UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

A5241, Version 2.0, 04/08/09:
The Optimized Treatment that Includes or Omits NRTIs (OPTIONS) Trial: A Randomized Strategy Study for HIV-1-Infected Treatment-Experienced Subjects Using the cPSS to Select an Effective Regimen

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

Your contacts for the study are:
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- Coordinator: Joseph Quinn, RN (215) 349-8092
- Study Nurse: Wayne Wagner, RN (215) 349-8092

24 Hour Emergency Number (215) 662-6059 Ask for the Immunodeficiency Program Doctor on call

Introduction:
You are being asked to take part in this research study because you are infected with HIV (the virus that causes AIDS) and because it appears that the HIV that you are infected with may be resistant to anti-HIV drugs from each of three classes of drugs that are currently widely recommended. This means that many of these drugs will no longer be able to control your viral load (the amount of HIV in your blood).

This study is sponsored by the National Institutes of Health (NIH). The doctor in charge of this study at this site is Dr. Pablo Tebas. Before you decide if you want to be a part of this study, we want you to know about the study.

This research study is supported by money from Boehringer Ingelheim Pharmaceuticals, Inc., Hoffmann-La Roche, Inc., Merck and Company, Monogram Biosciences, Pfizer, Inc. and Tibotec Therapeutics. In addition, the person leading this research study receives payment from Merck and Company and Tibotec Therapeutics for activities that are not a part of this study. These activities may include consulting, advisory board membership, giving speeches or writing reports. If you would like more information, please ask the researchers or the study coordinator.

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. If you agree to take part in this study, you will be asked to sign this consent form. You will get a copy to keep.

Why Is This Study Being Done?
This study is being done to:
- see how effective new anti-HIV drugs are
- test the safety and tolerability of taking these new types of anti-HIV drugs in different combinations
- see if using a combination of anti-HIV drugs that does not include any nucleoside analogue reverse transcriptase inhibitors (NRTIs) is as good as or leads to fewer side effects than a combination of anti-HIV drugs that does include NRTIs. NRTIs are one class of antiretroviral drugs that resemble the components that the virus needs to reproduce. NRTIs are substituted for these essential building blocks and disrupt the virus' ability to make more copies of itself. More information about this is below.
- Test a new way of selecting anti-HIV drug combinations for individuals. More information about this is below.
Including or not including NRTIs
Currently, treatment guidelines recommend the use of at least two active anti-HIV drugs (drugs that your HIV is not resistant to). Because the virus you are infected with is resistant to many of the currently approved drugs, this study will include new types of drugs. We hope that one of these new combinations of anti-HIV drugs will be able to lower your viral load.

Treatment guidelines also recommend the use of at least two NRTIs to help lower your viral load. Some people have bad side effects from NRTIs, so we would like to see if NRTIs are always necessary.

Selecting anti-HIV drugs for individuals
This study is also being done to test a new way of predicting how well drugs will work for a particular person. Doctors on the study team will study the results from a resistance test (a test to see how certain anti-HIV drugs, including the study drugs, might work to control your viral load) and a tropism assay (another test that shows whether one of the study drugs, maraviroc, might be able to control your viral load) along with information from your medical history. The medical history information includes what drugs you have taken in the past and whether you have ever had any bad effects from other drugs. Then the doctors will identify one or more of the study regimens as the best option(s) for you. They will also identify at least two NRTIs that may be the most effective for you.

The study-provided anti-HIV drugs that may be part of your study treatment are enfuvirtide (including supplies that will be needed to inject this drug), maraviroc, raltegravir (formerly known as MK-0518), darunavir, tipranavir, and etravirine. Ritonavir must be taken with darunavir and tipranavir, but will not be provided by the study. You will have to obtain ritonavir yourself. The study staff may be able to help you find a source for this drug. NRTIs will not be provided by the study; you will have to obtain NRTIs yourself. The study staff may be able to help you find a source for these drugs (see “What is the cost to me?”).

What Do I Have To Do If I Am In This Study?

Screening
If you think you would like to join this study, you will be asked to sign this consent form. After you have signed the form you will be asked some questions and will undergo some tests to see if it is safe for you to join the study. These evaluations may take about 1-2 hours.

- You will be asked questions about your health and medicines you have taken in the past.
- You will be asked about your gender.
- You will have about 3 tablespoons of your blood collected for routine safety laboratory tests, viral load, a resistance test and a tropism assay.
- Some blood may be used to check for hepatitis B (a virus that can affect your liver).
- If you are a woman who is able to become pregnant, a small amount of blood that has already been collected will be used for a pregnancy test. You might be asked to provide a small amount of urine, instead, for this test. You will not be able to enter the study if you are pregnant.
- You will have a physical examination.
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- You will be asked whether you have taken enfuvirtide in the past and about your willingness to take enfuvirtide, a drug which is given by injection twice a day. These injections of enfuvirtide are self-administered. The pharmacist will review with you how to draw up the syringe and administer the medication to yourself. If you have a care giver who will help you with this, the pharmacist or study nurse can provide training for them as well.
- You will be asked about the anti-HIV drugs you have taken in the past and whether there were any that your body has not tolerated.

NOTE: The answers you give to these questions may affect the number of treatment options that the study can provide you. If you have taken enfuvirtide in the past and are willing to take it on this study, there may only be one treatment option available to you. If you are not willing to take enfuvirtide, regardless of whether you have taken it before, there may only be one treatment option available to you. If you have taken maraviroc or another drug in the same class, you will not be able to take maraviroc as part of your study treatment. The study staff will be able to describe the study treatment options to you.

Results of all of these tests will be given to you when they become 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 researchers within the AIDS Clinical Trials Group (ACTG) may determine whether there are patterns or common reasons why people do not join a study.

On Study

There will be two steps in this study. If the results of your screening tests show that you are eligible and you decide to take part in this study you will enter the study on Step 1. You may or may not enter Step 2. If you do not enter Step 2 you will still receive the results of your resistance test and tropism assay if available.

Step 1:
You will continue taking your current anti-HIV drugs until you receive new anti-HIV study drugs in Step 2 of the study. Step 1 of the study will last up to 75 days (about 2 and a half months).

There will not be any visits until your doctor receives the results from your resistance test and tropism assay. These results will determine if you are eligible to stay in the study. It's possible that even if you are eligible, there may not be room for you in the group that you could be in. If this happens, your participation in the study will end. You will still receive the results of your resistance test and tropism assay.

Pre-Entry for Step 2:
You will return to the clinic for a pre-entry visit for Step 2.

Your doctor will receive information from the study team that will include all the possible options of anti-HIV study drug combinations that may help to lower your viral load. The recommendations from the study team will be based on a new way of predicting how well drugs will work for a particular person. Your physician and you will choose a study regimen from among these options. Neither you
nor your physician will be able to choose whether you will add or not add NRTIs to your study regimen.

If you choose a study regimen that contains enfuvirtide, then you will receive training on how to take enfuvirtide at this visit. Enfuvirtide is a drug that must be taken either by a needle and syringe or by using a needle-free device called a Biojector 2000. You will have a choice of taking this drug by injection or by using the Biojector. Training might include watching a video on how to take enfuvirtide. If you are unable to use the Biojector or syringe, a person you choose will be taught to use the Biojector or syringe to give you your enfuvirtide dose.

This visit will also include the following evaluations. These evaluations may take about one and a half hours.
- You will have a physical examination.
- You will be asked about medicines that you are currently taking.
- You will have about 2 tablespoons of your blood collected for routine safety laboratory tests, a viral load test, and your CD4+/CD8+ cell count (a measure of how well your body can fight infections)
- If you are a woman able to become pregnant, some your blood that has been collected will be used for a pregnancy test. You may be asked to provide a small amount of urine, instead, for the pregnancy test.

Results of any tests will be given to you when they become available. Throughout the remainder of the study, results of any tests that are done during the study will be given to you when they become available.

On Step 2
Entry Visit:
If you are eligible for Step 2, you will return to the clinic for the Step 2 entry visit within 2 weeks of the Pre-Entry visit for Step 2. In Step 2, you will return to the clinic for five visits in the first four months and then for 7 more visits, once every 8 to 12 weeks for the remainder of the study. You will be in Step 2 of the study for 96 weeks, or almost 2 years.

If it appears that there are enough study drugs that together may be able to lower your viral load well, then you will be placed into one of two treatment groups, Arm A or Arm B (see below). You will be assigned to one arm or the other by chance (as if by the toss of a coin). You have an equal chance of being assigned to either of the study treatment arms.

If it appears that there are only a few study drugs that might lower your viral load or that they might not lower it only a little, we will still try to pick the best combination of study drugs for you. You will be assigned to Arm C (see below).

You will not be able to choose which arm you are in, but you may be able to choose which study drugs you will take. You, the study staff, and your doctor will all know which arm you are in. We do not know if one arm’s treatment will be any better than the other. This study is designed to answer this question.
Study Drugs
Below is a list of the study drugs and how they are given. You will only take some of these drugs, not all of them.
- enfuvirtide: injection under the skin (or by using a needle-free device, Biojector 2000) 2 times a day
- maraviroc: 1 or 2 tablets twice a day by mouth
- raltegravir: 1 tablet by mouth 2 times a day
- darunavir + ritonavir: 2 darunavir tablets and 1 ritonavir capsule by mouth 2 times a day, with food
- tipranavir + ritonavir: 2 tipranavir and 2 ritonavir capsules by mouth 2 times a day, with food
- etravirine: 2 tablets by mouth 2 times a day, with food

The study groups are:
Arm A
If you are in this arm you will take a three- or more-drug combination of the drugs listed below. You may not be eligible to use all of these drugs.
- enfuvirtide
- maraviroc
- raltegravir
- darunavir + ritonavir
- tipranavir + ritonavir
- etravirine
You will also take at least two NRTIs

Arm B
If you are in this arm you will take a three- or more-drug combination of the listed below. You may not be eligible to use all of these drugs.
- enfuvirtide
- maraviroc
- raltegravir
- darunavir + ritonavir
- tipranavir + ritonavir
- etravirine
You must not take any NRTIs

Arm C
If you are in this arm you will take a combination of the drugs listed below. You may not be eligible to use all of these drugs.
- enfuvirtide
- maraviroc
- raltegravir
- darunavir + ritonavir
- tipranavir + ritonavir
- etravirine
You will also take at least two NRTIs
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You must arrive fasting (not having had anything to drink or eat except water and your pills for 8 hours before this entry visit). The evaluations listed below will take about 1-2 hours.

- You will have a physical examination.
- You will be asked about your health and about medications that you have taken since your last clinic visit.
- You will have about 2 tablespoons of blood collected to check your viral load, and your CD4+/CD8+ cell count, and to check the levels of cholesterol, triglycerides, and glucose.
- You may have about ½ tablespoon of blood collected for a test to see if you are infected with hepatitis C (a virus that can affect your liver).
- Some of your urine will be used for a routine urine test.
- If you are a woman who is able to become pregnant some your blood or urine that has already been collected will be used for a pregnancy test.
- About 2 tablespoons of blood will be collected and stored and may be used later for a resistance test and/or tropism assay.
- You will be asked some questions about how you have been feeling, about what you can do by yourself, and about how often you need to see a doctor or visit a clinic.
- You will be asked some questions about whether and how much you smoke.
- If you have chosen a regimen that includes enfuvirtide, you will receive additional training about how to take this drug.
- Depending on when you enter Step 2 of the study you may be asked some questions and to perform some simple tasks. These evaluations will focus on identifying any changes in your memory or in your ability to follow instructions.

Week 1 Visit
At this visit you will have the following evaluations. These evaluations will take about 1 hour.
- You will have a physical examination.
- You will be asked about your health and about medications that you have taken since your last clinic visit.
- You will have less than 1 tablespoon of your blood collected to check your viral load.
- If you are taking enfuvirtide, the clinic staff will talk with you about how you are taking it. The staff may ask you to show them how you are taking it. If this is the case, they will let you know ahead of time.
- If you are a woman who is able to become pregnant, you may need to have a blood or urine pregnancy test.

Weeks 4 through 96 (about 11 visits total)
- At these visits, you will have the evaluations listed below. Most of the visits will take 1-2 hours. One of the visits will take about 4 hours; this is explained below, under Special Evaluations. The study staff will be able to tell you about how long you will need to be in the clinic each time. You may be asked to bring all of your study medicine containers and your enfuvirtide vials back to the clinic while you are on the study.
- You will have a physical examination.
- You will be asked about your health and about medications that you have taken since your last clinic visit.
- You will have about 1 tablespoon of your blood collected to check your viral load.
- If you are a woman who is able to become pregnant, you may need to have a blood or urine pregnancy test.
Depending on when you enter Step 2 of the study, you may be asked every 24 weeks (about every 6 months for up to 2 years) to answer some simple memory questions and be asked to perform some simple tasks. These evaluations will focus on identifying any changes in your memory or in your ability to follow instructions.

You may also have some of the evaluations listed below at some of these visits. For some visits, you will need to arrive fasting (not having had anything to eat or drink for at least 8 hours). The study staff will remind you about when you need to fast before a study visit.

- You will have about 2 tablespoons of your blood collected for routine safety laboratory tests, CD4+/CD8+ cell count, and to check the levels of cholesterol, triglycerides, and glucose.
- You will be asked to provide a small amount of your urine to be used for a routine urine test.
- About 1 tablespoon of your blood will be collected and stored and may be used later for a resistance test.
- You will be asked some questions about how you have been feeling, about what you can do by yourself, and about how often you need to see a doctor or visit a clinic.
- You will be asked some questions about whether and how much you smoke.
- You will be asked to fill out a form with questions about how you remember to take your study drugs. Filling out this form may take up to 15 minutes of your time.
- If you are taking enfuvirtide, the clinic staff will talk with you about how you are taking it at 2 or more visits. The staff may ask you to show them how you are taking it. If this is the case, they will let you know ahead of time.

Special Evaluations:
At some of the visits that have already been described above, some of your blood will be collected to check the levels of the study drugs in your blood. It is possible that you will have to re-schedule one of these visits if you have missed doses of study drugs in the 3 days before these visits. The study staff will try to help you avoid having to re-schedule.

At one of your study visits between the 1st and the 6th month after taking study drugs:
- You must not take your study drugs until you arrive at the clinic. Once you arrive at the clinic, about 2 tablespoons of blood will be collected before you take your study drugs. Once you take your study drugs, you will wait at least 3 hours before another 2 tablespoons of blood are collected.

At another of your study visits between the 1st and the 6th month after taking study drugs:
- You must arrive at the clinic 5-14 hours after your last drug dose. About 2 tablespoons of blood will be collected.

At any other visit at which blood is collected to check the levels of the study drugs in your blood:
- About 2 tablespoons of blood will be collected.

Other Visits
Possible virologic failure
If one of the tests shows that your viral load is too high, you will be asked to return to the clinic. The evaluations will take about 1 hour.
- You will be asked about medicines that you have taken since your last clinic visit.
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- About 2 tablespoons of blood will be collected to re-check your viral load and for a possible resistance test.
- About 2 tablespoons of blood will be collected for resistance tests that could be done after the study is over.
- Based on the results of the tropism assay that was done in Step 1, about 1 tablespoon of blood may be collected for a tropism assay that might be done right away. Another 1 tablespoon of blood may be collected and stored for a tropism assay that could be done after the study is over.
- About 2 tablespoons of blood will be collected to check the levels of the anti-HIV drugs in your blood.
- The study staff will talk with you about how you are remembering to take your anti-HIV drugs.
- If you are taking enfuvirtide, the clinic staff will talk with you about how you are taking it.

You will be told the results of the viral load, resistance, and tropism tests that are done right away as soon as they are available.

Change in treatment
If you make a change in your study-provided treatment, you will be asked to return to the clinic. The evaluations will take up to 1 hour.
- You will have a physical exam.
- You will be asked about medicines that you have taken since your last clinic visit.
- About 2 tablespoons of blood will be collected to check the levels of the anti-HIV drugs in your blood.
- If you have been taking enfuvirtide, the clinic staff will talk with you about how you are or were taking it.
- Depending on when you joined the study, you may be asked some questions and be asked to perform some simple tasks. These evaluations will focus on identifying any changes in your memory or in your ability to follow instructions.

Leaving the study early, stopping all study treatment, stopping all NRTIs, or starting NRTIs. If you leave the study early or if you are in Arm A and stop all NRTIs, or if you are in Arm B and add an NRTI, you will be asked to return to the clinic for another visit. At this visit, you will have the evaluations listed below. This visit may take 1-2 hours. You will need to arrive fasting (not having had anything to drink or eat except water and your pills for 8 hours before this visit) for this visit. The study staff will remind you about when you need to fast before a study visit.

- You will have a physical examination.
- You will be asked about your health and about medicines that you have taken since your last clinic visit.
- You will have about 4 tablespoons of your blood collected for routine safety laboratory tests and to check your viral load, your CD4+/CD8+ cell count, to check drug levels in your blood, and to check the levels of cholesterol, triglycerides, and glucose. Some of this blood will be stored and may be used later for a resistance test and, possibly, a tropism assay.
- A small amount of your urine will be collected and used for a routine urine test.
- You will be asked some questions about how you have been feeling, about what you can do by yourself, and about how often you need to see a doctor or visit a clinic.
- You will be asked to fill out a form with questions about how you remember to take your study drugs. Filling out this form may take up to 15 minutes of your time.
- You will be asked about whether and how much you smoke.
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- If you have been taking enfuvirtide, the clinic staff will talk with you about how you are or were taking it.
- You will be asked some questions and you will be asked to perform some simple tasks. These evaluations will focus on identifying any changes in your memory or in your ability to follow instructions.

What If I Become Pregnant During This Study?
If you become pregnant while on study, you must stop taking the study drugs and see your doctor to get the best care possible. You will be asked to return to the clinic for a study visit at your earliest possible convenience to have the evaluations listed under “Leaving the study early” in the Other Visits section above performed. You may remain on study during your pregnancy or you may choose to leave the study. Either way, the clinic staff will be contacting you to find out about any events that happened during your pregnancy and about the health of the baby.

The possible risks to the unborn baby from the study drugs are stated above in the risks. Long-term follow-up is recommended for a baby whose mother takes anti-HIV drugs during pregnancy. The study staff will talk to you about long-term follow-up.

Other
Some of your blood that is left over may be stored (without information that could identify you) and used for ACTG-approved HIV-related research.

How Many People Will Take Part in This Study?
About 454 people will enter Step 2: 177 for Arm A, 177 for Arm B, and up to 100 people in Arm C. About 577 people may need to enroll in Step 1 for 454 people to start Step 2. Not every one who enters Step 1 will enter Step 2. About 10-15 people are expected to participate at the University of Pennsylvania.

How Long Will I Be in This Study?
If you enter the study but do not enter Step 2 of the study, you will be in this study for up to 75 days (a little more than 10 weeks). If you do enter Step 2, you will be in this study for up to 106 weeks (or a little more than 2 years) altogether: about 10 weeks in Step 1 and then about 96 weeks in Step 2.

Why Would the Doctor Take Me Off This Study Early?
Your doctor may need to take you off the study early without your permission if:
- The study is stopped or cancelled.
- A Data Safety Monitoring Board (DSMB) recommends that the study be stopped early (A DSMB is an outside group of experts who monitor the study.)
- You are not able to attend the study visits as required by the study.
- You are not able to enter Step 2 of the study.
- You do not start the study treatment.
- Your doctor believes that remaining on the study is no longer what is best for you.
Your doctor may also need to take you off the study drugs without your permission if:
- Continuing the study drugs may be harmful to you.
- You need a treatment that you may not take while taking study drugs.
- You are not able to take the study drugs as required by the study.
- You become pregnant or are breast-feeding.

If you must stop taking the study drugs before Step 2 of the study is over, your doctor will ask you to continue to be part of the study and return for some study visits and procedures through the end of Step 2.

**What If I Have To Stop Taking All Anti-HIV Drugs After I Start Them?**

**During the study:**
If you must permanently stop taking anti-HIV drugs before you are finished with Step 2 of the study, the study staff will discuss other options that may be of benefit to you.

**After the study:**
After you have completed Step 2 of the study, you and your doctor will decide what treatment you should have. If continuing to take the same or similar anti-HIV drugs would be of benefit to you, the study staff will discuss how you may be able to obtain them. You may be able to obtain them outside of the study. The study staff will talk with you about your choices.

**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 that may be related to the drug. If you have questions concerning the additional study drug side effects please ask the medical staff at your site.

There is a risk of serious and/or life-threatening side effects when non-study medicines are taken with the study drugs. For your safety, you must tell your doctor or the study nurse about all medicines you are taking before you start the study and also before starting any new medicines while on the study. Also, you must tell your doctor or the study nurse before enrolling in any other clinical trials while on this study.

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

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

Risks with Use of Enfuvirtide (ENF)

- Injection site reactions: Almost all people have skin reactions at the site where enfuvirtide is injected. Reactions may include: itching, swelling, redness, pain or tenderness, hardened skin, bumps. Most reactions are mild. Occasionally they may be severe or rarely associated with infections or collection of thick liquid (abscess) at the injection site.
- Lung infection (pneumonia). You should contact your healthcare provider right away if you have a cough, fever, or trouble breathing.
- Serious allergic reactions. Symptoms may include: trouble breathing, fever, nausea, vomiting, chills, shakes, skin rash, blood in your urine, swelling in your feet, dizziness, severe muscle weakness starting in your feet and quickly moving to your upper body (Guillain-Barre syndrome). Contact your healthcare provider right away if you get any of these allergic reaction symptoms and do not take any more enfuvirtide. Enfuvirtide should not be restarted if your doctor thinks that you had an allergic reaction that was related to enfuvirtide.

Other side effects of enfuvirtide may include:
- Numbness and tingling of the hands and feet
- Difficulty sleeping
- Depression, or anxiety
- Decreased appetite
- Sinus infections and other infections in other places, including the skin (herpes), and the blood (sepsis)
- Swollen glands (lymphadenopathy)
- Muscle pain
- Constipation
- Pancreatitis (swelling of the pancreas). If you develop pancreatitis, you may have one or more of the following: stomach pain, nausea, and vomiting.
- Abnormal blood tests including: increases in eosinophils (a special type of white blood cell), which sometimes can be a sign of an allergic reaction, increases in liver functions, which could mean you have liver damage and in rare cases may lead to liver failure.

If people without HIV infection mistakenly inject themselves with ENF, they may have a false-positive HIV antibody test by the ELISA assay. If you are having someone else give you ENF, then he or she should be told about this risk.

Injection risk when using needle-free system “Biojector”:
Shooting nerve pain and tingling lasting up to 6 months from injecting close to large nerves or near joints, and bruising and/or collection of blood under the skin have been reported.

If you are taking any blood thinners, or have hemophilia or any other bleeding disorder, you may be at higher risk of bruising or bleeding after using the needle-free system “Biojector.”
Risk of Transmitting Disease
When giving an injection by needle at home there is the small chance of a needle-stick injury, which can cause an infectious disease (such as HIV, HBV (hepatitis B), and/or HCV) to uninfected people in your household. Clinic personnel will review with you what to do if there is an accidental needle stick. Careful disposal of used needles in special containers that will be provided should be practiced.

Risks with use of Maraviroc (Maraviroc (MVC, Selzentry®), Pfizer, Inc

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

- Liver problems (liver toxicity) have occurred in people who took maraviroc. An allergic reaction may happen before liver problems occur. Stop taking maraviroc and call your Health Care 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, dark urine, vomiting, stomach pain, or elevated liver related function tests. People who are co-infected with hepatitis B or C 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
- Stroke

In addition to the serious side effects listed above, additional side effects include:

- Cough
- Fever
- Some infections, including herpes, colds, sore throat, sinus infections, flu and flu-like symptoms
- Rash
- Muscle aches, spasms and pain
- Stomach pain and bloating
- Dizziness
- Diarrhea
- Swelling of parts of the body
- 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.

Maraviroc 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 maraviroc. Before starting maraviroc, you should inform your health care provider if you are allergic to soy or peanuts.
Risks with use of Raltegravir (RAL, Isentress)

The following side effects have been associated with the use of raltegravir:
- Upset stomach
- Headache
- Tiredness
- Weakness
- Trouble sleeping
- Rash, which can be severe
- Feeling anxious
- Depression, suicidal thoughts and actions
- Paranoia (an abnormal sense of fear)
- Low blood platelet count
- Muscle tenderness, weakness or injury which can be serious and lead to kidney damage

Risks with Use of Protease Inhibitors (darunavir and tipranavir are protease inhibitors)
- Increases in the amount of triglycerides and/or cholesterol in the blood
- Development of diabetes or the worsening of high blood sugar

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

Risks with Use of Tipranavir (TPV, Aptivus) Given with Ritonavir (RTV, Norvir)
Reports of bleeding into the brain, which can lead to permanent disability or death, have been associated with the use of tipranavir + ritonavir. This risk may be increased if you are at risk for bleeding for another reason, or you are receiving other medications known to increase the risk of bleeding, including supplemental high doses of vitamin E.

People taking tipranavir together with ritonavir may develop severe liver problems, including liver failure which can result in death. People who have signs of liver disease before starting tipranavir and people with liver diseases such as hepatitis B or C have an increased risk for worsening of their liver disease. If you are developing liver damage, you may have one or more of the following reactions: tiredness, general feeling of illness or flu-like feeling, loss of appetite, nausea, pale stools, dark urine, yellowing of the skin or whites of your eyes, liver tenderness and increases in liver enzymes in the blood.

Additional side effects of tipranavir + ritonavir include:
- Stomach cramps or pain, heartburn, and abnormal bowel movements (stools), including loose or watery stools, which may result in dehydration
- Upset stomach (nausea, vomiting), decreased appetite
- Feeling weak and tired
- Headache
- Rash, which may be severe. Women taking estrogen hormones may have a higher risk of getting a rash.
- Pancreatitis (inflammation of the pancreas)

NOTE: Before starting tipranavir, you should inform your doctor if you are allergic to sulfa
medicines. While receiving tipranavir, you should inform your doctor if you have any unusual or unexplained bleeding.

**Risks with Use of Darunavir (DRV, Prezista) Given with Ritonavir**

People taking darunavir together with ritonavir may develop severe liver problems, which may be life-threatening. People who have increased liver function tests before starting darunavir and people with liver diseases such as hepatitis B or C have an increased risk of worsening liver disease.

- Rash. In some people, darunavir may cause a severe or life-threatening rash. Contact your healthcare provider if you develop a rash or a rash accompanied with fever, general malaise, fatigue, muscle or joint aches, blisters, mouth lesions, conjunctivitis (eye problems), hepatitis (liver problem).
- Diarrhea
- Nausea
- Stomach discomfort
- Vomiting
- Headache
- Runny nose and sore throat
- Abnormal increases in triglycerides and cholesterol in the blood
- Abnormal liver function blood tests
- Abnormal pancreatic blood tests

**NOTE:** Before starting darunavir, you should inform your healthcare provider if you are allergic to sulfa medicines.

**Risks with Use of Etravirine (ETR, Intecence)**

- Rash, which may be severe and life-threatening
- Diarrhea, upset stomach, and vomiting
- Abdominal pain
- Tiredness
- Numbness, pain, or tingling in the hands or feet
- High blood pressure
- Headache
- Increase in blood glucose
- Increases in cholesterol and triglycerides
- Decreased white blood cells
- Rhabdomyolysis (breakdown of muscle)
Risks with Use of NRTIs
Lactic acidosis and severe hepatomegaly (enlarged liver) with steatosis (fatty liver) that may result in liver failure, other complications and death have been reported with the use of antiretroviral nucleoside analogues alone or in combination. The liver complications and death have been seen more often in women on these drug regimens. Some nonspecific symptoms that might indicate lactic acidosis include: unexplained weight loss, stomach discomfort, cramps, nausea, dizziness, vomiting, fatigue, weakness, muscle pain, and shortness of breath.

There may be other side effects of NRTIs, depending on which NRTI you receive. The study staff will discuss these other possible side effects with you. All of the NRTIs used in this study are FDA-approved for treating HIV.

Unforeseen Risks
You might experience side effects or discomforts that are not listed in this form. Some side effects may not be known yet. It is possible that you will be the first patient to experience a particular effect. Tell the study doctor or study staff right away if you have any problems.

Are There Risks Related To Pregnancy?
The anti-HIV drugs in this study may be unsafe for unborn babies. If you are having sex that could lead to pregnancy, you must agree not to become pregnant or to attempt to make a woman pregnant. Because of the risk involved, you and your partner must use at least two methods of birth control, one of which must be a barrier method that you discuss with the study staff. You must continue to use both methods until 6 weeks after stopping your medicines. You must choose two of the birth control methods listed below:
- Condoms (male or female) with or without a spermicidal agent
- Diaphragm or cervical cap with spermicide
- IUD
- Hormone-based contraceptive

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

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 are infected with 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
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- no treatment
Please talk to your doctor about these and other choices available to you. Your doctor will explain the risks and benefits of these choices.

What About Confidentiality?
We will do everything we can to protect your privacy. 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. In addition, any publication of this study will not use your name or identify you personally.

People who may review your records include the U.S. Food and Drug Administration (FDA), University of Pennsylvania IRB, OHRP, National Institutes of Health (NIH), study staff, study monitors. 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.

Your records may be reviewed by the U.S. Food and Drug Administration (FDA), University of Pennsylvania IRB, National Institutes of Health (NIH), study staff, study monitors.

What Are the Costs To Me?
Taking part in this study may lead to added costs to you and your insurance company. In some cases it is possible that your insurance company will not pay for these costs because you are taking part in a research study.

There will be no cost to you for study provided drugs, clinic visits, examinations or laboratory and test procedures that are part of this study. If your study regimen includes ritonavir, any NRTIs, or other drugs not provided by the study, then you will be responsible for obtaining these drugs. These drugs could be costly.

The study will provide up to two real-time resistance tests. If your doctor believes that an additional test is necessary during the study, the study will not pay for the test. You may be responsible for paying for this test and it could be costly.

Will I Receive Any Payment?
You will be compensated $25 for each clinic visit you attend for Step 2 to cover transportation costs, parking, child care, etc and for your time and inconvenience. Thus, if you attend all study visits (13), the maximum compensation you will receive from the study is $325. If you need to come into the clinic for study required evaluations as described earlier in this consent (virologic failure confirmation, repeat lab tests), you will also be compensated $25 for these visits.

What Happens If I Am Injured? What Happens if My Baby Is Injured (In the Event That I Become Pregnant?)
If your baby or you have a medical emergency during the study you should go to the nearest emergency room. You may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

In the event that you are hurt or injured as a result of participation in this research study, please contact the investigator listed on page one of this form.

In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise offered from the University of Pennsylvania or the National Institutes of Health. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

**What Are My Rights As a Research Subject?**

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

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

**What Do I Do If I Have Questions Or Problems?**

For questions about this study or a research-related injury, contact:

- Pablo Tebas, MD (215-615-4321)
- Clinical Trials Unit (215 349-8092)

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

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

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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.

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For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

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Provide a brief description of above person authority to serve as the subject’s authorized representative.