SUBJECT INFORMATION AND INFORMED CONSENT FORM AND AUTHORIZATION TO DISCLOSE HEATLH INFORMATION

Title:	A Phase III Multicenter,Double-Blind,Randomized,Active Comparator-Controlled Clinical Trial to Evaluate the Safety and Efficacy of MK-1439A Once-Daily Versus ATRIPLA™ Once-Daily in Treatment-Naïve HIV-1 Infected Subjects
Study Name:	
Protocol No:	**MK-1439A-021**
Study Sponsor:	**Merck Sharp & Dohme Corp., (a subsidiary of Merck & Co. Inc.)**
Study Doctor:	Pablo Tebas, MD (215) 662-6059 (Immunodeficiency Program Doctor On Call) - 24-hour number (215) 349-8092 - office number

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You are being invited to take part in a research study. This consent document has information to help you decide if you want to participate. Take your time, read this document carefully, and ask the study doctor or staff any questions you may have. You should not sign this document until you understand all of the information presented in the following pages and until all of your questions about the research have been answered to your satisfaction.

If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by participating in this study.

The study doctor [or institution] will be paid by the Sponsor, Merck Sharp & Dohme Corp., for conducting this study.

The study has been approved by Schulman Institutional Review Board. Schulman Institutional Review Board is an independent committee established to help protect the rights of research subjects.

About This Study

You are being asked to participate in this research study because you have HIV that has not been treated before.

The purpose of this study is to:

- test the safety of the research study drug, MK1439A
- Evaluate the safety, tolerability and efficacy of MK-1439A q.d. compared to ATRIPLA ™

This is a research study to test an investigational drug (MK-1439A) that has not been approved by the United States Food and Drug Administration (FDA) for sale and the comparator study drug, ATRIPLA™ which is a drug that is available by prescription. There may be reasons why you are not allowed to take part in this study. Some of these reasons include:

- You are less than 18 years of age.
- You are not HIV-1 positive.
- You have a history or current evidence of a condition that might confound the results of the study or interfere with your participation for the full duration of the study.
- You are a current user of recreational or illicit drugs or have had a recent history of drug or alcohol abuse or dependence. Talk to the study doctor if you have a history of drug or alcohol use.
- You have been treated for a viral infection other than HIV-1 such as hepatitis B, with an agent that is active against HIV-1, including, but not limited to, adefovir, tenofovir, entecavir, emtricitabine or lamivudine.
- You have had documented or known resistance to study drugs including MK-1439, efavirenz, emtricitabine, lamivudine, and/or tenofovir.
- You have participated in a study with an investigational compound/device within 30 days prior to signing the informed consent or anticipate participating in such a study involving an investigational compound/device during the course of this study.
- You have used certain immune suppressing drugs within 30 days prior to treatment in this study or it is anticipated that you will need them during the course of the study. Note: Short courses of corticosteroids (a drug that is like a hormone produced by your body) will be allowed if needed to treat diseases such as asthma.
- You have a current (active) diagnosis of acute hepatitis.
- You have advanced liver disease as determined by your doctor.
- You are a female who is pregnant, breastfeeding, expecting to conceive, or expecting to donate eggs (at any time during the study, from the beginning of the study through 12 weeks following the last dose of study drug) or are a male who is expecting to donate sperm (at any time during the study, from the beginning of the study through 12 weeks following the last dose of study drug).
- You are or have an immediate family member (e.g., spouse, parent/legal guardian, sibling or child) who is investigational site or sponsor staff directly involved with this trial.

The study doctor or staff will discuss these and any other reasons why you may not be allowed to enter the study.

About 680 people will be in the study. You will be in the study about 104 weeks. This study will use competitive enrollment. This means that when a target number of subjects has entered the treatment phase of the study, all further enrollment will be closed. Therefore, it is possible that you could be in the screening phase, ready to enter the treatment phase, and be discontinued without your consent if the target number of subjects has already entered the treatment phase of the study.

What will I be asked to do?

If you take part in the study, you will need to do the following:

- Visit the study doctor about 13 times
- Discuss with the doctor your medical history.
- Complete a Study Medication Diary daily at home and an electronic questionnaire at the clinic during some of your visits.
- Tell your study doctor about any illnesses or other problems you have during the time you are in the study.
- Tell your study doctor about any medicines you take while you are in the study, including medicines you take with or without a doctor's prescription such as vitamins, herbal supplements, or aspirin.
- Fast (nothing to eat or drink) for at least 8 hours prior to Visit 2 (Day 1), Visit 6 (Week 24), Visit 8 (Week 48), and Visit 12 (Week 96). In addition, you will stay at the study site (approximately 2 hours) at Visit 6 (Week 24) and Visit 8 (Week 48). At these 2 visits, two blood samples will be collected, pre-dose and 30 minutes to 2 hours postdose (you will remain fasting until the second blood sample has been collected).
- Keep a card with you that will let any doctor you see know that you are in a study, so they can find out what the study is about.
- Take study drug(s) as instructed:
    - All study drugs will be taken once daily. The study drugs will be provided as tablets packed in bottles (labeled as Bottle A and Bottle B). You will be assigned to take tablets from bottles (A and B) each day. You will start to take your study drug on the day of randomization and will take one tablet, once a day from each of your assigned bottles during the study treatment period. One tablet from Bottle A (MK-1439A or matching placebo [a look-alike pill with no active ingredients, sometimes called a sugar pill]) will be taken once daily without regard to food at approximately the same time each day. One tablet from Bottle B (ATRIPLA™ or matching placebo) will be taken once daily at bedtime on an empty stomach.
    - Store study drug as instructed.
    - Write down when you take your study drug on the patient diary card given to you. Bring the diary card and all study drug containers with you to each study visit.

You will be assigned by chance to get either MK-1439 100 mg (with a placebo that matches ATRIPLA™) or ATRIPLA™ (with a placebo that matches MK-1439). You have a 50% chance of getting MK-1439A and a 50% chance of getting ATRIPLA™. The matching placebos are included in this study to make sure that your assigned treatment (MK-1439 or ATRIPLA™) remains blinded. Blinded means that neither you nor the study doctor will know which of the two study medications you are receiving. In case of an emergency, the study doctor can get this information.

If your blood tests show that you have liver lab results that are not normal, the study doctor or staff will ask you to provide additional samples of blood for testing to find out why your liver lab results are not normal. If you do decide to provide the samples, the study staff will discuss with you the amount of the additional samples of blood that will be taken and the tests that will be performed on the blood.

The tests that may be performed include HIV and viral hepatitis tests to find out if HIV or hepatitis is the reason your liver lab results are not normal. Depending on the region where you live, you may need to sign another consent form to have these tests done.

The results of all of your blood tests, just like all other laboratory test results, will be provided to the Sponsor. Positive HIV and viral hepatitis test results may be reportable to local health authorities according to local laws.

It is your decision whether to provide the additional samples and have these tests performed. However, if you decide not to provide the additional samples and have the tests done, you may need to leave the study for your own safety (as the cause of your abnormal liver lab results may not be able to be determined without them).

What will happen during the study visits?

When you come in for your study visits, the study doctor or staff may do any or all of the following to test whether the study drug is working and/or to monitor your health:

- Give you a Subject Identification Card.
- Dispense study drug and instructions.
- Review your medical and medication history.
- Perform a physical examination.
- Check your vital signs (including blood pressure, heart rate, temperature).
- Check if you have or have had any serious side effects.
- Perform an electrocardiogram (ECG) – to measure the electrical activity in your heart.
- Confirm if you (or your partner) are using appropriate acceptable methods of birth control.
- To test for hepatitis B and C. Positive hepatitis B and C test results may be reportable to local health authorities according to local laws.

Your personal information may be given out if required by law. If you test positive for HIV, Hepatitis B or Hepatitis C, by law we have to report the infection to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born. This is to keep track of how many people in the U.S. have HIV infection. It is also to make sure that states get enough money from the federal government to support the medical care of people living with HIV. The Health Department does not share the names of HIV infected people with anyone else. It removes all personal identifiers, such as your name, before giving information on the number of HIV infections to the federal government. Please note that it is likely that this information has been already reported to the PA Health Department as the HIV test being done for this study is not the first test for you.

- Collect blood and urine samples:
  - To test the amount of virus that is in the body.
  - To perform routine safety tests.
  - To perform a pregnancy test.
  - To measure the amount of study drug in your body. This process is known as pharmacokinetics (PK).
- A blood sample will be collected for planned genetic research. Your blood and tissue samples contain genes, which are made up of DNA (deoxyribonucleic acid) and which serve as the "instruction book" for the cells that make up our bodies. Genetic research is the study of DNA variation. Variation in your DNA can affect the way you respond to drug treatments. The Sponsor will look at variation in your DNA. Your DNA will be used to understand how genetics affect response to the treatment(s) administered. Your genetic information will be analyzed together with the clinical data collected in this study. Your blood sample may also be used to help develop new tests. The results are for research use only.
- You will also be asked to take part in optional future biomedical research. You will be asked to read and sign a separate informed consent that describes the optional future biomedical research.

What effects could the tests have on me?

You may feel discomfort during some of these tests or may experience some inconveniences. Some may also have risks, which may include:

- Blood samples: drawing blood from your arm may cause pain, bruising, bleeding, lightheadedness, and rarely, fainting or infection.
- The electrocardiogram (ECG) procedure may cause minimal discomforts during the attachment and removal of the ECG leads to and from the skin.
- Fasting for 8 hours could cause dizziness, headache, stomach discomfort or fainting.

About The Study Drug(s)

ATRIPLA™ is made by Bristol-Myers Squibb & Gilead Sciences, LLC and not by the Sponsor. The matching placebo for ATRIPLA™ is made by the Sponsor, according to laws about clinical testing, to look like ATRIPLA™. Neither the matching placebo nor this study is sponsored by, approved by, or affiliated with Bristol-Myers Squibb & Gilead Sciences, LLC.

MK-1439A

MK-1439A is being studied by the Sponsor to treat HIV-1 infection. MK-1439A is a single tablet made from 3 different drugs. The drugs that are in MK-1439A are MK-1439 (doravirine), lamivudine and tenofovir disoproxil fumarate. Lamivudine and tenofovir disoproxil fumarate have been approved to treat HIV-1 infection; MK-1439 (doravirine) is being studied by the Sponsor.

MK-1439A has been given to about 364 HIV-1 infected patients as a single dose of 100 mg doravirine/300 mg lamivudine/300 mg tenofovir disoproxil fumarate.

MK-1439

MK-1439 is being studied by Merck & Co., Inc. to see if it has any effect in treating HIV-1.

MK-1439 has been given as:

- Single doses up to 1200 mg and multiple daily doses up to 750 mg for 10 days and up to 100 mg for 17 days to about 284 healthy men.
- Single doses up to 100 mg to 162 healthy women, 12 healthy elderly women, 12 healthy elderly men, 6 men and 2 women with moderate hepatic impairment.
- Multiple doses up to 200 mg once daily for 7 days without other approved HIV medications to 12 young HIV-1 infected men.
- Multiple doses up to 200 mg once daily in combination with other approved HIV medications (combination therapy) to about 214 male and 18 female HIV-1 infected patients who have never taken HIV drugs before. This study is ongoing. So far, the longest period a patient has taken MK-1439 in this study is about 24 months. In this study, patients will take MK-1439 for up to two years.

Lamivudine

Lamivudine is an approved medication available by prescription. It is used to treat HIV-1.

Tenofovir

Tenofovir disoproxil fumarate is an approved medication available by prescription. It is used to treat HIV-1 and hepatitis B virus (HBV) infection.

ATRIPLA™

ATRIPLATM is an approved drug available by prescription in the United States and most major markets. ATRIPLATM is available as a solid oral tablet. It is used to treat HIV-1.

ATRIPLA™ contains 3 medicines, SUSTIVA® (efavirenz), EMTRIVA® (emtricitabine) and VIREAD® (tenofovir disoproxil fumarate also called tenofovir DF) combined in one pill. ATRIPLA™ can be used alone as a complete regimen, or in combination with other anti-HIV-1 medicines to treat people with HIV-1 infection. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

What side effects could the study drug(s) cause?

MK1439A

The following side effects were reported in 2% or more ofHIV-1 infected subjects participating in a study of MK-1439A, and the study doctor believes they may have been caused by MK-1439A:

- Abnormal Dreams
- Difficulty Falling asleep/staying asleep
- Nausea
- Diarrhea
- Fatigue
- Nightmare
- Dizziness
- Headache
- Sleepiness

The majority of side effects reported were mild or moderate in intensity.

MK1439

The following side effects have been reported in 2% or more of healthy men and women who were in studies of MK-1439:

- Dizziness/Dizziness with change in position
- Fever
- Nausea and stomach pain/discomfort
- Back Pain
- Drowsiness
- Headache/migraine
- Stuffy, runny or uncomfortable nose
- Diarrhea/ loose stools
- Fatigue
- Muscle or joint pain/stiffness

The following side effects have been reported more than once by HIV-infected men who were in a study of MK-1439 given alone for 7 days:

- Headache
- Nausea
- Diarrhea

The side effects seen with MK-1439 in healthy people or in HIV-infected men who were given MK-1439 alone were generally mild in intensity and did not last long.

Side effects rated as moderate in intensity were:

- One event of dizziness
- One event of knee pain
- One event of fatigue
- Two events of headache
- One event of inflamed small intestine
- One event of diarrhea
- One event of vomiting
- One event of hot flush
- Two events of change in a blood test that may show liver damage
- One event of high blood sugar

The following side effect was rated as severe in intensity:

- One person briefly fainted. The study doctor did not think this was related to MK-1439.
- One person for a brief time was feeling faint. The study doctor did not think this was related to MK 1439.

The following two side effects were serious:

- One person had changes in blood tests that may show liver damage. The study doctor thought the blood test changes were likely caused by a hepatitis virus infection which the person got before taking MK-1439.
- One person had sarcoidosis (inflammation of lymph nodes, lungs, liver, eyes, skin, or other tissues). The study doctor did not think this was related to MK-1439.The following side effects were considered related to MK-1439 and occurred in 2% or more of subjects when MK-1439 was given as:
- Doses ranging from 25 mg to 200 mg once daily in combination with other approved HIV medications for up to 96 continuous weeks in 115 HIV-1 infected men and 9 HIV-1 infected women.

- A dose of 100 mg once daily in combination with other approved HIV medications for up to 48 continuous weeks in 99 HIV-1 infected men and 9 HIV-1infected women.
  - Abnormal dreams
  - Diarrhea/loose stools
  - Dizziness
  - Difficulty falling and/or staying asleep
  - Headache
  - Nausea
  - Sleep Disorder
  - Nightmare
  - Tiredness

Most of these side effects were mild to moderate in intensity and short lived except for one report of difficulty falling asleep that was considered severe.

Four patients stopped the drug because of a side effect considered to be related to MK-1439 when given with other antiretroviral drugs:

- 1 due to weakness
- 1 due to epigastralgias (pain in the upper part of abdomen), insomnia (difficult falling or staying asleep), and nausea
- 1 due to a sleep disorder (disruption in sleep)
- 1 due to hallucinations

<u>Lamivudine</u>

The following serious side effects have been reported in some patients that were given Lamivudine:

- Inflammation of the pancreas
- Increased acid in the blood: symptoms may include feeling very weak or tired, unusual muscle pain, trouble breathing, stomach pain with nausea or vomiting, feeling cold (especially in your arms and legs), feeling dizzy or lightheaded, and having a fast or irregular heartbeat
- Worsening of hepatitis B (for patients that already have hepatitis B), if you stop taking Lamivudine
- Enlarged liver with changes in fat distribution in liver cells
- Changes in location and amount of body fat
- Changes in your immune system (Immune Reconstitution Syndrome) can happen when you start taking HIV medications. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time
- Bone problems, which may include bone pain or softening or thinning of bones (which may lead to fractures)

The following common side effects have been seen in people who have taken Lamivudine:

- Cough
- Diarrhea
- Difficulty falling and/or staying asleep
- Fever
- General feeling of being unwell
- Hair loss
- Headache
- Lack of energy
- Muscle and joint aches and pain
- Nasal symptoms, including irritation, running nose, and congestion
- Nausea
- Rash
- Stomach pain/cramps
- Vomiting

The following less common side effects have been seen in people who have taken Lamivudine:

- Body produces insulin (a hormone that lowers the level of sugar in your blood) but does not use it effectively
- Breakdown of muscle cells that cause kidney problems
- Chills
- Decrease in the number of cells in the blood that fight infection
- Decrease in the number of cells involved in blood clotting
- Depression
- Dizziness
- Failure to produce or decrease in the number of cells in the blood that carry oxygen
- Hepatitis

- High blood sugar levels
- Increase in liver tests which may be a sign of liver problems
- Increase in the amount of fat in the blood
- Increased cholesterol
- Indigestion
- Inflammation of the pancreas, which could result in abdominal pain and discomfort and could require hospitalization and intravenous treatment
- Lack of or decreased appetite
- Nerve changes that may result in numbness, pain or weakness. Tingling or numbness of the arms, legs, hands and feet.
- Serious, potentially life threatening allergic reaction
- Swollen Skin

The following side effects have been seen in people who have taken Lamivudine but who were not in studies:

- Hives
- Itching
- Weakness

<u>Tenofovir</u>

The most common side effects seen in people who have taken Tenofovir:

- Rash
- Diarrhea
- Headache
- Itchy skin
- Stomach pain
- Depression
- Pain
- Vomiting
- Weakness
- Dizziness
- Nausea
- Difficulty falling and/or staying asleep
- Stomach bloating
- Fever

Serious side effects that may be life threatening that have been seen in some patients taking Tenofovir include:

- Liver problems: symptoms may include your skin or the white parts of your eyes turning yellow, dark urine, light colored stool, loss of appetite for several days or longer, nausea and stomach pain.
- Increased acid in the blood: symptoms may include feeling very weak or tired, unusual muscle pain, trouble breathing, stomach pain with nausea or vomiting, feeling cold (especially in your arms and legs), feeling dizzy or lightheaded, and having a fast or irregular heartbeat.
- New or worsened kidney problems, including kidney failure.
- Bone problems, which may include bone pain or softening or thinning of bones (which may lead to fractures).
- Changes in your body's ability to fight infection.

Less common side effects seen in patients taking Tenofovir include:

- Back or chest pain
- Joint pain
- Muscle aches
- Nerve changes that may result in numbness, pain or weakness
- Anxiety
- Lack of energy
- Sinus infection
- Upper respiratory tract infection
- Common cold
- Pneumonia
- Upset stomach
- Sweating
- Weight loss
- Changes in the location and amount of fat throughout the body
- Increased gas
- Loss of desire to eat

The following additional side effects have been seen in people who have taken Tenofovir but were not in studies:

- Low levels of potassium in the blood, which can cause muscle cramps or an irregular heart beat
- Allergic reaction (may include rash, hives, swelling, trouble breathing)
- Breakdown of muscle cells that cause kidney problems

- Low phosphate levels, which may cause muscle weakness or breakdown, bone pain and confusion
- Muscle weakness
- Abnormal kidney function causing a loss of fluids
- Inflammation of the pancreas, a gland in the abdomen that produces insulin and substances that help food be digested
- Shortness of breath
- Excess protein in the urine
- Changes in blood test that may show damage to the pancreas, a gland in the abdomen that produces insulin and substances that help food be digested
- Increased urination

ATRIPLA™

Most frequent side effects:

- Change in blood tests that may show muscle damage
- Decreased phosphate in blood
- Diarrhea
- Dizziness
- Feeling Weak
- Headache
- Nausea
- Rash
- Vomiting
- Depression
- Difficulty sleeping
- Abnormal dreams

Other possible common side effects:

- Tiredness
- Allergic reactions
- Changes in tests that may show problem with pancreas
- Difficulty concentrating
- Stomach pain
- Disturbances of coordination and balance

- Drowsiness
- Feeling bloated
- Skin discoloration
- Gas
- Increased fat in blood
- Itching
- Loss of appetite
- Low white blood cell counts
- Pain
- Problem with digestion

Other uncommon side effects:

- Angry behavior
- Blurred vision
- Breakdown in muscle
- Breast enlargement in males
- Chills
- Confusion
- Decrease in potassium (salt in the body)
- Decreased sex drive
- Diminished sensibility
- Dry mouth
- Feeling of spinning or tilting
- Flushing
- Forgetfulness
- Hallucinations
- Incoherent speech
- Increase in cholesterol
- Increase in creatinine, a substance that shows how well your kidneys are working
- Increased appetite
- Low red blood cell count
- Misbelief
- Mood affected
- Muscle pain or weakness
- Paranoia
- Personality change
- Protein in urine
- Ringing in ears
- Seizure
- Strange thoughts
- Suicidal thoughts
- Suicide or suicide attempts
- Swelling of face, lips, tongue or throat
- Tremor
- Yellow eyes (jaundice)
- Loss of memory

The following side effects are rare:

- Abnormal vision
- Change in body fat
- Dark urine
- Fatty liver
- Feeling cold in extremities
- High volume of urine
- Irregular heartbeat
- Itchy rash, reaction to sunlight
- Kidney failure
- Light color stool
- Light headedness
- Palpitations
- Thinning or softening of bones
- Thirst
- Trouble breathing
- Disturbance of motor behavior

Other important side effects and information for patients taking ATRIPLA™:

- QT prolongation has been seen with the use of efavirenz. Efavirenz is one of the medicines in ALTRIPLA. QT prolongation is a disruption in the electrical activity of the heart.
- Lactic Acidosis - Some HIV medicines, like ATRIPLA™, can cause a rare but serious condition called lactic acidosis with liver enlargement. Nausea and tiredness that don't get better may be symptoms of lactic acidosis. In some cases, this condition can cause death. Women, overweight people, and people who have taken HIV medicines for a long time have a higher chance of getting lactic acidosis and liver enlargement. Lactic acidosis is a medical emergency and must be treated in the hospital.
- Severe hypersensitivity or life-threatening skin reactions or rash (including Stevens-Johnson syndrome and erythema multiforme) - Sometimes these skin reactions and skin rashes can become severe and require treatment in a hospital. Symptoms of a severe allergic reaction could include: trouble breathing, wheezing, dizziness or fainting, throat tightness or hoarseness, fast heartbeat or pounding in your chest (tachycardia), sweating, swelling of your face, lips or tongue, muscle or joint pain, blisters or skin lesions, mouth sores or ulcers.
- Severe skin reactions such as Stevens-Johnson syndrome and erythema multiforme; neuropsychiatric adverse reactions (including severe depression, death by suicide, psychosis-like behavior, seizures, severe hepatic events, inflammation of pancreas and lactic acidosis (sometimes fatal) have been reported.
- Changes in body fat can happen in people who take antiretroviral therapy. The changes may include an increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the back, chest, and stomach area. Loss of fat from the legs, arms, and face may also happen. The exact cause and long-term health effects of these conditions are not known.
- Changes in immune system (Immune Reconstitution Syndrome) can happen when you start taking HIV medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time.

- Liver problems which may be life-threatening - Slight increases in liver function tests have been reported. The increases in liver function tests usually resolved when medication was stopped, and in some cases the levels resolved without stopping. These increases rarely required permanently stopping the medication. Rarely, more severe liver reactions (including cases that have resulted in death) have been reported in patients with serious underlying medical conditions (for example, hepatitis infection).
- Convulsions have been observed in patients receiving efavirenz, generally in the presence of known medical history of seizures.
- Patients with liver disease including chronic hepatitis B or C, who are treated with combination antiretrovirals, have a higher risk of severe and potentially life-threatening liver problems. Your doctor may conduct blood tests in order to check how well your liver is working or may switch you to another medicine.
- If you have hepatitis B infection, your doctor will carefully consider the best treatment regimen for you. Tenofovir disoproxil and emtricitabine, two of the active substances in ATRIPLA™, show some activity against hepatitis B virus although emtricitabine is not approved for the treatment of hepatitis B infection. Symptoms of your hepatitis may become worse after discontinuation of ATRIPLA™.
- Diabetes and high blood sugar (hyperglycemia) - Some people who take combination HIV medicines including ATRIPLA™ can get high blood sugar, develop diabetes, or your diabetes can get worse.
- Women should not become pregnant while taking ATRIPLA™ and for 12 weeks after stopping it. Serious birth defects have been seen in the babies of animals and women treated with efavirenz (a component of ATRIPLA™) during pregnancy. It is not known whether efavirenz caused these defects. Tell your healthcare provider right away if you are pregnant. Also talk with your healthcare provider if you want to become pregnant.
- Women should not rely only on hormone-based birth control, such as pills, injections, or implants, because ATRIPLA™ may make these contraceptives ineffective. Women must use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control. Efavirenz, a component of ATRIPLA™, may remain in your blood for a time after therapy is stopped. Therefore, you should continue to use contraceptive measures for 12 weeks after you stop taking ATRIPLA™.

Are there any other risks?

Other less common side effects have been reported with the use of the drugs in this study. The study doctor or staff can discuss these with you.

Are there any risks that are not known?

There may be other side effects or risks that are not known at this time when the study drug is taken by itself or with other drugs. Any drug could cause you to have an allergic reaction that could become life-threatening if not treated promptly.

Are there pregnancy risks?

It is not known if the study drug(s) may affect an unborn or nursing baby. If you are pregnant, trying to become pregnant or breast-feeding, you may not be in the study. The study doctor will perform a blood and/or urine pregnancy test before the start of and during the study, if you are able to have a baby.

If you are able to have a baby, and not willing to remain truly abstinent (no sexual intercourse) you must use a reliable birth control method from the beginning of the study through 12 weeks following the last dose of study drug (even though your participation in the study will end after 14 days following the last dose of study drug). You must also agree to not donate eggs from the beginning of the study through 12 weeks following the last dose of study drug (even though your participation in the study will end after 14 days following the last dose of study drug).

The following birth control methods are allowed during the study:

Single method (one of the following is acceptable):

- intrauterine device (IUD)
- vasectomy of a female subject's male partner

Combination method (requires use of two of the following):

- diaphragm with spermicide (cannot be used in conjunction with cervical cap/spermicide)
- cervical cap with spermicide (only for females that have not birthed a child)
- contraceptive sponge (only for females that have not birthed a child)
- male condom or female condom (cannot be used together)
- hormonal contraceptive: oral contraceptive pill (estrogen/progestin pill or progestin-only pill), contraceptive skin patch, vaginal contraceptive ring, or subcutaneous contraceptive injection, contraceptive rod implanted into the skin.

You will need to follow your doctor's instructions regarding use of contraceptives after completion of the study. Your doctor may ask you to continue to use contraceptives for 12 weeks after the last study dose.

Use of barrier methods of contraception is strongly encouraged to reduce the risk of HIV-1 transmission during sexual contact.

If you become pregnant during the study you must notify the study doctor right away. The study drug will be stopped and you ***will*** be taken out of the study.

There may be risks if you are male and your partner is pregnant or trying to become pregnant. If you are male and your partner is able to become pregnant, you and your partner must use a reliable birth control method from the beginning of the study through 12 weeks following the last dose of study drug (even though your participation in the study will end after 14 days following the last dose of study drug). The following birth control methods are allowed during the study:

Single method (one of the following is acceptable):

- intrauterine device (IUD)
- vasectomy

Combination method (requires use of two of the following):

- diaphragm with spermicide (cannot be used in conjunction with cervical cap/spermicide)
- cervical cap with spermicide (only for females that have not birthed a child)
- contraceptive sponge (only for females that have not birthed a child)
- male condom or female condom (cannot be used together)
- hormonal contraceptive: oral contraceptive pill (estrogen/progestin pill or progestin-only pill), contraceptive skin patch, vaginal contraceptive ring, or subcutaneous contraceptive injection, contraceptive rod implanted into the skin.

Use of barrier methods of contraception is strongly encouraged to reduce the risk of HIV-1 transmission during sexual contact.

If your partner becomes pregnant during the study you must notify the study doctor right away. <u>You must also agree to not donate sperm from the beginning of the study through 12 weeks following the last dose of study drug (even though your participation in the study will end after 14 days following the last dose of study drug).</u>

Additional Information You Need to Know

Will I be told if new information is discovered during the study?

You will be told in a timely manner about significant new information that might affect your decision to stay in the study.

If I am injured from the study drug, who will pay the doctor and hospital bills?

If you are injured as a direct result of the study drug or a procedure required by the study plan, the study sponsor will pay the reasonable (customary treatment) costs of medical treatment.

The sponsor will determine if the injury is caused by the study drug and the reasonableness of the expenses taking into consideration the study doctor's evaluation, other physicians' evaluations of the subject, sponsor's experience with the study drug and other relevant factors.

The study sponsor or the University of Pennsylvania has no plans to provide any other form of compensation. You will not lose any of your legal rights or release the Sponsor, the study doctor, the study staff, or study site from liability for mistakes or intentional misconduct by signing this consent document.

If you are injured during this study, your study doctor will discuss with you the available medical treatment options.

What benefits could there be from taking part in the study?

If the study drug works, you may have some benefit. If the study drug does not work or if you are on placebo, you may not benefit. Information learned from the study may help other people in the future.

Will I be paid?

You will receive a payment of $50 dollars per visit to help cover the cost of travel and expenses (which may include such things as parking, baby-sitting, time off from work, meals, etc.). If all study required visits are completed, the total compensation for the study will be $650. As part of this study you will be given the option to receive a ClinCard (similar to a debit card). If you choose to receive the ClinCard, you will be given a separate consent to describe the program.

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

Will there be any charge for me to be in this study?

Some of the tests or treatments used in this study may be part of your routine medical care used to maintain your health even if you did not take part in this study. You or your insurance company may be billed for the cost of this routine medical care.

What are my options if I am not in the study?

You do not have to be in this study to receive treatment for your HIV infection. If you should decide not to participate in, or if you withdraw from this study, your options include:

- Alternative treatments for HIV infection include combinations of several medications given either as separate pills or in combination tablets. Typical treatments include 2 drugs from the nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) class and a drug from the non-nucleoside reverse transcriptase inhibitor (NNRTI), the protease inhibitor (PI) or the integrase inhibitor (InSTI) class. Your doctor will prescribe the best option according to the medications that are available, taking into account your personal condition and the treatment recommendations in your country.

If you have questions about alternate treatments and their potential benefits and risks, ask the study doctor for additional information.

The study doctor will discuss the risks and benefits of these options with you.

Who will be able to see my records and know that I am in the study?

Information from this study will be given to the sponsor. It will also be given to the U.S. Food and Drug Administration (FDA). Unless otherwise required by law, medical records which identify you and the consent document signed by you may be looked at and/or copied for research or regulatory purposes by:

- the study doctor and staff;
- the study sponsor;
- those working for or with the sponsor;
- the institutional review board; and
- government agencies in other countries where the study drug may be considered for approval

Because of the need to release information, complete confidentiality cannot be promised. The study results may be published in medical journals or presented at medical meetings, but your identity will not be revealed.

A more detailed explanation of how health information about you will be used and shared is included in a separate document called an Authorization**.** If you decide not to sign the Authorization you will not be permitted to participate in the study.

The authorization part of the consent gives more detailed information about how your personal health information may be used and disclosed by the University of Pennsylvania Health System (UPHS), the School of Medicine and the individual Principal Investigator, subject to University of Pennsylvania procedures.

What personal health information is collected and used in this study and might also be disclosed?

The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Name, address, telephone number, date of birth
- Social Security Number (if you receive more than $600 for participating in studies at PENN, we will need your SSN for the W-9)
- Personal and family medical history
- Current and past medications or therapies
- Results of physical exams, laboratory tests and procedures you will undergo during this research study

Why is your personal contact and health information being used?

Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study. In some situations, your personal health information might be used to help guide your medical treatment.

Which of our personnel may use or disclose your personal health information?

The following individuals may use or disclose your personal health information for this research study:

The Principal Investigator and the Investigator's study team

Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).

Who, outside of UPHS and the School of Medicine, might receive your personal health information?

As part of the study, the Principal Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

Individuals or organizations responsible for administering the study:

- Pharmaceutical sponsor (Merck Sharp & Dohme Corp): This is the company that supplies drugs for the study. Information regarding safety and adverse effects needs to be collected and monitored.

- Contract Research Organization: Monitors will visit the site on a regular basis to review data and assure accuracy and completeness of information before the data are analyzed.

Regulatory and safety oversight organizations

The Food and Drug Administration and regulatory agencies in other countries

The Office of Human Research Protections

The Study Monitoring Committee

Schulman Institutional Review Board

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations. Data are reported to the sponsor on Case Report Forms that identify you by your unique study number and not your name or medical record number. Information regarding your health, such as side effects of the study medications you experience will be reported only by code number. All samples collected for analysis will be labeled with your study number, visit number and date of your visit.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may UPHS and the School of Medicine be able to use or disclose your personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research repository (database). However, UPHS and the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so
- The University of Pennsylvania's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted by law

Will you be able to access your records?

You will be able to access some or all of your medical records after the study is over. The Principal Investigator is not required to release research information to you that is not part of your medical record.

Can you change your mind?

Yes, at any time you may withdraw your approval to allow the use and disclosure of your personal health information as described here. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study.

If you withdraw your permission to use any blood or tissue obtained for the study, the Sponsor may need to retain and use any samples that have already been collected to comply with its legal obligations and to maintain the scientific integrity of the study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. You will also be given the UPHS and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your personal health information.

WHAT IS AN ELECTRONIC MEDICAL RECORD?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

Will information about this research study be included in a Registry Databank?

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

Who do I call if I have questions about…

- The study: the study doctor at the telephone number listed on page 1 of this consent document.
- A study-related injury: the study doctor at the telephone number listed on page 1 of this consent document. If you go to the hospital or emergency room, tell the hospital doctor that you are taking part in a research study.
- My rights as a research subject or complaints about the study: Schulman Institutional Review Board at 1-888-557-2472 during business hours Monday – Friday 8:00 a.m. to 6:00 p.m. EST. You may write to Schulman Institutional Review Board at 4445 Lake Forest Drive, Suite 300, Cincinnati, Ohio 45242.

Can I refuse to be in the study and can I be asked to leave the study?

Your decision to participate in this study is voluntary. You may choose not to participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care.

If you decide to stop taking the study drug, please contact the study doctor.

If at some point you consider withdrawing from the study, you can decide if you are willing to continue to provide information or not. This would be helpful for the purposes of the study. To help you decide, the study doctor/staff can tell you which study procedures and information collection would still apply if you stop taking the study drug, but choose to remain in the study. If you leave the study for any reason, the study doctor may ask you to have some end-of-study tests.

The study doctor or the sponsor can stop your participation at any time without your consent for any reason, including the following:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled;
- For administrative reasons; or
- If the target number of subjects has entered the study treatment phase.

PRIMARY CARE PHYSICIAN/SPECIALIST NOTIFICATION OPTION

Please indicate below whether you want us to notify your primary care physician or your specialist of your participation in this study.

_____ Yes, I want the study doctor to inform my primary care physician/specialist of my participation in this study.

_____ No, I do not want the study doctor to inform my primary care physician/specialist of my participation in this study.

_____ I do not have a primary care physician/specialist.

_____ The study doctor is my primary care physician/specialist.

By signing below, I agree that:

- I have read and understand this informed consent document.
- I have had the chance to ask questions and they have been answered.
- I understand that taking part in this study is voluntary.
- I voluntarily consent to take part in this research study.
- I may choose not to be in the study or to leave the study at any time by telling the study doctor. I will not be penalized or lose any benefits to which I am otherwise entitled.
- I may have to leave the study without my consent if I need other treatment, do not follow the study plan, have a study-related injury, or for any other reason.
- If I leave the study for any reason, the study doctor may ask me to have some end-of-study tests.
- I do not give up any of my legal rights by signing this consent document.

I will receive a copy of this signed and dated consent document.

_____	_____	_____
Printed Name of Subject	Signature of Subject	Date (MM/DD/YYYY)
_____	_____	_____
Printed Name of Person Conducting Consent Discussion	Signature of Person Conducting Consent Discussion	Date (MM/DD/YYYY)

CONSENT FOR SUBJECTS WHO CANNOT READ

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness* Date

*Impartial Witness: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent and any other written information supplied to the subject. **Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance**