

**SUBJECT INFORMATION AND INFORMED CONSENT FORM
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION**

Protocol Title: A Phase 3b, Randomized, Double-Blind Switch Study to Evaluate the Safety and Efficacy of Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) Fixed Dose Combination (FDC) in HIV-1 Positive Subjects who are Virologically-Suppressed on Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (FTC/RPV/TDF)

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New Information

This study was originally planned to last for 48 weeks; this new consent extends the study treatment for an additional 48 weeks. The total length of blinded treatment is now about 2 years. The rationale for the study extension is to obtain long term safety and efficacy data on switching from Atripla and Complera to Odefsey.

INTRODUCTION TO RESEARCH STUDY

You have been asked to take part in a clinical research study involving an experimental drug named emtricitabine/rilpivirine/tenofovir alafenamide (F/R/TAF) fixed dose combination (FDC). An experimental drug means it has not been approved by any country for the treatment of HIV-1 infection. F/R/TAF will be compared to another drug named emtricitabine/rilpivirine/tenofovir disoproxil fumarate (F/R/TDF) FDC, commonly known as Complera/Eviplera.

Complera/Eviplera is approved by the Food and Drug Administration (FDA) in the United States and by the European Medicines Agency (EMA) in Europe for the treatment of HIV-1 infection in adults.

This Subject Information and Informed Consent Form (ICF) will tell you about the study. Your study doctor or study nurse will go over this ICF with you and answer any questions you may have regarding the study. Ask your study doctor or study nurse to explain any words or information in this ICF you do not clearly understand. After reading this ICF, you should understand: 1) the purpose of the study; 2) how taking part may help you; 3) any potential risks to you, and; 4) what is expected of you during the study.

Research studies are voluntary and include only those who wish to take part. If you agree to participate you will be asked to sign and date this ICF and be given a signed and dated copy to keep. No one can force you to take part in this study. Even if you decide not to be in the study or agree to take part now, you can change your mind and stop at any time without penalty or loss of benefits to which you would otherwise be entitled.

Your study doctor will be paid by the sponsor to conduct this research study.

PURPOSE OF THE STUDY

The purpose of this study is to evaluate if F/R/TAF works as well as F/R/TDF. It is also to see if F/R/TAF will maintain the control of your HIV-1 infection when compared to F/R/TDF. Safety, how well your body accepts the drug, and tolerability, how stable its effects are, will also be evaluated and are determined by the physical exams, laboratory tests, x-rays, and questions asked of you about problems you might experience during the study.

DESIGN OF THE STUDY

If you agree to take part in this study, you will be one of 550 subjects at about 150 study sites in North America and Europe. 10 people are enrolled in this study at the University of Pennsylvania. This study is open to male and female subjects, 18 years of age or older, who meet the study requirements. The study doctor has asked you to come to the clinic for a Screening visit to see if you are eligible to take part.

This is a randomized, double-blind study. Randomized means you will be selected by chance (like a flip of the coin) to receive one of 2 study treatments as follows:

Study Treatment Arm 1: F/R/TAF plus placebo to look like F/R/TDF

Study Treatment Arm 2: F/R/TDF plus placebo to look like F/R/TAF

You have an equal chance of being assigned to Study Treatment Arm 1 or Study Treatment Arm 2. 275 subjects will be assigned to each arm.

“Placebo” means the pill contains material with no active effect on your HIV but looks like the active study drug. “Active” means that the pill is designed to affect your HIV. Double-blind means neither you nor your study doctor will know which Study Treatment Arm you will be assigned to. However, your study doctor can find out which group you are in if there is an emergency.

All of your study drugs will be supplied by Gilead Sciences, Inc. (Gilead) which is also the sponsor of this study. The study drugs must be stored at room temperature between 15 °C and 30 °C (59 °F and 86 °F).

The study drugs should be taken *with food* by mouth once a day at about the same time each day. The directions for taking the study drugs will be on the bottles. It is very important that you take the study drugs every day as instructed by the study doctor or study nurse.

DURATION OF THE STUDY

Taking part in this study will last at least 96 weeks, not including the Screening visit. During this time, you will be required to visit the clinic at least 11 times (this is called the study period). The screening period (the time between the Screening and Baseline visits) will be up to 30 days.

Following your 96 weeks on study, you will continue to take the study drugs and attend visits every 12 weeks until the study is unblinded. Unblinded means the time when your study doctor and Gilead will learn to which study treatment arm you were assigned. Once this happens you will have the choice of continuing in the study or stopping participation. If you stay on the study, you will be given F/R/TAF and you, your study doctor, and Gilead will know which study drug you are taking.

If you choose to participate after the study is unblinded you will receive F/R/TAF for up to 48 weeks or until Gilead chooses to end the study.

SUBJECT RESPONSIBILITIES

If you decide to be in this study, there are certain rules you must follow before, during, and after the study period. Some are listed below, but there could be others that the study doctor will discuss with you:

- You must not become pregnant or get someone pregnant during this study, or for 90 days afterwards.
- It is very important that you tell your study doctor all of the information you know about your health and medications you may be taking throughout the study period. If you do not tell the study doctor everything you know, you may be putting your health at risk.
- You must return all of the used and unused study drug materials, including empty study drug bottles.

- You must follow all instructions given to you while you are participating in this study. If you do not, you may be removed from the study. If you are unsure about what you are supposed to do, ask the study doctor.
- Some insurance companies require people who are renewing a policy or getting a new policy to tell them about participating in a clinical study. You should check with your insurer to determine if taking part in this study will affect your existing insurance policy.

STUDY PROCEDURES

Screening Visit:

To help your study doctor decide if you may participate in this study and whether it is safe for you to do so, you will need to have screening procedures done. Please note that if at any point during the screening period you do not qualify for the study, not all of the procedures listed below may occur:

- You will be asked about your medical and HIV-1 history and any medications you are taking or have taken within the last 30 days.
- You will have a complete physical exam, including measurement of your weight, height, and vital signs (temperature, blood pressure, heart rate, and breathing rate).
- You will provide a urine sample for general health tests.
- You will have about 29 mL or 6 teaspoons of blood taken for general health tests and tests related to your HIV-1 such as: complete blood count (review of red and white blood cells as well as platelets) chemistry (measurement of substances in the blood to determine general health), CD4+ (white blood cell that fights infection), glomerular filtration rate or “eGFR” (measures kidney function), HIV-1 RNA (measure the amount of HIV in your blood), and Hepatitis B and C viruses.
- If you are female and able to become pregnant, a blood pregnancy test will be performed. To take part in this study, the pregnancy test must be negative.
- You will have a 12-lead electrocardiogram (ECG) conducted to check the functioning of your heart.
- You will complete a questionnaire about why you want to be in this study.

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.

Baseline/Day 1 Visit:

If your study doctor finds that you qualify to participate and you agree to continue, a Baseline/Day 1 visit will be scheduled within 30 days of the Screening visit. The following procedures will be performed:

- You will be asked about changes in your health and whether you have taken any new medications since the Screening visit.
- You will have a complete physical exam, including measurement of your weight and vital signs (temperature, blood pressure, heart rate, and breathing rate).
- You will provide a urine sample for:
 - General lab tests
 - Sample storage for possible additional tests
 - Renal (kidney) safety test (test the health of and how the study drug is affecting your kidneys)
 - This sample must be collected in a fasted state. “Fasted” means that you will not eat or drink anything except water for at least 8 hours before you provide your sample.
- If you are a female able to become pregnant, a urine pregnancy test will be performed. If the test is positive, a blood pregnancy test will be done to confirm the result; if confirmed, you will no longer be allowed to participate in the study.
- You will have about 28 mL or 6 teaspoons of blood taken for tests such as: complete blood count, chemistry, CD4+, eGFR, HIV-1 RNA, and Cystatin C (to monitor your kidney function), bone safety test (to measure your bone health), glucose (sugar in your blood), lipid profile [total cholesterol, HDL or good cholesterol, direct LDL or bad cholesterol, and triglycerides (type of fat found in your blood)].
 - The glucose, lipid profile, and bone safety samples must be collected in a fasted state.
- You will have about 9 mL or 2 teaspoons of blood taken for storage for virology (to study your HIV-1), safety tests, and possible additional tests.
- You will complete two questionnaires about your health called the Visual Analogue Scale (VAS) Adherence Questionnaire and SF-36 Questionnaire. The VAS is a visual scale that will estimate how much study drug you believe you have taken. The SF-36 contains questions about your general health and wellness while participating in the study.
- You will be counseled regarding the importance of taking all study drugs according to the instruction provided by your study doctor.
- You will receive your first bottles of study drugs and will be asked to begin taking your first dose within 24 hours after this visit.
- You must take the study drugs *with* food by mouth once a day at about the same time each day.

Weeks 4 to 96 Visits:

You will be asked to return to the clinic for study visits at: Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84 and 96 unless otherwise specified. The following procedures will be performed:

- You will be asked about changes in your health and whether you have taken any new medications since your last clinic visit.

- You will have a physical exam, if needed. A complete physical exam will be performed at **Weeks 24, 48, 72 and 96**.
- Measurement of your weight and vital signs (temperature, blood pressure, heart rate, and breathing rate).
- You will provide a urine sample for:
 - General lab tests
 - Sample storage for possible additional tests
 - Renal safety test (collected at **Weeks 24, 48, 72 and 96** only). You must have fasted prior to providing this sample.
- If you are a female able to become pregnant, a urine pregnancy test will be performed. If the test is positive, a blood pregnancy test will be done to confirm the result; if confirmed, you will no longer be allowed to participate in the study.
- You will have a 12-lead ECG conducted (**Weeks 24, 48, 72 and 96 only**).
- You will have about 20 mL or 4 teaspoons of blood taken for tests of: complete blood count, chemistry, CD4+, eGFR, and HIV-1RNA.
- Additionally, at Weeks 24, 48, 72 and 96, you will have about 20 mL or 4 teaspoons of blood taken for tests of: hepatitis B & C, glucose, bone safety and a lipid profile. You must have fasted prior to this blood draw.
- You will have about 3 mL or 1 teaspoon of blood taken to measure the amount of study drugs in your blood. This type of testing is called pharmacokinetics (PK). It tells the researchers how much time it takes for the study drug to be absorbed into your body and how long it stays in your body after it has been absorbed. You will be asked not to take your study drug on the morning of these visits. (**Weeks 4, 8, 12, and 24 only**)
- You will have about 3 mL or 1 teaspoon of blood taken at **Week 24** for PK. You will be asked to take your study drug in clinic at this visit.
- You will have about 11 mL or 2 teaspoons of blood taken for storage for virology, safety, and possible pharmacokinetic (PK) or additional tests.
- You will complete two questionnaires about your health: The VAS (**all visits**) and the SF-36 (**Weeks 24, 48, 72 and 96 only**).
- If you do not appear to be responding properly to the study drugs, you may be required to return to the clinic for an unscheduled visit to confirm whether or not you are truly failing your study treatment. About 12 mL or 3 teaspoons of blood will be taken during this visit to measure the amount of HIV-1 in your blood for genotype/phenotype testing. These tests help determine whether a variation in your HIV-1 gene has changed how the study drugs affect your HIV-1 virus. The study doctor will then decide whether or not a change to your study treatment regimen is required.
- You will be counseled regarding the importance of taking all study drugs according to the instruction provided by your study doctor.
- You will receive a 4-week supply of study drugs at Weeks 4 and 8. At Weeks 12, 24, 36, 48, 60, 72, 84 and 96 you will receive a 12-week supply of study drugs.
- You must take the study drugs *with* food by mouth once a day at about the same time each day.

- You will be required to bring your used and unused study drug bottles back to the clinic at each visit. The number of tablets will be counted. You will be asked about any missed doses since your last visit.

Post Week 96 Visits

You will be asked to return to the clinic for study visits every 12 weeks until the study is unblinded. The following procedures will be performed:

- You will be asked about changes in your health and whether you have taken any new medications since your last clinic visit.
- You will have a physical exam, if needed. A complete physical exam will be performed **every 48 weeks**.
- Measurement of your weight and vital signs (temperature, blood pressure, heart rate, and breathing rate).
- You will have a 12-lead ECG conducted (**every 48 weeks**).
- You will provide a urine sample for:
 - General lab tests
 - Sample storage for possible additional tests
- If you are a female able to become pregnant, a urine pregnancy test will be performed. If the test is positive, a blood pregnancy test will be done to confirm the result; if confirmed, you will no longer be allowed to participate in the study.
- You will have about 20 mL or 4 teaspoons of blood taken for tests of: complete blood count, chemistry, CD4+, eGFR, and HIV-1RNA.
- **Every 24 weeks** you will have about 15mL or 3 teaspoons of blood taken for tests of: glucose, a lipid profile and hepatitis B & C (only every 48 weeks). You must have fasted prior to this blood draw.
- You will have about 11 mL or 3 teaspoons of blood taken for storage for virology, safety, and possible PK or additional tests.
- You will complete the VAS questionnaire about your health.
- If you do not appear to be responding properly to the study drugs, you may be required to return to the clinic for an unscheduled visit to confirm whether or not you are truly failing your study treatment. About 12 mL or 3 teaspoons of blood will be taken for genotype/phenotype testing. The study doctor will then decide whether or not a change to your study treatment regimen is required.
- You will be counseled regarding the importance of taking all study drugs according to the instruction provided by your study doctor.
- You will receive a 12-week supply of study drugs.
- You must take the study drugs *with* food by mouth once a day at about the same time each day.
- You will be required to bring your used and unused study drug bottles back to the clinic at each visit. The number of tablets will be counted. You will be asked about any missed doses since your last visit.

Unblinding Visit

Once the study has been unblinded, you will be asked to return to the clinic within 30 days. You will have the choice of continuing in the study or stopping your participation. If you choose to stop, you will return for a 30 Day Follow-Up visit. The following procedures will be performed at this Unblinding visit:

- You will be asked about changes in your health and whether you have taken any new medications since your last clinic visit.
- You will have a complete physical exam.
- Measurement of your weight and vital signs (temperature, blood pressure, heart rate, and breathing rate).
- You will have a 12-lead ECG conducted.
- You will provide a urine sample for:
 - General lab tests
 - Sample storage for possible additional tests
 - Renal safety – You must have fasted prior to providing this sample.
- If you are a female able to become pregnant, a urine pregnancy test will be performed. If the test is positive, a blood pregnancy test will be done to confirm the result; if confirmed, you will not qualify for the extension phase of the study.
- You will have about 20 mL or 4 teaspoons of blood taken for tests of: complete blood count, chemistry, CD4+, eGFR, and HIV-1RNA.
- You will have about 5 mL or 1 teaspoon of blood taken for tests of: glucose, bone safety, and a lipid profile. You must have fasted prior to this blood draw.
- You will have about 11 mL or 3 teaspoons of blood taken for storage for virology and possible PK or additional tests
- You will complete two questionnaires about your health: the VAS and SF-36.
- If you do not appear to be responding properly to the study drugs, you may be required to return to the clinic for an unscheduled visit to confirm whether or not you are truly failing your study treatment. About 12 mL or 3 teaspoons of blood will be taken for genotype/phenotype testing. The study doctor will then decide whether or not a change to your study treatment regimen is required.
- You will be required to bring your used and unused study drug bottles back to the clinic at each visit. The number of tablets will be counted. You will be asked about any missed doses since your last visit.

Early Study Drug Discontinuation (ESDD) Visit

If you discontinue study drugs at any time before the Unblinding visit, you will be asked to return to the clinic within 72 hours of stopping study drugs. For safety purposes, you will be asked to continue to come to the scheduled study visits until the study is unblinded. Procedures at this visit will include:

- You will be asked about changes in your health and whether you have taken any new medications since your last clinic visit.
- You will have a complete physical exam.
- Measurement of your weight and vital signs (temperature, blood pressure, heart rate, and breathing rate).
- You will have a 12-lead ECG conducted.
- You will provide a urine sample for:
 - General lab tests
 - Sample storage for possible additional tests
 - Renal safety – You must have fasted prior to providing this sample. Required only if last test was more than 12 weeks before this visit.
- If you are a female able to become pregnant, a urine pregnancy test will be performed. If the test is positive, a blood pregnancy test will be done to confirm the result.
- You will have about 20 mL or 4 teaspoons of blood taken for tests of: complete blood count, chemistry, CD4+, eGFR, and HIV-1RNA.
- You will have about 5 mL or 1 teaspoon of blood taken for tests of: glucose, bone safety, and a lipid profile. You must have fasted prior to this blood draw. The bone safety tests are required only if the last tests were more than 12 weeks before this visit.
- You will have about 11 mL or 3 teaspoons of blood taken for storage for virology and possible PK or additional tests.
- You will complete two questionnaires about your health: the VAS and SF-36.
- If you do not appear to be responding properly to the study drugs, you may be required to return to the clinic for an unscheduled visit to confirm whether or not you are truly failing your study treatment. About 12 mL or 3 teaspoons of blood will be taken for genotype/phenotype testing. Your study doctor may recommend other treatments for your HIV.
- You will be required to bring your used and unused study drug bottles back to the clinic at each visit. The number of tablets will be counted. You will be asked about any missed doses since your last visit.

30-Day Follow-up Visit

You will be asked to attend a 30-Day Follow-up visit in the following cases:

- If you stop your study drugs, and do not wish to continue your regularly scheduled visits, you will be asked to return to the clinic 30 days after completion of the Early Study Drug Discontinuation visit.
- If you continue on study drugs until the Unblinding Visit and decide not to take part in the extension phase, you will be asked to return to the clinic 30 days after completion of the Unblinding visit.

Procedures at this visit include:

- You will be asked about changes in your health and whether you have taken any new medications since your last clinic visit.
- You will have a physical exam, as needed.
- Measurement of your weight.
- You will provide a urine sample for:
 - General lab tests
 - Sample storage for possible additional tests
- If you are a female able to become pregnant, a urine pregnancy test will be performed. If the test is positive, a blood pregnancy test will be done to confirm the result.
- You will have about 20 mL or 4 teaspoons of blood taken for tests of: complete blood count, chemistry, CD4+, eGFR, and HIV-1RNA.
- You will have about 5 mL or 1 teaspoon blood taken for storage for possible additional tests.

Restrictions During the Study

You may not take the following over-the-counter (OTC) medicines:

- *fluconazole (Diflucan[®]),*
- *Omeprazole (Prilosec[®]),*
- *esomeprazole (Nexium[®]),*
- *lansoprazole (Prevacid[®]),*
- *St. John's Wort,*
- *echinacea,*
- *milk thistle, or*
- *the Chinese herb Sho-Saiko-To (Xiao-Shai-Hu-Tang).*

Antacids that contain calcium, magnesium, or aluminum (for example, Tums[®] or Rolaids[®]) or ulcer medicine (for example, Carafate[®]) should only be taken at a minimum of 2 hours before or 4 hours after any dose of study drugs.

Heartburn medications such as cimetidine (Tagamet[®]), ranitidine (Zantac[®]), nizatidine (Axid AR[®]), or famotidine (Pepcid AC[®]) should only be taken 12 hours before or 4 hours after any dose of study drugs.

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

RISKS

This section provides information on the possible risks associated with participation in this study from study procedures and side effects from the study drugs. You may experience some, all, or none of these effects. However, life-threatening and even fatal side effects could occur. You will be monitored for all side effects.

You must tell the study doctor about any new medications, including prescription and non-prescription medicines, vitamins, herbal supplements, and new health problems that develop while you are participating in this study.

Tenofovir Alafenamide (TAF)

FTC/RPV/TAF is a fixed-dose combination (FDC) tablet containing three medications: emtricitabine (FTC), rilpivirine (RPV) and tenofovir alafenamide (TAF). The safety of FTC/RPV/TAF is based on studies of FTC+TAF; and studies of RPV.

Adverse drug reactions that have been identified in studies of patients treated with F+TAF are as follows:

Very common:

- headache,
- diarrhea and
- nausea.

Common:

- vomiting,
- abdominal pain,
- indigestion,
- passing gas,
- rash, and
- fatigue (feeling tired).

Common adverse drug reactions that have been identified in studies of patients taking RPV include:

- decreased appetite,
- depression,
- abnormal dreams,
- sleep disorders (either difficulty sleeping or feeling sleepy),
- headache,
- dizziness,
- abdominal pain,
- nausea,
- vomiting,
- rash,
- fatigue, and
- changes in liver tests.

Additional adverse reactions from regimens containing RPV (given with FTC+tenofovir disoproxil fumarate (TDF) as FDC) include:

- increased weight and
- severe skin reactions including rash accompanied by fever, swelling and liver problems.

Across all Phase 2 and Phase 3 studies in which 2,394 subjects received regimens containing F+TAF (given with elvitegravir+cobicistat (EVG+COBI) as FDC), eye disorders were uncommon, balanced between treatment groups, and most were considered by the investigator as unrelated to the study drugs. None were definitive for posterior uveitis, and none resulted in permanent discontinuation of study drugs. One subject in Study GS-US-292-0106 had an adverse reaction of intermediate uveitis (inflammation in the middle of the eye) that was considered related to study drug by the investigator but resolved while the subject continued on study drug without interruption.

FTC/RPV/TDF (Emtricitabine/Rilpivirine/Tenofovir DF, Complera/Eviplera)

FTC/RPV/TDF is a single tablet regimen containing three medications: rilpivirine (RPV, Edurant), Emtricitabine (FTC, Emtriva), and Tenofovir DF (TDF, Viread). The side effects on the individual components of FTC/RPV/TDF are listed below.

Tenofovir DF (TDF, Viread)

Very common potential side effects identified in 10% or more of HIV patients who received at least one dose of TDF 300 mg include:

- diarrhea,
- nausea,
- vomiting, and
- dizziness.

Gas was a common side effect (occurring in $\geq 1\%$ and less than 10% of patients). Those side effects were often mild or moderate in severity, and less than 1% of Viread treated patients discontinued treatment due to the events listed above.

In addition to the side effects reported from clinical trials the following possible side effects are also known:

- Allergic reaction
- Decreased phosphorus (a mineral in the body similar to calcium and found in your teeth and bones)
- Decreased potassium (a mineral in the body important for muscles to work well and to regulate blood pressure)
- High levels of lactic acid in the blood
- Shortness of breath
- High levels of amylase (an enzyme in saliva and your digestive tract used to break down foods) in the blood
- Inflammation of the pancreas
- Abdominal pain
- Abnormalities of tests that measure liver function (increased liver enzymes, most commonly AST, ALT, and gamma GT)
- Inflammation of the liver
- Fat buildup in the liver
- Rash

- Weakness
- Rapid breakdown of muscle tissue
- Muscular weakness
- Muscle disease
- Softening of the bone (expressed as bone pain and rarely contributing to breaks)

Cases of kidney damage have been reported in patients taking tenofovir DF who already have circulatory or specific kidney disease and 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 breaks 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, abnormally excessive excretion of urine resulting in dehydration and thirst, and increased creatinine (a blood measure of kidney function) in the blood have also been reported in patients taking tenofovir DF.

Cases of high levels of lactic acid in the blood, an enlarged liver and fat in the liver, including fatal cases, were reported in HIV-infected patients treated with anti-retroviral agents similar to tenofovir DF. The symptoms of high lactic acid levels 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 (feeling less hungry),
- nausea and
- lower abdominal pain.

Emtricitabine (FTC, Emtriva®)

Very common side effects seen in 10% or more of patients treated with FTC in combination with other anti-HIV drugs are:

- headache,
- diarrhea,
- nausea,
- and increased creatine kinase in your blood which may cause you to experience muscle pain and weakness.

Other common side effects occurring in $\geq 1\%$ and less than 10% of patients with FTC include:

- allergic reaction,
- dizziness,
- difficulty sleeping,
- abnormal dreams,
- lowered function of the liver and pancreas,
- vomiting,
- stomach pain,
- problems with digestion resulting in discomfort after meals,
- changes in skin color primarily on the palms and/or soles,
- weakness,
- pain,
- increased bilirubin (a yellowish-orange substance produced by the breakdown of hemoglobin from red blood cells) in the blood,
- increased triglycerides (fatty acid),
- increased glucose in the blood, and
- low white blood cell count, which can make you more prone to infection.

Additionally, cases of high levels of lactic acid in the blood, an enlarged liver and fat in the liver, including fatal cases, were reported in HIV-infected patients treated with anti-HIV agents similar to FTC.

Rilpivirine (RPV, Edurant[®])

The most commonly reported side effects in patients taking RPV include:

- depression,
- trouble sleeping,
- headache,
- rash,
- nausea,
- stomach pain,
- vomiting,
- tiredness,
- dizziness, and
- abnormal dreams.

If you experience severe depression or thoughts of harming yourself you must immediately inform the study doctor or study staff.

Other side effects, which may be severe, include:

- diarrhea,
- abdominal discomfort,
- gall stones,
- gall bladder disease,
- decreased appetite (feeling less hungry),

- sleep disorders,
- feeling sleepy,
- anxiety,
- kidney stones and
- kidney disease.

Changes in laboratory values include:

- increased creatinine in the blood (an indication of possible kidney damage),
- increased liver enzyme levels in the blood and increased bilirubin in the blood (indications of possible liver damage), and
- increases in cholesterol and triglycerides in the blood.

Switching From a Stable Regimen

You are currently taking medications that are effectively treating your HIV infection. You may be changing from a stable regimen that is working well to a new regimen during this study. When switching from one antiviral regimen to another, there is a risk that the virus will not be controlled with the new regimen, that the virus could develop resistance to the medications, and that the new regimen could cause new side effects. Viral load, possible resistance, and side effects will be frequently and carefully monitored during this study to minimize these risks.

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.

Autoimmune disorders such as Graves' disease (a disease in which the thyroid produces excessive thyroid hormones), polymyositis (a disease caused by inflammation leading to weakness of the muscles), and Guillain-Barre syndrome (a disease that occurs when the body's immune system 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 variable and can occur many months after starting treatment.

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

Blood Draws

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 Testing

Some of your blood will be tested for hepatitis B and C. The study doctor may be required by law to report the result of these tests to the local health authority.

Personal Questions Risks

You will be asked questions about personal issues during this study. There may be questions about your mood, about sexual functioning, about drug use, etc. These types of personal questions may make some subjects uncomfortable.

UNKNOWN/UNEXPECTED RISKS

In addition to the risks listed above, there are risks that are not known or do not happen often when subjects take these study drugs, including severe or life-threatening allergic reactions, interactions between study drugs or interactions with another medication. You will be informed in a timely manner, both verbally and in writing, of any new information, findings or changes to the way the research will be done that might influence your willingness to continue in this study.

PREGNANCY AND BREAST-FEEDING

The risks of the study drugs to an unborn baby or nursing child are unknown and may be hazardous. If you are a woman who is pregnant or intend to become pregnant, or if you are currently nursing a child, you cannot be in this study. You should be aware that on rare occasions in early pregnancy, the pregnancy test may be falsely negative and that a negative test result does not prevent pregnancy. If you think that you have become pregnant during the study or within 30 days of taking your last dose of study drugs, you must tell your study doctor immediately. If you become pregnant during the study, you will be removed from the study and the study doctor will refer you to seek obstetrical care and request to track your pregnancy.

BIRTH CONTROL REQUIREMENTS

The use of condoms is encouraged because they have been proven to decrease the risk of transmission of HIV and other sexually transmitted diseases.

Total abstinence from intercourse is acceptable. Periodic abstinence such as calendar, ovulation, basal temperature post-ovulation methods, and withdrawal are NOT acceptable methods of birth control.

Female Subjects:

If you are a female able to become pregnant, you must agree to use acceptable methods of birth control from **Screening**, throughout the study, and for at least **30 days** after the last dose of study drug. If you are a female using hormonal agents as one of your contraceptive methods, it is required that the same hormonal method be used for at least 3 months before study dosing, throughout the study and for at least 30 days after the last dose of study drug.

Effective methods of birth control in this study include:

- a combination of one hormonal method and one barrier method
- two barrier methods where one method is the male condom
- use of an intrauterine device (IUD) or tubal sterilization

Acceptable hormonal methods include:

- injectable progesterone
- progesterone implants
- combination oral contraceptive
- transdermal contraceptive patch
- vaginal ring

Acceptable barrier methods include:

- diaphragm with spermicide
- cervical cap with spermicide
- male condom

You must use either a hormonal method or a barrier method even if your partner has had a vasectomy.

Because the effectiveness of hormonal contraceptives may be decreased by other drugs, you must use both a non-hormonal method and a hormonal method of birth control in order to prevent possible pregnancy.

Male Subjects:

You must agree to use condoms consistently and correctly during heterosexual intercourse with women who are able to become pregnant and you must tell your partner to use one of the acceptable methods of contraception listed above and for at least 30 days after the last dose of study drugs. You must not donate sperm while enrolled in the study and for at least 30 days after the last dose of study drugs.

POSSIBLE BENEFITS OF THE STUDY

There is no guarantee that you will receive personal benefit from taking part in this study. The study drugs are not expected to cure you of your HIV infection. However, clinical research studies such as this are a way for doctors to determine if a drug is useful in fighting a disease. By taking part in this study, you and Gilead may benefit if F/R/TAF is effective in treating HIV infection.

Your taking part 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. By taking part in this study, you will have close medical monitoring of your health condition by blood tests and other evaluations during clinic visits.

TREATMENT OPTIONS

You have the option to discuss with your study doctor not to have treatment or to choose other antiretrovirals to treat your disease. These medicines include commercially available medicines. Your study doctor will discuss appropriate alternative treatment options and their risks and benefits 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 take part.

WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE

Taking part in this clinical research study is voluntary and you can refuse to take part or stop at any time without stating a reason. Your withdrawal will not result in penalty or loss or affect your access to other medical care to which you would otherwise be entitled.

Special care will need to be taken when determining if you need to stop the study drugs. Your study doctor will supervise any discontinuation of the study drugs with your health as the first priority. Your taking part in this study may be terminated at any time by: a) your study doctor, b) Gilead, Inc., c) the U.S. Food and Drug Administration (FDA), d) Chesapeake IRB (IRB, a group of people who review research studies to protect the rights and welfare of research participants), and other appropriate regulatory agencies.

Your study doctor may withdraw you from the study if it is considered important for your medical safety. If it is discovered that you did not give an accurate medical history or did not follow the instructions for the study given by your study doctor, 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 study drugs used in this study will be given to you at no 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.

PAYMENT FOR PARTICIPATION

You will be paid \$25.00 for your screening visit. For visits thereafter, Baseline and 10 visits through wk 96 (4, 8, 12, 24, 36, 48, 60, 72, 84 and 96) and every 12 weeks past week 96, you will be paid \$40 for every visit you attend. An additional payment of \$10 will be made at these visits if you bring back the study medication bottles dispensed at the last visit (empty or with any unused study drugs). Thus if you attend all required visits through week 96 and return your medication bottles for the study through wk 96, the maximum payment you can receive is \$575. If you stop taking study drugs early and complete the Early Study Drug Discontinuation Visit and return the study medication bottles, you will be compensated \$50. You will be compensated \$50 for the 30-Day Follow-Up Visit that occurs after the Early Study Drugs Discontinuation Visit. You will be compensated \$25 for any unscheduled visits requested by the study staff. The total payment you will receive for the study depends on how long you participate. All compensation will be provided on a ClinCard (a debit card).

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.

MEDICAL TREATMENT AND COMPENSATION FOR STUDY-RELATED INJURY

If you become sick or injured as a direct result of taking the study drug and/or following the study procedures, the 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. No other form of reimbursement for study-related injury or illness is offered by Gilead. You should immediately contact your study doctor at the contact information shown below in the event you experience any study-related illness or injury.

If you receive Medicare benefits, Gilead is required by law to report payments made to you for treatment, complications, and injuries that arise from this study. Information that you are taking part in the study, medical treatments received, Medicare claims, and other personal information about you such as your name, social security number, and date of birth, will be provided to the Centers of Medicare and Medicaid Services and its agents and/or contractors for this purpose.

You do not give up any legal rights by signing this form. You are not prohibited from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

SOURCE FOR ADDITIONAL INFORMATION

You can ask questions about this consent form or the study (before you decide to start the study or at any time during the study). Questions may include:

- Who to contact in the case of a research-related injury or illness.
- Any payment for being in the study.
- Your rights and your responsibilities as a study subject.
- Other questions.

Contact the study doctor or study staff with any questions or concerns. Their telephone number is printed on the first page of this form. If you have any questions or complaints about your rights as a research subject, contact:

- By mail:
 Study Subject Adviser
 Chesapeake IRB
 6940 Columbia Gateway Drive, Suite 110
 Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@chesapeakeirb.com

Please reference the following number when contacting the Study Subject Adviser:
Pro00010961.

GENERAL 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. All of your study data will be kept in a secure location. Your personal information may be given out if required by law. If you test positive for HIV, Hepatitis B or Hepatitis C, 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 (IRB), Gilead and/or Gilead'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.

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 infection (but at all times in compliance with applicable law and regulation).

By signing this consent form you agree that you will not be able to have access to your personal health information related to this study until the study is over. This is done to maintain the scientific integrity of the study. After the study is complete, you can obtain access to your information through your study doctor.

AUTHORIZATION TO USE AND DISCLOSE RECORDS

During this study your study doctor, study nurses and other study site personnel will record information about you, your health and your participation in the study on forms provided by Gilead. These forms are known as case report forms. You will not be able to participate in this study if you do not consent to the collection of this information about you.

The information collected about you, will be held by the study site, Gilead, and Gilead's authorized representatives. To ensure that your personal information is kept confidential, your name and any other information that allows you to be identified directly will not be entered on the case report forms or included in any records or samples your study doctor provides to Gilead or Gilead's authorized representatives. Instead, you will only be identified by your initials and a code. The code is used so that your study doctor can identify you if necessary.

Gilead and its authorized representatives will analyze and use the coded information they receive for the purposes of this study. Such purposes include:

- checking your suitability to take part in the study,
- monitoring your treatment with the study drugs,
- comparing and pooling your study treatment results with those of other subjects in clinical studies,
- establishing whether the study drugs meet the appropriate standards of safety set by the authorities,
- establishing whether the study drugs are effective,
- supporting the development of the study drugs,
- supporting the licensing application for regulatory approval of the study drugs anywhere in the world,
- supporting the marketing, distribution, sale and use of the study drugs anywhere in the world, and/or
- as otherwise required or authorized by law.

If necessary for these purposes, Gilead may share your information with its affiliates, people and companies with whom Gilead works, and regulatory or other governmental agencies. Although efforts will be made to protect your privacy, absolute confidentiality of your records cannot be guaranteed. Your medical information and records may be re-disclosed and no longer protected by federal privacy law.

As explained in this consent form, your participation in this study is voluntary and you may withdraw from the study at any time by informing your study doctor. By signing this consent, you authorize the collection and use of information about you as described in this consent. You may take back this authorization for the collection and use of information about you by informing your study doctor in writing at the address listed on the first page of this form. If you withdraw from the study or if you take back your authorization for the collection and use of information about you, your participation in the study will end and the study personnel will stop collecting information from you. Gilead will need to keep and use any research results, and may need to keep and use any samples, that have already been collected. Gilead must do this to comply with its legal obligations and to maintain the scientific integrity of the study. Your decision to withdraw from the study or to take back your authorization for the collection and use of information about you will not result in any penalty or loss of access to treatment or other benefits to which you are entitled.

This authorization has no expiration date, unless and until you revoke it. In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign this authorization document.

If you have any questions about the collection and use of information about you, you should ask your study doctor.

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 and regulatory agencies in other countries

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 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?

Since this is an open-label study, you will be able to access some or all of your medical records after the study is over. 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.

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).

RESEARCH STUDY REGISTRY

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

STORAGE AND USE OF BLOOD AND/OR URINE SAMPLES

A portion of your blood and/or urine taken at all visits after the Screening visit will be frozen and stored. Your stored samples and the information collected about you during the study may be used by Gilead or its research partners for HIV-1 geno/phenotyping assays or their development, for retesting the amount of HIV-1 in your samples, for measurement of antiviral drug levels in your samples, or for clinical laboratory testing to provide additional clinical data. At the end of this study, these samples may be held in storage by Gilead for up to 10 years.

Geno/phenotyping tests may be experimental; that is, these tests may not have been approved by the U.S. Food and Drug Administration (FDA). The results of such tests are designated “for research use only”, and the interpretation of the test results may not have direct benefit to you. Some of the information or analyses resulting from tests done on your samples will not be given to you or your study doctor. This information will not be placed in your medical records and will have no effect on your medical care.

No human genetic testing will be performed without your separate written consent.

Optional Blood Sample Storage for Future Research

As an optional part of this study, you are also being asked to allow the Study Sponsor to store your blood samples for future testing to learn more about how the study drug(s) has worked against HIV-1. From these samples, it might also be possible to learn more about what causes HIV-1, how to prevent HIV, or how to better treat HIV. These samples may also be used for purposes that are not yet known. No human genetic testing will be performed without your separate written consent.

If you choose to allow your samples to be banked for future research, about 11 mL (about 3 teaspoons) of blood will be drawn at each study visit (starting at Baseline/Day 1) to be frozen and stored. If you do not agree to banking of your samples, you can still take part in the main research study.

You should also know that the Sponsor and other researchers who may study your blood samples have an economic interest in developing new drugs and medical tests. The results of this research may lead to a commercial product for the diagnosis, cure, mitigation, treatment, or prevention of disease. You understand and agree that by consenting to the storage of your samples for possible future research, you authorize the use of your sample, the by-products of the sample, and any products developed from the sample as described by this form. The Sponsor or other researchers or research companies may patent or sell discoveries that result from this research. Neither the Sponsor nor the Study Doctor has any plans to compensate you if this happens.

Withdrawing consent to the storage and future testing of your sample will result in destruction of your sample. If you wish to withdraw your blood samples from testing, please contact the study doctor at the telephone number or address listed on the first page of this consent form. However, if you withdraw your consent after the sample has been tested, the test results and research study/sample-related information must remain in any database(s) that were created for the research study. The reason for this is to comply with regulations that require the Sponsor to make data available for review by the United States Food and Drug Administration (FDA) or other appropriate regulatory authorities, or if this research is used to support an application for FDA approval to market the study drug.

If you withdraw consent for participation in the main study or are discontinued from the main study, the blood sample you provided will continue to be available for storage and future testing unless you also withdraw your consent for this purpose as stated above.

Please initial next to one of the statements below to indicate whether or not you agree to allow storage of your samples for possible future research outside of the main research study.

Yes _____ No _____ I agree to allow my blood samples to be stored for future research outside of the main research study.

AGREEMENT TO BE IN THE STUDY

By signing this ICF, I acknowledge that:

- (1) I have carefully read and understand the information presented in this consent document.
- (2) The purpose and procedures related to this research study have been fully explained to me and I have had the opportunity to ask questions and all of my questions were answered to my satisfaction.
- (3) I have been informed of the parts of the program that are experimental and of the possible discomforts, symptoms, adverse events and risks that I might reasonably expect, and the possible complications, if any, that I might reasonably experience from both known and unknown causes as a result of my participation.
- (4) I understand that I am free to withdraw this authorization and to discontinue my participation in this program any time. The consequences and risks, if any, of withdrawing from the program while it is ongoing have been explained to me.
- (5) I understand that such withdrawal will not affect my ability to receive medical care to which I might otherwise be entitled.

Subject

Subject Printed Name	Signature	Date

Person Obtaining Consent

Printed Name & Title	Signature	Date

Witness (if applicable)

Witness Printed Name	Signature	Date