MC1181

Phase 2 Trial of Ixazomib Combinations in Patients with Relapsed Multiple Myeloma

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MAYO CLINIC

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC1181, "Phase 2 Trial of Ixazomib Combinations in Patients with Relapsed Multiple Myeloma" (ARM E ONLY)

IRB#: 11-001516

Principal Investigator: Dr. S. Kumar and Colleagues

Please read this information carefully. It tells you important things about this research study. A member of our research team will talk to you about taking part in this research study. If you have questions at any time, please ask us.

Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision.

To help you decide if you want to take part in this study, you should know:

- Taking part in this study is completely voluntary.
- You can choose not to participate.
- You are free to change your mind at any time if you choose to participate.
- Your decision won't cause any penalties or loss of benefits to which you're otherwise entitled.
- Your decision won't change the access to medical care you get at Mayo Clinic now or in the future if you choose not to participate or discontinue your participation.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you a copy of this form to keep. A copy of this form will be put in your medical record.

CONTACT INFORMATION

You can contact …	At …	If you have questions about …
Principal Investigators: Dr. Shaji Kumar	**Phone:** (507) 284-2511 **Institution Name and Address:** Mayo Clinic Rochester 200 First Street SE Rochester, MN 55905	▪ Study tests and procedures ▪ Research-related injuries or emergencies ▪ Any research-related concerns or complaints ▪ Withdrawing from the research study ▪ Materials you receive ▪ Research-related appointments
Mayo Clinic Institutional Review Board (IRB)	**Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681	▪ Rights of a research participant
Research Participant Advocate (The RPA is independent of the Study Team)	**Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu	▪ Rights of a research participant ▪ Any research-related concerns or complaints ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study
Patient Account Services	**Toll Free:** (844) 217-9591	▪ Billing or insurance related to this research study

Other Information:

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.

1. Why are you being asked to take part in this research study?

You are being asked to take part in this research study because your multiple myeloma has gotten worse and is not responding to the standard drugs for multiple myeloma. The plan is to have up to 183 people take part in this study at Mayo Clinic.

2. Why is this research study being done?

In this study, you will be treated with a drug called Ixazomib (MLN9708). It is thought that Ixazomib will interfere with the process of protein breakdown in the multiple myeloma cells.

This study is being done to find out the effects (good and bad) of Ixazomib used in combination with cyclophosphamide, daratumumab, and dexamethasone has on you and your Multiple Myeloma. Ixazomib, cyclophosphamide, daratumumab, and dexamethasone are all approved for use in treatment of relapsed myeloma, but not in the combination as indicated here.

As you read this form describing the study, ask any questions you have. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you decide. If you decide to participate, you may stop participating at any time during the study. You may decide not to participate. If so, none of your current benefits or normal health care will be affected in any way. When you feel comfortable that all your questions have been answered, and you wish to take part in this study, sign this form in order to begin your participation. Your signature means you have been told about the study and what the risks are. Your signature on this form also means that you want to take part in this study.

3. Information you should know

Who is Funding the Study?
Takeda/Millennium Pharmaceuticals, Inc. is funding the study. Takeda/Millennium Pharmaceuticals, Inc. will pay your study doctor or the institution to cover costs related to running the study and will supply the study drug ixazomib. Janssen Pharmaceuticals will provide the study drug Daratumumab.

Taking part in this research study will not change your rights and benefits. Taking part in this research study does not give you any special privileges. If you decide to not participate in this study, or stop in the middle of the study, no benefits are taken away from you. You do not have to be in this research study to receive or continue to receive medical care from Mayo Clinic.

You will be told of important new findings or any changes in the study or procedures that may affect you or your willingness to continue in the study.

4. How long will you be in this research study?

You will receive study treatment for as long as your multiple myeloma is responding to the treatment and you are not having side effects that cannot be managed. As of Addendum 30, study treatment will be discontinued. You will be in the study for up to 2 years after the end of treatment.

5. What will happen to you while you are in this research study?

Before you are enrolled in the study, you will undergo certain tests to ensure that it is safe for you to go on the study (listed in the table below). If you are eligible and agree to participate, you will take ixazomib by mouth on days 1, 8, and 15 of each cycle (for 3 out of 4 weeks).

Cyclophosphamide and dexamethasone pills will be taken on days 1, 8, 15 and 22. Daratumumab will be given to you intravenously, by inserting a needle into a vein, on days 1, 8, 15 and 22 for the first 2 cycles, then on days 1 and 15 for cycles 3, 4, 5 and 6, then on day 1 of all subsequent cycles. Each cycle is 28 days.

To start with you will receive ixazomab 4mg, cyclophosphamide 300 mg/m2 and dexamethasone 40 mg by mouth, and daratumumab 16 mg/kg through a vein. The doses may be adjusted as we go through the study based on your individual tolerance. Cyclophosphamide will be discontinued after 12 cycles, but the ixazomib, daratumumab and dexamethasone will continue.

While you are enrolled in this study, you will need to have blood tests done weekly for the first two cycles of treatment, which should take less than an hour. After 4 cycles of therapy, you can elect to have these tests done at a facility closer to home or at Mayo Clinic, if there are no ongoing side effects, whichever is more convenient to you. You will still need to return every two cycles. This visit will last approximately half a day and will include blood tests, a visit with

your doctor and study coordinator. Other tests such as x-rays and bone marrow tests may also be done in between if your physician feels that it is required for management of your myeloma. Below is a table that shows the procedures and study visits:

Before study registration	• Routine blood and urine tests and exams, including a blood test for hepatitis. Please note: If your hepatitis test result is positive you will need to have a second test done to make sure the results are the same. The researcher will tell you how to find medical help and counseling as needed, and you may not be able to take part in the study. Your health insurer or you will have to pay for the cost of the repeat test, any follow-up medical care, or counseling. If the hepatitis test results are positive, it is the state law that they be reported to the State Department of Health. The test results will also be put in your medical record. • Bone marrow aspirate and biopsy • Skeletal survey or Whole Body Low Dose CT (WBLDCT) • PET/CT or MRI, if clinically indicated • Pregnancy test (only for females who may still become pregnant) • EKG • Chest x-ray • Spirometry
Weekly for the first 2 cycles	• Routine blood tests
Every cycle	• Routine blood and urine tests and exams • Bone marrow aspirate and biopsy (done if you are suspected to have achieved a complete response) • Medication Diary • Physical Exam • If you have extramedullary disease, WBLDCT, PET/CT or MRI will be done at the end of Cycle 1 and then every three cycles (or as clinically indicated)
Follow-up Phase	• Clinically indicated tests that are required for the normal monitoring of your myeloma

As of amendment 27:
You may receive treatment locally, provided the ixazomib can be sent, and the daratumumab can be obtained at your local healthcare facility; and provided it is feasible to have the evaluations required by the protocol completed remotely or through your local healthcare facilities. You will need to return to the enrolling institution every 3rd cycle. Please note, if you receive daratumumab locally (not at Mayo Clinic Rochester, Arizona or Florida), it will be from the commercial supply and will be billed to you/your insurance and not paid for by the study.

If your disease gets worse while you are receiving the study drugs, the study treatment will be discontinued, and you will be able to switch to another treatment. However, once you stop this study treatment you will be followed every 6 months until you have been in the study for 2 years. If you have a complete response or discontinue treatment for any other reason, you will be followed every 3 months for one year after the end of your treatment, then be followed every 6 months until you have been in the study for 2 years beyond end of treatment.

6. What are the possible risks or discomforts from being in this research study?

POTENTIAL DISCOMFORTS AND RISKS OF IXAZOMIB

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:

Common risks of Ixazomib *(events occurring greater than 20% of the time)*

- Feeling sick to your stomach (Nausea)
- Throwing up (Vomiting)
- Loose Stool (Diarrhea)
- Constipation
- Feeling tired or weak
- Decreased number of blood cells (platelets) that help to clot the blood (which could put you at increased risk of bleeding (Thrombocytopenia)
- A low number of white blood cells, which are the infection fighting cells, which could put you at risk for infection (Neutropenia)
- A low number of a particular white blood cell, which is important to the immune system (Lymphopenia)
- Infection including shingles

- Decrease in red blood cells, which are the oxygen carrying cells which could make you feel tired (Anemia)
- Skin rash
- Swelling of extremities (arms and/or legs)
- Numbness and tingling (also known as peripheral neuropathy)
- Joint pain (arthralgia)
- Flu-like symptoms and other upper respiratory tract infections
- Lung infections including pneumonia
- A painful blistery red rash that is confined to one side of the body, similar to chicken pox (Herpes zoster)

Less likely risks of Ixazomib *(events occurring less than or equal to 20% of the time)*

- Decreased appetite
- Abdominal pain or distension
- Back pain
- Sensation of lightheadedness or vertigo (spinning sensation) (Dizziness)
- Blood chemical imbalance (Electrolyte imbalance)
- Excessive or abnormal loss of body fluids (Dehydration)

Rare risks of Ixazomib *(events occurring less than 2-3% of the time)*

- Low or high blood pressure
- Effects on your nervous system that may cause painful feelings or numbness or tingling in hands and feet. The nerves that control things like your heart rate, gut movement, and urinary bladder may be affected
- Inflammatory response associated with an increase in your white blood cell count, fever, and a change in certain protein levels and chemistries in the body
- Esophageal ulcer
- Chest pain
- Abnormal liver tests
- Decreased weight
- Fainting episodes
- Decreased level of consciousness
- Tremors
- Blood clots
- Inflammation of the lungs
- Increased blood pressure in the lungs
- Nosebleeds
- Muscle weakness
- Changes in mood

- Swelling around the eyes
- Muscle aches

Rare but serious risks of Ixazomib

- Life threatening severe skin rash
- Abnormal heart rhythms
- Worsening of your heart function (Congestive heart failure)
- Disorders that could affect the function of your lung that could be serious enough to result in death
- Liver failure
- Abnormal clotting of the blood in small blood vessels (Thrombotic Thrombocytopenic Purpura (TTP))
- A complication that may occur if the cancer cells die too quickly that includes inappropriate increase or decrease of various natural chemicals in the blood stream, called uric acid, phosphorus, potassium, creatinine, and calcium. Severe tumor lysis can result in kidney failure and may harm muscle or nerve function (Tumor lysis syndrome)
- High creatinine and renal failure. The amount of creatinine (a waste product made by your body) in your blood helps your doctor understand how your kidneys are working. High creatinine means your kidneys are having trouble working well. Patients who had lost body water 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).
- Blockage of your bowel function
- Severe rash that can lead to skin peeling and life-threatening complications (Stevens Johnson syndrome)
- A condition that can be associated with abnormal neurological function and seizures (posterior reversible encephalopathy syndrome; PRES)
- Inflammation of the spinal cord (transverse myelitis)
- Progressive multifocal leukoencephalopathy, a rare condition associated with inflammation in the brain has been reported, but it is not clear if it is related to the medication. The most prominent symptoms are clumsiness, progressive weakness, and visual, speech, and sometimes personality changes.
- Acute febrile neutrophilic dermatosis (Sweet's syndrome), this is a skin condition that causes fever and a painful skin rash that appears mostly on the arms, face and neck.

Ixazomib should not be taken if you have ever had a serious allergic reaction to boron or boron containing products.

Dexamethasone

Likely risks of dexamethasone (events occurring greater than 20% of the time)

- Stomach and throat ulcers or worsening of any ulcers you had before treatment
- Swelling and pain of the pancreas
- Weight gain around the stomach
- Puffiness (especially in the face)
- Buildup of fluids and a rise in blood pressure
- Possible rise in your blood sugar
- Changes in the blood levels of potassium
- Infection

Less likely risks of dexamethasone (events occurring less than or equal to 20% of the time)

- Muscle weakness
- Brittle bones
- Menstrual changes
- Itching, and other allergic reactions, some severe

Rare but serious risks of dexamethasone (events occurring less than 2-3% of time)

- Mood swings
- Depression
- Trouble sleeping
- Changes in personality
- Seizures
- Dizziness
- Patients who are more likely to get heart disease may have heart failure

Cyclophosphamide

Likely (happening greater than 20% of the time)

- Feeling sick to the stomach
- Throwing up
- Loss of appetite
- Watery stools
- Yellowing of the skin
- Lowering of your blood cell counts which could cause infection or bleeding and you may have to have a blood transfusion. Contact your study doctor right away if you develop any signs of infection such as fever, chills, persistent sore throat

Less likely (happening less than or equal to 20% of the time)

- Escape of the drug from the vein may cause soreness or severe pain and redness in that area; pain, redness, and soreness of a vein
- Temporary hair loss. Regrowth may have a different color or texture.
- Bladder irritation. This can cause pain, blood in the urine, unusual decrease in the amount of urine, dark urine, and scarring of the bladder. If you drink 8 to 10 glasses of water a day and empty the bladder frequently, you can avoid this side effect.
- Damage to the female sex organs. Women who are still having periods may not have them every month or they may stop altogether for a time. A woman may not be able to get pregnant again.
- Sores in the mouth

Rare but serious (happening less than 3% of the time)

- Secondary leukemia and/or myelodysplastic syndrome (damage to the bone marrow that affects normal blood cell production)
- Allergic reaction (rapid heartbeat, shortness of breath, wheezing, tightness in the throat)
- Black/bloody stools
- Severe stomach/abdominal pain
- Mental/mood changes
- Muscle weakness/spasms
- Swelling of the ankles/feet
- Sudden or unusual weight gain
- Headache
- Dizziness
- Metallic taste
- Abnormal liver tests
- Heart failure has been reported but rarely at the doses given in this study. This can also happen if cyclophosphamide is used in combination with radiation treatment or certain other chemotherapy drugs (e.g., doxorubicin). Seek immediate medical attention if you develop chest pain, jaw/left arm pain, trouble breathing, and irregular heartbeat.
- Scarring of the lungs causing coughing spells and shortness of breath

Side effects may be higher by using other drugs with cyclophosphamide. Phenobarbital raises the effect of cyclophosphamide on your blood cells. Other drug interactions have been reported. If you need anesthesia within 10 days of taking cyclophosphamide, you should let your anesthesiologist know about your treatment.

Daratumumab

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

- Increased risk of infections, including infection of the upper respiratory tract (such as nose, sinuses, throat, or upper airway), lung, lower airway (bronchitis), and/or pneumonia
- Fatigue, or lack of energy
- Weakness, lack of strength
- Nausea
- Anemia (lowered blood cell counts)
- Back pain
- Decreased white blood counts including neutrophils and lymphocytes
- Low platelets, which may increase the risk of bleeding and bruising (see "Blood Cell Effects: below)
- Decreased appetite
- Fever
- Cough
- Headache
- Numbness and tingling (neuropathy)
- Diarrhea
- Constipation
- Vomiting
- Rash, a noticeable change in the texture or color of your skin
- Shortness of breath (dyspnea), including wheezing
- Muscle spasms
- Swelling of hands, feet or limbs
- Sleeplessness (insomnia)
- Joint pain
- Infusion related reactions (see "Infusion Related Reactions" section below)

Common side effects with daratumumab (affects 1 to 10 in 100 patients)

- Urinary tract infection
- Influenza or flu like symptoms
- Chills
- Nasal congestion
- Abnormal heart rhythm
- Sepsis (a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs)
- High blood glucose levels
- Low blood calcium levels

- Loss of body fluids, also known as dehydration
- Irregular heartbeat (atrial fibrillation)
- High blood pressure
- Fluid in the lungs (pulmonary edema)
- Dizziness
- Fainting
- Inflammation of the pancreas
- Itchy skin
- Muscular pain in the chest
- 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
- A condition with your immune system in which not enough gamma globulin proteins (also known as antibodies) are produced (hypogammaglobulinemia). Decreases in gamma globulin proteins can increase the risk of infections

Uncommon risks of daratumumab (affects 1 to 10 in 1,000 patients)

- Hepatitis B virus reactivation (if you previously had hepatitis B, the infection could return)
- Cytomegalovirus infection (see separate section on infections below)
- COVID-19

When daratumumab is given at the same time with other drugs, some side effects of these drugs may happen more often or may be more severe. There may be other unexpected side effects.

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.

Get emergency medical help if you have any of following: hives; wheezing; difficulty breathing; swelling of your face, lips, tongue, or throat; or pain in chest.

The sponsor has tried different ways of giving the infusions to lessen these reactions. The sponsor will continue to monitor infusion-related reactions and make changes to the infusions 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, acetaminophen and antihistamine, before and after the infusion
    - The infusion may be slowed down or stopped
    - You may stay overnight in hospital after the infusion so medical staff can check you and to make sure you are monitored and managed appropriately.

Blood Cell Effects
Daratumumab can decrease white blood cell counts which help fight infections, and blood cells called platelets which help to clot blood. 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.

Infection
Different kinds of infection have been seen in patients receiving daratumumab. Most of them are upper 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, 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. It is important to tell your 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 also 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.

Allergic reactions/Anaphylaxis
Daratumumab is an antibody made from a protein. Protein drugs can cause allergic reactions (for example fever or chills, sometimes, it is very difficult to tell the difference with infusion related reactions) in some people.

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

Anaphylaxis is the worst type of allergic reaction, it can happen suddenly and often causes the throat to swell, an itchy rash and sometimes the blood pressure to drop. Anaphylaxis has not been seen with daratumumab so far. Your study doctor and their staff will be ready to treat such a reaction in case it happens. If this happens, you will not receive any more daratumumab infusions. You may not be able to be treated again with this type of medication. In the future, you should tell any other doctor you visit that you received daratumumab in this research study and if you had an allergic reaction.

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.

Interference with cross-matching blood for transfusions
Daratumumab can interfere with the standard test to identify compatible blood for transfusion support for up to six months after the last infusion. The blood transfusion center needs to be informed that you have received daratumumab so that additional steps can be taken to identify compatible blood products. As with any medication, allergic reactions are a possibility.

The risks of drawing blood include pain, bruising, and rarely, infection at the site of the needle stick.

Pregnancy and Birth Control:

RISK TO THE UNBORN CHILD (MEN AND WOMEN)

Female subjects: We do not know if the study drugs will affect mother's milk or an unborn child. Therefore, breast-feeding and pregnant women are not allowed to take part in the study. Due to unknown risks and potential harm to the unborn child/ infant, you should not become pregnant or nurse a baby while on this study.

You must have a negative pregnancy test prior to enrolling in the study.

Unless you cannot have children because of surgery or other medical reasons (you had an effective tubal ligation, or had the ovaries or the uterus removed; or you are post-menopausal), you must use two effective methods of birth control from the time of signing the informed consent form, for the entire study drug treatment period, and for 90 days after completing study drug treatment. It is strongly recommended that at least one of these two methods be highly effective (see examples below).

Highly effective methods	**Other effective methods (barrier**
Intra-uterine devices (IUD)	Latex condom with a spermicidal agent
Hormonal (birth control pills/oral contraceptives, injectable contraceptives, contraceptive patches, or contraceptive implants)	Diaphragm with spermicide; Cervical cap with a spermicide; Sponge with a spermicide
If one of the highly effective methods cannot be used, using two effective methods at the same time are recommended.	

You must use birth control methods as directed above, unless you completely avoid having heterosexual intercourse.

Male subjects: We do not know if using the study drugs will affect sperm. Therefore, due to potential risk, you should not get your partner pregnant during the study drug treatment period. Even if you are surgically sterilized (i.e., have had a vasectomy) you must agree to use an appropriate method of barrier contraception (latex condom with a spermicidal agent) during the entire study drug treatment period, and for 90 days after completing study drug treatment. Or, you should completely avoid having heterosexual intercourse.

Highly effective methods	**Other effective methods (barrier**
Vasectomy	Latex condom with a spermicidal agent
	Diaphragm with spermicide; Cervical cap with spermicide; Sponge with spermicide
If one of the highly effective methods cannot be used, using two effective methods at the same time are recommended.	

All subjects (male or female): If you or your partner becomes pregnant during this study, you must tell the study doctor immediately. The doctor will advise you of the possible risks to your unborn child and discuss options for managing the pregnancy with you.

For female subjects who become pregnant while on this study, the study drug will be stopped immediately, and the pregnancy will be followed until conclusion.

During the course of the study and for 3 months after stopping daratumumab. the last dose of daratumumab both male and female patients must use effective methods of birth control and not donate sperm/eggs.

Risk summary

Many side effects go away shortly after the (Ixazomib) is stopped, but in some cases side effects can be serious, long lasting, or may never go away. There may be a risk of death. Some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

7. Are there reasons you might leave this research study early?

Taking part in this research study is voluntary. You may decide to stop at any time. You should tell the researcher if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers, Millennium Pharmaceuticals Inc. or Mayo may stop you from taking part in this study at any time:

- if it is in your best clinical interest,
- if you do not follow the study procedures,
- if the study is stopped.

8. What if you are injured from your participation in this research study?

Where to get help:
If you have side effects from the study treatment, you need to report them to the researcher and your regular physician, and you will be treated as needed. Mayo will bill you or your insurer for these services at the usual charge. Mayo will not offer free medical care or payment for any bad side effects from taking part in this study.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

9. What are the possible benefits from being in this research study?

This study may not make your health better; however, the results of this study may help in the development of a potential new treatment for multiple myeloma and may help other patients with the disease in the future.

10. What alternative do you have if you choose not to participate in this research study?

You do not have to be in this study to receive treatment for your condition. Your other choices may include:

- Other treatment with approved drugs or care for your myeloma without being in a study
- Bone marrow transplantation
- Investigational drugs, which may be available for the treatment of your disease and their risks and benefits

You should talk to the researcher and your regular physician about each of your choices before you decide if you will take part in this study. If you decide not to take part in this study, your ability to get medical care will not be affected.

11. What tests or procedures will you need to pay for if you take part in this research study?

You and/or your health plan will need to pay for all tests and procedures that are part of this study because they are needed for your regular medical care. The study drugs ixazomib and Daratumumab will be given to you at no cost. You or your health plan will have to pay for the IV administration (and related costs) of the Daratumumab. You or your health plan might also have to pay for other drugs or treatments which are given to help you control side effects. **Please note, if you receive daratumumab locally (not at Mayo Clinic Rochester, Arizona or Florida), it will be from the commercial supply and will be billed to you/your insurance and not paid for by the study.**

Before you take part in this study, you should call your health insurer to find out if the cost of these tests and/or procedures will be paid for by the plan. Some health insurers will not pay for these costs. You will have to pay for any costs not covered by your health insurer.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

12. Will you be paid for taking part in this research study?

You will not be paid for taking part in this study.

13. What will happen to your samples?

Your samples will be used as described for this study. When the study is done, they will be destroyed.

14. How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

The study data sent by the study doctor to the sponsor does not include your name, address, social security number, or other information that directly identifies you. Instead, the study doctor assigns a code number to the study data and may use your initials. Some study data sent to the sponsor may contain information that could be used (perhaps in combination with other information) to identify you (e.g., date of birth). If you have questions about the specific health information that will be sent to the sponsor, you should ask the study doctor.

In addition to the uses listed above, companies that sponsor studies often use study data for other purposes that are not part of the study. For example, the company might use the study data for research purposes to support the scientific objectives of the study described in this consent document, to learn more about the effects (good and bad) of any drug, device or treatment included in the study, to better understand the disease(s) included in the study, or to improve the design of future studies. Also, the company might share the study data with other companies it

does business with. The company might do these things during the study, or after the study has ended, and would not have to ask for your permission to do so. The sponsor might still use study data, even after you stop your authorization, or the authorization expires, as long as the study data was collected before your authorization stopped or expired. The ways in which the study data could be used in the future may not be known now, so we can't give you the details.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Health information may be collected about you from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Why will this information be used and/or given to others?

- To do the research.
- To report the results.
- To see if the research was done correctly.

If the results of this study are made public, information that identifies you will not be used.

Who may use or share your health information?

- Mayo Clinic research staff involved in this study.
- Millennium Pharmaceuticals, Inc.
- Janssen Pharmaceuticals

With whom may your health information be shared?

- The Mayo Clinic Institutional Review Board that oversees the research.
- Other Mayo Clinic physicians involved in your clinical care.
- Researchers involved in this study at other institutions.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- The sponsor(s) of this study and the people or groups it hires to help perform this research.
- A group that oversees the data (study information) and safety of this research.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you.

However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Privacy Rights

You do not have to sign this form, but if you do not, you cannot take part in this research study.

If you cancel your permission to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

If you choose not to take part or if you withdraw from this study, it will not harm your relationship with your own doctors or with Mayo Clinic.

You can cancel your permission to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission lasts until the end of this study, unless you cancel it. Because research is an ongoing process, we cannot give you an exact date when the study will end.

ENROLLMENT AND PERMISSION SIGNATURES

Your signature documents your permission to take part in this research.

	/ /	: AM/PM
Printed Name	Date	Time

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

	/ /	: AM/PM
Printed Name	Date	Time

Signature