased sensitivity of the skin to the sun), itchiness, flushing, and gynecomastia (development of breast tissue in males).

There is a remote risk of Stevens-Johnson Syndrome which is an uncommon, potentially fatal condition that may begin with flu-like symptoms, such as headache, fever, cough, and body aches, and then progress to a more serious condition with rash, blistering and sloughing of the outermost layer of skin, burning eyes, visual impairment and blindness. Tell the study doctor right away if you experience any of these symptoms.

Because of possible serious and life-threatening side effects when taking Atripla® with other medications, including those you take without a prescription, tell your study doctor about all the medications you are taking or planning to take, including any herbal supplements such as St. John's Wort.

Please talk to your study doctor for more details on side effects or refer to the Atripla package insert for additional information.

Immune Reconstitution Syndrome

A condition called immune reconstitution syndrome can happen in some patients with advanced HIV infection (AIDS) when combination anti-HIV treatment is started. Signs and symptoms of inflammation from opportunistic infection that a person has or had may occur as the medicines work to control the HIV infection and strengthen immune system. Autoimmune disorders such as Grave's disease (an autoimmune disease in which the thyroid is overactive, producing an excessive amount of thyroid hormones), polymyositis (a persistent inflammatory muscle disease that causes weakness of the skeletal muscles, which control movement) and Guillain-Barre syndrome (a serious disorder that occurs when the body's immune system mistakenly attacks part of the nervous system, leading to nerve inflammation that causes muscle weakness) have also been reported to occur in the setting of immune reconstitution, however, the time to onset is more variable, and can occur many months after initiation of treatment.

Call your study doctor right away if you notice any signs or symptoms of an infection after starting study medication.

Allergic Reaction Risks
As with taking any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash.
- Difficulty breathing.
- Wheezing.
- Sudden drop in blood pressure.
- Swelling around the mouth, throat or eyes.
- A fast pulse.
- Sweating.

Please seek treatment and alert the study doctor and study staff immediately if you have any of these symptoms, or any other side effects, during the study.

Blood Draws
In addition to risks associated with the study drug, drawing blood from a vein may cause local pain, bruising, occasional lightheadedness, fainting, and very rarely, infection at the site of the blood draw.

ECG
After you have an ECG, you may have mild irritation, slight redness, and itching at the places on your skin where the recording patches are placed. You may have to have your chest shaved for this procedure.

Hepatitis B and C Testing Risks
At the Screening visit, you will be tested for hepatitis B and C, and the results of these tests may be reported to your local health authority. You will be told, face-to-face, the results of these tests. Counseling will be available to you if necessary.

Other
As with all drugs, unexpected or yet unknown side effects may occur. Any new information that becomes known during the study and that may affect your participation will be shared with you by your study doctor.

Viruses, which are resistant to the study drug, may develop during the course of study treatment. This may reduce your treatment options in the future. Throughout the study, your study doctor will monitor your HIV-1 levels for viral rebound (increases in HIV-1 levels after having previous results of lowered HIV-1 levels). If you are taking FTC/RPV/TDF STR, and your HIV-1 level when you entered the study was greater than 100,000 copies/mL, then you may have a greater chance of viral rebound occurring. Resistant mutations develop most rapidly in people who do not take their HIV-1 drug consistently. Therefore, it is important to take your study drug as prescribed by your study doctor.

You may have a side effect that requires your study doctor to end your participation in the study. You should contact your study doctor immediately if you feel that you cannot tolerate your study drug regimen.

Possible Benefits of the Study
There is no guarantee that you will receive personal benefit from participating in this study. The study drug is not expected to cure you of HIV. However, clinical research studies such as this are a way for

doctors to determine if a drug is useful in fighting a disease. By participating in this study, you and the Sponsor, Gilead Sciences, Inc., may benefit if FTC/RPV/TDF STR is effective in treating HIV-1 infection. In addition, previous studies have demonstrated that single tablet regimens have better adherence. Good adherence means that less doses are missed and therefore, your HIV may be better controlled. Your participation in this study may benefit the community, scientists and doctors who work with HIV by providing increased knowledge and information about the treatment of your disease. In addition, during your participation you will have close medical monitoring of your health condition by blood tests and other evaluations during clinic visits.

PREGNANCY AND BREAST FEEDING

The effects of FTC/RPV/TDF STR and Atripla® have not been fully evaluated on the developing fetus in humans. Animal studies do not indicate direct or indirect harmful effects of RPV, FTC, and TDF with respect to pregnancy. The effects of some anti-HIV medications (including the drug EFV, which is one of the drugs found in Atripla®) may be harmful to unborn babies. Changes have been seen in animals, and a small number of reports of neural tube defects (a problem with development of the spine and/or brain) in babies of women who were taking efavirenz in the early part of their pregnancy have been reported, but it is not certain that efavirenz was the cause.

Because the effects of FTC/RPV/TDF STR and Atripla® on a developing fetus as well as on exposed infants are unknown, any female able to become pregnant (i.e., a female subject of childbearing potential is a nonmenopausal female who has not had a hysterectomy, bilateral oophorectomy, or medically documented ovarian failure. This definition includes a young woman who has not yet started menstruating) must have a negative blood pregnancy test to enroll; females who are breast-feeding will not be enrolled in this study.

It is very important while you are in this study that you do not become pregnant if you are a female, or do not cause others to become pregnant if you are a male. Not having sex is the only certain way to prevent pregnancy.

Male subjects and female subjects of child-bearing potential and sexually active must agree to utilize protocol recommended methods of contraception during heterosexual intercourse from the screening visit throughout the study and for 12 weeks following the last dose of study drug.

Protocol recommended methods of contraception in this study are: 1)a combination of one hormonal method and one barrier method; (2) two barrier methods where one method is the condom; or (3) use of an IU, tubal sterilization or vasectomy and one barrier method , or be non-heterosexually active, practice sexual abstinence.

Acceptable hormonal methods include: injectable progesterone, progesterone implants, combination oral contraceptives, transdermal patch, and vaginal ring. Acceptable barrier methods include: diaphragm (with spermicide), cervical cap (with spermicide), and the condom. Female subjects must use either a hormonal method or a barrier method if the partner has a vasectomy. Female subjects who utilize hormonal contraceptives as one of their birth control methods must have used the same method for at least 3 months before study dosing. Hormone-based contraceptives may not be effective at preventing pregnancy when they are used with FTC/RPV/TDF STR and Atripla®. Please speak with your study doctor to determine the best method of birth control for you to use during this study.

Protocol-Recommended Contraceptive Methods

Contraception Combination Methods

Hormone Methods (choose one and use with a barrier method)	Barrier Methods (use both OR choose one and use with a hormone method OR other method)	Other Methods (choose one and use with a barrier method)
Estrogen and Progesterone • Oral contraceptives • Transdermal patch • Vaginal ring Progesterone • Injection • Implant	• Diaphragm with spermicide OR Cervical cap with spermicide • Condom (with or without spermicide)	Intra-uterine devices (IUDs) • Copper T 380A IUD • LNg 20 IUD • Tubal sterilization • Vasectomy

Even if you use highly effective birth control methods, you could still become pregnant. There is a slight chance that a pregnancy test could be wrong. If the pregnancy test is wrong, and you receive the study drug while pregnant, the study drug may harm an unborn baby.

If you are female and become pregnant or suspect that you have become pregnant while in the study and within 30 days of last dose of study drug, you will be required to stop taking the study drug and to notify your study doctor immediately. You will be discontinued from the study. The study doctor will request to track your pregnancy and will report the pregnancy and outcome to Gilead.

Other not yet identified side effects could occur to you, your embryo or fetus should you become pregnant during the time you participate in the study or after you have completed the study.

CONDOM USE

It has been proven that condom use decreases the risk of spreading HIV and hepatitis B between sexually active individuals. To decrease your risk of transmitting the virus to another individual and to decrease the risk of being infected with a different strain of HIV, we recommend that condoms be used for all sexual activity to include oral, vaginal, and anal sexual contact. Condom use is recommended in addition to your current form of birth control.

TREATMENT OPTIONS

You have the option to discuss with your study doctor not to have treatment or to choose other anti-HIV drugs to treat your disease. These medicines include commercially available medicines. Your study doctor will discuss appropriate alternative treatment options with you. You will be made aware of any new findings that become available during the course of the study that may affect your willingness to participate in this study

STATEMENT ABOUT PRIVACY

Records identifying you will be kept confidential and, to the extent permitted by applicable laws and/or regulations, will not be made publicly available. Your personal information may be given out if required by law. If you test positive for HIV, by law we have to report the infection to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born. This is to keep track of how many people in the U.S. have HIV infection. It is also to make sure that states get enough money from the federal government to support the medical care of people living with HIV. The Health Department does not share the names of HIV infected people with anyone else. It removes all personal identifiers, such as your name, before giving information on the number of HIV infections to the federal government. Please note that it is likely that this information has been already reported to the PA Health Department as the HIV test being done for this study is not the first test for you. In the event of any publication regarding this study, your identity will remain confidential.

Representatives from government agencies, including the U.S. Food and Drug Administration ("FDA"), institutional review boards, the Sponsor and/or the Sponsor's authorized representatives may need access to your original medical records and study records for the purpose of checking data collected for the study. By signing this consent form, you authorize this access.

To ensure that your information collected for this study will be kept private, your name will not be used whenever possible. A code will be used instead of your name. All of your study data will be kept in a secure location.

Your coded study information and samples may also be used for additional unanticipated medical and/or scientific research projects in the future relating to HIV-1 or the development of the FTC/RPV/TDF (but at all times in compliance with applicable law and regulation).

As explained in this consent form, study treatment in this study is randomized and "open-label" so you and your Study Doctor will know which study treatment arm you are assigned to. By signing this consent form you agree that you will not be able to have access to information about your participation in the study until the study is over. After that, you can obtain access to your information through your Study Doctor.

AUTHORIZATION TO USE AND DISCLOSE RECORDS

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 personal health information is collected and used in this study and might also be disclosed?

The following personal health 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
- Social Security Number (if you receive more than $600 for participating in studies at PENN, we will need your SSN for the W-9)
- Personal and family medical history
- Current and past medications or therapies
- Results of physical exams, laboratory tests and procedures you will undergo during this research

study

Why is your personal contact and health information being used?
Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study. In some situations, your personal health information might be used to help guide your medical treatment.

Which of our personnel may use or disclose your personal health information?
The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).

Who, outside of UPHS and the School of Medicine, might receive your personal health information?
As part of the study, the Principal Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

Individuals or organizations responsible for administering the study:

- Pharmaceutical sponsor (Gilead Sciences): This is the company that supplies drugs for the study. Information regarding safety and adverse effects needs to be collected and monitored.
- Contract Research Organization: Monitors will visit the site on a regular basis to review data and assure accuracy and completeness of information before the data are analyzed.

Regulatory and safety oversight organizations

- The Food and Drug Administration
- The Office of Human Research Protections
- The Study Monitoring Committee

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations. Data are reported to the sponsor on Case Report Forms that identify you by your unique study number and not your name, date of birth or medical record number. Information regarding your health, such as side effects of the study medications you experience will be reported only by code number. All samples collected for analysis will be labeled with your study number, visit number and date of your visit.

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 UPHS and the School of Medicine be able to use or disclose your personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research repository (database). However, UPHS and 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 to do so
- The University of Pennsylvania's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted by law

Will you be able to access your records?
During your participation in this study, you might not be able to access some or all of your medical records. For example, access to portions of your medical records may be denied in studies where your knowledge of study results included in such records could affect the reliability of the study. You will have access to your medical record information when the study is over or earlier, if possible. The Principal Investigator is not required to release research information to you that is not part of your medical record.

Can you change your mind?
Yes, at any time you may withdraw your approval to allow the use and disclosure of your personal health information as described here. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study.

If you withdraw your permission to use any blood or tissue obtained for the study, the Sponsor may need to retain and use any samples that have already been collected to comply with its legal obligations and to maintain the scientific integrity of the study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. You will also be given the UPHS and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your personal health information.

WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE
Special care will need to be taken when determining if you need to stop the study drug. Your study doctor will supervise any discontinuation of the study drug with your health as the first priority. Your participation in this study may be stopped at any time by a) your study doctor, b) Gilead Sciences, Inc., c) the FDA, d) the Institutional Review Board (a review group that gives approval to your study doctor to conduct this study), and (e) other appropriate regulatory agencies.

Your participation in this clinical research study is voluntary, and you can refuse to participate or stop at any time without stating a reason. Your withdrawal will not affect your access to other medical care.
Your study doctor may withdraw you from the study if it is considered important for your medical safety. If it is learned that you did not give an accurate medical history or did not follow the instructions for the study given by your study doctor and/or study nurse, you may be taken off the study at any time. If you are taken off the study, you will no longer receive the study drug.

COST OF TREATMENT

The FTC/RPV/TDF STR and Atripla® used in this study will be given to you free of charge. All clinic, professional, diagnostic, and laboratory fees for tests and procedures that are part of this study will be provided at no cost to you. You or your usual health care payer will be responsible for any other health care costs.

STUDY STAFF PAYMENT

Gilead Sciences, Inc. Is paying the study doctor and study staff for their work in this study

PAYMENT FOR PARTICIPATION

You will be paid $25.00 for your screening visit. For visits thereafter, Baseline, 12 visits through week 96 1, you will be paid $50 for every visit you attend. Thus if you attend all required visits for the study, the maximum payment you can receive is $675. If the drug is not commercially available by the end of the study, the study may continue until it is available through your doctor or Gilead discontinues its development. If this is the case, you will continue to receive $50 for every visit you attend for the study. If you need to come in for an unscheduled visit that is requested by the study staff, you also will be paid $10 for that visit. The total payment you will receive for the study depends on how long you participate.

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 an Individual Tax Identification Number or Social Security Number for tax purposes.

COMPENSATION FOR STUDY-RELATED INJURY

If you are injured or become sick as a direct result of taking the study drug and/or following the study procedures, University of Pennsylvania will provide you with medical treatment. The Sponsor, Gilead Sciences, Inc., will reimburse you or the University of Pennsylvania for the reasonable and necessary costs of such medical treatment, *provided* that you have followed the instructions of the Study Doctor. No other form of reimbursement for study-related injury or illness is offered by the Sponsor. You do not give up any legal rights by signing this form. You should immediately contact your Study Doctor at the contact information shown on the first page of this form in the event you experience any study-related illness or injury.

WHAT IS AN ELECTRONIC MEDICAL RECORD?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance

you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

SOURCE FOR ADDITIONAL INFORMATION

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

AGREEMENT TO BE IN THE STUDY

This Subject Information and Informed Consent Form contain important information to help you decide if you want to be in this study. If you have questions that are not answered in this form, please ask one of the study staff. Please answer the following questions by placing your **initials** in the line for **"Yes"** or **"No"**.

1. Have you had the opportunity to ask questions and discuss the study?	___ Yes ___ No
2. Have you received answers you find acceptable to all of your questions?	___ Yes ___ No
3. Have you received enough information about the study to make an informed decision?	___ Yes ___ No
4. Have you been told you are free to stop the study at any time without having to give a reason and without affecting your medical care?	___ Yes ___ No
5. Have you been told that your medical records may be reviewed and how the information will be used?	___ Yes ___ No
6. Do you agree to have your personal information collected during this study and blood samples stored for future commercial research related to the study treatment, prevention or diagnosis of HIV-1?	___ Yes ___ No
7. Have you been told that you will not have any rights to any discovery or inventions which result from future research and you will not receive any financial compensation in connection with any future research?	___ Yes ___ No

If you answered NO to any of the seven questions listed above you should not sign this form. Once you have had all your questions answered and you are comfortable participating in this study, please sign

below.

By signing and dating this form you agree that you are volunteering to be in this study.

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.

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

_____ ____/____/____
Signature of Research Subject Date

_____
Printed Name of Research Subject

STATEMENT OF PERSON EXPLAINING CONSENT

I have carefully explained to the subject the nature and purpose of the above study. There has been an opportunity for the subject to ask questions about this research study. I have been available to answer any questions that the subject has about this study.

_____ ____/____/____
Signature of Person Explaining Consent Date

_____
Printed Name and Title of Person Explaining Consent