HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

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

Protocol Title:	**A5324 FINAL Version 2.0, dated 8/25/17; Letter of Amendment #1, 3/29/2018; Letter of Amendment 2, 6/4/2018; Letter of Amendment #3, 8/22/18** A Randomized, Double-Blinded, Placebo-Controlled Trial Comparing Antiretroviral Intensification with Maraviroc and Dolutegravir with No Intensification or Intensification with Dolutegravir Alone for the Treatment of Cognitive Impairment in HIV
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Introduction:

You are being asked to take part in this research study because you are infected with the human immunodeficiency virus (HIV), the virus that causes AIDS. This study is sponsored by the National Institutes of Health (NIH). The doctors in charge of this study at this site are: Dr. Dennis Kolson and 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?

There are now several HIV treatment options for a person with HIV infection who has not yet been treated. Most people who receive treatment and take their medications as directed have a good test result. This is usually determined by measuring the amount of HIV in the blood (viral load). The best response is when HIV cannot be found (undetectable) in the blood. However, it has recently become clear that some people with HIV who are receiving effective HIV drugs continue to have more health problems than people without HIV infection. Sometimes, there is damage to organs in the body, including bone, kidneys, and the brain.

The reasons this study is being done are the following:

- To see how the study drug combinations affect your ability to use your fingers and hands, concentrate, learn and remember, speak and write, think, solve problems and make decisions.
- To see how well the study drug combinations lower your HIV viral load.
- To see how safe the study drug combinations are, how well people are able to take the study drug combinations, and how well their immune systems respond to the study drugs.
- To see how well the study drug combinations get into your blood.

The drugs we are testing in this study are maraviroc (MVC) and dolutegravir (DTG). Both of these drugs have been approved by the Food and Drug Administration (FDA) for treatment of HIV. MVC and DTG will be added to your current drug regimen.

Some participants in the study will not be given the drugs that we are testing. Instead, they will be given a placebo. Placebo pills are just pills with no active ingredient in them.

You will be given one of the following three drug combinations:

- Placebo for maraviroc (MVC) and placebo for dolutegravir (DTG)
  OR
- DTG active drug and placebo for MVC
  OR
- MVC and DTG active drugs

How Many People Will Take Part in This Study?
About 186 people will take part in this study. About 10-15 participants are expected to enroll at the University of Pennsylvania.

How Long Will I Be In This Study?
You will be in this study for about 96 weeks.

What Do I Have To Do If I Am In This Study?
If you would like to be in this study, after you have read and signed this informed consent form, you will come to the clinic for a screening exam to make sure you meet the requirements for joining the study.

At Screening
This visit will take about 1 to 2 hours. The tests for this visit may be done in more than one day if that will be easier for you. At the screening visit:

- Your HIV infection status will be confirmed. If there is no record available, another HIV test will be done.
- We will ask you questions about your medical history, any medications you are taking or have taken within the last 30 days, and about the anti-HIV drugs you are taking (such as how long you have been taking the anti-HIV drugs you are currently taking, if you stopped taking them for any reason for more than 7 days, etc.).
- You will have a physical exam and will be asked questions about your health.
- You will have about 1-2 tablespoons (25mL) of blood drawn to measure your viral load (the amount of HIV in your blood), to see if you are infected with the hepatitis C virus (an infection of the liver) if there is no record available, to see if you have syphilis (a type of sexually transmitted disease), and to have some other routine tests for safety. You will be told the results of these tests when they become available
- We will ask you to give a urine sample for safety testing. We will give you the results of this test as soon as it becomes available.

- You will be given a liver enzyme test, formerly called liver function test (LFT) to see if you have damage to your liver and if your liver is working well.
- You will be asked some questions about yourself, such age, educational level and primary language.
- You will take neuropsychological tests, which will take about 1 hour. During the neuropsychological tests you will answer questions, list items (such as naming foods, or animals, or some other groups you know), and do simple tasks. You will be asked questions to see if you forget things, have difficulty understanding facts, or difficulty with your behavior and interacting with others.
  - Problems with thinking and decision making are an important effect of HIV-1 infection on the brain. These problems are known as neurocognitive impairment, and impact specific areas of brain functioning such as your ability to use your fingers and hands, concentrate, learn and remember, speak and write, think, solve problems and make decisions. Neurocognitive impairment has been classified into diagnoses, HIV Associated Neurocognitive Disorders, which is abbreviated as HAND. The diagnosis of HAND can go from least to most severe.
  - The study team will determine if you have HAND and are eligible for the study based on combining the results of the neuropsychological testing, gathering data on other conditions that can impact brain functioning and therefore your thinking, and also seeing how these changes in thinking ability have affected your home, social and work life.
- If you are a woman able to become pregnant, we will ask you to give a urine sample or have an additional 1 teaspoon (5mL) of blood drawn to see if you are pregnant. You will not be able to enroll in this study if you are pregnant. You will be told the result of the test when it becomes available.
- You will be asked to complete some questionnaires that ask about how you are feeling, how well you are able to perform your daily activities and about your alcohol and drug use.

At Pre-Entry
If you are eligible for the study, you will come in for a pre-entry visit. This visit will last about 30 minutes. At this visit you will have about 5 tablespoons (75 mL) of blood drawn, which will be stored for future testing.

The screening and pre-entry visits may be on different days or on the same day.

At Study Entry Visit
If you are eligible for the study, you will come in for an entry visit. This visit will last about 1 hour. At this visit:

- You will have a physical exam and will be asked questions about your health and about any medicines you have taken or are taking.
- You will have about 1-2 tablespoons (25mL) of blood drawn to measure your viral load, to measure your CD4+ cell count (CD4+ cells are cells in your blood that fight infection), and to have some other routine safety tests including liver enzyme test. You will be told the results of these tests when they become available.
- If you are a woman able to become pregnant, you will have a pregnancy test within 2 days before entry into the study. Pregnant women cannot enter the study.
- You will have about 5-6 tablespoons (80 mL) of blood drawn, which will be stored for future testing that is required for the study. This is not optional.
- We will ask you to fill out a questionnaire to see how well you are taking your anti-HIV drugs.

We will randomize you to one of three groups:

- Group A: placebo for MVC and placebo for DTG
- Group B: DTG active drug and placebo for MVC
- Group C: MVC and DTG active drugs

Randomized means that we will assign you by chance to one of three groups. You have an equal chance of being assigned to any group, like flipping a coin.

This study is a double-blind study. This means that you and the study staff will not know which group you have been assigned. We are doing this research because we do not know which treatment group is best for you.

You will continue taking the anti-HIV drugs that you are currently taking. You will also be given a combination of MVC, DTG or placebo based on the group that you are randomly assigned to. You must start the new medications within three days after you are randomized. If you will start taking the new medications after the day you are randomized, you may need another pregnancy test before starting. If you are pregnant you cannot start the new medications.

After Entry

After your entry visit, you will come to the clinic at weeks 2, 4, 12, 24, 48, 72, and 96. These study visits will last about 1 to 2 hours, except week 12 which will last about 4 hours. During these visits:

- You will have a physical exam, and will be asked questions about your health and about any medicines you have taken or are taking, at every visit.
- You will take neuropsychological tests at weeks 24, 48, 72, and 96.
- We will draw about 2-7 tablespoons (30-105mL) of blood for routine safety tests, to measure your viral load, and to measure your CD4+ cell count. You will be told the results of these tests when they become available. You will have routine safety tests, including liver enzyme test, at weeks 4, 12, 24, 48, 72, and 96; viral load measured at weeks 12, 24, 48, 72, and 96; and CD4+ cell count measured at weeks 12, 24, 48, 72, and 96. We will also store some of your blood for future testing at every visit.
- We will draw an additional 1 teaspoon-1 tablespoon (5-15mL) of blood for pharmacokinetic studies (PK) (to measure the amount of study drug in your blood) at weeks 12, 24, and 48. At these visits we will draw blood before you take the study drugs. At week 12 we will also draw blood 2 and 4 hours after you take the study drugs. If one of the study drugs you will be taking are taken in the evening, 3 days before the PK studies at weeks 12, 24, and 48, you will have to switch taking that study drug from the evening to the morning. The study staff will contact you before that time to remind you when to make the switch. You must also not take the study drugs in the morning on the day of the weeks 12, 24, and 48 visits, and instead bring the study drugs with you to the clinic. The study staff will give you the doses in the clinic.
- We will ask you to give a urine sample at week 96 for safety testing. You will be told the result when it is available.
- We will ask you to fill out some questionnaires at weeks 24, 48, 72, and 96 that ask you about how you are feeling, how well you are able to perform your daily activities, and your alcohol and drug use. We will also ask you to fill out a questionnaire about how well you are taking your current anti-HIV drugs at weeks 4,12, 24, 48, 72, and 96. If you are having problems taking your anti-HIV drugs correctly, a site staff member will try to help.
- If you are a woman who can become pregnant, you will have a pregnancy test at every study visit. You will be told the result of this test when it becomes available.
- If one of the study drugs you will be taking are taken in the evening, three days before the PK studies at weeks 12, 24, and 48 you will have to switch taking that study drug from the evening to the morning. The study staff will contact you before that time to remind you when to make the switch. You must also not take the study drugs in the morning on the day of the weeks 12, 24, and 48 visits and bring the study drugs with you to the clinic. The study staff will give you the doses in the clinic.
- At weeks 12, 24, 48, and 72, your study drugs will be refilled.

- At weeks 36, 60, and 84, you will return for refill of your study drugs. If you are a woman and able to become pregnant, you will also have a pregnancy test. This visit should take about 30 minutes or less.

You should inform the study doctor before changing the other anti-HIV drugs that you are taking.

Optional Lumbar Puncture

In this study, there is an optional lumbar puncture. A lumbar puncture (also called a "spinal tap") removes fluid that surrounds the brain and spinal cord. This is done by numbing a small patch of skin on your back and inserting a needle in between the bones in your lower back. You will be asked to lie in a flat position (with one or no pillows) at the clinic for up to 30 minutes after the test. You should also drink plenty of liquids and not do too much activity for up to 24 hours after the test.

The lumbar puncture will be performed to measure inflammatory markers (a measure of the body's response to infection or damage) to see if your brain is affected by HIV.

- If you agree to participate in the optional lumbar puncture study, you will have a neurological exam at study entry and week 48. The neurological exam will see if you have any nerve damage or nervous system problems and will take about 30 to 45 minutes.
- If you had abnormal bleeding or bruising in the past or the study doctor feels you may be at risk of having abnormal bleeding, you will also have about 1 teaspoon (6mL) of blood drawn to check the number of platelets (the cells in the blood that stop bleeding) in your blood and to see how long it takes your blood to clot at study entry and week 48. You will be told the results of the tests when they become available.
- If you are eligible for the lumbar puncture, you will have a lumbar puncture at study entry and week 48. About 2 to 3 teaspoons of spinal fluid will be collected for routine and study-specific tests and HIV viral load.

Virologic Failure

You will be tested for virologic failure at weeks 12, 24, 48, 72, and 96. Virologic failure is when your anti-HIV drugs are not fully suppressing HIV in the blood. If the study staff sees that your viral load has gone up, you will be asked to have another viral load test done within 30 days. About 2 teaspoons (10mL) of blood will be drawn for the viral load test. We will also draw about 4 teaspoons (20 mL) of blood that will be used for tests that check which anti-HIV drugs have stopped working on the HIV in your blood (resistance test) and if a specific type of anti-HIV drug will be able to control your HIV (tropism test) if the repeat viral load test shows that your viral load is still up. We will also ask you to fill out a questionnaire about how well you are taking your current anti-HIV drugs.

If your viral load is still up and you are still taking study drug, you will be asked to stop the study drug, and come to the clinic within 2 weeks. You will be followed on study and off study treatment until the final study visit, week 96. If you have virologic failure at week 96, you will have a confirmation of virologic failure within 30 days, and you will be off study.

After you start your study drugs, you should not stop taking any of them unless you have discussed it with the study doctor. If you do not take your study drugs or other HIV medications consistently, this may result in viral rebound, a condition in which HIV levels in your blood become detectable. This could lead to drug resistance and a chance that the study drugs, or your other HIV medications, will no longer be effective. Discontinuing HIV medications can also result in immune system decline. If your blood test shows evidence of drug resistance, you will be taken off the study drugs but will be asked to continue follow-up in the study until you complete all visits and procedures.

Although very unlikely, you could develop viral rebound or drug resistance during this study. If drug resistance develops, your choices of HIV medications in the future could be limited.

If You Have to Stop Taking the Study Drugs Early or You Have to Stop the Study Early

If you have to stop taking the study drugs early or you have to stop the study early, you will come to the clinic for an additional visit. At this visit:

- You will have a physical exam and will be asked questions about your health and about any medicines you have taken or are taking.
- You will take neuropsychological tests.
- We will draw about 1 tablespoon (15mL) of blood to measure your viral load and CD4+ cell count. We will tell you the test results of when they become available.
- We will draw about 2 tablespoons (30mL) of blood and store the blood for future study-related virologic testing.
- If you are a woman who can become pregnant, you will have a pregnancy test. We will tell you the test result when it becomes available.
- We will ask you to fill out some questionnaires to see how you are feeling, how well you are able to perform your daily activities, if you have been hospitalized recently, and how well you are taking your current anti-HIV drugs
- We will ask you to give a urine sample for safety testing. We will give you the results of this test as soon as it becomes available.

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 the AIDS Clinical Trials Group (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.

Other

Some of your blood or spinal fluid (if you have a lumbar puncture) that is 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. Storage of leftover blood or spinal fluid is not a requirement to participate in the study and you may withdraw your approval for the storage of your leftover blood or spinal fluid at any time, and your samples will be destroyed. 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

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 start breastfeeding
- your primary care physician no longer thinks that participating in the study is in your best interest
- the study is stopped or cancelled
- you are not able to attend the study visits or perform the assessments as required by the study

The study doctor may need to take you off the study drugs without your permission if:

- you become pregnant or start breastfeeding
- You decide that you want to become pregnant or actively try to get pregnant
- You do not want to use one of the required birth control methods while on the study treatment
- 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

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 Drugs, Or Once I Leave The Study, How Would They Be Provided?

During the study:

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

After the study:

After you have completed your study participation, the study will not be able to continue to provide you with the drugs you received on the study. If continuing to take these or similar drugs would be of benefit to you, the study staff will discuss how you may be able to obtain them.

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. It is very important that you tell your study doctor of any changes in your medical condition while taking part in the study. If you have questions concerning the additional study drug side effects please ask the medical staff at your site. At any time during the study, if you believe you are experiencing any of these side effects, you have the right to ask questions on possible and/or known risks.

There is a risk of serious and/or life-threatening side effects when non-study drugs are taken with the study drugs. For your safety, you must tell the study doctor or nurse about all drugs you are taking (including non-prescription drugs, vitamins and herbal supplements) before you start the study and you must ask for approval for taking any new drugs while you are on the study. You must also tell the study doctor or nurse before enrolling in any other clinical trials while on this study.

Use of Combination Antiretroviral Drugs

Immune Reconstitution Syndrome:

In some people with advanced HIV infection, symptoms from other infections or certain diseases may occur soon after starting combination anti-HIV treatment 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 antiretroviral therapy, tell your healthcare provider right away.

The use of potent antiretroviral 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

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. If this happens, people could treat you unfairly or family members, friends, and/or the community might not accept you.

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.

Risk of Spinal Tap
- Leakage of cerebrospinal fluid (CSF) into the tissues in your back, which can cause headache
- Back pain or pain where the needle is inserted in the back
- Decreased blood pressure
- CSF leak
- Infection
- Fever
- Nerve injury (very rare)
- Bleeding
- Allergic reaction to medication used to numb the area where the spinal tap will be done.
- Allergic reaction to the substance (such as iodine) that is used to clean the area of the spinal tap to prevent infection could include itching, hives, swelling, shortness of breath, difficulty breathing, changes in blood pressure and heart rhythm, loss of consciousness, or in a rare case, death.

Headaches can be helped by lying down face up and by taking over-the-counter headache medicine. Severe headaches should be reported to the study staff or study doctor.

It may be uncomfortable for you to lie on your side while the lumbar puncture is being done and to lie flat on your back for the required time afterwards.

Risks of MVC (Selzentry)
The following serious side effects have been associated with the use of MVC:

- Liver problems (liver toxicity) have occurred in people who took MVC. An allergic reaction or serious skin reaction may happen before liver problems occur. Stop taking MVC and call the study doctor or your healthcare provider right away if you get any of the following signs or symptoms:
  - Rash on your body (allergic reaction)
  - yellowing of the skin or whites of your eyes (jaundice)
  - dark urine
  - vomiting
  - stomach pain
  - elevated liver-related function test.- People who are co-infected with hepatitis B might be at higher risk of having liver problems.

- Heart problems, including heart attack.
- Low blood pressure when standing up, which can cause dizziness or fainting. People who have serious kidney problems may be at increased risk for dizziness and fainting.

In addition to the serious side effects listed above, the most common effects of MVC in adults include:
- Colds
- Cough
- Fever
- Rash
- dizziness
- diarrhea
- Swelling of parts of the body
- Flu and flu-like symptoms

- Muscle aches, spasms and pain
- Stomach pain and bloating
- Sleeping problems
- Runny, congested nose
- Problems with urination
- Low amounts of white blood cell counts (neutropenia)

NOTE: Because of how the drug works in your body, there is a possible increased risk for getting other infections or cancer, although there is no evidence from the clinical trials of an increase in serious infections or cancer.

MVC contains soy lecithin. If you have a medical history of allergy to soy (soya or soybeans) or peanuts, you may develop an allergic reaction to MVC. Before starting MVC, you should inform the study staff or study doctor if you are allergic to soy or peanuts.

Risks of DTG (Tivicay)

The following serious side effects have been associated with the use of DTG. These include allergic (hypersensitivity) reactions and liver problems, including acute hepatic failure, which may be life-threatening.

Contact the study doctor or your healthcare provider right away if you develop a rash while taking DTG, especially if it is associated with any of the symptoms listed below, which could be signs of an allergic reaction. Stop taking DTG and get medical help right away if you develop a rash with any of the following signs or symptoms:

- Fever
- General ill feeling
- Extreme tiredness
- Muscle or joint aches
- Blisters or sores in mouth
- Blisters or peeling of the skin
- Redness or swelling of the eyes
- Swelling of the mouth, face, lips, or tongue
- Problems breathing

Contact the study doctor or your healthcare provider if you have any of the following symptoms that could be signs of liver problems:

- Yellowing of the skin or whites of the eyes (jaundice)
- Dark or tea-colored urine
- Pale-colored stools or bowel movements
- Nausea or vomiting
- Loss of appetite
- Pain, aching, or tenderness on the right side below the ribs
- Changes in liver test results, more common in people with hepatitis B or C

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People with pre-existing history of depression or other psychiatric illness may be at greater risk for suicidal thoughts, or attempts, which may lead to death. If your psychiatric condition worsens, or if you develop suicidal thoughts, call your healthcare provider right away.

Other side effects of DTG include:

- Trouble sleeping
- Abnormal dreams

- Tiredness
- Headache
- Anxiety (fear, worry)
- Depression
- Abdominal pain
- Flatulence (gas in the abdomen)
- Nausea, vomiting
- Muscle and joint aches

Dolutegravir and Pregnancy:
Early results from a large study in Botswana of pregnant women showed a possible increased risk of certain types of serious birth defects involving the brain and spinal cord in babies born to women who received DTG for HIV treatment at the time of becoming pregnant or early in their pregnancy. No cases of babies born with these types of birth defects have been reported among women who started DTG later in pregnancy.

Tell your study doctor or your healthcare provider about any side effect that bothers you or that does not go away.

Are There Risks Related To Pregnancy?
Recently, some new information about DTG from another study being done in Botswana was reported. This study found that women taking DTG when they became pregnant appeared to be more likely to have babies with an abnormality called a neural tube defect than women who were taking other HIV medicines when they became pregnant. A neural tube defect is an abnormality of the spine or brain that can be severe. This abnormality can cause babies to die. Neural tube defects usually happen in about 1 out of every 1000 babies. In the Botswana study, neural tube defects were found in about 1 out of every 100 babies born to women who were taking DTG when they became pregnant. A baby's neural tube is formed in the first 4 weeks after conception. In the Botswana study, no neural tube defects were found in babies born to women who started taking DTG during pregnancy, after the neural tube had formed. The drug company and regulatory authorities and different researchers are looking into this issue to see if DTG really does cause neural tube defects. In the meantime, the U.S. FDA and other groups have recommended that women who are going to start taking DTG have a pregnancy test first. They also recommend that women use birth control to prevent pregnancy while taking DTG. HIV-infected women who are able to become pregnant are allowed to participate in this study, but they must use birth control (intrauterine device [IUD] or hormone-based contraceptive) in order to not become pregnant while in this study. If you do become pregnant while on study and taking the study drugs, you must call the study doctor right away.

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. Because of the risk involved, you must use at least one method of birth control. You must continue to use birth control for 6 weeks after stopping your medicines. You must choose one of the birth control methods listed below:

- Intrauterine device (IUD) or intrauterine system
- Hormone-based contraceptive (contraceptive subdermal implant, combined estrogen and progestogen oral contraceptive, injectable progestogen, contraceptive vaginal ring, and percutaneous contraceptive patches)

If you do not want to use one of the birth control methods listed above, you will be taken off the study treatment, but asked to continue the study evaluations.

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. Women who can become pregnant will have testing for pregnancy at every study visit. If you think you may be pregnant at any time during the study, tell your study staff right away. If you decide at any time while you are in this study that you want to become pregnant and start trying to become pregnant, you must tell your study staff right away. If you are pregnant or trying to become pregnant, you will be taken off the study treatment, but asked to continue the study evaluations. The study staff will talk to you about your choices.

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.

NOTE: It is not known whether the study drug passes through breast-milk and may cause harm to your baby. If you are breastfeeding, you cannot take part in this study.

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 prescription drugs available to you
- treatment with experimental drugs, if you qualify
- no treatment

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

What About Confidentiality?

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 obtained 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, U.S. Office for Human Research Protections (OHRP), U.S. Food and Drug Administration (FDA), or other local, U.S. and international regulatory entities as part of their duties, University of Pennsylvania institutional review board (IRB), National Institutes of Health (NIH), , study staff, study monitors, the drug company supporting this study and its 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 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.

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 study visit, by law we have to report the result 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. In addition if syphilis or Hepatitis tests are positive, they will be reported to the local department of health.

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
- 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 office that support research operations.

Who, outside 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 keyed directly into a central, password protected database. 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.
- ViiV Healthcare Ltd: The pharmaceutical company that is supplying the drugs 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
- Food and Drug Administration

Once your personal health information is disclosed to others outside of 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 my 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.

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 the study drugs, Selzentry or Tivacay or placebo, study-related visits, physical examinations, required laboratory tests or other procedures. This study will not provide you with antiretroviral drugs. When the study is over, Selzentry and Tivicay will no longer be provided, if you or your provider wants to continue these medications, you/your insurance company would be responsible for the costs. You, your insurance company, or your health care system may need to assume the cost of drugs not provided by the study. 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 attended (screen, pre-entry, entry and weeks 2, 4, 12, 24, 48, 72 and 96. If you elect to have the lumbar puncture performed (at Entry and week 48), you will be compensated $200 for each procedure. Compensation will be given on a Clincard at the completion of each study visit. The maximum amount of compensation for the study is $500 if all study required visits are completed and attended. If both LP procedures are done, then the maximum will be $900. If you are required to come to the clinic for any additional visits, you will be compensated $35. 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 Participant?

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 participant, contact:

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

CONSENT

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

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.

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** 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.

Your permissions and signature

Optional LP

On page 5 of this form, we told you about an optional LP (lumbar puncture) procedure to be performed by Dr. Kolson. Please write your initials or make your mark in the boxes next to the option you choose.

☐ I agree to have a lumbar puncture performed.

☐ I do not agree to have a lumbar puncture performed.

Tests on Leftover Samples

On page 6 of this form we told you about storing your leftover blood or spinal fluid (with no information that will identify you) and using it for future ACTG-approved research. These samples may be stored for an indefinite period of time. Results of testing done on these samples may not be given to you because they will be done in the future. Please write your initials or make your mark in the box next to the option you choose.

☐ I allow my leftover samples to be stored and used for other studies related to HIV.

OR

☐ I do not allow my leftover samples to be used in any other studies.

If you agree to join this study, you will need to sign below. Before you sign this consent form, make sure of the following:

- You have read this consent form, or someone has read it to you.
- You feel that you understand what the study is about and what will happen to you if you join. You understand what the possible risks and benefits are.
- You have had your questions answered and know that you can ask more.
- You agree to join this study.

You will not be giving up any of your rights by signing this consent form.

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

IRB APPROVAL FROM:
11/06/2018 TO: 11/05/2019

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:
11/06/2018 TO: 11/05/2019