Appendix IV: Sample Screening and Enrollment Informed Consent Form

HPTN 083

A Phase 2b/3 Double Blind Safety and Efficacy Study of Injectable Cabotegravir Compared to Daily Oral Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC), For Pre-Exposure Prophylaxis in HIV-Uninfected Cisgender Men and Transgender Women who have Sex with Men

Version 3.0
October 31, 2019
DAIDS Document ID: 20725

Sponsored by: Division of AIDS, United States (US) National Institute of Allergy and Infectious Disease, US National Institutes of Health. Study products are provided by ViiV Healthcare and Gilead Sciences, Inc.

PRINCIPAL INVESTIGATOR: *[Insert Name*]

PHONE: [Insert Number]

GENERAL OVERVIEW

You are being asked to take part in an investigational research study related to the Human Immunodeficiency Virus, or HIV. HIV is the virus that causes Acquired Immunodeficiency Syndrome, or AIDS.

This study is being offered to approximately 5000 HIV-uninfected men who have sex with men (MSM) and transgender women (TGW) that have sex with men in Asia, North and South America, and South Africa. Before you decide whether to join the study, we would like to explain the purpose of the study, the risks and benefits to you, and what is expected of you.

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

There may be no direct benefits for you if you participate in this study. There also may be some risks with taking part in the study. Before you can make an informed decision about whether to take part in this study, you should understand the possible risks and potential benefits of being in this study. This informed consent form gives information about the study that will be discussed with you. Once you understand the study, and if you agree to take part, you will be asked to sign your name on this form.

Your participation is voluntary

This consent form gives information about the study that will be discussed with you. Once you understand the study, and if you agree to take part, you will be asked to sign your name or make your mark on this form. You will be offered a copy of this form to keep.

Before you learn about the study, it is important that you know the following:

- Your participation is voluntary. You do not have to take part in any of the tests or procedures in the study.
- You may decide not to take part in the study, or you may decide to leave the study at any time. [You will continue to receive the same services that you can get at [insert clinic name]].
- If you decide not to take part in the study, you can still join another study at a later time if there is one available and you qualify.
- You cannot join this study if you are taking part in another study of drugs or medical devices. You are asked to tell the study staff about any other studies you are taking part in or thinking of taking part in. This is very important for your safety.

BACKGROUND AND PURPOSE OF THE STUDY

You are being asked to participate in this study because you are at risk of getting infected with HIV. Ideally, as part of routine medical care, ways to decrease your risk of getting infected with HIV would be discussed with you. *[Sites to include next sentence if Truvada is locally available*]: A treatment you might be offered to decrease your risk of getting HIV is a pill call Truvada (TDF/FTC). It is one pill that contains two drugs, one called emtricitibine [FTC] and the other called tenofovir disoproxil fumarate [TDF]). It is approved by the U.S. Food and Drug Administration (FDA) for the treatment of HIV and also to prevent people from getting HIV. *[Non-US sites to fill in the current status of approval of TDF/FTC here].* The US FDA is the regulatory group that oversees the approval of all drugs in the US. The approval of TDF/FTC for the prevention of HIV is based in part on a previous study in men who have sex with men (MSM) and transgender women (TGW) who have sex with men, called iPrEX. The iPrEX trial enrolled close to 2,500 HIV-uninfected MSM and TGW who were at risk for getting HIV, to see whether TDF/FTC would lower their chances of getting HIV. The study showed that it did. The study also showed that people that took the drugs more regularly were more likely to not get HIV than those who did not take the drugs regularly. TDF/FTC is supposed to be taken every day in order to provide the highest chance of not getting HIV.

The main purpose of this study is to try to find out if a new drug, called cabotegravir (CAB), is as safe and will work as well as TDF/FTC in protecting you from getting HIV. CAB is available in the form of a pill and as an injection (shot). Researchers do not yet know if this injectable drug will work to protect people from getting HIV. This is why we are doing this study. In this study, you will take pills every day, and you will be get a shot every 8 weeks, after first getting two shots given one month apart.

STUDY GROUPS

If you decide to be in this study, you will be placed in to 1 of 2 groups. Each group will have approximately 2500 people in it. You will be followed for approximately four years, and include up to approximately 47visits to this clinic over that time.

Each person in each group will get injections and a daily pill. Injections are given as one shot in the buttock. The shot is given over time like this: you get one shot, then a month later you get another shot, and then after that you get a shot every two months. The pill should be taken every day.

The first group will get the real CAB drug in a pill and injections, and the second group will get the real TDF/FTC drug in a pill and an injection with no study drug in it. We do not want you or the study researchers to know which group you are in, because we want to know which drug works better to protect you from getting HIV. By not knowing, then we do not favor one group over the other. In order to do this, each group will also get placebos of the injections and the pills. Placebos look and feel like the real drug, but they do not contain any of the active ("real") drug or any other medicines. The placebo for the CAB injection is a nutrition infusion called Intralipid. The placebo for the pills will look, feel and taste the same as the real pills.

The study group that you will be in will be chosen randomly, like flipping a coin. You cannot choose your group, and the study staff cannot choose your group for you. You have an equal chance of being placed in one of the two groups. Both groups are very important to the study. In this study, you and the study researchers will NOT know which group you are in until the study is over.

No matter what group you are in, you must remember that we do not know if CAB works to protect you from getting HIV. We do know that taking TDF/FTC on a daily basis can be more than 90% protective against getting HIV infection. It is important to remember neither daily TDF/FTC nor CAB will protect you from getting sexually transmitted infections, like gonorrhea, chlamydia, syphilis, warts, or herpes. One of the best things you can do to protect yourself from getting HIV during sex is to us a condom every time you have sex.

The groups look like this, and each group moves through 3 Steps in the study [*sites may show a graphic to depict the groups and the steps*] like this:

Group A – this group gets real CAB pills and injections:

- Step 1: Real CAB pill AND placebo pill for TDF/FTC (2 pills total) every day for 5 weeks
- Step 2: Real CAB injections given as one shot, then another shot a month later, and then every 2 months after that AND placebo pill for TDF/FTC every day up to three years after enrollment
- Step 3: Real TDF/FTC pill every day for about a year, then move to local HIV prevention services

Group B – this group gets real TDF/FTC pills:

- Step 1: Real TDF/FTC pill AND placebo pill for CAB (2 pills total) every day for 5 weeks
- Step 2: Placebo CAB injection AND real TDF/FTC pill everyday up to three years after enrollment
- Step 3: Real TDF/FTC pill every day for about a year, then move to local HIV prevention services

In Step 1, everyone starts the study by taking pills for 5 weeks. This is to see if you have any serious side effects to the study drugs before you start getting the shots.

In Step 2, everyone takes pills and gets shots. This step will continue until three years after enrollment.

In Step 3, which starts on the same day as the last day of Step 2, everyone gets the real TDF/FTC every day for about a year, then your participation in the study will end and we will refer you to local HIV prevention services. There are no current plans for the study to offer the injectable CAB drug to study participants after the completion of the study.

If the results of this study show that CAB works to prevent HIV, we will tell you that and let you know if it may become available in your local area. Often times it can take a long while for a new drug to become available to the public once it has been shown that it works in a study like this.

STUDY PROCEDURES

Screening Visit

Your screening visit may occur after you read, discuss, understand, and sign this form, or will we schedule it for you at another time. We will help you understand the form and answer your questions before you sign this form. The procedures done for the screening visit will take about [*site to fill in time required*], and may be done at one or more visits.

At this visit, the study staff will:

- Ask you where you live and other questions about you, your medical health, your sexual practices, including if you are at a higher risk of getting HIV, and whether you use alcohol or drugs. [Sites in US to add this here: We will ask you to answer some additional questions about sexual practices using an assessment called SexPro, which may provide additional information about your HIV risk, and whether this study is appropriate for you.] [Sites in South America to add this here: We will ask you to answer some additional questions about sexual practices using an assessment called SexPro, which may provide additional information about your HIV risk.]
- Give you a brief physical exam to make sure you are healthy.
- Talk with you about HIV and ways to protect yourself from getting it and offer condoms and lubricant.
- Have an electrocardiogram (ECG) scan, which is a test to monitor your heart.

- Collect ~XX mL (about x teaspoons) of blood for HIV testing, Hepatitis B and C testing, to check your general health, to check the health of your liver, and for storage for study-related testing.
- [*Sites participating in the DXA substudy to include this:*] We may ask you to be a part of a group that gets a bone mineral density-energy x-ray absorptimetry (DXA) scan. A DXA scan is a special kind of x-ray using a small amount of radiation, allowing the doctor to see parts of the body better than a regular x-ray. We know that TDF/FTC may cause thinning or softening of bones in some people. We want to see whether there are changes to your bones during the study, and the DXA scan lets us evaluate your bones. We want to see if this is different between the TDF/FTC and CAB treatments. The scan will be done at the Enrollment visit (this visit), and 2 other times during the study (Weeks 57 and 105). The results of the DXA scans will be given to you at the end of the study.

The results of the HIV test will be available [*site to insert timeframe of RNA testing, and also EIA testing if being used*]. You will be contacted about the results of your other tests when they are available.

Confirmation of Eligibility:

Once all the results of the screening tests are known, the following will happen within 45 days after screening:

- You will be told your test results and what they mean.
- If you have a positive HIV, hepatitis B or C test you will not be eligible for the study, and you will be referred for the appropriate medical care (*sites to add specifics about this here as necessary*).
- If you are negative for HIV but the results from the other blood tests show that you might have some health problems, you may not be eligible for the study. Study staff will refer you to available sources of medical care and other services you may need. Later, if these problems resolve, you may be able to come back to find out if you are eligible at that time.

Step 1: Enrollment Visit (Week 0)

If you are eligible for this study and decide to take part in the study, you will be asked to return for the enrollment visit. This visit will last about xx hours. During the visit, the study staff will:

- Confirm where you live and how to contact you.
- Ask you some questions about yourself, like your age, and your racial/ethnic group [*sites that want to collect this during screening should move this to screening section.*]
- Talk with you about HIV and ways to protect yourself from getting it.
- Give you a complete physical exam, to include measuring your height, weight, blood pressure, pulse, and ask you about any other medicines you are taking.
- Collect a urine sample to see if there is sugar or protein in your urine.

- Collect ~XX mL (about x teaspoons) of blood for: HIV testing, Hepatitis B testing, syphilis, to check how much cholesterol is in your blood (a fatty substance in your blood), to check your general health, to check the health of your liver, and for storage for study-related testing and long-term storage (if you provide consent) *[Sites to delete if long term storage is not allowed]*. [*Sites to add this if allowed at your site. If not, delete: Additionally, if you provide consent, we will use a sample of your blood to see how the drugs work in your body by looking at your genes. Information about the testing related to your genes is found later in this consent form.*] For the cholesterol test, you will be instructed to not eat or drink anything other than what the study staff tell you is acceptable for 8-12 hours before your blood is drawn.
- Ask you questions about your sexual behavior.
- Ask you questions about your opinions about taking pills and getting injections.
- Perform a swab of your rectum and collect urine for gonorrhea and chlamydia.
- [*Sites participating in DXA substudy to include this*: If you agreed to be part of the DXA subset, you will undergo a DXA scan [*Note to sites participating in the DXA substudy - the first DXA may occur 30 days before the Enrollment visit or 7 days after in order to allow for flexibility in scheduling.*]
- We may ask you to be a part of a group that gets a bone mineral density-energy x-ray absorptimetry (DXA) scan. A DXA scan is a special kind of x-ray using a small amount of radiation, allowing the doctor to see parts of the body better than a regular x-ray. The subset will include 350 participants. The scan will be done at the Enrollment visit and 2 other times during the study (Weeks 57 and 105). If you are in this group, we will also check your blood to see how much Vitamin D is in it, and will ask you about your diet to see if you are eating foods with calcium in it. We will tell you if the DXA subset is no longer available to participate in. [*Sites that do not participate in the DXA subset to delete this entire bullet item*].
- Randomize you into one of the two study groups.
- Give you your study pills, and explain how to take them, and any side effects they may cause.
- Have a discussion about any challenges of taking a pill every day.
- Give you the results of tests when they are available.
- Offer you condoms and lubricants.

Step 1: Weeks 2 and 4 Visits

These visits will last about XX. During these visits, the study staff will:

- Confirm where you live and how to contact you.
- Talk with you about HIV and ways to protect yourself from getting it.
- Count your pills, and talk with you about ways to help you take your pills.

- Give you a brief physical exam, to include measuring your weight, blood pressure, pulse, and ask you if you have experienced any side effects from the study drugs, and ask you about any other medicines you are taking.
- Collect ~XX mL (about x teaspoons) of blood for HIV testing, to check your general health, the health of your liver and kidneys, and for storage.
- Have a discussion to help work through any challenges of taking a pill every day; if it seems to you or to the study staff that you are having challenges, we will try to help by working through these with you.
- Give you the results of your blood tests when they are available.
- Offer you condoms and lubricant.

If you have a side effect from the pills, or if you do not take enough of your pills, you may not be able to get the shots. If this happens, we will ask you to attend a visit once a year for three years from the time you enrolled in the study. The procedures for those visits are outlined later in this consent form document [*sites may also list the procedures here]*.

Step 2: Week 5 Visit – Visit for first injection

This visit will last up X hours. During this visit, the study staff will:

- Confirm where you live and how to contact you.
- Give you a brief physical exam, to include measuring your weight, blood pressure, pulse, ask you if you have experienced any side effects from the study drugs, and ask you about any other medicines you are taking.
- Talk with you about HIV and ways to protect yourself from getting it.
- Collect ~XX mL (about x teaspoons) of blood for HIV testing and for storage.
- Ask you to answer questions about your sexual behavior.
- Give you your study pills, and explain how to take them, and any side effects they may cause.
- Administer the first shot in your buttock
- Have a discussion to help work through any challenges of taking a pill every day; if it seems to you or to the study staff that you are having challenges, we will try to help by working through these with you.
- Give you the results of your blood test when they are available.
- Offer you condoms and lubricant.

Step 2: All other visits where injections occurs: Week 9, 17, 25, 33, 41, 49, 57, 65, 73, 81, 89, 97, 105, 113, 121, 129, 137, 145, 153 (an injection is not given at Week 153 but is a study visit),

In this step of the study, there will be approximately 19 visits where you will receive a shot and study pills. Injections will be given approximately every 2 months (8 weeks) after the first two are given one month (4 weeks) apart. These visits will last up to XX hours. During these visits, the study staff will:

[*Note: Sites may remove Week numbers in the text below if easier to depict it in a table or refer to the Schedule of Procedures and Evaluations*].

- Confirm where you live and how to contact you.
- Talk with you about HIV and ways to protect yourself from getting it.
- Give you a brief physical exam, to include measuring your weight, blood pressure, pulse. Ask you if you have experience any side effects from the shots you received, and ask you about any other medicines you are taking.
- Collect ~XX mL (about x teaspoons) of blood for:
    - HIV testing, to check your general health, the health of your liver, and for storage (every injection visit)
    - HCV testing about every year (Weeks 57, 105 and 153 only)
    - Syphilis testing about every 6 months throughout Step 2 (Weeks 33, 57, 81, 105, 129 and 153 only)
    - Testing to see how much cholesterol is in your blood two times during the study, one year apart (Weeks 57 and 105 only). For the cholesterol test, you will be instructed to not eat or drink anything other than what the study staff tell you is acceptable for 8-12 hours before your blood is drawn.
- Collect a urine sample to see if there is sugar or protein in your urine about every year for 3 years (Weeks 57, 105, and 153 only).
- Ask you to answer questions about your sexual behavior at every injection visit for about 2 years, and then every other injection visit for the rest of Step 2 (Weeks 5, 9, 17, 25, 33, 41, 49, 57, 65, 73, 81, 89, 97, 105, 121, 137, 153)
- Ask you questions about how you feel about taking pills and getting injections about every 6 months for two years and then once more a year later (Weeks 17, 41, 65, 89 and 137).
- *[Sites to include only for those sites participating in DXA subset:]* If you had a DXA scan (x-ray) when you started the study, we will ask you to have two more, about a year apart from each other (Weeks 57 and 105 only). We will also ask you questions about what you eat and if you take any vitamins or other supplements.
- Ask you to have an ECG scan about every year for 3 years (Weeks 57, 105, and 153 only).
- Perform a swab of your rectum and collect urine for gonorrhea and chlamydia about every 6 months throughout Step 2 (Weeks 33, 57, 81, 105, 129, and 153 only).

- Give you your study pills, and explain how to take them, and any side effects they may cause (at all injections visits).
- At Week 153 only or if you move to Step 3 early, collect any unused blinded oral study product
- Give you a shot (at all injection visits except for Week 153).
- Give you the results of your blood tests when they are available (at all injection visits).
- Have a discussion to help work through any challenges of taking a pill every day; if it seems to you or to the study staff that you are having challenges, we will try to help by working through these with you (at all injection visits).
- Offer you condoms and lubricant (at all injection visits).

Step 2: Post-Injection Visits: Weeks 6, 10, 19, 27, 35, 43, 51, 59, 67, 75, 83, 91, 99, 107, 115, 123, 131, 139, 147

[*Note: Sites may remove Week numbers in the text below if easier to depict it in a table or refer to the Schedule of Procedures and Evaluations*].

There will be up to approximately 19 visits following each visit where you got a shot. These visits will last up to XX hours. During these visits, the study staff will:

- Confirm where you live and how to contact you.
- Talk with you about HIV and ways to protect yourself from getting it.
- Give you a brief physical exam. Ask you if you have experience any side effects from the shots you received, and ask you about any other medicines you are taking.
- Collect ~XX mL (about x teaspoons) of blood for HIV testing, to check your general health, the health of your liver, the amount of the study drug that is in your blood, and for storage.
- Offer you condoms and lubricant.

Step 3: If you stopped getting injections early, you will go to Step 3. If you got all of your injections, you will go to Step 3 at Week 153 of Step 2, which is the same visit as Day 0 of Step 3. This step includes 4 more visits over about a year (Week 12, 24, 36, and 48).

Each visit will last up to XX hours. During these visits, the study staff will:

- Confirm where you live and how to contact you.
- Talk with you about HIV and ways to protect yourself from getting it.
- Give you a brief physical exam, to include measuring your weight, blood pressure, pulse, and ask you about any other medicines you are taking
- Collect ~XX mL (about x teaspoons) of blood for HIV testing, syphilis testing, to check your general health, the health of your liver, the amount of the study drug in your blood,

and for storage. Note: Blood will be collected for syphilis testing at Day 0 (which is the same as Step 2 Week 153), and Weeks 24 and 48. However, if you have had syphilis testing within 3 months of joining this part of the study, you will only have this done at Week 24 and Week 48.

- Perform a swab of your rectum and collect urine for gonorrhea and chlamydia (Day 0 (same as Step 2 Week 153), Week 24 and 48 only). If you have had this test within 3 months of joining this part of the study, you will only have this done at Week 24 and Week 48 only.
- Give you your study pills, and explain how to take them, and any side effects they may cause (Day 0, Weeks 12, 24, and 36 only).
- Ask you to answer questions about your sexual behavior (Day 0, Week 12, 24 and 48 only).
- Ask you questions about what it was like getting the injections and taking the study pills (this will only be asked if you have not been asked this in the few months before you started this step).
- Have a discussion to help work through any challenges of taking a pill every day; if it seems to you or to the study staff that you are having challenges, we will try to help by working through these with you.
- Give you condoms and lubricant.

If you move into Step 3 prematurely, some of the procedures above may not have to be performed, which will depend on when during the study you moved into Step 3. The procedures that may not have to be performed are: asking you about questions about your sexual behavior, urine collection and testing for GC/CT, and rectal swab collection and testing for GC/CT and syphilis testing.

It may be necessary for additional visit(s) and procedures in the event of unforeseen or unanticipated events or results; for example, you may have a side effect that requires repeat testing on your blood to ensure that the study drugs continue to be safe for you to use. Or, sometimes the results of some tests are not clear and additional testing is needed in order to confirm a test result. There also may be difficulties in sample shipping, processing, or testing; and/or if you are experiencing any symptoms or changes in your physical condition. There also may be a time that you are not able to complete all of the procedures in a visit and you have to come back the next day or another day, and additional blood may be needed when you come back in order to complete the requirements of the visit. In the event of any of these unforeseen or unanticipated results, we will explain to you what will happen and what procedures will need to be done.

After these visits are over, we will help you seek additional HIV prevention care [sites to add information here or elsewhere in the consent form].

Annual Visits

Procedures for HIV testing every year if you do not get shots or have completed or been in Step 3:

As we mentioned, the study begins with taking pills only for five weeks before you can start with the shots. During this time, you may get a side effect that would result in not moving to the part of the study where the shots are given. Or, you may not have taken enough of the pills. If any of this happens, you would not get shots, and we would ask you to attend a visit once a year until three years from your date of Enrollment in order to test you for HIV.

If you do get shots but stop getting them early, you will move to Step 3 of the study where you will get real TDF/FTC for approximately a year and come in for visits every three months for approximately a year. After that time, we will help you find prevention services in the local area, and we will ask you to attend a visit once a year until three years from your date of Enrollment in order to test you for HIV.

The procedures for these visits every year while Step 2 of the study is still ongoing are:

- Confirm where you live and how to contact you.
- Talk with you about HIV and ways to protect yourself from getting it.
- Give you a brief physical exam, and ask you about any medicines you are taking.
- Collect ~XX mL (about x teaspoons) of blood for HIV testing, the amount of the study drug in your blood, and for storage.
- Give you condoms and lubricant.

As we mentioned at the beginning of the consent form, you can decide to not participate in the study at any time during the study. If you decide this during a study visit, that study visit may be your last study visit. If you decide this in between visits, we will ask you to return any unused study pills.

Procedures if you become infected with HIV during the study

If you get HIV during the Step 1 of the study, you will stop taking your study pills, and you will be referred for local care and treatment of HIV and will be discontinued from the study. If you get HIV during Step 2 of the study (while you are getting shots), you will stop taking the study drugs and getting shots and we will ask you to come back for a visit every 3 months for about a year. During these visits we will take xx amount of blood [*sites to fill in*] to check your immune system, the amount of HIV in your blood, the health of your blood and liver, and for storage. We also will give you a brief physical exam during these visits, and ask you about any other medications that you are taking. If you get HIV during Step 3 of the study, you will stop taking the TDF/FTC (Truvada), and will be referred for local care and treatment of HIV. We may ask you to come in for additional visits to check on your health.

Permanently Stopping Your Study Product

There may be certain situations that occur where you will no longer get the study drugs while in the study, either because you decide you do not want to any longer, you get HIV, or the drugs are no longer safe for you to take. We may ask you to continue to come to the study visits even if you no longer get shots or take pills. We will fully explain to you what will be expected if you permanently stop taking the study drugs.

USE OF STUDY SAMPLES

In addition to the laboratory tests performed at each study visit, samples from all study participants will be used for other testing that is part of this study. This will include testing related to HIV and other infections, including testing for the drugs used in this study and other anti-HIV medications. If you get infected with HIV or hepatitis B or C during the study, some the stored blood may also be used to study the HIV and hepatitis virus, and the body's response to these infections. If you are taking sex hormones, your stored samples may also be used to study whether these medications interact with the anti-HIV medications used in this study. The samples used for this testing will be labeled with your study number and will be tested at special laboratory facilities that may be located in the US and other countries outside of [insert site country]. Results of this specialized testing will not be returned to the study site or you.

POSSIBLE FUTURE TESTS *[Sites may require a separate consent form for this]*

If you agree, your stored samples may also be used for future research related to HIV infection, hepatitis infection, and other infections transmitted through sex, and to better understand laboratory tests related to this study. [For sites that opt in for pharmacogenomics testing:] If you agree, your stored samples may also be used to study genes related to HIV infection and use of anti-HIV medications to prevent HIV infection. This testing is described in more detail below. You can agree to have your samples used for future research, even if you do not agree to have your samples used to study genes.

The stored samples will be labeled with your study number and will be tested at special laboratory facilities that may be located in the US and other countries outside of [insert site country]. Only approved researchers will have access to them. Results from this testing will not be returned to the study site or you. You will be asked to sign at the end of this consent form to give permission to use your stored samples for future research. Even if you do not give permission to store your blood for possible future research, you can still be in this study. You may also withdraw your consent to use your stored samples for future research at any time. We will then destroy your samples after all of the study-related testing has been completed. If you agree to have your stored samples used for future research, your left over blood will be stored for an indefinite period of time after the study ends.

RISKS AND/OR DISCOMFORTS

Study Medications

The side effects of cabotegravir include:

- Headache
- Diarrhea
- Fatigue
- Muscle aches
- Nausea
- Fever
- Dizziness

- Runny nose
- Sore throat
- Upper respiratory tract infection
- Vomiting (being sick)
- Difficulty sleeping
- Abnormal dreams/nightmares
- Depression
- Flatulence (gas or wind)
- Increase in the level of enzymes in the muscles (creatine phosphokinase)
- With the CAB that you get as a shot, some people in other studies have said they had pain, irritation, skin redness, bumps, swelling, itching, bruising in the area where they got the shot, some of which lasted a few weeks before resolving.

There have been some people who were taking this medicine who have had liver side effects. Some of these people were HIV-infected (HIV positive) and some had damage to their liver before taking the CAB study medication. While taking the study medication, their blood tests showed that their liver was irritated, although they felt well. The medications were stopped, and the liver blood tests returned to normal. In this study, anyone with HIV-infection, Hepatitis C (or B), or any liver irritation will not be allowed to be in the study.

Some people who have had a prior history of seizures (epilepsy) have had seizures (spells) while taking CAB. One person who did not have a previous history of seizures died after prolonged seizures. If you have ever had a seizure you will not be allowed to be in the study.

The shots you receive in this study are long acting, meaning they stay in your body for a long time – as long as a year or more. If you develop a side effect to the study drug after the shot, there will be no way to remove the drug from your body. If you are in Group A, the group that gets the real CAB, we will monitor your health for a year after your last injection. If you get infected with HIV while on the real CAB, it is possible that real CAB and other HIV drugs that are like it may not work to fight the virus.

If you develop a symptom from these drugs while the drugs are still in your body, every effort will be made to treat the side effects. The amount of drug will decrease overtime and will eventually disappear.

We will update you on any new side effects that we see in this study and other on-going studies, if those side effects appear to have come from the drug. If you have questions concerning the additional study drug side effects, please ask the medical staff at your site. As stated above, some of these risks are seen in HIV infected people taking these medications. It is not known if these side effects will occur as often and it could be that some of these side effects might be more or less serious in HIV uninfected people.

Side effects of TDF/FTC include:

Lactic acidosis (elevated lactic acid levels in the blood) and severe hepatomegaly (enlarged liver) with steatosis (fatty liver) that may result in liver failure, other complications or death have been reported

with the use of antiretroviral nucleoside analogues alone or in combination. The liver complications and death have been seen more often in women on these drug regimens. Some nonspecific symptoms that might indicate lactic acidosis include: unexplained weight loss, stomach discomfort, nausea, vomiting, fatigue, cramps, muscle pain, weakness, dizziness and shortness of breath.

Other side effects include:

- Upset stomach (nausea), vomiting, gas, loose or watery stools
- Abdominal pain
- Generalized weakness
- Dizziness
- Depression
- Headache
- Shortness of breath
- Increased cough
- Runny nose
- Allergic reaction: symptoms may include fever, rash, itching, upset stomach, vomiting, loose or watery stools, abdominal pain, achiness, shortness of breath, a general feeling of illness or a potentially serious swelling of the face, lips, and/or tongue.
- Skin darkening of the palms of hands and/or soles (bottom) of feet
- Bone pain and bone changes such as thinning and softening which may increase the risk of breakage (this side effect goes away after stopping TDF/FTC)
- Muscle pain and muscle weakness
- Sleeping problems; unusual dreams; tiredness
- Worsening or new kidney damage or failure
- Liver problems. If you are developing liver problems, you may have one or more of the following symptoms:
    - Abnormal liver function tests, which could mean liver damage
    - Yellowing of the skin or whites of your eyes,
    - Dark urine,
    - Pain on the right side of your stomach,
    - Loss of appetite, upset stomach or vomiting,
    - Pale colored stools,
    - Itchy skin.
- Increases in pancreatic enzyme (substances in the blood), which could mean a problem with the pancreas

- Increased triglycerides
- Increased creatine phosphokinase (CPK), which could mean muscle damage

Side effects of Intralipid when used as an intramuscular injection placebo include headache, anxiety, insomnia, vomiting, nausea, constipation, extremity pain, agitation, diarrhea, sedation, nasopharyngitis, upper respiratory infection, cough, urinary tract infection, decreased weight, and increased muscle tone.

When Intralipid is given as an intravenous infusion (into a vein directly) for nutrition, the following side effects have been reported (note that these side effects have not been reported when Intralipid is administered through an intramuscular injection):

Immediate or early adverse reactions, each of which has been reported to occur in clinical trials less than 1% of the time: trouble breathing, blue appearance to the skin at where the injection was given, allergic reactions, elevated levels of fat in your blood, increased chances of getting blood clots, nausea, vomiting, headache, flushing, increase in temperature, sweating, sleepiness, pain in the chest and back, slight pressure over the eyes, dizziness, and irritation at the site of the infusion;

Delayed adverse reactions such as: large liver, yellowing of the skin and eyes, large spleen, low blood cell counts, increases in liver function tests, and overloading syndrome (seizures, fever, increase in white blood count, large liver, large spleen, and shock).

Possible Injection Side Effects:

The injections will be given in the muscles of your buttocks (bottom "cheeks"). The injection could be given too deeply or not deeply enough, missing the muscle and entering your skin, blood, or a nerve. The risk of this is unknown but may result in higher levels of the injected medication in your system. Getting injections could also cause some people to feel lightheaded or feel like they might pass out, or 'faint'. This reaction, called a 'vasovagal reaction', can occur with many medical procedures and resolves quickly.

Blood Draws

Taking blood samples may cause some pain, bruise your arm, or make you feel lightheaded. In rare cases you may faint. There is also a slight chance of infection when blood is drawn. You may be nervous while you are waiting for your test results, particularly your HIV and sexually transmitted infection tests. You will receive counseling before and after these tests to help address your concerns.

Rectal Swabs

You may experience pain or discomfort in your rectum from the swab. In some cases, you may have some bleeding.

Sensitive Questions

The questions we will ask you about your sexual behavior may make you feel uneasy. However, you do not have to answer any question that you do not want to and you can stop answering the questions at any time.

DXA Scan *[Only sites participating in the DXA subset to include this section]*

If you receive the scan, note the following: We are exposed to radiation on a daily basis both from natural (sun and earth) and man-made sources. The average radiation dose from these sources for those living in the United States is 363 millirem per year. Exposure of up to 5,000 millirem of radiation is allowed in individuals who use radiation in their work (such as Radiologic Technologists and radiologists). Also, there is no evidence that a dose up to 5,000 millirem per year is associated with any risk. The radiation dose that you will receive from the DXA scans done for this research is less than 1% of this annual limit for radiation workers (if you receive the scans). The scanning machines will not cause any physical discomfort other than from having to lie still on the table for the duration of the test.

ECG

ECG patches may cause a skin reaction such as redness or itching. You may also experience localized skin discomforts and/or hair loss associated with the placement of ECG leads.

Genetic Testing

[*Sites that are able to conduct this testing should keep this section included; otherwise, this should be removed, as well as the signature lines on the signature page*]

We want to look at your genes that affect how your body changes and removes the drug used in this study. Gene differences between people can lead to different amounts of drug in the body. This may affect how well a drug protects people from HIV infection. If you consent, we will test your blood to get information about how your genes may have affected the drug levels in your body. The tests we will use to look at your genes are research tests and will be performed in a research laboratory. All of the samples will be identified with a coded number. The laboratory doing the testing will not know who you are. The results obtained for individual study participants (like you) will not be reported to the study sites or back to you. However, the combined results of the testing for all of the study participants will be available to the study sites and to the study participants at their request, once the analysis has been completed.

We also may also use your samples and information for more complete genetic testing. For example, researchers may do “genome-wide association studies,” also known as GWAS. A genome is all of your genes in total. Genes are made of even smaller “building blocks” that are arranged in a specific order. Many diseases can result from changes to this order or “sequence.” These changes may somewhat explain why some people get diseases like cancer or diabetes while others do not. These changes may partly explain the body’s response to disease and treatment. We are interested in understanding if the way the study medication interacts with your body has anything to do with your particular genes.

We may find information as we do this study that raises important other questions as to the safety of the study medication - - this new information may require that we do additional testing of left-over study

samples. We will let you know right away if we find any new information or any new concerns develop about the medication as the study continues.

Your genetic information may also be shared for future research purposes and may be stored in a central genetic database, but your personal information (like your name or anything else about you) will not be shared.

Social

There may also be some social risks to participating in this study. You may feel embarrassed or uncomfortable with some of the questions you will be asked, some of the procedures that will be done, or some of the test results that you will receive. The questions we will ask you about your sexual behavior may make you feel uneasy. However, you do not have to answer any question that you do not want to and you can stop answering the questions at any time. You may also experience stigma as a result of being involved in a study about HIV because people may assume that you are HIV-infected. In addition, there may be uncommon or previously unknown risks that might occur. You should report any problems to the researchers immediately.

Confidentiality

We will make every effort to protect your confidentiality during the study. However, it is possible that others may learn that you are part of this study and they may think that you are infected with HIV or are at high risk for infection with HIV. Because of this you could have trouble finding or keeping a job. You could also have problems with your family, friends and community.

HIV Infection

We told you earlier that we do not know if CAB works to protect you from getting HIV. If you are in the group that gets the real CAB, you still may be at risk of getting HIV. We do know that taking TDF/FTC every day can be very effective at preventing HIV infection. If it is not taken every day, you may not be well protected. Because of these risks, it is very important that you use condoms every time you have sex, no matter what group you are in.

Because the study medication is itself being studied to be an HIV treatment medication, if you become HIV infected while taking the study medication, there is a chance that other drugs used to treat HIV infection might not work. This is called drug resistance.

To reduce the possibility of developing drug resistance, you will be asked to work with your local study clinic team to begin HIV treatment after your last study medication injection. The study will not provide this treatment but may be able to help you find and/or pay for that treatment.

BENEFITS

There may be no direct benefit for you if you participate in the study. TDF/FTC is known to protect against getting HIV if taken daily as directed. CAB has not been shown to protect against getting HIV, which is the reason we are doing this study. Neither you nor we will know which real drug you are getting in this study.

We will test you for HIV, hepatitis B and hepatitis C during this study, and other sexually transmitted infections. We will refer you for Hepatitis B vaccination if it is indicated. The counseling you get during this study may help you to avoid HIV and other sexually transmitted infections. If you have or become infected with HIV, this counseling may help you to learn how to better care for yourself and avoid passing HIV to your sexual partners. If you become HIV infected, or have another sexually transmitted infection, we will refer you for care and/or treatment. During the study you will also have other tests to check on the health of your blood, and liver. If any health problems are found, you will be referred for care. At every visit you will be offered condoms and lubricant free of charge.

You or others in your community may benefit from this study later. The information gathered during this study may help to prevent the spread of HIV. This may be beneficial to you and your community.

NEW INFORMATION

You will be told any new information learned during this study that might affect your willingness to stay in the study. For example, if information becomes available that shows that the medication may be causing bad effects, you will be told about this. You will also be told when the results of the study may be available, and how to learn about them.

WHY YOU MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT

You may be withdrawn from the study without your consent if any of the following occur:

- You are unable or unwilling to follow all of the study procedures or instructions.
- You could be harmed by continuing to take the pill or getting an injection.
- The study is stopped or canceled.
- The study staff feels that staying in the study would be harmful to you.
- You are not able to attend clinic visits or complete all of the study procedures.
- Other reasons, as decided by the study staff.

ALTERNATIVES TO PARTICIPATION

[*Sites to include/amend the following if applicable:* There may be other studies going on here or in the community that you may be eligible for. If you wish, we will tell you about other studies that we know about. There also may be other places where you can go for HIV counseling and testing. We will tell you about those places if you wish.]

COSTS TO YOU

There will be no cost to you for study related visits, study products, physical examinations, laboratory tests, or other procedures specifically related to the study.

REIMBURSEMENT

You will receive [*sites to fill in*] for your time, effort, and travel to and from the clinic at each scheduled visit.

CONFIDENTIALITY

To keep your information private, your samples will be labeled with a code that can only be traced back to your study clinic. Your name, where you live, and other personal information will be protected by the study clinic. The results of any tests done on these samples will not be included in your health records without your permission. Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

Efforts will be made to keep your study records and test results confidential to the extent permitted by law. However, we cannot guarantee absolute confidentiality. You will be identified by a code, and personal information from your records will not be released without your written permission. Any publication of this study will not use your name or identify you personally. However, your records may be reviewed, under guidelines of the United States Federal Privacy Act, by the United States Food and Drug Administration (FDA); the sponsor of the study (United States National Institutes of Health [NIH]), the [*insert name of site*] Institutional Review Board (IRB), Ethic Committee (EC) study staff, study monitors, the companies that make the drugs used in this study, and (*insert applicable local authorities*].

[*For US sites only to include*] In addition to the efforts made by the study staff to help keep your personal information confidential, we have obtained a Certificate of Confidentiality from the U.S. Federal Government. This Certificate protects researchers from being forced to tell people who are not connected with this study, such as the court system, about your participation. The Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, we will tell the proper authorities.

The study staff will also use your personal information, if needed, to verify that you are not taking part in any other research studies. This includes other studies conducted by [site name] and studies conducted by other researchers that study staff know about.

Your records may be reviewed by:

- US FDA
- US NIH
- US Department of Heath and Human Services (DHHS), Office of Human Research Protection (OHRP)
- [insert names of applicable IRBs/ECs/other local eview bodies as applicable]

- Study staff
- Study monitors
- Companies that makes the study drug (ViiV Healthcare and Gilead Sciences, Inc.)
- Other U.S., local, and international regulatory entities may also review study records

[*Sites to include/amend the following if applicable:] [Local/state/national]* regulations require study staff to report the names of people who test positive for [HIV and other infections] passed during sex to the [*local health authority*]. Outreach workers from the [*health authority*] may then contact you about informing your partners, since they also should be tested. If you do not want to inform your partners yourself, the outreach workers will contact them, according to the confidentiality guidelines of the [*health authority*].

RESEARCH-RELATED INJURY

[*Sites to specify institutional policy*:] It is unlikely that you will be injured as a result of study participation. If you are injured, the [institution] will give you immediate necessary treatment for your injuries. You [*will/will not*] have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program to pay money or give other forms of compensation for such injuries either through this institution or the NIH. You do not give up any legal rights by signing this consent form.

PROBLEMS OR QUESTIONS

If you ever have any questions about the study, or if you have a research-related injury, you should contact [*insert name of the investigator or other study staff*] at [*insert telephone number and/or physical address*].

If you have questions about your rights as a research participant, you should contact [*insert name or title of person on the IRB or other organization appropriate for the site*] at [*insert physical address and telephone number*].

If you have questions about who to contact at the research site, you should contact [insert name of the investigator or community educator or CAB member] at [insert physical address and telephone number].

SIGNATURE PAGE

HPTN 083

A Phase 2b/3 Double Blind Safety and Efficacy Study of Injectable Cabotegravir Compared to Daily Oral Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC), For Pre-Exposure Prophylaxis in HIV-Uninfected Cisgender Men and Transgender Women who have Sex with Men

Version 3.0

October 31, 2019

SCREENING AND ENROLLMENT CONSENT

Insert signature blocks as required by the local IRB:] If you have read this consent form, or had it read and explained to you, and you understand the information, and you voluntarily agree to join the study, please sign your name or make your mark below. Also, please indicate by providing your initials in the spaces below the additional sample collection, genetic testing, or long-term storage that you agree to.

_____ I agree to take part in this study.

_____ I agree to have samples of my blood stored and used for future testing.

_____ I do not agree to have samples of my blood stored and used for future testing.

_____ I agree to allow my blood to be tested to see how my genes make the drug work in my body.

_____ I do not agree to allow my blood to be tested to see how my genes make the drug work in my body.

_____ [*Sites that participating in the DXA subset to add this*]: I agree to take part in the DXA subset.

_____ [*Sites that are participating in the DXA subset to add* this]: I do not agree to take part in the DXA subset.

_____ [*Sites that are participating in the DXA subset to add* this]: I have been told that the DXA subset is no longer available for participation.

_____ _____

Participant Name (print) Participant Signature and Date

_____ _____

Study Staff Conducting Consent Discussion (print) Study Staff Signature and Date

Witness Name (print) (As appropriate)	Witness Signature and Date