THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Pre-Transplant Immunosuppression for Matched Sibling and Related Haploidentical Hematopoietic Cell Transplantation for Patients with Severe Hemoglobinopathies

2020-0952

Study Chair: Kris Mahadeo

_____ _____
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).

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.

STUDY SUMMARY

The goal of this clinical research study is to learn about the long-term effectiveness (how well something works) of hematopoietic cell transplantation (HCT) in patients with severe blood diseases.

Hematopoietic cells are found in the bone marrow and produce blood cells. HCT injects healthy hematopoietic cells into the body to support blood cell production.

This is an investigational study. HCT is FDA approved and commercially available for the treatment of severe blood diseases. It is investigational to study the long-term effectiveness of HCT.

You will also receive drugs as part of this study (described under "Study Drug Administration") that are FDA approved and commercially available to help prepare

your body for HCT and lower your risk of developing a side effect called graft-versus-host disease (GVHD).

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

HCT 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. If you take part in this study, you may experience side effects, some of which may be severe or fatal.

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

You will receive 1 hematopoietic cell transplant, and follow-up after the procedure will last for 2 years.

You and/or your insurance provider will be responsible for the cost of HCT and the drugs given to prepare your body for the procedure and decrease the risk of graft-versus-host disease.

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

1. STUDY DETAILS

Screening Procedures

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

- You will have a physical exam.
- You will have an eye exam by an eye doctor.
- You will have an echocardiogram (ECHO), EKG, and either a cardiac MRI or MUGA scan to check your heart function.
- Blood (about 3 tablespoons) will be drawn for routine tests, immune system testing, cytokine testing, infectious virus testing, and to check the status of the disease. Cytokines are proteins that may affect the immune system. Infectious virus testing includes checking for cytomegalovirus (CMV), hepatitis B and C, herpes, vesicular stomatitis virus (VSV), human T-cell lymphotropic virus (HTLV) types 1 and 2, HIV (the AIDS virus), adenoviruses, and galactomannan (a sign of infection).

- Urine will be collected for routine tests.
- You will have imaging scans (CT scan, MRI, and/or an MRA [magnetic resonance angiogram]) to check your health.
- You may have a lung function test. During a lung function test, you will blow into a device to measure your lung volume and capacity.
- If you can become pregnant, part of the above blood sample 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 treatment options will be discussed with you.

Up to 40 patients will be enrolled in this study. Up to 25 will take part at MD Anderson.

Study Drug Administration

You will have some or all of the therapies below to help prepare your body for the transplant and lower your risks of developing GVHD. These are not meant to treat the disease. Negative days are days before you receive HCT on Day 0.

Immunosuppression Therapy

If you are found to be eligible to take part in this study, starting 68 days before HCT, you will have immunosuppression therapy to prepare your body for HCT. On **Days -68 to -64 and Days -40 to -36**, you will receive:

- Fludarabine by vein over about 30-60 minutes.
- Dexamethasone by vein over about less than 1 minute.

Antibody Desensitization Therapy

Antibodies are created by the immune system and may attack foreign cells or substances, such as transplanted hematopoietic cells. If the study doctor thinks it is needed, you may have antibody desensitization therapy before HCT to help your body accept the new hematopoietic cells. You may receive:

- Rituximab by vein over several hours depending on the dose level you receive on **Days -69, -41, -28, and -13.**
- Bortezomib by vein over less than 1 minute either on **Days -68, -65, -40, and -37** or on **Days -68, -65, -62, -58, -40, -37, -34, and -31**.

Please note: If you take part in this study and you receive rituximab, you may be given either rituximab or a biosimilar of that drug (which means it is identical to the study drug). Everything stated in this document about rituximab also applies to its biosimilar, including information about FDA approval status, side effects, and cost.

Conditioning Therapy

After completing immunosuppression therapy and antibody desensitization therapy (if you have it), you will have conditioning therapy to help prepare your body for HCT. You will receive:

- Rabbit ATG by vein on **Days -12 to -10**. The first infusion will take about 6 hours, and the second and third may only take about 4 hours.
- Fludarabine by vein over about 30-60 minutes on **Days -8 to -4**.
- Busulfan by vein over about 3 hours on **Days -7 to -4**.

Plasmapheresis
If the study doctor thinks it is needed, on **Day -12** when you start conditioning therapy, you may also have plasmapheresis to help prepare your body to accept the new hematopoietic cells.

For this procedure, you will need to stay seated in a chair and keep both arms still for about 3 hours. During this process, your blood will flow into the machine and then directly back into your bloodstream through the second line. Blood will be drawn from 1 arm through a catheter (needle and tube) connected to the plasmapheresis machine. Inside the machine, plasma (where the antibodies are located) will be separated from the rest of the blood and collected in a sterile bag. Then, the rest of the blood will be returned through a catheter to your other arm. A blood thinner called citrate will be added to the blood as it enters the machine in order to lower the risk of your blood clotting in the machine.

HCT
After completing conditioning therapy, you will receive a hematopoietic cell transplantation on **Day 0**. You will be hospitalized for the procedure and will stay in the hospital to be watched for side effects until the study doctor thinks it is safe for you to be discharged. This may last about 4-6 weeks.

Graft-Versus-Host Disease (GVHD) Therapy
GVHD occurs when transplanted donor cells attack the cells of the recipient's body. After HCT, you will receive the following drugs to help prevent GVHD:

- Cyclophosphamide by vein over about 2-3 hours on **Days 3 and 4**.
- Tacrolimus by vein as a continuous infusion starting on **Day 5**. After Day 5, you will continue to receive tacrolimus for 6-12 months. If the study doctor thinks it is safe, you may be able to take the drug by mouth. If this happens, the dose you receive and how often you take it will be discussed with you.
- MMF by vein over about 2 hours or by mouth on **Day 5**. After Day 5, you will continue to receive or take MMF every day, 2 times a day (every 12 hours) for another 60 days.

You will no longer be able to take the study drugs or receive HCT if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

You will 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.

Additional Treatments
As part of your standard of care, you may receive additional treatment (such as hydroxyurea or chelation therapy). You may have already been prescribed these

medications as part of your standard of care when you join the study. If this is the case, you will continue to receive those medications.

You will sign a separate consent form explaining how hydroxyurea and chelation therapy is given, including their risks.

Study Visits

During Immunosuppression Therapy

If you tested positive for infectious viruses at screening, every 2 weeks until immunosuppression therapy is completed, blood (about 3 teaspoons) will be drawn for infectious virus testing.

During Conditioning Therapy

Every day while receiving conditioning therapy:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests and to check the status of the disease.

On the Day of HCT

On **Day 0**, blood (about 3 teaspoons) will be drawn for routine tests.

After HCT

While you are hospitalized after HCT, blood (about 3-4 teaspoons) will be drawn for routine tests every day until the study doctor thinks it is no longer needed to draw blood daily. After that, blood will be drawn 3 times a week until you are discharged from the hospital and then 1 time every week after that until the study doctor thinks it is no longer needed.

Every week while you are hospitalized, blood (about 3 teaspoons) will be drawn for infectious virus testing.

Every week for 4 weeks and then every month for 6 months after that, blood (about 1-2 teaspoons) will be drawn for cytokine testing.

Every week for 6 weeks and then 2 times a month after that through Day 100:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests, immune system testing, and/or to check the status of the disease.

On **Days 90, 180, and 270**:

- You will have a physical exam.
- Blood (about 3 tablespoons) be drawn for routine tests, immune system testing, and/or to check the status of the disease.
- Urine will be collected for routine tests.
- You will have an EKG and ECHO to check your heart function (Day 180).
- You will have an MRI or MRA to check your health (Day 180).

- You may have a lung function test (Day 180).

On **Day 365** (1 year after HCT):

- You will have a physical exam.
- You will have an eye exam by an eye doctor.
- You will have an ECHO, EKG, and either a cardiac MRI or MUGA scan to check your heart function.
- Blood (about 3 tablespoons) will be drawn for routine tests, immune system testing, cytokine testing, and to check the status of the disease.
- Urine will be collected for routine tests.
- You will have imaging scans to check your health.
- You may have a lung function test.

Pharmacokinetic (PK) Testing

Blood (about 1 teaspoon each time) will also be drawn during this study for pharmacokinetic (PK) testing at the following time points. PK testing measures the amount of study drug in the body at different time points.

- On Days -12 to -10, before the dose and then 2 more times over the next 4 hours after the dose
- On Day -9, about 24 hours after the Day -10 dose
- On Day -5
- On Day 0, before HCT
- On Days 7, 14, 21, and 28

Follow-Up Visit

Two (2) years after HCT:

- You will have an ECHO and EKG to check your heart function.
- Blood (about 1 teaspoon) will be drawn for routine tests.
- You will have an MRI or MRA to check your health.

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 the study drug 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 the study drug. 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, rituximab, bortezomib, rabbit ATG, busulfan, cyclophosphamide, tacrolimus, mycophenolate mofetil, and plasmapheresis may each cause low blood cell counts (red, white and/or platelets):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood 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.
- 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.

Fludarabine Side Effects

Common (occurring in more than 20% of patients)

• fever • fatigue • pain • loss of appetite	• nausea • vomiting • low blood cell count (red, white, platelets)	• weakness • difficulty breathing • cough • infection

Occasional (occurring in 3-20% of patients)

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

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

• build-up of fluid in the tissue around the heart • weakness in wall of artery (possible serious bleeding complications) • multiple blood clots (possible organ dysfunction and/or failure) • bleeding in the brain • abnormal brain function (affecting balance and coordination) • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) • mental status change • coma • seizure • 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)	• painful blisters • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • dehydration • abnormal pancreas tests • bladder inflammation with bleeding (possible pain and/or urge to urinate) • bone marrow failure due to abnormal tissue growth • destruction of red blood cells and platelets due to abnormal antibodies • anemia due to destruction of red blood cells • condition causing increased bleeding and/or bruising • liver failure • nerve damage (possible numbness, pain, and/or loss of motor function)	• nerve damage affecting the eye and/or causing wrist weakness • paralysis • blindness • inflammation of an eye nerve • kidney failure • high blood levels of uric acid (possible painful joints and/or kidney failure) • bleeding in the lungs and/or airways • failure to breathe • low oxygen level in the blood (possible lightheadedness) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • 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)

Dexamethasone Side Effects

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

• high blood pressure • irregular, fast, and/or slow heartbeat • enlarged heart • heart failure • tearing of the walls of the heart (post-heart attack) • blood vessel inflammation (possible bleeding and/or bruising) • blood clots in a vein (possible pain, swelling, and/or redness) • blood clots in an artery (possible organ damage such as stroke and/or heart attack) • swelling (such as tissue and/or abdominal swelling) • dizziness • shock • fainting • headache • increased pressure between the skull and brain (possible headache, vision changes, and/or mental status changes) • seizure • depression • mood swings • personality changes • mental disorders • euphoria (unusual feelings of happiness or well-being) • difficulty sleeping • fatigue/lack of energy • anxiety	• hives • acne-like rash • hair loss (partial or total) • hair growth • sweating • tissue death • Cushing's syndrome (possible weakness, diabetes, and/or bone weakness) • decreased ability to process carbohydrates • high blood sugar (possible diabetes) • sugar in the urine • diabetes • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • low blood levels of potassium (possible weakness and/or muscle cramps) • abnormal blood acid/base balance (possible organ damage) • high blood levels of sodium (possible weakness and/or swelling) • body-wide loss of proteins (possible weakness and/or swelling)	• changes to the menstrual cycle • problems with production of sperm • bruising • weakness • inflammation of nerves (possible pain and/or loss of motor or sensory function) • joint pain • joint disease (possible pain) • pain or loss of function of the hips or shoulders due to bone death • broken bones • loss of muscle • muscle damage causing weakness • nerve damage (loss of motor or sensory function) • loss of bone strength (possible broken bones) • abnormal sensation (such as pins and needles) • tendon tear • collapse of bones in the spine • enlarged liver • abnormal liver tests (possible liver damage) • bulging eye • increased pressure in the eye (possible

• darkening and/or lightening of the skin • tiny dots on the skin • wound healing problems • skin rash, redness, and/or dryness • fragile and/or thinning skin • skin test reaction impaired (due to a lowered immune system) • stretch marks	• build-up of fat in abnormal areas • weight gain • increased appetite • digestive system bleeding • esophageal sore • hole in the intestines (possibly leaking contents into the abdomen) • nausea • itching near the anus • inflammation of the pancreas (possible abdominal pain) • stomach ulcer	vision loss, pain, and/or blurry vision) • cataracts (clouding of the lens of the eye) • hiccups • fluid in the lung (possible difficulty breathing) • infection • allergic reaction (such as skin reaction) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

Dexamethasone may cause stunted growth in children.

Dexamethasone may cause you to develop another type of cancer.

Dexamethasone may cause a false-positive or false-negative skin test (such as a test for tuberculosis [TB]). If you need to have a skin test performed, tell the doctor that you are taking dexamethasone.

Stopping dexamethasone suddenly may cause withdrawal symptoms (such as fever, muscle/joint pain, and fatigue). This is because dexamethasone affects your adrenal glands and may cause your body's hormone levels to change. The study doctor will help you stop dexamethasone safely, if you want to stop taking the study drug. Do not just stop taking dexamethasone.

Rituximab Side Effects

Common (occurring in more than 20% of patients)

• heart disorder • fever	• nausea	• nerve damage (possible numbness,

• fatigue • chills	• low blood cell counts (red, white) • low blood levels of phosphate (possible bone damage) • weakness	pain, and/or loss of motor or sensory function) • lung disease • infection

Rituximab may commonly cause infusion reactions such as difficulty breathing and/or tissue swelling. In some cases, life-threatening reactions such as sudden stopping of the heart and/or shock caused by heart damage may occur. It is not known how often these more serious reactions may occur.

Because rituximab is a mouse antibody that has been changed to make it similar to a human antibody, treatment with rituximab may commonly cause the body to make human antibodies to the mouse-based antibody. These antibodies are called HAMA or HACA. The potential response of your body to rituximab may lead to decreasing the effectiveness of mouse-based antibody therapies for you in the future. If you receive other drugs in the future that contain mouse proteins, you could develop an allergic reaction to those drugs.

Occasional (occurring in 3-20% of patients)

• high blood pressure • low blood pressure (possible dizziness/fainting) • chest tightness • swelling (arm/leg/ • tissue) • flushing • anxiety • headache • difficulty sleeping • dizziness • shivering • skin rash	• itching • night sweats • hives • high blood sugar (possible diabetes) • abnormal blood test • diarrhea • abdominal pain • weight gain • vomiting • upset stomach • low platelet counts	• abnormal liver and/or bone tests (possible liver damage) • pain (back/joint/muscle) • muscle spasms • difficulty breathing (possibly due to narrowing of the airways) • cough • runny nose • nosebleed • sore throat

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

• sudden stopping of the heart • fast and/or irregular heartbeat • heart failure • heart attack	• severe painful blisters • severe skin rash • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the	• abnormal sensation (such as pins and needles) • kidney damage/failure • inflammation inside the eye and/or of an

• blood vessel inflammation (possible bleeding, bruising, and/or rash) • shock caused by heart damage • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss)	skin and digestive tract) • high blood levels of uric acid (possible painful joints and/or kidney failure) • blockage and/or hole in the intestines (possibly leaking contents into the abdomen) • anemia due to destruction of red blood cells • thick blood (possible blockage of blood flow) • condition that looks like lupus (an immune system disease) • immune system reaction (possible organ damage) • decreased bone marrow function and inability to make red blood cells • liver damage/failure	eye nerve (possible vision problems) • bronchiolitis obliterans (damage of the small airways with difficulty breathing) • lung inflammation (possible difficulty breathing or chest pain) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • worsening of Kaposi's sarcoma • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

In people who have ever been infected with hepatitis B virus, there is a risk that the virus can flare up during treatment with drugs that affect your immune system, such as rituximab. This could lead to liver failure. The risk of hepatitis B virus flaring up may continue for several months after you stop taking rituximab. If you become jaundiced (yellowing of the skin and eyes) or develop viral hepatitis while taking rituximab or after stopping treatment, you should tell your study doctor right away. Your study doctor will discuss this risk with you and explain what testing is recommended to check for hepatitis.

Rituximab may also cause other viruses to reactivate. This includes JC virus (PML), cytomegalovirus, herpes simplex virus, parvovirus B19, varicella zoster virus, West Nile virus, and hepatitis C.

Talk to the study doctor before receiving any vaccines (for example, vaccines for measles, mumps, rubella, or polio). Receiving a vaccine while taking rituximab may increase the risk of serious infection or make the vaccine less effective.

Bortezomib Side Effects

Common (occurring in more than 20% of patients)

• fever • fatigue • skin rash • nausea • diarrhea	• constipation • loss of appetite • vomiting • low blood cell counts (red, white, and platelet)	• nerve pain • nerve damage (possible numbness, pain, and/or loss of motor function)

Occasional (occurring in 3-20% of patients)

• heart disease • low blood pressure (possible dizziness/ fainting)	• headache • weakness • dizziness • abdominal pain	• abnormal sensation (such as pins and needles) • difficulty breathing • injection site irritation/redness • reactivation of herpes

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

• heart failure • build-up of fluid in the tissue around the heart (possible heart failure) • severe heart problems • shock caused by heart damage • fainting • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • stroke • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or	• very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract) • hormonal deficiency that affects the body's ability to control blood pressure and react to stress • dehydration • decreased blood flow to part of the bowel (possibly causing tissue death) • destruction of red blood cells (possible kidney damage and/or failure) • blindness	• inflammation of an eye nerve • nerve damage (affecting the eye) • deafness • build up of abnormal protein in cells, causing organ failure (such as the kidneys and/or heart) • lung disease • fluid in the lungs (possible difficulty breathing) • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

coma, which may be permanent, or death) • skin condition with fever and skin lesions		

Exact frequency unknown

• sudden stopping of the heart • slow/fast/irregular heartbeat • blood clots in a vein (possible pain, swelling, and/or redness) • chest pain due to heart trouble • blood clots in an artery (possible organ damage such as stroke and/or heart attack) • blood clots in a vein (possible pain, swelling, and/or redness) • decreased supply of blood to the heart • deposits of an abnormal protein in the heart • abnormal EKG • heart attack • swelling (arm/leg/face) • high blood pressure • inflammation of the tissue around the heart (possible chest pain) • vein inflammation • brain disease • temporary stroke symptoms	• high blood sugar (possible diabetes) • 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) • weight loss • inflammation of the stomach/intestines • difficulty swallowing • blockage of the intestine or colon (possibly due to stool) • vomiting or coughing up blood • hole in the intestines (possibly leaking contents into the abdomen) • swelling of the vocal cords • inflammation of the pancreas (possible abdominal pain) • abdominal wall inflammation • tarry stool • paralysis of the intestines	• bleeding in the liver • blood clots in a vein to the liver (possible liver and/or digestive system damage) • difficulty walking • pain • uncontrolled movement • paralysis • broken bone(s) • blurry and/or double vision • painful red eyes • painful swelling of the eyelids • hearing problems • back-up of urine into the kidney • kidney stones • decreased kidney function (possible kidney failure) • kidney failure • high blood levels of uric acid (possible painful joints and/or kidney failure) • blockage in the lung (possible pain and/or shortness of breath) • cough • nosebleed • build-up of fluid around the lungs • low oxygen level in the blood due to inflammation in the

• bleeding in and/or around the brain • agitation • anxiety • chills • confusion • coma • paralysis of nerves in the spinal cord controlling the head and neck that help move the muscles of the face • difficulty forming or speaking words • difficulty sleeping • decreased function of the part of the nervous system that controls automatic functions (possible fatigue and/or low blood pressure) • fatigue/lack of energy • mental status changes • painful or abnormal skin sensations • suicidal thoughts • seizure • psychosis (loss of contact with reality) • itching • hives • tissue swelling • low blood sugar	• mouth blisters/sores (possible difficulty swallowing) • abnormal taste • chronic heartburn and indigestion • upset stomach • fluid in the abdomen • blood in the urine • inability to urinate • bladder inflammation with bleeding (possible pain and/or urge to urinate) • urge to urinate • loss of bladder control • DIC (breakdown of the blood clotting system - • possible severe bleeding, organ dysfunction, and/or organ failure) • blockage of the bile tract (possible body yellowing and/or abdominal pain) • liver damage/failure • abnormal liver tests (possible yellowing of the skin and/or eyes)	lungs (possible lightheadedness) • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • lung inflammation (possible difficulty breathing) • difficulty breathing (possibly due to lung damage) • severe life-threatening infection (possible low • blood pressure, kidney failure, and/or heart failure) • allergic reaction that may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) • bacteria in the blood

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) • high blood pressure • swelling (arm/leg) • fast heartbeat	• dizziness • fever • chills • headache • high blood levels of potassium (possible kidney failure) • abdominal pain • nausea	• diarrhea • low blood cell counts (white and/or platelets) • weakness • pain • difficulty breathing • 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).

Busulfan Side Effects

Common (occurring in more than 20% of patients)

• fast heartbeat • high blood pressure • chest pain • blood clots in the vein (possible pain, swelling, and/or redness) • swelling • flushing • headache • difficulty sleeping • anxiety • depression • dizziness • fever/chills • weakness • skin rash/itching • hair loss (partial or total)	• 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) • dry mouth • mouth blisters/sores (possible difficulty swallowing) • nausea/vomiting • loss of appetite • upset stomach • feeling of fullness • abdominal pain • diarrhea/constipation	• low blood cell counts (red, white, platelets) • abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • pain • abnormal kidney test (possible kidney damage) • lung disorder (possible damage, inflammation, and/or scarring) • cough • nosebleed • runny nose • difficulty breathing • allergic reaction

• high blood sugar (possible diabetes)		• injection site swelling

Occasionally (in 3-20% of patients), busulfan may cause liver damage due to blood clots.

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

• heart scarring (possible heart failure) • multiple blood clots (possible organ dysfunction and/or failure) • leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing) • inability to sweat • decreased production of adrenal hormones (possible weakness and/or low blood pressure)	• enlarged veins in the esophagus (possible bleeding) • decreased testicle size and function • low sperm count • inability to have children • liver damage, failure, and/or scarring • blockage of the bile tract (possible body yellowing and/or abdominal pain) • lack of tooth enamel • cataracts (clouding of the lens of the eye)	• immune response (causing muscle weakness) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

Busulfan may rarely cause you to develop another type of cancer (such as cancerous tumors or leukemia, a type of blood cancer).

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

• low blood pressure (possible dizziness/ fainting) • abnormal EKG • irregular heartbeat • heart failure • build-up of fluid around the heart (possible heart • failure) • enlarged heart	• shedding and scaling of the skin (possible fatal loss of bodily fluids) • change of skin color • acne • painful skin bumps • severe blisters • hair loss (partial or	• failure of the ovaries to produce hormones (possible stopped menstrual cycle) • increased amount of blood • enlarged liver • difficulty breathing due

• fatigue • agitation • confusion • coma • decreased brain function (possible paralysis and/or coma) • seizure • bleeding in the brain • delirium (loss of contact with reality) • hallucinations (seeing or hearing things that are not there)	• total), and it rarely may be permanent • weight gain • vomiting of blood • inflammation of the pancreas (possible abdominal pain) • intestinal blockage • decreased urine output • blood in the urine • difficult and/or painful urination • bladder inflammation with bleeding (possible pain and/or urge to urinate) • increased risk of bleeding	• to narrowing of the airways • coughing up blood • hiccups • throat inflammation/sore throat • fast breathing • build-up of fluid around the lungs • low oxygen level in the blood (possible lightheadedness) due to dehydration and low blood pressure • graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body) • infection

<u>Cyclophosphamide Side Effects</u>

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

• hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing) • nausea/vomiting • inability to regulate water/salt balance which can cause frequent urination and dehydration	• headache • abdominal pain • loss of appetite • diarrhea • problems with production of sperm and eggs • inability to have children • stopped menstrual cycle • low blood counts (red, platelet, white)	• fever with dangerously low white blood cell count (febrile neutropenia) • bladder inflammation and bleeding (possible pain and/or urge to urinate) • infection

Cyclophosphamide may cause you to develop another type of cancer (such as bladder cancer, acute leukemia [a type of blood cancer], lymphoma [a type of lymph

node cancer], thyroid cancer, and/or sarcoma [a type of cancer that can start in the soft tissue, bone, or other tissue].

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

• irregular heartbeat • build-up of fluid around the heart (possible heart failure) • build-up of blood in the sac around the heart (possible impaired heart function) • inflammation of the heart and/or the tissue around the heart (possible chest pain and/or bleeding) • heart damage/failure, death of heart tissue, or other severe heart problems • heart attack, which can be serious and life-threatening • blood clots in a vein (possible pain, swelling, and/or redness) • blood clots in an artery (possible organ damage such as stroke and/or heart attack) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • dizziness • very severe blistering skin disease (with ulcers of the skin and digestive tract) • severe sunburn-like rash at site of previous radiation (called radiation recall)	• wound healing problems • low blood levels of potassium (possible weakness) • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • hormonal deficiency that affects the body's ability to control blood pressure and react to stress • decreased supply of blood to the abdomen • digestive system bleeding • enlarged bowel (possible abdominal pain) • inflammation of the intestines (possible bleeding) • inflammation of the pancreas (possible abdominal pain) • liver damage (possibly due to blood clots) • jaundice (yellowing of skin and/or eyes) • high blood levels of uric acid (possible painful joints and/or kidney failure) • ovarian scarring • urinary tract or bladder scarring • decreased testicle size and function	• hearing loss • breakdown of muscle tissue (possible kidney failure) • death of kidney tissue (possible kidney failure) • difficulty breathing • lung inflammation (possible difficulty breathing) • problems with blood carrying oxygen (possible blue skin) • lung damage due to blood clots • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • multiorgan failure • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

• very severe blistering skin disease (loss of large portion of skin)	• blood in the urine • blurry vision	

<u>Tacrolimus Side Effects</u>

Common (occurring in more than 20% of patients)

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

Occasional (occurring in 3-20% of patients)

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

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

• low blood pressure (possible dizziness/ fainting) • abnormal EKG • irregular/fast/slow heartbeat • heart and/or lung failure • heart attack	• sweating • skin sores • wound healing problems • abnormal blood acid/base balance (possible organ damage)	• high red blood cell count (possible headache, dizziness, and/or stoke) • anemia due to destruction of red blood cells

• enlarged heart • decreased blood supply to the heart • decreased blood supply to the brain caused by stroke • blood vessel disorder (possible tissue death) • increased amount of blood • vein inflammation • blood clots in a vein (possible pain, swelling, and/or redness) • abnormal blood clotting • stroke • flushing • fainting • abnormal dreams • difficulty thinking • inability to speak • memory loss • difficulty writing • loss of coordination due to brain dysfunction • difficulty walking • chills • confusion • mood swings or changes (such as agitation, anxiety, depression, and/or nervousness) • nightmares • hallucinations (seeing or hearing things that are not there) • psychosis (loss of contact with reality) • seizure • acne • hair loss (partial or total) • shedding and scaling of the skin (possible fatal loss of bodily fluids) • hair growth • skin sensitivity to sunlight or sunlamps	• Cushing's syndrome (possible weakness, diabetes, and/or bone weakness) • low blood levels of iron (possible low blood red cell counts and/or weak fingernails) • high blood levels of uric acid (possible painful joints and/or kidney failure) • dehydration • throat inflammation (possible esophageal sore) • mouth blisters/sores • increased appetite • cramps • difficulty swallowing • gas • abdominal wall inflammation • hole in the intestines (possibly leaking contents into the abdomen) • slow emptying of food from the stomach into the intestines • stomach ulcer • intestinal blockage • fluid-filled sac in the pancreas • inflammation and bleeding of the pancreas (possible abdominal pain and/or tissue death) • weight gain/loss • bladder inflammation (possible pain, bleeding, and/or urge to urinate) • difficult, frequent, and/or painful urination	• blockage of the bile tract (possible body yellowing and/or abdominal pain) • liver damage • jaundice (yellowing of skin and/or eyes) • leg cramps • muscle pain, twitching, tightness, and/or spasms • painful joint inflammation • joint disease (possible pain) • loss of bone strength (possible broken bones) • immune response that causes the body to attack itself (causing muscle weakness) • nerve damage (loss of motor or sensory function) that is possibly due to pressure on the nerves • paralysis • walking/balance problems (possible falling) • vision problems (such as blurry vision and/or lazy eye) • painful red eyes • hearing loss • ear pain • ringing in the ears • kidney failure • infection-related kidney damage (possible kidney failure) • back-up of urine into the kidney

• change of skin color	• inability to produce urine • blood in the urine • vaginal inflammation • rectal disease • increased risk of bleeding	• death of kidney tissue (possible kidney failure) • voice changes • sore throat • hiccups • collapsed lung and/or fluid in the lung (possibly difficulty breathing) • runny nose • flu-like symptoms • allergic reaction • 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 • multiple blood clots (possible organ dysfunction and/or failure) • DIC (breakdown of the blood clotting system) (possible severe bleeding, organ dysfunction, and/or organ failure) • abnormal blood clotting in small blood vessels (possible stroke and/or other organ damage) • tissue swelling • coma • difficulty forming or speaking words • anxiety disorder causing inability to speak	• brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) • delirium (loss of contact with reality) • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin)	• destruction of red blood cells (possible kidney damage and/or failure) • increase in white blood cells • breakdown of muscle tissue (possible kidney failure) • liver failure • blindness • damage to an eye nerve (possible vision changes) • deafness • failure to breathe • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure)

• decreased brain function (possible paralysis and/or coma)	• inflammation and bleeding of the pancreas (possible abdominal pain) • decreased bone marrow function and inability to make red blood cells	• life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • multiorgan failure • 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.

Mycophenolate Mofetil Side Effects

Common (occurring in more than 20% of patients)

• high blood pressure • low blood pressure (possible dizziness/fainting) • swelling (such as arm/leg/face) • chest pain (possibly due to heart trouble) • fast heartbeat • headache • dizziness • difficulty sleeping • fever • anxiety • skin rash • 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) • high blood levels of fat (possible heart disease and/or stroke) • nausea/vomiting • diarrhea/constipation • abdominal pain • loss of appetite • upset stomach • fluid in the abdomen • increase in infection-fighting cells • low blood cell counts (red, white, platelets) • abnormal liver tests (possible liver damage) • pain • weakness	• tremors • abnormal sensation (such as pins and needles) • decreased kidney function • abnormal kidney test (possible kidney damage) • difficulty breathing (possibly due to narrowing of the airways) • build-up of fluid around the lungs • cough • 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 • extra heartbeats • sudden stopping of the heart • heart failure • build-up of fluid in the tissue around the heart • decreased blood circulation • abnormal blood clotting • blood clots in an artery and/or vein (possible organ damage such as stroke and/or heart attack) • blood vessel spasm (possible blockage of blood flow) • increased risk of bleeding • flushing • seizure • mood changes or swings (such as agitation, confusion, depression, and/or nervousness) • delirium and/or psychosis (loss of contact with reality) • hallucinations (seeing or hearing things that are not there) • difficulty thinking • fainting • chills and fever • fatigue/lack of energy • sleepiness • sweating • pale skin	• diabetes • low blood sugar • abnormal blood acid/base balance (possible organ damage) • Cushing's syndrome (possible weakness, diabetes, and/or bone weakness) • digestive system bleeding due to digestive system irritation • thirst/dehydration • abdominal swelling • difficulty swallowing • gum disease • thickened gums • mouth blisters/sores (possible difficulty swallowing) • dry mouth • inflammation of the stomach and/or intestines • stomach ulcer • weight gain or loss • gas • paralysis of the intestines • tarry or coffee ground-like blood in the stool • frequent and/or painful urination • inability to urinate • blood in the urine • decreased urine output • swelling of the scrotum • impotence	• painful joint inflammation • joint disorder • muscle tightness • numbness • nerve damage (loss of motor or sensory function) • loss of bone strength (possible broken bones) • leg cramps • cataracts (clouding of the lens of the eye) • vision problems (possible teary eyes, lazy eye, and/or painful red eyes) • deafness • ear pain • ringing in the ears • back-up of urine into the kidney • high blood levels of uric acid (possible painful joints and/or kidney failure) • kidney failure • death of kidney tissue (possible kidney failure) • voice changes • sore throat/throat inflammation • collapsed lung and/or fluid in the lung (possibly difficulty breathing) • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • runny nose

• acne • hair loss (partial or total) • hair growth • itching • thickened skin • skin sores • blistering skin rash • cyst (fluid-filled lump) • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)	• prostate disorder • increased amount of blood • wound healing problems • high red blood cell count (possible headache, dizziness, and/or stoke) • liver damage • jaundice (yellowing of skin and/or eyes)	• interrupted breathing • lung inflammation (possible difficulty breathing) • nosebleed • coughing up blood • hiccups • fast breathing • 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 • 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) • inability to process food due to stomach and/or intestinal damage • inflammation of the pancreas (possible abdominal pain)	• decreased bone marrow function and inability to make red blood cells • infection-related kidney damage (possible kidney failure) • 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>Plasmapheresis Side Effects</u>

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

• low blood pressure (possible dizziness/fainting)	• tingling and/or numbness • dizziness	• difficulty breathing • air entering the blood stream

• chest discomfort • irregular heartbeat • heart failure • chills • shock • seizure • fainting • anxiety • fatigue	• low blood levels of calcium (possible weakness and/or cramping) • nausea • vomiting • low blood counts (red, platelets) • destruction of red blood cells	• loss of blood (if the tubing breaks or the machine malfunctions) • discomfort, bruising, bleeding, and/or infection at the needle insertion site • infection

Citrate may cause numbness and/or tingling of the fingertips and/or around the mouth, weakness, and/or severe muscle cramps. Tell the study staff right away if you have any numbness/tingling, weakness, chills, and/or stiff arms.

You should avoid all aspirin and ibuprofen products for at least 3 days before and also during the plasmapheresis procedures. Any high physical activity, especially contact sports such as football and basketball, should be avoided for 24 hours after the plasmapheresis procedure.

Other Risks

You may receive **hydroxyurea and chelation therapy** as part of your standard of care. You will sign a separate consent form explaining these therapies, including their risks.

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.

During the **eye exam**, your pupils will be dilated with eye drops to allow a good view of the back of the eye. This will result in some blurred vision lasting for a few hours. You will not be able to drive during this time.

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.

During the **MRI/MRA**, 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/MRA staff and the scanning will be stopped if you wish. The MRI/MRA will require a catheter to be inserted into one of your veins in order to inject the MRI/MRA 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/MRA 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**. All study data will be stored in password-protected computers, and/or locked file cabinets for at least 3 years after the study ends and is closed with the IRB and will continue to be stored securely after the study. Only the study chair, collaborators, study staff/coordinators, data coordinators, research nurses, regulatory coordinators, and study monitors will have access to study data.

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. Talk with the study doctor about the birth control method(s) you should use during this study and how long to use them.

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. Kris Mahadeo, at 713-729-2873) 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. If you leave the study early, you will still have follow-up visits to check your health. If you withdraw from this study, you can still choose to be treated at MD Anderson.

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.

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.

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.

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.

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.

Conflict of Interest

The University of Texas MD Anderson has a royalty sharing agreement for IV busulfan.

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 Protocol **2020-0952**.

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

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
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.

WITNESS TO PARENTAL/GUARDIAN PERMISSION

I was present during the explanation of the research to be performed under Protocol **2020-0952**. The child participant was also present. In my opinion, the parent(s)/guardian provided permission for the child to participate in the research.

_____ _____
SIGNATURE OF WITNESS TO THE PARENTAL/GUARDIAN PERMISSION (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

_____
PRINTED NAME OF WITNESS TO THE PARENTAL/GUARDIAN PERMISSION

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

WITNESS TO ASSENT

I was present during the explanation of the research to be performed under Protocol **2020-0952**. The child participant was also present. In my opinion, the child assented to participate in the research. (Note: If obtaining assent, a witness signature is required.)

_____ _____
SIGNATURE OF WITNESS TO THE ASSENT (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

_____
PRINTED NAME OF WITNESS TO THE ASSENT

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 below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION