THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Safety Study of Daratumumab, Ixazomib, and Dexamethasone in AL Amyloidosis
2017-0243

Subtitle: Version Date 16Jun2021

Study Chair: Oren Pasvolsky

_____ _____
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 if the combination of daratumumab, ixazomib, and dexamethasone at standard doses can be given safely to patients with amyloid light chain (AL) amyloidosis.

Researchers also want to learn the recommended dose of the study drug combination.

This is an investigational study. Daratumumab given as an injection under the skin and ixazomib are FDA approved and commercially available for the treatment of another type of blood cancer called multiple myeloma, although not in combination. Daratumumab is FDA approved and commercially available for the treatment of AL amyloidosis in combination with bortezomib, cyclophosphamide, and dexamethasone. Dexamethasone is FDA approved and commercially available to help prevent or treat certain side effects. The combination of daratumumab and ixazomib with dexamethasone is not FDA approved for the treatment of AL amyloidosis. It is currently being used for research purposes only.

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

The study drugs 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 infusion related reactions with daratumumab or digestive system side effects (such as nausea, vomiting, and diarrhea) with ixazomib. You may have prolonged stays out of town, and there may be other standard treatment options.

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

You may continue taking the study drugs for up to 12 cycles, as long as the doctor thinks it is in your best interest.

Daratumumab and ixazomib will be provided to you at no cost while you are on study. You and/or your insurance provider will be responsible for the cost of dexamethasone.

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

1. STUDY DETAILS

Screening Tests

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

- You will have a physical exam.
- You will have EKGs and an echocardiogram (ECHO) to check your heart function.
- You will have lung function testing.
- Blood (about 2 tablespoons) will be drawn for routine tests. You will be screened for Hepatitis B and C. Some of the routine blood and urine tests throughout the study are to check the status of the disease. If you can become pregnant, the routine testing will include a pregnancy test. To take part in this study, you must not be pregnant.
- A 24-hour urine sample will be collected for routine tests. For the urine sample, you will be given a container and told how to use it.
- You will have a bone marrow biopsy to check the status of the disease and for cytogenetic testing. To collect a bone marrow 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. Cytogenetic testing looks at how genetic changes to cells may affect how the disease may react to the study drugs.

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

Up to 20 participants will be enrolled in this study.

Study Drug Administration

If you are found to be eligible to take part in this study, you will receive daratumumab, ixazomib, and dexamethasone. All participants will receive the study drugs at the same doses. Dexamethasone will be given at a lower dose during Cycle 1 and then a higher dose during Cycles 2 and beyond.

Each cycle is 28 days.

You will receive **daratumumab** as an injection under the skin over the abdomen on Days 1, 8, 15, and 22 of Cycles 1-2, then on Days 1 and 15 for Cycles 3-6, and on Day 1 of Cycles 7-12. The first 2 doses will be given over 6½ hours. After that, the doses may be given over 3½ hours if you have no bad reactions.

You will take **ixazomib** by mouth on Days 1, 8, and 15 of Cycles 1-12. You should take each dose of ixazomib on an empty stomach (no food or drink) at least 1 hour before or at least 2 hours after food, with about 8 ounces (1 cup) of water.

Swallow the ixazomib capsules whole. Do not break, chew, or open capsules. If you miss or vomit a dose of study drug at home, do not retake the missed or vomited dose. Wait and take the next scheduled dose.

Dexamethasone is given as a premedication before your dose of daratumumab to lower the risk of side effects. You will receive dexamethasone by vein over 15 minutes or by mouth on Days 1, 8, 15, and 22 of Cycle 1. Starting with Cycle 2 and beyond, dexamethasone will be given as a premedication before each dose of daratumumab and

then again the next day. During weeks when you do not have a daratumumab dose scheduled, you will receive dexamethasone as a single dose 1 time a week.

You will be given other standard drugs to help decrease the risk of side effects, such as infection and indigestion. You may ask the study staff for information about how the drugs are given and their risks.

You should bring any empty bottles and any unused study drug to the clinic at each visit. You will be given a diary to record when you take your study drug each day.

Study Visits

On **Day 1 of Cycles 1-12:**

- You will have a physical exam.
- Blood (about 4 tablespoons) will be drawn, and a 24-hour urine sample will be collected for routine tests.

On **Day 8, 15, and 22 of Cycles 1 and 2 and Day 15 of Cycle 3-6**, blood (about 1-2 tablespoons) will be drawn for routine tests.

These tests may be repeated if the doctor thinks it is needed.

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

Your participation on the study will be over after your last follow-up visit.

Follow-up Visits

About 90 days after your last study drug dose:

- You will have a physical exam.
- Blood (about 4 tablespoons) will be drawn, and a 24-hour urine sample will be collected for routine tests.
- You will have an ECHO to check your heart function.

If you stop the study drugs and the disease has not gotten worse, blood (about 4 tablespoons) will be drawn and a 24-hour urine sample will be collected for routine tests every 90 days (+/- 30 days). The testing will stop after 24 months or if the disease gets worse, whichever comes first.

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 the drugs are 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 drug/procedures.

Daratumumab and ixazomib each may cause low blood cell counts (red blood cells, white blood cells, and/or platelets).

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low white blood cell count increases your risk of infection (such as the flu, pneumonia, bronchitis, upper respiratory tract, shingles and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing. If you have an infection now, have a history of frequent infections, or if you feel sick, you should tell your study doctor right away. Signs of an infection may include fatigue, headache, fever, chills, aches and pains, coughing, congestion, chest tightness, or shortness of breath.
- 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.

Tell your healthcare provider if you develop any symptoms of infection such as fever, or any symptoms of decreased platelet counts such as bruising or bleeding.

Daratumumab Side Effects

To date, approximately 6,204 clinical trial patients have been treated with daratumumab IV (intravenous, directly into the vein) or SC (subcutaneous, underneath the skin of the abdomen). Of these 6,204 patients, about 2,161 received daratumumab alone, and about 4,272 patients received daratumumab in combination with other therapies.

Daratumumab is commercially approved for the treatment of multiple myeloma and AL amyloidosis.

Not all the possible side effects and risks related to daratumumab are known. New side effects may happen. You will be watched closely, and you will receive appropriate care if side effects happen. Please tell your study doctor if you have any of the side effects described below or any other ones not listed. You will be told of any new findings that may affect your decision to continue in this study.

The following side effects are observed when daratumumab was given to patients, either alone or in combination with other drugs.

Very common side effects with daratumumab (affects 1 in 10 patients or more).

- Infection of the upper respiratory tract such as nose, sinuses, throat or upper airway, including influenza and flu like symptoms
- Infection of the lungs (pneumonia)
- Infection of the lower airway (bronchitis)

- Low white blood cells (including neutrophils and lymphocytes); may increase the risk of getting an infection (see also separate section below)
- Low platelets; may increase the risk of bleeding and bruising (see separate section "Blood Cell Effects" below)
- Low red blood cells (anemia)
- Decreased potassium in the blood
- Decreased appetite
- Sleeplessness (insomnia)
- Abnormal sensation including numbness/tingling of hands, feet or limbs (sensory neuropathy, paresthesia)
- Headache
- High blood pressure
- Cough
- Shortness of breath (dyspnea), including wheezing
- Diarrhea
- Constipation
- Nausea
- Pain in the belly (abdomen)
- Vomiting
- Rash, a noticeable change in the texture or color of your skin
- Pain in the bones and muscles such as back pain or chest pain
- Joint pain
- Muscle spasms
- Swelling of hands, feet or limbs
- Fatigue or lack of energy
- Weakness, lack of strength
- Fever

Common side effects with daratumumab (affects 1 in 100 patients or more and fewer than 1 in 10 patients).

- Urinary tract infection
- COVID-19
- Sepsis (a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs)
- Hypogammaglobulinemia, a condition with your immune system in which not enough gamma globulin proteins (also known as antibodies) are produced. Decreases in gamma globulin proteins can increase the risk of infections
- High blood glucose levels
- Low blood calcium levels
- Loss of body fluids, also known as dehydration
- Dizziness
- Fainting
- Irregular heartbeat (atrial fibrillation)
- Fluid in lungs (pulmonary edema)
- Inflammation of the pancreas (pancreatitis)

- Itchy skin
- Chills
- Infusion-related reaction (see separate section “Infusion-Related Reactions” below)
- Injection site reaction: local reaction reported as mild pain or a burning sensation at the site of injection in the abdominal wall. Redness and hardening of the skin at the injection site was also observed and usually disappeared within a few hours after the administration

Uncommon side effects with daratumumab (affects 1 in 1,000 patients or more and fewer than 1 in 100 patients).

- Cytomegalovirus infection (see separate section on infections below)
- Liver infection (hepatitis) in those patients who are carriers of the hepatitis B virus

Infusion-Related Reactions

An antibody is a large protein that is generated as part of the normal immune system to neutralize foreign objects such as bacteria and viruses. Daratumumab is an antibody designed to specifically target and eliminate a specific harmful object in your body, in this case cancerous plasma cells. A non-local, hypersensitivity reaction to daratumumab that occurs during or shortly after an administration (IV or SC) is called an infusion-related reaction. It usually occurs during or within the first few hours after the start of the first administration. However, delayed reactions can happen up to 3-4 days after the administration. These reactions can be life-threatening and fatal outcomes have been reported.

Signs and symptoms of infusion-related reactions may include respiratory symptoms, such as stuffy nose, cough, throat irritation, as well as chills, vomiting and nausea. Most of the observed infusion-related reactions were mild or moderate, and ended by temporarily stopping the administration and/or giving medicines to treat the symptoms. Tell your doctor right away if you have above mentioned symptoms.

If you have a breathing problem now or had breathing problems in the past (like chronic obstructive pulmonary disease (COPD) or asthma), you should tell your study doctor. Also, if you start to have breathing problems while you are on the study you should tell your study doctor right away.

Severe reactions have occurred, including narrowing and obstruction of the respiratory airway (bronchospasm), low level of oxygen (hypoxia), shortness of breath, high blood pressure, swelling in the throat and fluid in the lungs (pulmonary edema), and complaints of the eyes, such as fluid in the eye (choroidal effusion), blurry vision (acute myopia), and increased pressure in the eye or eye pain (acute angle closure glaucoma). In addition, heart attack (myocardial infarction) has also occurred when daratumumab is given through the vein. Your study doctor and their staff will be ready to treat such a reaction in case it happens. In the future, you should tell any doctor you visit that you received daratumumab (an antibody) in this research study and if you had an allergic reaction including an anaphylactic reaction, the worst case of allergic reaction.

Anaphylactic reaction

Anaphylactic reaction is a serious allergic reaction that can develop quickly (in minutes to a few hours) and may cause death. Usually, a combination of the following side effects occurs: an itchy rash, throat or tongue swelling, shortness of breath, vomiting, lightheadedness, and low blood pressure. This type of reaction is for example seen when one is allergic to a bee sting or certain foods like peanuts.

Please inform your doctor immediately if you experience any of these signs and symptoms.

Anaphylactic reactions were rarely reported when commercially available daratumumab was used outside of clinical trials (also called post marketing experience). The reported cases of anaphylactic reaction were believed to be a more severe form of infusion related reactions.

More than 227,000 patients globally have been treated with daratumumab. Anaphylactic reaction has not been reported in clinical studies; therefore, the frequency is not known.

The sponsor will continue to monitor infusion-related reactions and make changes to the way daratumumab is administered and/or recommend additional medications as necessary.

In this study, the following will be done to reduce the chance of a daratumumab infusion related reaction:

- You will get medications, including steroids, paracetamol/acetaminophen, and antihistamine, before the infusion.
- If you have a reaction, the infusion will be paused, and the symptoms treated as needed. Dependent on the reaction, the infusion may continue at a slower rate. If you have a life-threatening reaction, you will need to stop further treatment with daratumumab, and your doctor will discuss alternative treatments with you.
- If you are considered higher risk for breathing problems (for example COPD, asthma), you may also get medications, including inhaled steroids, after the infusion.
- You may stay overnight in hospital after the infusion so medical staff can check you.
- You may need medications, including steroids, paracetamol/acetaminophen, and antihistamine, post infusion as well.

Infection

Different kinds of infection have been seen in patients receiving daratumumab. Most of them are respiratory tract infections. If you have an infection now, have a history of frequent infections, or if you feel sick, you should tell your study doctor right away. The majority of the observed infections so far were mild or moderate. Severe infections such as pneumonia from bacteria, influenza virus, respiratory syncytial virus, and COVID-19, and sepsis have also been reported. Your doctor may also recommend other medications to potentially prevent or reduce the risk of COVID-19 infection or severe infection. Tell the study doctor right away if you are diagnosed with COVID-19 (even if you have no or only minor symptoms) or have been exposed to someone with COVID-19 infection. It is important to continue general infection prevention practices such as washing hands,

wearing masks, social distancing, and avoiding public transportation or travel as much as possible.

Certain infections with viruses, such as shingles (Herpes Zoster virus) and cytomegalovirus, and liver infection (hepatitis B virus) have been observed with daratumumab. Patients who have had prior exposure to hepatitis B virus are at increased risk of recurrence of the virus. Your doctor will test you for the hepatitis B virus before beginning treatment on this study. If you test positive for the virus, you will be closely monitored for signs of infection during daratumumab treatment and until 6 months after the last dose of daratumumab, and you will be treated, if appropriate, by your doctor.

Blood transfusions:
If you need a blood transfusion, you will have a blood test first to match your blood type.

Daratumumab can affect the results of this blood test. These changes can last up to 6 months after your last dose. Your doctor will therefore test your blood type before you start treatment with Daratumumab. The test result will be placed on the patient identification wallet card you will carry for this study. Please tell all your health care providers that you are using daratumumab before receiving a blood transfusion.

When given as an injection under the skin, in addition to the above, daratumumab may cause an injection site reaction (pain, burning sensation, redness/hardening of the skin).

When given as an injection under the skin, daratumumab is combined with a substance called rHuPH20 (Hylenex) to help the body better absorb daratumumab. Hylenex may cause an injection reaction (possible redness, pain, swelling, rash/irritation, hardness, and tingling/numbness). You may develop an antibody against Hylenex. If you are allergic to Hylenex or any of its parts, you may have an allergic reaction. In males, it is also possible that your body's reaction to rHuPH20 may interact with sperm, but it is not known if this may affect your fertility.

Heart problems, in some cases fatal, have occurred in patients with AL amyloidosis. Your study doctor will monitor you closely. Call your study doctor right away if any of the following symptoms occur: chest pain, feeling faint, swollen legs, shortness of breath, or abnormal heart rhythm.

Ixazomib Side Effects

Based on studies of ixazomib, it is possible to predict some of the discomforts and risks. However, it is possible that ixazomib may cause risks that have not yet been observed in patients. The following risks might be seen:

- Low platelet count which may increase the chance of bleeding
- Skin rash which may range from some red areas, small flat spots, or small raised bumps that may or may not be itchy in a few areas or all over the body
- Nausea
- Vomiting
- Diarrhea
- Numbness or tingling or pain feelings in hands and feet

- Swelling or fluid buildup in the arms or legs
- Flu-like symptoms and other upper respiratory tract infections
- Arthralgia or joint pain
- Lung infections including pneumonia bronchitis or pneumonitis
- Herpes Zoster that can sometimes cause local pain that may last after recovery from the skin rash and does not go away for some time

Other discomforts and risks reported in studies with ixazomib, which may have been due to the patient's disease, ixazomib, other medications, or some combination of these include:

- Not feeling like eating
- Electrolyte imbalance (blood chemical imbalance)
- Loss of water from the body (dehydration) because of vomiting and/or loose stools
- High blood creatinine and renal failure which means your kidneys are having trouble working well; Patients who had lost body water (dehydration) because of vomiting and/or loose stools have had high levels of creatinine indicating that the kidneys were failing to function adequately. In some severe situations, less kidney function may require temporary treatment with a machine that supports the function of the kidney (dialysis).
- Feeling short of breath or difficulty breathing
- Feeling tired or weak
- Chills
- Cough
- Fever
- Headache
- Pain in the abdomen or back
- Muscle weakness
- Feeling dizzy or dizziness
- Lowered blood pressure that can commonly cause you to feel light headed, faint or pass out when you stand up
- Lowered white blood cells called lymphocytes
- Lowered red cells or anemia which may make you feel tired
- Lowered white blood cells called neutrophils that may increase your risk of infection and may be associated with fever
- Constipation
- Pain (muscular) in extremities
- Distortion of the sense of taste, i.e., an abnormal or impaired sense of taste
- Trouble falling asleep, staying asleep or both

Some discomforts and risks occur with lesser frequency than those mentioned above, but should be noted because they are severe, life-threatening or fatal. With limited experience and because these events occurred while patients were receiving other drugs as well, we do not know if ixazomib causes such problems. Severe, life-threatening or deadly conditions that may involve rash, blistering, skin peeling and mouth sores, including Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), Acute febrile neutrophilic dermatosis (Sweet's syndrome) and pemphigus vulgaris, have been reported in ixazomib studies when given in combination with other drugs. These rashes are disorders of the immune system, which differ from regular skin rashes and are generally more severe.

In addition, two rare neurological conditions have been reported in patients on ixazomib. Posterior reversible encephalopathy syndrome (PRES) which affects the brain and may cause headaches, changes in your vision, changes in your mental status, or seizures (fits), but is usually reversible.

Transverse myelitis, also a rare condition, is an inflammatory disease-causing injury to the spinal cord which has been reported in a patient receiving ixazomib. This condition may cause varying degrees of muscle weakness, reduced movement in legs, changes in the feelings of the toes and feet, unusual muscle tightness, feelings of pain, changes in bowel (constipation) or urinary (loss of control) function, or loss of leg movement. In general, recovery may be partial, complete, or not at all, but most patients experiencing transverse myelitis have good to fair recovery of symptoms. We do not know whether ixazomib causes transverse myelitis; however, as it happened to a patient receiving ixazomib, we are not able to exclude the possibility that ixazomib may have contributed to transverse myelitis.

Progressive multifocal leukoencephalopathy (PML) is a rare, serious infection of the brain that is caused by a virus. Persons with a weakened immune system may develop PML. PML can result in death or severe disability. PML has been observed rarely in patients taking ixazomib. It is not known whether ixazomib may contribute to the development of PML.

Thrombotic microangiopathy (TMA), including thrombotic thrombocytopenia purpura (TTP) and hemolytic uremic syndrome (HUS), are rare, serious blood disorders that cause low levels of platelets and red blood cells and result in blood clots in small vessels. Symptoms may include fatigue, fever, bruising, nose bleeds, and decreased urination. These disorders can occasionally be fatal. TMA, TTP, and HUS have been seen rarely in patients treated with ixazomib.

Overdose has been reported in patients taking ixazomib. Reports of accidental overdose have been associated with risks such as nausea, lung infections including aspiration pneumonia, multiple organ failure, and death. It is important to take only one dose of ixazomib at a time, and only at the prescribed interval.

Ixazomib should not be taken if you have ever had an allergic reaction to the active substance or any of the inactive ingredients used in its formulation.

The following side effects may also be a risk with ixazomib because they have been reported with another proteasome inhibitor, velcade, in patients with diseases requiring this type of treatment, or in patients who receive ixazomib in combination with other drugs for cancer treatment:

- Rapid death of cancer cells that may let large amounts of the cells into the blood that injure organs, such as kidneys (this is referred to as tumor lysis syndrome).
- Worsening of your heart function (congestive heart failure) that may require additional drugs for treatment or hospitalization.
- Disorders of your lung that could be serious enough to result in death
- Other drugs and supplements may affect the way ixazomib works. Tell your doctor

about all drugs and supplements you are taking while you are in this study.

Dexamethasone Side Effects

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

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

• difficulty sleeping • fatigue/lack of energy • anxiety • darkening and/or lightening of the skin • tiny dots on the skin • wound healing problems • skin rash, redness, and/or dryness • fragile and/or thinning skin • skin test reaction impaired (due to a lowered immune system) • stretch marks • hives • acne-like rash	• digestive system bleeding • esophageal sore • hole in the intestines (possibly leaking contents into the abdomen) • nausea • itching near the anus • inflammation of the pancreas (possible abdominal pain) • stomach ulcer • changes to the menstrual cycle • problems with production of sperm • bruising • weakness • increased thirst	• high risk of getting infections, including viral infections, fungal infections, bacterial, parasitic and opportunistic infections (such as seasonal flu or recurrence of herpes) • allergic reaction (such as skin reaction) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

Dexamethasone may cause 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.

Study Drug Combination Side Effects

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

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

The type of **genetic testing** being performed in this study will not provide you or your doctor information about diseases that are passed down in families. It will not tell the study researchers anything that will prevent you from getting health insurance, and it will not tell the study researchers anything about any diseases or conditions you may get in the future.

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
The effects of daratumumab and ixazomib on fertility, the human embryo, the fetus, or the breast-fed infant are unknown. If you are a woman, taking part in the study might harm your unborn child or breast-fed baby. Thus, you must agree not to become pregnant while you are in this study. Also, you cannot take part in this study if you are pregnant or breastfeeding a child. If you are a man, the effect of daratumumab and ixazomib on your sperm is unknown.

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 effective methods of birth control during the study and for at least 90 days after your last dose of study drug, if you are sexually active.

Birth Control Specifications:

Males:
Acceptable birth control includes surgical sterilization (vasectomy) combined with an effective barrier method listed below. As another option, it is acceptable to combine 2 effective barrier methods.

Females:

Unless you cannot have children because of surgery or other medical reasons (such as if you are post-menopausal), you must use 2 effective methods of birth control. It is strongly recommended that at least one of these 2 methods be highly effective (see examples below). If a highly effective method cannot be used, you should use 2 effective methods at the same time.

Highly effective methods:
- Intrauterine devices (IUD)
- Hormonal (birth control pills, injections, patches, or implants)

Other effective methods (barrier methods):
- Condom with or without spermicide
- Diaphragm with spermicide
- Cervical cap with spermicide
- Sponge with spermicide

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy. You must not donate sperm during the study and for 90 days after your last dose of study drug.

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. You must not donate eggs during the study and for 90 days after your last dose of study drug.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson, Janssen Scientific Affairs, LLC, or Takeda/Millennium 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.

Takeda/Millennium Pharmaceuticals may reimburse you for reasonable costs that are a direct result of your participation, such as travel expenses. You will need to provide receipts for your expenses to be eligible for reimbursement. Please ask the study staff about this possible reimbursement.

Additional Information

4. You may ask the study chair (Dr. Oren Pasvolsky, at 832-728-1403) 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 who can help you safely stop study treatment and then decide if you need to have any visits or tests to check on your health. 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.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Janssen Scientific Affairs LLC, Takeda/Millennium Pharmaceuticals, 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 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 supported by: Janssen Scientific Affairs, LLC and Takeda/Millennium 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 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 will 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

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:

- Dr. Christine Jing Ye (Co-Investigator)
- Dr. Krina Patel (Collaborator)
- Dr. Robert Orlowski (Collaborator)

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
- Janssen Scientific Affairs LLC and Takeda/Millennium Pharmaceuticals, who are supporters of this study, and/or any future sponsors/supporters of the study
- Adaptive Biotechnologies
- 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 official Sponsor of this study is MD Anderson Cancer Center. However, this study is supported through funding and study drug by Janssen Scientific Affairs, LLC and Takeda/Millennium Pharmaceuticals.

Bone marrow will be sent to Adaptive Biotechnologies for sequencing of Minimal Residual Disease (MRD).

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

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