THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Olaparib combined with High-Dose Chemotherapy for Refractory Lymphomas
2017-0073

Study Chair: Yago Nieto

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 the MD Anderson Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn abouts the safety and effectiveness of the combination of olaparib and high-dose chemotherapy (vorinostat, gemcitabine, busulfan, and melphalan, either with or without rituximab) in patients who have non-Hodgkin's or Hodgkin's lymphoma and are receiving an autologous stem cell transplant.

Please note: If you take part in this study and 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.

This is an investigational study. Olaparib is FDA approved and commercially available for the treatment of ovarian cancer. Vorinostat is FDA approved and commercially available for the treatment of lymphoma. Melphalan is FDA approved and commercially available for the treatment of myeloma. Busulfan is FDA approved and commercially available for the treatment of leukemia. Gemcitabine is FDA approved and commercially available for the treatment of lymphoma, breast cancer, and lung cancer. Rituximab is FDA approved and commercially available for the treatment of non-Hodgkin's lymphoma.

The use of these study drugs in combination to treat non-Hodgkin's or Hodgkin's lymphoma is investigational. The study doctor can explain how the study drugs are designed to work.

Treatment on this study 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 may choose not to take part in this study because it is a first in human study and there are other standard options.

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

You will be taken off study about 100 days after the transplant.

You will receive olaparib at no cost while you are on the study. You and/or your insurance provider will be responsible for the cost of all other study drugs and the stem cell transplant.

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. 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 cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

You had screening tests that are a routine part of the transplant preparation that helped show that you were eligible to take part in this study. The results of these routine tests will be collected from your study record to confirm that you are eligible to take part in this study.

If you can become pregnant, blood (about 1-2 teaspoons) will be drawn or urine will be collected within 28 days and within 72 hours before you receive the busulfan test dose (described below) to confirm you are not pregnant.

In stem cell transplants, 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 your stem cells are called "plus days."

Up to 50 participants will be enrolled in this study. All will take part at MD Anderson.

Busulfan Test Dose

You will receive a test dose of busulfan by vein over about 60 minutes. Before and after you receive this low-level test dose of busulfan, blood will be drawn several times to check how the level of busulfan in your blood changes over time. This is called pharmacokinetic (PK) testing. This information will be used to decide the next dose needed to reach the correct blood level that matches your body size. You will most likely receive this test dose as an outpatient during the week before you are admitted to the hospital. If it cannot be given as an outpatient, you will be admitted to the hospital on Day -13 (13 days before your stem cells are returned to your body) and the test dose will be given on Day -12.

Blood (about 1 teaspoon each time) will be drawn for PK testing about 11 times: once before your test dose of busulfan and 10 times over the 11 hours after the dose. The blood samples will be repeated again on the first day of high-dose busulfan treatment (Day -9). A temporary heparin lock line will be placed in your vein to lower the number of needle sticks needed for these draws.

If it is not possible for the PK tests to be performed for any reason, you will receive the standard fixed dose of busulfan.

Study Drug Administration

On **Day -11 through Day -3**, you will take olaparib by mouth 2 times a day, about 12 hours apart, with or without food, with a glass of water. The olaparib tablets should be swallowed whole and not chewed, crushed, dissolved, or divided. Olaparib tablets can be taken with or without food.

If you vomit after taking your olaparib dose, but you can see all the tablets are intact, you should retake that dose. If you miss or vomit a scheduled dose, you should take the scheduled dose up to 2 hours after that scheduled dose time. If more than 2 hours after the scheduled dose time, the missed dose should not to be taken and you should wait and take your next scheduled dose.

On **Day -10 through -3**, you will take vorinostat by mouth. The study staff will tell you how many olaparib and vorinostat tablets to take. You will also receive dexamethasone by vein over about 3-5 minutes 2 times each day. Dexamethasone is a standard drug given to help decrease the risk of certain side effects.

On **Day -10**, if you have a type of B-cell cancer, you will receive rituximab (a treatment used for certain lymphomas) by vein over about 3-6 hours as part of your standard care. The study doctor will tell you if you will receive rituximab.

On **Day -9**, you will receive gemcitabine by vein over 4½ hours.

On **Days -9, -8, -7, and -6,** you will receive busulfan by vein over about 3 hours.

On **Day -4**, you will receive gemcitabine by vein over 4½ hours and then melphalan by vein over 30 minutes.

On **Day -3**, you will receive melphalan by vein over 30 minutes.

On **Days -2 and -1**, you will rest (you will not receive chemotherapy).

On **Day 0**, you will receive your stem cells by vein over about 30-60 minutes.

As part of standard care, you will receive G-CSF (filgrastim) as an injection just under your skin 1 time each day starting on Day +5 until your blood cell levels return to normal. The study doctor will discuss this with you, including how filgrastim is given and its risks.

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.

You may be taken off study earlier if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Study Tests

Within 7 days before starting study treatment, you will have an EKG to check your heart function. This may be repeated during the study, if your doctor thinks it is needed.

As part of your standard care, you will remain in the hospital for about 3-4 weeks after the transplant. While you are in the hospital, blood (about 4 teaspoons) will be drawn every 1-2 days for routine tests. After you are released from the hospital until about 30 days after the transplant, you will need to stay in the Houston area to be checked for infections and side effects.

Between discharge and Day 30, you will come to the clinic 2-3 times per week and on Day 30 to have a physical exam, PET/CT scans to check the status of the disease, and blood drawn (about 4 teaspoons) for routine tests. The results of these routine tests will also be included in your study record.

About **100 days after the transplant**:

- You will have a physical exam.
- Blood (about 4 teaspoons) will be drawn for routine tests.
- You will have PET/CT scans to check the status of the disease.
- If the study doctor thinks it is needed, you may have an EKG, either an echocardiogram (ECHO) or MUGA scan to check your heart function, chest x-rays, and/or lung function tests. For a lung function test, you will breathe deeply and then blow into a device for a few seconds. Urine may also be collected for routine tests.
- If the study doctor thinks it is needed, you may 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 is numbed with anesthetic, and a small amount of bone marrow and bone is withdrawn through a large needle.

Other Information
You should not take Tylenol (acetaminophen) from 3 days before until 3 days after receiving busulfan and melphalan, since acetaminophen may cause serious liver damage if taken with busulfan and melphalan.

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

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.

Busulfan, gemcitabine, melphalan, olaparib, rituximab, and vorinostat 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.

Olaparib Side Effects

Common (occurring in more than 20% of patients)

• fatigue • headache • abdominal pain • nausea/vomiting • diarrhea	• constipation • loss of appetite • abnormal taste • enlarged red blood cells • low red blood counts • weakness • muscle/joint pain	• abnormal kidney test (possible kidney damage) • lung inflammation • runny nose • infection/pneumonia • flu

Occasional (occurring in 3-20% of patients)

• swelling	• skin rash	• low blood cell counts

• dizziness • low blood levels of magnesium (possible weakness, muscle cramps, and/or irregular heartbeat)	• upset stomach • mouth blisters/sores (possible difficulty swallowing)	(white/platelets) • back pain • difficulty breathing • cough

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

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

• allergic reaction

Vorinostat Side Effects

Common (occurring in more than 20% of patients)

• fatigue • high blood sugar (possible diabetes) • diarrhea	• nausea • abnormal taste • loss of appetite • weight loss	• low platelet count • abnormal kidney test (possible kidney damage)

Occasional (occurring in 3-20% of patients)

• abnormal EKG • swelling (arm/leg) • chills • dizziness • headache • fever • hair loss (partial or total)	• itching • dehydration • dry mouth • constipation • vomiting • loss of appetite • low red blood cell count	• muscle spasms • blockage in the lung (possible pain, shortness of breath, and/or failure to breathe) • cough • infection

Vorinostat may occasionally cause you to develop another type of cancer (such as squamous cell carcinoma (skin cancer).

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

• high blood pressure • chest pain • heart attack • blood clots in a vein (possible pain, swelling, and/or redness) • blood vessel inflammation (possible	• shedding and scaling of the skin (possible fatal loss of bodily fluids) • low blood levels of potassium (possible weakness and/or muscle cramps) • low blood levels of	• low white blood cell count • kidney failure • damage to the nervous system (causing numbness and/or paralysis) • loss of feeling or

bleeding and/or bruising) • tissue swelling • fatigue • stroke • fainting	sodium (possible headache, confusion, seizures, and/or coma) • digestive system bleeding • difficulty swallowing • inflammation of the stomach and/or intestines • gallbladder inflammation (possible abdominal pain) • inability to urinate	movement due to spinal cord damage • blockage in the tubes that drain urine from the kidneys • coughing up blood • blurry vision • deafness • bleeding in or from the tumor • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • bacteria in the blood

Vorinostat may rarely cause you to develop another type of cancer (such as lymphoma [cancer of the lymph nodes]).

Gemcitabine Side Effects

Common (occurring in more than 20% of patients)

• fever • skin rash • nausea/vomiting • low blood cell counts (red, white, platelets)	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes)	• abnormal kidney test (possible kidney damage) • blood in the urine

Occasional (occurring in 3-20% of patients)

• swelling (such as arm/leg) • abnormal sensation (such as pins and needles)	• fatigue • hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing)	• diarrhea • difficulty breathing • flu-like symptoms • injection site swelling, pain, and/or heat • infection

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

• irregular heartbeat • heart attack • heart failure • multiple blood clots (possible organ dysfunction and/or	• stroke • large skin blisters • decay of body tissue • severe sunburn-like rash at site of previous radiation (called	• liver damage due to blood clots • kidney failure • lung inflammation/ damage (possible difficulty breathing)

failure) • blood vessel inflammation (possible bleeding and/or bruising) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss)	radiation recall) • destruction of red blood cells (possible kidney damage and/or failure) • abnormal blood clotting in small blood vessels (possible stroke and/or other organ damage) • leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing)	• fluid in the lung (possible difficulty breathing) • difficulty breathing due to narrowing of the airways • 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)

Gemcitabine may cause brain injury that may result in headache, confusion, seizures, and/or vision loss. It is not known how often this may occur.

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 • 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) • 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) • 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 • 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)

• enlarged heart • multiple blood clots (possible organ dysfunction and/or failure) • leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing) • blistering skin rash • dryness of the skin and/or oral mucous membrane (mouth) • hair loss (partial or total) • 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) • blurry vision	• 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) • fatigue • agitation • confusion • coma • decreased brain function (possible paralysis and/or coma) • seizure	• shedding and scaling of the skin (possible fatal loss of bodily fluids) • change of skin color • acne/acne-like rash • blistering skin rash • painful skin bumps • severe blisters • hot flashes • weight gain • vomiting of blood • inflammation of the pancreas (possible abdominal pain) • decreased urine output • blood in the urine • difficult and/or painful	• increased amount of blood • enlarged liver • difficulty breathing due 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

• bleeding in the brain • delirium (loss of contact with reality) • hallucinations (seeing or hearing things that are not there)	urination	blood pressure • graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body) • infection

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)

Occasional (occurring in 3-20% of patients

• stopped menstrual cycle

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	• bright red blood in the stool • inability to have children • decreased testes function • abnormal liver tests (possible liver damage) • liver damage, possibly due to blood clots • jaundice (yellowing of skin and/or eyes)	• abnormal kidney test (possible kidney damage) • kidney failure • damage to DNA (possible new form of cancer)

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

• skin rash • skin sores at the injection site • hair loss (partial or total) • bone marrow failure	• lung damage (possible difficulty breathing) • lung inflammation (possible difficulty breathing)	• tissue death at the injection site caused by drug leakage • allergic reaction

Rituximab Side Effects

Common (occurring in more than 20% of patients)

• heart problems • fever • fatigue • chills • low blood levels of phosphate (possible phone damage)	• nausea • low blood cell counts (red, white) • weakness	• nerve damage (loss of motor or sensory function) • lung inflammation (possible difficulty breathing) • 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 • 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 • inflammation of the liver, gall bladder, and/or bile ducts	• abnormal liver and/or bone tests (possible liver damage) • pain (back/joint/muscle) • muscle spasms • lung inflammation • lung damage • 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)

• heart problems	• anemia due to destruction of red blood cells • decreased bone marrow function and inability to make red blood cells	• high blood levels of uric acid (possible painful joints and/or kidney failure) • abnormal sensation (such as pins and needles)

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.

Frequency Unknown

• sudden stopping of the heart • fast and/or irregular heartbeat • heart failure • heart attack • 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)	• severe painful blisters • severe skin rash • lesions due to skin infection • 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) • thick blood (possible blockage of blood flow) • liver damage • condition that looks like lupus (an immune system disease) • immune system reaction (possible organ damage) • liver damage/failure	• decreased kidney function (possible kidney failure) • inflammation inside the eye and/or of an eye nerve (possible vision problems) • low oxygen level in the blood (possible lightheadedness) • bronchiolitis obliterans (damage of the small airways with difficulty breathing) • flu • 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)

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.

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 the arteries • swelling (such as tissue and/or abdominal swelling) • dizziness • shock • fainting • headache • increased pressure in the skull or between the skull and brain (possible headache, vision changes, and/or mental status changes) • seizure	• 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) • diabetes • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • abnormal blood acid/base balance (possible organ damage) • low blood levels of potassium (possible weakness and/or muscle cramps) • high blood levels of sodium (possible weakness and/or	• changes to the menstrual cycle • problems with production of sperm • bruising • muscle weakness • inflammation of nerves (possible pain and/or loss of motor or sensory function) • 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

• depression • fatigue and anxiety • mood swings • personality changes • mental disorders • euphoria (unusual feelings of happiness or well-being) • difficulty sleeping • fatigue/lack of energy • darkening and/or lightening of the skin • tiny dots on the skin • impaired wound healing • skin rash, redness, and/or dryness • fragile and/or thinning skin • skin test reaction impaired (due to a lowered immune system) • stretch marks	swelling) • sugar in the urine • body-wide loss of proteins (possible weakness and/or swelling) • build-up of fat in abnormal areas • weight gain • increased appetite • digestive system bleeding • small red or purple spots in the mouth • 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	• enlarged liver • abnormal liver tests (possible liver damage) • bulging eye • increased pressure in the eye (possible vision loss, pain, and/or blurry vision) • cataracts (clouding of the lens of the eye) • hiccups • fluid in the lung (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) • infection • allergic reaction (such as skin reaction) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

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.

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

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

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

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

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

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

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

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

This study may involve unpredictable risks to the participants.

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

Birth Control Specifications: If you can father a child, you and your partner must use 2 highly effective forms of birth control while on study and for at least 6 months after your last dose of study drug(s).

If you can become pregnant, you must use a highly effective birth control method while on study and for at least 6 months after your last dose of study drug(s).

Ask your doctor about acceptable forms of birth control.

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.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, in the week before you are admitted to the hospital and then again on Day -5, blood (about 8 teaspoons) will be drawn for tests to check the effect of the treatment on the DNA (genetic material) of blood cells.

Optional Procedure #2: If you agree and the study doctor thinks it is possible, in the week before you are admitted to the hospital and then 1 time between Day -2 and Day +2, you will have a fine needle aspiration (FNA) of your lymph nodes to check the effect of the treatment on the DNA of cancer cells. To collect a fine needle aspirate, a small amount of tissue is withdrawn through a needle.

There are no benefits to you for taking part in any of those 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 procedure.

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.

Having a **fine needle aspiration** 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 site.

Genetic research may result in the development of beneficial treatments, devices, new drugs, or patentable procedures. There are no plans to provide you compensation from such developments. The results of any genetic tests may be put in your health records. If this information were released, it could be misused. Such misuse could be

distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

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 tests to learn how your DNA has been affected by the study treatment?

YES NO

Optional Procedure #2: Do you agree to have a lymph node FNA to check the effect of the treatment on the DNA of cancer cells?

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 Astra Zeneca Pharmaceuticals 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. Yago Nieto, 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. 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, Astra Zeneca Pharmaceuticals, 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.

9. This study is sponsored and/or supported by: Astra Zeneca Pharmaceuticals.

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 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. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

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

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

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

Conflict of Interest

Dr. Borje Andersson (collaborator) has a royalty sharing agreement for IV busulfan. Dr. Andersson also receives compensation from a consulting agreement with PDL Biopharma, the company that makes and supplies IV busulfan.

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
- Astra Zeneca Pharmaceuticals, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- licensees of study technology, 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.

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

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 **2020-0073**.

_____ _____
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

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