HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

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

Protocol Title:	**A5354 Version 1.0, dated 4/19/16, Letter of Amendment #1, 12/13/16; Letter of Amendment #2, 11/7/17** **Effect of Antiretroviral Treatment Initiated During Acute HIV-1 Infection on Measures of HIV-1 Persistence and on HIV-1-Specific Immune Responses A Limited-Center Trial of the AIDS Clinical Trials Group (ACTG)**
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Introduction:

You are being asked to take part in this research study for two main reasons:

1. You are acutely infected with the human immunodeficiency virus type 1 (HIV-1, the virus that causes AIDS). Acutely infected means that you are newly infected with HIV.
2. You are willing and able to start taking antiretroviral therapy (ART, anti-HIV drugs) right away.

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. This consent form is for the second part of this two-part 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?

The study is being done to:

- start ART early in those recently or acutely infected with HIV-1
- see how starting ART as soon as the infection is found affects the amount of HIV-1 in your blood and how well your body fights the HIV-1 infection
- look at the amount of HIV-1 DNA (genetic material for HIV-1) seen in CD4+ T-cells (infection-fighting cells in your blood) after 48 weeks of ART
- see how early treatment for HIV affects the numbers of HIV-1 infection fighting cells (CD4+ and CD8+ T-cells) in your blood

How Many People Will Take Part in This Study?
About 150 people (men and women 18 years of age and older) who have acute HIV-1 infection will take part in this study. About 5 people are expected to enroll at the University of Pennsylvania.

How Long Will I Be In This Study?
Most participants will be on this study for about 72 weeks or 1.5 years. This will include a Screen visit and an enroll visit followed by 9 clinic visits. These visits are detailed in Attachment A. There are 2 telephone contact evaluations at Study weeks 2 and 8.

What Do I Have To Do If I Am In This Study?
If you decide to join this study, you will first need to be screened for the study to make sure that you qualify. You will start taking ART at study entry. At study entry, a sample of your blood will be tested to confirm your HIV-1 infection. At the time of starting ART, an additional sample of your blood will be tested to see how far along you are with your HIV-1 infection; this is called Fiebig staging. There are three study groups determined by Fiebig staging. Based on your medical records of HIV testing and the results from the day that you start the HIV medications, the study team will determine which study group you will be included in. Both you and your doctor will know which drugs you are taking. The study staff will work with you to make sure you are taking your medication correctly.

The study will provide a single tablet that contains 4 different drugs. Three of these drugs treat HIV, and one is a drug that increases the levels of one of the anti-HIV drugs. The names of these drugs, which will be provided as a single tablet regimen, are: elvitegravir/cobicistat/emtricitabine/ tenofovir alafenamide (EVG/COBI/FTC/TAF) and has been approved by the US Food and Drug Administration.

If you are not able to take the study-provided medicine, then you will be allowed to take the best ART available to you, as prescribed by your primary care doctor. These non-study-provided ART must be obtained locally.

If you enter this study, you will need to come for study visits up to nine times in the first year, of which two of these visits will be done by telephone. If during these telephone visits, the study staff determines that you should be seen in person, you will be asked to go to the clinic. In the next year, you will have up to two clinic visits that will include the study staff contacting you by telephone the day after completing the optional procedures (gut biopsy and/or lumbar puncture). You will be notified by the study staff of when to expect to receive these telephone calls before you are actually called. Most clinic visits will last about 1 hour. If you elect to have leukapheresis at the Entry visit, this visit will last about 3 hours. The study staff will tell you how long each visit will last.

NOTES:
- If your laboratory tests from entry (as noted in the first paragraph of the “What Do I Have to Do If I Am In This Study?”) show that you do not qualify for the study, the study staff will tell you to stop the study supplied ART. You will be asked to complete the discontinuation evaluations, and your follow-up will end.
- After you enter the study, if your blood test shows that you have had HIV longer than expected at the time of entry, then your follow-up and HIV study treatment will end at week 24. Your study doctor will tell you the results of the tests by week 12 so you will have time to pursue HIV treatment outside of the study.
- If you stop taking your ART for 7 or more days in a row, the last peripheral blood mononuclear cells (PBMC, cells separated from the blood taken from you) and plasma (the liquid part of blood taken from you) collection will be done at week 48.

You may need to come to the clinic for extra visits if you develop side effects or if you need to switch to non-study-provided ART or if the level of HIV in your blood increases after it has been undetectable. More information about the study procedures is given at the end of this consent (Attachment A). During the study, you will receive results, when they are available, from any routine tests that are done during the study.

At most visits, we will collect blood samples for routine safety labs and study-required tests. Some of your blood will be stored (with protectors of identity) and used for immunologic, resistance, and genetic testing that is required for this study. Amounts of blood being drawn at each visit are listed at the end of the form.

You will get the usual adherence support (procedures to help you remember to take your ART).

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. 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. If you do not want this information to be recorded, you should not sign this consent form and not participate in the study. If you elect not to participate, all information collected thus far by the research team will be destroyed.

Extra Samples and Blood Collections

Part of the entry visit includes taking a larger amount of blood (large volume blood draw) than what is collected on a typical blood draw. At PENN, blood can also be collected during a medical procedure called leukapheresis, which may be performed in place of large volume blood collection (200 mls) at entry. The advantage of leukapheresis is there is minimal blood loss (30 mls). Only the white cells are collected and the red blood cells and platelets (clotting cells) are returned to the participant.White cells are replaced by the body within several days. Both procedures will be discussed with you and you and the study staff will decide which alternative is best for you. For the leukapheresis procedure, you will need to be in a semi-reclining or reclining position for about 2 hours. By collecting blood using this procedure, researchers are able to get many more white blood cells than is usually possible. For additional information, see Attachment B of Appendix I.

After week 48, you may be asked whether you agree to have additional procedures done and samples collected. You will be provided more information about these additional procedures during that visit. These additional procedures are optional and include leukapheresis or large volume blood collection, gut biopsy by flexible sigmoidoscopy, and lumbar puncture (see Appendix II for additional information). You will not receive the results of these procedures because they are for research purposes only. No matter what you decide, it will not affect your participation in the study.

NOTE: If you are pregnant or become pregnant on study, these optional procedures will not be done.

What if I have to stop taking both the study-provided and non-study provided ART?

During the study:

If you must stop taking ART for 7 or more days in a row before the week 24 study visit and you have not had an HIV-1 RNA test showing your viral load was <50 copies/mL, then you will be asked to complete the discontinuation evaluations before having to stop the study medications and being taken off the study. The study staff will discuss other options that may be available to you.

If you stop taking ART for 7 or more days in a row either during the first 24 weeks after you have had a HIV-1 viral load <50 copies/mL or after week 24,you will be asked by the study staff to return to the clinic to have a repeat HIV-1 viral load test that will check whether your ART regimen is working. This test is called a virologic failure (VF) confirmatory test. If the confirmatory test results show that your ART regimen is working for you, then you will remain in the study for continued follow-up and no more PBMC and plasma collection will be done after week 48. If the test results show that your ART regimen has failed, then you will be asked to complete the discontinuation evaluations before having to stop the study medication and being taken off the study. The study staff will discuss other options that may be available to you.

After the study:
After you have completed the study, the study will not provide you with study drugs. The study staff will talk with you about your choices. You and your doctor will decide what treatment you should have, and the study staff will discuss with you how you may be able to obtain ART after the study ends

What Are The Risks Of The Study?

The main risks of the procedures and study-provided drug are described below.

Risks of Social Harm
Although the study site will make every effort to protect your privacy and confidentiality, it is possible that other people could find out that you are in a study and this could cause problems for you. For example, other people might figure out that you are infected with HIV-1. If this happens, you could be treated unfairly or you could have problems being accepted by other family members, friends, and/or the community.

Risks of Drawing Blood
Taking blood may cause some discomfort, lightheadedness, bleeding, swelling, or bruising where the needle enters the body, and in rare cases, fainting or infection.

Risks of Leukapheresis:
Rarely, you may feel faint during or after leukapheresis. Side effects that can occur during the leukapheresis procedure include chills, nausea, and heartburn caused by the citrate anticoagulant that is used during the procedure to keep the collected cells from clumping together in the bag. This chemical may use up some of the calcium in your blood stream, and tingling in the face, lips, or hands may be noted. If this happens, study staff may slow the rate of infusion of this chemical and may offer you one or two calcium carbonate tablets to correct the calcium loss. After the leukapheresis procedure you may experience temporary discomfort, including irritation, swelling or bruising at the place where the needle was inserted into your vein to collect the blood. Leukapheresis can also occasionally cause: hives, numbness and tingling, or swelling of your feet and ankles.

Risks Related to Pregnancy
The ART 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 or to attempt to make a woman pregnant.

Because of the risk involved, you and your partner must use at least one effective method of birth control. You must continue to use birth control while receiving study drugs.

Remember: If you are having sex, you need to use condoms to prevent transmitting your HIV-1 infection to others.

Approved methods of birth control are listed below. The study staff will talk with you about your choices.

- Birth control medications that prevent pregnancy given as pills, shots, or placed on or under the skin
- Male or female condoms with or without a cream or gel that kills sperm
- Diaphragm or cervical cap with a cream or gel that kills sperm
- Intrauterine device

If you can become pregnant, you must have a pregnancy test, and the test result must be available at the study clinical research site before you can start ART. If you think you may be pregnant at any time during the study, you must tell the study staff right away. If you become pregnant during the study, you may choose to stay in the study and switch to a regimen that is recommended for pregnant women. The study staff will talk to you about your choices.

Risks of Genetic Testing

This research includes optional genetic testing and you will need to sign at the end of the consent if you agree. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or your doctor.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.

A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.

Risks of ART

All ART medications can have side effects. The drug regimen provided in this study may have side effects. Listed below are the more serious or common side effects that may be related to the study-provided drugs. Please note that these lists do not include all the side effects seen with the study-provided drugs. The staff will be able to tell you which are the most serious side effects. They will also be able to tell you what to do if you have any of these side effects. If you have questions concerning the additional study-provided drug side effects, please ask the medical staff at your site.

<u>Emtricitabine (FTC)</u>

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

- Headache
- Dizziness
- Tiredness
- Inability to sleep, unusual dreams

- Loose or watery stools
- Nausea or vomiting
- Abdominal pain
- Rash, itching, which sometimes can be a sign of an allergic reaction
- Darkening of the skin on the palms of the hands and/or soles of the feet
- Increased cough
- Runny nose
- Abnormal liver function tests, which could mean liver damage
- Increases in pancreatic enzyme (a substance in the blood), which could mean a problem with the pancreas
- Increased triglycerides (a type of fat found in the blood)
- Increased creatine phosphokinase (a substance found in the blood), which could mean muscle damage

NOTE: If you are infected with both hepatitis B and HIV-1, your liver function tests may increase and symptoms caused by hepatitis may get worse if you stop FTC.

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, such as FTC, when used 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.

Some side effects of FTC may not need any medical attention. As your body gets used to the medicine, these side effects may disappear.

<u>Tenofovir Alafenamide (TAF)</u>
The following side effects have been associated with the use of TAF:

- Nausea, vomiting, gas, loose or watery stools
- Generalized weakness
- Dizziness
- 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
- Allergic reaction: symptoms may include fever, rash, nausea, 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
- Bone pain and bone changes such as thinning and softening, which may increase the risk of breakage
- Muscle pain and muscle weakness
- Sleeping problems

NOTES:

- If you are infected with both hepatitis B and HIV-1, your liver function tests may increase and

symptoms caused by hepatitis may get worse if you stop TAF.
- Because there is only a small amount of information on TAF in pregnant and breastfeeding women, you should not use TAF during pregnancy or if breastfeeding.

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, such as TAF, when used 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.

Some side effects of TAF may not need any medical attention. As your body gets used to the medicine, these side effects may disappear.

Cobicistat (COBI)
The following side effects have been associated with the use of COBI:
- Abdominal or stomach pain
- Bloody urine
- Chills
- Clay-colored stools
- Dark urine
- Decreased frequency or amount of urine
- Dizziness
- Fast heartbeat
- Fever
- Headache
- Hives or welts, itching, or rash
- Hoarseness
- Increased thirst
- Irritation
- Joint pain, stiffness, or swelling
- Loss of appetite
- Lower back or side pain
- Nausea and vomiting
- Pain in the groin or genitals
- Redness of the skin
- Sharp back pain just below the ribs
- Swelling of the eyelids, face, lips, hands, lower legs, or feet
- Tightness in the chest
- Troubled breathing or swallowing
- Unpleasant breath odor
- Unusual tiredness or weakness
- Vomiting of blood
- Weight gain
- Yellow eyes or skin
- Dark-colored urine
- Muscle cramps or spasms
- Muscle pain or stiffness

- Diarrhea
- Discouragement
- Feeling sad or empty
- Irritability
- Loss of interest or pleasure
- Trouble concentrating
- Trouble sleeping
- Upper abdominal or stomach pain

Some side effects of COBI may not need medical attention. As your body gets used to the medicine, these side effects may disappear.

Elvitegravir (EVG)
The following side effects have been associated with the use of EVG:

- Diarrhea
- Headache
- Nausea
- Discouragement
- Feeling sad or empty
- Heartburn
- Indigestion
- Irritability
- Lack of appetite
- Loss of interest or pleasure
- Rash
- Stomach discomfort, upset, or pain
- Thoughts or attempts at killing oneself
- Trouble concentrating
- Trouble sleeping
- Unusual tiredness or weakness
- Vomiting

Some unwanted effects may be caused by EVG. In the event that any of these side effects do occur, they may require medical attention. Some of the side effects that can occur with EVG may not need medical attention. As your body adjusts to the medicine during treatment, these side effects may go away. Your health care professional may also be able to tell you about ways to reduce or prevent some of these side effects. If any of the aforementioned side effects continue, are bothersome, or if you have any questions about them, check with your health care professional.

Some side effects of EVG may not need any medical attention. As your body gets used to the medicine, these side effects may disappear.

Use of Combination Antiretroviral (ARV) Drugs
In some people with advanced HIV-1 infection, symptoms from other infections or certain diseases may occur soon after starting combination ART but can also occur later. Some of these symptoms may be life threatening. If you start having new symptoms, or notice that existing symptoms are getting worse after starting your ART, tell your health care provider right away.

The use of potent ARV 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

There is a risk of serious and/or life-threatening side effects when non-study-provided medications are taken with the study-provided drugs. For your safety, you must tell the study doctor or nurse about all medications you are taking before you start the study. It is also important that you do not start any new medications while on the study before discussing it with the study doctor or nurse. Also, you must tell the study doctor or nurse before enrolling in any other clinical trials while on this study.

Can I Join the Study If I Am Currently Pregnant or Breastfeeding?

If you are pregnant or breastfeeding, you are allowed to take part in the study as long as you meet the requirements of the study. If you are pregnant at the time of enrollment, you will be instructed by the study staff to take alternative, non-study-provided ART during your pregnancy or while breastfeeding.

What If I Become Pregnant During This Study?

If you become pregnant while on study, you must tell the study staff right away and see your doctor to get the best care possible. You will be asked to return to the clinic for a study visit at your earliest possible convenience. You may remain on study during your pregnancy or you may leave the study. Either way, the study staff will contact you to find out about any events that happen during your pregnancy and about the health of the baby.

If you choose to stay in this study, you will not be able to continue on the study-provided drug. You and your study doctor will decide what ART are best for you now that you are pregnant. If you are on study-provided EVG/COBI/FTC/TAF, you will need to change to alternative non-study-provided ART that is felt to be appropriate for use in pregnancy by your study doctor and/or primary care provider. You will continue to have regularly scheduled study visits, but you will not take part in the optional procedures and large volume blood collection.

This study will not provide care related to your pregnancy, the delivery of your baby, or the care of your baby. You must arrange for your care and your baby's care outside of this study. Your study doctor will help you find appropriate care.

Long-term follow-up is recommended for a baby whose mother takes ART during pregnancy. The study staff will talk with you about long-term follow-up and the possibility of enrolling your baby in a long-term follow-up study.

After your baby is delivered, you may be able to return to the study-provided drug regimen you were taking before you became pregnant. If you decide to breastfeed your baby, you must remain on your current non-study-provided ART.

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:

- You never started ART (study-provided or non-study-provided drugs) or started ART later than 48 hours after joining the study.
- An HIV-1 test shows that you are not infected with HIV or you have had HIV infection for a longer

period of time than expected or your laboratory tests from entry show that you do not qualify for the study.
- You miss 3 study visits in a row.
- Your viral loads show that the HIV medications you are taking are no longer working well for you; this is known as having VF.
- Your study doctor believes that remaining on the study is no longer what is best for you.
- You are unable to follow the requirements of the study or at the recommendation of the IRB/EC, NIAID, OHRP, other government agencies as part of their duties, or industry supporter.
- A Study Monitoring Committee (SMC), an outside group of experts that monitors the study, recommends that the study be stopped early or canceled.

The study doctor may also need to take you off the study treatment without your permission if:
- continuing the study drug infusion may be harmful to you, for example, if the study drugs are making you sick.
- you need a treatment that you may not take while on the study
- You become pregnant and/or start breastfeeding

If you must stop taking ART before the study is over or if you want to stop the study visits, then the study staff will ask you to return to the clinic for a final visit.

Are There Benefits to Taking Part in This Study?

It is possible that being in this study will be of no direct benefit to you and that the optional procedures being done will not change your clinical care.

It is also possible that being in this study benefits you in one of the following ways:
- Gives you access to ART for 1.5 years or 72 weeks.
- Gives you more detailed information about your HIV-1 infection than you could get from your local anti-HIV care center; having this information could help you get better treatment for your HIV-1 infection.
- Provides you with frequent health checks that could help identify problems early; having this information could help you get good treatment at the right time.

Finally, it is possible that your being in this study will provide information that will help others with HIV-1 infection

What Other Choices Do I Have Besides This Study?

Instead of being in this study, you have the choice of:
- treatment with the anti-HIV drugs available to you locally
- treatment with experimental drugs, if there is a study available locally for which 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?

Pregnancies that occur while on study will be reported to the Antiretroviral Pregnancy Registry.

We will do everything we can to protect your privacy. In addition to the efforts of the study staff to help keep your personal information private, we have a Certificate of Confidentiality from the US 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 ACTG, Office for Human Research Protections (OHRP), or other government agencies as part of their duties, University of Pennsylvania institutional review board (IRB), National Institutes of Health (NIH), study staff, study monitors, industry supporters or 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.

A description of this clinical trial will be available on ClinicalTrials.gov, as required by US law. This website will not include information that can identify you. At most, the web site will include a summary of the results. You can search this website at any time.

Your personal information may be given out if required by law. If you test positive for HIV, or if a CD4 or viral load is done at a research study visit, by law we have to report the result to the City of Philadelphia Health Department/PA Department of Health. Personal identifiers such as name, sex, date of birth, address, and phone number will be reported. For more information about the requirements reporting infectious diseases to the City of Philadelphia Health Department, please visit https://hip.phila.gov/ReportDisease. For more information about the requirements reporting infectious diseases to the PA Health Department, please visit: http://www.health.pa.gov/Your-Department-ofHealth/Offices%20and%20Bureaus/epidemiology/Pages/Reportable-Diseases.aspx#V620aZ3D9eU.
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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 and from the other HIV studies in which you have participated.
- Results of tests and procedures you will undergo during this research
- 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 information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right

- to evaluate and manage research functions

Who may use and share information about me?
The following individuals may use or share your information for this research study:

- The Principal Investigator and the Investigator's study team
- Other authorized personnel at Penn, including offices that 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 recorded on case report forms, keyed into a central database and electronically submitted to the Data Coordinating Center. The data will be cleaned and stored at this facility until it is ready to be analyzed.
- 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.
- Gilead Sciences: The pharmaceutical company that is supplying the drug for this study.
- 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.
- Government Agencies: Data from this study will be made available to the Food and Drug Administration and to the National Institutes of Health/Division of AIDS (DAIDS)/National Institute for Allergy and Infectious Disease (NIAID), for them to evaluate the safety and efficacy of the treatments being used in this study.

Regulatory and safety oversight organizations

- The Office of Human Research Protections

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 be able to use or disclose your personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research 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, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Information related to your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR. Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

What Are the Costs To Me?

You will not have to pay for the study-provided drug, EVG/COBI/FTC/TAF. If your doctor decides that other drugs would work better for you, then you might have to pay for those drugs. This could happen if you are unable or unwilling to take EVG/COBI/FTC/TAF or if you become pregnant while on study.

You will not have to pay for study visits, exams, and laboratory tests needed for this study. The study will perform one resistance test for all participants (at entry prior to taking the study medications) and possibly another resistance test in those participants whose ART regimen has failed (at the VF confirmatory visit). In addition, some of your blood may be tested at the end of the study to look at genetic factors. The results of these tests will not be available right away since the tests will be done later in the study.

Taking part in this study may lead to added costs to you or your insurance company. In some cases, it is possible that your insurance company or health care system 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 (screen, entry and 9 clinic visits); a total of 11 study visits. At weeks 2 and 8, a telephone visit will be done, and at the clinic visit after the phone contact, $10 will be compensated for the completed phone contact. Compensation will be given as a ClinCard (a debit card). The maximum amount of compensation for the study is $550 if all regular study required visits are completed and attended. If you are required to come to the clinic for any additional visits you will be compensated $25. If you participate in the optional procedures (leukapheresis, rectal biopsy or lumbar puncture) $150 will be compensated for EACH procedure. This will be in addition to the regular compensation schedule.

There is no other form of compensation available such as reimbursements for parking, tokens or child care. In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

What Happens If I Am Injured?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania or the National Institutes of Health to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this 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, tell the study staff .

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

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.

☐ a subsequent consent for this participant that does not alter the risks for investigational product or products, alternatives or benefits. Research staff will conduct the consent discussion.

☐ a subsequent consent for this participant that does alter the risks for investigational product or products, alternatives or benefits. The physician or nurse practitioner investigator will discuss the changes to these sections and the research staff will review changes that were made to other sections.

Human Genetic Testing
If you agree, some of your blood will be saved (with protectors of identity) and tested in the future to see how your own genes can help to show how your immune system and/or virus will respond to the ART, either successfully or unsuccessfully. You will not receive the results of these studies because they are for research purposes only.

Please **initial below** if you agree to have any of your blood used for genetic testing. You may change your mind at any time and your samples will be destroyed.

I am willing to have some of my blood stored for genetic testing_____.
OR
I am NOT willing to have my blood stored for genetic testing____.

Other
Please **initial below** whether you are willing to have some of your leftover blood (that is stored at the study site and/or at a central laboratory without information that could identify you) used for future ACTG-approved HIV-related research. This research may not be connected with this study. Future studies will be required to have IRB approval prior to use. You will not receive the results of these studies because they will likely be done after the study ends.

I am willing to have some of my leftover blood used for future non-A5354 research _____.
OR
I am NOT willing to have any of my leftover blood used for future non-A5354 research ____.

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.

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

Participant's Legally Authorized Representative (print) (As appropriate)	Legally Authorized Representative's Signature and 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

ATTACHMENT A: Study Visits

The study staff can answer any questions you have about individual study visits, the evaluations that will occur, or how long each visit will be. The table below can be used as a quick reference for you, along with the explanations that follow.

I. Study Schedule

Evaluation or Procedure	Screening[1]	Entry[2]	Most Other Visits[3]	Some Other Visits[4]	Special Visit[5]	Leaving or Stopping the Study Early[6]
Consent	√			√		
Acute HIV-1 infection documented	√					
HIV-1 infection confirmed and Fiebig stage testing		√				
Group assigned and ART started		√				
Physical exam		√	√			√
Medical History	√	√				
Medication History	√	√				
Blood collected		√	√		√	√
Pregnancy test		√	√			√
Resistance test		√			√	
Urine collected		√				√
Telephone follow-up with participants				√		
Adherence support		√	√	√	√	
Large volume blood draw		√		optional		
Optional procedures				√		
Approximate amount of blood		up to 359 mL	see footnote 3 below for blood volume details	see footnote 4 below for blood volume details	20 mL	9 mL

[1]Screening: After you have read and signed the consent form, the study staff will check your medical records for available documentation of your HIV-1 diagnosis; for instance, whether you are recently or acutely infected with HIV-1 to make sure that you meet the requirement for joining the study. You will be asked about anti-HIV and other kinds of medications you have taken in the past.

[2]Entry Visit: If you are eligible to join the study, you will enter the study and be placed into a group. At this visit, you will start taking ART. If you are unable or unwilling to take the study-provided drug, then you must have access to and can begin to take an alternative ART in order to enter the study.

NOTE: Large volume blood collection (about 320 mL of blood) will be done, and at some sites, optional leukapheresis may be done in place of large volume blood collection at entry.

[3]Most Other Visits: Most participants will be seen at 1 week, 4 weeks, 12 weeks, and 24 weeks after entering the study and then at 48 weeks and thereafter at weeks 60 and 72 (final study visit for participants whose test results show Fiebig I-V stages). Those participants whose test results show Fiebig VI will have their final study visit at week 24.

The approximate amount of blood (in mL/teaspoons) that will be drawn at the following study visits are listed as follow:

- week 1: 3 mL (half teaspoon)
- week 4: 79 mL (16 teaspoons)
- week 12: 83 mL (17 teaspoons)
- week 24: 83 mL (17 teaspoons)
- week 36: 10 mL (2 teaspoons)
- week 48: 173 mL (35 teaspoons)
- week 49: 63 mL, and possibly an additional draw if not enough blood was collected at week 48 for the virologic studies (13 teaspoons)
- week 60 or 72: see footnote 4 below

[4]Some Other Visits: At weeks 2 and 8 and the day after having the optional procedures (gut biopsy and/or lumbar puncture), you will be contacted by the study staff over the phone to check how you are doing. At week 36, you will come to the clinic to have a physical exam, a viral load test, and an adherence evaluation.

At weeks 60 and 72, you will have blood drawn (23 mL or about 5 tsp) for routine safety labs at each visit. Depending on whether or not you reached the main goal of the study at week 48, you may be asked as to whether you are willing to have additional procedures done and samples collected between weeks 60 and 72 (see Appendix II for details on these procedures). If you agree to the optional blood collection between weeks 60 and 72, either leukapheresis (equivalent to 30 mL of blood loss) or large volume blood draw (about 320 mL of blood as an alternative to leukapheresis) will be collected.

[5]Special Visit: If it seems that the ART regimen is not working or if you are having side effects from your treatment regimen, then you may be asked to come to the clinic for an extra visit.

[6]Leaving the Study Early: You will be asked to come to the clinic for an extra visit if you leave the study or stop the study treatment early.

II. Explanation of Evaluations

Consent and contact information collection
After you read the consent and have had a chance to ask questions about the study, you will sign the consent form if you want to continue to be evaluated for study participation. You will also be asked how to be contacted in case you miss a visit or there are problems with your tests, and whether you give the study team permission to contact you.

Acute HIV-1 infection documentation
The study staff will check your medical records to see if you had an HIV test done as part of local routine care and whether you were recently or acutely infected with HIV-1.

HIV-1 infection confirmation and Fiebig staging
Blood will be collected to confirm that you have HIV-1 infection, and an additional blood sample will be collected for Fiebig staging (a test to show how far along you are with your HIV-1 infection).

Group assignment and study treatment/locally-provided ART
You and the clinic staff will discuss your assigned group and the optimal ART options for you. These will be based on your acute HIV-1 diagnosis and medical history. At study entry, you will receive either study-provided or other non-study-provided ART based upon your discussion with the study site doctor.

The study staff and the study pharmacist will tell you how often to take your drugs and whether you should take them with food.

Physical examination
You will have a physical exam and will be asked questions about your health and about any medicines you have taken or are taking now.

Blood collection
Blood will be collected from you for various tests during the study. These include: routine safety laboratory tests, HIV-1 viral load (a test that shows how much HIV-1 is in your blood), CD4+ T-cell count (a test that shows how many infection-fighting cells you have in your blood), and liver function tests. At entry and at the confirmatory visit to check whether your ART regimen has failed, a sample will be collected for resistance testing (a test that shows whether the ART is working for you). Routine PBMC and plasma storage will be done.

Human genetic testing
Some of your blood will be tested to see whether the ART you are taking are making a difference by looking at your immune response (levels of infection fighting cells, CD4+ and CD8+ T-cells, in your blood) or whether development of resistance to ART is associated with different genes. You will not receive the results of these studies because they will be done in the future.

Pregnancy testing
If you are a woman who is able to become pregnant, then you may be asked to give a small urine or blood sample for a pregnancy test.

HIV-1 resistance testing
Your blood will be used to see which ART might work best for you.

NOTE: If resistance testing was done as part of routine care, the study doctor may review these results to make sure that your current ART is still the best for you.

Urine collection
You will be asked to provide a small amount of urine that will be used in safety tests.

Primary endpoint determination
At week 48, you will be asked to give blood samples for testing to determine whether you met the main goal of the study by looking at the total amount of HIV genetic material in infection-fighting cells at study week 48 (also known as the primary endpoint).

Site follow-up with participants via telephone
You will be asked about how you have been feeling and how well you are remembering to take your ART.

Adherence support
Everyone will get some adherence support from the site staff. This means that the study staff will explain to you in detail how to take the medications and help you find ways to take the medications correctly.

_____ **(initials) YES, (the information was reviewed)**

ATTACHMENT B: SAMPLES COLLECTION AND OPTIONAL PROCEDURE AT ENTRY

A. Explanation of Samples Collection and Optional Procedure

The samples collection and optional procedure below will advance the scientific goals of this study but will offer no direct benefit to participants. Neither you nor your doctor will receive any results from the samples collection and optional procedure because these tests are for research purposes only. If you choose not to participate in the optional procedure, it will not affect your ability to take part in this study.

NOTE: If you are pregnant, the samples collection and optional procedure will not be done.

- Large volume blood collection

  A large volume blood draw (320 mL) will be collected.

  NOTE: At PENN, leukapheresis may be done in place of large volume blood collection. Both procedures will be discussed with you and you and the study staff will decide which alternative is best for you.

- Leukapheresis (in place of large volume blood draw)

  The leukapheresis procedure may be performed at the Apheresis & Infusion Unit at the Hospital of the University of Pennsylvania. The procedure will take about 2 hours and the full visit will last about 3 hours. You will have to remain in a semi-reclining or reclining position for most of this time.

  Leukapheresis is a medical procedure that involves removing whole blood from an individual/donor and separating the blood into individual components so that leukocytes (white blood cells) can be removed. The remaining blood components are then put back into the bloodstream of the individual/donor. This will be done by inserting a needle attached to sterile tubing in one arm, and first sending your blood through a machine. This machine spins your blood to separate the red blood cells (cells that carry oxygen), the white blood cells (cells that fight infection) and the platelets (cells that help form clots). The white blood cells will be kept for testing. The rest of your blood will be returned to your body through another needle and tube in your other arm. Not all of your white blood cells are removed, and your body will make more white cells within a few days. Losing the number of white blood cells that are collected does not pose a danger to your health.

B. Risks Associated with Samples Collection and Optional Procedure

- Large volume blood collection

  Taking blood may cause some discomfort, lightheadedness, bleeding, swelling, or bruising where the needle enters the body, and in rare cases, fainting or infection.
- Leukapheresis (in place of large volume blood draw)

  Leukapheresis has been shown to be safe in HIV-infected donors and does not affect CD4+ T-cell count or immune status of short-term donors. The needle used is larger than normal blood draw and may be uncomfortable. Taking blood may cause some discomfort, lightheadedness, bleeding, swelling, or bruising where the needle enters the body, and in rare cases, fainting or

infection. Rarely, a participant may feel faint during or after leukapheresis. This sort of reaction can be handled by changing the participant's position or administering intravenous fluids. You may experience chills, nausea, and heartburn caused by the citrate anticoagulant that is used during the procedure to keep the collected cells from clumping together in the bag. This chemical may use up some of the calcium in your blood stream, and tingling in the face, lips, or hands may be noted. If this happens, study staff may slow the rate of infusion of this chemical and may offer you one or two calcium carbonate tablets to correct the calcium loss. Participants will be observed closely by an experienced blood bank technician during the procedure.

_____ **(initials) YES, (the information was reviewed)**