Northwestern University
Comprehensive Transplant Center
Consent Form and HIPAA Authorization for Research

PROTOCOL TITLE: Impact of two prednisone-free maintenance immunosuppressive regimens with reduced dose FK506+Everolimus vs. standard dose FK506+MMF on subpopulation of T and B cells, renal allograft function and gene expression profiles in renal allograft biopsies at 12, 24 and 36 months post-transplant. Prospective single center study in recipients of renal transplant allograft (Protocol Version 26Oct2017).

PRINCIPAL INVESTIGATOR: Lorenzo Gallon, MD

SUPPORTED BY: Novartis Pharmaceuticals

Conflict of Interest Disclosure
The following disclosure is made to give you an opportunity to decide if this relationship will affect your willingness to participate in this research study:

If your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before making your decision whether or not to be in the study.

Introduction
You are being asked to take part in a research study. This document has important information about the reason for the study, what you will do if you choose to take part, and the way we, Northwestern University, would like to use information about you and your health.

What is the reason for doing this study?
You are being asked to be part of this research study because you are going to receive a kidney transplant.

The immune system is your body's defense against infection and other disease. After transplantation, the body sees the new organ as "foreign" and tries to destroy or "reject" it. Immunosuppressive medications help to prevent your immune system from attacking your transplanted organ. The primary purpose of this study is to investigate the impact of two maintenance immunosuppressive treatment plans on your immune system.

The immunosuppressants used in this study are mycophenolate mofetil, tacrolimus and everolimus. All of these medications are approved for use by the United States Food and Drug Administration (FDA) to prevent your body from rejecting the kidney you receive during your kidney transplant surgery.

Randomization:
In this research study, you will be randomly placed into one of the two following groups. You will be placed into either group by chance using a process similar to the flip of a coin. Neither you nor the study staff will select what group you will be in.

(**Group 1**): tacrolimus and mycophenolate mofetil
(**Group 2**): tacrolimus and everolimus

What you will do if you choose to be in this study?

If you decide to take part in this study, your participation will last for about 3 years or 36 months after your transplant date, and will include 5 study visits. Visits for this study will occur at pre-transplant and then 3, 6, 12, 24 and 36 months post-transplant. If it is not possible for the final visit to occur at 36 months, this visit may take place up to 50 months post-transplant.

Screening/Baseline Data and Sample Collection

Once you have read and signed this consent form, information about you (age, gender and race) will be collected by study staff. We will collect additional data from your medical record, as explained on the following page. 50 mL or about 3.5 tablespoons of blood and a sample of your urine will be collected for research on the day of your surgery, before you receive your transplant.

At the time of transplant, a kidney biopsy will be performed as standard of care. We will collect a piece of tissue from this biopsy for research purposes.

Follow-Up Visits

You will be followed at the transplant center and receive similar care as participants not taking part in a research study. This study was designed so that follow-up information is collected when you would already be in the clinic as part of your normal care. All subjects in this study will be required to visit the clinic for study-related visits at the time points listed above. In the event that you are not scheduled for a 3, 6 12, 24 or 36 month visit as standard-of-care, we would ask you to come specifically for the study, at no additional cost to you. On average, a research-only visit may last from 15 to 30 minutes in length.

At each research follow-up, you will answer questions regarding your health. Blood and urine samples will be collected for research tests at each visit, in addition to any required for your normal care. About 50 mL or 3.5 tablespoons of blood will be collected specifically for research.
Tests strictly associated with this research protocol also involve kidney biopsy tissue. Kidney biopsies are done for standard of care once at 3 months, 12 months and 24 months post-transplant, and a piece of the kidney biopsy tissue from each of these visits will be used for our research study.

Medical History

We will review your medical chart to obtain your previous medical history. Information about your health history will be recorded in the study database. Other information collected from your medical record will include: your height and weight, serum creatinine, blood type, Rh factor, HLA & PRA (tests related to your immune system's compatibility for the kidney transplant), CBC, viral panel results (Hepatitis B, Hepatitis C, Human Immunodeficiency Virus (HIV), Cytomegalovirus (CMV), and Epstein–Barr virus (EBV), and immunosuppression medication levels.

Blood Samples

All transplant participants have blood drawn after their transplant. You will have some extra blood drawn for this research study according to the schedule above. In most cases, this blood can be collected when you are already having blood drawn for your clinic visit or a standard lab visit. The research samples will be sent to the Principal Investigator's (Dr. Lorenzo Gallon) research laboratory on Northwestern's medical campus. The amount of blood drawn for research purposes will not exceed 60 mL or 4 tablespoons of blood during a 6-week period.

Kidney Biopsy
A kidney biopsy is a procedure to remove and examine a small piece of kidney tissue. At Northwestern, it is recommended that all recipients have this procedure performed on their transplanted kidneys, at time of transplant and then at 3, 12 and 24 months post-transplant, These biopsies will be billed to you or your insurance company. If you choose to participate in this study, an additional piece of tissue will be taken for research during each of your routine care biopsies. Only the extra tissue sample taken for this study is considered a research-related test.

Urine Collection
You will have urine collected at the time points listed in the schedule above.

What are some of the risks and discomforts that may happen to people who are in this study?
According to a report sent by Novartis Pharmaceuticals in March 2014, some participants receiving everolimus in other research studies have experienced cardiac arrest, with some instances resulting in death. Based on these findings, your risk of cardiac arrest, and death as a result, may be increased with the use of everolimus.

In another report sent by Novartis Pharmaceuticals in May 2014, some participants in other research studies have experienced ascites which is a build-up of fluid in the abdomen causing bloating and discomfort. Based on these findings, your risk of ascites may be increased with the use of everolimus.

Additionally, taking part in this study may involve the following risks:

Blood Draws
The risks of drawing blood are pain, bruising, infection, redness, swelling at the site of the needle entry, and a small chance of fainting. Care will be taken to avoid these risks.

Biopsies
No biopsies will be performed solely due to your participation in this study. However, at your routine care biopsies, an extra piece of kidney tissue (possibly requiring an extra needle) will be taken for use in this study. Risks of a kidney biopsy include bleeding in or around the kidney that can lead to a fall in blood pressure and rise in heart rate. In some cases a hole can form between blood vessels inside the kidney. The hole is called a fistula. Most fistulas close on their own and do not present a problem. However, occasionally (in approximately 1 in 100 cases), a hole in a blood vessel can lead to bleeding, and may require a blood transfusion. Very rarely (in less than 1 in 1000 cases), the fistula can lead to a need for surgery or result in loss of the kidney. Additional risks of a biopsy include;infection, pain, bleeding at the site of needle entry and/or having blood in urine. There is a very small chance a small scar may form at the site of needle entry. To lessen these risks, the biopsy procedure will be done using ultrasound guidance. Ultrasound allows the doctor to see where to place the needle.

These risks for a kidney biopsy will be explained to you by your doctor. The risks of the kidney biopsy are not changed because you are in this study. However, an extra needle is sometimes required to get the research tissue for the study, and may minimally increase the risks associated with this procedure.

Genetic Information

Genetic testing will be performed on your blood samples for this study. Knowledge of these tests may make you feel emotionally uncomfortable. This genetic information is collected to see how your genes related to your immune system have responded to your immunosuppression medications. These tests are only for research. That means the results will not be shared with you, even if they containextra information about conditions you may have, or about certain types of treatments that may help you.

If you withdraw from the study your samples from these tests will be destroyed. Strict precautionary measures will be taken to ensure that this genetic information and any identifying information are only accessible to the appropriate research staff. We will password-protect the electronic documents containing genetic information, and keep all files with genetic information in locked areas to which only authorized staff have access.

What do I need to know about reproductive health/sexual activity if I am in this study?
The drugs associated with this study may be harmful to a fetus. Sexually active men and women should use an effective method of birth control while taking the anti-rejection drugs. Condoms or diaphragm with spermicide, intrauterine devices (IUD), hormonal pills, injections, or patches, surgical sterilization (vasectomy or tubal ligation) and complete abstinence are examples of effective methods of birth control. Only methods that use condoms provide adequate protection against sexually transmitted diseases.

If you or your partner becomes pregnant while on the study, you must inform your study nurse/physician immediately. You may be required to switch anti-rejection drugs, in which case other treatment options will be discussed with you. Information will be collected on your pregnancy and the outcome.

What are some of the benefits that are likely to come from my being in this study?
If you take part in this study there may be no direct medical benefit to you. The information learned from this study may someday benefit future kidney transplant recipients.

What other procedures or courses of treatment might be available to me?
You do not have to take part in this research study. Before you decide to take part in this study, you can speak with the Principal Investigator Dr. Lorenzo Gallon about these and other options available to you. Your decision to take part in this study will not affect your chances of receiving a kidney transplant or the amount of time you will wait for a transplant. The drugs used in this study are FDA approved and are available outside of this study.

Your study doctor will tell you about any new information (good or bad) from this research or other studies that relate to this study. If new information is provided to you, you may be asked to re-consent to continue your participation.

Are there any financial costs to being in this study*?*
While there will be tests and procedures done only for this study, there will be no additional costs to you for being in this study.

You will be responsible for the cost of your transportation, including parking. You will receive a voucher for up to 6 hours of free parking for your study visits. This voucher is only valid if you park in the 251 E. Huron Street Garage, which is connected to the Galter Pavilion and the Feinberg Pavilion (hospital) by the street overpass on the second floor. The garage is also known as "university parking garage A." If you park in any other garage, this parking voucher will not be

valid and you will need to pay for your own parking.

What should I do if I am injured as a result of being in this study?
If you have an injury or illness from taking the study drug or procedures required for this study, the reasonable medical expenses required to treat such injury or illness may be paid for by the study sponsor.

The coverage for such injury or illness is only available if the Northwestern University principal investigator has decided that the injury/illness is directly related to the study drug or study procedures and is not the result of a pre-existing condition or the normal progression of your disease, or because you have not followed the directions of the study doctor. If your insurance is billed, you may be required to pay deductibles and co-payments that apply. You should check with your insurance company about any such payments.

If I have questions or concerns about this research study, whom can I call?
You can call us with your questions or concerns. If you have any illness or injury during your time on this study, you should call us promptly. Lorenzo Gallon, MD is the person in charge of this research study. You can call him at telephone number 312-695-4457, Monday through Friday, from 9am to 5pm.

For problems arising evenings or weekends, you may call 312-695-8900 and ask to speak to the transplant research nurse on-call.

Reasons why you may be taken off study without your consent:
You may be removed from the study without your consent at any time for the following reasons:

- Your doctor or the study staff thinks that it is in your best interest not to continue in the study
- You are unable to complete required study visits
- The study is stopped by Northwestern University, or Novartis Pharmaceuticals

If you are discontinued from the study, the study staff will contact you to discuss the procedures and appropriate future treatment for your continued care.

What are my rights as a research subject?
If you choose to be in this study, you have the right to be treated with respect, including respect for your decision whether or not you wish to continue or stop being in the study. You are free to choose to stop being in the study at any time.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Your choice not to be in this study will not negatively affect the routine medical care to which you are otherwise entitled.

If you want to speak with someone who is not directly involved in this research, or have questions about your rights as a research subject, please contact the Northwestern University Institutional Review Board (IRB) Office. You can call them at 312-503-9338.

What about my confidentiality and privacy rights?
- We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal

health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

- Transplant history: Date of transplant, cause of renal disease
- Demographics: Age, race, ethnicity, gender
- Results of physical examinations
- Medical history
- Blood test results
- All medications
- Related events of interest: admissions to the hospital, rejection, infections, etc.

During this study you may be coming to the Northwestern Memorial Hospital clinical offices for research appointments or to get clinical services, such as lab tests, needed for the study. When that happens, you will be scheduled for these services through the NMH computer system. When a clinical exam or lab is done by NMH or one of its employees for the purpose of this research study, that information will be kept in both NMH's clinical records and in the study records.

The following groups of people may give the researchers information about you: All current and previous health care providers, including but not limited to Northwestern Medical Group (NMG) and Northwestern Memorial Hospital (NMH).

Your medical and research records will be confidential to the extent permitted by law. Data from this study will be entered into a computerized database through a secured website and only study staff with a password will be allowed to enter data. Efforts will be made to keep your personal information private; however, we cannot guarantee complete confidentiality. Your data will be identified by a code and not by your name. Personal information from your records will not be released without your written permission.

Once we have the health information listed above, we may share some of this information with the following people. Please note that any research information shared with people outside of Northwestern University and its clinical partners (or affiliates), the Northwestern University Institutional Review Board Office and Office for Research Integrity, the US Office of Research Integrity, the US Office for Human Research Protections, the US Food and Drug Administration will not contain your name, address, telephone or social security number or any other direct personal identifier unless disclosure of the direct identifier is necessary for review by such parties or is required by law [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigators office].

- Authorized members of the Northwestern University workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board (a committee which is responsible for the ethical oversight of the study).
- Clinical affiliates, including but not limited the Rehabilitation Institute of Chicago (RIC), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), Northwestern Lake Forest Hospital (NLFH), and the Ann & Robert H. Lurie Children's Hospital of Chicago (Lurie Children's). Your participation in this study may be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers.

- Clinical affiliates, including but not limited to Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH), for purposes including, but not limited to, the affiliate's provision of care to you and/or the affiliate's scheduling of appointments and/or billing activities.
- Other University research centers and University contractors who are also working on the study,
- Study monitors and auditors who make sure that the study is being done properly,
- Novartis Pharmaceuticals, who is sponsoring the study, and that company's contractors and partners.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).

Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings. If your individual results are discussed, your identity will be protected by using a study code number rather than your name or other identifying information. Examples of identifying information include medical record number, Social Security number, and address.

ClinicalTrials.gov

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

Please note that:

- You do not have to sign this consent form. If you do not, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits. However, you will not be allowed to take part in this research study.
- You may change your mind and "take back" (revoke) this consent at any time. Even if you revoke this consent, the Principal Investigator may still use or share health information that was obtained about you before you revoked your consent as needed for the purpose of this study. To revoke your consent for the use of your health information, you must do so in writing to:

Lorenzo Gallon, MD
Northwestern University
Transplant Surgery- Clinical Research
676 N. St. Clair Street, Ste. 1900
Chicago IL, 60611

- Unless you revoke your consent, it will not expire. If you "take back" (revoke) your consent to use any blood or tissue taken for the study, the Principal Investigator will make sure that these specimens are destroyed or will make sure that all information that could identify you is removed from these samples.

Consent Summary:
I have read this consent form and the research study has been explained to me. I have been given time to ask questions, and have been told whom to contact if I have more questions. I agree to be in the research study described above.

A copy of this consent form will be provided to me after I sign it. A copy of this signed consent document, information about this study and the results of any test or procedure done may be included in my medical record and may be seen by my insurance company.

_____ _____
Subject's Name (printed) and Signature Date

_____ _____
Name (printed) and Signature of Person Obtaining Consent Date