THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

**Informed Consent**

# INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

## A Pilot Study of Allogeneic Hematopoietic Cell Transplantation for Patients with High Risk Solid Tumors

2020-0496

Study Chair: Jeremy Connors

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

**STUDY SUMMARY**

*If you are reading and signing this form on behalf of a potential participant, please note: Any time the words "you," "your," "I," or "me" appear, it is meant to apply to the potential participant.*

The goal of this clinical research study is to learn about the safety and effectiveness of a combination of drugs (fludarabine, thiotepa, etoposide, melphalan, and rabbit anti-thymocyte globulin [rabbit ATG]) followed by an allogeneic hematopoietic stem cell transplant (HSCT) when given to patients with recurrent (has come back) or refractory (has not responded to treatment) high-risk solid tumors.

**This is an investigational study.** Fludarabine, thiotepa, etoposide, melphalan, and rabbit ATG are all FDA approved and commercially available. However, it is considered investigational to use these drugs together, at these doses, to treat high-risk solid tumors. Their use in this study is for research purposes only.

The study doctor can explain how the study drugs are designed to work.

The study drug combination and stem cell transplant may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. You may not want to take part in this study because you will be hospitalized and/or required to stay within 1 hour of the clinic for an extended amount of time. You may also experience side effects associated with the study drugs.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You will receive the study drug combination over a period of 6 days. You will have follow-up visits for 1 year after your stem cell transplant.

You and/or your insurance provider will be responsible for the cost of the study drugs and the stem cell transplant you receive during this study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive the standard treatment for the disease as determined by your primary treatment team outside of this study. You may receive other investigational therapy, if available. The study doctor will discuss the possible risks and benefits of these treatments. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

## 1. STUDY DETAILS

**Screening Tests**

Signing this consent form does not mean that you will be able to take part in this study. The following tests and procedures will be performed to help the study doctor decide if you are eligible:

- You will have physical exam.
- Blood (about 1-2 teaspoons) will be drawn for routine tests, immune system testing, circulating tumor cell (CTC) testing, tests to check your blood type, and tests to check for viruses such as cytomegalovirus (CMV), hepatitis B and C, herpes simplex virus (HSV), varicella-zoster virus (VSV), human t-lymphotropic virus (HTLV), and HIV (the AIDS virus). CTC testing checks the number of tumor cells in the blood.
- Blood (about 1-2 teaspoons) will also be drawn for use in distinguishing between your cells and the donor’s cells after your transplant.
- You will have an echocardiogram (ECHO), MRI, or MUGA scan to check your heart function.
- You have a CT scan of your chest to check your lung function. If the doctor thinks it is needed, you may also have a pulmonary function (breathing) test.

- You will have tests/procedures to check the status of the disease. Depending on the disease and what the study doctor thinks is needed, this may include:
    - Imaging scans (such as a PET scan)
    - Bone marrow aspirate/biopsy - to collect a bone marrow biopsy/aspirate, an area of the hip or other site is numbed with anesthetic, and a small amount of bone marrow and/or bone is withdrawn through a large needle.
    - Blood may be drawn for tumor marker testing – tumor markers may be related to the status of the disease.
- If you are able to become pregnant, blood (about 1 teaspoon) will be used for a pregnancy test. To take part in this study, you must not be pregnant.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other options will be discussed with you.

Up to 40 participants will be enrolled in this study. All will take part at MD Anderson.

**Study Drug Administration**

Negative days are days before your stem cell transplant. Day 0 is the day you receive your stem cell transplant. Positive days are days after your stem cell transplant.

You will be admitted to the hospital during this study. You will have a central line placed in your vein (called a Hickman catheter) before you start receiving the study drug combination. The Hickman catheter allows the study staff to draw blood daily without having to stick you with a needle many times. The catheter will also be used to give you blood, blood products, the stem cell infusion, antibiotics and other medicines, and nutrition through your vein. You will be kept in strict isolation in order to protect you from outside germs that cause infections.

In the days leading up to the stem cell transplant, you will receive fludarabine, thiotepa, etoposide, melphalan, and (if you are receiving an umbilical cord blood or matched unrelated donor transplant) rabbit ATG. This drug combination is called conditioning chemotherapy. These drugs are not intended to treat the disease directly but instead help prepare your body to receive the stem cell transplant.

**On Days -8, -7, and -6,** you will receive thiotepa and etoposide by vein. The thiotepa infusion should take about 2 – 4 hours. The etoposide infusion should take at least 60 minutes.

**On Days -5 and -4,** you will receive melphalan and fludarabine by vein. The melphalan infusion should take about 20 minutes. The fludarabine infusion should take about 1 hour.

**On Day -3,** you will receive fludarabine alone by vein over about 1 hour.

If you are receiving an umbilical cord blood or matched unrelated donor transplant only, **on Days -3 and -4,** you will also receive rabbit ATG by vein. The first infusion may take at least 6 hours for adults and 6-12 hours in pediatric patients. The second infusion may take at least 4 hours.

On **Days -2,** you will start to receive either tacrolimus or cyclosporine to help lower your chance of developing graft-versus-host disease (GVHD), described below in the Possible Risks section. You will receive the drug by vein as a continuous (non-stop) infusion every day until you are able to take it by mouth. You will continue to take tacrolimus/cyclosporine by mouth every day. It is expected that you will take this drug until about Day 60-100, depending on what kind of donor the stem cells came from, but it may be longer if the study doctor thinks it is needed. You will then be tapered off (gradually stop taking) tacrolimus or cyclosporine. The study doctor will discuss with you which drug you will take and how long/how often you will receive it.

On **Day 0**, you will have your stem cell transplant. You will receive the stem cells by vein. The study doctor will discuss with you how long the stem cell transplant will take.

You will also start taking mycophenolate mofetil (MMF) to help prevent GVHD. You will take it 3 times every day, about 8 hours apart. You will take it until about Day 60-100, depending on what kind of donor the stem cells came from, but it may be longer or shorter if the study doctor thinks it is needed.

During this study, you will also be given standard drugs to help decrease the risk of side effects. You may ask the study staff for information about how the drugs are given and their risks.

During this study, you may also receive platelet/blood infusions and/or be fed by vein for several weeks. The study doctor will discuss these procedures with you, if needed.

Between 4 and 8 weeks after your transplant, your new bone marrow should be creating enough red blood cells, white blood cells, and platelets and the new immune system should be developing as well. The study doctor will release you from the hospital when you have enough blood cells that are working properly.

## Study Visits

**Each day during your conditioning chemotherapy:**

- You will have a physical exam.
- Blood (about 3 teaspoons) will be drawn for routine tests.
- If you can become pregnant, blood (about 1 teaspoon) will be collected for a pregnancy test.

Blood (about 3 teaspoons) will be drawn for routine tests **daily after your stem cell transplant** until the study doctor thinks your blood cell counts have recovered.

**One (1) time a week for Weeks 1-6:**

- You will have a physical exam.
- Blood (about 3 teaspoons) will be drawn for routine tests.

**One (1) time a week until you are discharged from the hospital, then 1 time a week until you no longer require blood and/or platelet transfusions,** blood (about 3 teaspoons) will be drawn for routine tests.

On **Day 28:**

- Blood (about 2 – 3 teaspoons) will be drawn to determine the number of donor cells are present in your body following the transplant.

On **Day 42:**

- You will have a bone marrow aspirate to check the status of the disease.

**Two (2) times a month from Day 42 to Day 100:**

- You will have a physical exam.

On **Day 100**:

- Blood (about 3 teaspoons) will be drawn for routine tests and immune system testing.
- You will have tests/procedures to check the status of the disease. This may include the imaging scans, spinal tap, and/or bone marrow biopsy/aspirate as described in Screening Tests.

On **Day 180**:

- You will have a physical exam.
- Blood (about 4 teaspoons) will be drawn for routine tests, immune system testing, and tests to determine the number of donor cells are present in your body following the transplant.
- You will have tests/procedures to check the status of the disease. This may include the imaging scans, spinal tap, and/or bone marrow biopsy/aspirate as described in Screening Tests.

On **Day 270**:

- You will have a physical exam.
- Blood (about 4 teaspoons) will be drawn for routine tests and immune system testing.
- You will have tests/procedures to check the status of the disease. This may include the imaging scans, spinal tap, and/or bone marrow biopsy/aspirate as described in Screening Tests.

On **Day 365**:

- You will have a physical exam.
- You will have an ECHO, MRI, or MUGA scan to check your heart function.
- You will have a pulmonary function test to check your lung function.
- Blood (about 4 teaspoons) will be drawn for routine tests, immune system testing, and tests to determine the number of donor cells that are present in your body following the transplant.
- You will have tests/procedures to check the status of the disease. This may include the imaging scans, spinal tap, and/or bone marrow biopsy/aspirate as described in Screening Tests.

## 2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Fludarabine, thiotepa, etoposide, melphalan, rabbit ATG, tacrolimus, and mycophenolate mofetil may each cause low blood cell counts (red blood cells, platelets, and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.

### Fludarabine Side Effects

**Common (occurring in more than 20% of patients)**

| | | |
|---|---|---|
| • fever<br>• fatigue<br>• pain<br>• loss of appetite | • nausea<br>• vomiting | • weakness<br>• difficulty breathing<br>• cough<br>• infection |

| | | |
|---|---|---|
| | • low blood cell count (red, white, platelets) | |

**Occasional (occurring in 3-20% of patients)**

| | | |
|---|---|---|
| • chest pain (possibly due to heart trouble)<br>• heart failure<br>• heart attack<br>• fast and/or irregular heartbeat<br>• blood clots in a vein (possible pain, swelling, and/or redness)<br>• vein inflammation<br>• swelling<br>• chills<br>• stroke<br>• headache<br>• difficulty sleeping | • skin rash and/or itching<br>• sweating<br>• hair loss (partial or total)<br>• high blood sugar (possible diabetes)<br>• mouth blisters/sores (possible difficulty swallowing)<br>• diarrhea/constipation<br>• digestive system bleeding<br>• gallstones<br>• blood in the urine<br>• difficult and/or painful urination | • inability to urinate<br>• abnormal liver tests (possible liver damage)<br>• abnormal sensation (such as pins and needles)<br>• vision problems<br>• hearing loss<br>• sore/swollen throat<br>• lung damage/inflammation (possible difficulty breathing)<br>• coughing up blood |

**Rare but serious (occurring in fewer than 3% of patients)**

| | | |
|---|---|---|
| • build-up of fluid in the tissue around the heart<br>• weakness in wall of artery (possible serious bleeding complications)<br>• multiple blood clots (possible organ dysfunction and/or failure)<br>• bleeding in the brain<br>• abnormal brain function (affecting balance and coordination)<br>• progressive multifocal leukoencephalopath | • painful blisters<br>• very severe blistering skin disease (with ulcers of the skin and digestive tract)<br>• very severe blistering skin disease (loss of large portion of skin)<br>• dehydration<br>• abnormal pancreas tests<br>• bladder inflammation with bleeding (possible pain and/or urge to urinate) | • nerve damage affecting the eye and/or causing wrist weakness<br>• paralysis<br>• blindness<br>• inflammation of an eye nerve<br>• kidney failure<br>• high blood levels of uric acid (possible painful joints and/or kidney failure)<br>• bleeding in the lungs and/or airways<br>• failure to breathe<br>• low oxygen level in the blood (possible lightheadedness) |

| | | |
|---|---|---|
| y (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death)<br>• mental status change<br>• coma<br>• seizure<br>• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure) | • bone marrow failure due to abnormal tissue growth<br>• destruction of red blood cells and platelets due to abnormal antibodies<br>• anemia due to destruction of red blood cells<br>• condition causing increased bleeding and/or bruising<br>• liver failure<br>• nerve damage (possible numbness, pain, and/or loss of motor function) | • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)<br>• breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) |

Fludarabine may rarely cause you to develop another type of cancer (such as skin cancer and/or acute myeloid leukemia [a type of blood cancer].

**Frequency Unknown**

| | |
|---|---|
| • testes/sperm damage | • graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body) |

**<u>Thiotepa Side Effects</u>**

**It is not known how often the following side effects of thiotepa may occur.**

| | | |
|---|---|---|
| • chills<br>• fatigue<br>• fever<br>• headache<br>• weakness<br>• dizziness<br>• hair loss (partial or total)<br>• skin rash<br>• lightening of skin<br>• hives | • nausea/vomiting<br>• stopped menstrual cycle<br>• decreased production of sperm<br>• difficult and/or painful urination<br>• inability to urinate<br>• low blood cell counts (red, white, platelets)<br>• blood in the urine | • swelling of the vocal cords<br>• difficulty breathing due to narrowing of the airways<br>• wheezing<br>• nosebleed<br>• infection<br>• life-threatening allergic reaction (such as difficulty breathing, |

| | | |
|---|---|---|
| • abdominal pain<br>• loss of appetite | • blurry vision<br>• painful red eyes | low blood pressure, and/or organ failure)<br>• injection site pain |

**Rare but serious (occurring in fewer than 3% of patients)**

| | |
|---|---|
| • liver damage (possible caused by blood clots) | • bladder inflammation (possible pain, bleeding, and/or urge to urinate) |

Thiotepa may rarely cause you to develop another type of cancer (such as acute myeloid leukemia, a type of blood cancer).

**Etoposide Side Effects**

**Common (occurring in more than 20% of patients)**

| | | |
|---|---|---|
| • hair loss (partial or total) | • nausea | • vomiting<br>• low blood cell counts (red, white, platelets) |

**Occasional (occurring in 3-20% of patients)**

| | | |
|---|---|---|
| • loss of appetite<br>• diarrhea | • mouth blisters/sores (possible difficulty swallowing) | • liver damage |

**Rare but serious (occurring in fewer than 3% of patients)**

| | | |
|---|---|---|
| • low blood pressure (possible dizziness/fainting)<br>• heart attack<br>• decreased blood supply to the heart<br>• blood vessel spasm (possible blockage of blood flow)<br>• blood vessel inflammation (possible bleeding and/or bruising)<br>• fever<br>• brain injury that may be reversible (possible headache, | • severe sunburn-like rash at site of previous radiation (called radiation recall)<br>• very severe blistering skin disease (with ulcers of the skin and digestive tract)<br>• very severe blistering skin disease (loss of large portion of skin)<br>• enlarged bowel (possible abdominal pain) | • nerve damage (possible numbness, pain, and/or loss of motor function)<br>• blindness<br>• inflammation of an eye nerve<br>• lung inflammation and/or damage (possible difficulty breathing)<br>• blue skin<br>• drug leakage from the injection site (possible hardened tissue and/or tissue death) |

| | | |
|---|---|---|
| confusion, seizures, and/or vision loss)<br>• seizure | • failure of the ovaries to produce hormones (possible stopped menstrual cycle)<br>• abnormal blood acid/base balance (possible organ damage) | • closing of the throat<br>• allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) |

High-dose etoposide also may cause the following side effects. It is not known how often these side effects may occur.

| |
|---|
| • symptoms of drunkenness (possible flushing and/or dizziness) |

High-dose etoposide may cause you to develop another type of cancer (such as leukemia, a type of blood cancer).

**Melphalan Side Effects**

**Common (occurring in more than 20% of patients)**

| | | |
|---|---|---|
| • swelling (arm/leg)<br>• fever<br>• fatigue<br>• dizziness<br>• low blood levels of potassium (possible weakness and/or muscle cramps) | • low blood levels of phosphate (possible bone damage)<br>• diarrhea<br>• nausea<br>• vomiting<br>• loss of appetite<br>• constipation | • mouth blisters/sores (possible difficulty swallowing)<br>• abdominal pain<br>• abnormal taste<br>• upset stomach<br>• low blood cell counts (red, white, platelet) |

**Occurring in 1-10% of patients**

| | | |
|---|---|---|
| • bright red blood in the stool<br>• stopped menstrual cycle | • kidney failure | • allergic reaction that may be life threatening (such as difficulty breathing, low blood pressure, and/or organ failure) |

**Frequency Unknown**

| | | |
|---|---|---|
| • blood vessel inflammation (possible bleeding and/or bruising)<br>• flushing<br>• tingling<br>• hormonal deficiency that affects the body's ability to control blood pressure and react to stress | • inability to have children<br>• decreased testes function<br>• liver damage, possibly due to blood clots<br>• jaundice (yellowing of skin and/or eyes) | • abnormal kidney test (possible kidney damage)<br>• damage to DNA (possible new form of cancer) |

**Rare but serious (occurring in fewer than 3% of patients)**

| | | |
|---|---|---|
| • bone marrow failure<br>• lung damage (possible difficulty breathing) | • lung inflammation (possible difficulty breathing) | • tissue death at the injection site caused by drug leakage |

**ATG Side Effects**

Treatment with ATG may cause the body to make human antibodies to the rabbit- or horse-based antibody, depending on which one you receive. If you receive other drugs in the future that contain rabbit or horse proteins, you could develop an allergic reaction to those drugs.

**Rabbit ATG Side Effects**

It is not known how often the following side effects may occur.

| | | |
|---|---|---|
| • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)<br>• high blood pressure<br>• swelling (arm/leg)<br>• fast heartbeat | • dizziness<br>• fever<br>• chills<br>• headache<br>• high blood levels of potassium (possible kidney failure)<br>• abdominal pain<br>• nausea | • diarrhea<br>• low blood cell counts (white and/or platelets)<br>• weakness<br>• pain<br>• difficulty breathing<br>• infusion site pain/swelling/redness |

Rabbit ATG may cause cytokine release syndrome. This involves a release of a large amount of proteins into the blood stream. This may cause changes in blood pressure and heartbeat, flu-like symptoms (nausea, fever, and chills), and/or affect your lung/liver/kidney function. It may also cause certain brain-related symptoms, such as dizziness, weakness, confusion, difficulty speaking, and/or decreased brain function (possible paralysis and/or coma).

## Tacrolimus Side Effects

### Common (occurring in more than 20% of patients)

| | | |
|---|---|---|
| • high blood pressure<br>• swelling<br>• headache<br>• difficulty sleeping<br>• fever<br>• itching and/or skin rash<br>• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)<br>• high blood sugar (possible diabetes)<br>• low blood sugar | • high blood levels of fat (possible heart disease and/or stroke)<br>• diabetes<br>• diarrhea<br>• abdominal pain<br>• nausea/vomiting/upset stomach<br>• constipation<br>• loss of appetite<br>• fluid in the abdomen<br>• low blood cell counts (red, white, platelets)<br>• abnormal liver tests (possible liver damage, and possibly due to scarring and/or blood clots) | • tremors<br>• weakness<br>• abnormal sensation (such as pins and needles)<br>• pain<br>• abnormal kidney test (possible kidney damage)<br>• difficulty breathing (possibly due to lung damage)<br>• build-up of fluid around the lungs<br>• infection |

### Occasional (occurring in 3-20% of patients)

| | | |
|---|---|---|
| • chest pain (possibly due to heart trouble)<br>• build-up of fluid in the tissue around the heart | • fatigue<br>• dizziness<br>• inflammation of the stomach and/or intestines | • decreased urine output<br>• cough<br>• lung inflammation |

### Exact frequency unknown but occurring in fewer than 15% of patients

| | | |
|---|---|---|
| • low blood pressure (possible dizziness/ fainting)<br>• abnormal EKG<br>• irregular/fast/slow heartbeat<br>• heart and/or lung failure<br>• heart attack<br>• enlarged heart<br>• decreased blood supply to the heart<br>• decreased blood supply to the brain caused by stroke<br>• blood vessel disorder (possible tissue death)<br>• increased amount of blood<br>• vein inflammation<br>• blood clots in a vein (possible pain, swelling, and/or redness)<br>• abnormal blood clotting<br>• stroke<br>• flushing<br>• fainting<br>• abnormal dreams<br>• difficulty thinking<br>• inability to speak<br>• memory loss<br>• difficulty writing<br>• loss of coordination due to brain dysfunction<br>• difficulty walking<br>• chills<br>• confusion<br>• mood swings or changes (such as agitation, anxiety, depression, and/or nervousness)<br>• nightmares<br>• hallucinations (seeing or hearing things that are not there) | • sweating<br>• skin sores<br>• wound healing problems<br>• abnormal blood acid/base balance (possible organ damage)<br>• Cushing's syndrome (possible weakness, diabetes, and/or bone weakness)<br>• low blood levels of iron (possible low blood red cell counts and/or weak fingernails)<br>• high blood levels of uric acid (possible painful joints and/or kidney failure)<br>• dehydration<br>• throat inflammation (possible esophageal sore)<br>• mouth blisters/sores<br>• increased appetite<br>• cramps<br>• difficulty swallowing<br>• gas<br>• abdominal wall inflammation<br>• hole in the intestines (possibly leaking contents into the abdomen)<br>• slow emptying of food from the stomach into the intestines<br>• stomach ulcer<br>• intestinal blockage<br>• fluid-filled sac in the pancreas<br>• inflammation and bleeding of the pancreas (possible abdominal pain and/or tissue death) | • high red blood cell count (possible headache, dizziness, and/or stoke)<br>• anemia due to destruction of red blood cells<br>• blockage of the bile tract (possible body yellowing and/or abdominal pain)<br>• liver damage<br>• jaundice (yellowing of skin and/or eyes)<br>• leg cramps<br>• muscle pain, twitching, tightness, and/or spasms<br>• painful joint inflammation<br>• joint disease (possible pain)<br>• loss of bone strength (possible broken bones)<br>• immune response that causes the body to attack itself (causing muscle weakness)<br>• nerve damage (loss of motor or sensory function) that is possibly due to pressure on the nerves<br>• paralysis<br>• walking/balance problems (possible falling)<br>• vision problems (such as blurry vision and/or lazy eye)<br>• painful red eyes<br>• hearing loss<br>• ear pain<br>• ringing in the ears<br>• kidney failure<br>• infection-related kidney damage (possible kidney failure) |

| | | |
|---|---|---|
| • psychosis (loss of contact with reality)<br>• seizure<br>• acne<br>• hair loss (partial or total)<br>• shedding and scaling of the skin (possible fatal loss of bodily fluids)<br>• hair growth<br>• skin sensitivity to sunlight or sunlamps<br>• change of skin color | • weight gain/loss<br>• bladder inflammation (possible pain, bleeding, and/or urge to urinate)<br>• difficult, frequent, and/or painful urination<br>• inability to produce urine<br>• blood in the urine<br>• vaginal inflammation<br>• rectal disease<br>• increased risk of bleeding | • back-up of urine into the kidney<br>• death of kidney tissue (possible kidney failure)<br>• voice changes<br>• sore throat<br>• hiccups<br>• collapsed lung and/or fluid in the lung (possibly difficulty breathing)<br>• runny nose<br>• flu-like symptoms<br>• allergic reaction<br>• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) |

Tacrolimus may cause you to develop another type of cancer (such as bladder, thyroid, or skin cancer).

**Rare but serious (occurring in fewer than 3% of patients)**

| | | |
|---|---|---|
| • sudden stopping of the heart<br>• multiple blood clots (possible organ dysfunction and/or failure)<br>• DIC (breakdown of the blood clotting system) (possible severe bleeding, organ dysfunction, and/or organ failure)<br>• abnormal blood clotting in small blood vessels (possible stroke and/or other organ damage)<br>• tissue swelling<br>• coma<br>• difficulty forming or speaking words<br>• anxiety disorder causing inability to speak<br>• decreased brain function (possible paralysis and/or coma) | • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss)<br>• progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death)<br>• delirium (loss of contact with reality)<br>• very severe blistering skin disease (with ulcers of the skin and digestive tract)<br>• very severe blistering skin disease (loss of large portion of skin)<br>• inflammation and bleeding of the pancreas (possible abdominal pain)<br>• decreased bone marrow function and inability to make red blood cells | • destruction of red blood cells (possible kidney damage and/or failure)<br>• increase in white blood cells<br>• breakdown of muscle tissue (possible kidney failure)<br>• liver failure<br>• blindness<br>• damage to an eye nerve (possible vision changes)<br>• deafness<br>• failure to breathe<br>• increased blood pressure in the lungs (possible difficulty breathing and/or heart failure)<br>• life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)<br>• multiorgan failure<br>• graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body) |

Tacrolimus may rarely cause you to develop another type of cancer (such as lymphoma [a type of lymph node cancer] or leukemia [a type of blood cancer]).

Tacrolimus also may cause heart damage. It is not known how often this may occur.

**Cyclosporine Side Effects**

**Common (occurring in more than 20% of patients)**

| | | |
|---|---|---|
| • high blood pressure<br>• headache | • hair growth<br>• nausea | • tremors<br>• decreased kidney function |

Cyclosporine may commonly cause an increased risk of infection, such as a viral or bacterial infection or pneumonia. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

**Occasional (occurring in 3-20% of patients)**

| | | |
|---|---|---|
| • swelling<br>• high blood levels of fat (possible heart disease and/or stroke) | • diarrhea<br>• thickened gums<br>• abdominal pain<br>• upset stomach | • female reproductive disorder<br>• abnormal sensation (such as pins and needles)<br>• leg cramps |

**Rare but serious (occurring in fewer than 3% of patients)**

| | | |
|---|---|---|
| • abnormal blood clotting in small blood vessels (possible stroke and/or other organ damage)<br>• increased pressure in the skull (possible headache, vision changes, and/or mental status changes)<br>• brain damage that may be reversible (possible headache, confusion, seizures, and/or vision loss)<br>• loss of consciousness | • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death)<br>• abnormal salts, minerals, or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizures)<br>• destruction of red blood cells (possible kidney damage and/or failure) | • blockage of the bile tract (possible body yellowing and/or abdominal pain)<br>• abnormal liver tests (possible liver damage and/or yellowing of the skin/eyes)<br>• breakdown of muscle tissue (possible kidney failure)<br>• swelling of the eye nerve (possible vision loss)<br>• fluid in the lung (possible difficulty breathing)<br>• life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) |

Cyclosporine may cause you to develop another type of cancer, such as lymphoma (a type of lymph node cancer).

**Mycophenolate Mofetil Side Effects**

**Common (occurring in more than 20% of patients)**

| | | |
|---|---|---|
| • high blood pressure<br>• low blood pressure (possible dizziness/fainting)<br>• swelling (such as arm/leg/face)<br>• chest pain (possibly due to heart trouble)<br>• fast heartbeat<br>• headache<br>• dizziness<br>• difficulty sleeping<br>• fever<br>• anxiety<br>• skin rash<br>• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure) | • high blood sugar (possible diabetes)<br>• high blood levels of fat (possible heart disease and/or stroke)<br>• nausea/vomiting<br>• diarrhea/constipation<br>• abdominal pain<br>• loss of appetite<br>• upset stomach<br>• fluid in the abdomen<br>• increase in infection-fighting cells<br>• low blood cell counts (red, white, platelets)<br>• abnormal liver tests (possible liver damage)<br>• pain<br>• weakness | • tremors<br>• abnormal sensation (such as pins and needles)<br>• decreased kidney function<br>• abnormal kidney test (possible kidney damage)<br>• difficulty breathing (possibly due to narrowing of the airways)<br>• build-up of fluid around the lungs<br>• cough<br>• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) |

Mycophenolate mofetil may cause long-lasting anemia. Mycophenolate mofetil may cause a viral or bacterial infection.

**Occasional (occurring in 3-20% of patients)**

| | | |
|---|---|---|
| • irregular/slow heartbeat<br>• extra heartbeats<br>• sudden stopping of the heart<br>• heart failure<br>• build-up of fluid in the tissue around the heart<br>• decreased blood circulation<br>• abnormal blood clotting<br>• blood clots in an artery and/or vein (possible organ damage such as stroke and/or heart attack)<br>• blood vessel spasm (possible blockage of blood flow)<br>• increased risk of bleeding<br>• flushing<br>• seizure<br>• mood changes or swings (such as agitation, confusion, depression, and/or nervousness)<br>• delirium and/or psychosis (loss of contact with reality)<br>• hallucinations (seeing or hearing things that are not there)<br>• difficulty thinking<br>• fainting<br>• chills and fever<br>• fatigue/lack of energy<br>• sleepiness<br>• sweating<br>• pale skin<br>• acne<br>• hair loss (partial or total)<br>• hair growth<br>• itching<br>• thickened skin | • diabetes<br>• low blood sugar<br>• abnormal blood acid/base balance (possible organ damage)<br>• Cushing's syndrome (possible weakness, diabetes, and/or bone weakness)<br>• digestive system bleeding due to digestive system irritation<br>• thirst/dehydration<br>• abdominal swelling<br>• difficulty swallowing<br>• gum disease<br>• thickened gums<br>• mouth blisters/sores (possible difficulty swallowing)<br>• dry mouth<br>• inflammation of the stomach and/or intestines<br>• stomach ulcer<br>• weight gain or loss<br>• gas<br>• paralysis of the intestines<br>• tarry or coffee ground-like blood in the stool<br>• frequent and/or painful urination<br>• inability to urinate<br>• blood in the urine<br>• decreased urine output<br>• swelling of the scrotum<br>• impotence<br>• prostate disorder<br>• increased amount of blood<br>• wound healing problems | • painful joint inflammation<br>• joint disorder<br>• muscle tightness<br>• numbness<br>• nerve damage (loss of motor or sensory function)<br>• loss of bone strength (possible broken bones)<br>• leg cramps<br>• cataracts (clouding of the lens of the eye)<br>• vision problems (possible teary eyes, lazy eye, and/or painful red eyes)<br>• deafness<br>• ear pain<br>• ringing in the ears<br>• back-up of urine into the kidney<br>• high blood levels of uric acid (possible painful joints and/or kidney failure)<br>• kidney failure<br>• death of kidney tissue (possible kidney failure)<br>• voice changes<br>• sore throat/throat inflammation<br>• collapsed lung and/or fluid in the lung (possibly difficulty breathing)<br>• increased blood pressure in the lungs (possible difficulty breathing and/or heart failure)<br>• runny nose<br>• interrupted breathing<br>• lung inflammation (possible difficulty breathing)<br>• nosebleed<br>• coughing up blood |

| | | |
|---|---|---|
| • skin sores<br>• blistering skin rash<br>• cyst (fluid-filled lump)<br>• underactive thyroid gland (possible weight gain, heart failure, and/or constipation) | • high red blood cell count (possible headache, dizziness, and/or stoke)<br>• liver damage<br>• jaundice (yellowing of skin and/or eyes) | • hiccups<br>• fast breathing<br>• flu-like symptoms |

MMF may occasionally cause you to develop another type of cancer (such as skin cancer).

**Rare but serious (occurring in fewer than 3% of patients)**

| | | |
|---|---|---|
| • heart valve damage<br>• progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) | • hole in the intestines (possibly leaking contents into the abdomen)<br>• inability to process food due to stomach and/or intestinal damage<br>• inflammation of the pancreas (possible abdominal pain) | • decreased bone marrow function and inability to make red blood cells<br>• infection-related kidney damage (possible kidney failure)<br>• lung damage (possible difficulty breathing) |

MMF may rarely cause you to develop lymphoma (cancer of the lymph nodes).

**Frequency Unknown**

| | |
|---|---|
| • birth defects | • pregnancy loss |

**Using the study drugs together** may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

**<u>Other Risks</u>**
The **allogeneic stem cell transplant** infusion may cause allergic reactions and/or shortness of breath. The donor cells may fail to grow and multiply in your body (graft failure). If this occurs, you may have a high risk of infections and/or bleeding. You may need frequent blood transfusions. Graft failure can be treated with growth factors or a second transplant, but these treatments do not work all the time.

Once inside your body, the cells from your donor may react against your normal tissues, causing a reaction called graft-versus-host disease (GVHD). Acute GVHD may occur within the first several months after the transplant and may cause skin rash, diarrhea, and/or liver damage. Chronic GVHD may develop after the third

month after the transplant and is considered a long term complication involving the lungs, eyes, mouth, liver, skin, joints, digestive system, and/or muscles.

**Veno-occlusive disease** (liver damage caused by blood clots) is a common complication that results from high doses of chemotherapy. Patients who experience this develop swelling, weight gain, jaundice (yellowing of skin and/or eyes), abnormal liver function, abdominal swelling, and stomachache or shoulder pain. These usually occur in the first month after transplant. Although most patients recover completely, veno-occlusive disease can lead to death. If you develop these symptoms, you will receive drugs to treat them.

Some complications of transplantation may occur many years later. Some children experience delays in growth. There may be hormonal problems that affect your thyroid or damage to the ovaries or testes, which lead to infertility. Your hormone level will be monitored yearly following your transplant. The chemotherapy can also affect any organ system including your heart, lungs and kidneys. You may develop cataracts, which are cloudy spots on the lens of the eyes that blur vision. They can occur many years after the transplant. If you notice a change in your eyesight following transplant, you should notify your doctor immediately. If children do not have their adult teeth at the time of transplant, their tooth development may be delayed. Tooth decay and gum disease are also common. It will be important to see a dentist regularly following transplant. Some children will develop learning disabilities, growth problems, bone problems, nervous system problems, and psychosocial issues following their transplant.

**Blood draws** may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **bone marrow biopsies/aspirates** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

**Spinal taps** may cause headaches, sensitivity of the eyes to light, nausea, vomiting, confusion, drowsiness and/or pain at the injection site. They may cause fever, infection, and/or bleeding. Spinal taps may cause inflammation/bleeding around the brain and/or the covering of the spinal cord, which can lead to nerve damage. In rare instances, spinal taps may cause seizures, leakage of spinal fluid, and/or blockage of spinal fluid, which can lead to brain swelling. Severe infections of the spinal fluid or bleeding within the brain can result in coma and/or death. Repeated spinal taps may result in learning or memory difficulties.

**EKGs/ECHOs** may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

**MUGA scans** may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

**CT scans** send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

A **PET scan** may cause you to feel "closed in" while lying in the scanner. However, the scanner is open at both ends and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or technicians will give comfort or the scanning will be stopped.

The PET scan exposes your body to radiation. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel "closed in" and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality.**

This study may involve unpredictable risks to the participants.

**Pregnancy Related Risks**

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: Talk to your study doctor about appropriate methods of birth control during this study.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

## 3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

## Additional Information

4. You may ask the study chair (Dr. Jeremy Connors, at 713-792-6624) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. It may be dangerous to suddenly stop study treatment, and the study doctor can discuss ways to safely withdraw. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   If you stop being in the research, already collected data may not be removed from the study database. The study staff may ask if they can continue collecting the results of routine care from your medical record. If you agree, this data will be handled the same as research data.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

## Future Research

### Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and/or shared with other researchers and/or institutions for use in future research.

**Samples**
Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

**Genetic Research**
Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

**Authorization for Use and Disclosure of Protected Health Information (PHI):**

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

   Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected. If you withdraw from the study, the study staff may ask if they can continue collecting the results of routine care from your medical record.

E. 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.

**CONSENT/AUTHORIZATION**
**(Adult Participants Only)**

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

**LEGALLY AUTHORIZED REPRESENTATIVE (LAR)**

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

**WITNESS TO CONSENT**

I was present during the explanation of the research to be performed under this protocol.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

**PERSON OBTAINING CONSENT**

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

**PARENT/GUARDIAN PERMISSION**

I have read and understand the description of this research. I have had a chance to discuss the study and ask questions. My questions have been answered. I give permission for my child or ward to take part in this study.

_____ _____
SIGNATURE OF PARENT/GUARDIAN DATE

_____
PRINTED NAME OF PARENT/GUARDIAN

_____ _____
SIGNATURE OF PARENT/GUARDIAN DATE
Signature of Other Parent (Optional, unless required by the IRB.)

_____
PRINTED NAME OF PARENT/GUARDIAN

__X__ The IRB has determined that the signature of both parents is required.

If not obtaining both parental signatures, please indicate reason below:

____Other parent is deceased, unknown, incompetent, or not reasonably available.

____Parent/Guardian signing above has sole legal responsibility for the care and custody of the child.

____The IRB has determined that the signature of both parents is NOT required.

**ASSENT OF MINOR**

***(Entire section must be completed if the participant's intellectual age is at least 7 and less than 18 years. Participants with an intellectual age of 7 - 12 are not required to sign.)***

If written assent is not obtained on an age-appropriate participant, check reason why not:

____ 1.) The participant's intellectual age is less than seven.

____ 2.) The participant dissented, but the participant's parent(s)/guardian felt that the intervention(s) or procedure(s) involved in the research hold out the possibility of a direct benefit that is important to the health and/or well being of the participant and is available only in the context of this research study.

____ 3.) Other: _____

I have been told what I will be asked to do in this study.

I have been told that I do not have to be in this study. If I decide not to be in this study, no one will be mad at me. I may quit at any time, but if I do, I may need to take a different treatment.

I have had a chance to talk about the study and ask the study doctor questions. All of my questions have been answered. I agree to be in this study and do what I am asked to do so long as I want to stay in this study. I agree that the study doctor can put me on this study. By signing this paper, I am not giving up any of my legal rights. I have been given a copy of this document.

_____ _____

SIGNATURE OF MINOR (Age 13-17) DATE

_____

PRINTED NAME OF MINOR

**TRANSLATOR**

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line.)