UNIVERSITY OF CALIFORNIA LOS ANGELES
CONSENT TO PARTICIPATE IN RESEARCH

A single armed, unblinded, non-randomized feasibility study of hematopoietic stem cell infusion following a conditioning regimen of total lymphoid irradiation (TLI) and anti-thymocyte globulin (ATG) in patients with a pre-existing, well-functioning HLA-identical kidney transplant

Consent form for RECIPIENT Participants

INTRODUCTION

Dr. Jeffrey Veale and associates from the Department of Urology at the University of California, Los Angeles are conducting a research study. This study is being funded by OneLegacy Foundation.

WHY AM I BEING INVITED TO TAKE PART IN A RESEARCH STUDY?

We invite you to take part in a research study because you received a kidney transplant from a sibling whose HLA makers are identical to yours.

WHAT SHOULD I KNOW ABOUT A RESEARCH STUDY?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.
- You can discuss this study with friends and family.
- You can also discuss it with your health care doctor or request a second opinion.

WHY IS THIS RESEARCH BEING DONE?

The purpose of this study is to learn if an investigational treatment will allow kidney transplant recipients to better accept their new kidney and stop immunosuppressive medicines such as tacrolimus, mycophenolate mofetil, and steroids (medications that help prevent graft rejection). “Investigational” means that the treatment has not been approved by the US Food and Drug Administration (FDA) or other regulatory authorities.

The investigational treatment being tested is an infusion of donor blood stem cells following treatment with a drug called Rabbit Anti-Thymocyte Globulin (also known as rATG or Thymoglobulin) and radiation therapy (known as total lymphoid irradiation or TLI) to the lymph nodes and spleen. Both rATG and TLI weaken your immune system’s response to your transplanted kidney and blood stem cells. The blood stem cells you receive will be donated by the same sibling who previously donated their kidney to you.

rATG is an antibody against a type of immune cell called the T cell. Infusion of rATG results in destruction of T cells, which will lower the immune system.

You will start the investigational treatment within 3 months and up to 5 years after your kidney transplant. This treatment allows immune cells from the donor and recipient to live side by side, a condition referred to as “mixed chimerism.” Researchers think that mixed chimerism is responsible for creating a state of “tolerance” in kidney transplant recipients in which all immunosuppressive medications can be stopped without rejection of the transplanted kidney.

With current standard treatments for transplants, up to 10% of patients will experience rejection during the first year. Most rejections can be treated successfully, but about 30% of patients eventually lose their kidney at the end of 10 years. Kidney transplant patients need to take immunosuppressive medications for life and these medications can have serious negative side effects, such as increased risk of infections, cancer, high blood pressure, diabetes, high cholesterol levels, and heart disease. One of these medications can even lead to a recurrence of kidney failure.

In this study, we will test if the investigational treatment allows patients to stop immunosuppressive medications after their kidney transplant. We will also determine if the investigational treatment has an impact on the rate of kidney rejection and the side effects of immunosuppressive medications. It is possible that some patients might eventually be able to stop their immunosuppressive medications altogether. However, it is also possible that the investigational treatment will be less effective at preventing rejection and cause new and worse side effects.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

20 people will take part in this study at UCLA (10 recipients and 10 donors).

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

Before you begin the study:
You will undergo routine teaching, assessment by the Nephrology team, laboratory testing, and procedures to find out if you are a good candidate for stem cell transplantation. Once you complete your evaluation and your doctors confirm you are a good candidate for stem cell transplantation, you may be considered for the study. To participate in this study, you must have a living donor sibling who previously donated their kidney to you. If an appropriate living donor is identified and cleared for stem cell donation you may qualify to participate.

You will be asked to sign and date this consent form before any research study tests are done. Once the consent form has been signed, the study doctor will do additional screening tests to find out if you can be in the research study. Completing the screening tests does not mean that you can be in the research study. It is possible that you will not qualify to be in this research study based on your screening tests. If this happens, your study doctor will tell you why you cannot take part in this study.

The following procedures, which are not part of your routine care, will be done to screen you for the study.

- You will have blood taken for stem cell transplant safety tests to make sure you are a good candidate for stem cell transplant. These tests will screen you for different diseases. In addition, you will have blood taken for research tests. The amount of blood to be drawn will vary at different visits but it will never be more than approximately eight tablespoons of blood. The amount of blood collected for research be approximately 6 tablespoons of blood.
- You will have an appointment with the BMT doctors to determine if it is safe to proceed with stem cell transplant.
- You will have an appointment with Radiation Therapy doctors to determine if it is safe to proceed with TLI.
- You may need to do a chest x-ray, depending on the date of your last x-ray.
- You may need to do an electrocardiogram (measures your heart's electrical activity), depending on the date of your last electrocardiogram.
- You may need to do an echocardiogram (an ultrasound of your heart), depending on the date of your last echocardiogram.
- You will complete one questionnaire that asks about how you are feeling, your activity level, and how your transplantation affects your life. The questionnaire is called the Modified Transplant Symptom Occurrence and Symptom Distress Scale – Revised 59 (MTSOSD-R 59).
- You may undergo a colonoscopy, pap smear, or mammogram depending on your current symptoms and medical history to make sure you are a good candidate for stem cell transplant.

During the study:

Overview:

If you qualify and enroll in the study, you will receive an investigational treatment with stem cell transplantation following a regimen of rATG and TLI. Stem cell transplantation is not a routine treatment for pre-existing kidney transplant recipients. It is therefore considered investigational for this study.

You will receive the stem cell transplantation after completing a rATG and TLI regimen. You will receive your first dose of rATG on Day 0 and will continue to receive rATG for 4 more days after your first dose (total of 5 doses of rATG). rATG will be given through a peripheral venous catheter (a small tube in a small vein). rATG may be held for severe neutropenia – having lower-than-normal levels of neutrophils (a type of white blood cell) in your blood.

You will also begin receiving TLI on Day 0 and will receive 10 radiation treatments over 11 days. It is possible that delays in administration of TLI may also be necessary due to your clinical condition (for example, significant post-operative pain, nausea and/or vomiting, etc.).

“Port” x-rays help determine the field shape (area to be radiated) of each section is correct. You will receive 1 set of “Port” x-rays for the duration of the treatment (at least 2 x-rays per area, so at least 6 Port x-rays per day).

“Isocenter” x-rays help to verify the center of each area and are taken in a pair of 2 x-rays as well. This is to ensure the middle, or what we call isocenter corresponds with the plan. It helps to determine if you need to be moved a few millimeters and in which direction you need to be adjusted. 1 group set of Isocenter x-rays will be taken daily (at least 2 x-rays per area, so at least 6 Isocenter x-rays per day).

Should there be delays or interruptions in TLI due to any cause, then the radiation schedule will be adjusted appropriately based on clinical judgment as will the clinical assessments, labs, and administration of stem cells. TLI doses will resume according to the same schedule (i.e. excluding holidays and weekends). The schedule for the infusion of the cellular product will be adjusted as needed to occur on the same day as the completion of TLI. If, however, the interruption exceeds 3 consecutive days, you may need to be withdrawn from the treatment protocol.

After TLI is complete, you will receive two infusions of your donor's blood-forming and immune cells. The infusions are done approximately one hour apart on the same day. Each infusion contains a different type of cell from your donor. The first infusion will consist of donor blood-forming stem cells (CD34+) delivered to the bedside in a bag which is then connected to the central catheter. The second infusion will consist of donor immune cells (CD3+) in a syringe which is then injected into the central catheter. These cells will have been processed on a device that is approved by the FDA. This is an investigational treatment.

After your stem cell transplant, you will be treated with routine anti-rejection medications (tacrolimus, mycophenolate mofetil, and corticosteroids) and medications to prevent infections (trimethoprim-sulfamethoxazole, valganciclovir or ganciclovir, acyclovir, letermovir, nystatin, and possibly fluconazole). However, you will take acyclovir for a longer time than most kidney transplant recipients to prevent shingles.

Throughout the study, you will have blood tests to monitor the levels of creatinine in your blood. Creatinine is a measure of kidney function. If your doctors notice a significant (more than 30%) and unexplained change in your creatinine level, you may be asked to undergo a kidney biopsy. During a kidney biopsy, your doctor will place a thin needle through your skin into the kidney transplant to remove a small piece of tissue for examination. The biopsy is done under ultrasound (sonar) guidance and local anesthesia (numbing medicine). This will help your doctors determine if your body is rejecting your transplanted kidney. Kidney biopsies that are done when your doctors suspect rejection are part of your routine care. You will be asked to provide extra blood for research tests if your doctors suspect rejection.

If your chimerism test shows no evidence of donor stem cells at Week 12, you may be asked to complete a research bone marrow exam. This is not part of your routine care. The exam has two steps. The first step is bone marrow aspiration, where the doctor will

put a needle into the back of your hip bone and pull liquid bone marrow cells up into a syringe. The second part of the exam is a bone marrow biopsy. During the biopsy, the needle will be turned into your hip bone to get a solid piece of your bone marrow. Before the needle is inserted for aspiration and biopsy, you will receive a local anesthetic (numbing medicine) to lessen pain and discomfort of the needle. The exam usually takes around 10 minutes and is well tolerated. The bone marrow will be examined for the type and quantity of cells and the percentage of you and your sibling's cells (chimerism).

If you participate in this study, you will need to come to UCLA for follow-up appointments for 4 years after your transplant. What will happen during these visits is described in the section below.

Before Your Stem Cell Transplant

Before your stem cell transplant, you will return for two visits with the Radiation Therapy team and one visit with the BMT team:

1) Visit 1 – within 12 weeks
    a. You will have an appointment with the BMT doctors to determine if it is safe to proceed with stem cell transplant
    b. You will have an appointment with the Radiation Therapy team for consultation and planning before the stem cell infusion
2) Visit 2 – within 4 weeks of your scheduled transplant. During this visit, the Radiation Therapy team will plan your radiation fields (sites where radiation will be received) for TLI. To map your radiation fields, you will undergo a CT scan during this visit.

Day 0 to Day 11 (day of stem cell transplantation)

Before your stem cell transplant infusion, you will need to come into the clinic for at least 10 days. On Days 0 to 4 and Days 7 to 11, doctors will perform a physical exam, a review of your current medications, a review of symptoms and side effects that you are experiencing, and safety blood and urine tests.

You will receive your first dose of rATG on Day 0 and will continue to receive rATG for 4 more days after your first dose (total of 5 doses of rATG). After the final dose of rATG on Day 4, your study doctor will give you a prescription for prednisone. You will take prednisone on your own for up to 6 days. You will take a different dose of prednisone every day. A medication diary will be provided to document the prednisone doses. Please bring this diary with you to every visit.

You will begin radiation therapy once a day for 5 consecutive days on Day 0 to Day 4 and Day 7 to 11. For each radiation therapy session – including Day 1 – you will have 3 sets of x-rays taken to locate where to deliver the radiation treatment. You will have a visit with a radiation oncologist on Day 3 or 4.

You will have a two-day break from radiation treatment (Day 5 and Day 6).

Since you need to come into the clinic often, it is recommended that you live near the hospital until Day 14. This will also help you access emergency care quickly if you need it.

After your stem cell transplant infusion, you may be treated with several immunosuppressive medications as part of your transplant care. These may include:
(1) Corticosteroids
(2) Mycophenolate Mofetil (MMF)
(3) Tacrolimus

You may also take several routine medications that help prevent infection, such as TMP/SMX and Nystatin. In addition, valganciclovir or ganciclovir, acyclovir, and fluconazole may be given to you depending on your infectious disease history and based on the tests you took prior to your transplant. All these medications may be part of your routine care. However, the length of time you need to take acyclovir is longer for this study because you will receive investigational treatment. Your doctor will decide which of these medications you need.

The following may take place each day:

Day 0
- Physical exam with the Nephrology, Radiation Oncology, and Bone Marrow Transplant (BMT) doctors.
- Review of medications you are taking and side effects
- Blood tests and tacrolimus blood test for safety. Approximately 1 tablespoon of blood will be collected.
- rATG infusion
- Undergo TLI, including 1 set of Port x-rays and 1 group set of Isocenter x-rays

Day 1
- Physical exam with the Nephrology and/or BMT doctors if needed
- Review of medications you are taking and side effects
- Safety blood and urine tests and tacrolimus blood test if needed. Approximately 1 tablespoon of blood will be collected.
- rATG infusion
- TLI, including 1 group set of Isocenter x-rays

Day 2
- Physical exam with the Nephrology and/or BMT doctors if needed
- Review of medications you are taking and side effects
- Safety blood and urine tests and tacrolimus blood test if needed. Approximately 1 tablespoon of blood will be collected.
- rATG infusion
- TLI, including 1 group set of Isocenter x-rays

Day 3

- Physical exam with the Nephrology, Radiation Oncology doctors, and/or BMT doctors if needed
- Review of medications you are taking and side effects
- Safety blood and urine tests and tacrolimus blood test if needed. Approximately 1 tablespoon of blood will be collected.
- rATG infusion
- TLI, including 1 group set of Isocenter x-rays

Day 4
- Physical exam with the Nephrology and BMT doctors.
- Review of medications you are taking and side effects
- Safety blood and urine tests and tacrolimus blood test if needed. Approximately 1 tablespoon of blood will be collected.
- rATG infusion
- TLI, including 1 group set of Isocenter x-rays

Day 7
- Physical exam with the Nephrology and/or Bone Marrow Transplant (BMT) doctors if needed.
- Review of medications you are taking and side effects
- Safety blood and urine tests and tacrolimus blood test if needed. Approximately 1.5 tablespoons of blood will be collected.
- An infectious disease test called CMV DNA PCR will be performed.
- Undergo TLI, including 1 group set of Isocenter x-rays

Day 8
- Physical exam with the Nephrology and/or BMT doctors.
- Review of medications you are taking and side effects
- Safety blood and urine tests and tacrolimus blood test if needed. Approximately 1 tablespoon of blood will be collected.
- TLI, including 1 group set of Isocenter x-rays

Day 9
- Physical exam with the Nephrology and/or BMT doctors if needed
- Review of medications you are taking and side effects
- Safety blood and urine tests and tacrolimus blood test if needed. Approximately 1 tablespoon of blood will be collected.
- TLI, including 1 group set of Isocenter x-rays

Day 10
- Physical exam with the Nephrology and/or BMT doctors if needed
- Review of medications you are taking and side effects
- Safety blood (approximately 1 tablespoon) and urine tests if needed
- TLI, including 1 group set of Isocenter x-rays

Day 11
- Physical exam with the Nephrology, Radiation Oncology, and/or BMT doctors.

- Review of medications you are taking and side effects
- Safety blood and urine tests and tacrolimus blood test. Approximately 1 tablespoon of blood will be collected.
- TLI, including 1 group set of Isocenter x-rays
- Infusion of investigational blood stem cells from your sibling donor, which is not routine. There will be two separate infusions, each containing a different type of cell from your donor. The first infusion will consist of donor blood-forming stem cells (CD34+) delivered to the bedside in a bag, which is then connected to your central catheter. The second infusion will consist of donor immune cells (CD3+) in a syringe which is then injected into the central catheter. The infusions will be done approximately one hour apart. The providers may give you pre-treatment medications such as acetaminophen (Tylenol), diphenhydramine (Benadryl), and dexamethasone (a type of steroid) before your infusions. These medications are given routinely to help reduce side effects of stem cell infusions.
- Begin taking routine medication called Mycophenolate Mofetil (MMF), which helps prevent graft rejection.

Day 14
- Physical exam with the Nephrology and/or BMT doctors.
- Review of medications you are taking and side effects
- Safety blood and urine tests. Approximately 1 tablespoon of blood will be collected.

Weeks 3 to 4
- Physical exam with the Nephrology and/or BMT doctors.
- Review of medications you are taking and side effects
- Safety blood tests and tacrolimus blood test and/or urine test
- Infectious disease tests called CMV DNA PCR, BK PCR, EBV PCR, and serum IgG. Less than one tablespoon of blood will be collected.

Weeks 5 to 12
- Physical exam with the Nephrology and/or BMT doctors.
- Review of medications you are taking and side effects
- Safety blood and urine tests and tacrolimus blood test
- An infectious disease test called CMV DNA PCR will be collected at Weeks 5, 7, 9, and 11. Infectious disease tests called BK PCR, EBV PCR, and serum IgG will be collected at Weeks 8 and 12. Less than one tablespoon of blood will be collected.
- On Weeks 6 and 10, you will complete blood tests for research and to measure chimerism. Approximately 6 tablespoons of blood will be collected.
- At Week 12, you will also be asked to complete one quality of life questionnaire.
- If your chimerism test shows no evidence of donor stem cells, you may be asked to complete a bone marrow exam, described in the Overview section. The bone marrow exam would need to be completed within 7 days of Week 12.

Months 4 to 6
You will come to clinic every week for blood tests to measure your tacrolimus levels.

You will also need to come to clinic every other week to see the Nephrology team. The following will be done during these visits:
- Physical exam
- Review of medications you are taking and side effects
- Safety blood and urine tests
- An infectious disease test called CMV DNA PCR
- Once a month, you will complete the following extra blood tests:
    - Infectious disease blood tests called EBV, BK, and IgG. Less than one tablespoon of blood will be collected.
    - Blood tests for research and to measure chimerism. Approximately 6 tablespoons of blood will be collected.

At Month 6, you will complete the following additional tests:
- Additional blood draws for research tests (less than one tablespoon)
- 1 quality of life questionnaire

Between month 3 and 6 after your transplant, some of the blood draws could be performed by your primary care provider at the study doctor's discretion. This will only be in certain cases and only if you have been approved to reside more than three hours from the study site. The study team will explain if this applies to you.

Months 7 to 12

You will come to clinic every other week to complete safety blood and urine tests and blood tests to measure your tacrolimus levels. The blood and urine tests will be done more frequently so that doctors can closely monitor your safety.

You will also need to come to clinic once a month to see the Nephrology team. The following procedures will be done during these visits:
- Physical exam
- Review of medications you are taking and side effects
- Safety blood and urine tests. Certain tests, such as CMV DNA PCR, EBV and serum IgG may be collected. Serum IgG will only be done through Month 7. Less than one tablespoon of blood will be collected.

At Months 8 and 10, you will complete the following additional tests during your monthly visit:
- Blood tests for research and to measure chimerism. Approximately 6 tablespoons of blood will be collected.

At Month 12, you will complete the following procedures in addition to what is listed above:
- Blood tests for research and to measure chimerism. Approximately 6 tablespoons of blood will be collected.
- 1 quality of life questionnaire

If your tests show that your transplanted kidney is not being rejected, and if your chimerism tests show the presence of donor immune cells that last at least 6 months, your doctors will tell you to stop taking tacrolimus in Month 12.

Months 13 to 15
You will come to clinic 1 time per week to complete safety blood tests. These tests are being done so that doctors can closely monitor your safety.

You will also need to come to clinic 1 time per month to see the Nephrology team. The following procedures will be done during these visits:
- Physical exam
- Review of medications you are taking and side effects
- Safety blood and urine tests

At your Month 15 visit, additional blood (approximately 6 tablespoons) will be drawn for research tests and chimerism testing.

Your doctor may also start screening you for cancer as part of your routine care as the immunosuppressive medications used to prevent rejection of your kidney transplant may increase the risk of cancer or make a pre-existing cancer worse. The frequency and type of screening depend on your sex and age. You should speak with your study doctor about what screening tests you need.

Months 16 to 48
You will come to the clinic every other week from Month 16 through Month 18 to complete safety blood tests. Starting at Month 19, you will come to clinic 1 time per month for safety blood tests. These tests are being done more often so that doctors can closely monitor your safety. If needed, laboratory tests can be drawn at a local laboratory, closer to your home.

You will need to come to clinic every other month to see the Nephrology team. The following procedures will be done during these visits:
- Physical exam
- Review of medications you are taking and side effects
- Safety blood and urine tests

During Months 18, 21, 24, 30, 36, 42, and 48, you will have additional blood (approximately 6 tablespoons) taken during your visit for research tests and chimerism testing.

At Months 24, 36, and 48, approximately 2 tablespoons of additional blood will be taken for research tests. An infectious disease test called BK PCR will also be taken. You will also be asked to complete 1 quality of life questionnaire.

Other Visits That May Be Required For Safety

If your doctors notice a significant (more than 30%) and unexplained change in your creatinine level, you may be asked to undergo a kidney biopsy.

HOW LONG WILL I BE IN THIS STUDY?

We expect that you will be in this research study for 4 years after the infusion of donor blood stem cells.

WHAT KINDS OF RISKS OR DISCOMFORTS COULD I EXPECT?

Known risks and discomforts:
The possible risks and/or discomforts associated with the research treatment and procedures described in this consent form are listed below. Your study doctor can help manage these side effects and prevent them from getting worse. It is important that you tell your study doctor all of your side effects in a timely manner so that he/she can help treat them.

1. Graft-versus-Host Disease: Receiving stem cells from another person may cause a reaction called graft-versus-host disease (GVHD). This happens if the donor cells you received attack your tissues. This is a common problem after bone marrow transplantation. In this study, we filter the donor stem cells to make them safer and lower your risk of GVHD. In addition, you will get a much smaller amount of immune cells compared to traditional bone marrow transplant patients. You will also take anti-rejection medicines for 1 year which lowers your chance of getting GVHD even more. When this treatment approach has been used at other transplant centers, there have been no cases of GVHD.

   There are two types of GVHD: (1) acute GVHD, which usually occurs in the first 100 days after your transplant, and (2) chronic GVHD, which occurs later. Signs and symptoms of acute GVHD include skin rashes, diarrhea (loose stools), and liver abnormalities. Chronic GVHD may affect multiple areas of your body including the skin, mouth, liver, stomach, and intestines. Both acute and chronic GVHD are treated with many of the same medicines used to prevent kidney rejection, including tacrolimus, MMF, and prednisone. GVHD may go away with treatment, but in some cases it may last for the rest of your life and may even be fatal (result in death). Although this is a possible risk, the chances of this happening are extremely low. In the over 40 patients who received the same investigational treatment at Stanford University, there were no cases of GVHD and no deaths from GVHD.

2. Total Lymphoid Irradiation (TLI): Radiation therapy has been used for decades in the treatment of cancer, auto-immune diseases and for rejection of kidney transplantation. Radiation therapy works by damaging the DNA within cells which leads to their death. The amount of radiation used in this study is 1/3rd of that used to treat cancer of the lymph nodes (also known as lymphoma).

Common side effects:

- Low white blood cell count (also known as neutropenia): this can lead to an increased risk of infection. It is temporary and will wear off in a couple of days to weeks after stopping radiation therapy.
- Low red blood cell count (also known as anemia): This can lead to fatigue. It is temporary and wears off in a couple of days to weeks after stopping radiation therapy.
  Nausea, some loss of appetite and weakness. These side effects should wear off in two to three days after radiation therapy is stopped. Subjects may receive routine anti-emetic medications to prevent or treat nausea. Please note that the most commonly prescribed anti-emetics are Ondansetron (Zofran), Granisetron (Kytril), Chlorpromazine (Compazine), and Metoclopramide (Reglan).

Less common side effects:

- Increased risk of viral infections. As part of this study, you will stay on antiviral medicines to reduce your risk of infection.

Rare but serious side effects:

- Increased risk of developing certain cancers, such as thyroid cancer, breast cancer, skin cancer, and lung cancer in smokers. Based on the published data from Stanford University, the risk of these “secondary” cancers is quite low. You will be monitored with routine cancer screening after your transplant. If you develop cancer, your doctor will assess you as needed.
- There is a risk of infertility due to irradiation to the ovaries or testes. Your testicles or ovaries will be shielded during TLI to reduce this risk as much as possible. The true risk of infertility is not known because of the already high infertility rate in patients with end-stage kidney disease.

3. Infusion of Blood Stem Cells: stem cell infusion is a common practice for the treatment of blood cancers. In this study, the infusion is not to cure cancer, but to create a “chimeric” state. A “chimeric” state is when your donor’s bone marrow and immune system exists within you. The co-existence of both immune systems allows for the development of “tolerance” and the lowering or end of immunosuppressive medications.

Common side effects:

- nausea
- flushing in
- headache

Less common side effects:

- fever
- cough

- wheezing

Rare but serious side effects:

- Low blood pressure
- Irregular heartbeat
- Acute renal failure

4. rATG

   Common side effects:

   - High blood pressure
   - Swelling of arms or legs
   - Increased heartbeat
   - Chills, fever, headache, pain, malaise
   - Rash
   - High potassium level in blood
   - Abdominal pain
   - Diarrhea
   - Nausea
   - Low white blood cell count
   - Low platelet count
   - Weakness
   - Shortness of breath
   - Infection in the bloodstream

   Less common side effects:

   - Dizziness

   Rare but serious side effects:

   - Difficulty swallowing
   - Hives, itching, rash
   - Puffiness or swelling of eyelids or around the eyes, face, lips, or tongue
   - Serum Sickness, which causes symptoms such as fever, general ill feeling, hives, itching, joint aches, joint stiffness, swollen lymph nodes and skin rash

5. Tacrolimus

   Serious but common side effects:

   - high blood sugar (diabetes): frequent urination, increased thirst or hunger, blurred vision, confusion, drowsiness, loss of appetite, fruity smell on your breath, nausea, vomiting, or stomach pain
   - kidney problems

- nervous system problems: headache, confusion, seizures, changes in your vision, changes in behavior, coma, tremors, numbness and tingling
- high levels of potassium in your blood
- high blood pressure
- changes in the electrical activity of your heart (QT prolongation)
- heart problems (myocardial hypertrophy): shortness of breath, chest pain, feeling lightheaded, feeling faint
- severe low red blood cell count (anemia)

Common side effects:

- infections in general, including cytomegalovirus (cmv) infection
- tremors (shaking of the body)
- constipation
- diarrhea
- headache
- stomach pain
- trouble sleeping
- nausea
- high blood sugar (diabetes)
- low levels of magnesium in your blood
- low levels of phosphate in your blood
- swelling of the hands, legs, ankles, or feet
- weakness
- pain
- high levels of fat in your blood
- high levels of potassium in your blood
- low red blood cell count (anemia)
- low white blood cell count
- fever
- numbness or tingling in your hands and feet
- inflammation of your airway (bronchitis)
- fluid around your heart

6. Cyclosporine

Common side effects:

- headache
- diarrhea
- heartburn
- gas
- increased hair growth on the face, arms, or back
- growth of extra tissue on the gums

- acne
- flushing
- uncontrollable shaking of a part of your body
- burning or tingling in the hands, arms, feet, or legs
- muscle or joint pain
- cramps
- pain or pressure in the face
- ear problems
- breast enlargement in men
- depression
- difficulty falling asleep or staying asleep

Serious but less likely or rare side effects:

- unusual bleeding or bruising
- pale skin
- yellowing of the skin or eyes
- seizures
- loss of consciousness
- changes in behavior or mood
- difficulty controlling body movements
- changes in vision
- confusion
- rash
- purple blotches on the skin
- swelling of the hands, arms, feet, ankles, or lower legs

7. Mycophenolate Mofetil (MMF)

Serious but common side effects:

- Low white blood cell counts (especially neutrophils) – Neutrophils fight against bacterial infections. You have a higher chance of getting an infection when your white blood cell count is low. This is most common from 1 month to 6 months after your transplant.
- Low red blood cell count – Red blood cells carry oxygen to your body tissues. You have a higher chance of getting severe anemia when your red blood cell count is low.
- Low platelet count – Platelets help with blood clotting.
- Stomach problems – Stomach problems including intestinal bleeding, a tear in your intestinal wall (perforation) or stomach ulcers can happen in people who take MMF. Bleeding can be severe and you may have to be hospitalized for treatment. Call your study doctor right away if you have sudden or severe stomach-area pain or stomach-area pain that does not go away, or if you have diarrhea.
- Inflammatory reactions - Some people taking MMF may have an inflammatory

reaction with fever, joint stiffness, joint pain, and muscle pain. Some of these reactions may require hospitalization. This reaction could happen within weeks to months after your treatment with MMF starts or if your dose is increased. Call your study doctor right away if you experience these symptoms.

Common side effects:

- diarrhea
- blood problems including low white and red blood cell counts
- infections
- blood pressure problems
- fast heartbeat
- swelling of the lower legs, ankles, and feet
- changes in laboratory blood levels, including high levels of blood sugar (hyperglycemia)
- stomach problems including diarrhea, constipation, nausea and vomiting
- rash
- nervous system problems such as headache, dizziness and tremor

8. Valganciclovir

Common side effects:

- Diarrhea
- Nausea
- Vomiting
- Pain, tenderness, or swelling of the abdomen
- Eye pain,
- Constipation
- Headache
- Weight loss
- Back, join, or muscle pain
- Mouth ulcers
- Depression
- Anxiety
- low white cell, red cell, and platelet cell counts in blood tests
- fever
- fatigue
- headache
- sleeplessness
- urinary tract infection

- shaky movements (tremors)

Serious but less likely or rare side effects:

- seeing specks, flashes of light, or a dark curtain over everything
- decreased urination
- blood in urine
- vision problems
- swelling of the hands, arms, feet, ankles, or lower legs
- hives
- rash
- itching
- yellowing of skin or eyes; loss of appetite; dark urine; and/or light-colored bowel movements
- unintentional trembling or shaking movements
- numbness, pain, burning, or tingling in the hands or feet
- seizures

9. Ganciclovir

Common side effects:

- nausea
- vomiting
- diarrhea
- constipation
- stomach pain
- belching
- loss of appetite
- changes in ability to taste food
- dry mouth
- mouth sores
- unusual dreams
- nervousness
- depression
- sweating
- flushing
- joint or muscle pain or cramps

Serious but less likely or rare side effects:

- Seeing specks, flashes of light, or a dark curtain over everything
- decreased urination

- hives
- rash
- itching
- swelling of the hands, arms, feet, ankles, or lower legs
- numbness, pain, burning, or tingling in the hands or feet
- shaking hands that you cannot control
- difficulty breathing or swallowing
- chest pain
- mood changes
- seizures

10. Acyclovir

Common side effects:

- upset stomach
- vomiting
- diarrhea
- dizziness
- tiredness
- agitation
- pain, especially in the joints
- hair loss
- changes in vision

Serious but less common or rare side effects:

- hives
- rash or blisters
- itching
- difficulty breathing or swallowing
- swelling of the face, throat, tongue, lips, eyes, hands, feet, ankles, or lower legs
- hoarseness
- fast heartbeat
- weakness
- pale skin
- difficulty sleeping
- fever, sore throat, chills, cough, and other signs of infection
- unusual bruising or bleeding
- blood in the urine
- stomach pain or cramps
- bloody diarrhea

- decreased urination
- headache
- hallucinations (seeing things or hearing voices that do not exist)
- confusion
- aggressive behavior
- difficulty speaking
- numbness, burning, or tingling in the arms or legs
- temporary inability to move parts of your body
- shaking of a part of your body that you cannot control
- seizures
- loss of consciousness

11. Letermovir

Common side effects:
- Nausea
- Vomiting
- Diarrhea
- Stomach pain
- Swelling of arms or legs
- Cough
- Headache
- Fatigue (extreme tiredness)

Less common side effects:
- Fast or irregular heartbeat

12. TMP/SMX

Common side effects:
- Nausea
- Vomiting
- Loss of appetite
- Rash
- Itching

Serious but less likely or rare side effects:
- rash (hives)
- difficulty breathing or swallowing
- sore throat
- fever or chills
- severe diarrhea (watery or bloody stools) that may occur with or without fever

and stomach cramps (may occur up to 2 months or more after your treatment)
- shortness of breath
- cough
- unusual bruising or bleeding
- yellowing of the skin or eyes
- paleness
- red or purple skin discolorations
- joint or muscle pain/aches
- mouth sores
- bluish-colored fingernails, lips, or skin

13. Nystatin

Common side effects:
- Nausea
- Vomiting
- Diarrhea
- Stomach pain

Rare but serious side effects:
- Irritation or burning of the mouth
- Hives
- Rash or itching
- Difficulty breathing or swallowing

14. Fluconazole

Common side effects:
- headache
- dizziness
- skin rash
- nausea
- vomiting
- diarrhea
- stomach pain
- heartburn
- change in ability to taste food

Serious but less likely or rare side effects:
- extreme tiredness
- unusual bruising or bleeding

- lack of energy
- loss of appetite
- pain in the upper right part of the stomach
- yellowing of the skin or eyes
- flu-like symptoms
- dark urine
- pale stools
- seizures
- rash
- blistering or peeling skin
- hives
- itching
- swelling of the face, throat, tongue, lips, eyes, hands, feet, ankles, or lower legs
- difficulty breathing or swallowing

15. Methylprednisolone (intravenous)

Common side effects:

- headache
- dizziness
- slowed healing of cuts and bruises
- acne
- thin, fragile, or dry skin
- red or purple blotches or lines under the skin
- skin depressions at the injection site
- increased body fat or movement to different areas of your body
- difficulty falling asleep or staying asleep
- inappropriate happiness
- extreme changes in mood changes in personality
- extreme tiredness
- depression
- increased sweating
- muscle weakness
- joint pain
- dizziness
- irregular or absent menstrual periods
- increased appetite
- hiccups

Serious but less likely or rare side effects:

- black or tarry stool sore throat, fever, chills, cough, or other signs of infection
- seizures

- vision problems
- swelling of the eyes, face, lips, tongue, throat, arms, hands, feet, ankles, or lower legs
- difficulty breathing or swallowing
- shortness of breath
- sudden weight gain
- rash
- hives
- itching
- confusion
- abnormal skin patches in the mouth, nose, or throat
- numbness, burning, or tingling in the face, arms, legs, feet, or hands

16. Prednisone (oral)

Common side effects:

- headache
- dizziness
- difficulty falling asleep or staying asleep
- inappropriate happiness
- extreme changes in mood
- changes in personality
- bulging eyes
- acne
- thin, fragile skin
- red or purple blotches or lines under the skin
- slowed healing of cuts and bruises
- increased hair growth
- changes in the way fat is spread around the body
- extreme tiredness
- weak muscles
- irregular or absent menstrual periods
- decreased sexual desire
- heartburn
- increased sweating

Serious but less likely or rare side effects:

- vision problems
- eye pain, redness, or tearing
- sore throat, fever, chills, cough, or other signs of infection
- seizures

- depression
- loss of contact with reality
- confusion
- muscle twitching or tightening
- shaking of the hands that you cannot control
- numbness, burning, or tingling in the face, arms, legs, feet, or hands
- upset stomach
- vomiting
- lightheadedness
- irregular heartbeat
- sudden weight gain
- shortness of breath, especially during the night
- dry, hacking cough
- swelling or pain in the stomach
- swelling of the eyes, face, lips, tongue, throat, arms, hands, feet, ankles, or lower legs
- difficulty breathing or swallowing
- rash
- hives
- itching

17. Kidney Transplant Biopsy: kidney transplant biopsies are part of routine care for kidney transplant patients when their doctor suspects kidney rejection (for indication). At some centers outside of UCLA, kidney biopsies are done to screen for subclinical rejection, a condition where the kidney is functioning well, but a low level of rejection is present (surveillance biopsies). Surveillance biopsies are not routinely performed at UCLA. Kidney biopsies are being done more frequently in this study for research and safety purposes.

<u>Common side effects:</u>

- blood in the urine, which resolves within 1 to 2 days following the procedure
- local discomfort and/or pain

<u>Less common side effects:</u>

- infection at the biopsy site on your skin
- infection at the biopsy site on your kidney

<u>Rare but serious side effects:</u>

- bleeding into the kidney transplant which may result in loss of the kidney transplant
- hematoma (also known as bruising) around the kidney transplant

18. Bone Marrow Biopsy: bone marrow biopsies are a part of routine care for bone

marrow transplant patients to monitor their response to treatment and examine the cause of abnormal blood counts. Bone marrow biopsy will be performed for this study only if tests show lack of chimerism.

Common side effects:

- pain and/or discomfort

Less Common side effects:

- local bleeding and/or hematoma, which may cause temporary nerve injury to your gluteal nerve (a nerve that runs through the muscles in your buttocks)
- local infection to the skin and bone

Rare but serious side effects:

- severe bleeding
- injury to specific blood vessels within the area near the biopsy site, which may require blood transfusion and/or surgery to repair the injury.

19. Blood Draws: blood draws are a routine part of transplant care and necessary to monitor the function of the transplant, immunosuppressive drug levels and for possible side effects from the medications. In this study, blood draws are done more frequently than for routine care.

Common side effects

- discomfort and/or pain
- bruising

Less common side effects

- fainting

20. Colonoscopy: Colonoscopies are generally a safe procedure with a low risk of serious side effects or complications.

Common side effects

- abdominal cramping or bloating
- nausea, vomiting, or rectal irritation caused by procedure or by the preparatory bowel cleansing

Less Common side effects

- Blood from rectum or in stool after biopsy (tissue sample) or polyp removal
- A bad reaction to the pain medicine or the sedative (medicine used to provide a relaxing, calming effect)

Rare but serious side effects

- A perforation (hole) in the intestinal wall

You may have undergone this procedure as part of your routine care for kidney transplantation.

21. Pap smear: Pap smears are generally a safe procedure with a low risk of serious side effects or complications.

Common side effects

- Mild cramping
- Light bleeding or spotting

You may have undergone this procedure as part of your routine care for kidney transplantation.

Radiation Risks:
The potential long-term effects from this radiation doses that you will receive as part of this study is uncertain. There is a risk of short term and long-term medical side effects associated with radiation exposures of this level that your doctor feels may be justified by the serious nature of the disease. The short term effects from high radiation doses associated with this study are vomiting, diarrhea, blood count changes, and kidney damage. The long term side effects from high radiation doses associated with this study could include secondary cancer. The additional radiation exposure from other procedures are within the acceptable limits for diagnostic studies involving ionizing radiation and are routinely used in medicine. The person obtaining your consent can answer any questions you have, and provide detailed written information about the amount of radiation resulting from this study.

CT Scan:
CT scans involve the risks of radiation (see above). In addition, if contrast material (iodine dye) is used, there is a slight risk of developing an allergic reaction, which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock, or rarely, death. The contrast material may also cause kidney problems, especially if you are dehydrated or have poor kidney function. The study doctors will ask you about any allergies or related conditions before the procedure. If you have any of these problems, you may not be allowed to have a CT scan.

Having a CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner, or by lying in one position for a long time. If contrast material is used, you may feel discomfort when it is injected. You may feel warm and flushed and get a metallic taste in your mouth. Rarely, the contrast material may cause nausea, vomiting or a headache.

X-rays for Chest/Abdomen/Pelvis:
An x-ray (radiograph) is a noninvasive medical test that helps physicians diagnose and treat medical conditions. An x-ray examination is a painless procedure. X-rays involve the risks of radiation (see above).

A chest x-ray produces images of the heart, lungs, airways, blood vessels and the bones of the spine and chest.

An Abdominal x-ray is a commonly performed diagnostic x-ray examination that produces images of the organs in the abdominal cavity including the stomach, liver, intestines and spleen.

An X-ray of the pelvis focuses specifically on the area between your hips that holds many of your reproductive and digestive organs.

For some X-rays, your doctor will inject you with a contrast dye before the procedure to improve the images. The dye, usually iodine, can cause some side effects, including:

- hives
- itching
- lightheadedness
- nausea
- a metallic taste in your mouth
- In rare cases, the dye can cause a severe reaction, such as:
- anaphylactic shock
- very low blood pressure
- cardiac arrest

Mammogram:
A mammogram is an x-ray picture of the breast designed to detect tumors and other abnormalities. An x-ray is a noninvasive medical test that helps physicians and treat medical conditions. It involves the risks of radiation (see above).

You may have undergone this procedure as part of your routine care for kidney transplantation.

Reproductive Risks:
The effects of the investigational treatment on fetal (unborn baby) and infant development is not known. Therefore, it is important that you avoid getting pregnant to prevent exposing a fetus to study treatment. If you are currently pregnant or breast feeding, you may not participate in this study. If you are a woman who is able to become pregnant, a blood pregnancy test will be done at screening and must be negative before you can enter the study. If you enroll in the study and you are a woman, you must agree to avoid sexual intercourse or use a birth control method that the study doctors judge to be effective (such as hormonal treatments, condoms, or an intrauterine device) for at least 12 months after your transplant. Doctors routinely recommend this for all women who receive kidney transplants. You must notify the study doctor immediately if you become pregnant.

Questionnaire:

The MTSOSD-R 59 is a questionnaire that you will be given during the study. There are questions related to anxiety or depression that may make you uncomfortable. This questionnaire is used for research and is not used to guide clinical care; please let your doctor know if you are feeling anxious or depressed.

Unknown risks and discomforts:
The long-term risks of immunosuppressive therapy used in this study are unknown. The investigational treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything new that might make you change your mind about taking part in the study.

ARE THERE ANY BENEFITS IF I PARTICIPATE?

Possible benefits to me:
Taking part in this study may or may not make your health better. The possible benefits you may experience from being in this study include longer survival of your transplanted kidney and being able to stop immunosuppressive medications. It may be possible for you to stop these immunosuppressive medications completely. This could lower the risk of side effects from these medications and improve your quality of life. However, there is no guarantee or promise that the investigational treatment will benefit you. The investigational treatment may even be harmful.

Possible benefits to others or society:
This study will help the researchers learn more about managing immunosuppression in kidney transplant patients. Hopefully this information will help in the treatment of future patients who might benefit from combined kidney and stem cell transplants.

WHAT OTHER CHOICES DO I HAVE IF I DON'T WANT TO PARTICIPATE?

Participation in research is completely voluntary. You can decide to participate or not to participate.

You may wish to talk with your treating physician about your choices before deciding if you will take part in this study. If you decide not to take part in this study, your other choice will be to receive routine treatment for your condition without being in a study. This means you will be placed on continual immunosuppressive medication after your transplant.

CAN THE RESEARCHERS REMOVE ME FROM THIS STUDY?

The researchers may end your participation in this study for a number of reasons including if your safety and welfare are at risk, you do not follow instructions or you miss scheduled visits. The researchers or the study sponsor might also decide to stop the study at any time.

If you are a woman and become pregnant while you are on the study, the researchers may end your participation in the study.

If you decide to stop being part of the study, are removed from the study, or the study is stopped, you will be asked to return for follow-up visits once a year for four years (during Months 12, 24, 36, and 48) as part of your routine care. The data collected about you up to the point of withdrawal will remain part of the study and may not be removed from the study database.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT CONFIDENTIAL?

The researchers will do their best to make sure that your private information is kept confidential. Information about you will be handled as confidentially as possible, but participating in research may involve a loss of privacy and the potential for a breach in confidentiality. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security.

Use of personal information that can identify you:
No identifiable information about you will be kept with the research data. All identifiable information about you will be replaced with a code. A list linking the code and your identifiable information will be kept separate from the research data.

How information about you will be stored:
All research data and records will be maintained in a secure location at UCLA. Only authorized individuals will have access to it. Some research data and records will be stored electronically on a secure network with encryption and/or password protection.

People and agencies that will have access to your information:
The research team, authorized UCLA personnel, the study sponsor (OneLegacy Foundation), and regulatory agencies such as the Food and Drug Administration (FDA), may have access to study data and records to monitor the study. Research records provided to authorized, non-UCLA personnel will not contain identifiable information about you. Publications and/or presentations that result from this study will not identify you by name.

Employees of the University may have access to identifiable information as part of routine processing of your information, such as lab work or processing payment. However, University employees are bound by strict rules of confidentiality.

Because this study involves the treatment of a medical condition and/or medical procedures, a copy of this consent form will be placed in your medical record. This will allow the doctors that are caring for you to obtain information about what medications and/or procedures you are receiving in the study and treat you appropriately.

How long information from the study will be kept:

Research study files and specimens will be kept indefinitely after completion of the study.

USE OF DATA AND SPECIMENS FOR FUTURE RESEARCH

My data and/or specimens, including de-identified data and/or specimens may be kept for use in future research.

ARE THERE ANY COSTS FOR TAKING PART IN THIS STUDY?

The study will pay for the cost of supplying and administering the study drug/device, and all required study items and services as described in this consent form.

WILL I BE PAID FOR MY PARTICIPATION?

You will not be paid for your participation in this research study. Your parking will be paid for in the form of a parking voucher for visits which involve only research-related tests.

WHAT OTHER THINGS SHOULD I CONSIDER BEFORE PARTICIPATION?

Use of My Specimens:
Any specimens (e.g. tissue, blood) obtained for the purposes of this study will become the property of the University of California. Once you provide the specimens you will not have access to them. The University may share your specimens in the future with other researchers or outside institutions. Information that identifies you will not be shared with anyone outside of UCLA. The specimens will be used for research and such use may result in inventions or discoveries that could become the basis for new products or diagnostic or therapeutic agents. In some instances, these inventions and discoveries may be of potential commercial value and may be patented and licensed by the University. You will not receive any money or other benefits derived from any commercial or other products that may be developed from use of the specimens.

If any donor blood stem cells are left over after your treatment, they will be thrown away.

Researcher or Institutional Financial Interests in this Study

Jeffrey Veale, MD, the principal investigator of the study, is an unpaid member of the OneLegacy Advisory Board.

The David Geffen School of Medicine at UCLA has received a grant from OneLegacy foundation.

WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

The Research Team:
You may contact the following study doctors at the numbers below with any questions or concerns about the research or your participation in this study. You may also call the UCLA Page Operator at (310) 825-6301 to reach them 24 hours a day, 7 days a week.

Jeffrey Veale, MD at (310) 267-7727
Erik Lum, MD at (310) 267-2555
Caspian Oliai, MD at (310) 794-4955

UCLA Office of the Human Research Protection Program (OHRPP):
If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, you may contact the UCLA OHRPP by phone: (310) 206-2040; by email: participants@research.ucla.edu or U.S. mail: UCLA OHRPP, Box 951406, Los Angeles, CA 90095-1406.

Public Information about this Study:
ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. 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.

WHAT HAPPENS IF I BELIEVE I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call their at the number listed above.

If you are injured as a result of being in this study, UCLA will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or the study sponsor OneLegacy Foundation, or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call the UCLA Office of the Human Research Protection Program at (310) 206-2040 or send an email to participants@research.ucla.edu.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You can choose whether or not you want to participate. Whatever decision you make, there will be no penalty to you and you will not lose any of your regular benefits.

- You have a right to have all of your questions answered before deciding whether to take part.
- Your decision will not affect the medical care you receive from UCLA.
- If you decide to take part, you can leave the study at any time.
- If you decide to stop being in this study you should notify the research team right away. The researchers may ask you to complete some procedures in order to protect your safety.
- If you decide not to take part, you can still get medical care from UCLA.

HOW DO I INDICATE MY AGREEMENT TO PARTICIPATE?

If you agree to participate in this study you should sign and date below. You have been given a copy of this consent form and the Research Participant's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

Use of Data and Specimens for Future Research:
My data and/or specimens may be kept for use in future research to learn about, prevent or treat other health-related problems (check one below).

- ☐ Yes
- ☐ No

Contact for Future Research
UCLA researchers may contact me in the future to ask me to take part in other research studies.

- ☐ Yes
- ☐ No

SIGNATURE OF THE PARTICIPANT

_____
Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF PERSON OBTAINING CONSENT

_____ _____
Name of Person Obtaining Consent Contact Number

_____ _____
Signature of Person Obtaining Consent Date