MC210809 / 21-006597

Evaluating Mechanisms of Immunomodulator Sensitivity and Resistance in Multiple Myeloma

NCT05288062

Document Date: 01/24/2024

MAYO CLINIC

Name and Clinic Number

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Not to be used after: **January 23, 2025**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC210809, Evaluating Mechanisms of Immunomodulator Sensitivity and Resistance in Multiple Myeloma

IRB#: 21-006597

Principal Investigator: Wilson Gonsalves, M.D., and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this study is to find out how patients will respond to one cycle of standard treatment with a type of drug called an immunomodulatory drug (sometimes referred to as IMiDs), combined with a corticosteroid drug. Examples of an immunomodulatory drug include lenalidomide and pomalidomide. These drugs work through a variety of mechanisms to affect the function of the immune system. They are widely used as treatment for multiple myeloma and remain the backbone of therapy for both newly diagnosed patients and patients that have relapsed disease. An example of a corticosteroid drug is dexamethasone. Dexamethasone is a strong anti-inflammatory agent and is also widely used to treat patients with multiple myeloma.

	You have been asked to take part in this research because you have been diagnosed with multiple myeloma or smoldering myeloma.
What's Involved	For each patient (study participant), the study will be conducted in 3 periods: screening period, treatment period, and follow-up period. You will be required to come to the study site for study visits; this is similar to making an appointment with your study doctor. In addition to your regular appointments and procedures, you will be asked to have a bone marrow aspirate/biopsy done for research at the end of Cycle 1. This will be paid for by the research study. You will also be asked to participate in another study that will ask about the use of your blood and bone marrow biopsy samples. You and your study doctor will plan as many visits as needed to complete the study assessments and procedures for the protocol.
Key Information	All the study drugs are approved by the FDA for treatment of patients with multiple myeloma or smoldering myeloma, this includes patients who are newly diagnosed and haven't yet received treatment, as well as patients who have already received treatment. There are risks to the study drugs that are described later in this document. Some of the very common side effects are fatigue, nausea, low platelet count, low hemoglobin count, infections, decreased appetite, vomiting, and diarrhea. Many side effects go away shortly after the treatment is stopped, but in some cases side effects can be serious, long lasting problems, or may never go away. There may be side effects that are unknown. The risks associated with study participation are completely described later in this form. It is important to review the risk section carefully. It is not known whether this treatment will be better or worse for you than what your doctor would normally choose. By participating in this research study, you may help doctors answer this question. You do not have to participate in this study to receive treatment for your condition. Your study doctor will discuss the risks and benefits of other treatments with you before you decide whether or not you want to participate in this study.

Approval Date: **January24, 2024**
Not to be used after: **January 23, 2025**

Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

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

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

Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Wilson Gonsalves, M.D. Phone: 507-284-2511 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55905 **Co-Principal Investigator:** Sikander Ailawadhi, M.D. Phone: (904) 953-2000 **Institution Name and Address:** Mayo Clinic Hospital Jacksonville, FL 32224 **Co-Principal Investigator:** Rafael Fonseca, M.D. **Phone:** (480) 301-8000 **Institution Name and Address:** Mayo Clinic Hospital 5777 E Mayo Blvd Phoenix, AZ 85054
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681

MAYO CLINIC

Name and Clinic Number

Approval Date: **January24, 2024**
Not to be used after: **January 23, 2025**

If you have questions about …	You can contact …
▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

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

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

You are being asked to take part in this study because you have been diagnosed with a type of blood cancer called Multiple Myeloma or Smoldering Myeloma that requires treatment.

The plan is to have about 190 take part in this study at Mayo Clinic.

Why is this research study being done?

The purpose of this study is to find out how patients will respond to 1 cycle of treatment with a type of drug called an immunomodulatory drug (sometimes referred to as IMiDs), combined with a corticosteroid drug. Examples of an immunomodulatory drug include lenalidomide and pomalidomide. These drugs work through a variety of mechanisms to affect the function of the immune system. They are widely used as treatment for multiple myeloma and remain the backbone of therapy for both newly diagnosed patients and patients that have relapsed disease. An example of a corticosteroid drug is dexamethasone. Dexamethasone is a strong anti-inflammatory agent and is also widely used to treat patients with multiple myeloma.

All the drugs used in this research study are FDA approved.

Information you should know

Who is Funding the Study?
This study is being funded by a philanthropic foundation that supports cancer research. They will pay the institution to cover costs related to running the study.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

You will be in the study for up to 6 months (cycles). If your multiple myeloma worsens or you have side effects from the study medications you may not be in the study for 6 months (cycles).

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

If you agree to take part in this study, we will ask you to sign this consent form to see if you are eligible. Routine tests for your cancer will be done.

Screening Period
Prior to starting treatment on this trial, you will have specific procedures and tests to make sure you are eligible to be in this study.

They include:

- Medical history (including any medications that you are taking now or have taken in the past)
- Review of your current medical condition(s)
- Physical examination (including height and weight)
- Vital signs (blood pressure, heart rate, temperature)
- Whole body low dose CT scan or PET/CT if deemed necessary
- Routine blood tests (including CBC, chemistry panel, INR/PT and TSH)
- Blood tests done specifically to assess your disease
- Urine tests done specifically to assess your disease
- Pregnancy test if you are able to become pregnant
- Bone marrow aspirate and biopsy

These tests are part of regular care for your cancer. If some of these tests have been done recently, you may not need to repeat them.

If you qualify to participate in the study, and agree to participate you will receive the study treatment.

Treatment Period
This study consists of 4 groups (also called cohorts):

Group A (cohort A)
This group is for patients who have been diagnosed with smoldering multiple myeloma.

Group B (cohort B)
This group is for patients who have been newly diagnosed with multiple myeloma and haven't received any treatment yet.

Group C (cohort C)
This group is for patients who have been diagnosed with multiple myeloma and have already received initial treatment, but their multiple myeloma has gotten worse (called relapsed and/.or refractory).

Group D (cohort D)
This group is for patients who have been diagnosed with multiple myeloma and their multiple myeloma is getting worse while on treatment with lenalidomide which is being used as a maintenance treatment (relapsed after lenalidomide maintenance).

Please note: If you choose to participate in this study, those enrolled in groups (cohorts) B, C, or D will not have standard of care treatment for cycle 1. For example, patients with multiple myeloma that is newly diagnosed (Cohort B), relapsed and refractory (Cohort C) or relapsed after lenalidomide maintenance (Cohort D) will receive at least one cycle of a doublet (2 drugs) based therapy alone that includes either lenalidomide or pomalidomide with dexamethasone instead of conventional standard of care regimens that include a combination of triplet (3 drugs) or quadruplets (4 drugs) drug combination regimens. After the first cycle, participants will be able to receive conventional standard of care regimens for cycles 2 and beyond.

Treatment is given in either 21- or 28-day cycles. Cycle 1 is 21 days and cycles 2-6 are 28 days. You will receive the following treatment:

Groups A and B Cycle 1
You may receive lenalidomide or lenalidomide and dexamethasone, your doctor will tell you what you should take. The directions for taking the lenalidomide are below and your doctor will give you the directions for the other treatment drugs.

- Lenalidomide is taken by mouth Days 1-14
    - Lenalidomide is a capsule and should be taken at about the same time each day. The capsules should not be opened, broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food.
    - If you miss a dose of lenalidomide: If less than 12 hours has passed since missing a dose, you can take the dose. If more than 12 hours has passed since missing a dose at the normal time, you should not take the dose, but take the next dose at the normal time on the following day. If you miss a dose let your study doctor know.

You will have the following tests/visits:
- After Cycle 1 (before Cycle 2), you will have a research bone marrow biopsy.
- After Cycle 1 (before Cycle 2), you will have a research blood sample, about 4 tablespoons (i.e., 60 mL).

Groups A and B Cycles 2-6
You may receive lenalidomide or lenalidomide and dexamethasone, or lenalidomide and another agent. Your doctor will tell you what you should take. The directions for taking the lenalidomide are below and your doctor will give you the directions for the other treatment drugs.

- Lenalidomide is taken by mouth Days 1-21
    - Lenalidomide is a capsule and should be taken at about the same time each day. The capsules should not be opened, broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food.

- If you miss a dose of lenalidomide: If less than 12 hours has passed since missing a dose, you can take the dose. If more than 12 hours has passed since missing a dose at the normal time, you should not take the dose, but take the next dose at the normal time on the following day. If you miss a dose let your study doctor know.

Groups C and D Cycle 1
You will receive lenalidomide and dexamethasone or pomalidomide and dexamethasone. Your doctor will tell you what you should take.

- Lenalidomide is taken by mouth Days 1-14
  - Lenalidomide is a capsule and should be taken at about the same time each day. The capsules should not be opened, broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food.
  - If you miss a dose of lenalidomide: If less than 12 hours has passed since missing a dose, you can take the dose. If more than 12 hours has passed since missing a dose at the normal time, you should not take the dose, but take the next dose at the normal time on the following day. If you miss a dose let your study doctor know.
- Pomalidomide is taken by mouth Days 1-21
  - The capsules should be taken about the same time each day. The tablets should not be broken or chewed. The tablets should be swallowed whole with water.
  - If a dose of pomalidomide is missed, it should be taken as soon as possible on the same day. If it is missed for the entire day, it should not be made up.
  - As part of your clinical care, you will automatically be enrolled in the Pomalyst® REMS program in order to obtain pomalidomide. Before you can be enrolled in this program, you must read and agree to all the instructions. Due to the risks of the drug, pomalidomide is only available through this program. More information is available on this website http://www.pomalystrems.com/patient.html
- Dexamethasone is taken by mouth Days 1, 8, and 15
  - The tablets should be taken about the same time each day. The tablets should not be broken or chewed. The tablets should be swallowed whole with water.
  - If you forget a dose, take it as soon as you remember it. However, if more than 12 hours have passed since missing a dose at the normal time skip the missed dose. Do not take a double dose (two doses at the same time) to make up for a forgotten

You will have the following tests/visits:
- After Cycle 1 (before Cycle 2), you will have a research bone marrow biopsy
- After Cycle 1 (before Cycle 2), you will have a research blood sample , about 4 tablespoons (i.e., 60 mL).

Groups C and D Cycles 2-6:
You will receive lenalidomide plus dexamethasone or pomalidomide plus dexamethasone, Your doctor will tell you what to take.

- Lenalidomide is taken by mouth Days 1-21
  - Lenalidomide is a capsule and should be taken at about the same time each day. The capsules should not be opened, broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food.
  - If you miss a dose of lenalidomide: If less than 12 hours has passed since missing a dose, you can take the dose. If more than 12 hours has passed since missing a dose at the normal time, you should not take the dose, but take the next dose at the normal time on the following day. If you miss a dose let your study doctor know.
- Pomalidomide is taken by mouth Days 1-21
  - The capsules should be taken about the same time each day. The tablets should not be broken or chewed. The tablets should be swallowed whole with water.
  - If a dose of pomalidomide is missed, it should be taken as soon as possible on the same day. If it is missed for the entire day, it should not be made up.
  - As part of your clinical care, you will automatically be enrolled in the Pomalyst® REMS program in order to obtain pomalidomide. Before you can be enrolled in this program, you must read and agree to all the instructions. Due to the risks of the drug, pomalidomide is only available through this program. More information is available on this website http://www.pomalystrems.com/patient.html

For all groups, during cycles 2-6, you may receive an additional anti-myeloma agent at the discretion of your physician. It would be given to you as standard of care if your doctor thinks this will help your treatment. Your doctor may determine that it is beneficial to you to continue on the treatment regimen even after the 6th cycle when you would have completed the study.

All groups:
You will have the following tests/visits:

- Medical history (including any medications that you are taking now or have taken in the past)
- Review of your current medical condition(s) every cycle
- Physical examination (including height and weight) every cycle
- Vital signs (blood pressure, heart rate, temperature) every cycle
- Routine blood tests every cycle (including CBC, chemistry panel)
- Blood tests done specifically to assess your disease
- Urine tests done specifically to assess your disease
- Pregnancy test every cycle (if you are able to become pregnant)
- Clinical bone marrow aspirate and biopsy (as clinically indicated)

- Medication Diary to be completed every cycle
- Research blood test before cycle 1. This will only be done if you agree to participate in another research study, IRB#521-93, 919-04 or 14-009163 and sign a consent form for that study)
- Research bone marrow aspirate and biopsy before cycle 1. This will only be done if you agree to participate in another research study, IRB#521-93, 919-04, or 14-009163 and sign a consent form for that study) (before cycle 1)

Follow-up Period
There will be a follow-up visit within 7 days after you finish the study treatment.

You will have the following tests/visits while receiving treatment:

- Medical history (including any medications that you are taking now or have taken in the past)
- Review of your current medical condition(s)
- Physical examination (including height and weight)
- Vital signs (blood pressure, heart rate, temperature)
- Whole body low dose CT scan or PET/CT
- Routine blood tests (including CBC, chemistry panel)
- Blood tests done specifically to assess your disease
- Urine tests done specifically to assess your disease
- Clinical bone marrow aspirate and biopsy (if clinically indicated)
- Optional research bone marrow and aspirate
- Optional research blood sample

Optional research bone marrow biopsy and aspirate and blood sample

After you have completed treatment, we would like to request a sample of bone marrow for research. This would be done at the same time as your clinical bone marrow biopsy.

Please check one.

I agree to provide a bone marrow sample for this optional biopsy:

☐ Yes ☐ No Please initial here: _____Date: _____

After you complete treatment, we would like to request a blood sample for research. This would be done at the same time as your clinical blood draw.

Please check one.

I agree to provide a blood sample for this optional blood test

☐ Yes ☐ No Please initial here: _____Date: _____

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

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

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

It is possible that the symptoms of your condition will not improve during the study or may even worsen. Treatment with the study treatment may also involve risks to your future health that we currently do not know about. You will be closely monitored for any side effects that may occur. Side effects that have been reported with the study treatments are described below. If you have any questions about these, please ask the study doctor.

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

Lenalidomide

The following are likely risks of lenalidomide:

- Low white blood cells (neutropenia) and lymphopenia or a decrease in white blood cells that can make you more prone to infections
- Low platelets (thrombocytopenia) have been observed which may require reduction or interruption of the dose of lenalidomide that you receive.

- Deep venous thrombosis (blood clots in veins, usually in your calf) and lung emboli (blood clot in lungs). You need to seek medical care if you experience shortness of breath, chest pain, or arm or leg swelling.
- Fatigue or feeling tired
- Constipation or difficulty moving your bowels
- Diarrhea or loose/frequent bowel movements
- Infections involving various organs
- Peripheral neuropathy, causing numbness or tingling in extremities

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

- Allergic reaction and tumor lysis syndrome have been reported. Tumor lysis syndrome refers to disturbances of your electrolytes which is caused by rapid killing of cancer cells in the blood. This may be seen after initiation of cancer treatment and may result in kidney damage and heart problems such as an abnormal heartbeat.
- Diarrhea
- Fatigue, lack of energy
- Low red blood cells (anemia)
- Constipation
- Swelling of hands, feet or limbs
- Difficulty sleeping
- Muscle cramp/spasms
- Back pain
- Joint pain
- Nausea
- Fever
- Infection of the nose, sinuses, and/or throat
- Cough
- Rash
- Itching and dry skin
- Lack or loss of strength
- Shortness of breath
- Dizziness
- Headache
- Decreased appetite
- Tremor
- Abnormal thyroid function or inflammation of thyroid gland
- Abdominal pain or distension
- Gastrointestinal bleeding

- Bowel obstruction
- Abnormalities of liver tests
- Allergic reactions to drug
- Abnormalities of mineral levels in blood
- Heartburn

Serious side effects occurring in 1% or more of patients and not listed in bold above

- Neutropenia associated with a fever
- Pulmonary embolism or blood clot in or around the lungs
- Deep vein thrombosis or blood clots in a larger blood vessel
- Atrial fibrillation or irregular heartbeat
- Progression of the disease being studied including multiple myeloma
- Pneumonia or an infection of the lungs
- Sepsis or an infection of the blood
- Dehydration
- Kidney failure which can cause increases or decreases in the amounts of chemicals in your blood which can cause irregular heartbeats, muscle twitching, seizures, and/or death.
- Myocardial infarction (heart attack)
- Stroke (bleeding in the brain or clotting)

Rare cases of the following events have been reported:

- Angioedema- an allergic skin disease characterized by patches of swelling involving the skin and/or the lining of your nose, mouth, and gastrointestinal tract.
- Anaphylaxis- serious potentially life-threatening type of allergic reaction that may cause breathing difficulty, dizziness, low blood pressure, and loss of consciousness.
- Stevens-Johnson syndrome and toxic epidermal necrolysis- serious allergic skin reactions that begin as a rash in one area and later cover more of the body leading to detachment of the top layer of skin (could be body-wide). Medical journals have reported patients with allergic skin reaction with thalidomide who also developed the same type of reaction with lenalidomide
- Drug reaction with eosinophilia and systemic symptoms (DRESS). This is a drug reaction and may cause fever, rash, hepatitis, nephritis, pneumonitis, myocarditis, and/or pericarditis

- Tumor lysis syndrome- metabolic complication that can occur during or without treatment of cancer. These complications are caused by the break-down products of dying cancer cells and include hyperkalemia (high potassium), hyperphosphatemia (high phosphorus), hyperuricemia and hyperuricosuria (high uric acid in blood and urine), hypocalcemia (low calcium), and consequent acute uric acid nephropathy and acute renal failure (kidney damage).
- Tumor Flare reaction- a condition that involves any of the following increase in the size of the cancerous lymph nodes, rash and slight fever.
- Rhabdomyolysis- a serious condition involving the destruction of skeletal muscle that can lead to kidney failure. Signs and symptoms include dark, red, or cola colored urine and muscle tenderness, stiffness, aching (myalgia) or weakness.
- Increase in blood levels of lipase due to inflammation of pancreas gland.
- Abnormalities of blood clotting
- Bone marrow failure
- Decrease in lymphocytes (type of white blood cells)
- Enlarged spleen
- Abnormal heart rhythms
- Congestive heart failure (condition where the heart becomes weak and cannot pump enough blood to the rest of the body
- Decreased function of adrenal gland
- Decreased hearing
- Vision abnormalities
- Clotting in blood vessels of intestines
- Seizures
- Graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body) (graft vs. host disease)

Also Reported on Lenalidomide Trials but with the Relationship to Lenalidomide Still Undetermined:

- Tissue swelling (angioedema)
- Rhabdomyolysis is a breakdown of muscle fibers. It occurs when muscle cells die and release cell contents into the blood stream. It can cause muscle pain and a number of health problems, including damage to the kidneys. If severe, this could be life threatening (rhabdomyolysis)

These events have the potential to be fatal.

Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking study drug. In some cases, side effects can be serious, long lasting or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Hematological Toxicity
Lenalidomide is associated with significant neutropenia (decrease in white blood cells that help fight infection) and thrombocytopenia (decrease in platelets that help with blood clotting). You will have your blood counts checked frequently when starting treatment with lenalidomide.

Deep Vein Thrombosis and Pulmonary Embolism
Lenalidomide has demonstrated an increased risk of deep vein thrombosis (DVT, blood clot in a larger blood vessel) and pulmonary embolism (PE, a blood clot in or around the lungs) in some people with certain medical conditions. The study staff will ask you about any risk factors you may have. [If you have a history of blood clots your doctor will prescribe either heparin or coumadin for the first four months of the study treatment. The doctor may continue to prescribe the medication or aspirin for the remainder of your course of study treatment. All other patients will receive (at the discretion of the treating physician) either oral low–dose aspirin or another treatment to prevent blood clotting during study participation.] Patients unable or unwilling to undergo treatment for prevention of blood clots will not be eligible to participate in this study. You will be instructed on the signs and symptoms of DVT and PE and if symptoms occur you should contact your study doctor promptly.

Second new cancers
According to researchers, patients with cancer have a higher risk of developing a second new cancer when compared to people without cancer. In clinical studies of newly diagnosed multiple myeloma, a higher number of second cancers were reported in patients treated with induction therapy (treatment as first step to reducing number of cancer cells) and/or bone marrow transplant then lenalidomide for a long period of time compared to patients treated with induction therapy and/or bone marrow transplant then placebo (a capsule containing no lenalidomide). Patients should make their doctors aware of their medical history and any concerns they may have regarding their own increased risk of other cancers.

Other Risks
If any physician other than the study doctor prescribes medication for you for another condition or you are taking any over-the-counter medications or vitamins, you must inform the study staff. This is important because the interaction of some medications may cause serious side effects.

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.

Your condition may not get better or may become worse while you are in this study.

Risks Associated with Pregnancy

Lenalidomide is related to thalidomide. Thalidomide is a known to cause severe life-threatening human birth defects. Findings from a monkey study indicate that lenalidomide caused birth defects in the offspring of female monkeys who received the drug during pregnancy. If lenalidomide is taken during pregnancy, it may cause birth defects or death to any unborn baby. Females must 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.

Lenalidomide is detected in trace quantities in human semen according to a study. The risk to the fetus in females of childbearing potential whose male partner is receiving lenalidomide is unknown at this time. For these reasons male patients receiving lenalidomide must use a latex condom while taking lenalidomide, when temporarily stopping lenalidomide, and for 28 days after permanently stopping lenalidomide treatment during any sexual contact with a pregnant female or a female of childbearing potential even if you have undergone a successful vasectomy.

Patients should not donate blood during treatment therapy or for 28 days following discontinuation of lenalidomide.

You must NEVER share lenalidomide with anyone else.

Lenalidomide will hurt unborn babies. The manufacturer of this drug has a pregnancy prevention program for any patient who takes this drug. Your doctor can explain to you such a program. There are additional side effects that have been seen in patients that have taken lenalidomide. Please ask your study doctor for information regarding these side effects.

POTENTIAL DISCOMFORTS AND RISKS OF POMALIDOMIDE (CC-4047, Pomalyst®)

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

- A low number of white blood cells, which are the infection fighting cells, which could put you at risk for infection (neutropenia or leukopenia)
- A low number of a particular white blood cell, which is important to the immune system (lymphopenia)

- Feeling tired (fatigue)
- Difficulty passing stool (constipation)
- Feeling sick to your stomach (nausea)
- Decreased number of blood cells (platelets) that help to clot the blood (which could put you at increased risk of bleeding (thrombocytopenia)
- Decrease in red blood cells, which are the oxygen carrying cells, which could make you feel tired (anemia)
- Back pain
- Shortness of breath or difficulty breathing (dyspnea)
- Loose stools (diarrhea)
- Bronchitis
- Upper respiratory tract infection
- Pneumonia
- Dizziness
- Nerve damage (peripheral neuropathy)
- Decreased appetite
- Swelling of limbs (peripheral edema)
- Fever (Pyrexia)
- Bone pain
- Muscle spasm
- Cough
- Kidney failure (renal failure)
- Increased blood creatinine which is associated with kidney failure
- Sudden onset of kidney failure (Acute renal failure)
- Nausea
- Generalized weakness (asthenia)
- Itchiness (Pruritus)

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

- When pomalidomide or related drugs (i.e. thalidomide and lenalidomide) have been used along with corticosteroids and certain other chemotherapy drugs, there has been an increased risk of individuals developing blood clots including blood clots in the big veins of the limbs (deep vein thrombosis) or in the lungs (pulmonary embolism). Your doctor may request or require that you take aspirin or another blood thinner in this situation.
- Abdominal pain
- Sore mouth, nose, or throat (nasopharyngitis)
- Drop in blood pressure
- Headache

- Chest pain
- Feeling shaky (tremor)
- Infections including potentially life threatening infections
- Muscle aches
- Muscle weakness
- Nerve damage with numbness and abnormal sensations (peripheral sensory neuropathy)
- Abnormal sensations (Paresthesia)
- Abnormal balance (Gait disturbance)
- Damage to multiple nerves (Polyneuropathy)
- Decreased sensations (Hypoesthesia)
- Pain due to nerve damage or irritation (Neuralgia)
- Nerve damage with difficulty in movement (peripheral motor neuropathy)
- Joint swelling or achiness
- Dry or itchy skin
- Blushing or redness to face (flushing)
- Decreased function of the thyroid gland, which can result in feeling tired and weight gain that may first show up as an increased levels of thyroid stimulating hormone (hypothyroidism). If your thyroid function becomes abnormal, your doctor may have you take a thyroid replacement pill daily.
- Difficulty emptying the bladder (urinary retention)
- Pelvic pain
- Rash
- Throwing up (vomiting)
- Decreased sodium levels in the blood (hyponatremia)
- Abnormally high calcium in the blood stream, that can result in fatigue, confusion, feeling sick to your stomach, throwing up, difficulty passing stool, abnormal heartbeat, coma, and death (hypercalcemia)
- Abnormally low calcium in the blood stream, that can result in muscle cramps, abdominal cramps, spasms (hypocalcemia)
- Abnormal levels of potassium in the blood (hyper- or hypokalemia)
- Death
- Excessive sweating (hyperhidrosis)
- High blood sugar (hyperglycemia)
- Gastrointestinal bleeding
- Airway and lung infection (bronchopneumonia)
- Shingles (Herpes zoster)
- Severe infection secondary to low neutrophil count (neutropenic sepsis)
- Fever related to low neutrophil count (Neutropenic fever)

- Respiratory tract infection
- Pneumonia caused by Pneumocystis jiroveci
- Pneumonia caused by respiratory syncytial virus
- Pneumonia with involvement of lobes of lungs (Lobar pneumonia)
- Pneumonia caused by streptococcal bacteria (Streptococcal pneumonia)
- Elevated liver enzymes (alanine aminotransferase elevation, Aspartate aminotransferase elevation, Gamma-glutamyltransferase elevation)
- Elevated liver function test
- Confusion
- Depressed level of consciousness
- Drop in all blood counts resulting in anemia, low white blood cell count (leucopenia), and low platelet count (thrombocytopenia) (pancytopenia)
- Spinning sensation (vertigo)
- Nosebleed (epistaxis)
- General physical health deterioration
- Swelling face (Face edema)
- Generalized itchiness (Generalized pruritus)
- Impairment of kidney function (Renal impairment)
- Loss of protein in urine (Proteinuria)
- Bleeding in gastrointestinal tract (Gastrointestinal hemorrhage)
- Bleeding from hemorrhoids (Hemorrhoidal hemorrhage)
- Bleeding from rectum (Rectal hemorrhage)
- Bleeding gum (Gingival bleeding)
- Passage of fresh blood per anus (Hematochezia)

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

- Chest wall pain
- Inability of the heart to properly pump blood to the lungs (right ventricular failure)
- Bleeding from the stomach large intestine and/or small intestine (gastrointestinal bleeding)
- Narrowing of the stomach or intestines (gastrointestinal stenosis)
- Chest pain that occurs when your heart doesn't get enough oxygen, which can be a warning sign of a heart attack (angina - unstable)
- An irregular heartbeat that results from the top/upper chambers of the heart “quivering” instead of beating normally (atrial fibrillation)
- Fast heart rate (tachycardia) or slow heart rate (bradycardia)
- Decrease in the ability of the heart to pump blood, because of weakening of the heart muscle (congestive heart failure)

- Lack of oxygen to the heart muscle which can cause damage to the heart (heart attack)
- Feeling like your heart is "fluttering or skipping" (heart palpitations)
- Bleeding in the brain (cerebral hemorrhage)
- Lack of oxygen to the brain caused by either bleeding in the brain or blood clot. Also called a stroke (cerebral vascular accident)
- Memory impairment
- Blood creatinine increased
- Excessive or abnormal loss of body fluids (dehydration)
- Failure to thrive
- Anxiety
- Feeling sad or blue (depression)
- Difficulty falling or staying asleep (insomnia)
- Changes in mood
- Kidney stones (nephrolithiasis)
- Collection of fluid in the space around the lung (pleural effusion)
- Inability of the lungs to function properly (respiratory failure)
- High blood pressure (hypertension) or low blood pressure (hypotension)
- Acute inflammation of the liver including hepatitis, liver failure, jaundice (yellowing of skin and whites of eyes) (hyperbilirubinemia)
- Inflammation of supporting tissue of the lungs (interstitial lung disease)
- Possible second cancer with prolonged use
- Blurred vision
- Decreased level of phosphorus in the blood (hypophosphatemia)
- Decreased albumin in the blood (hypoalbuminemia)
- Low levels of magnesium in the blood (hypomagnesemia)
- Night sweats
- Changes in the voice or hoarseness (dysphonia)
- Nosebleed (epistaxis)
- Very sleepy, difficulty arousing (lethargy)
- Fainting (syncope)
- Excessive sleepiness (somnolence/depressed level of consciousness)
- Change in taste sensation (dysgeusia)
- Dry mouth
- Chills
- Recurrent areas of skin or mucosal swelling of sudden onset, usually disappearing within 24 hours; an allergic reaction to the medication (angioedema and urticaria) an exaggerated or inappropriate immune response (hypersensitivity) to pomalidomide
- Hepatitis B viral activation

- Hepatitis
- Kidney failure and blood chemistry abnormalities secondary to destruction of cancer cells by anti-cancer treatment (tumor lysis syndrome)
- Skin cancer (basal cell carcinoma and squamous cell carcinoma)
- Development of a new cancer during cancer treatment (second primary malignancies) including blood and bone marrow cancers (Hematologic malignancies), solid organ tumors (solid tumors), and skin cancers.
- Inflammation of the lungs
- Inflammation of lung tissue (pneumonitis)
- Pneumonia caused by staphylococcal bacteria
- Pneumonia caused by fungi
- Pneumonia caused by viruses
- Pneumonia caused by influenza virus
- Increased blood urea level which can be related to kidney failure
- Decreased creatinine renal clearance which is related to kidney failure
- Decreased glomerular filtration rate which is related to kidney failure
- Decreased urine output (Oliguria) which can be related to kidney failure
- Destruction of kidney tubules (Renal tubular necrosis)
- Kidney failure of sudden onset mostly related to dehydration (Acute pre-renal failure)
- Chemical changes in body related to kidney failure (Azotemia)
- Eyelid edema
- Eye swelling or swelling around eyes (Periorbital edema)
- Lip swelling
- Swollen tongue
- Swelling in the mouth (Edema mouth)
- Swelling in the throat (Pharyngeal edema)
- Severe skin reaction with wide-spread fluid sac (bullous) formation and skin shedding (Stevens-Johnson syndrome)
- Severe skin reaction with wide-spread skin destruction and shedding (Toxic epidermal necrolysis)
- Drug reaction with eosinophilia and systemic symptoms
- Itchiness due to drug allergy (Allergic pruritus)

Risks Associated with Pregnancy

Pomalidomide is related to thalidomide. Thalidomide is a known to cause severe life-threatening human birth defects. If pomalidomide is taken during pregnancy, it may cause birth defects or death to any unborn baby. Females must not become pregnant while taking pomalidomide.

You have been informed that the risk of birth defects is unknown. If you are female, you agree not to become pregnant while taking pomalidomide.

Pomalidomide is detected in trace quantities in human semen according to a study. The risk to the fetus in females of childbearing potential whose male partner is receiving pomalidomide is unknown at this time. For these reasons male patients receiving pomalidomide must use a latex condom while taking pomalidomide, when temporarily stopping pomalidomide, and for 90 days after permanently stopping pomalidomide treatment during any sexual contact with a pregnant female or a female of childbearing potential even if you have undergone a successful vasectomy.

Patients should not donate blood during treatment therapy or for 28 days following discontinuation of pomalidomide.

You must **NEVER** share pomalidomide with anyone else.

Female subjects of childbearing potential must be willing to use 2 methods of birth control or be surgically sterile or abstain from heterosexual activity for 28 days prior to starting pomalidomide, during the course of the study, and through 30 days after last dose of pomalidomide and carfilzomib. Female subjects of childbearing potential are those who 1) have achieved menarche at some point, 2) have not undergone a hysterectomy or bilateral oophorectomy or 3) have not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months). Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the subject.

Male subjects must agree to practice abstinence or use an effective barrier method of contraception starting with the first dose of pomalidomide through 6 months after last dose of pomalidomide and carfilzomib if sexually active with a female of childbearing potential. Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the subject. Other acceptable methods of contraception are condoms with contraceptive foam, oral, implantable or injectable contraceptives, contraceptive patch, intrauterine device, diaphragm with spermicidal gel, or a sexual partner who is surgically sterilized or post-menopausal.

All subjects must agree to follow the local requirements for pomalidomide counseling, pregnancy testing, and birth control; and be willing and able to comply with the local requirements (for example, periodic pregnancy tests, safety labs, etc.).

Dexamethasone

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

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

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

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

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

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

As with any medication, allergic reactions are a possibility.

Pregnancy risk
If you are a female of childbearing potential, you must agree to the following:

- abstain from heterosexual intercourse
  OR
- to use birth control as follows:
  - Two methods of reliable birth control (one method that is highly effective and one additional barrier method), beginning 4 weeks before starting treatment and continuing for 4 months after completing treatment.

You must also agree not to donate eggs for the purpose of reproduction during treatment and continuing for 4 months after completing treatment.
If you are a male, you must agree to the following:

- Refrain from donating sperm
- Abstain from heterosexual intercourse
  OR
- Agree to use contraception/barrier as follows:
  - Agree to use a male condom, even if you have undergone a successful vasectomy, and your female partner must use an additional highly effective contraceptive method

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

Standard of Care risks
Your doctor will discuss the risks of bone marrow aspirate and biopsy, blood draw, and WBLDCT (or PET/CT), as these tests and procedures are part of your standard clinical care. You will be exposed to radiation from the WBLDCT or PET/CT. The amount of radiation has a low risk of harmful effects.

If your doctor prescribes another treatment drug for you to receive during cycles 2-6, they will discuss those risks.

Are there reasons you might leave this research study early?

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

In addition, your doctor, the researchers, or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best interest,
- If you do not follow the study rules,
- If the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may

continue to be used.
We will tell you about any new information that may affect your willingness to stay in the research study.

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

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

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

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

The treatment being used in the trial contains medicines that are typically used for treatment of myeloma. We hope the information learned from this study will benefit other people with multiple myeloma in the future.

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

You do not have to be in this study to receive treatment for your condition. Your other choices may include the commonly used treatment regimens that include the currently approved drugs. You should talk to the researcher and your regular physician about each of your choices before you decide if you will take part in this study.

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

You won't need to pay for tests and procedures which are done just for this research study. These are:

- Research bone marrow aspirate done at the end of Cycle 1

You and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care. These tests and procedures are:

- Medical history (including any medications that you are taking now or have taken in the past)
- Review of your current medical condition(s)
- Physical examination (including height and weight)
- Vital signs (blood pressure, heart rate, temperature)
- Whole body low dose CT scan or PET/CT
- Routine blood tests
- Blood tests to assess your disease
- Urine tests to assess your disease
- Pregnancy test if you are able to become pregnant
- Bone marrow aspirate and biopsies that are done as part of your routine care
- Standard of care drugs, Lenalidomide, Pomalidomide and Dexamethasone
- Any other standard of care drug prescribed by your doctor

You will also be responsible for any co-payments and deductibles. Before you take part in this study, you should call your insurer to find out if the cost of these tests and/or procedures will be covered. You will have to pay for any costs not covered by your insurance.

If you have questions about any costs to you that may result from taking part in the research, please speak with the Principal Investigator. If you wish, arrangements can be made for you to speak with someone in Patient Financial Services about these costs.

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

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

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

There is a very small chance that some commercial value may result from the use of your sample. This could include new products like a drug or a test to diagnose a disease. If that happens, you will not be offered a share in any profits.

Will your information or samples be used for future research?

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

Your information or samples collected for this study will not be used or shared for future research studies even if the identifiable information such as your name, Mayo Clinic number or date of birth is removed.

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

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. All of your research samples given to Mayo Clinic will be labeled with a code number and kept in locked storage. Only your study team will be able to link your samples with your identity. No one working with your samples will know your identity. If the results of the research are made public, information that identifies you will not be used.

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

Your health information may be collected from:

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

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

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

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and <u>not</u> employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

MAYO CLINIC

Name and Clinic Number

Approval Date: **January24, 2024**
Not to be used after: **January 23, 2025**

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

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

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

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

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

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
PL 3-02
200 1st Street SW
Rochester, MN 55905

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

Please be sure to include in your letter or email:

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

MAYO CLINIC

Name and Clinic Number

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Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

Enrollment and Permission Signatures

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

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

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

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature