IRB NUMBER: STUDY20180025
IRB APPROVAL DATE: 4/14/2020
IRB EFFECTIVE DATE: 4/14/2020
IRB EXPIRATION DATE: 4/13/2021

Title of Project: HIV Reservoir Reduction with Interleukin-2
Principal Investigator: Dr. Benigno Rodriguez

INTRODUCTION

We invite you to take part in a research study at the Case Western Reserve University (CWRU)/University Hospitals Cleveland Medical Center (UHCMC) Clinical Trials Unit. You are being asked to take part in this research study because you are infected with the human immunodeficiency virus (HIV), the virus that causes AIDS. This study is supported by research funding provided by Gilead.

The doctor in charge of this study at this site is: Dr. Benigno Rodriguez. Before you decide if you want to be a part of this study, we want you to know about the study.

First, we want you to know that:

Taking part in this research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your research team before you agree to the study.

This is a consent form. It gives you information about this study. The study staff will talk with you about this information. You are free to ask questions about this study at any time. 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.

You are invited to participate in a voluntary research trial that will examine the potential role of interleukin-2 (IL-2), a drug that is used to treat certain cancers, in decreasing the number of cells in your body that contain HIV. We call this the Latent Reservoir.

WHY IS THIS STUDY BEING DONE?

IL-2 is a molecule that is naturally produced by a certain part of the body's immune system, called T cells. In HIV infected patients, IL-2 treatment cycles can increase CD4 counts but these CD4 T cell increases do not seem to prevent complications from HIV. In an earlier study however, persons receiving a combination of HIV medicines plus cycles of IL-2 had lower numbers of cells in blood and lymph node that contained HIV than persons who received HIV medicines alone. In a few of these patients, the HIV medicines were stopped and HIV levels in blood became detectable telling us that these persons were not cured of infection.

The purpose of this study is to find out if IL-2 will decrease the numbers of cells in the body that contain HIV capable of infecting new cells. We call these HIV viruses "replication competent". It is important to do this study so that we can examine the levels of HIV in immune cells in each

person both before and after IL-2 treatment and to learn how IL-2 might decrease levels of virus in the body.

HOW THE STUDY WORKS

Entry into the study will only be permitted if you, in the opinion of the protocol team, have a good level of knowledge about the potential risks and benefits of participation. In addition, you must agree to comply with study requirements and clinic policies. You must also agree to allow extra research blood specimens to be collected and stored (frozen) for potential future use in studies related to HIV infection or the immune system. If you are actively engaging in substance abuse or you have a history of substance abuse that may interfere with protocol compliance or compromise your safety, you may also be excluded. You may also be excluded if you have a history of certain medical condition or if certain laboratory tests are outside of the normal range.

If you are eligible to participate in the study, you will undergo a pre-treatment leukapheresis procedure approximately 4 to 8 weeks before your first dose of IL-2. The procedure called leukapheresis is explained below in this document. You will continue your antiretroviral therapy (HIV medicines) and receive eight cycles of IL-2, which is the drug that will be used in the study. The antiretroviral therapy during study will be based a continuation of your current therapy and the costs for this treatment will be your responsibility or the responsibility of your insurer as they are now. You can continue to receive your usual medical care through your usual provider while you are on the study.

The medicine used in the study, called IL-2, is given by injection into the tissue under the skin using a syringe and needle. You will receive one of these injections twice a day for 4 days, and then again 8 weeks later for a total of eight periods of 4 days each.

A healthcare professional will show you how to administer these injections yourself. At the beginning of the study, and several times later, you will be asked to give yourself the injections in the clinic under the supervision of a member of the research staff to make sure that you can do it safely, and to give you a chance to ask any questions you might have about the injection.

You will be instructed as to how to inject IL-2. The staff will observe you give yourself the first IL-2 injection to make sure that you can do it safely, and to give you a chance to ask any questions you might have about the injection. Once you have given yourself the first dose, you will receive the remaining doses that you will need for the cycle already loaded into sterile syringes. The study staff will give you detailed instructions on how to store the medication, how to handle the pre-filled syringes, and how to administer each dose. You will then leave the clinic and will inject IL-2 yourself twice a day for a total of 4 days (a total of 8 injections including the first injection in the clinic). These 8 injections make up the first cycle of IL-2 administration.

It is possible that the study investigators will decide to provide only some, but not all, of the doses needed to complete a cycle at the time of your visit to the clinic. If this happens, you may be asked to ensure that you are physically available at a stable address to receive the remaining doses for a cycle through a courier service. This means that your identity may become known to personnel working for the courier service.

You will get a total of eight cycles of IL-2 during the study (one cycle every 8 weeks). The procedure will be the same for each cycle as described above for the first cycle, except you will not be asked to administer the first dose in the presence of study staff every time. Cycles are defined as 8 calendar weeks, including the 4-day period of IL-2 administration. The dose will be 5 million units of IL-2 given as an injection under the skin (subcutaneously) twice a day, once in the morning and once at night. Each of the eight IL-2 cycles will last four days, and will not be extended if doses are missed. At the start of your first cycle of IL-2 treatment, you will be taught how to manage potential side effects. If you are unable to self-administer the IL-2, your doctor or nurse will talk to you about possibly returning to the clinic for injections.

You will also be evaluated, by phone contact with the study staff, during each cycle (usually on days 2 and 4) for the presence of significant adverse effects, defined as those that, in the Principal Investigator's opinion, may be related to the study drug and require a change in treatment. You may be asked to return to the clinic if a physical examination/assessment is needed to evaluate any symptoms you may be experiencing.

If serious side effects develop during the injection period, the dose of IL-2 may need to be reduced, temporarily discontinued, or even stopped.

Eight weeks after your last IL-2 treatment cycle or if you must end IL-2 treatments for any other reason, you will be asked to return to the Clinical Trials Unit for an interval history and if indicated a targeted physical examination. At this time, you will have another leukapheresis to collect immune cells and plasma to examine the effects of IL-2 treatment on immune function and on the HIV reservoir.

WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?

If you decide to take part in this research study, you will be asked to sign this consent form. Before signing it, ask your study nurse or doctor to explain anything that you do not fully understand. 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. This will be done at the screening visit, which may take about 1.5 hours.

<u>Screening visit</u>

This visit will occur about 8 to 16 weeks prior to the start of the study treatment.

- Your HIV infection will be confirmed. If there is no record available, you will have another HIV-1 test.
- You will have a physical exam, which includes a vein assessment for leukapheresis.
- You will be asked about your health and medicines you have taken in the past or are taking now.
- Approximately 2 tablespoons of blood will be drawn for routine tests of blood, kidney, thyroid, and liver function, a test for hepatitis B and hepatitis C, and for tests of immune function and HIV levels.
- If you have female reproductive organs, you will only be allowed to participate in the study if you cannot become pregnant (for example, because you have your womb or ovaries removed, you are past menopause, or had your tubes tied). Study personnel will

ask you about your medical history in order to determine this and a pregnancy test will be done at this visit.

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, sex, race), clinical (for example, disease condition, diagnosis), and laboratory (for example, CD4+ T cell count, viral load) information is being collected from you to help the study team determine whether there are patterns or common reason why people do not join the study. This information may be held for an indefinite length of time. Information will be stored using code numbers without information that could identify you.

Please indicate with your initials below whether you agree to the use of some of your information if you decide not to take part in this study or if you do not meet the eligibility requirements.

_____YES _____NO

Pre-treatment leukapheresis visit (see also below)

If you are determined to be eligible to participate in the study, then this visit will occur approximately 4-8 weeks prior to the start of the study treatment and will include:

- You may have a physical exam and will be asked about your health and medicines you have taken since the previous visit or are taking now.
- Approximately 2 tablespoons of blood will be drawn for routine tests of blood, kidney, thyroid, and liver function and for tests of immune function.
- The leukapheresis procedure will be done at this visit.
- The leukapheresis samples obtained will be stored for detailed tests of HIV levels and for additional tests of immune function.
- This visit will take approximately 4 hours.

Initial Treatment Visit (Cycle 1 Day 0)

This visit will occur about 4-8 weeks after the pre-treatment leukapheresis visit.

- At this visit, you may have a physical exam and will be asked about your health and medicines you have taken since the previous visit or are taking now.
- Approximately 6 tablespoons of blood will be drawn for routine tests of blood cell, kidney, thyroid, and liver function, for tests of immune function, and for detailed testing of virus levels.
- You will be instructed as to how to inject IL-2. You will be observed as you give yourself the first injection under the skin.
- You will be given a dosing log along with instructions of how to complete while you were administering IL-2 injections.
- Information about managing expected side effects will be reviewed with you during this visit and will be given to you to take home for future reference.
- You will be observed in the clinic for at least 4 hours after the injection.
- This visit will take approximately 5 to 6 hours.

IRB NUMBER: STUDY20180025
IRB APPROVAL DATE: 4/14/2020
IRB EFFECTIVE DATE: 4/14/2020
IRB EXPIRATION DATE: 4/13/2021

Subsequent Treatment Cycles (Cycles 2,3,4,5,6,7,8 Day 0)

- At these visits that occur about 8 weeks apart, you may have a physical exam and will be asked about your health and medicines you have taken since the previous visit or are taking now.
- Approximately 6 tablespoons of blood will be drawn for routine tests of blood cell, kidney, thyroid, and liver function, for tests of immune function, and for testing of HIV levels. Detailed testing of HIV levels will be done at cycle 4 and 8.
- You will be instructed as to how to inject IL-2. You will be observed as you give yourself the first injection of cycle 4 and 8 under the skin.
- You will be given a dosing log along with instructions of how to complete while you were administering IL-2 injections.
- Information about managing expected side effects will be reviewed with you during this visit and will be given to you to take home for future reference.
- This visit will take approximately 1 to 1.5 hours.

Day 2 and 4 after beginning each Treatment cycle

You will be contacted by a study nurse who will ask you how you are feeling and how you are tolerating the treatment. You may be asked to come to the clinic for physical exam and/or laboratory testing, if you are experiencing side effects that require additional evaluation or intervention.

Day 7 after Treatment cycles 1,4 and 8:

- At this visit, you may have a physical exam and will be asked about your health and medicines you have taken since the last visit or are taking now.
- Approximately 6 tablespoons of blood will be drawn for routine tests of blood cell, kidney and liver function, for tests of immune function, and for detailed testing of virus levels.
- This visit will take approximately 1 hour.

Final study visit and unscheduled study visits

This visit will occur approximately 8 weeks after day 0 of treatment cycle 8. If you stop participating in the study prematurely, then you will be asked to come to clinic for this final study visit approximately 6-10 weeks after day 0 of the last treatment cycle. This visit will include a leukapheresis procedure.

- You may have a physical exam and will be asked about your health and medicines you have taken since the previous visit or are taking now.
- Approximately 8 tablespoons of blood will be drawn for routine tests of blood cell, kidney, thyroid, and liver function, for tests of immune function, and for detailed testing of HIV levels.
- The leukapheresis samples obtained will be stored for detailed tests of HIV levels and for additional tests of immune function.
- This visit will take approximately 4 hours.

IRB NUMBER: STUDY20180025
IRB APPROVAL DATE: 4/14/2020
IRB EFFECTIVE DATE: 4/14/2020
IRB EXPIRATION DATE: 4/13/2021

You may be asked to return to clinic to have a repeat blood draw in order to confirm a laboratory results at a time that is not part of the original schedule. These unscheduled visits typically last 30 minutes or less, and will involve only a few questions and a routine blood draw.

In the unlikely event that we detect through laboratory testing that your immune system has developed antibodies against the study drug, you may be asked to return to the clinic for a blood draw, a review of any medical issues you have had in the meantime, and a routine physical examination. If the lab tests show that the antibodies are still in your system, these visits may be required approximately every 3 months for up to a year. These visits typically last 30 minutes or less.

Leukapheresis

Your participation in this study will involve the collection of white blood cells by a process call leukapheresis. During leukapheresis, blood is removed from either peripheral veins or a central venous catheter and passed through a blood cell separator (apheresis machine). For this study, veins are used. Blood is removed from a vein in one arm with passage of the blood through the cell separator, the cells are removed, and the remainder is returned to a vein in the other arm. This machine uses a centrifuge to separate the blood into its various components (red blood cells, white blood cells, cells that help the blood to clot, and plasma). The white blood cells will be collected in a sterile bag and the rest of the blood components will be given back to you through the veins in your arm. White blood cells are the cells which fight infection. During the collection you will receive an anticoagulant (a drug to prevent the clotting of blood) which will be ACDA (citrate) and/or heparin. The anticoagulant is added to keep your blood from clotting during this procedure. The procedure could take up to 4 hours. Your samples will be collected for this study and may be stored indefinitely and used in other research protocols.

You will come to the Special Immunology Unit and be taken to the Seidman Ambulatory Stem Cell Transplant Unit at University Hospitals Cleveland Medical Center.

Four to eight weeks after the leukapheresis, you will return to the Clinical Trials Unit where you will undergo a brief history and, if indicated, a targeted physical examination. Blood will be taken for immune and viral studies.

USE OF YOUR STORED SAMPLES

During your participation in this study, blood will be collected by standard blood drawing techniques. In addition, blood components will be collected by leukapheresis. Some blood samples will be used for this research study. We will also store some of your blood samples. These samples will be kept and used in future research to learn more about HIV, the immune system and/or other medical conditions.

Generally, the results from the research done with your stored samples will not be given to your private doctor and will not be put in your medical record. This is because the test results, unlike routine medical testing, may be experimental or preliminary. The relevance of these tests to your care may be unknown.

IRB NUMBER: STUDY20180025
IRB APPROVAL DATE: 4/14/2020
IRB EFFECTIVE DATE: 4/14/2020
IRB EXPIRATION DATE: 4/13/2021

Your stored samples most of the time will be labeled with a code (such as a number) that only the study team can link to you or with an identifier such as your name. Any identifying information about you will be kept confidential to the extent permitted by law.

FUTURE STUDIES

In the future, other investigators (at CWRU or elsewhere) may wish to study your stored samples for studies unrelated to the current protocol. When the study team shares your materials, they may share it with no identifying information or with a code. Some information about you, such as your gender, age, health history, or ethnicity may also be shared with other investigators.

Any future research using your samples in studies unrelated to the current protocol will be reviewed by the investigator's Institutional Review Board (IRB), a special committee that oversees medical research studies to protect the rights and welfare of human subject volunteers.

Your stored materials will be used only for research and will not be sold. The research done with your materials may be used to develop new products in the future but you will not receive payment for such products.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 20 people will take part in this study.

HOW LONG WILL I BE IN THIS STUDY?

You will be in this study for up to 80 weeks.

WHY WOULD THE DOCTOR TAKE ME OFF THIS STUDY EARLY?

The study doctor may need to take you off the study early without your permission if you miss study visits, if you have not been compliant with your antiretroviral treatment regimen or with your IL-2 treatments, or if you become pregnant.

The study doctor may also need to take you off the study drug without your permission if you develop side effects that cannot be controlled, if it is determined that your participation in the study is no longer in your best interest, or upon instructions from the sponsors of the study or from the Food and Drug Administration, the Institutional Review Board, or any other regulatory agency involved in the oversight of this study.

IL-2 treatment may temporarily increase levels of HIV in blood. This is possibly the way by which IL-2 can decrease the size of the reservoir. If the study staff sees that your viral load has gone up, you will be asked to repeat your blood test to see if your viral load has returned to levels below levels of detection. If your viral load remains elevated above 200 copies/mL on three consecutive measurements after any one cycle of IL-2 administration and you have been compliant with your antiretroviral treatment regimen, you may decide to discontinue participation in the study.

If you must stop taking the study drug before the study is over, the study doctor may ask you to continue to be part of the study and return for some study visits and procedures.

If you must permanently stop taking IL-2 before your study participation is over, the study staff will discuss other options that may be of benefit to you. After you have completed study participation, the study will not be able to continue to provide you with IL-2 that you received on the study.

WHAT ARE THE RISKS AND/OR DISCOMFORTS RELATED TO THE STUDY?

Your participation in this study will require a minimum of thirty visits to the Clinical Trials Unit as indicated above. These visits will involve physical assessments and blood tests for research and safety monitoring and may be time consuming and inconvenient. The major risks of the study are primarily those associated with IL-2 therapy.

Potential Risks associated with IL-2 therapy

The IL-2 used in this study may have side effects, some of which are listed below. Please note that these lists may not include all the possible side effects that could be seen with IL-2. These lists include the more serious or common side effects with a known or possible relationship. If you have questions concerning additional side effects, please ask the Clinical Trials Unit staff.

The most common side effects include:

- Flu-like symptoms such as fever, chills, feeling tired
- Nausea
- Rash
- Redness or hard lumps in the areas where IL-2 is injected; the lumps may take weeks to months to resolve.

Persons who receive IL-2 may develop abnormal function of the thyroid gland. This has happened to participants who are enrolled in this research study.

Abnormal function of the thyroid gland can cause fatigue, changes in bowel habits, skin and hair changes, slow or fast heartbeat, irregular heart rhythm, swelling of the thyroid gland, intolerance to cold or heat, changes in sleep pattern, appetite changes, and changes in body weight and composition, including weight gain or weight loss. In some cases, thyroid abnormalities in persons who received IL-2 have been reversible, but it is not known how often that happens. Thyroid abnormalities can be treated with medications. If you develop thryroid abnormalities, it is possible that you will be required to take medication for life.

Your thyroid function will be measured at the beginning of the study and at the beginning of each IL-2 cycle. At the same time, levels of antibodies against the thyroid in your blood will be measured. Antibodies are proteins made by the immune system that help defend against substances or particles that may be harmful, such as bacteria, but occasionally may be directed against a person's own tissues. Persons who have antibodies against the thyroid appear to be more likely to develop thyroid abnormalities during IL-2 treatment. If any of these test results becomes abnormal at any time, you will be asked to discontinue the IL-2 treatment.

Other side effects include:

- Vomiting, loose or watery stools, stomach pain, loss of appetite
- Joint or muscle aches, sweats
- Abnormal liver tests, which may mean liver damage
- Skin peeling or itching
- Sores in the mouth
- Flushing
- High blood sugar
- Anxiety, sleeping problems, change in mood, headache, dizziness
- Abnormal kidney function
- Swelling, which is caused by leakage of fluid from the blood vessels into the surrounding tissues
- Low blood pressure and fast heartbeat
- Decreases in the amount of certain elements in the blood (calcium, magnesium, phosphate, sodium)
- A decrease in the number of red blood cells, which may cause weakness, dizziness, and fatigue
- A decrease in the number of platelets, which help the blood to clot
- Shortness of breath, cough, wheezing and nasal/sinus stuffiness
- Development of antibodies against IL-2
- Inflammation of the gallbladder

The following side effects have occurred infrequently:

- Severe allergic reactions, with breathing/swallowing difficulties and hives
- Serious heart problems, which may include angina (chest pain), abnormal heart rhythm, heart attacks or
  decreased pumping ability
- Development or worsening of certain auto-immune/inflammatory diseases
- Serious neurological or psychiatric side effects (for example, delerium, mania, depression, attempted suicide, loss of consciousness, convulsions, memory loss, swelling of the brain, or nerve disorders, such as disease of the nerve supplying the eye)
- Damage to an area of the brain or to other organs, caused by low blood supply
- Kidney failure (which may be fatal)
- Worsening of viral hepatitis and liver failure
- Blood clot formation in a vein or artery.
- Pancreatitis, an inflammation of the pancreas.
- Development or worsening of Kaposi’s sarcoma
- Significant bacterial infections
- Death

Il-2 may lead to a temporary increase in the amount of HIV in your blood. With combination ARV medications, that is less likely to occur.

Sometimes, when people who have received IL-2 are given a certain type of dye for X-ray examinations, a reaction may occur that includes symptoms such as fever, chills, nausea, vomiting, itchiness rash, diarrhea, low blood pressure, swelling, and low urine output.

IRB NUMBER: STUDY20180025
IRB APPROVAL DATE: 4/14/2020
IRB EFFECTIVE DATE: 4/14/2020
IRB EXPIRATION DATE: 4/13/2021

Risks associated with blood drawing

Blood drawing from a vein may cause some discomfort, and occasionally some bleeding or bruising at the site. Rarely, people may faint while having blood drawn. Blood drawing will not exceed 450 milliliters (1 pint) over any 8-week period, which is within the safety guidelines for blood drawing practiced at the Clinical Trials Unit.

Risks associated with Stored Specimens

The greatest risk is the unplanned release of information from your medical records. The chance that this information will be given to an unauthorized person without your permission is very small. Possible problems with the unplanned release of information include discrimination when applying for insurance and employment. Similar problems may occur if you disclose information yourself or agree to have your medical records released.

Risks associated with leukapheresis

The potential risks of peripheral intravenous catheter placement for leukapheresis include:

- Pain
- Anxiety
- Bruising, including a form of bruising called a hematoma
- Light-headedness
- Fainting
- Chills
- Very rarely, infection

You may also have a greater chance of bleeding for a few hours after leukapheresis, since a blood thinner (heparin or citrate) is used in the leukapheresis machine, to which you will be connected through IV lines. Leukapheresis allows only immune cells to be removed from your blood, while re-circulating and giving back your red blood cells. Side effects are uncommon.

In rare cases, if blood in the cell separator (apheresis machine) clots (thickens) or the centrifuge stops working, the leukapheresis may be stopped and a loss of up to one half (½) pint of blood could result. If this happens we will ask you not to donate blood for at least 2 months. In extreme cases, subjects may require a blood transfusion.

Potential risks involved in this type of blood donation process are usually minimal and may include:

- A sour taste in the mouth,
- A lowering of your blood calcium levels,
- Tingling/numbness around the mouth and face
- Nausea
- Vomiting
- Fainting
- Blood loss
- Low platelets
- Anemia
- Infection
- Low potassium
- Bleeding

- Heparin induced clotting
- Fluid overload

These are temporary effects and may be reversed by the addition of fluid during the leukapheresis process.

In extremely rare cases complications could include introduction of air into the blood stream, seizures, or death. The numbness/tingling, nausea, vomiting and seizures may be due to the anticoagulant ACD-A used in the procedure. Using the least possible amount of anticoagulant minimizes these effects. Bleeding may occur, especially after the procedure. The risk of infection that can occur from the needle insertion into the arm is minimized by the use of gloves and an aseptic cleaning procedure. The introduction of air into the blood stream is prevented by air detectors and alarms in the cell separator, which are monitored by a trained technologist or nurse.

You should discuss these risks and side effects with the study doctor /study nurse. There also may be other risks and side effects that we cannot predict. Other procedures may be performed to make side effects less serious and uncomfortable. Many side effects go away shortly after the blood draw is stopped, but in some cases side effects can be serious or long lasting or permanent.

ARE THERE RISKS RELATED TO PREGNANCY?

IL-2 has not been studied adequately in pregnant women. Animal studies do not suggest that IL-2 causes birth defects, but it is not known whether or not this is true in humans. Because it is not known whether IL-2 may be harmful during pregnancy, you will not be allowed to participate in the study if you are a woman who can become pregnant.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

If IL-2 treatment decreases the size of the HIV reservoir, this might be of some benefit to you but such a benefit is uncertain. It is important to recognize that although there have been numerous studies evaluating the risks and benefits of IL-2, it remains an experimental medication in the treatment of HIV infection, and it is possible that taking this therapy could make things worse. In that situation, having taken no treatment would have been better than participating in this trial.

Another possible benefit for you from this study is a more intensive immunologic and virologic monitoring of your HIV-1 infection than usually done in clinics. The clinical significance of some of these test results is still unknown, however. Additionally, what we learn from this study may help us to improve the treatment of other people who are infected with HIV.

IRB NUMBER: STUDY20180025
IRB APPROVAL DATE: 4/14/2020
IRB EFFECTIVE DATE: 4/14/2020
IRB EXPIRATION DATE: 4/13/2021

WHAT ARE ALTERNATIVES TO PARTICIPATION?

An alternative to participating in this study is simply to remain on your licensed antiretroviral combination treatment and continue to be followed by your private physician over time.

WILL I RECEIVE ANY PAYMENT?

You will receive compensation for your time according to the type of study visit, as follows:

- You will receive $40 for the screening visit, if you live less than 15 miles away from the clinic. You will receive $50 for the screening visit, if you live 15 miles or more away from the clinic.
- You will receive $60 for the visits on day 0 of cycles 1, 4, and 8 ($180 total for those 3 visits), if you live less than 15 miles away from the clinic. You will receive $70 for the visits on day 0 of cycles 1, 4, and 8 ($210 total for those 3 visits), if you live 15 miles or more, away from the clinic.
- You will receive $210 for each visit that includes a leukapheresis, if you live less than 15 miles away from the clinic. There are two scheduled visits that include a leukapheresis: the initial leukapheresis visit (done before you start study treatment) and the final or premature discontinuation visit ($420 total for those 2 visits if leukapheresis is done at both of them). You will receive $220 for each leukapheresis visit ($440 total for those 2 visits if leukapheresis is done at both of them), if you live 15 miles or more away from the clinic.
- You will receive $40 for each of the other study visits, if you live less than 15 miles away from the clinic. You will receive $50 for each of the other study visits, if you live 15 miles or more away from the clinic (the total will vary because you may be required to return for unscheduled visits).

Your parking will be paid for each study visit. The mileage for the above determinations of compensation is the round-trip distance from your residence to the Foley Building, 2061 Cornell Road, Cleveland, Ohio. The mileage will be determined by an AIDS Clinical Trials Unit research nurse per Google Maps. If you travel by public transportation, you will be provided with 2 one-trip bus passes.

To receive payment you must agree to complete a W-9 form, which requires you to provide an address and social security number to the accounting department. This payment to you may be considered taxable income by the IRS. Subjects will be issued a 1099-Misc form only if payment exceeds $600 in a fiscal year from all studies in which you are participating. If you are an employee of Case Western Reserve University, you will be asked to provide your employee ID number, and compensation provided to you will be reported to the Payroll Department.

ARE THERE ANY COSTS FOR MY PARTICIPATION IN THE STUDY?

There will not be any direct cost to you for participating in the study.

NEW FINDINGS

You will be told of any new information learned during the study that might cause you to change your mind about staying in the study. At the end of the study, you will be told when study results may be available and how to learn about them.

WHAT IF I AM INJURED?

If injury occurs as a result of your involvement in this research, medical treatment is available from University Hospitals Cleveland Medical Center or another medical facility but you/your medical insurance will be responsible for the cost of this treatment. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered a "research injury". There are no plans for payment of medical expenses or other payments, including lost wages, for any research related injury. To help avoid injury, it is very important to follow all study directions.

WHAT ABOUT CONFIDENTIALITY?

You will be consented in a private exam room within the Special Immunology Unit at University Hospitals Cleveland Medical Center by Dr. Lederman or one of the research nurses. All laboratory specimens will be identified by coded number only to maintain your confidentiality. The study-required samples will be kept in a secure area in Dr. Lederman's Immunology Assessment Laboratory (2109 Adelbert Road, BRB Room 1048B) and only the research team will have access to the samples. The samples and data are identified only by code numbers and only limited research staff has access to the list of participants. This access is password protected and can be monitored.

All records will be kept locked. All computer entry and networking programs will be done with coded numbers only. Information about your participation will not be shared with individuals who are not directly involved with the research participant or as identified in the privacy of protected health information section below.

If the study team decides at any time that some of the doses needed for each cycle will be shipped rather than delivered to you in person, your identity will be known to the shipping company. In that event, you may be required to show proof of identity and/or to sign your name in order to receive the shipment.

Privacy of Protected Health Information

The Health Insurance Portability & Accountability Act (HIPAA) is a Federal law that helps to protect the privacy of your health information and to whom this information may be shared within and outside of University Hospitals. This Authorization form is specifically for a research study entitled "HIV Reservoir Reduction with Interleukin-2" and will tell you what health information (called Protected Health Information or PHI) will be collected for this research study, who will see your PHI and in what ways they can use the information. In order for the Principal Investigator, Dr. Benigno Rodriguez, and the research study staff to collect and use your PHI, you must sign this authorization form. You will receive a copy of this signed Authorization for your records. If you do not sign this form, you may not join this study. Your decision to allow the

use and disclosure of your PHI is voluntary and will have no impact on your treatment at University Hospitals. By signing this form, you are allowing the researchers for this study to use and disclose your PHI in the manner described below.

Generally the Principal Investigator and study staff at University Hospitals and Case Western Reserve University who are working on this research project will know that you are in a research study and will see and use your PHI. The researchers working on this study will collect the following PHI about you: Your name, your medical history, a list of your current medications, you will have a physical examination and you will be given IL-2. This PHI will be used to find out if IL-2 will decrease the number of cells in the body that contain HIV capable of infecting new cells. Your access to your PHI may be limited during the study to protect the study results.

Your PHI may also be shared with the following groups/persons associated with this research study or involved in the review of research: Gilead Sciences, Inc. (the sponsor); other staff from the Principal Investigator's medical practice group; University Hospitals, including the Clinical Research Center and the Law Department; Government representatives or Federal agencies, when required by law.

Your permission to use and disclose your PHI does not expire. However, you have the right to change your mind at any time and revoke your authorization. If you revoke your authorization, the researchers will continue to use the information that they previously collected, but they will not collect any additional information. Also, if you revoke your authorization you may no longer be able to participate in the research study. To revoke your permission, you must do so in writing by sending a letter to:

Dr. Benigno Rodriguez
2061 Cornell Road, 4th Floor
Foley Building
Cleveland, OH 44106

If you have a complaint or concerns about the privacy of your health information, you may also write to the UH Privacy Officer, Management Service Center, 3605 Warrensville Center, MSC 9105, Shaker Heights, OH 44122 or to the Federal Department of Health and Human Services (DHHS) at DHHS Regional Manager, Office of Civil Rights, US Department of Health and Human Services Government Center, JF Kennedy Federal Building, Room 1875, Boston, MA 02203. Complaints should be sent within 180 days of finding out about the problem.

The researchers and staff agree to protect your health information by using and disclosing it only as permitted by you in this Authorization and as directed by state and Federal law. University Hospitals is committed to protecting your confidentiality. Please understand that once your PHI has been disclosed to anyone outside of University Hospitals, there is a risk that your PHI may no longer be protected; however other Federal and State laws may provide continued protection of your information.

U.S. NATIONAL INSTITUTES OF HEALTH (NIH) CLINICAL TRIAL DATABASE

A description of this clinical trial will be available on http:///www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website

will include a summary of the results. You can search this website at any time to find out information about the trial and basic results.

WHAT DO I DO IF I HAVE QUESTIONS OR PROBLEMS?

If you have questions about this research study, please contact Dr. Benigno Rodriguez at 216-844-2342 between the hours of 9am-5pm daily from Monday through Friday. After hours please call 216-207-7244, enter pager number 35333, and then enter the phone number where you can be reached. The research nurse on-call is available 24 hours a day, 7 days a week and will return your call.

SUMMARY OF YOUR RIGHTS AS A PARTICIPANT IN A RESEARCH STUDY

Your participation in this research study is voluntary. Refusing to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed. In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating. If you experience physical injury or illness as a result of participating in this research study, medical care is available at University Hospitals Cleveland Medical Center (UHCMC) or elsewhere; however, UHCMC has no plans to provide free care or compensation for lost wages.

DISCLOSURE OF YOUR STUDY RECORDS

Efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. The University Hospitals Cleveland Medical Center Institutional Review Board may review your study records. If this study is regulated by the Food and Drug Administration (FDA), there is a possibility that the FDA might inspect your records. In addition, for treatment studies, the study sponsor and possibly foreign regulatory agencies may also review your records. If your records are reviewed your identity could become known.

CONTACT INFORMATION

_____ has described to you what is going to be done, the risks, hazards, and benefits involved. The Principal Investigator, Dr. Benigno Rodriguez, can also be contacted at 216-844-2432. If you have any questions, concerns or complaints about the study in the future, you may also contact them later.

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research-related injury; or other human subject issues, please call the University Hospitals Cleveland Medical Center's Research Subject Rights phone line at (216) 983-4979 or write to: President, Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 1400, Cleveland, Ohio, 44106-7061.

IRB NUMBER: STUDY20180025
IRB APPROVAL DATE: 4/14/2020
IRB EFFECTIVE DATE: 4/14/2020
IRB EXPIRATION DATE: 4/13/2021

Title of Project: HIV Reservoir Reduction with Interleukin-2
Principal Investigator: Dr. Benigno Rodriguez

SIGNATURE

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

x		
Signature of Participant	Date	Time
x		
Printed Name of Participant		
x		
Signature of Witness	Date	Time
x		
Printed Name of Witness		
x		
Signature of person obtaining informed consent	Date	Time
x		
Printed name of person obtaining informed consent		