Protocol Title: E- PRISM (Precision Intervention Smoldering Myeloma): A Phase II Trial of Combination of Elotuzumab, Lenalidomide and Dexamethasone in High-Risk Smoldering Multiple Myeloma

DF/HCC Principal Research Doctor / Institution: Irene Ghobrial, MD/Dana Farber Cancer Institute

DF/HCC Site-Responsible Research Doctor(s) / Institution(s): Andrew Yee, MD / Massachusetts General Hospital; Irene Ghobrial, MD/ Broad Institute

A. INTRODUCTION

You are invited to take part in a clinical trial, a type of research study because you have smoldering multiple myeloma (SMM). Patients with smoldering multiple myeloma do not have symptoms but are at risk for progressing to active multiple myeloma. Multiple myeloma is a cancer of the plasma cell, which is an important part of the immune system. Patients with active multiple myeloma generally require treatment. There are currently no approved therapies for smoldering multiple myeloma.

This research study is a way of gaining new knowledge about a new drug called “elotuzumab”. For purposes of this research, you will be referred to as a “participant”. This research study is evaluating a new drug called “elotuzumab” as a possible treatment for smoldering multiple myeloma.

It is expected that about 51 people will take part in this research study.

Bristol-Myers Squibb and Celgene are supporting this research study by providing funding for the research study and the study drug.

This research consent form explains why this research study is being done, what is involved in participating in the research study, the possible risks and benefits of participation, alternatives to participation, and your rights as a research participant. The decision to participate is yours. If you decide to participate, please sign and date at the end of this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future.

B. WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is a Phase II clinical trial, which tests the effectiveness of an investigational drug(s). The investigational drugs used in this research study are elotuzumab, lenalidomide and dexamethasone. Recent research studies have shown that early treatment of smoldering multiple myeloma may delay or prevent the progression to active multiple myeloma. The purpose of this research study is to learn whether the combination of elotuzumab and lenalidomide or the combination of elotuzumab, lenalidomide and dexamethasone works in treating your smoldering multiple myeloma.

"Investigational" means that the FDA (the U.S. Food and Drug Administration) has not approved the combination of elotuzumab, lenalidomide and dexamethasone as a treatment regimen for your specific disease.

The FDA has approved lenalidomide for the treatment of many types of cancer including multiple myeloma, and myelodysplastic syndromes. Dexamethasone, also FDA approved, is a type of steroid and is usually combined with other chemotherapy for the treatment of blood cancers, such as myeloma and leukemias. Elotuzumab is approved by the FDA for treatment of multiple myeloma, and is currently being evaluated for use in the treatment of several other types of cancers, including smoldering multiple myeloma.

C. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. Instead of being in this research study, you have other options which may include the following:

- Take part in another research study.
- Receive no therapy specific to your cancer.

Please talk to the research doctor about your options before you decide whether you will take part in this research study.

D. WHAT IS INVOLVED IN THE RESEARCH STUDY?

Sometimes it is hard to keep track of all of the details and procedures that are part of a research study. We will describe them in this consent form and you can refer to this at any time during the research study. We can also provide you with a calendar that will be an easy reference for you to keep track of the procedures and treatments required at each timepoint in the study.

Before the research starts (screening): After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **A medical history** includes questions about your health, current medications, and any allergies.
- **Performance status** evaluates how you are able to carry on with your usual activities.
- **An assessment of your disease (Metastatic Bone Survey)** by CT (Computerized Tomography) scan, MRI (Magnetic Resonance Imaging) and PET (Positron Emission Tomography) scans.
- **Physical Exam** including height and weight as well as checking your body for signs and symptoms of cancer.
- **Electrocardiogram (ECG)** measures the electrical activity and health of the heart.
- **Blood or Urine Pregnancy Test** is required if you are a woman who is able to get pregnant. The test will need to be negative within 24 hours of starting Cycle 1 and then again every cycle thereafter on Day 1.
- **Urine Test (in clinic) to assess your overall health.**
- **Blood tests** to check your overall health (1-2 tablespoons of blood).
- **Bone marrow aspirate and biopsy** will be done to evaluate your disease. For the bone marrow aspirate, a sample of bone marrow cells is taken by a needle and inserted into a bone in your body. For the biopsy, a small piece of bone is removed. These tests are done under local anesthesia.

If these tests show that you are eligible to participate in the research study, you will begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Additional Optional Research procedures to be performed at the time of screening:

- **Blood Sample:** Approximately 2 tablespoons of blood will be drawn for research to assess your disease status by DNA and RNA sequencing.
- **Bone Marrow Aspirate Sample:** for bone marrow procedures that are done as standard of care, a small amount of extra bone marrow cells will be taken for research tests. This additional sample will be taken at the same time as the other sample; you will not need an additional procedure. Even if your doctor determines the bone marrow sample is not required for

your type of disease, this sample will still be taken for research purposes. The research tests will help determine how Elotuzumab affects your disease

- **Buccal Swab** will be collected when you are in clinic at the beginning of the study (or at any time during the trial). The purpose is to harvest your normal DNA. You will not be provided with results about the genetic tests, nor will the information be placed in your medical record

After the screening procedures confirm that you are eligible to participate in the research study and you are ready to begin treatment.

If you take part in this research study, you will be given a study drug-dosing diary for each treatment cycle. Each treatment cycle lasts 28 days (4 weeks), during which time you will be taking each drug on different days of the cycle. The diary will also include special instructions for taking the study drug.

The tables below outline the schedule of drug administration for this study.

Study Drug Dosing Table: (28 Day Cycles)

Cycles 1-2

Drug	*Route*	*Schedule*
Elotuzumab	IV	Days 1,8,15, 22
Lenalidomide	Oral	Days 1-21
Dexamethasone	Oral and IV	Days 1,8,15, 22

Cycles 3-8

Drug	*Route*	*Schedule*
Elotuzumab	IV	Days 1 and 15
Lenalidomide	Oral	Days 1-21
Dexamethasone	Oral and IV	Days 1,8,15

If you complete treatment on either cohort through cycle 8, please see your maintenance schedule below:

Maintenance

Drug	*Route*	*Schedule*
Elotuzumab	IV	Day1
Lenalidomide	Oral	Days 1-21
Dexamethasone**	Oral and IV	Day 1

**Dexamethasone may be given on days 8 and 15 in maintenance at your provider's discretion.

Elotuzumab Administration: This drug will be administered intravenously (through your vein) by the study team in clinic over about 60 minutes. Your physician may also order other medications to be administered before you get dosed in order to decrease the risk of experiencing an infusion reaction related to the administration of the drug. Depending on if you do experience an infusion reaction, these drugs may be changed.

Lenalidomide Administration: This drug will be given as a single dose that you will take orally once daily on the days instructed. You must record all administrations of this drug at home and in clinic in the study drug diary provided to you.

Dexamethasone Administration: This drug will be given both orally and intravenously (through your vein). You must record all oral administrations of this drug in your study drug diary provided to you.

On Study Visits: Please see research required test table below.

If specified, visits will involve the following:

- **Medical History and Physical Exa**m will be performed and you will be asked questions about your general health and specific questions about any problems that you might be having and any medication changes.
- **Electrocardiogram (ECG)** will be conducted to measure the electrical activity and health of the heart (Only required at screening, at end of treatment or if clinically indicated).
- **Blood or Urine Pregnancy Test** is required if you are a woman who is able to get pregnant. The test will need to be negative within 24 hours of starting Cycle 1 and then again every cycle thereafter on Day 1.
- **24 hour Urine Sample** will be required, which you will return to clinic on Day 1 of each cycle for some patients whose disease is assessed by their urine result. This is to perform a specific test that shows signs of disease that sometimes does not show in blood or marrow.
- **Blood tests will be done** to check your overall health (1-2 tablespoons).
- **Bone marrow aspirate and biopsy** will be done to evaluate your disease. For the bone marrow aspirate, a sample of bone marrow cells is taken by a needle and inserted into a bone in your body. For the biopsy, a small piece of bone is removed. These tests are done under local anesthesia. Your physician may require this procedure more often to assess your disease.
- **Scans (or Imaging tests)** will assess your tumor by MRI or PET/CT at the end of your treatment.

- **Side effects** will be evaluated
- **Buccal swab** is a way to coll**ect DNA** from the cells on the inside of your cheek

Research Study Schedule
Cycle 1 and 2 (28 Day Cycles)

	Baseline	Day 1	Day 8	Day 15	Day 22	End of Treatment
Medical History and Physical Exam	X	X				X
Routine Blood Tests	X	X	X	X	X	X
Urine Test	X	X				X
Pregnancy Test (If applicable)	X	X				
MRI and PET/CT	X					X
EKG	X					X
Bone Marrow Aspirate and Biopsy	X					X
Research Blood Sample	X	X				X
Research Marrow Sample	X					X
Buccal Swab*	X					

* Buccal Swab can be obtained at any time during the trial

Cycle 3 through 24 (28 Day Cycles)

	Day 1	Day 8	Day 15	End of Cycle 8 or Cycle 9, Day 1	End of Treatment	Follow Up- Every 3 Months
Medical History and Physical Exam	X				X	X
Routine Blood Tests	X		X		X	X
Urine Test	X				X	X
Pregnancy Test (if applicable)	X					
MRI and PET/CT					X	
EKG					X	
Bone Marrow Aspirate and Biopsy	X			X	X	
Research Blood** Sample	X			X	X	
Research Marrow Sample				X	X	

** Research blood samples are requested at Day 1 of each cycle in addition to baseline, EOT, and to confirm disease response

Planned Follow-up: We would like to keep track of your medical condition for up to three years after you stop treatment. We would like to do this by calling you on the telephone or during a visit to your doctor's office to see how you are doing.

E. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be on the study treatment for up to 18 months and be followed for an additional 3 years.

The research doctor may decide to take you off the research study for many reasons including if:

- It is considered to be in your best interest
- The study treatment or procedures are found to be unsafe or ineffective
- There is any problem with following study treatments and procedures
- Your condition worsens
- A decision is made to close the study
- Or for other unforeseen reasons that make it necessary to stop your participation in the research study

If you are removed from the research study, the research doctor will explain to you why you were removed.

In addition, you can stop participating in the research study at any time, however, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study. If you decide to stop participating in this research study, we encourage you to talk to the research doctor and your primary doctor first.

F. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study. One risk is that you may get a study drug that does not help treat your disease or that makes your condition or disease worse. Another risk is that there may be side effects.

All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Everyone in the research study will be watched carefully for side effects. You will be monitored during the administration of study drugs to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the study drug. Some side effects can be mild; but others can be long lasting and may never go away. Some may be life-threatening or fatal.

Since the effect of the study drug(s) taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs, herbal preparations and nutritional supplements that you are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

Since this is the first clinical study of these three drugs combined for the treatment of smoldering multiple myeloma, information on expected combination

drug side effects in humans is limited, although potential side effects for each of the three drugs are well known and listed below:

Risks Associated with Elotuzumab

Likely (More than a 20% chance that this will happen)

- Tiredness
- Fever
- Swelling of the injection site, joints, and/or areas of the face
- Diarrhea
- Constipation
- Nausea
- Low white blood cell counts which can put you at risk for developing an infection, which can be life threatening
- Low red blood cell counts (anemia) which can make you feel tired, lightheaded or short of breath, and may require you to have red blood cell transfusions

Occasional (Between a 3-20% chance that this will happen)

- Allergic type infusion reactions that may occur during or after elotuzumab administration and include symptoms such as chills, fever, nausea, rash, flushing, chest discomfort, increased sweating, high blood pressure, abdominal pain, swelling around the eyes or muscle spasms
- Vomiting
- Mouth sores or pain
- Upset stomach or heartburn
- General weakness
- Back pain
- Bone, joint or muscle pain
- Chest pain
- Pain, numbness or tingling in the arms, hands, legs or feet
- Dizziness
- Difficulty sleeping
- Tremor
- Taste change
- Cough
- Shortness of breath
- Voice changes
- Nose bleeds

- Hiccups
- Poor appetite
- Increase in blood sugar
- Changes in electrolytes (body salts), which do not usually cause any symptoms but can sometimes cause tiredness, muscle weakness, cramping, rigidity, irregular heartbeat or seizures. This can be severe and possibly life threatening. This could require hospitalization and intravenous treatment
- Decreased weight
- Changes in liver or kidney function tests which can indicate damage to cells in the liver and kidney
- Increase in susceptibility to infections of the throat, mouth, lung, sinus, blood, kidney, bladder, skin, stomach or intestine
- Itching or hives
- Anxiety
- Depression
- Low blood pressure which might make you feel dizzy or light-headed
- Blurred vision or reduced vision

Rare (Less than a 1-3% chance that this will happen or serious side effects in at least 1 patient)

- Abnormal walking or falling
- Irritability or agitation
- Sudden death due to gastric perforation, multi-organ failure, sepsis, pneumonia, or vascular event
- Mood changes
- Confusion
- Dry eyes
- Cataract (clouding of lens of eye)
- Pink eye (inflammation of the eye)
- Dry mouth or skin
- Skin inflammation
- Hair loss
- Gas or bloating
- Difficulty swallowing
- Hemorrhoids
- Inflammation of the colon which can cause abdominal pain, loss of appetite, fatigue, diarrhea, cramping, fecal urgency and bloating (colitis).

- Inflammation of the liver which can lead to jaundice, poor appetite, and malaise (hepatitis)
- Neck or jaw pain
- Toothache
- Joint or muscle stiffness
- Sleepiness
- Memory loss
- Fainting
- Runny or stuffy nose
- Sinus congestion
- Wheezing
- Fluid in lungs
- Inflammation of the lung
- Viral infections such as herpes virus or the flu
- Fever with low white blood cell counts (febrile neutropenia), a condition marked by fever and lower-than-normal number of neutrophils in the blood which could increase the risk of infection
- Life threatening infections/infections leading to death
- Dehydration
- Excess amount of uric acid in the blood, (gout), which can cause pain in the joints as well as decrease kidney function.
- Blood clots in the veins of the leg or lung
- Localized collection of blood outside the blood vessel (ecchymosis or hematoma) that are usually due to a weakening in the wall of a blood vessel
- Inflammation of the vein(s)
- Kidney damage or failure
- Problems with urination or bladder control
- Pain while urinating
- Frequent urination
- Ringing in ears
- Rapid or slow heart rate
- Abnormal heart rhythm, which may be life threatening or fatal
- Palpitations
- Heart failure
- Irregular heart beat that is slow due to impaired electrical conduction across the heart (3rd degree AV block)
- Heart attack
- Inflammation of the heart muscle
- Weight gain

- Increased destruction of red blood cells that leads to anemia (hemolysis) that can cause a reduction in the delivery of oxygen to the tissues, fatigue, increased heart rate, chills, dark urine, yellow skin, and rapid heartbeat

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 side effects 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.

Risks Associated with Lenalidomide

Lenalidomide has been studied in healthy volunteers and in patients with cancer of the blood and other organs of the body as well as in patients with other diseases. As with any other experimental treatment there may be side effects or risks associated with lenalidomide, some of which are not yet known. The early treatment of smoldering multiple myeloma with lenalidomide is an investigational approach.

The following is a list of the most medically significant or most common side effects reported in completed and ongoing studies considered to be related to lenalidomide. In some cases, side effects can be serious, long-lasting, may never go away, or can cause death. This list is not complete, but your study doctor will answer any questions you might have and provide you with more information.

The use of lenalidomide therapy has been known to hinder the collection of your own stem cells in patients with multiple myeloma. If your disease progresses to multiple myeloma and you are deemed a candidate for autologous (using your own cells) stem cell transplant, it is unknown if the long term use of lenalidomide therapy will rule out stem cell collection from your peripheral blood.

Likely (More than a 50% chance that this will happen)

- Low number of red blood cells (anemia) which can cause tiredness, shortness of breath, and may require a blood transfusion
- Constipation or difficult bowel movements
- Diarrhea or loose/frequent bowel movements
- Fatigue

- A serious or life threatening decrease in the number of a type of white blood cell (neutrophil/ granulocyte) that helps to protect against infection which causes an increased risk of infection
- Decreased number of a type of blood cell that help to clot blood (platelet). This may result in bleeding.

Frequent (Chance of 10-50% that this will happen)

- Abnormally low level of thyroid gland hormone. This may cause fatigue, weight gain, fluid retention, sensitivity to cold and mental apathy. Can be serious or life threatening.
- Nausea or the urge to vomit
- Vomiting
- Chills
- Swelling or tingling of the arms and legs
- Fever
- Infection, which may be serious and life threatening
- A decrease in the number of a type of white blood cell (lymphocyte) and decrease in the total number of white blood cells (leukocytes) which may increase the risk of infection.
- Weight loss
- Loss of appetite
- Back, joint and muscle pain
- Muscle cramps/spasms
- Dizziness (or sensation of lightheadedness, unsteadiness, giddiness, spinning or rocking)
- Headache or head pain
- Difficulty sleeping or falling asleep
- Cough
- Shortness of breath
- Itching
- Skin rashes that may be flat (macular), raised (papular) or red and irritated.
- Excess sweating
- Formation of a blood clot that may break loose and be carried by the blood stream to plug another blood vessel. May be serious and life threatening.
- Abnormal liver function tests that mean the liver is not functioning properly and can cause fatigue, jaundice (yellowing of the skin or eyes). Although this is usually mild and reversible, this can be serious or life threatening

Rare (Chance of less than 1% that this will happen)

- Inflammation of the pancreas. This may cause abdominal pain and require hospitalization and intravenous treatment. It may be accompanied by increased blood levels of a fat digesting enzyme called lipase.
- Serious life-threatening allergic reaction requiring immediate medical treatment. The reaction may include extremely low blood pressure, swelling of the throat, difficulty breathing, and loss of consciousness.
- Tumor lysis syndrome, which is the result of rapid destruction of cancer cells that can occur after treatment of cancer has started and may cause an electrolyte imbalance, increased uric acid buildup (gout), and kidney damage
- Decreased production of blood cells by the bone marrow (marrow aplasia) including cells that fight infection, clot the blood, and carry oxygen to tissue
- Temporary growth in tumor or worsening of tumor related problems
- Tissue death of a part of the brain without inflammation
- Sudden decrease of kidney function. When the kidneys do not work properly, wastes can build up in your blood, leading to swelling in the arms and legs, tiredness and weakness. This could become severe, requiring hospitalization and dialysis to clean the wastes out of your blood. If the wastes are not removed from your blood, this could cause seizures and be life threatening.
- Severe reaction of the skin and gut lining that may include rash and shedding or death of tissue. This can include conditions in which the death is skin tissue causes the outer layer of the skin to separate from the middle layer and be serious and life threatening.
- Development of a second cancer including leukemia.
- Lenalidomide is a member of a class of drug that causes damage to a fetus (teratogen). It is important that **mandatory** contraceptive measures be used while taking lenalidomide. It also requires special prescription forms (RevAssist) and **frequent counseling.** Your physician will discuss this with you.

There may be an increased risk of second cancers in patients who are on lenalidomide maintenance therapy after a bone marrow transplant.

In addition, lenalidomide has been shown to increase the level of digoxin in the blood in some patients. Please tell your doctor if you are taking digoxin.

Risks Associated with Dexamethasone

Occasional (Chance of less than 10% that this will happen):

- Increased blood sugar. If you have diabetes, this may lead to a need to adjust your medications used to treat the diabetes.

- Increased appetite.
- Weight gain.
- Fluid retention (edema), which can cause a buildup of fluid in the body or extremities causing swelling.
- Elevation of blood pressure
- Mood changes (depression, or abnormal feelings of well-being and excitement)
- Difficulty sleeping
- Skin changes leading to thinning and easy bruising
- Gradual changes to bones that may increase their risk of breaking
- Muscle weakness
- Stomach irritation/ulcer
- Increased risk of infection
- Acne

Rare (Less than 1% chance that this will happen):

- Loss of potassium, which may lead to weakness and abnormal heart beats.
- Increased eye pressure in patients with glaucoma which may cause damage to the optic nerve and vision loss
- Gradual development of cataracts, or a clouding of the lens of the eye causing hazy or blurry vision
- If used for a long time it can suppress the function of the normal glands that make steroids (adrenal glands) leading to the need for continued replacement with steroid medication.
- Glaucoma, or optic nerve and vision damage which can be caused by an increase in pressure within the eye
- Pancreatitis or an inflammation of the pancreas causing pain in the upper abdomen that can become severe and cause nausea, vomiting, and could require hospitalization and may be life threatening.

Cancer research often includes biopsies, scans, x-rays that are also provided as routine care. The following describes the side effects of procedures done only for the purposes of research.

Risks Associated with Bone Marrow Biopsies:

Risks associated with bone marrow biopsies include pain, redness, swelling, excessive bleeding, bruising or infection at the needle site and or scarring at the biopsy site. An allergic reaction to the local anesthetic medication used to numb the skin over the biopsy site may occur. These risks can be discussed with the study doctor.

Uncommonly, complications from biopsies can be life threatening. As with any interventional procedure, other potentially serious complications from bleeding or organ damage may occur. These might require additional surgical intervention.

Radiation Risks Associated with Scans and X-Rays:

While you are in this research study, CT scans, Bone Scans, and x-rays utilizing radioactivity may be used to evaluate your disease. The frequency of these exams is the same as what you would receive as standard care. In the long term, over many years, there is a very low risk of developing a new cancer as a result of the radiological evaluation and treatment for your cancer.

Risks Associated with MRI Scans:

When having an MRI (Magnetic Resonance Imaging) scan, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your research doctor. Your doctor may give you a medication to make you feel more comfortable. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

Reproductive Risks:

The drugs used in this research study may affect a fetus. While participating in this research study, you should not become pregnant or father a baby, and should not nurse a baby. Let your doctor know immediately if you become pregnant or find out that you are going to be the father of a child. We can provide counseling about preventing pregnancy for either male or female study participants.

In the event that your partner becomes pregnant, it may be critical to share information regarding your participation in this research study with that person. Your research doctor should also be told if this happens. The study sponsor may want to collect data on your partner's pregnancy. The research doctor can provide you with the study sponsors contact information and your partner can decide whether or not they want to provide this information. For more information about what to do if your partner becomes pregnant please contact your research doctor.

Lenalidomide is related to thalidomide. Thalidomide is known to cause severe

life-threatening human birth defects. Findings from a laboratory study indicate that lenalidomide caused birth defects in the offspring of females who received the drug during pregnancy. If lenalidomide is taken during pregnancy, it may cause birth defects or death to any unborn baby. Females should not become pregnant while taking lenalidomide. You have been informed that the risk of birth defects is unknown. If you are female, you agree not to become pregnant while taking lenalidomide

Patients with blood cancers who take lenalidomide and dexamethasone have a greater chance of having blood clots. Because of this, it is recommended patients discuss the use of birth control pills or hormone replacement therapy with the study doctor to better understand the risks and benefits of these choices

Pregnancy Risk – Females:
If you are a female of childbearing potential*, you will be required to have a negative pregnancy tests prior to receiving lenalidomide.

- For the purposes of this study, a female of childbearing potential is a sexually mature female who:

    - Has not undergone a hysterectomy (the surgical removal of the uterus) or bilateral oophorectomy (the surgical removal of both ovaries)
    - Has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time during the preceding 24 consecutive months)

You will be required to use TWO reliable forms of birth control, one highly effective method and one additional effective method at the same time or practice complete abstinence from heterosexual intercourse during the following time periods related to this study: 1) throughout lenalidomide therapy, including interruptions in therapy; and 2) for at least 28 days after discontinuation of lenalidomide

Pregnancy Risk – Males:
Lenalidomide is present at very low levels in human semen of healthy men for three days after stopping the drug according to a study. For some men, such as men with kidney problems, lenalidomide may be present in semen for more than three days. For these reasons, to be safe, all male patients receiving lenalidomide must use a latex condom during any sexual contact with a pregnant female or with a female of childbearing potential while you are participating in this study, including during times when lenalidomide is temporarily stopped, and for at least 28 days after permanently stopping therapy, even if you have had a successful vasectomy. You must NEVER donate blood, sperm, or semen while

you are participating in this study and for at least 28 days after you have stopped therapy.

All Patients:

You must **NEVER** share lenalidomide (or other study drugs) with someone else. You must **NEVER** donate blood while you are participating in this study and for at least 28 days after you have been discontinued from the study. You must receive counseling and complete phone surveys as required by the **Revlimid REMS**® program. Females of childbearing potential that might be caring for you should not touch the lenalidomide capsules or bottles unless they are wearing gloves. Any unused lenalidomide should be returned to the study staff.

Non-Physical Risks:

Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

G. WHAT ARE THE BENEFITS OF THE RESEARCH STUDY?

This study may or may not help you because researchers do not know how elotuzumab/lenalidomide/dexamethasone or elotuzumab/lenalidomide will compare to the usual approach. This study may help researchers learn things that may help people in the future.

H. CAN I STOP BEING IN THE RESEARCH STUDY AND WHAT ARE MY RIGHTS?

You have the right to choose not to sign this form. If you decide not to sign this form, you cannot participate in this research study.
You can stop being in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop. Leaving the research study will not affect your medical care outside of the research study.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

It is important to tell the research doctor if you are thinking about stopping so your research doctor can evaluate the risks from stopping the elotuzumab/lenalidomide/dexamethasone or elotuzumab/lenalidomide.

I. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

We may use your samples and information to develop a new product or medical test to be sold. The sponsor and hospital may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

J. WHAT ARE THE COSTS?

Taking part in this research study might lead to added costs to you or your insurance company.
You will not be charged for elotuzumab or lenalidomide.

You or your insurance company will be charged for portions of your care during this research study that are considered standard care, such as dexamethasone. You may be responsible for co-payments and deductibles that are typical for your insurance coverage.

Dexamethasone is commercially available which means that the FDA has approved it for use in patients with your type of cancer. Because there is evidence that supports using this drug in patients with your type of cancer, you or your insurance company will be billed for the cost of dexamethasone.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- Dana-Farber Cancer Institute: (617) 632-3455
- Massachusetts General Hospital: (617) 726-2191

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

K. WHAT HAPPENS IF I AM INJURED OR SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for Dana-Farber/Partners CancerCare (DF/PCC) on behalf of the Dana-Farber/Harvard Cancer Center (DF/HCC) to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

L. WHAT ABOUT CONFIDENTIALITY?

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file. It may also become part of a DF/HCC research database.

The results of this research study may be published. You will not be identified in publications without your permission.

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.

M. FINANCIAL DISCLOSURES

It is possible that certain researchers on this study may have earned money from, or own some publicly-traded stock in, the company that makes or is developing the study drug. The amount of money that a researcher may earn and still take part in research is limited by the Harvard Medical School Faculty of Medicine Policy on Conflicts of Interest and Commitment. If you have further questions, please speak with a member of the study team or contact the Dana-Farber Cancer Institute Office of Research Integrity at 617-432-4557 or researchintegrity@dfci.harvard.edu

N. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research doctor or study staff as listed below:

Dana-Farber Cancer Institute

- Irene Ghobrial, MD: Irene_Ghobrial@dfci.harvard.edu

If you are experiencing an urgent medical issue, please go to the nearest emergency medical facility, or contact our site to have your physician paged.

24-hour contact: DFCI: Irene Ghobrial, MD (617) 632-3352 and ask for your physician to be paged at beeper 41651

Massachusetts General Hospital

- Andrew Yee, MD: Ayee1@mgh.harvard.edu

Broad Institute

- Irene Ghobrial, MD: Irene_Ghobrial@dfci.harvard.edu

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at DFCI (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

O. PRIVACY OF PROTECTED HEALTH INFORMATION

Federal law requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;

- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug for the purpose of this or other research relating the study drug and its use in cancer; and,
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- Bristol-Myers Squibb, who is supporting this research study by providing funding for the research study and the study drug
- Celgene, who is supporting this research study by providing funding for the research study and the study drug
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or

necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”
- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”

P. PRIVACY OF PROTECTED HEALTH INFORMATION

A federal law (Genetic Information Non-Discrimination Act, GINA) will help lower the risk from health insurance or employment discrimination on the basis of genetic information. The federal law does not include other types of misuse by life insurance, long term care or disability insurance. If you want to learn more about the GINA Law, which went into effect in 2009, you can find information

about it on the internet or ask the study staff. In addition to the federal law, some states have laws that also help to protect against genetic discrimination.
While we believe that the risks to you and your family are very low, we cannot tell you exactly what all of the risks are from taking part in genetic research studies. Your privacy and confidentiality will be protected to the fullest extent possible.

Optional Research studies:

Optional Assessment Participation: You have the option of volunteering to participate in several correlative studies that are optional throughout this trial. These samples are not required, and do not affect your participation in the main research study. You will not be given results from these tests. Please refer to Section D for details about the procedures and their frequencies.
Please read the following carefully and indicate your decision by initialing and dating below.

1. You will be asked to provide a buccal swab (an inner cheek skin sample) for DNA analysis as it relates to your disease. This is optional for the following time point: **(Study #1)**

    - At any time during the trial

I agree to give a sample of my DNA (Buccal swab) for this research study (Study #1)

Yes:☐

No:☐

Initials _____ Date _____

DFCI Protocol Number:	14-338	Approved Date (DFCI IRB Approval):	02/11/2020
Date Posted for Use:	02/12/2020		

2. A bone marrow biopsy is mandatory at screening, to confirm that your disease has responded, and at end of treatment however, extra marrow fluid samples will be taken for extended research on cellular immunity.

Approximately 1 extra tablespoon of bone marrow aspirate will be used for this research and is optional at the following time points: **(Study #2)**

- Prior to treatment
- To confirm disease response (whenever that may occur while on study) or when clinically indicated by your doctor
- End of treatment

Approximately 2 tablespoons of blood will be used for this research and is optional at the following time points: **(Study #2)**

- Prior to treatment
- Each Day 1 from Cycle 1-24
- To confirm disease response (whenever that may occur while on study)
- End of treatment

I agree to give additional samples of my blood and bone marrow for research purposes (Study #2)

Yes:☐

No:☐

Initials _____ Date _____

DFCI Protocol Number:	14-338	Approved Date (DFCI IRB Approval):	02/11/2020
Date Posted for Use:	02/12/2020		

Q. DOCUMENTATION OF CONSENT

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

Signature of Participant or Legally Authorized Representative

Date

Relationship of Legally Authorized Representative to Participant

DFCI Protocol Number: 14-338	Approved Date (DFCI IRB Approval): 02/11/2020
Date Posted for Use: 02/12/2020	

Adult Participants

To be completed by person obtaining consent:

The consent discussion was initiated on _____ (date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative, or, where the participant is a minor, the participant's parent or legal guardian.

For Adult Participants

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

☐ 1b) Participant is illiterate

The consent form was read to the participant who was given the opportunity to ask questions.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

☐ 2) The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

☐ 2a) gave permission for the adult participant to participate

☐ 2b) did not give permission for the adult participant to participate

DFCI Protocol Number: 14-338	Approved Date (DFCI IRB Approval): 02/11/2020
Date Posted for Use: 02/12/2020	