A Multicenter Phase 1-DEC (Dose Expansion Cohort) Open-label Study of Iberdomide (CC-220) in Combination With Elotuzumab and Dexamethasone for Relapsed/Refractory Multiple Myeloma

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STUDY INFORMATION:

Study Title: A Multicenter Phase 1-DEC (Dose expansion cohort) Open-label Study of Iberdomide (CC-220) in Combination with Elotuzumab and Dexamethasone for Relapsed/Refractory Multiple Myeloma

Study site(s): Icahn School of Medicine at Mount Sinai, The Blavatnik Family Chelsea Medical Center, Mount Sinai Hospital - Brooklyn

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SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in joining. Participation in the study is voluntary. You can agree to join or not. Your decision will not limit your ability to receive care at Mount Sinai. You should only agree to take part if you understand the study and if all of your questions about the research study are answered. If you do join the study, the research team must share any new information with you that may change your mind about taking part.

The purpose of this research study is to test the effectiveness (how well the drug works) when a medicine called dexamethasone combined with a medicine used for myeloma called elotuzumab with an investigational drug called iberdomide. The ability of iberdomide at reducing disease in relapse myeloma has been seen in some subjects participating in other studies that are still ongoing. The benefits of this combination therapy will be determined by looking at the decrease in your myeloma proteins and evaluating how long the results last. This study will also evaluate how well this combination is tolerated (does not cause unacceptable side effects). Since

one of the study objectives is to identify a dose that is safe and effective, the dose you receive may be higher or lower than other participants depending on how other patients have tolerated the dose being used. Dose of the study drug may be increased if it is considered safe to identify the best dose to use in a larger group of patients. The current treatments used for myeloma are not able to cure it and the disease tends to come back. At times, the side effects of these treatments can be very debilitating. This study will try to see if this combination of drugs could be better than what is already available.

If you choose to take part, you will be asked to

- Agree to not share your study medication.
- Perform a series of tests that are routinely done and include blood and urine samples, imaging x-rays, bone marrow biopsies and medical exam to see if you are a good candidate to participate in the study.
- Show up to clinic once a week for the first two months and then once every other week. During these visits, you will have blood tests and evaluated to see how your body and the cancer is responding to the treatment. This is routinely done when receiving any type of treatment for myeloma, but a few extra tests will be included in the blood samples taken. During some of those visits, you will also be receiving some medications that make part of your treatment in this study. A bone marrow biopsy will be done approximately 6 weeks from the start of treatment to see how the treatment is working; this procedure would normally not be done outside of a clinical trial. If your doctor thinks that you have responded very well to treatment and wants to confirm that, a bone marrow biopsy may be repeated. This biopsy can also be done if there is suspicion that the disease is getting out of control.

If you choose to take part, the main risks to you include side effects from elotuzumab and iberdomide and discomfort from procedures required for this study. For details on all the risks, please refer to the “Reasonably Foreseeable Risks” section.

Possible benefits may be access to a treatment that could help control your cancer. It could also help other patients like you that require treatment for myeloma that has relapsed. The investigational drug will be provided at no extra cost while on study.

If you are interested in learning more about this study, please continue to read below.

_____

STUDY PARTICIPATION:

You may qualify to take part in this research study because you have multiple myeloma that has been treated and has returned or is not responding to the current treatment. Even though you have received a combination of medicines that have different ways of working, you have not been treated with the drugs used on this study.

Your participation in this research study is expected to last as long as you tolerate treatment and are having a good result in controlling your myeloma.

The number of people expected to take part in this research study at the Mount Sinai is 15-20. The total number of people expected to take part in this research study across all sites is 31.

Funds for conducting this research study are partially provided by Bristol Myers Squibb.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

DESCRIPTION OF WHAT IS INVOLVED:

If you agree to take part in this research study, here is what may be involved:

The research activities will take place in the myeloma clinic of the Icahn School of Medicine at Mount Sinai. Throughout the study, you will interact with the study team that includes your study doctor, study nurses and coordinators, as well as infusion nurses, schedulers, social worker, phlebotomists, patient navigator, and clinic staff.

When you start treatment in the study, you will receive three drugs directed at reducing your myeloma> elotuzumab, iberdomide, and dexamethasone. Treatment will be given in periods of 28 days called “cycles”.

Elotuzumab is given through the vein at a dose of 10mg/kg once a week for the first two months. After that, it will be given at a dose of 20mg/kg once a month. The infusion normally takes 1-3 hours. Prior to each dose of elotuzumab, you will receive medications to prevent allergic reactions by mouth or through the vein.

Dexamethasone will be given as one or more tablets and/or as an infusion through the vein. On the days that elotuzumab is given, you will receive 40mg (20 mg if you are older than 75) of dexamethasone through the vein between 45 and 90 minutes before elotuzumab. The weeks you do not receive elotuzumab, you will take 40 mg of dexamethasone by mouth (20 mg if older than 74) once a week.

Iberdomide will be taken at one of four daily doses:0.75mg, 1 mg, 1.3 mg, or 1.6 mg. This will be taken daily for 21 days and will rest the remaining 7 days of the 28-day cycle. Iberdomide should be taken according to the label and should not be broken, chewed, or opened. If you forget to take your iberdomide and it has been

more than 12 hours since your regular dosing, you will skip that dose. On days that you receive elotuzumab, iberdomide should be taken at least 2 hours after completing the infusion.

Study Procedures
There are three periods to the study: screening, treatment and follow-up periods

Screening
The Screening Period of the study can take a few weeks to complete. The screening period is to see if you are eligible for the study and it will involve a variety of procedures including lab tests, imaging studies, procedures, and a physical exam.

Visit 1- (Screening Visit) At least 24 hours before the screening visit, you will receive a copy of the consent form in order for you to read and understand the risks, benefits and the procedures involved as a result of taking part in the study. At the Screening Visit, you will be asked to read and sign this informed consent before any study-related procedures that are not standard of care are performed. It is your right as a subject to have the study fully explained to you and you can ask that your study doctor explain or go over any parts of this informed consent that you do not understand before any study-related tasks begin. The following tests and procedures will be performed by the study staff to determine if you qualify to participate in this study:

- Review of your medical history.
- Review of medications you are currently taking and have taken in the past including herbal medications.
- A physical examination including measurement of your weight and vital signs (temperature, blood pressure, and heart rate).
- You will be asked about the symptoms you are having from your disease (performance status)
- Collection of your blood (approximately 4 teaspoons/20 mLs) for laboratory tests, which measure your blood chemistry, including kidney and liver function, count your red and white blood cells and platelets, measure your thyroid function, and check for hepatitis B or C infection. You must not have known HIV and your hepatitis B and C tests must be negative for you to participate in the study.
- You will be told of the results of the testing for Hepatitis B and C, and counseled as to the meaning of the results, whether they are positive or negative. If the test indicates that you are infected with Hepatitis B or C, you will receive additional counseling about the significance of your care and possible risks to other people. Researchers are required by law to report all positive results to the New York State Department of Health. The test results will be released only as permitted by applicable law. If you do not want to be tested for Hepatitis B or C, you should not agree to participate in this study.
- Collection of a urine or blood sample for a pregnancy test for women who can become pregnant 10-14 days before starting study drug. Results of the pregnancy test must be negative for you to

participate in this study. A pregnancy test must also be performed within 24 hours before the first dose of study medication is given. Results of the pregnancy test must also be negative for you to receive study drug.

- Collection of urine and blood for laboratory tests to evaluate your multiple myeloma. You will need to collect a 24-hour urine sample before your first day of study drug.
- A bone marrow sample will be taken via needle aspirate (a procedure in which a needle is inserted into the bone). A bone marrow biopsy (tissue sample) may also be taken if necessary (e.g. if aspirate cannot be obtained). The biopsy is optional and not required for you to participate in the study if the aspirate is available. The bone marrow sample will be used to assess your myeloma and for research purposes.
- Imaging studies (computed tomography (CT) scan, or magnetic resonance imaging (MRI) may be done if your study doctor suspects tumors outside your bones (called plasmacytomas) and considers it important as part of standard of care management.
- You will have a chest x-ray and a series of x-rays of your body (skeletal survey) to observe your myeloma at starting point.
- You will complete a series of questions to evaluate your symptoms and signs of how your disease is affecting your daily activities.
- If, based on the results of the screening visit tests and procedures, you qualify to participate in the study, you will return to the study doctor's office to begin the treatment period.

Treatment Period (28-day dosing cycles)

You will receive the study drug in cycles; each cycle will be 28 days long. Cycle 1 and 2 will require 4 total visits at Days 1, 8, 15 and 22. During these two cycles, your visits may take up to 7 hours. Cycle 3 will require 2 visits at days 1 (up to 4 hours) and 15 (up to 1.5 hours) Cycle 4 consecutive cycles after cycle 4 will require 1 vist at day 1 (up to 4 hours). If your study treatment is discontinued, you will need to complete an end of treatment visit that may take up to 3 hours to assess your disease progression. Once you discontinue from participating in this study, you will be contacted every 3 months to learn about your health, which may take up to 15 minutes.

At each visit that you receive study medication, you may also receive a brief physical exam, blood tests, vital signs, and an assessment of side effects you may be having.
If you experience any changes in your body or develop any new or worsening side effects during any part of the study, you should inform the study doctor or nurse immediately.
During the Treatment Period, you will be asked questions about your condition including:

- How your cancer is affecting your daily activities.
- Medications you took or are taking. This includes herbal supplements and over-the- counter medicines.

- What side effects you experienced. During your clinic visits, you should report any new or worsening medical problems since your last visit to the study doctor or other study personnel taking care of you.

The following procedures will be performed and/or collected at 1 or more visits:

- Physical examination
- Weight
- Vital sign measurements (blood pressure, heart rate, and temperature). If you develop a reaction during the infusion, you will continue to have your vital signs measured until the study doctor determines it is no longer necessary.
- You will be asked about the symptoms you are having from your disease (performance status)
- Urine or blood pregnancy test if you are a woman who can become pregnant (result must be negative to receive study drug).
- Blood samples will be drawn to assess 1 or more of the following:
- Your blood chemistry, including kidney and liver function, count your red and white blood cells and platelets (about 2 1/2 teaspoons or 13 mLs);
- Collection of urine and blood for laboratory tests to evaluate your multiple myeloma will be done every 4 weeks to evaluate how your disease is responding to treatment. You will need to bring a 24-hour urine sample with you.
- Additional blood samples will be drawn before and after infusions on day 1 and 15 of the first two cycles to assess your immune response and levels of the drug in your blood for study purposes. You will have from 2 teaspoons/10mLs to about 4 teaspoons/20 mLs total of blood drawn
- Another collection of your blood (approximately 8 teaspoons/ 40 mLs) for biomarker tests (substances in your blood, such as proteins) will be done at screening and prior to receiving treatment on day 1 and day 15 of the first two cycles. Measuring biomarkers in the blood may help predict whether or not someone is likely to benefit from a drug
- Additional tests including a bone marrow aspiration (or biopsy in some cases), bone survey, or other imaging studies like an MRI, CT scan, or PET/CT scan may be done if your study doctor believes it is needed.
- If your disease worsens, you may be asked for permission to obtain another bone marrow aspirate.
- You will complete a series of questions using paper forms, to assess your signs and symptoms and how the disease is affecting your daily activities.

  Study treatment may be stopped based on your disease assessments or if you are having side effects that make you unable to tolerate study therapy. Based on discussions between you and your study doctor, you may discontinue treatment if you decide to after having discussed it with your study doctor.

Follow-up

When you stop study treatments you will begin the last part of the study, the follow-up period. You will have one more evaluations, which will mark the end of treatment and may include the same blood, imaging, and biopsy tests like those during treatment. After this period, your study doctor will continue to assess your health condition to see if you received other therapies afterwards or had complications from the disease.

Test results that are for research purpose and not part of standard care will not be shared with you. Because this project involves the use of medications or a medical device, it is necessary that a note of your participation is made in the electronic medical record. That way anyone treating you will be aware of your participation and may be able to avoid any unfortunate outcomes that could arise if your research participation were unknown.

Because this research study involves the use of study drugs, a note must be included in your electronic medical record that you are taking part in the research. This way, anyone involved in your medical care will know that you are a study participant, and they can work to avoid any problems or negative outcomes that could arise if they do not know.

Genetic Testing

As a part of this study, you will be required to provide blood and bone marrow samples to study your genetic material (genomic testing). The purpose of this genomic testing is to help us understand how your genes affect response to the study treatments administered, the drug target and what it does, and/or your disease. DNA and RNA will be isolated from these samples. Genes are made up of DNA, which is the substance in cells that carries genetic (inherited) information. Genes help determine the characteristics of each individual, such as hair and eye color. This may include whether or not people are likely to get a certain disease, or how their disease may respond to study drug treatment. RNA is the substance that is made based on the information contained in the genes.

Your DNA and RNA samples will be used for genomic research to better understand how safe the study drug is, how well it works, what the drug target does, and the causes of multiple myeloma as well as related diseases and how to treat or prevent them. This genomic research includes reading the content (sequence) of your genes and studying variations in your DNA and RNA. These variations can affect the way you respond to study drug treatments and/or your disease. Your genetic information will be analyzed together with the health information collected in this study to determine if there are any connections between the two. Your sample may also be used to help develop new tests. The results of this analysis are for research use only and will not be returned to you.

Pregnancy

If you can possibly get pregnant, a blood or urine test for pregnancy will be done 10-14 days before you begin the study and the pregnancy test will be repeated 24 hours before receiving the first dose of study medication. A urine pregnancy test will be repeated on a weekly basis for the first month and then on a monthly basis. If you have irregular menstruation, the frequency of the pregnancy test after the first month will be every 15 days. You will be required to continue testing while on treatment and up to a month after the last dose of iberdomide. If you have not had a period in over 24 months and are considered postmenopausal, you do not need to have pregnancy tests repeated. The same applies if you have had a hysterectomy or removal of both ovaries.

You cannot be included in the study if you are or become pregnant, as the study drug could harm your fetus. You also should not be in the study if you are producing milk to feed a child as the study drug could harm your baby.

Unless you are at least one year past menopause or have had a successful operation to make pregnancy impossible, you should use 2 methods of effective birth control. Unless you are sexually abstinent (not having genital sex) the recommended methods of birth control are:

- The consistent use of approved hormonal birth control (pill, patches, or rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual activity),
- Sterilization (a vasectomy, getting tubes tied, or a hysterectomy).

Additional Effective contraceptive method:

- Male Latex or synthetic condom
- Diaphragm
- Cervical cap

All birth control methods (other than abstinence and sterilization) are only effective if you use them properly, start them at least one month before you begin the research study, and continue using them throughout the research study and for five months after the research study ends. If you are unsure whether the method of birth control you use is approved to use while you are in this study, you should ask the Lead Researcher before you begin the study. If you are less than one-year post-menopausal, you could still become pregnant. If you or your partner becomes pregnant, or may be pregnant, at any time within the five months after receiving the last dose of the treatment, you must tell a person from the research team immediately. The team may stop the study drug and refer you/your partner to an obstetrician/gynecologist for follow-up.

Should you/your partner become pregnant, whether or not you/your partner have the baby, the people funding and overseeing the research may ask for information on the pregnancy, even if you are no longer part of the study. You/your partner will be asked for additional written consent to share this information if that happens.

Semen/Sperm:

Drugs can be found in semen and alter sperm. Since you are taking part in a study using experimental drugs or treatments, it is recommended that 1) you use a condom, 2) you do not get a partner pregnant or expose them to semen, and 3) you do not donate semen. These recommendations apply one month before you start taking the study drug, while you are taking the study drug, and for 7 months after you stop taking the study drug. This is because levels of the study drug may be present in the sperm and/or semen even after you stop taking the study drug. You are encouraged to tell your partner(s) and/or their doctor(s) that you are participating in this clinical trial.

USE OF YOUR DATA AND/OR SAMPLES:

The researchers would like your permission to keep your personal information (such as, name, address, date of birth, social security number), study data and/or samples (blood, tissue, urine, saliva, or any other body matter) to use or share in future studies. You can still be part of the study if you do not allow us to use or share them. Please select Yes or No to each of the questions below. To decline all future uses/sharing please select 'No' each time.

(1) Will you allow the researchers to store your data and/or samples to use in future research studies?

Please initial your choice: Yes_____ No_____

If you select No, please stop here and move to the next section, '**Your Responsibilities If You Take Part in This Research**' section below."

If yes, please continue to the next question and tell us how your personal information, study data and/or samples may be used in future research studies.

(2) Do you give the researchers permission to keep the data and/or samples, so they could use them in future studies that are **directly related** to the purpose of the current study?

Please initial your choice: Yes_____ No_____

(4) Do you give the researchers permission to keep the data and/or samples indefinitely, so they could use them for future studies that are **not related** to the purpose of the current study (for example a different area of research)?

Please initial your choice: Yes_____ No_____

(4.1) From time to time, researchers outside of medicine and related sciences would like to use data and/or samples. This might be in the fields such as anthropology, human origins, mapping human migration patterns. Do you give permission for researchers **outside the field of medicine** to use your data and/or samples?

Please initial your choice: Yes_____ No_____

a. If the future research in a different area can be done without having to know that the data and/or samples came from you personally, that will be done.
b. If the future research in a different area requires that it is known specifically who the data and/or samples came from, then one of the following will be done:
   I. If you allowed the researchers to contact you in the future, they may be able to contact you to explain why your data and/or samples is needed and what will be done with it. Your permission will be asked to use your data and/or samples in that research project.
   II. If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical (for example, because you have moved), your data and/or samples may still be used. The Institutional Review Board (IRB) will be asked for permission to use the data and/or samples linked to your identity. The IRB can give permission for researchers to use and share identifiable health information without contacting you, but only if it determines that sharing the data and/or samples will not be more than minimal risk to you or your privacy. The IRB is a committee of doctors and scientists and nonscientists, including people not associated with this hospital or medical school, whose job it is to protect people who participate in research.

(5) Do you give permission to have your data and/or samples given **to other researchers,** including those at Mount Sinai, other medical or scientific institutions and for-profit companies, for use in research within the limits you have chosen above?

Please initial your choice: Yes_____ No_____

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

- If you decide to take part in this research study, you will be responsible for the following things: *Keeping all appointments and follow instructions from your doctor and the study team.*
- *Taking all the prescribed medications.*
- *Calling the study team to let them know of any symptom or side effect you may be having on a timely manner.*
- *Telling your doctor and study team all the medications you are taking.*
- *Discussing any medical treatments that you plan on having while on study.*
- *Telling your doctor and study team of any changes in your health.*
- *Letting your doctor and study team know of any new medications prior to starting them to make sure there is no interactions with the study drugs.*
- *Using birth control methods as described in the Description of What's Involved section.*
- *Notifying of any changes in address, contact information, or social situation.*
- *Be willing to refrain from blood donations during study drug therapy and for 90 days after therapy*

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

You will not be paid for taking part in this study. Being in this study will not cost you anything extra. Researchers will not pay you for your travel or the time it will take for you to be in the study.

It is possible that products may someday be developed with the help of your data and/or samples, and there are no plans to share any profits from such products with you.

POSSIBLE BENEFITS:

It is important to know that you may not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may be access to a treatment that could help control your cancer. It could also help other patients like you that require treatment for myeloma that has relapsed. The investigational drug will be provided at no extra cost while on study.

POSSIBLE RISKS AND DISCOMFORTS:

Treatment for cancer will often have side effects that may be mild or life-threatening. There may be unknown risks. Your doctor may prescribe medication to manage the side effects or can decide to delay or hold therapy. Any concerning side effects discovered during the study will be shared with you. Some side effects that may be expected from the drugs used in this study include:

Risks from Iberdomide

The study drug, iberdomide, is being studied in people with multiple myeloma (MM) which is a cancer of plasma cells, a type of white blood cell that normally produces antibodies that are used by your immune system to stop bacteria and viruses. Iberdomide is also being studied in systemic lupus erythematosus (SLE), an autoimmune disease that occurs when your body's immune system attacks your own tissues and organs. As of 13-Oct-2023, 17 clinical studies with iberdomide have been/are being conducted: 9 clinical pharmacology studies (7 in healthy participants, 1 in participants with hepatic impairment, and 1 in participants with renal impairment), 2 studies in participants with SLE, 3 studies in participants with lymphoma, and 3 studies in participants with MM. Across these studies, 1056 total participants were exposed, including 672 participants in multiple myeloma.

There is always a risk involved in taking any drug, but you will be carefully watched for any side effects. There may be risks or side effects that are unknown or cannot be foreseen at this time. You are encouraged to report anything that is bothering you to your study doctor or nurse. You can ask your study doctor questions or request more information about side effects and other possible risks at any time.

You are encouraged to report anything that is bothering you to your study doctor or nurse. You can ask your study doctor questions about side effects at any time.

Your study doctor may give you medicines to help lessen the side effects. Your study doctor may adjust the study drugs to try to reduce side effects. Some side effects go away soon after you stop the study drug. In some cases, side effects can be serious and long lasting. Sometimes they never go away or may cause death.

Side effects of iberdomide known to occur in MM patients:
Very common (occurring in at least 1 out of 10 people) (greater than 10%):

- Anemia, or a drop in your hemoglobin (iron deficiency)
- Neutropenia, or a drop in your neutrophil counts (lower than normal number of a certain type of white blood cells in your body) which could increase risk of infections
- Rash

- Thrombocytopenia, or a drop in your platelets (lower than normal number of platelets in the blood, making you more susceptible to bruising)
- Upper respiratory tract infection
- Numbness or painful tingling (neuropathy) of hands or feet
- Diarrhea

Common (occurring in at least 1 out of 100 and less than 1 out of 10 people) (1% to 10%):

- Febrile neutropenia, which is a condition marked by fever and a lower-than-normal number of neutrophils in the blood)
- Lower respiratory tract infection
- Pneumonia
- Blood clots in a vein or artery in different areas of the body such as lung, this type of blood clot is called a pulmonary embolism, leg, this is called a deep vein thrombosis and brain that can cause a stroke or a transient ischemic attack

Uncommon (occurring in at least 1 out of 1,000 and less than 1 out of 100 people) (0.1% to 1.0%):

- Deep Vein Thrombosis (DVT) (the formation of one or more blood clots (a blood clot is also known as a “thrombus,” while multiple clots are called “thrombi”) in one of the body's large veins, most commonly in the lower limbs (e.g., lower leg or calf))
- Pulmonary Embolism (PE) (a clot of material (an embolus) that blocks blood from getting to the lungs. It is usually caused by a blood clot that starts somewhere else in the body and travels to the lungs)

Other adverse events have been reported with iberdomide in clinical studies as listed below; however, it is not known at this time if they are caused by the administration of iberdomide.

- Fatigue or asthenia (weakness)
- Swelling (peripheral edema)
- Fever
- Headache
- Nausea
- Constipation
- Pain, including back, joint, bone
- Difficulty breathing
- Cough

- Decreased appetite
- Decreased kidney function (acute kidney injury)
- Abdominal pain
- Dry mouth
- Muscle spasm
- Abnormal liver tests which may indicate a liver problem (alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased)
- Muscular pain in the chest
- Vomiting
- Nerve problem which may result in numbness, pain, tingling (peripheral neuropathy)
- Dizziness
- Itching
- Weight loss

Iberdomide has different effects on cells of the immune system, which is the part of the body that protects you from developing infections, and the use of iberdomide could increase your risk of infection or prolong an infection. It may interfere with the response to certain vaccines, making it unsafe to receive "live" vaccines or making some vaccines not work and leaving you unprotected. If you have ever had a serious infection, including infection of the liver (also called viral hepatitis) or an infection of the lungs called tuberculosis, you must tell the study doctor.

Blood clots have been reported in participants receiving medications from the same drug class as iberdomide and have also been experienced by patients in the lupus studies with iberdomide. Since iberdomide may increase the risk of developing blood clots, you will be required to take an antithrombotic medication (medication that prevents or reduces the chance of developing a blood clot), such as daily aspirin.

It is possible that the condition for which you are being treated may worsen during the study. You will be closely monitored. If your condition becomes worse, your doctor may stop your participation in this study. The doctor will treat you as he/she feels is best.

Iberdomide has been given to animals to find out what side effects may happen in people. The relevance of these animal findings (listed below) to human risk is unknown. Side effects with iberdomide seen in animals include the following: decrease in the number of white blood cells (the cells that help you fight infections); decrease in the number of red blood cells, which may make you feel weak or tired; decrease in the number of platelets (the cells that help your blood to clot); changes in the lymphatic system (a part of the immune system), including decreases in lymphocytes in the blood and spleen; diarrhea (watery feces); and dehydration (loss of skin elasticity/loss of bodily fluids). There were reports of inflammatory changes in the eye; however, these effects disappeared 28 days after stopping iberdomide.

In a 9-month study in monkeys and in a fertility study (approximately 65 days of treatment) in male rabbits, a decrease in the amount of sperm producing cells was observed in male monkeys and rabbits given iberdomide at doses higher than the highest dose used in ongoing or planned in multiple myeloma studies in humans. In male monkeys, reversibility of this finding was not evaluated; however, similar finding in male rabbits was resolved approximately 65 days after the last iberdomide dose. It is not known at what time after start of iberdomide treatment this decrease will occur. It is not known if there might be a similar effect in men taking iberdomide and how this might affect their ability to father children. There were no effects of iberdomide in the sex organs of female monkeys and male/female rats.

Risks from Elotuzumab

Elotuzumab has been administered to patients alone (without other drugs for myeloma) and with other myeloma drugs such as lenalidomide, thalidomide or bortezomib. Listed below are side effects reported in elotuzumab clinical trials. Based on these trials, the events below are considered related to elotuzumab treatment when used in combination with other myeloma treatments (e.g. lenalidomide/dexamethasone or bortezomib/dexamethasone).

Very Common (occurring in 10% or more of patients):

- low white blood cell count (decreased lymphocytes)
- cough
- weight decreased
- Infections: including sore throat and lung infection
- shingles (also known as herpes zoster infection)

Common (occurring in between 1% and < 10% of patients):

- allergic reaction (also called hypersensitivity)
- altered mood
- reduced sensitivity to touch (also called hypoaesthesia)
- night sweats
- chest pain
- infusion related reactions that may occur during or after elotuzumab administration and include symptoms such as chills, fever, or high blood pressure

Other unexpected reactions may occur. It is also possible that your immune system could make antibodies against elotuzumab, which would limit how well it works against the myeloma. Blood samples will be taken during the study to test for the development of an immune reaction to elotuzumab.

All serious adverse events will be closely monitored. If any new information about the study drug or any other information becomes available which may influence your decision to continue in the study, you will be told in a timely manner.

Risk from Dexamethasone

Dexamethasone has been used to treat a variety of illnesses, including multiple myeloma. The potential side effects include the following:

Likely (occurring in greater than or equal to 30% of patients):

- upset stomach
- vomiting
- headache
- dizziness
- difficulty sleeping
- mood swings
- restlessness

Less likely (occurring in 10%-29% of patients):

- feeling anxious
- feeling achy
- increased hair growth
- easy bruising
- irregular or absent menstrual periods in women
- high blood pressure
- increased blood sugar levels
- skin thinning

Infrequent but Serious (occurred in less than 10% of patients):

- low hormone levels which can cause you to feel unusually tired, weak, and to lose your appetite
- confusion
- increased risk of infection because of a weakened immune system
- ulcers
- weakened heart, which can cause shortness of breath
- thinning of the bones which can make them more likely to break
- swelling of the pancreas
- slow wound healing
- skin rash
- swollen face, lower legs, or ankles
- vision problems
- cold or infection lasting a long time
- muscle weakness
- bleeding from the intestine

Other potential risks may include:

- Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.
- Risks associated with bone marrow biopsies and aspirates include pain, redness, swelling, excessive bleeding, or bruising at the site of the procedure. Other potential complications include abnormal wound healing, fever, infection, and allergic reaction to the medication used to numb the skin over the biopsy site.
- The risks of a blood draw include pain, bruising, and the slight possibility of infection at the place where the needle goes in. Some people feel dizzy or may faint during or after a blood draw.
- In addition to these risks, this research study may hurt you in ways that are not known. The unknown risks could be minor or major (death).
- If you are pregnant or become pregnant, this research may hurt your baby or your pregnancy in ways that are unknown. The unknown risks could be minor or major (death) for the pregnancy. You should not become pregnant or get someone pregnant while you take part in this study. Please read the acceptable methods of birth control found under the Description of What Is Involved section of this document.
- Economic risks (for example, having to pay money out of pocket for research or medical expenses, loss of health insurance, missing work or school)

- Group Risks - Although your name will not be given to researchers, basic information such as your race, ethnic group, and sex may be shared. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes or discrimination.
- Privacy Risks - Your name and other information that could directly identify you (such as an address, date of birth, or social security number) will never be placed into a database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Since the database contains genetic information, a break in security may also pose a potential risk to blood relatives as well as yourself. For example, it could be used to make it harder for you (or a relative) to get or keep a job or insurance. If your private information was misused, it is possible you would experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.
- Insurance Risks - There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). This law makes it illegal for health insurance companies, group health plans, and most employers of over 15 people to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

OTHER OPTIONS TO CONSIDER:

You may decide not to take part in this research study. If you decide not to take part, this will not affect the clinical care you receive at Mount Sinai. The choice is totally up to you.

Instead of being in this research study, there are other treatment options available. These options may be dependent on your individual situation, which your doctor will discuss them prior to signing this consent. These could include available treatment combinations, other clinical trials, or no treatment at all.

The important risks and possible benefits of these alternatives are listed below:

- *Approved combination therapies have been established to be safe in humans but may have suboptimal responses to your disease.*
- *Other clinical trials may use therapies that have uncertain results or unknown side effects.*

IN CASE OF INJURY DURING THIS RESEARCH STUDY

If you are injured or made sick from taking part in this study, you will get medical care. The group funding this research study will pay you for any reasonable and necessary medical expenses to diagnose and treat research-related injury or illness. This does not prevent you from seeking payment for injury related to malpractice or negligence. You can contact the Lead Researcher for more information.

The Centers for Medicare and Medicaid Services (CMS) is the government agency that oversees Medicare and Medicaid. Funding agencies who make payments for injuries related to studies must report payments to CMS. In order to do this, the funder must have certain information about you, such as your name, date of birth, Social Security Number, Medicare or Medicaid ID numbers, date of injury, and description of injury. The funding agency is only allowed to use this information to report payments related to the injury should this be necessary or as otherwise specified in the Authorization to Use and Disclose Protected Health Information section, which is included below.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this study at any time. No matter what you choose, your care and benefits through Mount Sinai will not be negatively impacted.

If you decide to stop being in the study, please contact the Lead Researcher or the research staff.
You may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page. Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you decide to stop being in the research study, the following may occur: any benefit you may have been getting from the study drug may stop and your disease could worsen. Stopping therapy does not guarantee treatment with other drugs if the options are limited.

If you stop being in the research study, the research team may not remove information they have already placed in the study database, and may continue to use that data as part of this study. The research team may ask you whether they can continue to collect information from your medical record.

If you decide you don't want your data and/or samples to be used for research anymore, you can contact the researcher and ask to have your data and/or samples withdrawn or labeled so that they will not to be used in additional projects or shared. If your data and/or samples have already been shared with researchers, those researchers will be asked to stop using them. However, if any data and/or samples have already been shared without your identity or a linking code, it won't be possible to retrieve them. Data and/or samples that have already been used will not be affected by your decision. If your data and/or samples have already been deposited in an external repository, the study team will request that your data and/or samples be removed.

Withdrawal without your consent: The Lead Researcher, the funder or Mount Sinai may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the research team have not been followed, the Lead Researcher believes it is in your best interest, or for any other reason. If data and/or samples have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Lead Researcher at phone number 212-241-7873.

If there is an emergency, please call 911 or go to the emergency room. Let the emergency room staff know you are in a research study so they can contact the Lead Researcher if needed.

DISCLOSURE OF FINANCIAL INTERESTS:

Researchers sometimes get paid for consulting or doing work for companies that produce drugs, biologics or medical devices. If you have questions regarding industry relationships, you are encouraged to talk to the Lead Researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

The company sponsoring this research study makes the drug being tested and has a financial interest that could be affected by the outcome of this research study.

The companies sponsoring this research study includes Multiple Myeloma Research Consortium and Bristol Myers Squib. Bristol Myers Squib manufactures the drugs being tested and so has a financial interest that could be affected by the outcome of this research study. The researchers however, do not have a direct financial interest in the sponsor or the product being studied.

Dr. Cesar Rodriguez Valdes (the Lead Researcher in this study), Dr. Hearn Cho, Dr. Adriana Rossi, Dr. Sundar Jagannath, Dr. Shambavi Richard, Dr. Joshua Richter and Ms. Donna Catamero (researchers in this study) are paid consultants for Bristol Myers Squibb, a study co-sponsor and developer of the study drugs Iberdomide and Elotuzumab.

Dr. Cho receives financial compensation as the Chief Medical Officer of the Multiple Myeloma Research Foundation, co-sponsor of the study.

In addition, Dr. Rodriguez Valdes, Dr. Rossi, Dr. Jagannath, Dr. Richard, Dr. Richter, Dr. Larysa Sanchez, Dr. Samir Parekh, and Ms. Kiah Purcell (researchers in this study) are paid consultants for other companies that research and develop treatments for multiple myeloma.

If you have questions regarding paid relationships that your physician/researcher may have with industry, you are encouraged to talk with your physician/researcher, or check for industry relationships posted on individual faculty pages on our website at http://icahn.mssm.edu/.

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MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As part of this study, some of your private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

What is protected health information (PHI)?
PHI is the combination of two things:

1. PHI contains information that identifies you. It will be used to contact you and link you to your health information, like name, date of birth, medical record number, and address.
2. PHI also contains health information, including information about your mental and physical health from your visits to doctors or hospitals, or from study visits.

Every time you visit a hospital or your doctor, PHI is created and recorded in your medical record by your healthcare providers. In the same way, the PHI created as part of this study will be linked to who you are and your medical information.

What PHI is collected and used in this research study, and might also be shared with others?

As part of this study, the research team at the hospital(s) involved in the research will collect your name, address, telephone/fax numbers, dates directly related to the individual (birth, admission, discharge, date of death, etc.), social security number, medical records number, health plan numbers, biometric identifiers, and photographic images.

During the study, the researchers will gather information by:

- Reviewing and/or taking your medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate, and temperature.
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- Reviewing genetic tests.

Why is your PHI being used?

Researchers need the information that identifies you so they can contact you during the study. They need your health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let others know who you are or that you took part in the study. If researchers publish or present study results at scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who you are, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your care or treatment. The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example:

- The Mount Sinai Program for the Protection of Human Subjects is responsible for overseeing research on human participants and may need to see your information.
- If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your PHI?

As part of the study, the Lead Researcher, research team and others in the Mount Sinai workforce may disclose your PHI, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Lead Researcher.)

- The United States Department of Health and Human Services (DHHS) and the Office of Human Research Protection (OHRP) (the government organization that is responsible for protecting human research participants).
- Other collaborating research center(s) and their associated research/clinical staff who are working with the researchers on this project: Multiple Myeloma Research Foundation
- Research data coordinating office and/or their representative(s) who will be responsible for collecting results and findings from all the centers: Emory Winship Cancer Institute
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration.

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Lead Researcher will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board (IRB) allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, *OHRP, as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access.* The results of this research may be published. However, your name and other identifying information will be kept confidential.

For how long will Mount Sinai be able to use or disclose your PHI?

Your authorization for use of your PHI for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The research team is not required to release research information to you that is not part of your medical record.

Do you need to give the researchers permission to obtain, use or share your PHI?
NO! If you decide not to let the research team obtain, use or share your PHI, you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment, or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
If you decide to stop being in the study, please contact the Lead Researcher or the research staff.
The research team may ask you whether they can continue to collect information from your medical record. You will also have to decide if you wish to limit the continued use of the information collected during the study. Under US privacy laws you may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.
Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study. If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your PHI.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If researchers are reviewing your medical records or asking questions about your medical history or conditions, it is possible that they may learn information related to your HIV status. If that is the case, the following information concerns you. If researchers are not reviewing your medical records or asking questions about your medical history or conditions, then you may ignore the following section.

Notice Concerning HIV-Related Information
If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 416-0197. These agencies are responsible for protecting your rights.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

ADULT PARTICIPANT:
Your signature below documents your permission to take part in this research study and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

_____	_____	_____	_____
Signature of Participant	Printed Name of Participant	Date	Time

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

_____	_____	_____	_____
Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time

WITNESS SECTION:

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant, and that consent was freely given by the participant.

_____	_____	_____	_____
Signature of Witness	Printed Name of Witness	Date	Time