UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

Gilead Sciences, Inc
GS-US-236-0115, Amendment 2 27-JUN-2012

A Phase 3b Randomized, Open-Label Study to Evaluate Switching from Regimens Consisting of a Ritonavir-boosted Protease Inhibitor (PI/r) plus Emtricitabine/Tenofovir Fixed-Dose Combination (FTC/TDF) to the Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir Disoproxil Fumarate Single-Tablet Regimen (EVG/COBI/FTC/TDF) in Virologically-Suppressed, HIV-1 Infected Patients

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

NEW INFORMATION
This Informed Consent Form is revised to provide updated information about change in frequency of one of the side effects of STRIBILD.

Frequency of suicidal ideation and suicide attempt in patients with a pre-existing history of depression or psychiatric illness has been changed from uncommon (occurred in more than or equal to 0.1% and less than 1% of patients) to common (occurring more than or equal to 1% and less than 10% of patients).

INTRODUCTION
You have been asked to volunteer for a clinical research study involving an experimental combination medication for the treatment of HIV-1 infection. This study is sponsored by Gilead Sciences, Inc. The experimental combination medication being evaluated in this study is one pill containing two experimental medications [elvitegravir (EVG) and cobicistat (COBI)] and two medications that are approved by the FDA for the treatment of HIV-1 infection. The two FDA approved medications that are included in the experimental combination tablet are Emtriva® (emtricitabine) which 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 EVG/COBI/FTC/TDF single tablet regimen (STR). On August 27, 2012 the United States Food and Drug Administration (FDA) approved Stribild™ (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg), a complete once-daily single tablet regimen (STR) for HIV-1 infection for treatment-naïve adults. Although this drug is now approved by the FDA, in this study, this drug is still considered an experimental combination medication.

This Subject Information and Informed Consent Form tells you about the study. Your Study Doctor or study nurse will go over this 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 consent form you do not clearly understand. You should understand the purpose of the study, how taking part may help you, any potential risks to you, and what is expected of you during the study.

If you agree to take part, you will be asked to sign and date this consent form and will be given a signed and dated copy to keep. No one can force you to take part in this study. Even if you 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.

PURPOSE OF THE STUDY

The purpose of this study is to see if HIV-infected subjects currently taking an antiretroviral (ARV) regimen consisting of a ritonavir-boosted protease inhibitor (PI/r) plus FTC/TDF (Truvada®) can safely switch to EVG/COBI/FTC/TDF STR without increasing the amount of virus in their blood.

The safety and effectiveness of EVG/COBI/FTC/TDF STR will also be compared to an antiretroviral regimen consisting of a ritonavir-boosted protease inhibitor plus Truvada®.
The safety and how well these drug combinations are tolerated will be determined based on vital signs, physical exams, laboratory tests and questionnaires about your, HIV treatment satisfaction, HIV treatment adherence, Quality of Life, and any 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 420 subjects at approximately 120 study sites in North America and Europe**.** About 10 persons are expected to enroll in this study at the University of Pennsylvania.

This study is open to male and female subjects, aged 18 and 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 an open-label study, which means that you and your study doctor will know whether you are receiving EVG/COBI/FTC/TDF STR or an antiretroviral regimen consisting of a ritonavir-boosted protease inhibitor plus Truvada®. 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: Approximately, 280 subjects will be randomized to Study Treatment Arm 1. If you are randomized to Study Treatment Arm 1 you will switch from your current antiretroviral regiment to a single tablet regimen of elvitegravir (EVG) 150 mg/cobicistat (COBI) 150 mg/emtricitabine (FTC) 200 mg/tenofovir disoproxil fumarate (TDF) 300 mg also referred to as EVG/COBI/FTC/TDF single tablet regimen (STR) for 96 weeks.

If at Week 96, EVG/COBI/FTC/TDF STR is **not** commercially available in your country you will have the option to (1) complete the study or (2) continue receiving EVG/COBI/FTC/TDF STR in an extension phase of the study until EVG/COBI/FTC/TDF STR becomes commercially available in your country, or until Gilead Sciences chooses to stop the development of the EVG/COBI/FTC/TDF STR.

Study Treatment Arm 2: Approximately, 140 subjects will be randomized to Study Treatment Arm 2. If you are randomized to Study Treatment Arm 2 you will continue taking your antiretroviral regimen consisting of a ritonavir-boosted protease inhibitor plus emtricitabine (FTC) 200 mg and tenofovir disoproxil fumarate (TDF) 300 mg [Truvada®] for 96 weeks.

If at Week 96, EVG/COBI/FTC/TDF STR is **not** commercially available in your country, you will have the option to (1) complete the study or (2) **switch** to EVG/COBI/FTC/TDF STR and stay on study until EVG/COBI/FTC/TDF STR becomes commercially available in your country, or until Gilead Sciences chooses to stop the development of the EVG/COBI/FTC/TDF STR.

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 2:1 ratio, which means that your chance of being assigned to Study Treatment Arm 1 is two times greater than 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.

EVG/COBI/FTC/TDF STR tablets will be supplied by Gilead Sciences, Inc., the Sponsor of this study. If you are assigned to Study Treatment Arm 2, Truvada® (FTC/TDF) will also be supplied to you by Gilead Sciences, Inc. through week 96. EVG/COBI/FTC/TDF STR tablets and Truvada® tablets must be stored at room temperature. Your study doctor or study nurse will review the proper storage of all study drugs used in this study with you. **EVG/COBI/FTC/TDF STR tablets must be taken once a day at approximately the same time every day with a meal.** If you are in **Study Treatment Arm 2**, you should take all your medications **as directed**. It is very important that you take your study drugs every day as instructed by the study doctor.

DURATION OF THE STUDY

The screening period (the time between the Screening visit and Baseline visit) may last up to 30 days. You will receive the study drug(s) for a minimum of 96 weeks (22 months). You will be required to visit the clinic up to 13 times.

If you are enrolled in Treatment Arm 1, and choose to continue taking EVG/COBI/FTC/TDF STR after Week 96, you will attend visits every 12 weeks starting at week 96 until EVG/COBI/FTC/TDF STR becomes commercially available in your country, or until Gilead Sciences chooses to stop the development of the EVG/COBI/FTC/TDF STR.

If you are in Study Treatment Arm 2, you will have the option to either complete the study or to switch to EVG/COBI/FTC/TDF STR at Week 96. If you choose to switch to EVG/COBI/FTC/TDF STR, you will attend study visits every 12 weeks starting at Week 96 until EVG/COBI/FTC/TDF STR becomes commercially available in your country or until Gilead Sciences chooses to stop the development of the EVG/COBI/FTC/TDF STR.

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:

- It is important that you do not become pregnant or get someone pregnant during this study, because the study drug may harm an unborn baby.
- It is very important that you tell your study doctors 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 as the study drug may be harmful in persons with certain illnesses or may interact with some medications.
- It is important to return all of the used and unused study drug bottles so that the research team can monitor how much medication you are taking.
- It is important to 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

All study procedures are listed in Study Procedures Table following this section. Please note that the Study Procedures Table is in addition to the explanations and instructions noted below and the guidance provided by your study doctor.

- 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.
- Read and complete the following questionnaires at selected visits:
  - questionnaires about your HIV treatment satisfaction,
  - questionnaire about why you are enrolling in this study (Screening visit only)
  - questionnaires regarding your treatment adherence, and
  - questionnaires regarding your Quality of Life
- Vital signs (blood pressure, temperature, respiratory rate, and heart rate).
- A complete physical examination, weight, and height (height only at Screening visit).
- A urine sample for laboratory tests.
- If you are a female able to become pregnant, a blood pregnancy test will be required at the Screening visit. If the blood pregnancy test is positive, you will not be eligible to participate in the study.
- If you are a female able to become pregnant, a urine pregnancy test will be performed at every visit beginning at the Baseline visit. If the urine pregnancy test is positive, the result will be confirmed by a blood pregnancy test. If the blood test is positive, you will not be allowed to participate in this study.
- About 32 mL (about 6 teaspoons) (5 mL = 1 teaspoon) of blood will be taken at each visit, except at Week 48 at which 44 mls or 9 teaspoons will be drawn, to perform the following as specified in the Study Procedures Table:
  - General health tests and tests related to your HIV, such as chemistry, complete blood count, kidney function, CD4 cell count (white blood cell that fights infection). Tests for hepatitis B and hepatitis C (Screening visit only), and to measure the amount of HIV-1 in your blood.
  - Determine the amount of study drugs in certain types of your blood cells called peripheral blood mononuclear cells (PBMCs) (Baseline visit only).
  - Measure the level of sugar and fats in your blood. This blood should be drawn in the morning prior to eating (in a fasting state) at the Baseline Visit, Weeks 4, 8, 12, 24, 36, 48, 96 and every 48 weeks after Week 96. 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.
  - If you do not appear to be responding properly to the study drugs, 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 treatment. A blood sample will be drawn during this visit to measure the amount of HIV-1 in your blood and for genotype/phenotype testing.
- A 12-lead ECG (electrocardiogram) to check the functioning of your heart (Screening visit only).
- Questions regarding any changes 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.

If your Study Doctor finds you eligible to take part, and you agree to continue, a "Baseline" (Day 1) Visit will be scheduled within 30 days of the Screening Visit.

In this study, there will be plasma storage samples for virology, PK, or clinical testing and serum storage samples for possible additional clinical testing. If you agree to have your samples stored for future research, you will be asked to give an additional 15 mL (about 3 teaspoons) of your blood as outlined in the Study Procedures Table below. Providing samples for future research is voluntary and will be explained in detail, later in this consent form.

You will be dispensed bottles of study drug as outlined below:

- **Study Treatment Arm 1:**
  - You will receive a 4-week supply of study drug at Baseline, Weeks 4, and 8
  - You will receive a 12-week supply of study drug at Weeks 12, 24, 36, 48, 60, 72 and 84. If you are continuing on the study after Week 96, you will receive a 12-week supply of study drug at each visit.
  - **It is important to take the EVG/COBI/FTC/TDF tablet once a day at the same time every day <u>with a meal</u> as this will maintain drug levels in the therapeutic range.**
  - You will be counseled regarding the importance of taking all study drugs.

- **Study Treatment Arm 2:**
  - You will receive a 4-week supply Truvada® and a prescription for ARV medications and be responsible for filling that prescription, at Baseline, Weeks 4, and 8.
  - You will receive a 12-week supply of Truvada® and a prescription for ARV medications and be responsible for filling that prescription, at Weeks 12, 24, 36, 48, 60, 72 and 84.
  - If you are continuing on the study after Week 96, you will discontinue all previous ARV medications (Truvada plus PI/r) and switch to the EVG/COBI/FTC/TDF STR at Week 96. You will receive a 12-week supply of study drug beginning at Week 96 and at each subsequent study visit.
  - **From Baseline to Week 96, it is important to take Truvada® and PI/r medications as directed. If you decide to switch to EVG/COBI/FTC/TDF STR at Week 96, you must take the EVG/COBI/FTC/TDF STR once a day at the same time every day <u>with a meal</u>.**
  - You will be counseled regarding the importance of taking all study drugs.

- You will be required to bring your used and unused EVG/COBI/FTC/TDF STR or Truvada® drug bottles back to the clinic at each visit. The study drugs (number of tablets) will be counted. You will be asked about any missed doses since your last visit.

<u>Restrictions During the Study</u>

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 4, 8, 12, 24, 36,48, 96, and every 48 weeks after Week 96.

It is important to check with the study doctor before taking any medications or health supplements for the length of the study. They may affect the levels of study medication or have an interaction with them.

GS 0115: Switch from Ritonavir-boosted Protease Inhibitor (PI/r)+ FTC/TDF to the Single-Tablet Regimen (EVG/COBI/FTC/TDF)

Study Procedures Table

Procedure (What is Going to Happen)	Screen	Baseline (Day 1)	End of weeK 4, 8, 12, 24, 36, 48, 60, 72, 84 and 96	Post Week 96 (every 12 weeks)	Early study termination (ET)	30-Day Follow up Visit/ Telephone Call
Review and sign Informed Consent	X					
Review your Medical History	X					
Review medications you are taking	X	X	X	X	X	X
Review any changes in your health since signing the consent form and last visit	X	X	X	X	X	X
Physical Examination will be performed	X	X	As Needed, Required at Wk 96	If needed	X	
Vital Signs will be taken (including weight. Height at Screening only)	X	X	X	X	X	
Blood and urine samples will be taken[a]	X	X	X	X	X	
Additional blood for storage will be collected (if you provide additional consent for this)		X	X	X	X	
Approximate Total Amount of Blood Taken - **mL in Europe (Teaspoons in US)**	23 (5)	37 (7)	32 (6); week 48, 44 ml (9)	32 (6)	32 (6)	
A 12-lead ECG will be performed	X					
You will complete a questionnaire about why you are enrolling into the study	X					
You will complete questionnaires regarding your HIV treatment satisfaction	X		X (weeks 4 & 24 only)		X	
You will complete questionnaires regarding your HIV Symptoms		X	X		X	
You will complete questionnaires regarding your general health	X	X	X (weeks 24,48, 72 & 96 only)			
You will complete questionnaires regarding your treatment adherence		X	X		X	
Receive study drug		X	X	X		
Return unused study drug and containers and review study drug taken since last visit			X	X	X	

a. Blood samples for: chemistry, hematology, kidney functions, sugar and fats, amount of HIV in your blood, PBMC (Baseline visit only), blood & urine pregnancy tests for females able to have children. If you do not appear to be responding properly to the study drugs, 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 treatment. A blood sample will be drawn during this visit (and at the Early Study Termination visit) to measure the amount of HIV-1 in your blood and for genotype/phenotype testing

RISKS

Study Drugs

EVG/COBI/FTC/TDF STR (STRIBILD) COMMON ADVERSE EVENTS

EVG/COBI/FTC/TDF STR is a combination medication containing four medications: elvitegravir (EVG), Cobicistat (COBI), Emtriva® (FTC), and Viread® (TDF) in a single tablet form.

A total of 194 healthy subjects were dosed with the EVG/COBI/FTC/TDF STR as part of 5 Phase 1 clinical studies. In addition, 48 HIV-1 infected, ARV treatment-naïve subjects have been dosed with EVG/COBI/FTC/TDF in an ongoing, blinded Phase 2 study. As of 10 April 2012, 916 HIV-1 infected subjects, both ARV treatment-naïve and ARV treatment-experienced, had been dosed with the EVG/COBI/FTC/TDF STR in ongoing Phase 3 studies. The following adverse events to treatment were identified.

Very common (more than or equal to 10%): diarrhea, nausea, fatigue, headache, depression, difficulty sleeping (insomnia).

Common (more than or equal to 1% or less than 10%): stomach pain (abdominal pain), indigestion (dyspepsia), gas (flatulence), vomiting, dizziness, abnormal dreams, rash, abnormal kidney function test (increased blood creatinine), kidney failure (renal failure) and suicidal ideation and suicide attempt in patients with a pre-existing history of depression or psychiatric illness..

Uncommon (more than or equal to 0.1% and less than 1%): a certain type of kidney disease (Fanconi syndrome)

Side effects on the individual components of EVG/COBI/FTC/TDF single tablet regimen (STR) are described below

EVG; ELVITEGRAVIR SIDE EFFECTS

Elvitegravir is an investigational drug as it has not been approved by the FDA at this time. EVG is in a class of drugs called integrase inhibitors and is being studied as a new treatment for HIV infection.

As of 30 June 2011, a total of 390 HIV-infected subjects and 960 healthy subjects have been dosed with EVG as an individual agent in clinical studies. In addition, approximately 358 HIV-1 infected treatment experienced subjects have been dosed in an on-going blinded Phase 3 study. Additionally, 194 healthy subjects and 48 HIV-infected treatment naïve have been dosed with EVG in a single tablet regimen containing EVG, COBI, FTC, and TDF as part of Phase 1 and 2 clinical studies. As of 10 April 2012, 916 HIV-1 infected subjects, both ARV treatment-naïve and ARV treatment-experienced, had also received elvitegravir as part of the EVG/COBI/FTC/TDF STR in ongoing, Phase 3 studies.

No additional side effects for EVG have been observed in clinical studies of EVG as an individual agent in addition to those listed above for EVG/COBI/FTC/TDF.

FTC; Emtriva® SIDE EFFECTS (Emtricitabine)

The most common side effects seen in patients treated with emtricitabine in combination with other anti-HIV drugs are: headache, diarrhea, nausea, and rash, which were generally mild. Other common side effects with emtricitabine 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 (a substance produced after medications are broken down by the liver that can make your skin yellow) in the blood, increased glucose (sugar) 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 (a muscle protein) in 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 emtricitabine. 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 emtricitabine package insert for additional information.

TDF; Viread® SIDE EFFECTS
(Tenofovir DF)

Tenofovir DF has been studied in approximately 12,000 HIV-infected adults for as long as 480 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 tenofovir DF.

In addition to side effects reported from clinical trials the following side effects have also been identified after tenofovir DF was approved in HIV-infected patients treated with combination therapy that has included tenofovir DF 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 tenofovir DF. 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 tenofovir DF 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 tenofovir DF.

Bone toxicity, including a decrease in bone mineral density, was seen in animals following treatment with tenofovir DF. Decreases in bone mineral density have been seen in humans. The risk of bone fractures associated with these types of changes is unknown.

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

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

COBI; COBICISTAT SIDE EFFECTS

Cobicistat is an investigational drug as it has not been approved by the FDA at this time. COBI does not have any antiviral activity and is being developed as a "booster" drug for other HIV treatment drugs.

As of 30 June 2011, 561 healthy subjects have been dosed with COBI as an individual agent as part of 17 Phase 1 studies and in 50 HIV-infected treatment naïve subjects in an ongoing blinded Phase 2 study. Approximately 350 HIV-infected treatment naïve subjects have received COBI as an individual agent in an ongoing, blinded study. Additionally, 194 healthy subjects and 48 HIV-infected treatment naïve subjects have been dosed with COBI in a single tablet regimen containing EVG, COBI, FTC, and TDF in clinical studies. As of 10 April 2012, 916 HIV-infected treatment naïve subjects, both ARV treatment-naïve and ARV treatment-experienced, had also received COBI as part of the EVG/COBI/FTC/TDF STR in ongoing, Phase 3 studies.

No significant changes in serum immunoglobulins (antibodies), ECG, thyroid hormone levels or urine characteristics have been seen in clinical studies to date. In two ongoing studies in which approximately 100 HIV-positive subjects are receiving COBI, mild decreases in estimated kidney function were observed. A follow-up study in healthy subjects showed that actual kidney function does not change. This phenomenon is seen with two other commonly used FDA-approved drugs, trimethoprim (an antibiotic) and cimetidine (an antacid). Your kidney function will be closely monitored throughout your participation in this study with blood and urine tests.

No additional side effects for COBI have been observed in clinical studies of COBI as an individual agent in addition to those listed above for EVG/COBI/FTC/TDF.

FTC/TDF; Truvada® Side Effects
(Emtricitabine/Tenofovir DF)

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

Other HIV medication Side Effects

Please ask your study doctor for information about the risks and benefits of other HIV-1 medications you are taking in Study Treatment Arm 2 for treatment of HIV-1 infection.

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 Graves' disease (a disease in which the thyroid produces excessive thyroid hormones), polymyositis (a disease of 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. 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.

Study Procedures

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 B and C Testing Risks

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

UKNOWN/UNEXPECTED RISKS AND DISCOMFORTS

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 drugs, 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). Resistant mutations develop most rapidly in people who do not take all of their HIV-1 drugs. Therefore, it is important to take all your study drugs 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.

PREGNANCY AND BREAST-FEEDING

The effects of EVG/COBI/FTC/TDF STR, or Truvada alone or in combination with other HIV medications have not been fully evaluated on the developing fetus in humans. Animal studies do not indicate direct or indirect harmful effects of EVG, FTC, TDF, and Truvada with respect to pregnancy. Because the effects of EVG/COBI/FTC/TDF STR, or Truvada alone or in combination with other HIV medications on a developing fetus as well as on exposed infants are unknown, any female able to become pregnant must have a negative blood pregnancy test to enroll. A female subject of childbearing potential is a nonmenopausal female who has not had a hysterectomy, both ovaries removed (bilateral oophorectomy), or medically documented ovarian failure. This definition includes a young woman who has not yet started menstruating. You will be asked to have a pregnancy test to be sure you are not pregnant at the start of the study, during the study and at the end of the study. 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.

Male subjects and female subjects of childbearing 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 30 days following the last dose of study drug. For subjects on Treatment arm 2, contraception should be consistent with the approved package inserts.

Protocol-recommended contraceptive methods are: (1) a combination of one hormonal method and one barrier method; (2) two barrier methods where one method is the male condom; or (3) use of an IUD or tubal sterilization (see table below). Acceptable hormonal methods include: injectable progesterone, progesterone implants, combination oral contraceptives, transdermal patch, and vaginal ring. Acceptable barrier methods include: diaphragm, cervical cap, and the male condom. Female subjects must use either a hormonal method or a barrier method if the partner has a vasectomy. If a subject has undergone tubal sterilization or has had a Copper T 380A IUD or LNg 20 IUD inserted, no other contraception is needed.Female subjects who utilize hormonal contraceptive as one of their birth control methods must have used the same method for at least three months prior to study dosing. It is recommended that an oral contraceptive contain 30 µg of ethinyl estradiol if administered with EVG/COBI/FTC/TDF.

If tubal sterilization is performed using the Essure procedure, a procedure where a radiographic dye is injected into the uterine cavity to verify that the tubes are blocked (hysterosalpingogram (HSP)), must be performed approximately 3 months after the Essure procedure. Prior to this verification, Essure is not

considered a reliable form of contraception and the contraception methods described below must be used.

Protocol-Recommended Contraceptive Methods

<table>
<tr><th rowspan="2">Methods to Use by Themselves</th><th colspan="2">Combination Methods</th></tr>
<tr><th>Hormone Methods
(choose one and use with a barrier method)</th><th>Barrier Methods
(use both OR choose one and use with a hormone method)</th></tr>
<tr><td rowspan="2">Intra-uterine devices (IUDs)
• Copper T 380A IUD
• LNg 20 IUD

Tubal sterilization</td><td>Estrogen and Progesterone
• Oral contraceptives
• Transdermal patch
• Vaginal ring
Progesterone
• Injection
• Implant</td><td>• Diaphragm
OR
Cervical cap
• Male condom</td></tr>
<tr><td colspan="2">Partner’s vasectomy must be used along with a hormone or barrier method.</td></tr>
</table>

* It is recommended that an oral contraceptive contain 30 µg of ethinyl estradiol if administered with EVG/COBI/FTC/TDF.

All subjects must undergo appropriate contraceptive counselling. The Investigator will counsel subjects on the most effective method(s) for avoiding pregnancy during the study.

Use of condoms should be encouraged for all participants because they have been proven to decrease the risk of transmission of HIV and other sexually transmitted diseases. The use of spermicide is not recommended if the subject or subject’s partner is HIV-infected.

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 all the study drugs 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 (problems during pregnancy, health of the baby at delivery, ie. Weight, APGAR scores) 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.

Possible Benefits of the Study

There is no guarantee that you will receive personal benefit from participating in this study. The study drugs are 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 the combination pill of EVG/COBI/FTC/TDF STR is safe and effective in treating HIV-1 infection. 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.

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. 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.

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 EVG/COBI/FTC/TDF STR (but at all times in compliance with applicable law and regulation). Your stored samples will be labeled with a study identification number, a bar coded number, and your initials. If your stored samples are shared with other researchers, they will only contain an identification number that does not identify you.

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 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.

WITHDRAWAL FROM STUDY
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 drugs.

COST OF TREATMENT

The EVG/COBI/FTC/TDF STR tablets used in this study will be given to you free of charge. If you are assigned to Study Treatment Arm 2 Truvada® will be given to you free of charge, also. 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, 11 visits through week 96, you will be paid $50 for every visit you attend. Thus if you attend all required visits for the study through week 96, the maximum payment you can receive is $575. If the drug is not commercially available by the end of week 96, the study will continue until it is available through your doctor or Gilead discontinues its development. If you continue past week 96, you will continue to receive $50 for every visit you attend for the study. If you choose not to participate after week 96, you will come in for an end of study visit ($50). 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 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 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 below in the event you experience any study-related illness or injury.

If you receive Medicare benefits, the Sponsor, Gilead Sciences, Inc., 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.

WHO CAN I CALL WITH QUESTIONS, COMPLAINTS OR IF I'M CONCERNED ABOUT MY RIGHTS AS A RESEARCH SUBJECT?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you

want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

RESEARCH STUDY REGISTRY

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

STORAGE AND USE OF PLASMA AND SERUM SAMPLES

A portion of your blood drawn at visits outlined in the Study Procedures Table will be frozen and stored. Your stored samples and the information collected about you during the study may be used by the Study Sponsor or its research partners for viral mutation testing, 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. No human genetic testing will be performed without your separate written consent. At the end of this study, these samples may be held in storage by Gilead Sciences, Inc. for up to 10 years.

Viral mutation testing detects changes or "mutations" in certain regions of the virus being studied. A mutation in an HIV-1 gene can change how antiretroviral drugs affect the HIV-1 virus. Some mutations can prevent certain antiretroviral drugs or drug treatments from reducing the level of HIV-1in your blood. When this occurs, the HIV-1 has become "resistant" to that drug and possibly other similar drugs. These tests may be experimental; that is, these tests may not have been approved by the 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.

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).

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 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 be also be used for purposes that are not yet known.

If you choose to allow your samples to be banked for future research, an additional 15 ml (3 teaspoons) of blood will be drawn at Baseline Visit and Weeks: 4, 8, 12, 24, 36,48, 60, 72, 84 and 96. If EVG/COBI/FTC/TDF STR is not commercially available in your country at week 96, and you decide to continue in the study after Week 96, sampled will also be stored every 12 weeks after Week 96. 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. 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

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.

By signing this informed consent form, 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 (or legally authorized representative)

Subject Printed Name (or legally authorized representative)	Signature	Date

<Description of Legal Representative's Authority (e.g., parent or legal guardian)>

Person Obtaining Consent

Printed Name & Title	Signature	Date

Witness (if applicable)

Witness Printed Name	Signature	Date