HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

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

Protocol Title:	**A5359, Version 1.0,07/05/2018; Letter of Amendment #1, 7/30/19** A Phase III Study to Evaluate Long-Acting Antiretroviral Therapy in Non-adherent HIV-Infected Individuals **A Multicenter Trial of the AIDS Clinical Trials Group (ACTG)**
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Introduction:

You are being asked to take part in this research study because you are infected with HIV and you have had problems taking daily medications. This study is sponsored by the National Institutes of Health (NIH). The doctor in charge of this study at this site is: Dr. Pablo Tebas. Before you decide if you want to be a part of this study, we want you to know about the study.

This is a consent form. It gives you information about this study. The study staff will talk with you about this information. You are free to ask questions about this study at any time. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. If you agree to take part in this study, you will be asked to sign this consent form. You will get a copy to keep.

Why Is This Study Being Done?

This study is being conducted to test if injectable, long-acting anti-HIV drugs that are given every month can be used safely and effectively in individuals who are infected with HIV and who have had problems taking daily medications in the past. This study is also being conducted to evaluate how well are these medications tolerated.

The drugs being looked at in this study are oral cabotegravir, oral rilpivirine, long-acting injectable cabotegravir and long-acting injectable rilpivirine. A long-acting drug means it stays in the body much longer compared to the usual form of the medications. Only oral rilpivirine is currently approved by the U.S. Food and Drug Administration (FDA) for treating HIV/AIDS in treatment-naïve (persons who have never receive antiretroviral therapy) individuals. Oral cabotegravir, long-acting cabotegravir and long-acting rilpivirine are experimental drugs.

How Many People Will Take Part in This Study?
350 people will take part in this study. About 8-10 people are expected to enroll at the University of Pennsylvania

What Do I Have To Do If I Am In This Study?
If you agree to join this study, you will be asked to sign this consent form. After you have signed the form, you will be asked some questions and will undergo some tests at the screening visit to see if it is safe for you to join the study.

Screening
The screening visit will take about 1-2 hours. About 2 tablespoons of blood will be drawn.

- You will be asked about your medical history including your HIV history.
- You will be asked about any medicines you have taken in the last 12 months.
- You will also be asked about any anti-HIV medications that you may have ever taken.
- You will have a physical exam. The study staff will check your vital signs such as temperature, blood pressure, breathing, weight, and pulse.
- You will have blood drawn for routine blood tests and HIV viral load (VL, the amount of virus in your blood sample) and CD4+ cell count (the number of white blood cells that fight infection).
- You may have blood drawn for resistance testing (a test to see if the virus in your blood is likely to respond to study drugs).
- You may have blood drawn to test for hepatitis B and C (viruses that can affect your liver).
- You will have an electrocardiogram (ECG).
- You will have urine collected for urinalysis.
- You will be asked to complete a questionnaire that will ask questions about: mental health, smoking, alcohol and substance use.
- If you are a woman able to become pregnant, you will have a pregnancy test. Pregnant women, or women who want to become pregnant in the next 4 years, cannot enter the study.
- An HIV test may be required to document your HIV status.
- You will be asked to provide forms of additional contact including, but not limited to: mailing address, email address, home/cell phone, and additional emergency contacts (for example, someone from your family, a friend, or case manager).
- You will be asked to sign a release of information to allow the study staff to consult with your HIV provider regarding your study participation.

If you do not enroll into the study
If you decide not to take part in this study or if you do not meet the eligibility requirements, we will still use some of your information with your permission. As part of this screening visit, some demographic (for example, age, gender, race), clinical (for example, disease condition, diagnosis), and laboratory (for example, CD4 cell count, viral load) information is being collected from you so that ACTG researchers may help determine whether there are patterns or common reasons why people do not join a study. No personal identifiers will be included with this information.

Entry
Within 60 days of your screening visit, you will come to the clinic for entry evaluations. This visit will last about 2 hours and you will need to be fasting. You will have about 4 tablespoons of blood drawn. You will also have some questionnaires given at entry.

- You will have a physical exam.
- You will be asked about any medicine changes you have had since your screening visit.
- You will have blood drawn for routine blood tests, CD4+, and HIV viral load.
- You will have blood drawn for storage for future HIV-related ACTG approved research tests.

- You will have urine collected for a drug screen, which will test for the presence of recreational drugs. The test results will be available to the study investigator and may be available to your doctor. You may be referred for additional services based on the results of these tests.
- You will have a blood draw for dried blood spots (drops of blood collected on a piece of paper) and will also have the option to provide about 100 strands of hair (obtained within 1 cm of the scalp) collected to measure levels of anti-HIV medications.
- If you are a woman able to become pregnant, a pregnancy test will be done before you begin your study medications.
- You will be asked to come to the clinic fasting (no food or drink except water, decaffeinated black coffee without sugar, and your prescription drugs for the 8 hours just before the visit) for lipid testing. If you did not fast before a required fasting visit, you will be asked to come back to the clinic for another blood draw after you have fasted.
- You will be asked to complete a questionnaire that will ask questions about: mental health, domestic violence, healthcare utilization and medication adherence.

If you qualify to participate in this study, you will initially be prescribed an oral anti-HIV regimen that your doctor will recommend based on your previous drug regimens and the results of your HIV resistance tests. Your anti-HIV drugs will be provided to you at this visit. If your drugs start making you sick or stop working for you, your doctor can switch you to another regimen.

Post-Entry Step 1

During Step 1, the study doctor will consult with your HIV provider to determine which anti-HIV medications will be safe and most likely to decrease your HIV VL. The study will provide these anti-HIV medications to you at no charge and this step will last approximately 24 weeks. During this step, you will be closely monitored to see if the drugs that you were started on are working and you will be asked to return to clinic at Step 1, weeks 2, 4, 8, 12, 16, 20, and 24. Visits will last about 1 hour. You will have about 3-4 tablespoons of blood drawn. At most of the visits, you will have:

- You will have a physical exam and be asked about any medications that you may be taking.
- You will be given questionnaires to complete, which may include questions about how you take your medications, health and behavior questions, and about your smoking, alcohol and drug use habits and demographics. You will also have pill counts where you will be asked to bring back all left over pills and pill bottles so that we can see how well you are taking the medications.
- You will have blood collected for routine blood tests, HIV viral load, CD4+ and CD8+, and study drug levels (including plasma and dried blood spots). You will not have blood taken at Step 1, week 2.
- If you are a woman who can become pregnant and/or if you think you might be pregnant, you will be asked to provide a blood or urine specimen for pregnancy testing. If you are taking dolutegravir, you will be asked to provide a specimen for pregnancy testing at every visit.
- You will be asked to give urine specimens for recreational drug testing (these samples will be stored for future analysis) and to monitor for possible drug effects on your kidney function.
- Blood may be drawn and stored for future HIV-related ACTG approved research tests.
- You will have the option to provide about 100 strands of hair (obtained within 1 cm of the scalp) collected to measure levels of anti-HIV medications. This test will be an optional procedure.

Conditional Economic Incentives (CEI)

Because taking your pills every day is an important part of making sure the treatment works, you will receive additional financial compensation (also known as conditional economic incentives or CEI) if you achieve some specific “milestones” related to the results of your treatment during this first part of the study, according to the following plan:

- $75 if you complete a study visit at Step 1, week 2.

- $75 if you have a ten-fold decrease (for example from 1000 copies to 100 copies) in your HIV VL at Step 1, week 4, and a 100-fold (for example from 10,000 copies to 100 copies) decrease in your HIV VL at Step 1, week 8, visit compared to your VL at the beginning of the study entry.
- $150 if your HIV VL is less than 200 copies at Step 1, weeks 12 and 16, and less than 50 copies at Step 1, week 20.

It is important to report any side effects you are experiencing to the research staff. They will help you manage your side effects or can suggest other options for treatment.

If you do not achieve the milestones, you will not receive the additional compensation (but you will receive the usual compensation given for attending your study visit). You will, however, be allowed to continue on the study and you may be eligible for the next available financial compensation. For example, you may not qualify to compensation at Step 1, week 4, but you could still receive financial compensation at Step 1, weeks 8, 12, 16, and/or 20, based on these milestones. The CEI will stop at Step 1, week 20.

The CEIs in this study are intended to enhance your possibility of reaching an undetectable HIV VL by the end of Step 1. This is important because you can only be eligible for randomization (assigned by chance as if by the toss of a coin) in Step 2 if your HIV VL is less than 50 copies, in order for you to be a candidate to receive long-acting therapy. CEIs have shown to be most helpful for short periods of time; in most studies, the effect of using them stops after an individual stops receiving them. Therefore, we only plan to provide CEIs during Step 1, for up to 20 weeks. After week 20 in Step 1, all CEIs will be discontinued for all participants.

After the CEIs are discontinued, you may feel disappointed about not receiving them. This is expected and should improve overtime. Keep in mind that you will still receive the usual compensation for your participation in the study, as it is customary in the studies performed by the AIDS Clinical Trials Group. The study personnel will be able to answer any questions you may have about the CEIs. As mentioned, the CEIs are only intended to be a temporary intervention as part of a research study.

<u>Step 2</u>
To be eligible to move on to Step 2, your HIV VL will need to be less than 50 copies at the Step 1, week 20, visit. If your HIV VL is greater than 50 copies but less than 400 copies, you will need to come in for a retest within 2 weeks. If your HIV VL is less than 50 copies by Step 1, week 20, or at your retest, you will be randomized (assigned by chance as if by the toss of a coin) to one of two groups in the next phase of the study, known as Step 2 randomization visit. Your chance of being assigned to one of the groups is one out of two (50%). You will be told which group you are in. The groups are as follows:

Group A – Switch your anti-HIV regimen to an initial short course of daily oral cabotegravir and rilpivirine tablets for 4 weeks, followed by long-acting injectable cabotegravir + long-acting injectable rilpivirine administered to you every 4 weeks.
Group B – Continue on your current regimen.

If you are assigned to Group A, your anti-HIV regimen will be switched to a combination of oral cabotegravir + oral rilpivirine for 1 month. After 1 month on the new oral medication, you will return to the clinic to have your safety labs checked to make sure that it will be safe for you to receive the medication as a long acting injectable. If your lab results confirm that it is safe for you to receive an injection, you will be asked to come to the clinic within 1 week to receive your first injection of long-acting anti-HIV medications.

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At that visit, you will receive 2 injections: a loading dose of 3 mL (less than a teaspoon) of long- acting cabotegravir plus a loading dose of 3 mL of long-acting rilpivirine, both in the gluteal muscle (in the buttocks). You will need to return to clinic within 4 weeks for an additional dose of long-acting anti-HIV medications. In all of the following visits, you will receive 2 injections which will include 2 mL of long-acting cabotegravir plus 2 mL of long-acting rilpivirine, both in the gluteal muscle. You will be asked to return to the clinic every 4 weeks for injections and study procedures. on Step 2, weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52.

If you are assigned to Group B, you will continue your current anti-HIV regimen. You will be asked to return to the clinic for a visit on Step 2, weeks 4, 8, 16, 24, 36, 48, and 52. Visits will last about 1 hour.

During most of these visits in Step 2 (regardless of which group you are randomized to), you will have about 3-4 tablespoons of blood drawn. In addition, you will have:

- You will have a physical exam, including an evaluation of the site where you are receiving the injection (Group A only).
- You will have an ECG at Step 2, Randomization, and Step 2, week 48.
- You will be asked about any side effects and about any medications that you may be taking.
- You will be given questionnaires to complete, which may include questions about how you take your medications, pill counts, mental health and behavior questions, domestic violence, stigma, self-efficacy, treatment satisfaction, demographics and about your smoking, alcohol and drug use habits.
- You will have blood collected for routine blood tests, HIV viral load, CD4+ and CD8+, and study drug levels. You may also have and HIV resistance test (HIV genotype).
- You will have the option to provide about 100 strands of hair (obtained within 1 cm of the scalp) collected to measure levels of anti-HIV medications. This test will be an optional procedure.
- You may be asked to give urine specimens for drug toxicology and to monitor for possible drug effects on your kidney function.
- If you are woman who is capable of becoming pregnant, you will be asked to give a urine specimen for a pregnancy test. You must have a negative pregnancy test result before receiving each injection. If you are taking dolutegravir, you will be asked to provide a specimen for pregnancy testing at every visit.
- Blood may be drawn and stored for future HIV-related ACTG approved research tests.
- At Step 2 randomization and Step 2 week 48, you will be asked to come to the clinic fasting (no food or drink except water, decaffeinated black coffee without sugar, and your prescription drugs for the 8 hours just before the visit) for lipid testing. If you did not fast before a required fasting visit, you will be asked to come back to the clinic for another blood draw after you have fasted.

<u>Step 3</u>
To be eligible to move on to Step 3, your HIV VL will need to be less than 50 copies at the Step 2, week 48 visit. If your HIV VL is greater than 50 copies but less than 400 copies, you will need to come in for a retest within 2 weeks. If your HIV VL is less than 50 copies by Step 2, week 52, you may enter into Step 3.

In Step 3, all participants will receive the long-acting injectable medications. If you had previously been receiving the long-acting injectables, you will continue to do so and come to the clinic every 4 weeks during this Step through week 52. If you have never received long-acting medications, your anti-HIV regimen will be switched to a combination of oral cabotegravir + oral rilpivirine for 1 month. After 1 month on the new oral medication, you will return to the clinic to have your safety labs checked to make sure that it will be safe for you to receive the medication as a long acting injectable. If your lab results confirm that it is safe for you to receive an injection, you will be asked to come to the clinic within 1 week to receive your first injection of long-acting anti-HIV medications. You will need to return to clinic

within 4 weeks for an additional dose of long-acting anti-HIV medications. All participants in Step 3 will come to the clinic every 4 weeks for injections and study procedures on Step 3, Registration and on Step 3, weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52. Visits will last about 1 hour. In Step 3, you will have about 1-2 tablespoons of blood drawn. At most visits, you will have:

- You will have a physical exam including an evaluation of the site where you are receiving the injection.
- You will have an ECG at Step 3, Registration, and Step 3, week 48.
- You will be asked about any side effects and any medications that you may be taking.
- You will be given questionnaires to complete, which may include questions about smoking, mental health, self-efficacy, stigma, domestic violence, treatment satisfaction, alcohol and drug use, and health care utilization.
- You will have blood collected for routine blood tests, HIV viral load, CD4+ and CD8+, and for drug concentrations. You may also have an HIV resistance testing (HIV genotype).
- You will have an evaluation of the site where you are receiving the injections.
- You will have the option to provide about 100 strands of hair (obtained within 1 cm of the scalp) collected to measure levels of anti-HIV medications. This test will be an optional procedure.
- You may be asked to give urine specimens for drug toxicology and to monitor for possible drug effects on your kidney function.
- If you are woman who is capable of becoming pregnant, you will be asked to give a urine for a pregnancy test. You must have a negative pregnancy test result before receiving each injection.
- Blood may be drawn and stored for future HIV-related ACTG approved research tests.
- At week 52, you will be asked to come to the clinic fasting (no food or drink except water, decaffeinated black coffee without sugar, and your prescription drugs for the 8 hours just before the visit) for lipid testing. If you did not fast before a required fasting visit, you will be asked to come back to the clinic for another blood draw after you have fasted.

If you are a woman who is able to become pregnant, a pregnancy test will be done at various visits in Steps 1, 2 and 3, if pregnancy is suspected, to make sure that you are not pregnant. Pregnancy testing must be performed before each injection. You will need to inform the study staff know if you change your birth control method or if you suspect you might be pregnant.

Step 4

If you received at least one dose of long-acting injectable medication during the study, you will need to be observed on oral HIV medications for 52 weeks after your last dose of injectable therapy. You will complete the study visits for the Step you are in (either Step 2 or Step 3) and then enter Step 4 to complete 52 weeks total on oral HIV medications. Please note that after completing Step 3, long-acting injectable medication will not be provided by the study, and will only be available to participants if it is available through your doctor's office. If you decide to continue this treatment, you may not need to enter Step 4.

In Step 4 of the study, you will obtain HIV pill medications from your doctor. You will come for study visits every 6 months for 1 year. You will have labs drawn and complete questionnaires at those study visits. Visits will last about 1 hour. You will have about 1-2 tablespoons of blood drawn. At most visits, you will have:

- You will have a physical exam. At Step 4, Registration, you will have an evaluation of the site where you receive your final injection.
- You will be asked about any side effects and any medications that you may be taking.
- You will be given questionnaires to complete, which may include questions related to your mental health, self-efficacy, treatment satisfaction, smoking, substance use, and how you take your medications.

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- You will have blood collected for routine blood tests, HIV viral load, CD4+, CD8+ and drug concentrations.
- You may be asked to give urine specimens and to monitor for possible drug effects on your kidney function. You may also have an HIV resistance testing (HIV genotype).
- If you are woman who is capable of becoming pregnant and you think you may be pregnant, you will be asked to give a urine sample for a pregnancy test. If you are taking dolutegravir, you will be asked to provide a specimen for pregnancy testing at every visit.
- At Step 4 registration and week 52 you will be asked to come to the clinic fasting (no food or drink except water, decaffeinated black coffee without sugar, and your prescription drugs for the 8 hours just before the visit) for lipid testing. If you did not fast before a required fasting visit, you will be asked to come back to the clinic for another blood draw after you have fasted.
- Blood may be drawn and stored for future HIV-related ACTG approved research tests.

Virologic Failure Confirmation Visit

If your HIV VL has not decreased enough or your HIV VL increases at or after entry into Step 2, you will return for an additional visit and have a second HIV VL test between 7 - 21 days of the previous HIV VL testing. At this visit you will have:

- You will have blood drawn for HIV VL, CD4+ and CD8+ and drug concentrations. You may also have a blood draw for HIV resistance testing (HIV genotype)
- You will have a blood draw for dried blood spots (if this happens during Steps 1 or 2) and will also have the option to provide about 100 strands of hair (obtained within 1 cm of the scalp) collected to measure levels of anti-HIV medications (if this happens during Steps 1 through 3).
- You will be given a questionnaire to complete, which will include questions about how you take your medications.

Your doctor may keep you on your current study drugs, or you may be switched to another study drug regimen selected by your doctor. If you are switched to a different study drug regimen not provided by the study, you will need to obtain that regimen from your doctor. You will continue to come in for your regular study visits as described above until the end of the study.

Premature Discontinuation of Study Therapy Visit

If you stop taking the study drugs before the end of the study or if you had virologic failure, you will be asked to return to the clinic for additional evaluations. This visit will last about 1 hour. You will have about 3 tablespoons of blood drawn. You also will be asked to continue to be part of the study and attend study visits even though you are no longer taking the study drugs.

- You will have a physical exam. The clinic staff will check your vital signs such as temperature, blood pressure, breathing, and pulse. You may have an evaluation of your injection site if you were receiving injections.
- You will be asked about the reasons why you discontinued the study drugs, about side effects and about any medicine changes you have had since screening.
- You will have blood drawn for routine blood tests, HIV viral load, CD4+ and CD8+, drug levels, and HIV genotype (if clinically indicated). You will also have a lipid profile if you are in Step 4.
- You will have a blood draw for dried blood spots (Step 2 only) and will also have the option to provide about 100 strands of hair (obtained within 1 cm of the scalp) collected to measure levels of anti-HIV medications.
- You will be given questionnaires to complete, which may include questions about how you take your medications, pill counts, health and behavior questions, and about your smoking, alcohol and drug use habits.
- You may be asked to give urine specimens.
- If you are woman who is capable of becoming pregnant, you will be asked to give a urine for a pregnancy test.

- Blood may be drawn and stored for future HIV-related ACTG approved research tests.

Final Visit
When you complete the study or if you leave the study early, you will be asked to come in to the clinic for final study evaluations. This visit will last about 1 hour. You will have about 4 tablespoons of blood drawn.

- You will have a physical exam. The study staff will check your vital signs such as temperature, blood pressure, breathing, and pulse. You may have an evaluation of your injection site if you were receiving injections.
- You will be asked about any medicine changes you have had since your last visit.
- You will have blood drawn for routine blood tests which may include HIV viral load, CD4+ and CD8+, drug levels. You may have an HIV genotype drawn if clinically indicated. You will also have a lipid profile if you are in Step 4.
- You will have blood drawn and stored for future HIV-related ACTG approved research tests.
- You will have a blood draw for dried blood spots (Step 2 only) and will also have the option to provide about 100 strands of hair (obtained within 1 cm of the scalp) collected to measure levels of anti-HIV medications.
- You will be given questionnaires to complete, which may include questions about how you take your medications, pill counts health and behavior questions, and about your smoking, alcohol and drug use habits.
- You may be asked to give urine specimens.
- If you are woman who is capable of becoming pregnant, you will be asked to give a urine for a pregnancy test.
- Blood may be drawn and stored for future HIV-related ACTG approved research tests.

You will be given the results of the pregnancy (if done), CD4+ and CD8+ cell counts, viral load, routine blood tests, glucose, cholesterol, triglycerides, hepatitis B and C.

OPTIONAL TESTS

Hair Collection
You have the option to provide about 100 strands of hair (obtained within 1 cm of the scalp) collected to measure levels of anti-HIV medications. Hair collection is not a requirement to participate in the study and you may withdraw your approval for hair collection, at any time.

Other Biologic Samples
Some of your blood, serum (part of the blood), plasma (part of the blood), cells, hair and dried blood spots that are left over after all required study testing is done may be stored (with usual protectors of identity) and used for ACTG-approved HIV-related research, including studies about immunology, virology, and metabolic testing that is required for this study. Storage of leftover blood (approximately 3-4 teaspoons) is not a requirement to participate in the study and you may withdraw your approval for the storage of your leftover samples, at any time. These samples may be held for an indefinite length of time. We cannot ensure that you will be told of the results of the research done on these samples.

Other Information
Your research site will collect your contact information including your address in order to keep in touch with you. In addition, in order to get a better understanding of the impact of your surrounding environment on your health, we are asking that we collect ONLY the first 3 digits of your zip code for a future analysis. Collection of this information is not a requirement to participate in the study.

How Long Will I Be In This Study?
You will be followed for a maximum duration of 180 weeks (about 3 and a half years) on this study. This includes 24 weeks in Step 1, 52 weeks in Step 2, 52 weeks in Step 3, and up to 52 weeks in Step 4, if the long-acting study medication is not commercially available at the end of Step 3.

Why Would The Doctor Take Me Off This Study Early?
The study doctor may need to take you off the study early without your permission if:

- The study is stopped or cancelled by the ACTG, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), National Institutes of Health (NIH), other government agencies, the drug companies supporting this study, or the site's Institutional Review Board (IRB). (An IRB is a committee that watches over the safety and rights of research participants.)
- A Data Safety Monitoring Board (DSMB) recommends that the study be stopped early (a DSMB is an outside group of experts who monitor the study).
- You are not able to attend the study visits as required by the study.
- You become imprisoned or involuntarily incarcerated in a medical facility and miss too many study visits and/or are unable to take your study drugs.
- Request of your primary care provider if s/he thinks the study is no longer in your best interest.
- If the study investigator feels that you may not be able to complete all of the necessary steps of the study or if continuing on the study may be harmful to you.

The study doctor may also need to take you off the study drug(s) without your permission if:

- Continuing the study drug(s) may be harmful to you
- You need a treatment that you may not take while on the study
- You are not able to take the study drug(s) as required by the study
- You become pregnant or are breast-feeding.

If you must stop taking the study drug(s) before the study is over, the study doctor may ask you to continue to be part of the study and return for some study visits and procedures.

If I Have To Permanently Stop Taking Study-Provided Medications Or Once I Leave The Study, How Would These Medications Be Provided?

During the study:
If you must permanently stop taking study-provided medications before your study participation is over, the study staff will discuss other options that may be of benefit to you.

After the study:
After the completion of the study, it is important that you continue treatment for your HIV infection. The study staff will discuss with you what your best options are for continuing treatment. This may be long-acting injectable drugs, if they are commercially available or oral anti-HIV therapy. This will be determined in conjunction with your doctor.

What Are The Risks Of The Study?
The drugs used in this study may have side effects, some of which are listed below. Please note that these lists do not include all the side effects seen with these drugs. These lists include the more serious or common side effects with a known or possible relationship. If you have questions concerning the additional study drug side effects, please ask the medical staff at your site.

There is a risk of serious and/or life-threatening side effects when non-study medications are taken with the study drugs. For your safety, you must tell the study doctor or nurse about all medications you are

taking before you start the study and also before starting any new medications while on the study. Also, you must tell the study doctor or nurse before enrolling in any other clinical trials while on this study.

Risks of the Questionnaires
You may feel embarrassed or uncomfortable answering the questions in the questionnaires, which will ask mental health questions related to depression, anxiety, suicidal thoughts, as well as substance use and alcohol use.

If your answers reveal that you are having suicidal thoughts you will be seen by a study clinician before you leave the clinic and you may be referred for psychiatric care. If your answers reveal a substance use problem to study staff, you may be referred for drug abuse treatment if you agree with being referred.

Risks of Drawing Blood
Taking blood may cause discomfort, bleeding, and bruising where the blood is drawn. Occasionally, there is swelling in the area where the needle enters the body and there is a small risk of infection. There is also a risk of lightheadedness, fainting, and blood clots.

Risks of Hair Collection
For participants who consent to the hair collection, we will collect about 100 strands of your hair. To do this, we will obtain a hair sample from the back of your head and cut close to the scalp with scissors. A noticeable place on the scalp where hair was cut may be visible. Cutting hair will not cause any pain. We will try to cut hair from underneath hair on top of it to hide where the hair was cut from.

Risks of Fasting
Some individuals find fasting to be bothersome. It may make some individuals feel anxious, irritable, or hungry. Participants who are required to take their morning medications with food should wait until after the visit has been completed to take their medications.

Risks of Combination Antiretroviral Therapy
Immune Reconstitution Inflammatory Syndrome (IRIS): In some people with advanced HIV infection, signs and symptoms of inflammation from other infections may occur soon after anti-HIV treatment is started.

The use of potent anti-HIV drug combinations may be associated with an abnormal placement of body fat and wasting. Some of the body changes include:
- Increase in fat around the waist and stomach area
- Increase in fat on the back of the neck
- Thinning of the face, legs, and arms
- Breast enlargement

STANDARD OF CARE TREATMENTS
The drugs in this section are the possible choices for the study doctor and your provider to select for your antiretroviral treatment. You will **not** be taking all of these medications. The study doctor will discuss which treatment you will receive and the risks associated with that particular regimen.

Risks with the Use of Nucleoside Analogues: Emtricitabine (FTC, Emtriva™), Tenofovir alafenamide fumarate (TAF, a component of Genvoya™, Odefsey ™ and Descovy™), Abacavir (ABC, Ziagen™), Lamivudine (3TC, Epivir™), Abacavir+Lamivudine (ABC/3TC, Epzicom™ and a component of Triumeq™)

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.

In addition, the following side effects have been associated with the use of Nucleoside Analogues:

- Upset stomach, vomiting, gas, loose or watery stools
- Generalized weakness
- Vague overall feeling of discomfort; Decrease in appetite
- Hypersensitivity reaction
- Depression
- Headache
- Abdominal pain
- Worsening or new kidney damage or failure
- Inflammation or swelling and possible damage to the pancreas and liver
- Shortness of breath
- Rash, itching, which sometimes can be a sign of an allergic reaction
- Muscle pain and muscle weakness
- Numbness, tingling, and pain in the hands or feet
- Bronchitis
- Pain (not specific)
- Allergic reaction: symptoms may include fever, rash, upset stomach, vomiting, loose or watery stools, abdominal pain, achiness, shortness of breath, a general feeling of illness or potentially serious swelling of the face, lips, and/or tongue
- Bone pain and bone changes such as thinning and softening which may increase the risk of breakage
- Headache
- Dizziness
- Tiredness
- Inability to sleep, unusual dreams
- Increased cough
- Runny nose
- Abnormal liver function tests, which could mean liver damage
- 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
- Low cells counts such as anemia, low white count and/or low platelets

NOTE: If you are infected with hepatitis B, you are not eligible for the study. Before starting abacavir, your healthcare provider should test you to determine if you are at risk of developing a severe allergy to abacavir.

Risks with the Use of Protease Inhibitors: Darunavir (DRV, Prezista™) and cobicistat (Prezcobix™:
The use of protease inhibitors may be associated with the following:

- Increases in the amount of triglycerides and/or cholesterol in the blood
- Development of diabetes or the worsening of high blood sugar

- There have been reports of increased bleeding in HIV-infected persons with hemophilia who were treated with protease inhibitors. It is not known if protease inhibitors were the cause of these bleeding episodes.

The risks of DRV or DRV/cobicistat include:

- Severe liver problems, which may be life-threatening. People who have increased liver function tests before starting DRV and people with liver diseases such as hepatitis B or C have an increased risk of worsening liver disease. If you are developing liver problems, you may have one or more of the following symptoms:
  - Yellowing of the skin or of the 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.
  - Rash, which may be severe or life-threatening. Contact your healthcare provider if you develop a rash. If you develop any skin changes with the following symptoms, stop using the DRV/cobicistat combination and contact your healthcare provider right away:
    - Fever
    - Tiredness
    - Muscle or joint pain
    - Blisters
    - Mouth sores
    - Red or inflamed eyes
  - Changes in blood test results that may show problems with the liver, kidneys and cholesterol levels
  - Inflammation of the pancreas. When the pancreas becomes inflamed, it can cause pain in the stomach, nausea, vomiting
  - Joint stiffness and bone pains may occur, rarely death of bone tissue and collapse of the bone may occur

Additional side effects include:

- Diarrhea
- Nausea
- Stomach pain
- Vomiting
- Headache

Before starting DRV, you should inform your healthcare provider if you are allergic to sulfa medicines.

DRV/cobicistat (Prezcobix®) when taken with some other medicines, like tenofovir, can cause new or worsening kidney problems, which can lead to kidney failure.

NOTE: Your healthcare provider can provide more complete information about the side effects of protease inhibitors. Before starting Darunavir (DRV, Prezista™ and a component of Prezcobix™), you should inform your healthcare provider if you are allergic to sulfa medicines.

Risks with Use of Integrase Inhibitors: Dolutegravir (DTG, Tivicay™ and a component of Triumeq™) and Elvitegravir/cobicistat (EVG/cobi, a component of Stribild™ and Genvoya™).

The following side effects have been associated with the use of Integrase Inhibitors:

- Upset stomach
- Headache
- Tiredness
- Weakness
- Trouble sleeping
- Vertigo
- Rash, which may be severe
- Feeling anxious
- Depression, suicidal thoughts and actions
- Paranoia (an abnormal sense of fear)
- Low blood platelet count
- Muscle pain, tenderness, or weakness, which can be serious and lead to kidney damage
- Abnormal liver function tests
- Changes in body fat
- Abnormal heart rhythm if receiving certain antiarrhythmics such as dofetilide.
- Participants with underlying hepatitis B or C may be at increased risk for worsening or development of transaminase elevations with use of Dolutegravir.
- Cancers have been seen in people who took raltegravir with other HIV drugs. The types of cancers seen are typical for people with very sick immune systems. It is unknown if the cancers were related to raltegravir use.
- Contact your health care provider right away if you develop a rash while taking dolutegravir, especially if it's associated with any of the following symptoms:
- Fever; Blisters or sores in your mouth; Blisters or peeling skin; Redness or swelling of your eyes; Swelling of your mouth, face, lips, or tongue; Trouble breathing
- Contact your health care provider right away if you have any of the following symptoms that could be signs of liver problems:
- Yellowing of your skin or whites of your eyes (jaundice); Dark or tea-colored urine; Pale-colored bowel movements; Nausea or vomiting; Loss of appetite; Pain, aching, or tenderness on your right side below your ribs

INVESTIGATIONAL TREATMENTS

Risks with Use of Rilpivirine (RPV, Edurant™ and a component of Complera™ and, Odefsey™) and RPV Long Acting injections:

More than 500 people have received RPV LA injections in clinical trials. The following side effects have been seen with rilpivirine in HIV-infected patients in clinical trials. Note that oral rilpivirine (Edurant) is an approved medicine that may be prescribed by your doctor.

The following serious side effects have been associated with the use of rilpivirine:

- Depression or mood changes. Be sure to contact your healthcare provider immediately if you are feeling sad or hopeless, feeling anxious or restless, or having thoughts of hurting yourself (suicide) or have tried to hurt yourself.
- Rash, which may be severe or life-threatening. Contact your healthcare provider if you develop a rash or other skin changes, especially if either is associated with any of the following:
  - Fever
  - Blistering on the skin or ulcers in the mouth
  - Eye redness or swelling of the face, moth, or other parts of the body

- Liver problems can happen. People who have abnormal liver tests before starting rilpivirine and people with liver diseases like hepatitis B or C have an increased risk of worsening liver disease. If you are developing problems, you may have one or more of the following symptoms:
  - Yellowing of the skin or of the 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.

Additional side effects include:
- Headache
- Trouble sleeping
- Abdominal pain
- Fatigue

NOTE: Some people taking rilpivirine have had liver problems. People with a history of hepatitis B virus (HBV) or hepatitis C virus (HCV) infection or who have elevated results on liver function tests may have an increased risk of developing new or worsening liver problems while taking rilpivirine.

In healthy participants, there was no clinically relevant effect on QTc interval (one of the measurements of the electrical activity of the heart as recorded on the electrocardiogram [ECG], and related to heart rate) at a dose of RPV 25 mg once daily. A modest increase in the QTc interval (change in electrical activity) has been observed with RPV at a dose of 75 mg once daily or higher (i.e. higher than used in this study). In HIV infected patients treated with RPV once daily, the change in electrical activity was similar with RPV as in the control group in the phase IIb study after 240 weeks as well as in the phase III study after 96 weeks There is a very small chance this change in electrical activity may lead to more serious heart problems such as abnormal heart rhythms (arrhythmias) and very rarely this could lead to sudden death. These risks may be higher when RPV is combined with certain other drugs with a known risk for such abnormal heart rhythms. However, to date, no such heart rhythm irregularities or sudden deaths have been observed in clinical studies with RPV. Your doctor will check for these drugs prior to starting the study.

Cabotegravir (CAB) Tablets and CAB Long Acting Injections
As of December 2017, an estimated 2169 people (including people with HIV, people who do not have HIV and who are taking PrEP, and people who do not have HIV and are not taking PrEP) have received CAB in studies sponsored by ViiV Healthcare. These included blinded studies (where people did not know what treatment they were receiving). In these studies, 1269 of the estimated 2169 people took the LA formulation.

The following serious effects may occur with the use of CAB:
- Hypersensitivity reactions. This is a type of allergic reaction that may start as a rash. If you develop a rash while taking CAB, contact your healthcare provider right away, especially if you also have:
  - Blisters or peeling skin
  - Fever
  - General ill feeling
  - Extreme tiredness
  - Muscle or joint pain
  - Blisters or sores in your mouth

  - Redness of the eyes
  - Swelling around your eyes, face, mouth, lips, or tongue
  - Trouble breathing
- Liver problems. Contact your healthcare provider right away if you have any of the following possible symptoms of a liver problem:
  - Yellowing of your skin or of the whites of your eyes (jaundice)
  - Dark or tea-colored urine
  - Pale colored stools
  - Nausea (feeling sick to your stomach) or vomiting
  - Loss of appetite
  - Pain, aching, or tenderness on your right side, below your ribs
- Depression, suicide attempts, or suicide, especially in people with pre-existing history of depression or other mental health problems. If your mental health problems worsen or if you develop suicidal thoughts, call your healthcare provider right away.
- Seizures/convulsions: If you have a history of seizures at any point in your life, please let your study doctor know.

Additional side effects include:

- Headache
- Upper respiratory tract infection. Symptoms may include
  - Sore throat
  - Cough
  - Runny nose
  - Fever
  - Trouble breathing
- Fever
- Fatigue
- Nausea
- Diarrhea
- Lack of energy or weakness
- Abdominal pain and discomfort
- Back pain
- Trouble sleeping
- Abnormal dreams
- Dizziness
- Joint aches and pains
- Muscle pain and/or breakdown of muscles
- Abnormal liver blood tests
- Increase in the level of enzymes produced in the muscles (creatine phosphokinase)

<u>General Side Effects of Injections - Long Acting Medications</u>

The injections you receive in this study are long acting, meaning they stay in your body for a long time. Following an injection of CAB LA or RPV LA, the medications stay in your body for months. In some people, low levels of CAB and RPV may be present in your body for more than a year. If you develop a side effect to CAB LA or RPV LA after the injection there will be no way to remove the drug from your body. You will be taking these drugs as tablets first, which stay in the body for a shorter amount of time. This will help the study staff understand if you would have problems with the drugs when received as an injection.

If you develop a symptom from these drugs, every effort to treat the symptoms will be made. The amount of drug will decrease overtime and will eventually disappear.

During the time that drug is leaving your body, your HIV virus could develop resistance (stop working) to these medicines, even if it is many weeks or months since you last took the drug. When discontinuing long acting HIV treatment, it will be very important to start taking other HIV medications, as recommended by your doctor, to help prevent your HIV from developing resistance to HIV medications.

Injection Site Reactions:
Side effects at the location where you received injections (termed Injection Site Reactions) been seen with both CAB LA and RPV LA. Common side effects could include:

- Pain or redness, swelling, itching, bruising, lumps, and irritation where you receive the injection(s). Most reactions resolve in a week or less.
- The injections that you receive will be given to you in the muscles of your buttocks (gluteal muscle).

Other Possible Injection Complications:
The injections will be given in the muscles of your buttocks (“bottom” or “cheeks”). It is possible that the person giving you your injection could accidentally give the injection too deeply or not deeply enough, missing the muscle and entering your skin, blood stream or a nerve. The risks of injecting a long acting drug outside of the muscle are not well understood, but could include having drug levels that are either too low or too high. The risk of having levels that are too low is that the drug may not work against your HIV virus. The risks of having high levels of CAB in your body are not well known. The risk of having high levels of RPV in your body are not well known, but one possible risk could include a change in your heart beat, which in severe cases can be life-threatening. In rare cases, symptoms such as feeling lightheaded, numbness or tingling, difficulty breathing, chest or stomach discomfort, sweating, nausea and/or feeling anxious have occurred after an injection with RPV LA. In these cases, high blood levels of RPV have been observed, which may be due to an accidental injection of part of the medication into a blood vessel instead of the muscle. Not all patients in whom an accidental injection in a blood vessel was suspected reported such symptoms. Most of the symptoms resolved within minutes. Your doctor may need to administer treatment to help resolve these symptoms. Every precaution will be taken to ensure that the correct size needle and injection technique is used to reduce these risks. You will also be monitored for safety events during the study. If your doctor is concerned that the injection was not given correctly, he or she may ask you to stay in the clinic up to 2 hours after the injection to monitor how you are doing and may order tests to monitor your safety. If you are concerned about this risk, speak to your doctor.

Receiving injections can cause some people to feel lightheaded or feel like they might pass out. Fainting can also occur. This reaction, called a “vasovagal reaction”, has been reported with other injectable medicines, and resolves quickly.

After receiving RPV LA injectable, the drug may be found in the body for longer than a year (longer than 12 months). This means you also may have drug in your body for longer than a year after the last injection. No safety issues are expected with this. We don’t know when all of the study drug will completely leave your body. We do know that levels of the drug in your body slowly decrease over time and we know that some people still have low levels of drug in their body a year or longer after receiving the last injection. You have to keep taking the treatment to avoid that the virus becomes resistant to rilpivirine due to low RPV plasma concentrations, and other types of HIV medications would have to be used to treat your HIV infection.

Are There Risks Related To Pregnancy?

You should not take part in this study if you are pregnant or intend to become pregnant in the next 4 years. Mothers should not breastfeed a baby while on this study. The drugs used in this study may be unsafe for unborn babies. If you are having sex that could lead to pregnancy, you must agree not to become pregnant. If you are a woman who can get pregnant, you must talk to your study doctor about birth control and use it all of the time. You must continue to use birth control until 30 days after stopping your oral anti-HIV medicines and 52 weeks after stopping your injectable anti-HIV medicines (i.e., 52 weeks after receiving the last dose of injectable anti-HIV medicine). You must choose one of the birth control methods listed below:

- Contraceptive subdermal implant
- Intrauterine device or intrauterine system
- Combined estrogen and progestogen oral contraceptive
- Injectable progestogen
- Contraceptive vaginal ring
- Percutaneous contraceptive patches

If you can become pregnant, you must have a pregnancy test before you enter this study. The test must show that you are not pregnant. If you think you may be pregnant at any time during the study, tell your study staff right away. If you become pregnant while on study, the study staff will talk to you about your choices.

If you become pregnant at any time during the study, tell your study staff right away. The study staff will ask you to stop taking study provided medications but continue your study visits.

If you become pregnant while on study, the study staff would like to obtain information from you about the outcome of the pregnancy (even if it is after your participation in the study ends). If you are taking anti-HIV drugs when you become pregnant, your pregnancy will be reported to an international database that collects information about pregnancies in women taking anti-HIV drugs. This report will not use your name or other information that could be used to identify you.

Breastfeeding

It is unknown whether the study drug passes through the breast-milk and may cause harm to your infant. You must not breast-feed if you are in this study.

In one study evaluating CAB in pregnant rats and their newborn pups, there was a higher rate of pups that died at the time of delivery or shortly after delivery in the rats that received a 1000 milligrams per kilogram dose of CAB compared to pregnant rats who did not receive CAB. This finding did not occur in pregnant rats who received two lower doses (0.5 and 5 milligrams per kilogram) of CAB. The blood levels of CAB given in this study are expected to be lower than the blood levels in pregnant rats where this finding was observed. The significance of this finding on human pregnancies is not known. Birth defects have not been observed in animal studies with CAB, to date.

Risk of neural tube defects with the HIV-1 Integrase inhibitor dolutegravir

In one ongoing birth outcome study, early results show that 4/426 (0.9% or nearly 1 in every 100) pregnancies of women who were taking dolutegravir at the time they became pregnant had babies with serious brain and spine defects, compared to 0.1% (one in every 1000) pregnancies of women who were not taking dolutegravir. These defects happen early in pregnancy, within the first month, before many women even know they are pregnant.

Cabotegravir is not the same drug as dolutegravir. We do know that cabotegravir and dolutegravir belong to the same class of medications and work in a similar way to treat HIV infection. We do not know if cabotegravir can cause nervous system defects in babies.

Are There Benefits to Taking Part in This Study?

If you take part in this study, there may be a direct benefit to you, but no guarantee can be made. It is also possible that you may receive no benefit from being in this study. Information learned from this study may help others who have HIV.

What Other Choices Do I Have Besides This Study?

Instead of being in this study you have the choice of:

- Treatment with other prescription drugs available to you
- Treatment with experimental drugs, if you qualify
- No treatment

Please talk to your doctor about these and other choices available to you. Your doctor will explain the risks and benefits of these choices.

What About Confidentiality?

We will do everything we can to protect your privacy. Some of the questionnaires you will complete while in this study reveal very personal information about your mental health and substance use. Site staff will do all they can to keep your information private, but if you want referral for treatment or site staff feel referral to other providers for treatment of these conditions is necessary, some of the information may need to be shared with these other providers. In addition to the efforts of the study staff to help keep your personal information private, we have gotten a Certificate of Confidentiality from the U.S. Federal Government. This certificate means that researchers cannot be forced to tell people who are not connected with this study, such as the court system, about your participation. Also, any publication of this study will not use your name or identify you personally.

People who may review your records include the ACTG, Office for Human Research Protections (OHRP) or other local, US, and international regulatory entities as part of their duties, Food and Drug Administration (FDA), University of Pennsylvania institutional review board (IRB) (a committee that protects the rights and safety of participants in research), National Institutes of Health (NIH), study staff, study monitors, drug companies supporting this study, and their designees. Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.

Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to yourself or others, we will be required to tell the proper authorities including a clinical provider if indicated.

Your personal information may be given out if required by law. If you test positive for infectious diseases (HIV, Hepatitis B or 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

A description of this clinical trial will be available on 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 any time.

HIPAA AUTHORIZATION
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 information about me may be collected, used or shared with others?
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, dates directly related to you such as date of birth and clinic visits.
- Personal and family medical history
- Current and past medications or therapies
- Information from questionnaires administered in the study.
- Results of tests and procedures you will undergo during this research study and from the other HIV studies in which you have participated.
- Social Security Number, Medical record number

Why is my information being used?
Your information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- evaluate and manage research functions.

Who may use and share information about me?

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need access to 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.)
- Authorized members at the University of Pennsylvania, School of Medicine who coordinate this study and support research operations.
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB.

Who, outside the School of Medicine, might receive my 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:

- ACTG Data Coordinating Center, Frontier Science Technology Research Foundation (FSTRF): Data for this study will be keyed into a password protected, secure central database. Statistical Data Analysis Center (SDAC): Approved data will be downloaded from FSTRF to the statistical

data center for the AACTG at the Harvard School of Public Health. Specific study reports will be periodically provided to the study team and data safety review board to monitor if the trial is safe.

- Contract Research Organization (PPD, Inc): Monitors from PPD will visit the AACTG on a quarterly basis to review data and correct mistakes before the data are sent to SDAC for analysis.
- ViiV Healthcare and Janssen Pharmaceuticals The pharmaceutical companies supplying the drugsfor this study.
-

Regulatory and safety oversight organizations

- The Office of Human Research Protections
- The Study Monitoring Committee
- National Institutes of Health/Division of AIDS (DAIDS)/National Institute for Allergy and Infectious Disease (NIAID)

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations. Data are reported to the sponsor on Case Report Forms that identify you by your unique study number and not your name, date of birth or medical record number. Information regarding your health, such as side effects of the study drug 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 the School of Medicine use or disclose my35 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 database. However, 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
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?
Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You must do so in writing to the Principal Investigator at Infectious Disease Division, 502 Johnson Pavilion Philadelphia PA 19104. 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, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research 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.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

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.

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).

What Are the Costs To Me?

There will be no cost to you for study-related visits, physical examinations, laboratory tests or other procedures. You or your insurance company may need to assume the cost of drugs not provided by the study. In some cases, it is possible that your insurance company will not pay for these costs because you are taking part in a research study.

Will I Receive Any Payment?

You will be compensated $50 for each study visit you attend. For Step 1 the visits are: Screening, Pre-Entry and Entry and weeks 2, 4, 8, 12, 16, 20, and 24 (10 visits). During the induction phase (first 20 weeks) you will be compensated additionally if you achieve certain VL “milestone” as follows:

- $75 if you complete a study visit at Step 1, week 2.
- $75 if you have the expected decrease in your HIV VL at Step 1, weeks 4 and 8.
- $150 if your HIV viral load is less than 200 copies at Step 1, weeks 12, and 16, and less than 50 copies at Step 1, week 20.

If you do not achieve the milestones, you will not be compensated (except for the usual compensation given for attending your study visit) but you will be allowed to continue on the study and you may be eligible for the next financial compensation (for example, you may not qualify to compensation at Step 1, week 4, but you could still receive financial compensation at Step 1, weeks 8, 12, 16, and/or 20, based on these milestones). The CEI will stop at Step 1, week 20.

The total financial compensation for completing all study visits and for reaching all ‘milestones’ during the first 20 weeks of the study is $500 (study visits) + *potential $675 for milestones.*

$50 compensation will be provided for each visit attended as part of Steps 2 to 4.

For the optional hair collection, we will give you $20 each time you opt to give a sample. Hair is collected at the following study visits: Entry, Step 1 Weeks 12 and 24; Step 2 Randomization, and weeks 8, 24, 36 and 48; Step 3 Randomization and weeks 12, 24, 36 and 48 and anytime on study if your viral load needs to be checked if it is elevated.

Compensation for the screening visit will be given as cash; compensation for the remainder of the study visits will be provided on a ClinCard (a debit card). There is no other form of compensation available such as reimbursements for parking, tokens or child care.

Please note that if you receive more than $600.00 compensation in one year for participation in research studies at the University of Pennsylvania, you must provide a Individual Tax Identification number or Social Security Number for tax purposes.

What Happens If I Am Injured?

If you are injured as a result of being in this study, you will be given immediate treatment for your injuries. The cost for this treatment will be charged to you or your insurance company. There is no program for compensation either through this institution or the National Institutes of Health. You will not be giving up any of your legal rights by signing this consent form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

What Are My Rights As a Research Subject?

Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. Your healthcare provider will treat you the same no matter what you decide.

We will tell you about new information from this or other studies that may affect your health, welfare, or willingness to stay in this study. If you want the results of the study, let the study staff know.

What Do I Do If I Have Questions Or Problems?

If you have questions about this study or a research-related injury, please contact the research team listed on page 1 of this consent form.

For questions about your rights as a research subject, contact:

- Director of Regulatory Affairs at the University of Pennsylvania by phoning (215) 898-2614

CONSENT

If this consent is the initial consent for this participant, the study staff will provide an overview of the study, required visits, treatment regimen, risk and all elements of consent. The physician investigator(s) or licensed Nurse Practitioner will conduct a focused discussion about risks, benefits and alternatives.

If this consent is a subsequent consent for this participant, since there are updates to the risk the physician investigator(s) or licensed Nurse Practitioner will conduct a focused discussion about risks, benefits and alternatives.

Conditional Economic Incentives (CEI)

Please indicate and initial below to ensure that you understand that:

a) The CEIs will only be implemented during Step 1 and;
b) All CEIs will be discontinued for all participants after week 20.

_____ Study Participant's initials

Optional Components of the study

Allowing your samples to be stored for this use is optional. Please indicate below if you agree to have your other biologic samples, including blood, serum (part of the blood), plasma (part of the blood), cells, hair and dried blood spots that are left over after all required study testing is done stored for later use. No matter what you decide, it will not affect your participation in the study.

For other biologic samples:

_____ (initials) YES, I agree **OR** _____ (initials) NO, I do not agree

For hair samples:

_____ (initials) YES, I agree **OR** _____ (initials) NO, I do not agree

If you decide now that any of your samples can be stored for research to be done at a later date, you may change your mind at any time. If you change your mind, you must contact your study doctor or nurse and let them know that you do not want your samples used for research to be done at a later date. Every effort will then be made to destroy your left-over samples.

Zip Code Information

Please indicate and initial below whether you approve the collection of the first 3 digits of your zip code.

_____ (initials) YES, I agree **OR** _____ (initials) NO, I do not agree

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

IRB APPROVAL FROM: 09/17/2019 TO: 08/12/2020

A copy of this consent form will be given to you. You will also be given the University of Pennsylvania Health System and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your health information.

RESEARCH STAFF CONSENT

Name of Subject (Please Print)	Signature of Subject	Date/Time

Name of Person Obtaining Consent (Please Print)	Signature	Date/Time

INVESTIGATOR CONSENT

The risks, alternatives, and benefits have been reviewed with me by the Investigator, and I understand what we have discussed.

Name of Subject (Please Print)	Signature of Subject	Date/Time

I verify I have reviewed risks, alternatives, benefits with this subject, who demonstrates good understanding.

Investigator Name (PRINTED)	Signature	Date/Time

IRB APPROVAL FROM: 09/17/2019 TO: 08/12/2020