UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

Gilead Sciences, Inc
GS-US-292-0119, Amendment 2,17-OCT-2013

A Phase 3 Open-Label Study to Evaluate Switching from Optimized Stable Antiretroviral Regimens Containing Darunavir to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Single Tablet Regimen (STR) plus Darunavir (DRV) in Treatment Experienced HIV-1 Positive Adults

CONSENT TO PARTICIPATE IN A RESEARCH STUDY AND RESEARCH SUBJECT HIPAA AUTHORIZATION

Your contacts for this study at the Hospital of the University of Pennsylvania [HUP] are:

Site address: 502 Johnson Pavilion, Philadelphia, PA 19104

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Study Nurses:	Wayne Wagner, RN, MSW	(215) 349-8092

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

YOUR RIGHTS

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

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

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

PURPOSE OF THE STUDY

The treatment of HIV infection requires the combination of several medications in order to decrease the amount of virus in the body, improve immune function and delay the progression of the disease. This has generally required patients to take a large number of pills each day, and many experience a loss of effectiveness of their current medication regimen over time or unacceptable side effects. Therefore, it is important to develop new drug regimens. In addition, the combination of drugs into a single tablet reduces the number of pills a patient has to take and makes it more convenient to stick to the prescribed drug regimen.

You have been asked to take part in a clinical research study involving an experimental drug named Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Single Tablet Regimen (E/C/F/TAF STR) plus Darunavir (Prezista®) (DRV) which is approved by the FDA for the treatment of HIV-1. An experimental drug means that the FDA has not approved it for use by the general public.

The purpose of this study is to evaluate safety and to determine whether E/C/F/TAF STR plus DRV is effective against HIV-1 in subjects on current antiretroviral regimens (ARV) in virologically suppressed, HIV-1 positive subjects. The sponsor, Gilead Sciences, also manufactures STRIBILD, which is a single tablet that contains Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate, which is FDA approved. This study will look at another formulation of Tenofovir which is thought to have less toxicity for your kidneys. Safety and tolerability will be determined on the basis of physical exams, laboratory tests, and questions about any problems you might experience during the study.

You have been asked to participate in this study because you have HIV, are currently receiving treatment for HIV that includes Darunavir (DRV) and your current regimen is working well (keeps the HIV virus under control so it cannot be detected in your blood, i.e "virologically suppressed").

This study also includes two types of pharmacokinetic analyses. "Pharmacokinetics or "PK"" is the study of actions a drug takes within the body including how it is absorbed by the body (such as through the mouth, stomach or intestine), how it moves throughout the body, how it is metabolized (processed, converted and used) by the body, and how it is removed from the body. As part of the main study, levels of HIV in the blood and drug levels of the study drugs will be determined at various study visits. In addition, there is an OPTIONAL sub-study that is more comprehensive: drug levels are measured at multiple time points in a 24 hour period.

DESIGN OF THE STUDY

If you agree to participate, you will be one of 170 subjects recruited from about 100 study sites in North America. At Penn, about 5 people are expected to participate in this study.

This is an open label study, which means you and your Study Doctor will know what study drug(s) you are receiving.

This study will have two Cohorts, 20 subjects will participate in Cohort 1. Cohort 2 will consist of 150 subjects.

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.

Cohort 1

20 subjects will enroll in the Cohort 1. If you are enrolled in Cohort 1 you will receive E/C/F/TAF plus DRV once daily. After 20 subjects have completed Week 4 of study treatment in Cohort 1, the study enrollment will stop and how safe and effective the treatment is will be reviewed. Once this review is completed and no concerns are found, Cohort 2 will begin enrollment. Subjects in Cohort 1 will continue to receive treatment during this review period.

Cohort 2

Cohort 2 is a randomized cohort, which means you will be selected by chance (like a flip of a coin) to receive one of the two study treatments listed below:

Study Treatment Group 1: Single tablet regimen of E/C/F/TAF plus DRV once daily: 100 subjects.

Study Treatment Group 2: Subjects will remain on current, pre-existing antiretroviral regimen that includes DRV: 50 subjects

The randomization for this cohort is in a 2:1 ratio, which means that your chance of being assigned to Study Treatment Group 1 is two times greater than your chance of being assigned to Study Treatment Group 2.

DURATION OF THE STUDY

For both cohorts: the screening period (the time between the Screening visit and Day 1 visit) may last up to 30 days. Once you are confirmed to be eligible to participate in the study, and you state

that you want to take part in the study, your participation in this study will last about 48 weeks for either cohort, not including the screening visit. Following confirmation of your eligibility, you will be required to visit the study center at least 10 times (at Weeks 2, 4, 8, 12, 16, 24, 36 and 48).

After 48 weeks of treatment, all subjects will be given the option to participate in a rollover study to receive E/C/F/TAF plus DRV and attend study visits every 12 weeks until E/C/F/TAF becomes commercially available or until Gilead Sciences elects to terminate development of E/C/F/TAF. Subjects who complete treatment through the Week 48 Visit and decide not to participate in the rollover study will be required to complete a 30-day Follow-Up Visit.

If you decide to participate in the study, you can stop your participation at any time. Also, your participation in this study may be stopped at any time as described on the section "**WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE**" of this consent form. This means that your participation in the study may be shorter than described above.

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.
- 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.
- You must return all of the used and unused study drug and/or empty bottles to the clinic at each visit.
- 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

To help the study doctor determine your eligibility and safety to participate in this study, you need to be seen at the study center within 30 days before the study starts. After you sign the informed consent form and receive a copy of the informed consent form, you will have screening procedures done. Note that all of the procedures listed below may not be performed if at any point during the evaluation you fail eligibility.

Day 1 (baseline)

You will be asked to come back to the study center within 30 days after the Screening visit for the Day 1 (baseline) visit. You must not have anything to eat or drink, except water, for at least 8 hours before the visit. Eating or drinking may affect the results of your urine and blood testing.

All study procedures are listed in the Study Procedures Table following this section. Each Cohort will follow the same procedure schedule. 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,
    - questionnaires regarding your treatment adherence, and
    - questionnaires regarding your Quality of Life
- A 12-lead ECG (electrocardiogram) to check the functioning of your heart.
- A urine sample for laboratory tests (urinalysis and urine chemistry) including a pregnancy test if you are a female. Some of the urine collected will be tested to see if the study drugs have any effect on your kidneys.
- If you are a female able to become pregnant, a blood pregnancy test will be required at screening. 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 required throughout the study. If the urine pregnancy test is positive, a blood pregnancy test will be done to confirm the result; if confirmed, you will not be able to participate in the study.
- About 20-60 mL (about 4-12 teaspoons) (5 mL = 1 teaspoon) of blood will be taken at each visit 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), parathyroid function (thyroid is a gland that makes hormones which regulate metabolism), tests for hepatitis B and C viruses, a single PK blood sample, and to measure the amount of HIV-1 virus in your blood.
- About 14 mL (about 3 teaspoons) of blood will be collected and stored to allow the possibility of conducting clinical tests at a later date (for example, to check whether the HIV in your blood can develop resistance to this anti-HIV drug). Storage of these samples is optional and you will need to give your consent (on page 17 of this consent). If you do not agree, the extra sample will not be drawn.
- At Weeks 4, 24 and 48 subjects receiving E/C/F/TAF plus DRV will take your study drug with food at the clinic. You will have a PK blood sample collected between 15 minutes and 4 hours. You will then return to the clinic 20 to 24 hrs later to provide a blood sample.
- 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. Approximately 12 mL (about 2 ½ teaspoons) of blood will be drawn during this visit to measure the amount of HIV-1 in your blood and for genotype/phenotype testing. Phenotype testing is a technique used to determine whether a mutation in the HIV-1 gene changes how anti-HIV drugs affect the HIV-1 virus. The study doctor will then decide whether or not a change to your study treatment regimen is required.

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.

You will be asked to come back to the study center within 30 days after the Screening visit for the Day 1 (baseline) visit. You must not have anything to eat or drink, except water, for at least 8 hours before the visit. Eating or drinking may affect the results of your urine and blood testing. You will also need to be fasted for visits 12, 24 and 48.

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

- If you are in Cohort 1 or randomized to Treatment Arm 1, you will receive a 4-week supply of study drugs at Weeks 4, 8, and 12. You will receive an 8-week supply of study drugs at Week 16. At Weeks 24, 36 and 48 you will receive a 12-week supply of study drugs. All study medication should be taken once a day at the same time every day with food. You will be counseled regarding the importance of taking all study drugs.
- You may need to continue to provide DRV with a prescription from your doctor for both cohorts and treatment arms
- If you are randomized to Treatment Arm 2 you will continue to supply your ARV with a prescription from your doctor.
- You will be required to bring your used and unused study drug bottles back to the clinic at each visit. The study drug (number of tablets) will be counted. You will be asked about any missed doses since your last visit.

Early Study Drugs Discontinuation (ESDD) Visit

If you discontinue study drugs at any time before the study is complete, you will be asked to return to the study center within 72 hours of stopping study drugs. Procedures at this visit will include those listed in the study procedures table.

30-Day Follow-Up

If you discontinue your study drugs, and do not wish to continue attending regularly scheduled visits, you will be asked to return to the study center 30 days after the completion of the Early Study Drugs Discontinuation visit. Procedures at this visit will include those listed in the study procedures table.

Study Procedures Table for Cohorts 1 and 2

Procedure (What is Going to Happen)	Screening	Baseline (Day 1)	End of week:			
			2, 4, 8, 12, 16, 24, 36, 48	Post Week 48 (every 12 weeks)	ESDD	30-Day Follow up Visit/
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	Weeks 24 and 48 and as needed.	As Needed	X	If needed
Vital Signs will be taken (including weight. Height at Screening only)	X	X	X	X	X	X
Blood and urine samples will be taken[a]	X	X	X	X	X	X
Additional blood and urine for storage will be collected (if you provide additional consent for this)		X	X	X	X	X
Approximate Total Amount of Blood Taken - **Teaspoons in US (mL in Europe**)	4 tsp (20mL)	7tsp (33.5mL)	10 tsp (49mL) Weeks 2 & 8-16 & 36. 12 tsp (61mL)	9tsp (43mL)	9tsp (43mL)	5 tsp (25mL)

			Week 4.13 tsp (67mL) Weeks 24 & 48			
A 12-lead ECG will be performed	X		X (Weeks 24 and 48 only)		X	
You will complete a questionnaire about your satisfaction with current medications		X	X (Weeks 24 and 48 only)			
You will complete questionnaires regarding your general health		X	X (weeks 24, 48 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	

Restrictions During the Study

You will be told not to eat or drink anything except water for at least 8 hours before your blood is drawn and your urine is collected at Day 1 (baseline) visit, Weeks 12, 24, and 48.

You cannot take any antacids that contain calcium, magnesium, or aluminum (for example, Tums® or Rolaids®), Carafate® (an ulcer medicine), or vitamins/mineral supplements that contain calcium, iron or zinc for a minimum of 2 hours before and 2 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.

Pharmacokinetic (PK) Sub-study

A pharmacokinetic sub-study will be performed in the E/C/F/TAF plus DRV arm only at or between the Week 2, Week 4, or Week 8 visits in approximately 15 subjects at some study sites. The sub-study will include intensive PK sampling and there will be a separate additional Consent Form to review and sign for subjects who choose to and are eligible to participate.

RISKS

You are participating in a study to assess the safety and efficacy of treatment simplification to E/C/F/TAF plus DRV. The E/C/F/TAF tablet has been studied in several trials and the adverse events (problems) noted in those studies is provided below. However, the individual components have also been studied alone or as part of other combination regimens. In order for you to be more fully informed about the risks for the study, the components have also been summarized. If you are selected to receive this regimen, there is no guarantee that this regimen will be better than your current HIV medication. There is the possibility that it could be worse at controlling HIV than your current regimen.

EVG/COBI/FTC/TAF (E/C/F/TAF)

E/C/F/TAF is a single-tablet regimen (STR, or "combination pill") containing four medications: elvitegravir (EVG), cobicistat (COBI), Emtriva® (FTC), and tenofovir alafenamide (TAF).

As of November 2012, 112 HIV-positive subjects have been dosed with the E/C/F/TAF combination pill as part of a Phase 2 study to evaluate the drug's safety and ability to suppress HIV viral load to undetectable levels (efficacy). After 6 months of therapy, 87% of subjects had undetectable viral loads (HIV-1 RNA < 50 copies/mL). Treatment was generally well tolerated as most adverse events or side effects (AEs) were mild and not associated with treatment discontinuation. No new or unexpected adverse events occurred. Subjects taking E/C/F/TAF had smaller changes in markers of kidney function and bone mineral density than subjects on a TDF-based regimen. The differences were statistically significant and may have important clinical relevance for individual patients. The frequency and type of adverse events and laboratory abnormalities was comparable to the TDF-based regimen.

In addition, more than 100 HIV-negative subjects have been dosed with the E/C/F/TAF combination pill as part of a Phase 1 study to evaluate the level of each drug in the blood (pharmacokinetics). No deaths or serious side effects occurred during the study. One subject discontinued from the study because of a nonserious adverse event of increased creatine phosphokinase (CPK) levels in the blood that was assessed as related to study drug. Elevated CPK can be an indicator of heart or muscle damage, although this particular patient was otherwise asymptomatic. The most frequently reported side effect was constipation. Other side effects included nausea, dizziness, headache, breast tenderness, and papular (small raised red bumps) rash. No subject in any treatment arm developed any clinically significant abnormalities (changes that were outside of the normal range) on ECG throughout the study.

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

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

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 in the blood, increased glucose in the blood, allergic reaction, hives, adverse effects on the function of the liver and pancreas, and low white blood cell count. A reduction in your white blood cell count can make you more prone to infection. You may also experience increased creatine kinase in your 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.

Tenofovir alafenamide (TAF)

Tenofovir alafenamide (TAF) is a new form of the anti-HIV drug, tenofovir. TAF as an individual agent has been administered to more than 40 HIV-positive subjects in two separate studies. In study GS-US-120-1101, subjects received higher doses of TAF (50 mg and 150 mg) than the TAF dose in this study. Side effects that were seen in more than two subjects were headache, nausea, and gas (flatulence). In Study GS-US-120-0104, adverse events observed in more than two subjects were nausea and fatigue. One serious adverse event of chest pain was reported, but not considered related to study drugs. In addition, TAF has been given to over 83 HIV-negative subjects.

A study in dogs detected eye problems (posterior uveitis) in some dogs when TAF was given at the highest doses. There have not been cases of uveitis related to TAF in clinical studies, however, during this study you should immediately report any visual disturbances or eye pain you experience to your doctor and be evaluated.

TAF is a drug similar to Tenofovir disoproxil fumarate (TDF), Viread®, an approved medication by the FDA for the treatment of HIV and hepatitis B infection. Although the side effects for TAF are not known yet, the adverse effects are expected to be similar to Viread. The side effects for Viread® are listed below.

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.

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

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

Darunavir (Prezista®) with low dose ritonavir (DRV/rtv)

The most frequently observed side effects (seen in more than 10 percent of subjects) of DRV/rtv were diarrhea, headache, abdominal pain, nausea, vomiting, changes in body fat and skin rash, mostly mild or moderate in severity.

Skin rash, when it occurs maybe accompanied with fever and/or increase in liver enzymes (transaminases). It usually develops within the first 4 weeks of treatment with DRV/rtv, is often mild or moderate in severity, often resolves within one week and does not necessarily lead to treatment interruption. However in some cases, the rash has been severe or life-threatening. Rare cases of Stevens-Johnson syndrome and other severe skin reactions have been reported in patients taking DRV/rtv in combination with other anti-HIV drugs, as well as other medications. The signs and symptoms can include severe rash (including the mouth and lips) with fever, weakness, fatigue (malaise), muscle or joint pain, blisters, swollen eyelids (conjunctivitis), inflammation of the liver (hepatitis) and/or increase of white cells in the blood (eosinophilia). It usually requires immediate admission to the hospital. This condition usually goes away when all medications are stopped. If you develop a rash or any skin abnormality, you should report it to your Study Doctor.

Different antiretroviral (ARV) drugs, including DRV/rtv, may affect fat and sugar metabolism and may cause diabetes. The most frequently observed laboratory abnormalities with DRV/rtv are increases in blood fats (triglycerides and cholesterol) and sugars (glucose). Rare cases of pancreatitis (inflammation of the pancreas that can cause abdominal pain and vomiting which can be sometimes life threatening) have been reported in patients taking DRV/rtv and other ARV drugs.

Uncommon cases of liver disorders (including inflammation of the liver that can cause fatigue, loss of appetite, nausea, jaundice, dark urine, liver tenderness) have been reported in patients taking DRV/rtv and other ARV drugs. Patients with liver diseases such as hepatitis B and/or hepatitis C may have worsening of their condition. Some of the liver disorders, which occur or worsen when taking DRV/rtv can be severe and might be sometimes life threatening.

Liver and pancreatic function, in addition to other organs' function will be monitored throughout the study.

There have been reports of increased risk of bleeding in patients with hemophilia and DRV/rtv. Report all bleeding episodes to your Study Doctor.

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 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.

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 may be reported to your local health authority. You will be told, face-to-face, the results of these tests. Counseling will be available to you if necessary.

UNKNOWN/UNEXPECTED RISKS AND DISCOMFORTS

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 to take part in this study.

PREGNANCY AND BREAST-FEEDING

The effects of E/C/F/TAF have not been fully evaluated on the developing fetus in humans. Animal studies do not indicate direct or indirect harmful effects of E/C/F/TAF and TDF with respect to pregnancy. Because the effects of E/C/F/TAF on a developing fetus as well as on exposed infants are unknown, any female able to become pregnant (i.e., A female subject of childbearing potential is a nonmenopausal female who has not had a hysterectomy, bilateral oophorectomy, or medically documented ovarian failure. This definition includes a young woman who has not yet started menstruating) must have a negative blood pregnancy test to enroll; females who are breast-feeding will not be enrolled in this study.

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

If you are a sexually active male or female, it is required that you use a protocol recommended method of birth control from the screening visit throughout the study and for 30 days following the last dose of study drug.

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 (without spermicide); 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. If you are female and use hormonal contraceptives as one of your birth control methods you must have used the same method for at least 3 months before study drug dosing. Since the effect of the study drugs on hormonal contraceptives is unknown, if you are on hormonal contraceptives you must agree to a barrier method in addition to continuing your current hormonal contraceptives. Acceptable barrier methods include: diaphragm, cervical cap, and the male condom (without spermicide). If you are female, you must use either a hormonal method or a barrier method if the partner has a vasectomy.

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>

If you are a female who is sexually active and able to become pregnant, please speak with your study doctor to determine the best method of birth control for you to use during this study. Hormone-based contraceptives may not be effective at preventing pregnancy when they are used with study drug.

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

If you are female and become pregnant or suspect that you have become pregnant while in the study and within 30 days of last dose of study drug, you will be required to stop taking 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 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 (except for lambskin) 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. The use of spermicide is not recommended if you or your partner is HIV-infected. Male subjects must agree to use condoms during heterosexual intercourse and avoid sperm donations while enrolled in the study and for 30 days after administration of the last dose of study drug.

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 taking part in this study, you and the Sponsor, Gilead Sciences, Inc., may benefit if E/C/F/TAF is 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.

WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE

Special care will need to be taken when determining if you need to stop the study drug. Your study doctor will supervise any discontinuation of the study drug with your health as the first priority. Your participation in this study may be stopped at any time by a) your study doctor, b) Gilead Sciences,

Inc., c) the FDA, d) the Institutional Review Board (a review group that gives approval to your study doctor to conduct this study), and (e) other appropriate regulatory agencies.

Your participation in this 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 a change to your treatment regimen is required or 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

E/C/F/TAF STR will be given to you free of charge. If you are enrolled into Cohort 1 or randomized into Cohort 2 Treatment Arm 1, you will also be given DRV free of charge. In addition, if you were prescribed Truvada® as part of your pre-existing antiretroviral regimen and are randomized into Cohort 2 Treatment Arm 2, you will be given Truvada® free of charge. All clinic, professional, diagnostic, and laboratory fees for tests and procedures that are part of this study will be provided at no cost to you. You or your usual health care payer will be responsible for any other health care costs.

PAYMENT FOR PARTICIPATION

You will be paid $50.00 for your screening visit. For visits thereafter, Baseline and 9 visits through wk 48 (2, 4, 8, 12, 16, 24, 36, and 48), you will be paid $50 for every visit you attend. Total compensation through week 48 of the study is $550. If you elect to participate in the rollover study and take E/C/F/TAF, you will be compensated $50 for each visit you attend. If you stop taking study drugs early and complete the Early Study Drug Discontinuation Visit, 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 $50 for any unscheduled visits requested by the study staff. The total payment you will receive for the study depends on how long you participate.

In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

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 on page 1 of this form 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.

STATEMENT ABOUT PRIVACY

Records identifying you will be kept confidential and, to the extent permitted by applicable laws and/or regulations, will not be made publicly available. Your personal information may be given out if required by law. If you test positive for HIV, 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.

To further protect your confidentiality on the study, you will be assigned a code number. This code number will be used to label all your samples for testing and the information collected about you as part of your study visits will be entered into a database by this code number. Records that have your name and personal information will have restricted access and stored in locked cabinets in a secure facility.

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 E/C/F/TAF (but at all times in compliance with applicable law and regulation).

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, email address, complete dates for visits, etc, social Security Number, medical record number
- 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 Independent Data 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).

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 URINE SAMPLES

A portion of the urine samples taken at each visit, except screening, will be frozen and stored. The stored urine samples may be used by the Sponsor or its research partners for possible additional clinical analyses. At the conclusion of this study, these samples may be retained in storage by Gilead Sciences, Inc. for a period up to 10 years.

STORAGE AND USE OF BLOOD SAMPLES

A portion of your blood sample drawn at each visit, except screening, will be frozen and stored. These stored blood samples and the information collected about you during the study may be used by the Study Sponsor or its research partners for HIV-1 genotyping/phenotyping assays or their development, for retesting the amount of HIV-1 in your blood, for measurement of antiviral drug levels in the blood, for future testing to learn more about how the study drug has worked against HIV-1 or clinical laboratory testing to provide additional clinical data. At the conclusion of this study, these samples may be retained in storage by Gilead Sciences, Inc. for a period up to 10 years.

Genotype testing detects changes or "mutations" in certain genetic regions of the HIV-1 virus. Phenotype testing is used to determine whether a mutation in an HIV-1 gene changes how anti-HIV drugs affect the HIV-1 virus. Some mutations can prevent certain anti-HIV drugs or drug regimens from reducing the level of HIV-1 in your blood. When this occurs, the HIV-1 has become "resistant" to that drug and possibly other similar drugs. Genotype and phenotype tests may be experimental; that is, these tests may not have been approved by the FDA. The results of such tests are for research use only, and the interpretation of the test results may not have direct benefit to you. At the conclusion of this study, these samples may be retained in storage by Gilead Sciences, Inc. for a period up to 10 years.

No human genetic testing will be performed without your expressed consent.

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

If you choose to allow your samples to be banked for future research, about 14 mL (about 3 teaspoons) of blood will be drawn at all study visits (starting at 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. 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

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 to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

Subject

Subject Printed Name	Signature	Date

Person Obtaining Consent

Printed Name & Title	Signature	Date

Witness (if applicable)

Witness Printed Name	Signature	Date

Legally Authorized Representative (if applicable)

Legally Authorized Representative Printed Name	Signature	Date