

**A PHASE 1 OPEN LABEL CLINICAL TRIAL OF THE SAFETY AND TOLERABILITY
OF SINGLE ESCALATING DOSES OF AUTOLOGOUS T CELLS TRANSDUCED
WITH VRX496 IN HIV POSITIVE PATIENTS**

**PATIENT CONSENT FORM
UNIVERSITY OF PENNSYLVANIA**

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(Ask for VIRxSYS Study Team Member on Call)

INVITATION TO PARTICIPATE: The doctors at University of Pennsylvania Hospital are studying HIV infection and are attempting to find better ways of diagnosis and treatment. This is called clinical research.

You are being asked to participate in this research study because you are HIV positive and continue to have HIV virus in your blood even though you have received treatment. Your participation in this study is entirely voluntary. In order to decide whether or not you should agree to be part of this research study, you should understand enough about its possible risks and benefits to make an informed decision. This process is known as informed consent.

This form gives detailed information about the research study that your doctor will discuss with you. Once you understand this study, you will be asked to sign this form if you wish to participate.

A company called VIRxSYS Corporation supports this research. This means that the research team at the University of Pennsylvania is being given funds to carry out the study.

PURPOSE: The purpose of this study is to test the safety and tolerability of Autologous (your own) T Cells Transduced (mixed) with VRX496 (VRX496 modified T cells) in HIV positive patients like you. "VRX496" is an anti-HIV gene transfer product that will be put into some of your T cells in the laboratory (changing your T cells).

We are studying VRX496 to see whether it can improve your immune system by changing some of your T cells so they can fight HIV and survive longer (HIV usually kills T cells it infects). After your cells are modified with VRX496 they will be put back in you where they may prevent the HIV from reproducing in the modified cells. If successful, this would help reduce the HIV infection and keep your CD4 cell counts from decreasing. However, since this study is primarily a safety study, the experimental treatment may not work and there may be no benefit.

VRX496 modified T Cells is an experimental treatment and not approved for general use in the United States but has been approved for use in this study. This research study will see what doses of VRX496 modified T Cells can be given safely to potentially reduce the HIV infection in your body while keeping your CD4 cell counts from decreasing.

We will study whether VRX496 modified T cells cause any side effects. We will study different doses of VRX496 modified T cells to determine which dose level is the safest and might work to help your body fight the HIV virus.

You should not be in this study if any of the following statements apply to you:

- You are pregnant or nursing a child.
- You have a recent (within 1 year) history of drug abuse
- You are currently taking a cortisone-like drug or have taken a cortisone-like drug within the past 30 days.
- You have taken hydroxyurea (hydrea) with the past 30 days.
- You have a history of cancer
- You have participated in a prior gene therapy trial or are currently taking part in another research study.

There may be other reasons why you cannot take part in this study that will be discussed with you by the study doctor or his/her staff.

PROCEDURES: If you decide to participate, you will be one of twelve (12) patient-subjects enrolled in this study divided into four (4) groups of three (3) patient-subjects each. If you are presently receiving treatment for HIV, you will be asked not to change your treatment for the duration of the study (6 months). All of the patient-subjects on this study will receive one dose of VRX496 modified T Cells. VRX496 modified T Cells are created using your own blood that has been treated with VRX496. The procedure used to collect your blood is described in this section.

All 4 groups of patient-subjects will receive different increasing doses of the study medication. Because of this, the first group of three patient-subjects to be treated in this study will receive lower doses of the study medication than later patient-subjects. We will watch all patient-subjects closely for side effects to be sure that it is safe to give the higher doses. You will be in this study for approximately 6 months from the time that you receive the VRX496 modified T Cells and will be need to complete all follow up appointments.

The study doctor will ask you to return once a year for your lifetime to have a medical history and repeat blood tests done.

The study doctor or his staff will ask you to read and sign this Informed Consent form after all of your questions have been answered.

At screening time you will have approximately 4 teaspoons of blood drawn for laboratory tests as well as an ECG (an electrocardiogram involves having wires placed on your chest to measure the electrical activity of your heart). Measurements of your blood pressure, heart rate, breathing rate, urinalysis, pregnancy test (if applicable), body temperature, height and weight will be recorded and your doctor will ask you questions about your medical history to make sure that you meet the requirements of this research study.

If all of these test show that you are qualified to be in this research study, you will then have a procedure performed called “apheresis” before you receive the study medication and then again at 6 months following the infusion of study medication. This procedure will require that you return to the University of Pennsylvania Medical Center’s blood bank to have it performed.

Apheresis is a special type of blood donation that involves collecting your blood. Blood is removed by inserting a needle and a small tube in your vein. A machine separates the different parts of your blood so that the lymphocytes or white blood cells can be separated from the rest of your blood, which includes the red cells and platelets. The blood is prevented from clotting within the tubing of the machine by adding a chemical/medication called acid-citrate-dextrose (ACD). You will be given back the remaining part of your blood through the tube in your arm, together with ACD and salt solution (saline).

After the apheresis procedure you may experience temporary discomfort, including irritation, swelling or bruising at the place where the needle was inserted into your vein to collect the blood. Apheresis can also occasionally cause: nausea, vomiting, seizures, blood loss, infection, skin rash, flushing, hives, numbness and tingling, or swelling of your feet and ankles.

The procedure usually takes between 2-3 hours to complete and takes place in the blood bank at the hospital. Trained personnel in the blood bank supervise the procedure. After the apheresis procedure is completed you will be told when to return to the hospital to receive your study medication (VRX496 modified T Cells).

Within 24 hours before you receive the dose of VRX496 modified T Cells you will have a repeat physical examination including measurements of blood pressure, urinalysis, heart rate, respiratory rate and temperature, you will have approximately 4 teaspoons of blood drawn and a urine sample taken for laboratory tests. If you are a woman of childbearing potential you will also have a repeat blood pregnancy test performed. The study doctor or his staff will ask you about any new medications that you have taken since your first visit to the hospital for this study.

You will receive the VRX496 modified T Cells intravenously (through a vein in your arm using a needle and a small tube) in the Clinical Research Center (CRC) facility at the hospital. The date and time of this infusion will be arranged by you and your study nurse. The study medication will take approximately 30 minutes to infuse (go into your vein). Approximately 10-20 minutes after the infusion is complete you will have approximately 2 teaspoons of blood drawn for laboratory tests. It will be necessary for you to remain in the CRC for at least two hours after the infusion is completed. The nurses will check your blood pressure, heart rate, breathing rate and temperature frequently during this time to be sure that they remain normal. If you do not experience any uncomfortable effects from the infusion you will be able to leave the hospital.

You will return to the CRC 24 hours after receiving the VRX496 modified T Cells to have repeat blood taken (approximately 3 Tablespoons), a physical examination including blood pressure, heart rate, breathing rate and temperature. The study doctor or staff will also ask you about any medications that you have taken or any symptoms that you may have experienced after receiving the VRX496 modified T Cells.

You will return to the CRC at 2 days, 3 days, 7 days, 14 days, 21 days and 28 days after receiving the VRX496 modified T Cells to have a physical examination, including blood

pressure, heart rate, breathing rate and temperature, blood tests (approximately 3 Tablespoons) performed. On day 7 and day 28 you will be asked to provide a urine sample. Your study doctor or his staff will also ask you about any medications that you are taking and any symptoms that you may have experienced since you received the VRX496 modified T Cells.

You will be asked to return to the clinic 3 months and 6 months after receiving the VRX496 Modified T Cells to have approximately 3 teaspoons of blood drawn for laboratory tests at each visit, a urine sample and a physical examination.

At your 6-month visit you will undergo a second apheresis procedure in the blood bank at the hospital. This second apheresis procedure is performed to see how your T cells have responded to the study medication and will not be reinfused at a later time.

After the apheresis procedure you may experience temporary discomfort, including irritation, swelling or bruising at the place where the needle was inserted into your vein to collect the blood. Apheresis can also occasionally cause: nausea, vomiting, seizures, blood loss, infection, skin rash, flushing, hives, numbness and tingling, or swelling of your feet and ankles.

The procedure usually takes between 1-2 hours to complete and takes place in the blood bank at the hospital. Trained personnel in the blood bank supervise the procedure.

After 6 months you will be asked to come back once a year for blood tests (1-1/2 teaspoons), and to have a medical history taken for your lifetime. These blood tests are done to look for side effects and to see if your immune system has responded to the VRX496 modified T Cells.

You will provide your current address and telephone number to the study doctor and will update this information throughout the research study so that he or his research staff will be able to contact you with any new information. It will be very important for you to keep the 3 and 6 months and yearly follow up visits to your doctor.

In order for the study doctors to learn more about your disease and the effects of the VRX496 modified T Cells, you should also know that at the time of your death, no matter when this occurs and what the cause, permission for an autopsy will be requested from your family. Please inform your family that this request is important and may have benefit to future clinical investigations studying HIV infection.

RISKS: The following adverse events may be observed with VRX496 T Cells:

- Metallic taste in the mouth
- Increase in blood pressure
- Low heart rate
- Allergic reaction
- Seizures
- Nausea and vomiting
- A decrease in hemoglobin and hematocrit (red blood cell number, called anemia)
- Increase in viral load or decrease in T cell count
- Changes in your T cells as a result of their modification with VRX496

COSTS AND FINANCIAL RISKS: There will be no costs to you for participating in this study. Autologous T Cells Transduced with VRX496 will be supplied free of charge by VIRXSYS Corporation.

BENEFITS: If the experimental treatment works you may have some benefit. However, since this is a primarily a safety study, the experimental treatment may not work and there may be no benefit.

PREGNANCY ISSUES: Due to the effect of this drug, there could be serious harm to unborn children (or children who are breast-feeding) and it could also jeopardize the health of the mother. In addition, it is possible that harmful side effects that are not yet known could occur to both the mother and unborn or breast-feeding child. For this reason, if you are pregnant, you will inform the investigator and understand you will not be included in the study. If you are still capable of becoming pregnant, you will be given a serum pregnancy test prior to entry into the study and again within 24 hours of receiving the VRX496 modified T Cells. You also understand that you will practice a medically accepted method of birth control (such as abstinence, hormonal birth control and barrier methods) during your participation in the study. Further, you understand that while you are taking this drug you should not become pregnant, and if you do become pregnant, you must discontinue the drug and consider termination of the pregnancy. If you are a male you should also take precautions to prevent a pregnancy by use of a medically accepted method of birth control.

ALTERNATIVES: You do not have to participate in this study to receive the experimental treatment for your HIV disease. If you decline participation in this study you will continue to be treated by your primary physician.

COMPENSATION: You will receive \$500.00 for your participation in this study. The payment schedule is as follows:

- \$100.00 after the apheresis procedure has been completed,
- \$150.00 after the infusion of VRX496 modified T cells and the completion of the 24 hour blood work,
- \$75.00 after Day 28 visit (only if all visits are completed as scheduled),
- \$75.00 for completion of the 3 month visit and
- \$100.00 for completion of the 6 month visit (only after the apheresis procedure is completed).

CONFIDENTIALITY: You understand that every attempt will be made by the investigators to maintain all information collected in this study strictly confidential, except as may be required by court order or by law. You further understand that authorized representatives of the Sponsor; VIRXSYS Corporation, the University of Pennsylvania, as well as the Food and Drug Administration (FDA), will have access to and may copy, both your medical records and records from your participation in this study. This access is necessary to insure the accuracy of the findings and your safety and welfare. If any publication or presentations result from this research, you will not be identified by name.

Name of Investigator
(if different from above)

Signature of Investigator
(if different from above)

Date/Time