Informed Consent Form

Maintenance Therapy with Carfilzomib, Pomalidomide and Dexamethasone (CPd) in High-Risk Myeloma Patients: A Phase 2 Study with a Safety Run-in

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EMORY | WINSHIP CANCER INSTITUTE
A Cancer Center Designated by the National Cancer Institute

You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title: **Maintenance therapy with carfilzomib, pomalidomide and dexamethasone (CPd) in high-risk myeloma patients**

Principal Investigator: Ajay K. Nooka MD MPH

Investigator-Sponsor: Ajay K. Nooka MD MPH

Study-Supporter: Amgen Pharmaceuticals

Introduction
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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.

What is the purpose of this study?
You are being asked to participate in this research study which will be using three different study drugs in as maintenance therapy among high risk myeloma patents. The purpose of the study is to evaluate how long the disease will be in remission using the combination of these three agents (carfilzomib, pomalidomide and dexamethasone). The study will also help to find out what effects, good and/or bad, the combination of carfilzomib, pomalidomide, dexamethasone have on you and your cancer. The study will assess the effects of the drug on multiple myeloma.

Carfilzomib and pomalidomide have been approved by the Food and Drug Administration (FDA) to treat relapsed and refractory multiple myeloma, but not as maintenance therapies. Dexamethasone has been used for treatment of myeloma for several decades. In this study, carfilzomib is an investigational study drug because it is not approved in the United States by the FDA for use in maintenance setting after an autologous stem cell transplant. Carfilzomib in combination with pomalidomide and dexamethasone as maintenance therapy in this case is considered experimental.

Emory will enroll up to 40 subjects at the Winship Cancer Institute.

What will I be asked to do?

If you decide to take part in this research study, you will undergo the following procedures:

Procedures to determine if you are eligible to take part in a research study are called "screening" procedures. For this research study, the screening procedures include those listed below. These procedures may overlap with procedures you would undergo as part of your routine care, and may be done regardless of whether you join this study. They will be done as an outpatient, and will involve 3-4 hours of your time. You will be seen by a physician, nurse practitioner or physician's assistant, nurses and medical technicians. All tests must be completed within 28 days from the day you receive you first treatment (Cycle 1 Day 1), unless otherwise indicated. You must sign this informed consent form before any research procedures may be done.

- A review of your medical history and confirmation of high risk status
- A review of any medication(s) you are currently taking
- Performance status (how well you are able to do your normal activities)
- Vital signs (blood pressure, pulse, and temperature) will be recorded
- A neurologic assessment including a physical evaluation and a questionnaire
- An echocardiogram (ECHO) test or Multi Gated Acquisition Scan (MUGA) (a test that measures how much blood your heart pumps on each beat)
- Height and weight will be recorded
- Blood samples (about 3 teaspoons) will be taken for routine tests to check your blood counts (numbers of each type of blood cell), chemistries (to evaluate your overall health status by checking things such as your kidney and liver function within 72 hours of starting treatment. Tests to assess your blood clotting will also be done.
- An EKG, or electrocardiogram (a test that measures the rhythm of your heart to make sure your heart is functioning properly)
- If you are a woman capable of having children, you will have another blood test to determine if you are pregnant before entering the study (about 1 teaspoon will be collected within 14 days of starting the study)
- Blood tests to assess the status of your myeloma
- A 24-hour urine collection will be done
- Standard radiologic imaging procedures may be done if you have a plasmacytoma (a solid tumor) to measure the size of your tumor(s) – this can include CT scans (computerized tomography), MRIs (magnetic resonance imaging), and/or other imaging tests within 28 days of starting treatment
- Skeletal survey - x-rays of the skull, long bones, pelvis and chest. This will be done if it has not been done in the past 12 weeks
- Bone marrow biopsy and aspirate
- Hepatitis B virus (HBV) testing

If you qualify for the study and decide to take part in the study, you will be given the study drugs carfilzomib, pomalidomide and dexamethasone.

Drug administration:

Maintenance Phase:
You will begin maintenance therapy within 28 days after signing consents. Maintenance will be continued until withdrawal of consent, disease relapse, unacceptable toxicity or no further clinical benefit is experienced.

Maintenance therapy consists of Carfilzomib at the dose of 56 mg/m^2 given on days 1, 8, and 15 only. Pomalidomide at a dose of 2 mg orally days 1-21 every 28 days will be continued, but your doctor may escalate to 4 mg after making sure that you are tolerating the 2 mg dosing well after the first 2 months of therapy. In the event that a dose reduction is required due to a newly encountered toxicity on day 1 of the first maintenance cycle, a reduced dose will be initiated for the maintenance therapy. Dexamethasone is also given

by mouth single daily oral dose of 40 mg/day on 1, 8, and 15 only. In the event that you fail to maintain a disease response during the maintenance phase, you may resume therapy at the dose levels and frequency of Carfilzomib, pomalidomide and/or dexamethasone tolerated before the initiation of the maintenance phase.

Pre-treatment medications:

- Treatment with carfilzomib can cause a condition called TLS (tumor lysis syndrome). TLS is an accumulation of substances in the blood as a result of rapid cancer cell destruction. In order to decrease the risk of TLS it is important for you to be well hydrated. You will be required to drink at least 6-8 cups of fluid per day starting 2 days prior to your first day of treatment, continuing for as many days as directed by your doctor or nurse. Your doctor will also administer fluids through one of your veins before and after each dose of carfilzomib if needed. Your doctor will determine if you will need to continue to follow this schedule throughout the study. You may also be treated with a pill taken by mouth called allopurinol. Allopurinol is used to help prevent one of the effects of TLS, an increase in uric acid. Your doctor will determine if you need to take this.

Additionally, anti-viral medication will be prescribed for you while you are taking carfilzomib and/or pomalidomide.

- Aspirin or low molecular weight heparin based on your risk for developing a blood clot will be prescribed to reduce or prevent the incidence of blood clots associated with pomalidomide. Your doctor will determine your risk for the choice of agent needed to prevent a blood clot.

Additional medications such as antibiotics, anti-fungal or other medication may be given to you depending on your side effects as determined by your doctor.

The pre-medications are all FDA-approved drugs that are commercially available. Your doctor may also replace other drugs or dosages for the pre-medications based on preference.

Monitoring / Follow-up Procedures:
You will undergo the procedures listed below (called “monitoring” or “follow-up” procedures). They are considered part of your standard medical care and would be performed whether or not you were participating in a research study. These procedures will all take place at the Emory, and will be performed by your study doctor, or a nurse, physician assistant, nurse practitioner, or lab technician. The tests are detailed below. You will be required to keep a pill dairy for the oral drug pomalidomide.

These procedures will be completed on Day One of each cycle (except Cycle One), unless otherwise indicated. The monitoring/follow-up procedures include:

- A review of any medication(s) you are currently taking
- Performance status (how well you are able to do your normal activities)
- A review of any symptoms or side effects you might be having Physical examination and neurologic assessment and questionnaire
- Vital signs (blood pressure, pulse, and temperature) will be recorded
- Weight will be recorded
- Blood samples (about 3 teaspoons) will be taken for routine tests to check your blood counts (numbers of each type of blood cell) and chemistries (to evaluate your overall health status by checking things such as your kidney and liver function) (This can be done the day prior to each Day One.)
- Pregnancy test for women of child bearing potential on within 14 days prior and on day 1 of first cycle and on day 1 of each cycle
- The skeletal survey will only be repeated as needed based on your symptoms.
- X-rays and/or scans to measure a plasmacytoma will be repeated every 12 weeks, to confirm a response or as needed based on your symptoms.
- Blood tests to assess the status of your myeloma will be repeated prior to every cycle

- A 24-hour urine test to assess the status of your myeloma will be repeated prior to each cycle
- A bone marrow aspirate may be repeated to confirm your response to treatment

Routine blood tests to check your blood counts will be performed on day 1 of each cycle and prior to each dose of carfilzomib throughout each 28 day cycle. This includes blood counts (numbers of each type of blood cell) and chemistries. For the visits on Day 1 of each cycle, the procedures will take approximately 2 hours to complete and does not include time needed for the management of your therapy.

RESEARCH-ONLY PROCEDURES FOR ALL SUBJECTS IN THIS STUDY:
The following research-only procedures apply to all subjects involved in this research study.

In addition to the blood test, a bone marrow aspirate will be obtained prior to the start of treatment. The bone marrow aspirate will be usually done routinely (not for research purposes) after transplant for evaluating response. We will use this test for screening and will only be done once at this time point, a sample approximately 20 milliliters or 4 teaspoons will be taken.

End of Study Visit:
Once your participation in the study is stopped, for any reason, you will have an end of study visit with the tests noted below. These procedures are part of your standard medical care (routine clinical care) that would be performed whether or not you were participating in a research study. These tests will be performed by your study doctor, or a nurse, physician assistant, nurse practitioner, or lab technician under your study doctor's supervision. The tests will take about 3 to 4 hours, and will include:

- Physical examination and neurologic assessment with the questionnaire
- Vital signs (blood pressure, pulse, and temperature) will be recorded
- Weight will be recorded
- Performance status (how well you are able to do your normal activities)
- Blood samples (about 2 teaspoons) will be taken for routine blood tests to check your blood counts (numbers of each type of blood cell) and chemistries (to evaluate your overall health status by checking things such as your kidney and liver function)

Once you come off study for any reason, your condition will be followed for an additional 4 weeks. If you are removed from the study for unacceptable adverse events, you will be followed until resolution or stabilization of the adverse event occurs. You will then be contacted every 3 months to check on the status of your health and future treatment.

How will my medicine be provided?
The medicine that you will take will be dispensed by the pharmacy and delivered to the principal investigator or study team member. The principal investigator or health care providers on his/her research team will provide the medicine to you. If you have questions about the medicine, you should ask the principal investigator or study nurse. You may also call the pharmacy if you have questions about the medicine. The number for the pharmacy is included on your medicine package.

You will be taking the study drug home, keep it out of the reach of children or anyone else who may not be able to read or understand the label. Do not let anyone else take the study drug besides you. Please note the pomalidomide intake in the study diary.

Who owns my study information and samples?
If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study.

What are the possible risks and discomforts?
Drugs for cancer are strong and have side effects. As with any experimental procedure, there may be adverse events or side effects that are currently unknown. Side effects can go away shortly after drug administration is stopped, but some risks could be long-lasting, permanent, serious, life threatening, or even cause death. You should talk to your study doctor about any side effects you have while taking part in the study. The risks involved with this study are listed below. You will be kept fully informed of any events that occur during the course of this clinical study which might affect your safety. If there is new information that might affect your safety, you will be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

If there is any new important safety information or other information that could affect your willingness to participate in this study, the study doctor will let you know.

a. Are there any risks from taking part in this study?
There may be risks to being in this study from carfilzomib, pomalidomide, dexamethasone or from some of the procedures or tests done in this study. Also, your condition may get better but it could stay the same or even get worse.

If you participate in this study, you or your family members should tell the study doctor or the study staff immediately if you have any unusual health problems, injuries, or side effects, even if you do not think these problems are caused by the study or by the study drug(s).

If there is any new important safety information or other information that could affect your willingness to participate in this study, the study doctor will let you know.

b. What are the likely risks with carfilzomib

Carfilzomib may cause all, some, or none of the side effects listed below. These side effects can be mild but could also be serious and some may even result in death. There may also be unknown side effects from taking carfilzomib alone or with other drugs you may be taking.

As of 19-Jan-2020 approximately 4694 subjects have received carfilzomib in Amgen-sponsored clinical trials and business-partner-sponsored clinical trials.

As of 03-Apr-2020, approximately 6924 subjects have received carfilzomib in investigator-sponsored trials (ISTs).

As of 19-Jan-2020 since it was first approved for sale, approximately 149785 patients have been prescribed carfilzomib (Kyprolis®) for treatment.

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

- Heart problems, including a history of 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 or 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

Talk to your doctor or nurse if any of these apply to you before using carfilzomib. You may need extra tests to check that your heart, kidneys and liver are working properly.

Conditions You Need To Look Out For

You must look out for certain symptoms while you are taking carfilzomib to reduce the risk of problems. Carfilzomib can make some conditions worse or cause serious side effects. Tell your doctor or nurse as soon as possible if you get any of these:

- Chest pains, shortness of breath, or if there is swelling of your ankles and feet, which may be symptoms of heart problems.
- Difficulty breathing, including shortness of breath at rest or with activity or a cough, rapid breathing, feeling like you can't breathe in enough air, wheezing, or cough, which can be signs of lung problems.
- Extremely high blood pressure, severe chest pain, severe headache, confusion, blurred vision, nausea and vomiting, or severe anxiety, which may be signs of a condition known as hypertensive crisis.
- Shortness of breath with everyday activities or at rest, irregular heartbeat, racing pulse, tiredness, dizziness, and fainting spells, which can be signs of a condition known as pulmonary hypertension.
- Swollen ankles, feet or hands, loss of appetite, passing less urine, or abnormal blood test results, which may be symptoms of kidney problems or kidney failure.
- Irregular heartbeat, kidney failure or abnormal blood test results which may be associated with Tumor Lysis Syndrome, which can be caused by the rapid breakdown of tumor cells.
- A reaction to carfilzomib infusion, which can include the following symptoms: fever, chills or shaking, joint pain, muscle pain, facial flushing or swelling, swelling of the throat, weakness, shortness of breath, low blood pressure, fainting, chest tightness, or chest pain.
- Unusual bruising or bleeding, such as a cut that does not stop bleeding in a normal amount of time or internal bleeding such as coughing up blood, vomiting up blood, dark tarry stools, or bright red blood in your stools.
- 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).
- Yellowing of your skin and eyes, abdominal pain or swelling, nausea or vomiting, which could be signs of liver problems, including liver failure. If you have previously had hepatitis B virus infection, treatment with Kyprolis may cause hepatitis B virus infection to become active again.
- 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/Hemolytic Uremic Syndrome (TTP/HUS).

- Headaches, confusion, seizures, blindness, and high blood pressure (hypertension), which may be symptoms of a neurologic condition known as Posterior Reversible Encephalopathy Syndrome (PRES).
- 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 central nervous system infection known as Progressive Multifocal Leukoencephalopathy (PML).
- Some patients that have Hepatitis B virus (HBV) may have reactivation of the virus while receiving carfilzomib (occurs in 1 in 1000 patients)
- Following a comprehensive analysis of the clinical trials and post market reports, Amgen has determined that acute pancreatitis is a risk associated with carfilzomib.
    - From the carfilzomib clinical trials, there were 12 cases with a possible association to carfilzomib, all of which were serious, 4 led to treatment interruption and 1 led to treatment discontinuation. There was one fatal case which occurred in a patient who experienced worsening renal function that required dialysis, a urinary tract infection, sepsis, and a myocardial infarction on the day he died.
    - From the post-marketing setting, there were 8 cases with a possible association to carfilzomib, all of which were serious, 4 led to treatment interruption and 1 led to treatment discontinuation.
    - In many cases, the co-administration of dexamethasone (which is known to be associated with the development of acute pancreatitis 1,2,3) was present. None of these cases had a fatal outcome.
    - The incidence of acute pancreatitis in Amgen sponsored clinical trials is 0.2% and the post market reporting rate is 29.3 cases per 100,000 person-years.
    - Based on the manufacturer's analysis of the clinical trials and post market analysis, a potential for risk of acute pancreatitis with carfilzomib was reported. Data from clinical trials demonstrate 12 cases of pancreatitis with a 'possible association' all considered as serious adverse events including one fatality related to the adverse event. In the post market setting, 8 cases of pancreatitis were reported, all considered as serious adverse events, no fatality reported.

The chance of these and other side effects happening to you is shown in the table below:

Body System	Very Common (may affect more than 1 in 10 people)	Common (may affect up to 1 in 10 people)	Uncommon (may affect up to 1 in 100 people)	Rare (may affect up to 1 in 1000 people)
Blood	Low red blood cell count, which may cause tiredness and fatigue; Low platelets, which may cause	Fever associated with low white blood cell count	Thrombotic microangiopathy (see 'Conditions you need to look out for') Thrombotic thrombocytopenic purpura (TTP) (see 'Conditions	Hemolytic uremic syndrome (HUS) (see 'Conditions you need to look out for')

Body System	Very Common (may affect more than 1 in 10 people)	Common (may affect up to 1 in 10 people)	Uncommon (may affect up to 1 in 100 people)	Rare (may affect up to 1 in 1000 people)
	easy bruising or bleeding; Low white blood cell count, which may decrease your ability to fight infection		you need to look out for')	
Heart		Heart failure*, and heart problems including rapid, strong or irregular heartbeat; Heart attack	Sudden loss of the 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.	Swelling and irritation of the lining around the heart
Lung	Shortness of breath; Cough, cough with phlegm	Blood clots in the lungs; Fluid in the lungs; Nose bleed; Change in voice or hoarseness; Pain in throat; Wheezing; Pulmonary hypertension (see 'Conditions you need to look out for')	Lung problems (see 'Conditions you need to look out for'); Bleeding in the lungs	Swelling of the throat
Eye		Blurred vision; Cataract		
Gastrointestinal	Diarrhea; Nausea; Constipation; Vomiting	Stomach Pain; Indigestion; Toothache	Bleeding in the stomach and bowels; Blockage of the intestines;	Hole in the stomach, small intestine, or large bowel

Body System	Very Common (may affect more than 1 in 10 people)	Common (may affect up to 1 in 10 people)	Uncommon (may affect up to 1 in 100 people)	Rare (may affect up to 1 in 1000 people)
			Inflammation of the pancreas gland	
General	Tiredness (fatigue); Fever; Swelling of the hands, feet or ankles; General weakness	Chills; Pain; Feeling unwell; Infusion site reactions such as pain, swelling, irritation or discomfort where you received the injection into your vein	Multi-organ failure	
Liver		Liver problems including an increase in your liver enzymes in the blood	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)	
Infections	Respiratory tract infection; Pneumonia; Bronchitis; Inflammation of the nose and throat	Runny nose or nasal congestion; Urinary tract infection; Flu-like symptoms (influenza); Serious infection in the blood; Viral infection; Infection and/or irritation of your stomach and bowels; Lung infection	Severe infection of the blood causing low blood pressure and low blood flow to the different organs Reinfection of the liver with the hepatitis B virus (see 'Conditions you need to look out for')	Infection of the back of the eye (cytomegalovirus).

Body System	Very Common (may affect more than 1 in 10 people)	Common (may affect up to 1 in 10 people)	Uncommon (may affect up to 1 in 100 people)	Rare (may affect up to 1 in 1000 people)
Infusion complications		A reaction to receiving the drug injection into your vein (see: A reaction to carfilzomib infusion in 'Conditions you need to look out for')		
Metabolism	Decreased appetite	Dehydration	Tumor lysis syndrome (TLS) (see "Conditions you need to look out for')	
Bone and Muscle	Back pain; Joint pain; Pain in limbs, hands or feet; Muscle spasms	Bone and muscle pain; Chest pain; Muscle weakness; Aching muscles		
Nervous System	Headache; Dizziness; Numbness	Abnormal sensation such as tingling or decreased sensation in arms and/or legs	Bleeding in the brain; Posterior reversible encephalopathy syndrome (PRES) (see 'Conditions you need to look out for')	
Psychiatric	Insomnia (difficulty sleeping)	Anxiety		
Kidney		Kidney problems, including decreased ability to make urine, and kidney failure needing dialysis		
Skin		Rash; Itchy skin; Redness of the skin;		

Body System	Very Common (may affect more than 1 in 10 people)	Common (may affect up to 1 in 10 people)	Uncommon (may affect up to 1 in 100 people)	Rare (may affect up to 1 in 1000 people)
		Increased sweating		
Tests	Changes to blood tests (decreased blood levels of potassium, increased blood levels of creatinine)	Changes to blood tests (decreased blood levels of sodium, magnesium, protein, calcium or phosphate, increased blood levels of sugar, calcium, uric acid, potassium, bilirubin, or c-reactive protein)		
Immune System			Allergy to carfilzomib	
Blood Vessels	High blood pressure (hypertension)	Low blood pressure (hypotension); Blood clots in the veins; Flushing	Stroke; Bleeding; Extremely high blood pressure (see 'Conditions you need to look out for')	
Ear and labyrinth		Ringing in the ears		

* 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.

The following side effects have been seen in people 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, nausea 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 fatigue, 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.

c. What are the risks of using carfilzomib in combination with other drugs?
Tell the study doctor or the study staff about any drugs you are taking, have recently taken, or are planning to take, including herbal remedies, supplements, and drugs you take without a prescription. The side effects of using carfilzomib in combination with other drugs are unknown at this time. Please discuss any concerns you may have with the study doctor.

d. What are the likely risks with pomalidomide
Pomalidomide will be administered as a capsule, by mouth on Days 1–21, for all cycles. Pomalidomide may be taken at a time of day that is convenient for you. However, it is suggested that you take pomalidomide at approximately the same time of day for consistency. Swallow pomalidomide capsules whole with water at the same time each day. Do not break, chew, or open the capsules. If you miss a dose of pomalidomide, take it as soon as you remember on the same day. If you miss taking your dose for the entire day, take your regular dose the next scheduled day (**DO NOT** take double your regular dose to make up for the missed dose). You should inform your study doctor and/or nurse of any missed doses of pomalidomide. If you take more than the prescribed dose of pomalidomide, you should seek emergency medical care if needed and contact study staff immediately. Females of childbearing potential who might be caring for you should not touch the pomalidomide capsules or bottles unless they are wearing gloves.

Pomalidomide (CC-4047) has been studied in healthy volunteers and in patients with cancer of the blood and other organs of the body as well as in patients with other diseases. As with any other experimental treatment there may be side effects or risks associated with pomalidomide, some of which are not yet known.

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

Very Common Events (>10%): those occurring in more than 10 out of 100 persons who receive pomalidomide:

- Decrease in the number of cells that help your blood to clot
- Pneumonia
- Decrease in a type of white blood cells (with or without fever)
- Muscle cramps
- Changes in bowel movement
- Decrease in the cells carrying oxygen to your body
- Decreased appetite
- Fever
- Pain
- Fatigue (tiredness)
- Nausea
- Dyspnea (shortness of breath)
- Swelling including arms and legs

Common Events (1- 10%): those occurring in 1 to 10 out of 100 persons who receive pomalidomide:

- Infection
- Dizziness
- Vomiting
- Rash

- Abnormal shaking
- Changes in sensations including decreased sense of touch, burning sensation, or tingling
- Sore throat
- Kidney not working well, difficulty in passing urine
- Confusion
- Abnormal blood tests
- Less alert
- Blood clots in legs or lungs
- Itching

Rare (<1%): those occurring in <1 out of 100 persons who receive pomalidomide:
- There are no rare events to report

Other Important Serious Side Effects: (Events that do not meet the criteria for inclusion into above criteria but are considered important enough for subjects to be made aware)
- New cancers including acute myeloid leukemia (AML) (a cancer of the bone marrow which affects your white blood cells have been seen in diseases where AML is considered to be part of the disease progression), Adrenal carcinoma (cancer of the adrenal gland), Bladder transitional cell carcinoma (cancer of the urinary bladder), Renal cell carcinoma (kidney cancer), Myelodysplastic syndrome (MDS: a group of diseases that affect your blood and bone marrow), Skin cancers, and Thyroid cancer.
- Inflammation of your lungs
- Tumor Lysis Syndrome- Tumor lysis syndrome is caused by rapid killing of tumor cells during treatment. When the tumor cells die, they release their contents into the bloodstream. If cell killing is very rapid, this can affect the subject's blood chemistries and the kidneys. In severe cases, this can lead to shutdown of kidney function, requiring dialysis.

If you have any questions or you don't understand any of the side effects, please ask your study doctor.

ADDITIONAL PRECAUTIONS
We do not know if pomalidomide has any effect on your being able to have a child in the future. Please speak with your doctor about family planning options for the future.

Other than the patient, females who are able to become pregnant and males who are able to father a child, should not touch or handle the pomalidomide capsules or the powder they contain.

You should not be donating blood during the study period and for at least 8 weeks after you come off the study.

In order to participate in the study you must register into and follow the requirements of the Pomalyst REMS™ program of Celgene Corporation. This program provides education and counseling on the risks of fetal exposure, blood clots, and reduced blood counts. You will be required to receive counseling, follow the pregnancy testing and birth control requirements of the program that are appropriate for you and take surveys regarding your compliance with the Pomalyst REMS™ program.

Before you consent to participating in this study, your study doctor will discuss with you the full requirements of the Pomalyst REMS Program and must agree to follow.

While in this study, if any physician or healthcare provider, other than the Study Doctor, prescribes medication(s) for you for another condition or reason, or you are taking any: over-the-counter medications; vitamins; herbal, holistic or homeopathic remedies, etc.; you must inform the study doctor or his/her staff immediately. Please also let your Study Doctor know all of your present and past diseases and allergies. This is important because a possible interaction with some medications, vitamins, and remedies may cause serious side effects, and/or may still be unknown.

d. What are the likely risks with Dexamethasone
Dexamethasone has been approved for use in humans since 1971 and a thorough understanding of the side effects has been established.

Very common Events (>10%): those occurring more than 10 out of 100 persons who receive dexamethasone:

- Stomach upset, irritation or stomach ulcers
- Increased blood sugar
- Increased blood pressure and swelling from retaining fluid
- Decreased production of your body's stress hormone cortisol
- Increased susceptibility to infection
- Insomnia (trouble sleeping)
- Mood changes, depression, anxiety
- Restlessness
- Vomiting
- Diarrhea
- Fever
- Decreased platelet count
- Increased risk of cataracts and glaucoma
- Bone thinning (osteoporosis)
- Muscle loss
- Problems with healing
- Weight gain
- Easy bruising
- Irregular or absent menstrual periods
- Headache
- Dizziness
- Increased hair growth
- If you experience any of the following symptoms, let your doctor know immediately:
- Skin rash
- Swollen face, lower legs, or ankles
- Vision problems
- Cold or infection that lasts a long time
- Muscle weakness or cramps
- Black or tarry stool

e. What are the reproductive risks of carfilzomib and pomalidomide:
Female Participants
Pregnant or breastfeeding women, and women planning to become pregnant, should not participate in this study.
If you are unable to become pregnant for one of the following reasons, the use of birth control methods is not required during this study:

- Your healthcare provider has confirmed that you are postmenopausal.
- You have had your uterus, or both ovaries, or both fallopian tubes removed.

If you could become pregnant, you:

- Should let your sexual partner know you are in this study
- Must agree to practice abstinence (not have sex) or use an acceptable method(s) of effective birth control 4 weeks before, during treatment and for an additional 30 days after the last dose of carfilzomib and/or pomalidomide.

- Must discuss your pregnancy prevention method with the study doctor to ensure it is acceptable for you. You should be aware that no one birth control method is 100% effective.

Carfilzomib and/or pomalidomide could decrease the effectiveness of contraceptive methods taken by mouth. There is an increase in the risk of developing a blood clot (venous thromboembolism) with the use of carfilzomib. This is also a risk with some oral contraceptives. You should be aware of this risk when choosing a method of birth control.

Highly effective methods of birth control for Female Participants or their Male Partner include:

- Combined (estrogen and progestogen) hormonal methods: pills, vaginal ring, or skin patch
- Single hormonal methods (progestogen) to stop release of the egg from the ovary: [pills, shots/injections, implants (placed under the skin by a healthcare provider)]
- Intrauterine device (IUD)
- Intrauterine hormonal-releasing system (IUS)
- Surgery to tie both fallopian tubes (bilateral tubal ligation/occlusion)
- Your male partner has had a vasectomy and testing shows there is no sperm in the semen
- Sexual abstinence (not having sex)

  It is not known if carfilzomib and/or pomalidomide is transferred into breast milk. If you are breastfeeding and wish to be in this study, you will be required to discontinue nursing during treatment with carfilzomib and/or pomalidomide and for an additional 30 days after stopping carfilzomib.

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Male Participants

If your female partner is unable to become pregnant for one of the following reasons, the use of birth control measures is not required during this study:

- Her healthcare provider confirmed that she is postmenopausal.
- She has had her uterus, or both ovaries, or both fallopian tubes removed. If you have had a vasectomy and testing shows there is no sperm in the semen, or your female partner has had a surgery to tie both fallopian tubes (bilateral tubal ligation/occlusion), you do not need to use additional methods of contraception during this study. Otherwise, if your female partner could become pregnant, you:
- Should let her know you are in this study.
- Must 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 and/or pomalidomide. You should be aware that no one birth control method is 100% effective.
- Your female partner should also consider using an acceptable method of effective contraception such as:
- Intrauterine device (IUD)
- Intrauterine hormonal-releasing system (IUS)
- Hormonal birth control method: pill, shots/injections, implants (placed under the skin by a healthcare provider), skin patches
- Female barrier method: diaphragm, cervical cap, contraceptive sponge (a female condom is not an option because there is a risk of tearing when both partners use a condom.)

You must not donate sperm during treatment and for an additional 90 days after the last dose of carfilzomib or pomalidomide.

Female and Male Participants

The pregnancy, breastfeeding, and birth control information in this document is specific to carfilzomib and/or pomalidomide. There may be additional risks to an unborn child or breastfed baby from other chemotherapy that you may receive during the study. This may require that you change the type and/or length of time that you

must use birth control or length of time that you must avoid breastfeeding. Please discuss this with the study doctor.

f. What if you become pregnant or breastfeed during the study?
If you decide to participate in this study, you must agree to not become pregnant or to breastfeed.

If you think you are pregnant or inadvertently become pregnant or breastfeed during treatment and for an additional 30 days after stopping carfilzomib and/or pomalidomide, you must tell the study doctor or study staff right away. Treatment with carfilzomib may be stopped. The study doctor will notify Amgen and Celgene of the pregnancy or that you are breastfeeding. You will be asked to provide information on the pregnancy or breastfeeding outcome for you and the baby.

g. What if your partner is pregnant when you begin this study or becomes pregnant during the study?
If your partner is pregnant when you begin this study or becomes pregnant during treatment and for an additional 90 days after stopping carfilzomib and/or pomalidomide, you must tell the study doctor or study staff right away. To prevent exposure of the unborn child to carfilzomib through semen, you will be required to practice sexual abstinence (not have sex), or you must wear a condom during vaginal sex.

The study doctor will notify Amgen and Celgene of the pregnancy and ask to obtain information on the pregnancy outcome for both the mother and baby.

What are the other risks and discomforts associated with this study?
Risks and side effects of venipuncture/intravenous needle insertion:
Infrequent (occurs in 1% to 10% of people - from 1 to 10 out of 100 people): mild pain and discomfort at the injection or needle insertion site as well as possible infection, bleeding, bruising, and soreness.

Rare (occurs in less than 1% or people - less than 1 out of 100 people): severe pain, swelling, infection from the actual injection, dizziness and/or and fainting.

Risks and Side Effects of EKG (Electrocardiogram):
Rare – Occurs in less than 1% of people (less than 1 out of 100 people):
Side effects that may be associated with the EKG electrode placement are skin irritation, redness, and chafing of the skin at the placement site.

Risks and Side Effects of Bone Marrow Aspirate and Biopsy
Possible side effects of a bone marrow aspirate and biopsy include bleeding, infection, bruising, pain or discomfort at the biopsy site and possible side effects from the local anesthetic (pain or bruising at the injection site).

The bone marrow test is performed by using a needle to obtain a small sample of bone marrow from the pelvic bone. The main discomfort associated with this test is pain when the bone marrow is being withdrawn. In order to make the procedure more comfortable, you will get a local anesthetic to numb the area. A mild sedative may also be given to you. While you are sedated, you will be able to respond to commands.

Radiation Risks and Side Effects (Skeletal Survey/X-ray):
You will be exposed to radiation from nuclear medicine, CT scans and other x-rays. These procedures are necessary for your medical care and will occur even if you do not participate in this study. The radiation dose estimate that you will receive is equal to or less than the radiation exposure allowed to be received by a radiation worker for 2 years. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. Although the risk from radiation is cumulative it is not expected to adversely affect your condition or treatment. The Emory University Radiation Safety Committee has reviewed and approved the use of radiation in this research study.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Will I benefit directly from the study?

This study is not designed to benefit you directly. The high-risk myeloma may improve while you are in this study but it may not, and it may even get worse. It is possible that you may not receive any direct benefit from this study. You may receive the information about your health. This study is designed to learn more if the combination of carfilzomib, pomalidomide and dexamethasone will help control the disease. The study results may be used to help others in the future.

Will I be compensated for my time and effort?

Your participation in this study is entirely voluntary and you will not receive any payment for participation. Your participation in the study may result in discoveries or products. The discoveries and products may have commercial value. If there is commercial value, you will not receive any compensation from the discoveries or products.

What are my other options?

Other choices instead of taking part in this study include the use of other forms of maintenance therapy with bortezomib, lenalidomide and dexamethasone (RVD), lenalidomide alone, bortezomib alone, or other experimental programs. Another choice is no maintenance treatment for your cancer and you may be treated at the time myeloma relapses. You should talk to your doctor about each of these choices before you decide if you will take part in this study.

How will you protect my private information that you collect in this study?

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Storing and Sharing your Information

De-identified data from this study may be shared with the research community at large to advance science and health. Data from this study may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Medical Record

If you have been an Emory Healthcare patient before, then you already have an Emory Healthcare medical record. If you have never been an Emory Healthcare patient, you do not have one. An Emory Healthcare medical record will be made for you if an Emory provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory Healthcare medical record you have now or any time during the study.

Emory Healthcare may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory Healthcare medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record.

Tests and procedures done at non-Emory places may not become part of your Emory medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you get ill or injured from being in the study, Emory will help you get medical treatment. Emory and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Ajay K. Nooka at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

Costs

You will not be charged for any tests specifically required for this research study, but you or your insurance company will be billed for tests or procedures that are considered part of your normal cancer care. This includes treatment costs that would be billed if you were not on this study, including but not limited to drugs, routine laboratory tests, x-rays, scans, surgeries, routine medical care, and physician charges.

Payment for drugs and procedures that are considered part of your normal cancer care will be billed to you or your insurance company. Your health insurance company may not pay for these charges because you are in a research study. If your insurance company does not pay for costs associated with this research study that are part of your normal cancer care, then you will be billed for these costs. You are responsible for paying for any insurance co-pays (if applicable to your policy), any deductible indicated by your insurance policy, and any charges your insurance company does not pay. You will not be charged for the study drug (carfilzomib). You and your insurance company will be billed for the costs of pomalidomide and dexamethasone.

So that you do not have unexpected expenses from being in this study, ask your study doctor for a list of the tests or procedures that are considered part of your normal cancer care, including the treatment of side effects.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for.

If you do not have insurance, Emory will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study

You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

You can be taken off the study (with or without your consent) for any of these reasons:

- you experience adverse events
- your condition gets worse
- new information becomes available that necessitates removing you from the study
- funding for the study is stopped
- it is in your best medical interest, in the opinion of your study doctor, for you to stop study participation.

You may be removed from this study if your tumor grows, unacceptable side effects occur, you withdraw your consent, or your doctor or the study sponsor thinks you should stop receiving the study drug. If you do not follow the study instructions given to you by the study doctor, you may be taken off of the study. Amgen Pharmaceuticals, the FDA, and/or the Institutional Review Board may decide to stop the study, and you would then be taken off of the study.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the study.

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information. We will use and disclose your PHI for the administration and payment of any costs relating to subject injury from the study.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- Dr. Nooka is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The research team and the Sponsor may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Food and Drug Administration.
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
    - Study-supporter: Amgen Pharmaceuticals
    - Celgene Pharmaceuticals
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at: [redacted]

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the main study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. The Sponsor, and people and companies working with the Sponsor on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information
Contact Dr. Ajay K. Nooka at [redacted]

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at [redacted]:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____ ____:____ am / pm
Signature of Subject (18 or older and able to consent) **Date** **Time (please circle)**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____ ____:____ am / pm
Signature of Person Conducting Informed Consent Discussion **Date** **Time (please circle)**