Informed Consent Form And Authorization To Disclose Health Information

Sponsor / Study Title:	**Division of Allergy, Immunology, and Transplantation (DAIT), National Institute of Allergy and Infectious Diseases (NIAID) / "A Phase 2, Double-Blind, Placebo-Controlled Trial of Mycophenolate Mofetil alone or with Voclosporin for Systemic Lupus: Examining Distinct Immunophenotypes to Validate and Enhance Rational Treatment (The DIVERT Trial)"**
Protocol Number:	**ALE10**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

1. TITLE OF CLINICAL RESEARCH STUDY

A Phase 2, Double-Blind, Placebo-Controlled Trial of Mycophenolate Mofetil alone or with Voclosporin for Systemic Lupus: Examining Distinct Immunophenotypes to Validate and Enhance Rational Treatment (The DIVERT Trial, ALE10)

2. PRINCIPAL INVESTIGATOR

«PiFullName»

3. YOUR PARTICIPATION IS VOLUNTARY

We will explain this research study to you. Time will be taken for you to ask questions.

- Taking part in this study is your decision.
- You may change your mind at any time.
- You will be given a copy of this consent form for your records.

4. CONSENT KEY INFORMATION

This section is a summary of the research study to help you decide whether or not to participate. Detailed information is provided after the key information.

Why is this research being done?
The main reason this research study is being done is to see if mycophenolate mofetil (MMF) by itself is helpful for treatment of Systemic Lupus Erythematosus (SLE, lupus) compared to a placebo (an inactive substance).

The research is also being done to see if adding voclosporin will help treat your lupus if you do not respond to MMF.

The study doctors want to look for a way to predict who will respond positively to MMF by testing blood samples from you before you start the study drug. The study will look for specific factors in your blood (transcription profiles) that they hope will help them determine which participants will do well while taking MMF.

What happens if you take part in this research study?
If you decide to join this study, you will be scheduled to come to the study site for up to 16 research visits over a year's time. You will be on this study for up to a year. At these research visits you will have the following procedures:

- Physical exam.
- Blood work.
- ECG (Electrocardiogram that records the electrical signals from your heart).
- Complete questionnaires and participate in assessments for your lupus.

Is there any way being in this research can hurt me?
All procedures and study drugs in this study have some level of risk.

The possible risks associated with the study drugs are:

- Increased Risk of Infection. You will be at an increased risk of developing a variety of infections, including opportunistic infections (types of infections that happen when the immune system is weakened) due to immunosuppression (weakening of the immune system).
- Reproductive and breastfeeding risks. MMF is known to cause birth defects and early term loss of pregnancy.
- Increased risk of your lupus flaring depending on what study treatment(s) you receive or what part of the study you are in.
- Cancer Risks. If the study drug is taken for a long time, there is an increased risk of developing certain types of cancers, especially skin cancers.

Will being in this research study help me in any way?
There might be no direct medical benefit to you for being in this study. The information learned from this study may someday benefit people with Systemic Lupus.

What other choices do I have besides taking part in this research?
Before you decide to take part in this study, your study doctor will talk with you about other options available to you. There may be other treatments available for Systemic Lupus. There also may be other research studies that you can choose to join.

Who is sponsoring this study?
This study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). The study is being conducted through the Autoimmunity Centers of Excellence (ACE) network.

DETAILED CONSENT INFORMATION
The rest of the consent document includes detailed information about this study.

5. INTRODUCTION

Systemic Lupus Erythematosus (SLE, lupus) is a complex disease in which the body's own immune system may cause damage to different parts of the body. Lupus may affect any or all of the following: the skin, the joints, the kidneys, the nervous system, the heart, the lungs, and the blood. Sometimes lupus can get better by itself and then worsen again even without making any changes in your medications. This is one reason it is a disease that is difficult for doctors to treat.

Treatment for lupus currently consists of medications that help control the many features of the disease and its symptoms, but these medications cannot cure the disease itself. Patients usually take several different medications to help control their symptoms. Once the disease is quiet and under control, it is hard to tell if the medications are controlling the disease or if the disease is just going through a natural decrease in the disease activity. Not all medications work for all patients. We do not have a way to know if a medicine will work for each patient ahead of time.

You are being invited to be part of this study because:

- You have lupus.
- Your lupus is active but is not at risk to cause serious damage in a specific organ (brain, kidneys, heart or lungs).

Why is this research being done?

The main reason this research study is being done is to see if MMF is helpful for treatment of lupus when other lupus medications have been stopped. There has never been a study with this many participants at multiple clinics that tries to determine if MMF by itself is a good study treatment for lupus that is not involving the kidneys.

The research is also being done to see if voclosporin will help treat lupus when it is added to MMF if you do not respond well enough to MMF.

Both MMF and voclosporin, as used in this study, are investigational. This means the U.S. Food and Drug Administration (FDA) has not approved MMF and voclosporin for this use.

The study doctors want to understand if there is a way to predict who will respond positively to MMF by looking at your bloodwork. The study will look for specific factors in your blood (transcription profiles) that they hope will help them determine which participants will do well while taking MMF. Transcription profiles are like the blueprints from your genes that guide the body how to make certain proteins. If there are more or less of some of these blueprints it shows that more or less proteins will be made. The proteins of interest are those that regulate your immune system.

6. STUDY COMPONENTS

Who is sponsoring this study?

This study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). The study is being conducted through the Autoimmunity Centers of Excellence (ACE) network.

How many people will be in the study? How many study sites will conduct this study?
About 120 participants will be in this study at about 15 study sites in the United States.

How long will I be in this study?
You will be in this study for up to 56 weeks.

What will I be doing if I join the study? If you choose to take part in this study, you will need to sign and date this consent form before we do any study procedures. This study is divided into three stages:

- Stage 1: Screening and study treatment with one or more steroid shots to control the lupus while other lupus medications are withdrawn,
- Stage 2: Randomization to MMF or placebo (sugar pill with no active study drug), and
- Stage 3: Re-randomization to MMF and voclosporin or MMF and placebo.

Stage 1: Screening Lupus Medication Withdrawal
Once you have signed and dated this consent form, the screening phase of the study is started. Your study team can tell you how long this visit will take. You will be in the screening phase for up to 28 days.

Medical History and Physical Exam: During the screening visit, you will be asked about your medical history, your lupus history, any recent vaccines you have had, and any medication you may take. You will be given a full physical exam (including vital signs), urine and blood tests, and a test for pregnancy (if you are female and able to have children). This includes testing your blood (and sometimes a skin test) for several infections, including HIV (the virus that causes AIDS), tuberculosis, hepatitis, and COVID-19. If you test positive for HIV, tuberculosis (TB), or hepatitis, the study doctor may have to report this information to local health authorities. Approximately 2 tablespoons of blood will be needed for the tests.

Electrocardiogram (ECG): An ECG will be performed as part of the screening visit. An ECG test measures the rate and regularity of your heartbeat. Electrodes (sticky sensors attached to wires) are attached to your arms, legs, and chest to record the electrical activity of your heart.

Participant Reported Questionnaires: You will be asked to complete questionnaires about how you are feeling and how your lupus is affecting your life. These questionnaires should take approximately 15 to 20 minutes to complete.

Steroid Injection: Since you currently have active lupus, you will receive a steroid injection into your muscle to help manage any symptoms you may be having during the screening period. If your symptoms do not improve, you can have up to two additional injections during the screening period. Depending on availability, the steroid injection will be methylprednisolone 80 mg or triamcinolone acetonide 60 mg. Your study doctor will be able to tell you which steroid you will receive. The risks of both are described below.

Lupus Medication Withdrawal: The study doctor will stop your current lupus medication during the screening period except that you can stay on up to 10 mg/day of prednisone and hydroxychloroquine if you have been taking it. These medications may be stopped the same day as you sign and date the consent form or later in the screening period.

COVID-19 Testing: You will be tested for COVID-19 within 2 days prior to the randomization visit and at the beginning of the randomization visit. If your test is positive, you will not be able to continue in the study until you have tested negative. See additional information related to COVID-19 in the Section below called **Information related to COVID-19**.

Research Labs: These research tests will help us learn more about lupus, help us learn more about the immune system, and help us learn how your lupus responds to study drugs and study treatment. The research testing being conducted may look at large chunks of your DNA (whole exome testing) or all of your DNA at once (whole genome testing). You will not be given the results of the research lab tests. Approximately 3 tablespoons of blood will be collected for research labs.

After all screening tests and lupus medication withdrawal are complete and you qualify for the study, you will move to Stage 2 of the study.

Stage 2: Randomization to MMF or placebo
If you qualify for Stage 2, you will be assigned randomly (like flipping a coin, 50/50 chance) to receive either MMF or placebo. Neither you nor the study doctors will know what you are taking. The first few weeks we will slowly increase the dose of MMF to avoid side effects. Once you are on full dose of MMF/placebo you will take this study drug for up to 48 weeks or as long as your lupus remains quiet. The below chart explains the dose of MMF/placebo you will receive and the number of pills you will need to take.

Study Day	**MMF strength in milligrams/Placebo**	**Number of pills**
Day 1-7	500mg in the AM and 500mg in the PM MMF/Placebo	2 in the AM/2 in the PM
Day 8-14	500mg in AM and 1000mg PM/Placebo	2 in the AM/4 in the PM
Day 15 until end of Stage 2	1000mg in the AM and 1000mg in the PM/Placebo	4 in the AM/4 in the PM

Below is a schedule of the visits and procedures that you will have during Stage 2. Following this schedule is a detailed explanation of each of these procedures. You will be in Stage 2 for up to 48 weeks if your lupus remains quiet.

Stage 2 Week Number	**0**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44**	**48**	**End of Study Safety Visit**
Stage 2 Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	
Randomization	**X**													
Physical Exam	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Vital Signs	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Lupus Assessment	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Participant Reported Questionnaires	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Clinical Labs	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Research Labs	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Approximate Blood Volume for Clinical Labs	**1 TBS**	**1 TBS**	**1 TBS**	**1.5 TBS**	**1 TBS**	**1 TBS**	**1.5 TBS**	**1 TBS**	**1 TBS**	**1 TBS**	**1 TBS**	**1 TBS**	**1.5 TBS**	**1.5 TBS**
Approximate Blood Volume for Research Labs	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**

TBS = Tablespoons

Review of your Health and Medications. You will be asked about any health events since the last visit, and you will review all the medication you are currently taking. Study staff will ask you specific questions about your lupus symptoms and any problems these may be causing you since the last time you were at the study site.

Brief Physical Exam: A brief physical exam will be conducted at each visit to monitor your health.

Vital Signs: Weight, temperature, blood pressure, respiration rate, and pulse will be obtained at all visits.

Clinical Labs: Clinical labs include blood and urine. The table above lists the total amount of blood to be collected at each visit for clinical labs. These tests are to monitor your general health. If you are a woman of childbearing potential, urine will be collected for a pregnancy test at each visit. You will be given the results of the clinical lab tests.

Research Labs: The table above lists the total volume of blood to be collected at each visit for research testing. These research tests will help us learn more about lupus, help us learn more about the immune system, and help us learn how your lupus responds to study drugs and study treatment. The research testing being conducted may look at large chunks of your DNA (whole exome testing) or all of your DNA at once (whole genome testing). You will not be given the results of the research lab tests.

If you are doing well on the study drug (MMF or placebo), you will stay in Stage 2 for up to 48 weeks.

If your illness begins to worsen at any time during the first 24 weeks of Stage 2, you and your study doctor will discuss moving into Stage 3. Prior to moving into Stage 3, if you and the study doctor think that another steroid shot is likely to help you, you can be given another shot. After this steroid shot you will move to Stage 3 of the study.

If your illness begins to worsen at any time during the first 24 weeks of Stage 2 and the study doctor thinks that another steroid shot would not be sufficient to help you, you will stop the study drug and new lupus medication will be provided to you outside of the study. You will continue to have study visits until week 24 or 4 weeks after the last dose of study drug, whichever is longer.

If your illness begins to worsen after week 24 of the study, you will stop the study drug and new lupus medication will be provided to you outside of the study. You will be scheduled to have one final study visit four weeks after you stopped the study drug.

Stage 3: Re-randomization to MMF and voclosporin or MMF and placebo
If you qualify for Stage 3, you will be assigned randomly (like flipping a coin, 50/50 chance) to receive either MMF and placebo or MMF and voclosporin. Neither you nor the study doctors will know which of these you are taking. If you were taking placebo during Stage 2, we will slowly increase the dose of MMF to avoid side effects exactly like we did in Stage 2. All participants will take voclosporin 23.7mg twice a day.

If during the first two weeks of Stage 3 you and the study doctor think that another steroid shot is likely to help your symptoms, you can be given another shot.

If your illness does not get worse, you will be in Stage 3 for up to 28 weeks.

Below is a schedule of the procedures that you will have during Stage 3.

Stage 3 Week Number	**0**	**2**	**4**	**8**	**12**	**16**	**20**	**24**	**End of Study Safety Visit**
Stage 3 Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	
Randomization	**X**								
Physical Exam	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**
Vital Signs	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
SLE Assessment	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**
Participant Reported Questionnaires	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**
Clinical Labs	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Research Labs	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**
Approximate Blood Volume for Clinical Labs	**0.5 TBS**	**0.5 TBS**	**1TBS**	**1 TBS**	**1.5 TBS**	**1 TBS**	**1 TBS**	**1.5 TBS**	**1.5 TBS**
Approximate Blood Volume for Research Labs	**0**	**0**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**	**3.5 TBS**

During Stage 3, If your lupus worsens and requires additional medication, you will be taken off the study drug and start the new medication outside of this study. You will be scheduled to come back for a stopping study visit four weeks after stopping study drug.

7. RISKS ASSOCIATED WITH PROCEDURES AND STUDY DRUGS

The risks associated with the study drugs in this study are described below.

Steroids: Triamcinolone acetonide and methylprednisolone acetate are corticosteroids. Corticosteroids are drugs that are given in many diseases to reduce inflammation and suppress the immune system. Corticosteroids are associated with several side effects. There are side effects that will be seen with short term use and with long term use. These are described below.

Side effects seen with short term use as being used in this study:

- High blood pressure
- Fluid retention
- Insomnia (not being able to sleep)
- Agitation

Side effects seen with long term use are:

- Nausea, abdominal pain, and ulcers
- High blood pressure
- Low potassium and calcium
- Osteoporosis (a bone disease where bones become weak)
- Cushing's syndrome (a disorder with physical and mental changes that result from having too much cortisol in the blood for a long period of time)
- High blood sugar
- Increased risk of infections
- Cataracts
- Glaucoma with possible damage to the nerves of the eye
- Enhanced risk of eye infections
- Acne, thinning of the skin, and bruising
- Aseptic necrosis (bone death because of bad blood supply)
- Hirsutism (hair growth on unexpected body areas)

Rare allergic reactions may happen with corticosteroid use and could be serious.

Side effects seen with Intramuscular injection of triamcinolone only are:

- Pain at the injection site
- Abscess (an infection deep in the tissue) near the injection site
- Skin atrophy (the breakdown and thinning of the skin) near the injection site
- Changes (darkening or lightening) in skin color near the injection site

Mycophenolic acid, MMF (CellCept®): MMF is an immunosuppressant (weakening the immune system) drug that is U.S. Food and Drug Administration (FDA) approved for the prevention of organ rejection after a transplant. MMF is not FDA approved to treat lupus. However, it is recommended by the American College of Rheumatology and American Society of Nephrology as a first line treatment for lupus nephritis and is a recognized standard of care for lupus. MMF use in this study is experimental.

Serious side effects of MMF include:

Infection Risks

An increased risk of developing bacterial, fungal, or viral infections. Certain viruses can live in your body and cause active infections when your immune system is weak. Viral infections that can happen with MMF include:

- Shingles, other herpes infections, and cytomegalovirus (CMV). CMV can cause serious tissue and blood infections.
- Hepatitis B and C viruses. Hepatitis viruses can affect how your liver works. Talk to your study doctor about how hepatitis viruses may affect you.

Brain Infection Risks

A brain infection called Progressive Multifocal Leukoencephalopathy (PML). In some participants, MMF may cause an infection of the brain that may cause death. You might be at an increased risk for this brain infection because MMF weakens your immune system. Call your study doctor right away if you have any of the following symptoms:

- Weakness on one side of the body
- You do not care about things you usually care about (apathy)
- You are confused or have problems thinking
- You cannot control your muscles

Yeast and Fungal Infection Risks

Yeasts and other types of fungal infections can happen with MMF and can cause serious tissue and blood infections. Call your study doctor right away if you have any of the following signs and symptoms of infection:

- Temperature of 100.5°F or greater
- Cold symptoms, such as a runny nose or sore throat
- Flu symptoms, such as an upset stomach, stomach pain, vomiting or diarrhea
- Earache or headache
- Pain during urination
- White patches in the mouth or throat
- Unexpected bruising or bleeding
- Cuts, scrapes, or incisions that are red, warm, and oozing pus

Cancer Risks

An increased risk of developing certain types of cancers, especially skin cancers. You should avoid exposure to sunlight and UV light should be limited by wearing protective clothing and using a broad-spectrum sunscreen with a high protection factor. (The use of sunscreen is also important for your general lupus care.) Tell the study doctor if you have:

- Unexplained fever
- Prolonged tiredness
- Weight loss
- Lymph node swelling
- A brown or black skin lesion with uneven borders, or one part of the lesion does not look like the others
- A change in the size and color of a mole
- A new skin lesion or bump
- Any other changes to your health

Reproductive Risks

Reproductive and breastfeeding risks. MMF is known to cause birth defects and early term loss of pregnancy. If you can become pregnant, you must agree to use two acceptable forms of birth control while taking MMF and for six weeks after you stop taking MMF. It is not known if MMF passes into breast milk.

If you are a sexually active male whose partner can become pregnant, you should use reliable contraception while taking MMF and for 90 days after you stop taking MMF. You should not donate sperm or blood products while you are taking MMF and for 90 days after you stop taking MMF.

Additional side effects include:

Low blood cell counts. People taking high doses of MMF each day may have a decrease in blood counts, including:

- White blood cells, especially neutrophils. Neutrophils fight against bacterial infections. You have a higher chance of getting an infection when your white blood cell count is low.
- Red blood cells. 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.
- Platelets. Platelets help with blood clotting.

Tell your study doctor right away if you have any signs of infection, including any unexpected bruising or bleeding. Also, tell your study doctor if you have unusual tiredness, lack of energy, dizziness, or fainting.

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.

MMF should not be taken with certain types of vaccinations (live vaccines). Some vaccines may not work as well during study treatment with MMF. Please speak with the study doctor about any plans you have about taking any vaccine.

Voclosporin (Lupkynis™): Voclosporin is an immunosuppressant approved by the FDA for use with other immunosuppressive treatments for the adult patients with active lupus nephritis (LN) but it has not been studied or approved for people with lupus who don't have nephritis. The use of Voclosporin in this study is experimental.

Serious side effects of voclosporin include:

Increased Risk of Infection. You are at an increased risk of developing a variety of infections, including opportunistic infections (types of infections that happen when the immune system is weakened) due to immunosuppression and you should contact the study doctor if you develop any symptoms of infection such as:

- Fever
- Sweats or chills
- Cough
- Flu-like symptoms
- Muscle aches
- Warm, red, painful areas on the skin.

An increased risk of developing certain types of cancers when taken for a long time, especially skin cancers. You should avoid exposure to sunlight and other forms of UV light should be limited by wearing protective clothing and using a broad-spectrum sunscreen with a high protection factor. Tell your study doctor if you have any changes in the skin.

Kidney Function Risks

Kidney problems. Kidney problems are common side effects of voclosporin and may be serious and chronic. The study doctor will check your kidney function while you take voclosporin.

High blood pressure. High blood pressure is a common side effect of voclosporin and may be serious. The study doctor will monitor your blood pressure while you take voclosporin and may ask you to check your blood pressure at home.

Nervous system problems. Nervous system problems are a common side effect of voclosporin and may be serious. Call your healthcare provider or go to the nearest hospital emergency room right away if you get any of these symptoms while taking voclosporin. These could be signs of serious nervous system problems:

- Confusion
- Changes in alertness

- Muscle tremors
- Numbness and tingling
- Headache
- Seizures
- Vision changes

High levels of potassium in your blood. The study doctor may do certain tests to check your potassium levels while you take voclosporin.

Anemia. Anemia is condition in which you lack enough healthy red blood cells to carry enough oxygen to your body's tissues. Having anemia can make you feel tired and weak.

QT prolongation. QT prolongation is a heart rhythm condition that can potentially cause fast, chaotic heartbeats. These rapid heartbeats might trigger you to suddenly faint. In some severe cases, QT prolongation can cause sudden death.

Reproductive and breastfeeding risks. The available information about voclosporin use in pregnant participants is limited and it cannot be determined if there is a risk of study drug-associated birth defects, miscarriage, or other negative outcomes for the mother or child. Voclosporin should not be taken during pregnancy. If you can become pregnant, you must agree to use two acceptable forms of birth control while taking voclosporin.

There is no information on the presence of voclosporin in human milk, the effects on the breastfed child, or the effects on milk production. Breastfeeding is not recommended during study treatment and for at least 7 days after the last dose of voclosporin.

Certain types of drugs (CYP3A4 inhibitors) can change how your body reacts to voclosporin. You must tell your study doctor when you start taking any new medications.

You should avoid eating grapefruit or drinking grapefruit juice while taking voclosporin.

Voclosporin should not be taken with certain types of vaccinations (live vaccines). Please speak with the study doctor about any plans you have about taking any vaccine.

The risks associated with the study procedures in this study are described below.

Lupus Medication Withdrawal: During the screening period your lupus medications will be stopped. This could cause your lupus to flare or get worse, although you will be receiving the steroid shot to avoid this happening. If you do start to flare, please contact the study doctor. There is also a risk that the study doctor will stop your lupus medications during the screening period, but you will not qualify for the study. If this happens you will be referred to your rheumatologist to start new lupus medication.

ECG: You may have minor discomfort, like removing a bandage, when the electrodes are removed. Rarely, a reaction to the electrode adhesive may cause redness or swelling where the patches were placed.

Blood Draw: A blood draw can cause temporary pain and bruising in the area where the blood sample was drawn. Lightheadedness or rarely fainting due to transient lowering of the blood pressure can occur.

Participant Reported Questionnaires: You may find it inconvenient to participate in these surveys. Being asked to think about your health and healthcare related information could make you feel worried or anxious. You do not have to answer any questions which make you feel uncomfortable.

Study treatment and procedures in this research study may involve risks that are not possible to predict. You will be informed of any new risks that may be identified during the study. Please ask your study doctor or the study staff to explain any procedures or risks that you do not understand.

Information related to COVID-19

- MMF, voclosporin, and steroids suppress your immune system and may increase your susceptibility to getting a COVID-19 infection. Also, infection could be more severe because of receiving these study drugs. This is true with any infection when taking drugs that suppress the immune system. These study drugs may also interfere with the amount of protection you would receive from a COVID-19 vaccine.
- If at any time during the study, you test positive for COVID-19, you develop COVID-19 symptoms, or have had close contact (within 6 feet for a total of 15 minutes or more over a 24-hour period) with someone with confirmed COVID-19, you must contact your study doctor immediately. You may be scheduled to have another COVID-19 test.

  If you join this study, you will be taking medications that are immune compromising. If you see your primary care physician or go to an urgent care facility because of COVID-19 symptoms or are in close contact with someone who has tested positive, you should inform the health care provider that because of the medications you take, you are considered immunocompromised and may be eligible for COVID-19 treatments. We will provide you with a wallet sized information card that you can share with your health care provider.
- Other treatments for COVID-19 may become available and if you test positive you should talk to your study doctor about every option available.
- The study staff also strongly recommends any other suggested vaccinations (including the seasonal fu vaccination) prior to joining this study. Speak to your study doctor about receiving any vaccines during the study.
- Measures to protect yourself and others from COVID-19 infection are outlined on the Centers for Disease Control website at the following link: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html. To decrease your risk of infection with SARS-CoV-2, we strongly recommend that you follow these recommendations, which include wearing a mask, practicing social distancing, and frequent handwashing/use of hand sanitizer.

8. POTENTIAL BENEFITS

If you agree to take part in this study, there may be no direct medical benefit to you.

Information learned from this study may someday benefit people in the future.

9. ALTERNATIVES TO PARTICIPATION

The study doctor and/or study staff will talk with you about this study and other options available to you. You may choose not to be in this research study.

10. NEW FINDINGS

The study doctor will tell you about any new information that may affect your willingness to continue in this study.

11. VOLUNTARY WITHDRAWAL FROM STUDY

You may decide not to take part or to leave the study at any time. If you choose not to join the study, or you decide to leave the study, there is no penalty or loss of benefits in your routine medical care or any other benefit(s) that you would otherwise be entitled to receive. The study staff will schedule you to return to the study site for a final visit so that your medical condition can be clarified after the study drug(s) have left your system.

You should talk to your study doctor who will discuss future treatment and procedures for your continued care.

12. REASONS WHY YOU MAY BE TAKEN OFF THE STUDY WITHOUT YOUR CONSENT

You may be removed from the study without your consent at any time. Reasons why you may be removed from the study include, but are not limited to, the following:

- The study doctor thinks it is not in your best interest to continue in this study.
- You are unable to complete required study treatments and examinations.
- The study is stopped by the Institution, the Sponsor(s), the Food and Drug Administration (FDA), or other health authorities.

If you are removed from the study, your study doctor will contact you to discuss stopping procedures and your future care.

13. PREGNANCIES, BREASTFEEDING AND BIRTH CONTROL

You cannot participate in this study if:

- You are currently pregnant or breast feeding.
- You plan to get pregnant in the next 18 months.

Study treatments and procedures involved in this research study may involve unexpected risks to your unborn or nursing child. The study drug (MMF) can cause birth defects. If you are female, a pregnancy test will be performed prior to your enrollment.

To prevent risk to the fetus, it is important that female participants or female partners of male participants take care to avoid becoming pregnant during this study. Avoiding sexual activity is the only certain method to prevent pregnancy. However, if sexually active, female participants of reproductive potential must use reliable method(s) of contraception (birth control) unless you are unable to become pregnant because of prior surgical sterilization. Acceptable contraceptive methods must begin from 4 weeks prior to starting the study to 6 weeks after completion of the study.

If you are on oral contraceptives, there is a potential for decreased effectiveness while taking MMF. It is important to know that even with use of these birth control measures, pregnancy could still result. The risks of receiving the study drug while pregnant include risk to the fetus and potential loss of the pregnancy. Male participants are strongly encouraged to use contraception with female partners. Men should not donate semen during therapy and for 90 days following discontinuation of mycophenolate mofetil.

If you become pregnant during the study, the study doctor will instruct you to stop taking the study drugs.

If you become pregnant, the study staff will collect information about the pregnancy, its outcome, and the health of the child after birth.

Since there are pregnancy risks associated with MMF, the FDA created an education program, Mycophenolate REMS (Risk Evaluation and Mitigation Strategy) to prevent unplanned pregnancies, reduce fetal exposure to MMF, collect information on pregnancies, and inform patients about the risks of MMF. Your study doctor has enrolled, and we strongly encourage you to discuss the program with your study doctor and to participate in the MMF REMS program as well. A description of this program is available at https://www.mycophenolaterems.com/PatientOverview.aspx.

The following chart lists the acceptable methods of contraception consistent with the MMF REMS program. The study doctor will review the chart and you must agree to one of the options listed as part of study participation.

Mycophenolate REMS Program Acceptable Methods for Females of Reproductive Potential

<table>
<tr><td colspan="4">Acceptable Contraception Methods for Females of Reproductive Potential*</td></tr>
<tr><td>Option 1

Methods to Use Alone</td><td colspan="3">Intrauterine devices (IUDs)
Tubal sterilization
Participant’s partner had a vasectomy</td></tr>
<tr><td colspan="4">OR</td></tr>
<tr><td rowspan="2">Option 2

Choose One Hormone Method AND One Barrier Method</td><td>Hormone Methods
choose 1</td><td></td><td>Barrier Methods
choose 1</td></tr>
<tr><td>Estrogen and Progesterone
Oral contraceptive pill
Transdermal patch
Vaginal ring

Progesterone-only
Injection
Implant</td><td>AND</td><td>Diaphragm with spermicide
Cervical cap with spermicide
Contraceptive sponge
Male condom
Female condom</td></tr>
</table>

OR			
Option 3 Choose One Barrier Method from each column (must chose two methods)	Barrier Methods choose 1		Barrier Methods choose 1
	Diaphragm with spermicide Cervical cap with spermicide Contraceptive sponge	AND	Male condom Female condom

* Females of reproductive potential include girls who have entered puberty and all women who have a uterus and have not passed through menopause.

14. COSTS TO YOU

The costs of all study drugs, tests and procedures described above that are required by the study will be paid for by the National Institute of Allergy and Infectious Diseases, (NIAID) through the Autoimmune Centers of Excellence (ACE). You will be responsible for any expenses related to your routine clinical care. Please ask your study doctor about any expected added costs that you may incur. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may lead to added costs to you or your insurance company.

15. PAYMENTS (REIMBURSEMENT)

«Compensation»

You will be paid up to a total of $xx.xx if you complete this study. You will be paid for the visits you complete according to the following schedule:

- $xx.xx for Visits xxx.
- $xx.xx for Visits xxx.
- $xx.xx for Visits xxx.

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid _____ ["following each completed visit", "monthly", "quarterly", "at the end of your participation in the research study", "following each completed visit or at the end of your participation in the research study, whichever you prefer"].

If you have any questions regarding your compensation for participation, please contact the study staff.

[OR]

You will not receive any monetary compensation for your participation in this study.

[If applicable:] We will reimburse you for the cost of ***[describe: e.g., traveling to your study visits]***. You will be reimbursed approximately ***[e.g., 2 weeks, 1 month, etc.]*** after you submit your travel receipts to the study staff.

16. RESEARCH-RELATED INJURY

If you are injured or get sick while in this study, it is important to tell your study doctor listed on page one of this consent form. The study doctor may arrange to see you at the study site or may direct you to an emergency care center.

Emergency medical treatment will be available to you. The study site will bill you or your insurance company in the normal way for the cost of such care. No payment or additional compensation is available to you for such injuries. There is no provision for medical care at no cost to you or monetary compensation from the study sponsor, the NIAID, or NIH. You do not lose any legal rights by signing and dating this form.

17. HIV POLICY

You will be tested for HIV as part of the screening visit before you start in the study. If you are found to be HIV positive you will not be able to participate in the study. Your medical records will be kept confidential to the extent permitted by law. However, as mentioned earlier in this consent form, the study doctor may be required by law to report the result of this test to the local health authority.

18. CONFIDENTIALITY

Your medical and research records will be confidential to the extent permitted by law. Efforts will be made to keep your personal information private. However, we cannot guarantee complete confidentiality.

You will be identified by a code, and personal information from your records will not be released without your written permission. You will not be identified in any publication or in the sharing of your data about this study. After the study is completed, the data may be placed in a central storage location. These data will not include your name or other information that can identify you. The purpose is to make study data available to other researchers. Information from this study may be put into databases along with information from other studies. There are different kinds of databases; some are publicly accessible, and some are restricted. Anyone on the internet can access publicly accessible databases. Only researchers who apply and are approved can access restricted databases. Traditionally used identifying information about you (such as name, phone number, address) will NOT be included or shared with others.

Your privacy is important to us and we will use safety measures to protect your privacy. Despite all the safety measures that we use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them.

While we will not use information that is traditionally used to identify you, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It is also possible there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you. There may also be other privacy risks that we have not foreseen.

As a NIH funded study, you are further protected through a policy that prevents the study doctor from releasing any sensitive information about you that may identify you. This does not prevent you or a family member from voluntarily releasing information about this research.

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.

Organizations that may look at and/or copy your medical records for research, quality assurance and data analysis include:

- The National Institute of Allergy and Infectious Diseases, (NIAID) sponsor of the research.
- NIAID representatives, agents, employees, contractors, and other persons assisting in conducting, monitoring, or analyzing the study.
- The U.S. Food and Drug Administration.
- Other State and Local health authorities.
- Pharmaceutical companies(s) and their commercial partners may review your medical and research records for regulatory purposes.

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research participants.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the study that is needed for auditing or program evaluation by the agency which is funding this study or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

19. WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00060226.

20. FUTURE USE OF YOUR DATA/BIOLOGIC MATERIALS

Information about you, including your biospecimens, collected for this study may be shared with other researchers. It may also be used for other research studies. We will make sure that your identity cannot be linked to the information we share. We will not ask you for additional permission before sharing the information.

We are asking your permission to store samples of blood and urine collected during the study to be used in the future for tests that aren't yet planned.

Your stored samples will be used to obtain knowledge about genetic information in relation to the immune system. Genetic tests study an individual's inherited characteristics, found in DNA, which is present in each of the cells of your body. DNA contains information needed to construct and operate the human body. Whole genome sequencing may be performed.

The results of tests performed on stored samples or reports resulting from the analysis of your samples will not be given to you or your doctor and they will not be put in your medical record. They will not identify you and will not affect your routine medical care.

There is no benefit to you from the storage of samples and information. However, the use of your samples and information may help researchers learn more about your disease or the genetics related to a specific condition. The purpose of storage and sharing data is to make information available for use in health research and to share what is stored with other researchers. Collecting, storing, sharing information, and making it available for other studies may help people in the future. Coded information put into databases together with other stored information from many studies conducted in different places allow researchers to study the combined information and learn even more about health and many different diseases.

Samples will be stored at Oklahoma Medical Research Foundation. If you decide to allow storage, your samples and information may be stored for an unknown length of time.

Although your stored research samples will not be sold, the information obtained from the research performed on your samples may in the future lead to the development of commercial products. You will not receive any money from research using your stored samples and information.

There may be unknown risks associated with the storage of samples and information. For example, if the future research involves genetic testing it is possible that it could be traced back to you because your genes are specific to you. We will make every attempt to protect your confidentiality and to make sure that your personal identity does not become known.

You can change your mind at any time and ask to have your samples destroyed. This request should be made in writing to the study doctor. If you make this request, all remaining stored samples will be destroyed. However, the results of any previous tests using your stored samples will be used. Your decision regarding the storage of samples or the information resulting from the analysis of your samples will not affect your ability to participate in this study. The future use of your samples and information may contribute to learning more about disease or help to study the genetics related to a specific condition.

Please indicate your response below:

I agree to the storage and sharing of samples (urine, blood and/or tissue) for genetic tests not currently planned.

☐ Yes ☐ No

_____
Initials of Research Participant

I agree to the storage and sharing of samples (urine, blood and/or tissue) and information resulting from the analysis of my samples for other tests not currently planned.

☐ Yes ☐ No

_____
Initials of Research Participant

21. FUTURE CONTACT

May we contact you by phone to find out if you are interested in hearing about new research studies or to ask you about how your current health is? Contact would be made by the lead study doctor's staff. If you decide at any time that you no longer want to be contacted, please tell us, and we will stop calling you.

Would you like us to contact you about future research studies or to ask you about how your current health is?

☐ Yes ☐ No _____
Initials of Research Participant

If you say "no" to this question, this will not affect your participation in this study.

22. SIGNATURE PAGE

Please sign and date below if you agree to take part in this study.

- You have read the informed consent and/or had it explained to you
- You were given the opportunity to ask questions about the information, and
- You voluntarily agree to take part in the study

_____	_____	_____
Research Participant's Name *(Typed or printed)*	Research Participant's Signature	Date

Signature of person explaining and obtaining the consent:

_____	_____	_____
Name and Title *(Typed or printed)*	Signature	Date

WITNESS SIGNATURE FOR PARTICIPANTS WHO CANNOT READ
The study participant has indicated that he/she is unable to read. The consent document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____	_____
Signature of Impartial Witness	Date

(NOTE: This consent form with the original signatures MUST be retained on file by the study doctor. A copy must be given to the research participant. A copy should be placed in the research participant's medical record, if applicable.)

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Representatives of the National Institute of Allergy and Infectious Diseases (NIAID).
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study, if applicable.
- A data safety monitoring board which oversees this study, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study drug works and is safe.
- To compare the study drug to other drugs.
- For other research activities related to the study drug.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law (HIPPA) and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____
Printed Name of Participant

_____
Signature of Participant Date

_____
Printed Name of the Person Obtaining the Authorization Date

_____
Signature of the Person Obtaining the Authorization Date

WITNESS SIGNATURE FOR PARTICIPANTS WHO CANNOT READ

The study participant has indicated that he/she is unable to read. This Authorization document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date