Official Title: *LCI-HEM-MYE-CRD-002*: A Phase II Study of Carfilzomib- Revlimid-Dexamethasone-Elotuzumab in Relapsed/Refractory Multiple Myeloma
NCT# 03361306
IRB-Approved Date: *09/15/2022*

Atrium Health

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Sponsor / Study Title:	**Levine Cancer Institute/ "PHASE II STUDY OF CARFILZOMIB, REVLIMID, DEXAMETHASONE AND ELOTUZUMAB IN RELAPSED/REFRACTORY MULTIPLE MYELOMA"**
Protocol Number:	**LCI-HEM-MYE-CRD-002**
Principal Investigator:	**Manisha Bhutani, MD**
Telephone:	[redacted] **(24 Hours)** [redacted] **(24 Hours)**
Address:	**Levine Cancer Institute** [redacted]

Please read this form carefully. Take time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign and date your name at the end of this form. You cannot take part in this research study until you sign and date this form.

This form is for use in a research study that may involve subjects who may or may not have the capacity to consent to take part in the study. Accordingly, when the subject cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the subject rather than the person (legally authorized representative) who is signing this form for the subject. In cases where the subject's representative gives consent, the subject should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the subject regains the capacity to consent, informed consent should be completed and the subject offered the ability to leave the study if desired.

INTRODUCTION

Dr. Bhutani and her associates (the investigators) are asking you to participate in a research study at Levine Cancer Institute (LCI) and Atrium Health to study the efficacy of the study treatment [elotuzumab, carfilzomib, lenalidomide and dexamethasone] in patients who have multiple myeloma which has come back/worsened (relapsed/refractory) after initial treatment.

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You are being asked to take part in this study because you have multiple myeloma, and your condition has worsened after initial treatment.

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to decide on study participation. You have also been told that you have the option not to participate. You may discuss your decision with your friends and family. You can also discuss it with your healthcare team. If you have any questions, you can ask your study doctor for more explanation.

This study is being carried out under the sponsorship of Levine Cancer Institute (LCI). Bristol-Myers Squibb [BMS] is the company that makes elotuzumab (Elo) and will be providing the drug in this study.

WHY IS THIS STUDY BEING DONE?

Research studies are done to find out the best way to treat patients.

Normal plasma cells are found in the bone marrow and are an important part of the immune system. Multiple myeloma (MM) is a cancer formed by malignant (cancerous) plasma (blood) cells. Despite major advances in therapy, MM is still considered an incurable malignancy.

The study drug elotuzumab, has been clinically shown to be effective in treating relapsed/refractory MM in combination with either bortezomib, or lenalidomide and dexamethasone. Elotuzumab in combination with lenalidomide and dexamethasone and also with pomalidomide and dexamethasone is currently approved by the Food and Drug Administration (FDA) for the treatment of patients with multiple myeloma. Carfilzomib is also FDA approved for treating multiple myeloma and frequently given in combination with lenalidomide and dexamethasone for treatment of relapsed/refractory MM. Based on these findings, this study will look at how subjects with relapsed/refractory MM respond to a combination treatment with the following drugs: elotuzumab, carfilzomib, lenalidomide and dexamethasone. The combination of these four drugs is not FDA approved and is experimental.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

You will be one of approximately 40 subjects to participate in this study at the Levine Cancer Institute.

HOW THE STUDY WORKS

Before the study starts, you or your legally authorized representative will be asked to sign and date this consent form. If you agree to participate in the study and sign and date the consent form, the study doctor will do some tests and procedures to find out if you can be in the study. These baseline tests and procedures include:

- Medical and disease history

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- Physical exam, including height and weight
- Vital signs (body temperature, breathing rate, heart rate, blood pressure)
- ECOG performance status (assesses daily living abilities)
- Pregnancy tests (blood) for females of childbearing potential
- Electrocardiogram (ECG – a measure of the heart's electrical activity and ECHO (echocardiogram – heart test done using sound waves) or MUGA (multigated acquisition scan) – to check the pumping action of the heart
- Document all current medications
- Bone marrow aspirate (sample) for disease evaluation and correlative studies
- Blood draw for disease evaluation and to check blood count and blood chemistries.
- Urine sample for disease evaluation collected over a 24-hour period
- PET/CT (positron emission tomography/computed tomography – special types of x-rays) scan or MRI (magnetic resonance imaging – pictures made using strong magnets and a computer) if your study doctor feels it is necessary to evaluate your disease
- Bone skeletal survey (various x-rays of all the bones in the body)
- Blood work to test for exposure to the hepatitis B virus. The study doctor may be required by law to report the result of these tests to the local health authority.

Many of these tests may be repeated during the course of this research study. After you have completed the first cycle of treatment during induction, the required office visits with your study doctor (physical exam and performance status) may be done as a virtual visit, per your study doctor's discretion.

Note: If you have previously been enrolled in the study, have not previously been tested for the hepatitis B virus and are currently receiving treatment with carfilzomib, you will be required to have a blood test to check for exposure to the hepatitis B virus, as mentioned in the procedures above.
All study treatment will be given on an outpatient basis. If you are having unfavorable side effects, the study treatment may be stopped for a while, or the dose of the study drug(s) may be reduced. Your study doctor will also discuss with you whether it is in your best interest to continue the treatment with the study drugs. You will continue study treatment until your disease worsens (progresses) or study treatment is interrupted for any other reason.

This study will be conducted in two parts: Induction and Maintenance Phase

<u>Induction Phase (Cycles 1-4):</u>

You will receive 4 cycles, each lasting for 28 days, of the following:

- Carfilzomib - 20/56 mg/m^2 IV (intravenous – through a vein) over 30 minutes on Days 1, 8, and 15 of all cycles.
- Lenalidomide - 25 mg by mouth on Days 1 through 21 of all cycles.
- Dexamethasone on Days 1, 8, 15 and 22. On days that you receive elotuzumab: 28 mg by mouth (between 3 and 24 hours before elotuzumab infusion) and 8 mg IV (receive a dose intravenously before elotuzumab infusion). On days that you do not receive elotuzumab, you

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will take dexamethasone 40 mg by mouth. The dose of dexamethasone may be reduced per your study doctor's decision.

- Elotuzumab - 10 mg/kg through an IV on Days 1, 8, 15, and 22 of Cycles 1 and 2, and elotuzumab 20 mg/kg over 1-2 hours on Days 1 of Cycles 3 and 4 (Prior to each elotuzumab dose you will receive additional medications, including antihistamines and acetaminophen, to prevent an allergic reaction to the elotuzumab.) over approximately 1-4 hours, with the first few doses to infuse at approximately 3-4 hours and later doses at approximately 1-2 hours if you tolerate the initial doses without a reaction. The first dose you receive at the 20 mg/kg dose (Cycle 3 Day 1) may be infused more slowly than the previous dose to make sure you can tolerate the infusion.

Maintenance Phase from Cycle 1 until end of study treatment:

- Lenalidomide - 15 mg by mouth on Days 1 through 21
- Elotuzumab - 20 mg/kg through an IV over approximately 1-2 hours on Day 1 of each cycle

The following tests and/or procedures will be done when you come to the clinic prior to each cycle:

- Physical exam (Day 1 of each cycle). The required office visits with your study doctor (physical exam and performance status) may be done as a virtual visit, per your study doctor's discretion.
- Vital signs prior to each infusion of elotuzumab
- ECOG performance status (Day 1 of each cycle)
- ECG prior to each cycle of induction treatment
- Pregnancy test (blood or urine) for females of childbearing potential once a week during the first cycle of induction and then prior to each cycle of study treatment thereafter
- Blood draw to check blood cell counts, blood chemistries and disease response. Blood counts and chemistries will also be checked prior to each carfilzomib dose. Disease response will be checked once every 2 cycles starting with Cycle 14 of maintenance.
- 24- hour urine collection sample for disease evaluation (only required if your study doctor determines this test is necessary to evaluate how your disease is responding to study treatment)
- Blood draw for correlatives studies prior to every cycle of induction, prior to the first 2 cycles of maintenance study treatment, and then prior to every third maintenance cycle
- Bone marrow aspirate for disease evaluation and research purposes after induction treatment is completed and again if you have a complete response to the treatment (no signs of myeloma in your blood or urine). This may also be repeated if your disease worsens. This will be determined by your study doctor.

After you complete the intervention (Post-Intervention; one visit):

An end of study treatment visit will be done when you stop study treatment for any reason. The visit will occur approximately 30 days after your last dose of study treatment. During this visit, the following procedures and tests will be done:

- Physical exam. The required office visits with your study doctor (physical exam and performance status) may be done as a virtual visit, per your study doctor's discretion.
- ECOG
- Vital Signs
- ECG
- Lab Assessments
- Concomitant Medication

Follow-up:

If you stop study treatment for any reason other than disease progression, you should continue to have disease assessments until your disease worsens or you start another therapy. You will be contacted by phone once every 3 months if you are not seen in the clinic.

RISKS/ DISCOMFORTS OF SUBJECTS

As with all research studies, the study drugs and study procedures may involve unknown risks. Any medication can have temporary or permanent side effects and can cause unforeseen adverse reactions. The study drug may not control your multiple myeloma.

General

During the intravenous (given into your vein) administration of elotuzumab or other drugs like carfilzomib, there may be pain or bruising at the infusion site. Other risks include fainting, bleeding, swelling, or (rarely) infection. If elotuzumab should accidentally be injected under your skin during administration, a local skin reaction may occur (for example, redness, swelling, tenderness, stiffness).

There are risks associated with blood draws, and these include pain, fainting, bruising, bleeding, swelling, or (rarely) infection where the needle or catheter is put in your arm for taking the blood sample.

You may have side effects while on the study. Everyone taking part in the study will be monitored carefully for any side effects. Side effects may be mild or very serious. Your study doctor may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study drug. In some cases, side effects can be serious, long lasting, or may never go away.

Elotuzumab

Very Common (occurring in 10% or more subjects):

- Tiredness (Fatigue)
- Diarrhea
- Vomiting

- Fever (Pyrexia)
- Constipation
- Headache
- Cough
- Nerve pain or numbness and tingling in the hand/arms and/or feet/legs (Peripheral neuropathy)
- Pain in extremities
- Sore throat, cold symptoms (Nasopharyngitis)
- Pain in throat (oropharyngeal pain)
- Low white blood cell count (lymphopenia, leukopenia)
- Decreased appetite
- Weight decreased
- Lung infection (pneumonia)
- Upper respiratory tract infection
- Cataracts

Common (occurring in between 1% and less than 10% of subjects):

- Infection with the herpes virus, which can result in a painful skin rash (shingles) or cold sores in the mouth
- Chest Pain
- Allergic Reaction (also called hypersensitivity)
- Infusion related reactions that may occur during or after elotuzumab administration and include symptoms such as chills, fever, or high blood pressure
- Reduced sensitivity to touch (Hypoesthesia)
- Altered mood
- Cough with phlegm
- Night sweats
- Deep vein thrombosis (development of a clot in a vein)
- Changes to blood tests (decreased blood levels of sodium, magnesium, protein, calcium or phosphate, increased blood levels of sugars, calcium, potassium)

Uncommon (occurring in less than 1% of subjects):

- Anaphylactic reaction (severe, potentially life-threatening allergic reaction). Symptoms can include difficulty breathing, low blood pressure, dizziness and hives/itching)
- Secondary primary malignancies (development of another type of cancer)
- Hepatoxicity (injury to your liver as a result of treatment with the drug)

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.

Carfilzomib

You will be told about the known risks, which are the side effects reported previously by others who took carfilzomib. However, your study doctors do not know all the side effects that you may experience. As with all investigational drugs, all risks may not have been identified at this time. There may be serious unexpected or unforeseen risks while taking carfilzomib, including death. It is known that nearly everyone who takes carfilzomib will have some side effects while on the study drug. Many of these side effects may be mild but some side effects can be serious and even fatal.

Before you take carfilzomib, your study doctor needs to know if you have any:

- Heart problems, including a history or chest pain, heart attack, heart failure, high blood pressure, irregular heartbeat, or if you have ever taken a medicine for your heart
- Lung problems, including a history of shortness of breath at rest of with activity
- Kidney problems, including kidney failure or if you have ever received dialysis
- Liver problems, including a history of hepatitis; particularly previous hepatitis B virus infection, fatty liver, or if you have ever been told your liver is not working properly
- Unusual bleeding, including easy bruising, bleeding from an injury, such as a cut that does not stop bleeding in a normal amount of time, or internal bleeding, which can indicate you have low platelets
- Blood clots in your veins
- Any other major disease for which you were hospitalized or received medication

Please notify your study doctor as soon as possible if you experience blurred or double vision, vision loss, difficulty speaking, weakness in an arm or a leg, a change in the way you walk, problems with your balance, persistent numbness, decreased sensation or loss of sensation, decreased alertness, memory loss or confusion which may be symptoms of a rare brain infection known as Progressive Multifocal Leukoencephalopathy (PML).

Very Common Side Effects (occurring in more than 10% of subjects):

- Low red blood cell count, which may cause tiredness
- Low platelets, which may cause easy bruising or prolonged bleeding
- Low white blood cell count, which may decrease your ability to fight infection
- Shortness of breath
- Cough, cough with phlegm
- Diarrhea
- Queasy/feeling like you need to throw up (nausea)
- Constipation
- Vomiting

- Tiredness (fatigue)
- Fever
- Swelling of the hands, feet or ankles
- General weakness
- Respiratory tract infection
- Lung infection (pneumonia)
- Infection of the tubes of the lungs (bronchitis)
- Inflammation of the nose and throat
- Decreased appetite
- Back pain, joint pain, pain in limbs, hands or feet
- Muscle spasms
- Headache
- Dizziness
- Numbness
- Insomnia (difficulty sleeping)
- Changes to blood tests (decreased blood levels of potassium, increased blood levels of creatinine)
- High blood pressure (hypertension)

Common Side Effects (occurring in up to 10% of subjects):

- Fever associated with low white blood cell count
- Heart failure, and heart problems including rapid, strong or irregular heartbeat. The risk of developing heart failure when receiving carfilzomib is higher if you are 75 years of age or older. This risk is also higher if you are Asian
- Heart attack
- Blood clot in the lungs
- Fluid in the lungs
- Nosebleed
- Change in voice or hoarseness
- Pain in throat
- Wheezing
- Pulmonary hypertension, symptoms include shortness of breath with everyday activities or at rest, irregular heartbeat, racing pulse, tiredness, dizziness, and fainting spells
- Blurred vision
- Cataract (clouding of the lens of the eye)
- Stomach pain
- Indigestion
- Toothache
- Chills, pain, feeling unwell

- Infusion site reactions such as pain, swelling, irritation or discomfort where you received the drug injection into your vein
- Liver problems including an abnormal increase in your liver enzymes in the blood
- Runny nose or nasal congestion
- Urinary tract infection
- Flu-like symptoms (influenza)
- Serious infection in the blood (sepsis)
- Viral infection
- Infection and/or irritation of your stomach and bowels
- Lung infection
- Dehydration (lack of fluids)
- Bone and muscle pain
- Chest pain
- Muscle weakness
- Aching muscles
- Abnormal sensation such as tingling or decreased sensation in arms and/or legs
- Anxiety
- Kidney problems, including decreased ability to make urine, increased creatinine in the blood, and kidney failure needing dialysis
- Rash, itchy skin, redness of the skin
- Increased sweating
- Changes to blood tests (decreased blood levels of sodium, magnesium, protein, calcium or phosphate, increased blood levels of sugars, calcium, uric acid, potassium bilirubin, or c-reactive protein)
- Low blood pressure (hypotension)
- Leg pain (which could be a symptom of blood clots in the deep veins of the leg)
- Chest pain or shortness of breath (which may be a symptom of blood clots in the lungs).
- Flushing (skin or face become red and hot)
- Ringing in the ears
- A reaction to carfilzomib infusion, which can include the following symptoms: fever, chills or shaking, joint pain, muscle pain, facial red, hot skin or swelling, swelling of the throat, weakness, shortness of breath, low blood pressure, fainting, chest tightness, or chest pain.

Uncommon Side Effects (occurring in up to 1% of subjects):

- Bleeding, bruising, weakness, confusion, fever, nausea, vomiting and diarrhea, and acute kidney failure, which may be signs of a blood condition known as Thrombotic Microangiopathy (including Thrombotic Thrombocytopenic Purpura [TTP])
- Sudden loss of heart function
- Reduced blood flow to the heart
- Abnormal amount of fluid between the heart and the lining around the heart

- Heart muscle disease which may cause shortness of breath and tiredness
- Lung problems, symptoms include difficulty breathing, including shortness of breath (dyspnea) at rest or with activity or a cough, rapid breathing, feeling like you can't breathe in enough air, wheezing, or cough.
- Bleeding in the lungs
- Bleeding in the stomach and bowels
- Blockage of the intestines
- Inflammation of the pancreas gland
- Multi organ failure
- Yellowing of your skin and eyes, stomach pain or swelling, queasy/feeling like you need to throw up or vomiting, which could be signs of liver problems, including liver failure. If you have previously had hepatitis B virus infection, treatment with carfilzomib may cause hepatitis B virus infection to become active again
- Liver failure
- Itchy skin, yellow skin, very dark urine and very pale stools which may be caused by a blockage in the flow of bile from the liver (cholestasis)
- Severe infection of the blood causing low blood pressure and low blood flow to the different organs
- Irregular heartbeat, kidney failure or abnormal blood test results which may be associated with Tumor Lysis Syndrome, a condition that can occur after treatment of a fast-growing cancer. As tumor cells die, they break apart and release their contents into the blood. This causes a change in certain chemicals in the blood, which may cause damage to organs, including the kidneys, heart, and liver
- Bleeding in the brain
- Headaches, confusion, seizures, blindness, and high blood pressure (hypertension), which may be symptoms of a neurologic condition known as Posterior Reversible Encephalopathy Syndrome (PRES)
- Allergy to carfilzomib
- Stroke
- Bleeding
- Extremely high blood pressure, severe chest pain, severe headache, confusion, blurred vision, queasy/feeling like you need to throw up and vomiting, or severe anxiety, can be signs for a condition known as hypertensive crisis

Rare (occurring in up to .1% of subjects)

- Hemolytic uremic syndrome (HUS) (condition that can occur when small blood vessels in your kidneys become damaged and inflamed which can cause clots to form resulting in kidney failure, which could be life-threatening)
- Swelling and irritation of the lining around the heart
- Swelling of the throat
- Hole in the stomach, small intestine, or large bowel

- Infection of the back of the eye (cytomegalovirus)

Other risks include fainting, bleeding, swelling, or (rarely) infection. If carfilzomib should accidentally be injected under your skin during administration, a local skin reaction may occur (for example, redness, swelling, tenderness, stiffness).

The following side effects have been seen in subjects who received carfilzomib. It is unknown if they were caused by carfilzomib, you may or may not experience these side effects:

- Tiredness, infection, and easy bruising or bleeding which may be symptoms of a blood condition known as Myelodysplastic syndrome/Acute Myeloid Leukemia (MDS/AML).
- Tenderness or pain in the abdomen that gets more intense with motion or touch, abdominal bloating or distention, queasy/feeling like you need to throw up and vomiting, diarrhea, constipation or the inability to pass gas which may be symptoms of swelling of the thin tissue that lines the inner wall of the abdomen and covers most of the abdominal organs.

Driving and Using Machines
You may experience tiredness, dizziness, fainting, and/or a drop in blood pressure after treatment with carfilzomib. This may impair your ability to drive or operate machinery. If you have these symptoms, you should not drive a car or operate machinery.

Hydration Risks
There may be risks associated with over hydrating (having too much fluid in your body) so it is important to follow your doctor's instructions regarding how much water or other fluids you should drink. Over hydration can cause side effect to your heart, lungs, and kidneys.

Dexamethasone

The potential side effects include the following:

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

- Difficulty sleeping
- Fatigue

Less Likely (occurring in 10%-29% of subjects):

- Low red blood cells or platelets
- Blurred vision
- Constipation or diarrhea
- Upset stomach, heartburn, or ulcer
- Fever
- Swelling of the arms or legs
- Upper respiratory tract infection
- Weight gain

- High blood sugar
- High blood pressure
- Increased appetite
- Muscle cramps
- Bone pain or back
- Joint pain
- Muscle weakness or muscle aches
- Headache
- Dizziness
- Tingling in the hands or feet
- Mood changes (depression, or abnormal feelings of well-being and excitement)
- Skin changes leading to thinning and easy bruising
- Gradual changes to bones that may increase their risk of breaking

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

- Low white blood cell counts
- Vomiting
- Abdominal pain
- Pneumonia
- Low blood potassium
- Pain in the arms or legs
- Tremor
- Altered taste sensation
- Numbness in the hands or feet
- Bronchitis
- Inflammation of the nose or throat
- Gradual development of cataracts
- If used for a prolonged period of time, steroids can suppress the function of the normal glands that make steroids (adrenal glands) leading to the need for continued replacement with steroid medication
- Glaucoma, which means having high pressure within the eyeball possibly leading to blindness. May require medical intervention to prevent visual impairment.
- Pancreatitis, which is an inflammation of the pancreas causing pain in the upper abdomen. This could become severe and cause nausea and vomiting, fever and rapid heart rate. This could require hospitalization and may be life threatening.

Lenalidomide

The FDA has added a new black box warning for subjects with MM receiving lenalidomide in combination with dexamethasone: There is a significantly increased risk of venous thromboembolic events such as deep vein thrombosis and pulmonary embolism (blood clot in the lung), as well as risk of arterial thromboembolic events such as arterial thromboembolism, myocardial infarction and

stroke. Arterial embolism is a sudden interruption of blood flow to an organ or body part due to an embolus adhering to the wall of an artery blocking the flow of blood, the major type of embolus being a blood clot (thromboembolism).

If you are receiving the combination of carfilzomib, lenalidomide and dexamethasone as part of this study, your study doctor will discuss the possible use of blood thinners due to this risk. There are numerous risks to being on blood thinners. The main risk is bleeding. Your study doctor will discuss these risks with you.

There is an increased risk of developing a second type of new cancer that has been seen in prior studies using these drugs. If you have questions about this risk, please speak with your study doctor.

Listed below are side effects associated with lenalidomide.

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

- Low number of white blood cells (with or without fever) know as leukocytes, neutrophils, granulocytes, or lymphocytes
- Low number of red blood cells (Anemia)
- Decrease in platelet cells that help your blood clot (Thrombocytopenia)
- Abdominal (stomach) pain
- Feeling weak and unwell (Asthenia)
- Chills
- Pneumonia
- Bronchitis
- Upper respiratory tract infection
- Sinusitis (sinus infection)
- Urinary tract infection
- Gastroenteritis (infection in the stomach and intestines)
- Kidney failure
- Flu (Influenza)
- Sore throat (Nasopharyngitis, pharyngitis)
- Stuffy nose (Rhinitis)
- Weight loss
- Cataracts (eye lens cloudy)
- Insomnia (not sleeping well)
- Decrease in blood potassium (Hypokalemia)
- Decrease in blood calcium (Hypocalcemia)
- Poor appetite
- Nerve pain or numbness and tingling in the hand/arms and/or feet/legs (Neuropathy, Peripheral neuropathy)

- Dizziness
- Shaking (Tremor)
- Headache
- Abnormal taste (Dysgeusia)
- Blurred vision
- Cough
- Blood clots in the legs or lungs (Pulmonary embolism, Deep vein thrombosis)
- Shortness of breath (Dyspnea)
- Nose bleeding (Epistaxis)
- Constipation
- Diarrhea
- Nausea
- Vomiting
- Dry skin
- Abnormal liver function tests
- Tingling of skin (Paresthesia)
- Itching
- Rash
- Feeling sad (Depression)
- Indigestion
- High blood sugar (Hyperglycemia)
- Muscle pain, spasms, or cramps
- Joint or bone pain
- Fatigue (feeling tired)
- Leg/feet swelling (Edema, peripheral edema)
- Fever
- Reduced sense of touch (Hypoesthesia)
- Back pain

Common (occurring in between 1% and less than 10% of subjects):

- Abnormally low number of all blood cells – red blood cells, white blood cells, and platelets (Pancytopenia)
- Dehydration
- Low or high blood pressure
- Bruising
- Upper abdominal pain
- Dry mouth
- Increased liver function tests (Alanine aminotransferase increased, Gamma-glutamyl transferase increased)
- Gout

- Increased risk of falling
- Increased sweating
- Muscle weakness
- Chest pain
- Toothache
- Fainting
- Stroke
- Heart attack
- Heart failure
- Fast heart rate
- Reduced blood flow and oxygen to heart tissue (Myocardial ischemia)
- Infections that are caused by virus such as cold sores, genital herpes, and/or shingles (Herpes simplex, Herpes zoster, Ophthalmic herpes zoster)
- Reduced or blocked flow of bile from liver (Cholestasis)
- Swelling of blood vessels (Vasculitis)
- Destruction of red blood cells (Hemolytic anemia)
- Lethargy, drowsiness, listlessness (lack of energy), or apathy (lack of interest)
- Increased C-Reactive Protein (liver protein that indicates inflammation in body)
- Diabetes
- Vertigo (loss of balance)
- Respiratory distress
- Decreased sensation in nerves (Peripheral sensory neuropathy)
- Increase in Iron (Iron overload)
- Decrease in blood phosphate (Hypophosphatemia)
- Decrease in blood magnesium (Hypomagnesemia)
- Decrease in blood sodium (Hyponatremia)
- Increase in blood calcium (Hypercalcemia)
- Myelodysplastic syndrome (blood cancer causing decreased red blood cells, white blood cells, and platelets)
- Leukemia (Acute Myeloid Leukemia, T-Cell Type Acute Leukemia)
- Skin Cancer (Basal Cell Carcinoma, Squamous Cell Carcinoma)
- Bacterial meningitis (inflammation of the membranes (meninges) surrounding your brain and spinal cord)
- Bacterial infection underneath or in the skin (Cellulitis, Erysipelas)
- Lung infection
- Respiratory tract infection
- Blood infection (Sepsis, Bacteremia)
- Joint infection
- Skin redness
- Increased uric acid in the blood (Hyperuricemia)

- Hematoma (swelling of skin filled with blood)
- Clot in vein (Thrombosis)
- Tumor flare (sudden increase in tumor size)
- Tumor lysis syndrome. Tumor lysis syndrome is caused by rapid killing of tumor cells during study treatment. When the tumor cells die, they release their contents into the bloodstream. Irregular heartbeat, kidney failure, or abnormal blood test results may be associated with Tumor Lysis Syndrome
- Night sweats
- Mood swings

Uncommon (occurring in 0.1% and less than 1% of subjects):

- Appendicitis (infection of the appendix)
- Bursitis infective (infection of the sac of fluid in tissue called the bursa)
- Worsening of symptoms of chronic obstructive pulmonary disease
- Kidney infection
- Allergic reaction (Hypersensitivity to the study drug)
- Inflammation and infection of the colon caused by the bacteria Clostridium difficile

Rare (occurring in 0. 01% and less than 0.1% of subjects):

- Rapid killing of tumor cells which may cause abnormal electrolytes or kidney damage (called tumor lysis syndrome)
- Inflammation of the lung
- Severe, potentially life-threatening, skin reaction involving the lining of the nose, mouth, stomach, intestines, or rash that leads to damage and shedding of the top layer of skin (Stevens Johnson syndrome (SJS) and Toxic epidermal necrolysis (TEN))
- A potentially life-threatening skin reaction (such as rash or skin peeling), elevated level of eosinophils (eosinophilia), fever, and/or swollen lymph nodes (lymphadenopathy) with other organ complications such as inflammation of the liver (hepatitis), inflammation of the kidney nephrons (nephritis), inflammation of the lungs (pneumonitis), inflammation of the heart (myocarditis), and/or inflammation of the sac surround the heart (pericarditis) (Drug reaction with eosinophilia and systemic symptoms (DRESS))

<u>Other Risks:</u>

Bone Marrow Biopsy: You may experience pain and/or discomfort at the site of the needle insertion. The amount of pain and/or discomfort depends on your pain tolerance, which differs from person to person. Some people describe a sharp pain in the bone where the needle is inserted. Other patients describe it as a long, hard punch or kick. This pain and/or discomfort only lasts a few seconds during the actual procedure. Tenderness over the area may last for a few days. Bleeding from the site or infection may occur but is rare.

You will be asked to sign a separate procedure consent prior to undergoing a bone marrow biopsy, and any other risks associated with these procedures will be discussed with you by your study doctor

and/or clinic staff. You will be monitored carefully during these procedures by specially trained medical staff.

Blood Sampling: Taking blood from a vein in your body may cause some pain, redness, or bruising at the injection site. In addition, lightheadedness, fainting, or an infection (rare) at the blood draw site is possible. If you feel faint, you should immediately lie down to avoid falling.

Radiological Exams (PET/ CT scans and x-rays): PET/CT scans and standard x-rays use x-ray radiation. Radiation has the potential to cause cancer or harm an unborn child. The amount of radiation you will receive during a CT scan is very low and most doctors agree that the benefits outweigh the risks. Some CT scans and PET scans will require you take a "contrast solution" either by mouth or by injection into a vein. You may experience discomfort from lying still in an enclosed space for a prolonged period of time.

Although rare, the contrast solution used in PET/CT scans may cause an allergic reaction such as nausea, vomiting, itching, skin rash, or in very rare instances swelling of the throat and difficulty breathing. If you feel any of these symptoms of an allergic reaction you must tell the clinical staff immediately so that you can be treated quickly.

MRI Risks: During MRI scanning, you may feel some heat and hear banging noises. Some patients experience a "closed-in" sensation or claustrophobia while inside the MRI machine, and this can be uncomfortable for some individuals. Some MRI scans need preparation beforehand; if there are special preparations you will be told about them prior to the day of your scan. You may have an injection of a type of dye just before the scan to help define certain organs more clearly. The injection may make you sick to your stomach or have pain, warmth, swelling, bruising, a small blood clot or infection at the injection site. Rarely, you may get a rash or other sign of allergy from the injection. If you have a history of kidney problems, you must inform the technologist or physician as you may not be able to receive an injection during the MRI exam. You must inform staff before the MRI if you have any metal implanted in your body, such as some hip replacements, hearing aids, pacemakers, bullets, or jewelry that cannot be removed. You may not be able to have an MRI since this type of scan uses very powerful magnets.

ECG (Electrocardiogram) Risks: An ECG traces the electrical activity of the heart. You may have mild irritation, slight redness, or itching at the sites on your skin where the recording patches are placed.

Reactivation of Varicella zoster virus (VZV): Due to carfilzomib administration, there is a risk of reactivation of this virus. Your healthcare provider will prescribe antiviral medication, to prevent it from happening. You will be prescribed this medication unless your healthcare provider feels it is not in your best interest to take it.

Blood clots: Due to lenalidomide administration it is possible that you may develop blood clots in your legs or lungs (occurs in 10% or more of subjects receiving lenalidomide). At the discretion of your healthcare provider, you may be prescribed medication to prevent blood clots. If you experience symptoms that could indicate a blood clot in your leg or lung (warmth/tenderness/

redness in your leg or shortness of breath, chest pain, and/or cough), notify your health care provider immediately.

Reproductive Risk:

There may be a possibility that the study drugs may damage an unborn child, and for this reason, if you are pregnant, plan to become pregnant, or nursing, you may not participate in this study. If you become pregnant during the study, you will be immediately discontinued from the study, and your study doctor will need to follow up with your pregnancy and your child's health. If you believe you are pregnant, please contact your study doctor immediately. The same applies to you if you are a male subject with potential reproductive partners. If you are a female of childbearing potential, you must agree to use a highly effective method of birth control plus a second acceptable or highly effective method from the time of informed consent until 6 months after the last dose of study treatment.

Highly effective methods

- Hormonal contraception associated with inhibition of ovulation
- Placement of intrauterine device or intrauterine system
- Vasectomized partner
- True abstinence

Acceptable methods

- Condom with spermicidal foam/gel/film/cream/suppository
- Occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/ suppository
- Hormonal contraceptives

Unacceptable methods

- Abstinence at certain times of the cycle only, such as during the days of ovulation or after ovulation (based on symptoms or temperature)
- Pre-ejaculatory withdrawal

If you are a male who is sexually active with a female of childbearing potential, you must agree to practice abstinence (not have sex) or you must always use a condom with spermicide during treatment and for an additional 90 days after the last dose of carfilzomib. You must not donate sperm during treatment and for an additional 90 days after the last dose of study treatment. Your female partner should also consider the contraception recommendations above.

WILL I BENEFIT FROM PARTICIPATING IN THIS STUDY?

Taking part in this study may or may not improve the symptoms of your condition. There may be no benefit to you and your condition may not improve. While you are in this study, your study doctor will follow your condition closely. By taking part in the study you may help future patients.

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WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

You may choose not to take part in this study or to leave the study at any time. Instead of taking part in this study, you may choose to receive standard medical treatment for your condition. Standard medical treatments for your condition may include standard chemotherapy, standard radiation therapy, hormone therapy, radio-immunotherapy (treatment with a radioactive substance that is linked to an antibody), other medications, or other experimental treatment. You can also choose to have no treatment at all.

If you decide that you don't want any more active treatment, one of your options is called "comfort care", also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible. If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

The risks and benefits of other treatments will be explained to you. The study doctor will answer any questions you have about these other alternative treatments. You can also discuss these options with your own health care provider.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

If you choose to take part in the study, you and/or your health plan/insurance will need to pay for all your routine care procedures. Levine Cancer Institute will provide you with the study drug, elotuzumab, at no charge. There is no additional cost to you to take part in this study. Some health insurance plans may not cover certain procedures and medical treatments. You may wish to discuss coverage with your insurance company before agreeing to participate in this study.

You will not receive payment for taking part in this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage You can print a copy of the "Clinical Trials and Insurance Coverage" information from this web site. Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

You may wish to discuss coverage with your insurance company before agreeing to participate in this research study.

STUDY STAFF PAYMENT/FINANCIAL DISCLOSURE

None of the doctors asking you to participate in this study has received or will receive money or other benefits for personal use from the companies (Amgen and Incyte) that developed some of the drugs used in this study.

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COMPENSATION FOR INJURY

In the event that you are injured as a result of your participation in this study, we will provide or arrange for treatment as necessary. This treatment, as well as other medical expenses, will be billed to you or your insurance company in the usual manner. You will be responsible for deductibles, co-payments, and co-insurance. There are no plans to pay or give you other compensation for the injury. You do not waive any legal rights by signing this consent form.

If you become ill or are hurt while you are in the study, get the medical care that you need right away.

For insurance or other payment reporting purposes, we may need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because we may have to check to see if you receive Medicare and if you do, report the payment we make to Medicare.

In no way does signing this consent form waive your legal rights nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

WHAT IF I WANT TO QUIT THE STUDY LATER ON?

Your participation in this study is completely voluntary. You should feel under no pressure to be in the study. If you decide not to be in the study, your decision will not in any way harm your relationship with your doctors or with Atrium Health or Levine Cancer Institute and there is no penalty or loss of benefits to you. You are free to stop being in the study if you change your mind after entering it. This would not harm your relationship with your doctors or with Atrium Health or LCI and there is no penalty or loss of benefits to you. If you choose to withdraw from the study, please notify the study doctor in writing at the address on the first page of this form.

Information already contributed to the study will remain in the study even if you choose to withdraw. If you leave the study for any reason, you will be asked to have the procedures completed for the final visit. If you decide to no longer participate in the study for any reason, you have the option not to allow Levine Cancer Institute to use your tissue samples for future testing by contacting the study doctor at the telephone number or address listed on the first page of this form. Tissue samples will be destroyed only if they have not already been tested.

Your study doctor or Levine Cancer Institute can remove you for any reason at any time from this study without your consent. Reasons include but are not limited to:

- The judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
- Your failure to follow the instructions of the study doctor for study procedures and / or investigational drug compliance.
- The study is stopped by Levine Cancer Institute.

Your study doctor will explain the reasons for your removal and will help arrange for your continued

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care, if needed.

NEW INFORMATION ABOUT THE STUDY

You will be told about any new information found during the study that may affect your decision about whether you want to continue to take part.

CONFIDENTIALITY

The records of this study will be kept confidential. In any sort of report we might publish, we will not include any information that will make it possible to identify a patient. Your record for this study may, however, be reviewed and/or photocopied by Bristol-Myers Squibb, Atrium Health, or by representatives of the Food and Drug Administration or other government agencies. To that extent, confidentiality is not absolute.

To ensure that your information collected for this study will be kept confidential, your name will not be used whenever possible. A code will be used instead of your name. All of your study data will be kept in a secure location.

A description of this clinical trial will be available on 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.

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AUTHORIZATION TO USE AND DISCLOSE YOUR PROTECTED HEALTH INFORMATION

If you wish to participate in this research study, you

_____

Printed Name of Research Subject

must sign this Authorization. By signing this Authorization, you give all healthcare providers, including Atrium Health, permission to use or disclose (release) your protected health information, both past and present, for the research study described here:

Levine Cancer Institute – LCI-HEM-MYE-CRD-002: "PHASE II STUDY OF CARFILZOMIB, REVLIMID, DEXAMETHASONE AND ELOTUZUMAB IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

The protected health information that we may use or disclose (release) for this research may include all information in your medical record, such as results of physical examinations, medical history, lab tests, or certain health information indicating or relating to a particular condition.

The health information listed above may be used by and/or disclosed (released) to:

- Study investigator and research staff
- Study sponsor and/or its associated companies, Levine Cancer Institute, Bristol-Myers Squibb (BMS)
- Regulatory or other governmental authorities of the United States or other countries based on this study
- Other persons or agents authorized by the study sponsor
- Atrium Health employees
- Other persons or agencies as required by law or allowed by federal regulations
- Data coordinating centers that will receive and process PHI; and/or;
- Advarra Institutional Review Board (Advarra IRB) or Data Safety and Monitoring Boards.

Atrium Health is required by law to protect your protected health information. By signing this Authorization, you authorize Atrium Health to use and/or disclose (release) your protected health information for this research study. Those persons who receive your protected health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your protected health information with others without your permission, if permitted by laws governing them. Your protected health information may then no longer be protected by the Privacy Rule.

Please note that you do not have to sign this Authorization, but if you do not, you may not receive research-related treatment through this study. However, Atrium Health may not condition (withhold or refuse) your other Atrium Health providers treating you on whether you sign this Authorization.

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You may change your mind and withdraw (take back) this Authorization at any time, except to the extent that Atrium Health or the Sponsor has already used or disclosed your protected health information based on this Authorization. To withdraw this Authorization, you must write to the Study Doctor at the address listed on the first page of this form

No publication or public presentation about the research described above will reveal your identity without another Authorization from you. If all protected health information that does or can identify you is removed, the remaining information will no longer be subject to this Authorization or federal rules (such as the Privacy Rule) and may be used or disclosed for other purposes.

When the research for which the use or disclosure is made involves treatment and is conducted by Atrium Health: To maintain the integrity of this research study, you generally will not have access to your personal health information related to this research until the study is complete.

At the conclusion of the research study and at your request, you generally will have access to your protected health information. Access to your protected health information in a medical record is described in the Notice of Privacy Practices provided to you by Atrium Health.

When conducting research, the data and results may be used or disclosed for further treatment outcomes research or to research a secondary result. This Authorization will remain in effect after the end of the current study, and any future related secondary study unless it is revoked by you in writing as described above.

_____

Signature of Research Subject or Research Subject's Legally Authorized Representative

_____

Printed name of Research Subject or Research Subject's Legally Authorized Representative

_____

Date

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

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An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  [redacted]
- or call **toll free**: [redacted]
- or by **email**: [redacted]

Please reference the following number when contacting the Study Subject Adviser: Pro00023493.

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STATEMENT OF CONSENT

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records. **I am not giving up any of my legal rights by signing this form.**

_____ _____/____/ _____ _____
Signature of Research Subject Date Time

_____
Printed Name of Research Subject

_____ _____/____/ _____ _____
Signature of Legally Authorized Representative (*If Applicable*) Date Time

_____
Printed Name of Legally Authorized Representative (*If Applicable*)

STATEMENT OF PERSON EXPLAINING CONSENT

I have carefully explained to the subject or the subject's legally authorized representative the nature and purpose of the above study. There has been an opportunity for the subject to ask questions about this research study. I have been available to answer any questions that the subject or the subject's legally authorized representative has about this study.

_____ ____/_____/_____ _____
Signature of Person Explaining Consent Date Time

_____
Printed Name of Person Explaining Consent

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