THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Addition of Inotuzumab Ozogamicin Pre- and Post-Allogeneic Transplantation
2018-0860

Subtitle: WI240288 – Version 24, 22 November 2024

Study Chair: Issa F. Khouri

_____ _____
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 safety of inotuzumab ozogamicin when given with fludarabine, with or without bendamustine, melphalan, and rituximab before and after a stem cell transplant. Researchers also want to learn if inotuzumab ozogamicin when given after a stem cell transplant can help control leukemia and lymphoma.

Fludarabine, bendamustine, melphalan, and rituximab are commonly given before stem cell transplants.

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

This is an investigational study. Inotuzumab ozogamicin is FDA approved and commercially available for the treatment of acute lymphoblastic leukemia (ALL).

Fludarabine, bendamustine, melphalan, and rituximab are FDA approved and commercially available for use in chronic lymphocytic leukemia (CLL). It is considered investigational to use inotuzumab ozogamicin in combination with fludarabine, bendamustine, melphalan, and rituximab to treat lymphoma and leukemia.

Treatment on this study may help to control the cancer. However, the addition of inotuzumab ozogamicin to allogeneic transplant may not improve your outcome and could worsen your outcome. Future patients may benefit from what is learned in this study. 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 should know there are other standard treatment options available without taking part in this study.

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

You will be on study for up to about 3 years.

Inotuzumab ozogamicin will be provided at no cost to you while you are on study. You and/or your insurance provider will be responsible for the cost of the stem cell transplant and fludarabine, bendamustine, melphalan, and rituximab.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive a stem cell transplant and/or other chemotherapy outside of this study. You may choose to 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

Up to 44 participants will be enrolled in this study. All will take part at MD Anderson.

Screening Tests

You had screening tests that are a routine part of the evaluation for stem cell transplantation that helped show that you were eligible to take part in this study. Tests may be repeated if not performed within 30 days before starting study treatment.

Study Drug Administration

For a stem cell transplant, the days before you receive your stem cells are called minus days. The day you receive the stem cells is called Day 0. The days after you receive the stem cells are called plus days.

Patients with leukemia will receive a different treatment plan than patients with lymphoma.

***If you have leukemia or aggressive lymphoma**:*

On **Day -13**, you will receive inotuzumab ozogamicin by vein over 1 hour. You will be given standard drugs to help decrease the risk of allergic reaction. You may ask the study staff for information about which drugs may be given and their risks.

On **Day -6**, you will be admitted to the hospital and given fluids by vein to hydrate you.

On **Days -5, -4, and -3**, you will receive fludarabine by vein over about 1 hour.

On **Day -2**, you will receive fludarabine by vein over about 1 hour and melphalan by vein over 30 minutes.

On **Day -1**, you will rest.

On **Day 0**, you will receive the stem cell transplant by vein.

On **Days +3 and +4** you will receive cyclophosphamide by vein over 3 hours. Cyclophosphamide is given to lower the immune system in order to lower the risk of graft-versus-host disease (GVHD -- when transplanted immune tissue, such as donor NK and stem cells, attacks the tissues of the recipient's body). You will also receive mesna by vein over 30 minutes every 4 hours for a total of 10 mesna doses on Days +3 and +4. Mesna is given to lower the risk of side effects to the bladder caused by cyclophosphamide. In addition, you will be given hydration starting 2 hours before each dose of cyclophosphamide.

You will be given standard drugs to help decrease the risk of side effects. Per your standard of care, you will receive ursodiol to help prevent veno-occlusive liver disease, filgrastim-sndz to help with the growth of white blood cells, and tacrolimus and mycophenolate mofetil (MMF) to help prevent graft-versus-host disease (GVHD). You may receive other standard of care drugs to help decrease the risk of side effects, if your doctor thinks it is needed. You may ask the study staff for information about which drugs may be given and their risks.

If you have indolent lymphoma:

On **Day -13**, you will receive inotuzumab ozogamicin by vein over 1 hour. You will be given standard drugs to help decrease the risk of allergic reaction. You may ask the study staff for information about which drugs may be given and their risks.

On **Day -6**, you will be admitted to the hospital and given fluids by vein to hydrate you. If you have a CD20-positive cancer, you will receive rituximab by vein over 4-6 hours.

On **Days -5, -4, and -3**, you will receive fludarabine by vein over about 1 hour and bendamustine by vein over about 30 minutes to 1 hour.

On **Days -2 and -1,** you will rest.

On **Day 0**, you will receive the stem cell transplant by vein.

On **Days +1 and +8**, you will receive rituximab by vein over 4-6 hours.

On **Days +3, and +4,** you will receive cyclophosphamide by vein over 3 hours. Cyclophosphamide is given to lower the immune system in order to lower the risk of graft-versus-host disease (GVHD -- when transplanted immune tissue, such as donor NK and stem cells, attacks the tissues of the recipient's body). You will also receive mesna by vein over 30 minutes every 4 hours for a total of 10 mesna doses on Days +3 and +4. Mesna is given to lower the risk of side effects to the bladder caused by cyclophosphamide. In addition, you will be given hydration starting 2 hours before each dose of cyclophosphamide.

You will be given standard drugs to help decrease the risk of side effects. Per your standard of care, you will receive ursodiol to help prevent veno-occlusive liver disease, filgrastim-sndz to help with the growth of white blood cells, drugs to prevent infection, and tacrolimus and mycophenolate mofetil (MMF) to help prevent graft-versus-host disease (GVHD). You may receive other standard of care drugs to help decrease the risk of side effects, if your doctor thinks it is needed. You may ask the study staff for information about how the drugs are given and their risks.

If you receive haploidentical or mismatched stem cell transplants:

On **Day -13**, you will receive inotuzumab ozogamicin by vein over 1 hour. You will be given standard drugs to help decrease the risk of allergic reaction. You may ask the study staff for information about which drugs may be given and their risks.

On **Day -6**, you will be admitted to the hospital and given fluids by vein to hydrate you.

On **Days -5 and -4,** you will receive fludarabine by vein over about 1 hour.

On **Days -3 and -2**, you will receive fludarabine by vein over about 1 hour and melphalan by vein over 30 minutes.

On **Day -1,** you will receive 1 dose of total body irradiation (TBI) over 30-40 minutes.

On **Day 0**, you will receive the stem cell transplant by vein.

On **Days +3, and +4,** you will receive cyclophosphamide by vein over 3 hours. Cyclophosphamide is given to lower the immune system in order to lower the risk of graft-versus-host disease (GVHD -- when transplanted immune tissue, such as donor NK and stem cells, attacks the tissues of the recipient's body). You will also receive mesna by vein over 30 minutes every 4 hours for a total of 10 mesna doses on Days +3 and +4. Mesna is given to lower the risk of side effects to the bladder caused by

cyclophosphamide. In addition, you will be given hydration starting 2 hours before each dose of cyclophosphamide.

You will be given standard drugs to help decrease the risk of side effects. Per your standard of care, you will receive ursodiol to help prevent veno-occlusive liver disease, filgrastim-sndz to help with the growth of white blood cells, drugs to prevent infection, and tacrolimus and mycophenolate mofetil (MMF) to help prevent graft-versus-host disease (GVHD). You may receive other standard of care drugs to help decrease the risk of side effects, if your doctor thinks it is needed. You may ask the study staff for information about how the drugs are given and their risks.

Maintenance
All patients treated on the bendamustine, fludarabine, and rituximab arm will receive 2 cycles of inotuzumab ozogamicin as maintenance therapy (treatment after transplant). Your doctor will decide when you are ready to receive Cycle 1 based on your health status. The first 24 participants treated on the fludarabine and melphalan arm may receive intrathecal maintenance per standard of care. Intrathecal means the drug is given directly into your cerebrospinal fluid (CSF) through an Ommaya reservoir. You will sign a separate consent form for this intrathecal administration.

The first 24 participants treated on the fludarabine and melphalan arm will not receive post-transplant inotuzumab ozogamicin maintenance on study, but later, participants treated on the fludarabine and melphalan arm may receive the same maintenance dose and schedule of inotuzumab ozogamicin as the participants treated on the bendamustine, fludarabine, and rituximab arm. Patients with Ph+ acute leukemia may receive standard of care maintenance with tyrosine kinase inhibitors (TKIs) after Day +100. Your study doctor will let you know when these drugs will be given.

Cycle 1 maintenance treatment will be started between 45 and 100 days after your transplant. On Days 1 and 8, you will receive inotuzumab ozogamicin by vein over 1 hour.

Cycle 2 maintenance treatment will be started 28 to 100 days after the start of Cycle 1. On Day 1 and Day 8, you will receive inotuzumab ozogamicin by vein over 1 hour.

Before you start receiving treatment during maintenance, you will have an EKG and blood (about 2 teaspoons) will be drawn for routine tests.

You may be taken off study early if the disease gets worse, if you have any intolerable side effects, if you are unable to follow study directions, if your doctor thinks it is in your best interest, if the study is stopped, or if you choose to leave the study early.

You should talk to the study doctor if you want to leave the study early. If you are taken off study early, you still may need to return for routine post-transplant follow-up visits, if your transplant doctor decides it is needed.

If you are thinking about dropping out of this study, please tell the study doctor. The doctor can tell you about the effects of stopping treatment. You and the doctor can talk about what follow-up care and testing would help you the most.

If you leave the study, your test results and information cannot be removed from the study records.

Study Visits

Before Day -13:

- Blood (about 4 tablespoons) will be drawn for routine tests, to test for infectious diseases, such as HIV and hepatitis, and to check the status of the disease.
- You will have a bone marrow aspiration and biopsy to check the status of the disease. To collect a bone marrow aspiration/biopsy, an area of the hip or other site is numbed with anesthetic, and a small amount of bone marrow and bone is withdrawn through a large needle.
- You will have an EKG to check your heart function.
- You will have a CT scan to check the status of the disease. If the doctor thinks it is needed, you will also have a PET scan.
- If you have had Gilbert's Disease, you will have an abdominal ultrasound to check your gallbladder.

As part of standard care, you will stay in the hospital for about 3-4 weeks after the transplant. After you are sent home from the hospital, you must stay in the Houston area to be checked for infections and other transplant-related side effects until about 3 months after transplant. During this time, you will return to the clinic at least 1 time each week and blood (about 2 teaspoons) will be drawn for routine tests.

About **1, 3, 6, and 12 months after transplant** and, if your doctor thinks it is needed, at **Years 2 and 3:**

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine tests, to check the status of the disease, and to learn how the transplant has taken.
- If your doctor thinks it is needed, you will have a bone marrow aspiration and biopsy to check the status of the disease,
- You will have a CT scan. If your doctor thinks it is needed, you will have a PET scan.

Other Information

Ask your doctor before taking other drugs, since they may interfere with the study drugs or cause side effects.

It is very important that you do not eat grapefruit or drink grapefruit juice during the study. Grapefruit has an ingredient called bergamottin, which can affect some of the drugs, including tacrolimus, used in this study. Common soft drinks that have bergamottin are Fresca, Squirt, and Sunny Delight.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. 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.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs or transplant.

Bendamustine, cyclophosphamide, fludarabine, inotuzumab ozogamicin, melphalan, mesna, and rituximab each may 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 difficulty breathing.

Inotuzumab Ozogamicin Side Effects

Common (occurring in more than 30% of patients)

• fatigue • fever • nausea	• abnormal digestive blood test (possible inflammation of the pancreas)	• low blood cell counts (platelets/white/red) • abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes)

Occasional (occurring in 3-30% of patients)

• headache • chills • veno occlusive disease (severe liver problems	• abdominal swelling/pain • abnormal taste • diarrhea • constipation	• mouth blisters/sores (possible difficulty swallowing) • liver damage • nosebleeds

due to blockage in the liver blood vessels) • high blood levels of uric acid (possible painful joints and/or kidney failure)	• vomiting • loss of appetite • fluid in the abdomen • abnormal blood test (possible pancreas damage)	• immune reaction (possible loss of drug function) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Inotuzumab ozogamicin may cause liver damage due to blood clots. This risk may be higher if you have a stem cell transplant after receiving the drug.

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

• liver damage due to scarring • liver thickening	• liver failure • bleeding in the brain (possibly severe and/or life-threatening) • infusion reaction (such as fever and low blood pressure) • allergic reactions	• breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

Tell the study staff about heavy alcohol use, any history of liver damage, and if you have had a stem cell transplant.

<u>Bendamustine Side Effects</u>

Common (occurring in more than 20% of patients)

• fatigue • fever • headache • nausea • vomiting	• diarrhea • constipation • loss of appetite • low blood counts (red, white, platelets)	• abnormal liver tests (possible liver damage/yellowing of the skin and/or eyes) • cough

Occasional (occurring in 3-20% of patients)

• low blood pressure (possible dizziness/fainting) • worsening of existing high blood pressure • fast heartbeat • chest pain	• high blood sugar (possible diabetes) • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood	• upset stomach • dry mouth • abnormal taste • high blood levels of uric acid (possible painful joints and/or kidney failure)

• swelling (arm/leg) • anxiety • depression • chills • dizziness • difficulty sleeping • itching and/or dry skin • skin rash • increased sweating • night sweats • dehydration	pressure, organ failure, heart problems, changes in mental status, and/or seizure) • weight loss • mouth blisters/sores (possible difficulty swallowing) • abdominal pain and/or swelling • chronic heartburn and indigestion	• pain • weakness • throat pain • wheezing • stuffy nose • difficulty breathing • allergic reaction • infusion reaction (possible chills, pain, and/or hives) • infection

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

• heart failure • heart attack • irregular heartbeat • skin rash (possibly fever/lymph node swelling/inflammation of internal organs/abnormal blood cell counts) • blistering skin rash • death of skin • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• very severe blistering skin disease (loss of large portion of skin) • liver damage • destruction of red blood cells • kidney failure • lung damage/ inflammation (possible difficulty breathing) • 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) • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • drug leakage from the injection site

Bendamustine may rarely cause you to develop another type of cancer (such as lung cancer, acute myeloid leukemia [a type of blood cancer], and/or myeloproliferative syndrome [a type of bone marrow cancer]).

Bendamustine may cause reactivation of certain infections, including hepatitis B, cytomegalovirus (CMV), tuberculosis (TB), and herpes zoster. You should be tested for hepatitis B before you start treatment with bendamustine. If the test results indicate that you have hepatitis B, experts in liver disease will advise your doctor whether you require treatment for the hepatitis B and you will be followed closely for any signs of reactivation for several months after you stop taking bendamustine.

Severe infections (including infections that usually occur more often or are more severe in people with weakened immune systems) may occur in patients treated with bendamustine. Some of these infections can lead to tissue and organ injuries and

death. Treatment with bendamustine may lower some of your white blood cell counts 7 to 9 months after you finish treatment with bendamustine. When treatment with bendamustine is combined with another drug called rituximab, your white blood cell counts may lower even more. These low white blood cells counts can make you more likely to develop infections. You should report any symptoms of infection to your doctor, such as fever, cough, or difficulty in breathing. If there are any signs of infections, your doctor will consider stopping treatment with bendamustine.

Cyclophosphamide Side Effects

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

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	• 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)	• 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

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)	• 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)	• 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)

Melphalan Side Effects

Common (occurring in more than 20% of patients)

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

Occurring in 1-10% of patients

• bright red blood in the stool • 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) • flushing • tingling • hormonal deficiency that affects the body's ability to control blood pressure and react to stress	• inability to have children • decreased testes function • liver damage, possibly due to blood clots • jaundice (yellowing of skin and/or eyes)	• abnormal kidney test (possible kidney damage) • damage to DNA (possible new form of cancer)

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

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

Mesna Side Effects

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

• flushing • dizziness • fever • increased sensitivity of the senses • headache • sleepiness • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• skin rash, blisters, and/or sores • very severe blistering skin disease (loss of large portion of skin) • loss of appetite • constipation • diarrhea • gas • nausea/vomiting • abnormal taste/change in taste	• blood in the urine • pain • shivering • painful red eyes • cough • sore throat • runny nose • flu-like symptoms • injection site swelling, pain, and/or heat

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

• high blood pressure • low blood pressure (possible dizziness/fainting)	• fast heartbeat • low platelet count	• allergic reaction that may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

Rituximab (or biosimilar) Side Effects

Common (occurring in more than 20% of patients)

• fever • fatigue • chills	• nausea • low blood cell counts (red, white) • weakness	• nerve damage (loss of motor or sensory function) • 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) • swelling (arm/leg/tissue) • flushing • anxiety • headache • difficulty sleeping • dizziness • 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 • chest pain due to heart trouble • heart failure • heart attack • blood vessel inflammation (possible bleeding, bruising, and/or rash) • shock caused by heart damage • inflammation of the brain and spinal cord (possible altered 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) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss)	• severe painful blisters • severe skin rash • infections of skin and mucous membrane • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract) • 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 • muscle inflammation and weakness	• abnormal sensation (such as pins and needles) • kidney damage/failure • inflammation inside the eye and/or of an eye nerve (possible vision problems) • bronchiolitis obliterans (damage of the small airways with difficulty breathing) • lung inflammation (possible difficulty breathing) • 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.

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.

Other Risks

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

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.

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.

Graft Failure: There is less than a 1% risk that the stem cells will not grow. Such a graft failure might be fatal unless you could get a second transplant.

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

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.

Side Effects of One Dose of Total Body Irradiation

It is not known how often the side effects of radiation therapy may occur.

• hair loss • dry mouth • abnormal taste	• nausea • vomiting	• cataracts (clouding of the lens of the eye)

All radiation adds up over a lifetime and may increase the risk of new cancer forming.

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 and will continue to be stored securely after the study.

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 and for 30 days after your last dose of study drugs, if you are sexually active.

Birth Control Specifications: Acceptable methods of birth control include: a hormonal birth control, intrauterine device (IUD), diaphragm with spermicide, or condom with spermicide.

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 may result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

OPTIONAL PROCEDURE #1: If you agree, blood (about 2 teaspoons) will be drawn for before your transplant and re-transplant and at then about 3 months, 6 months, and 1 year after your transplant for genetic testing that may help researchers understand more about the disease.

OPTIONAL PROCEDURE #2: If you agree, leftover samples of your last bone marrow biopsy and/or leftover samples from a previous lymph node biopsy will be used for genetic testing that may help researchers understand more about the disease. An additional bone marrow biopsy and lymph node biopsy will not be performed.

There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedures.

Optional Procedure 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.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of "yes" or "no" for each of the following optional procedures:

OPTIONAL PROCEDURE #1: Do you agree to have blood drawn for genetic testing that may help researchers understand more about the disease??

YES **NO**

OPTIONAL PROCEDURE #2: Do you agree to allow leftover bone marrow biopsy tissue and/or leftover samples from a previous lymph node biopsy to be used for genetic testing that may help researchers understand more about the disease?

YES **NO**

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 or Pfizer, Inc. 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. Issa F. Khouri, at 713-792-8750) 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. You may be asked whether the study doctor can collect data from your routine medical care. If you agree, this data will be handled the same as

research data.
The study staff may ask if they can continue collecting the results of routine care from your medical record.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Pfizer, Inc., 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.

   Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not contact you to let you know what they have found.

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

9. This study is sponsored and/or supported by: Pfizer, Inc.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

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

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or 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 samples are used for future research. If this 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 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 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.

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

Genetic 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

Outside relationships are disclosed to and approved by the Conflict of Interest Committee, which reviews these relationships for compliance with institutional policy. This review helps the IRB to assure that financial relationships do not have an impact on the conduct of this study. The following members of the study staff have disclosed compensation from the funding source(s) of this study:

- Elias Jabbour (Study Co-Chair)
- Partow Kebriaei (Study Co-Chair)

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
- Pfizer, Inc., who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- Any future sponsors and/or licensees of the study technology
- Genomic Testing Cooperative
- Center for International Blood and Marrow Transplantation Research (CIBMTR) and National Marrow Donor Program (NMDP)
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

Samples collected during the study (including the optional procedure) will be sent to Genomic Testing Cooperative in Irvine, California. No clinical information will be shared with Genomic Testing Cooperative or its representatives.

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.

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

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

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

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

____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.

__X__ 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