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Fred Hutchinson Cancer Center
University of Washington

Consent to take part in a research study:

Isatuximab, Carfilzomib, Pomalidomide, and Dexamethasone (Isa-KPd) for Patients with Relapsed/Refractory Multiple Myeloma

RG1121154

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UWMC Paging Operator
Please ask the operator to page the hematology/oncology fellow on call.

Important things to know about this study.

You are invited to participate in a research study. The purpose of this research is to determine the effectiveness of isatuximab in combination with carfilzomib, pomalidomide, and dexamethasone (KPd) at treating patients with relapsed/refractory multiple myeloma.

People who agree to join the study will be asked to attend up to 30 visits over the course of 24 months. The study involves physical examinations, blood draws, bone marrow biopsies/aspirates, study drug infusions, and PET/CT scans.

We do not know if isatuximab combined with KPd would help treat multiple myeloma, and it could even make your condition/disease worse. Isatuximab combined with KPd could cause side effects such as pneumonia, shortness of breath, fever, infection, and others, as described below in this form.

You do not have to join this study. There are multiple treatment regimens approved by the FDA for people with multiple myeloma who have had previous treatment for their disease, some of which show clear benefits. This study is not yet an approved, standard method of treatment. You can choose to receive standard methods to treat your multiple myeloma instead of participating in this study. We will give you details about the purposes, procedures, risks and possible benefits related to this study. We will explain

other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

We invite you to join this research study.

We invite you to join this research study because you have relapsed or refractory multiple myeloma. Up to 37 people will join this study.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in the study. You are free to say "yes" or "no", or to drop out after joining. If you say "no," you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

Why are we doing this study?

We are doing this study to examine whether or not isatuximab combined with carfilzomib, pomalidomide, and dexamethasone (KPd) is effective at treating people with relapsed or refractory multiple myeloma.

We are studying isatuximab in combination with carfilzomib, pomalidomide, and dexamethason (KPd). Isatuximab (Sarclisa®) is approved by the FDA in combination with pomalidomide and dexamethasone to treat multiple myeloma.

In this study, we want to learn what effects, good or bad, isatuximab combined with KPd has on people with multiple myeloma. If you join this study, we would give you isatuximab combined with KPd and watch carefully for any side effects.

What research tests, procedures, and treatments are done in this study?

If you join this study, we would do these tests and procedures at different times during the study:

- **Medical history.** You will be asked questions about your medical history. This includes ongoing medical conditions you have and drugs you are taking.
- **Physical examination.** Physical exams will assess your overall health status and include measuring your vital signs. This includes temperature, heart rate, breathing rate, and blood pressure. Your weight and your height will also be recorded. You will also be asked how easily you perform daily activities.
- **Routine laboratory tests**. Blood samples will be taken for routine tests. About 2-3 teaspoons of blood will be taken and your blood will be tested for

levels of certain components to see if it is safe for you to receive treatment. Urine will be collected for analysis.

- **Research Laboratory tests.** If you agree, approximately 1 teaspoon of blood will be taken for other research testing at your screening visit. Approximately 3 teaspoons teaspoon of blood would be taken at Day 1 of each cycle on treatment. Approximately 3 teaspoons teaspoon of blood would be taken at the End of Treatment visit. The results will not be reported in your medical record.
    - If you agree, approximately 2 additional teaspoons of blood will be taken for future research purposes.
- **Pregnancy test**. If you are a female who could become pregnant, you will have a pregnancy test. A blood or urine sample will be taken for this test.
- **Tumor imaging.**
    - Positron emission tomography (PET) scan. PET is another imaging technique. It produces a 3-dimensional picture of processes going on at the cellular level in the body. A whole-body PET may be done if there is known/suspected radiographically measurable disease.
- **Bone marrow aspirate and biopsy**. Bone marrow aspiration and biopsy may be done to see if your cancer has spread to the bone marrow. For the bone marrow aspirate, a sample of bone marrow cells is taken by a needle inserted into a bone in your body. For biopsy, a small piece of bone is removed. These tests are done under local anesthesia.
    - If you agree, approximately 2 teaspoons of bone marrow aspiration will be taken for future research purposes.
- **Echocardiogram (ECHO) or multiple-gated acquisition scan (MUGA)**. An ECHO is a non-invasive tool (i.e., it does not break the skin or physically enter the body) that uses sound waves to create a picture of the heart. A MUGA looks at how well the bottom chambers of the heart are pumping blood.

After you have finished taking isatuximab combined with KPd, you would enter the **follow-up** part of the study. The study team will conduct a follow up assessment every three months for up to 5 years per standard of care one of the following occurs; disease progression, initiating a non-study cancer treatment, withdrawing consent, study termination, or becoming lost to follow up. The follow up assessment will consist of a phone call, an email, or looking through your medical records".

Study Calendar

Procedures	Screening (-28 days)	Treatment																End of Treatment	Follow-up (every 3 months)
		Cycle 1 (+/- 3 days per visit)							Cycles 2 through 6 (+/- 3 days per visit)						Cycles 7 + (+/- 14 days per visit)				
		D1		*D8*		*D15*		*D22*	*D1*		*D8*		*D15*		*D1*		*D15*		
Informed Consent	X																		
Medical History	X																		
Physical Exam	X	X							X						X				
Vital Signs	X	X		X		X		X	X		X		X		X		X	X	
Tumor Imaging	X								X						X				
Bone Marrow Biopsy/Aspirate[1]	X																	X	
ECHO/MUGA	X																		
Blood Draws	X	X							X						X			X	
Lab/Monitoring	X	X							X						X			X	
Pregnancy Test (if applicable)	X	X																	
Post-Study Disease Status																		X	X
Treatment Administration																			
Isatuximab		X		X		X		X	X				X		X		X		
Carfilzomib		X		X		X			X		X		X		X		X		
Pomalidomide		X		X		X			X		X		X		X		X		
Dexamethasone		X		X		X		X	X		X		X		X		X		

[1]May be waived by the Primary Investigator

How long would you stay in this study?

If you join this study, you would stay in this study for about 6 years.

You would receive isatuximab and KPd for 24 months. After that, the study team will conduct a follow up assessment about every three months over a period of 5 years to assess your anti-cancer therapy status.

Doctors could take you out of this study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.
- The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

Long-term follow-up means keeping track of someone's medical condition for a long time. If you join this study, we would call you to see how you are doing. We would also ask your doctor to send a copy of your medical records. This information will help us learn about the long-term effects of isatuximab combined with KPd.

You do not have to be in long-term follow-up. You could say "yes" or "no". Either way, you could still join this study. If you drop out of the study, you would be asked if we could call you to see how you are doing.

If you choose not to join long-term follow-up, you would not be contacted regularly, and we would not ask your doctor to send medical records, but we might still need to contact you for some other reason.

What are the side effects (risks)?

In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study. Isatuximab and KPd could cause side effects we do not know about yet. We carefully watch everyone in the study for side effects.

If you join this study, we would tell you if we discover new side effects that could affect you.

This form lists side effects of *individual* drugs. Other side effects could occur when we use these drugs *together*.

Side effects may be mild or very serious. Medicines could be given to help lessen side effects. Many side effects go away soon after you stop taking isatuximab and KPd. In some cases, side effects can last a long time or never go away. There also is a risk of death.

Risks of Isatuximab

Likely side effects (more than 10% of patients) of isatuximab are:

- Infusion related reaction, very common, mostly mild to moderate, but occasionally can be serious and systemic, including life-threatening allergic reactions that may cause cardiac arrest, high or low blood pressure, swelling and redness, and difficulty breathing
- Fatigue
- Nausea
- Anemia (low number of red blood cells), which may cause tiredness, or may require blood transfusions
- Cough
- Diarrhea
- Headache
- Difficulty breathing
- Back pain
- Vomiting
- Fever
- Chills
- Decreased appetite
- Constipation
- Chest discomfort
- Swelling of arms, legs
- Neutropenia (low neutrophil count, a type of white blood cell), which could increase your risk of infections

Less likely side effects (between 5% and 10% of patients) of isatuximab are:

- Insomnia
- Muscle, joint or bone pain
- Flushing
- Pain in extremities
- Thrombocytopenia (low platelet count)
- Pneumonia
- Dizziness
- Stuffy/runny nose
- Abdominal pain
- Nosebleeds
- Wheezing
- Hypercalcemia (increased calcium in the blood)
- Decreased weight
- Increased blood creatinine
- High blood pressure
- Hypokalemia (decreased potassium in the blood)
- Urinary tract infection
- Acute kidney injury
- Weakness
- Distorted sense of taste
- Mouth and/or throat pain

- Peripheral sensory neuropathy (tingling or numbness in the arms or legs)
- Coughing which produces mucus
- Reactivation of a previous infection with a liver virus known as Hepatitis B

Other possible side effects

Some people who received isatuximab in combination with other anticancer drugs have reported other side effects. We do not know if isatuximab caused these side effects. They are:

- Cytokine release syndrome, a condition associated with the release of cytokines, small proteins that are a part of your immune system. Symptoms may include headache, fevers, chills, shortness of breath, rapid heartbeat, changes in blood pressure, and/or muscle aches.
- Development of secondary cancers, including skin cancer and other kinds of cancer
- Tumor Lysis Syndrome (the inability of your body to get rid of chemicals from the dying cancer cells that have been quickly broken down), which may cause kidney damage which may require dialysis

Risks of Carfilzomib

Likely side effects (more than 20% of patients) of carfilzomib are:

- High blood pressure
- Shortness of breath
- Infection, especially when the white blood cell count is low
- Bruising, bleeding
- Anemia (low number of red blood cells), which may cause tiredness, or may require blood transfusions
- Headache
- Nausea and diarrhea
- Pain
- Muscle spasm
- Fever
- Cough, cold symptoms such as stuffy nose, sneezing or sore throat
- Difficulty sleeping
- Tiredness

Less likely side effects (between 4% and 20% of patients) of carfilzomib are:

- Heart stops beating, heart attack, or heart failure which may cause shortness of breath, swelling of ankles, or tiredness
- Damage to the heart
- Bleeding from multiple sites including the brain, which may cause headache or confusion
- Swelling or fluid around the lungs which may cause shortness of breath
- Blood clot
- Infection

- Internal bleeding, which may cause belly pain, black tarry stool or blood in vomit
- Liver damage which may cause yellowing of eyes and skin, or swelling
- Kidney damage which may cause swelling, may require dialysis
- Tumor Lysis Syndrome (the inability of your body to get rid of chemicals from the dying cancer cells that have been quickly broken down), which may cause kidney damage which may require dialysis
- Swelling of arms, legs
- Vomiting
- Constipation
- Muscle weakness
- Chills
- Loss of appetite

Rare but serious side effects (less than 4% of patients) of carfilzomib are:

- Posterior reversible encephalopathy syndrome which may cause headache, seizure, or blindness
- Acute respiratory distress syndrome which may cause damage to the lungs or severe shortness of breath
- Blood clot which may cause bleeding, confusion
- Reaction during or following infusion of the drug which may cause fevers, chills, rash or low blood pressure

Risks of Pomalidomide

Likely side effects (more than 20% of patients) of pomalidomide are:

- Neutropenia (low numbers of neutrophils, a type of white blood cell)
- Anemia (low number of red blood cells), which may cause tiredness, or may require blood transfusions
- Thrombocytopenia (low platelet count)
- Fatigue
- Weakness
- Swelling of arms, legs
- Fever
- Nausea
- Constipation
- Diarrhea
- Back pain
- Chest pain
- Muscle spasms
- Upper respiratory tract infection
- Pneumonia
- Decreased appetite
- Increased levels of calcium in the blood
- Difficulty breathing
- Dizziness
- Peripheral neuropathy (tingling or numbness in the arms or legs)
- Rash

Less likely side effects (between 4% and 20% of patients) of pomalidomide are:

- Chills
- Leukopenia (decreased white blood cells)
- Vomiting
- Muscle, bone, and/or joint pain
- Muscle weakness
- Urinary tract infection
- Sepsis, which may lead to shock, organ failure, and may be fatal
- Decreased levels of potassium in the blood
- High blood sugar
- Decreased levels of sodium in the blood
- Dehydration
- Decreased levels of calcium in the blood
- Cough
- Nosebleeds
- Headache
- Tremor
- Dry skin
- Sweating
- Increased levels of creatinine in the blood
- Weight loss
- Anxiety
- Confusion
- Insomnia
- Kidney failure

Rare but serious side effects (less than 4% of patients) of pomalidomide are:

- Lymphopenia (decreased lymphocytes, a type of white blood cell), which can lead to increased infections

Risks of Dexamethasone

Likely side effects (more than 20% of patients) of dexamethasone are:

- High blood pressure which may cause headaches, dizziness
- Pain in belly
- Infection
- Diabetes
- Loss of bone tissue
- Damage to the bone which may cause joint pain or loss of motion
- Mood swings
- Swelling of the body, tiredness, bruising
- Increased appetite and weight gain in belly, face, back and shoulders
- Difficulty sleeping
- Skin changes, rash, acne

Less likely side effects (between 4% and 20% of patients) of dexamethasone are:

- Blood clot which may cause swelling, pain, shortness of breath

- Kidney stones
- Glaucoma
- Cloudiness of the eye, visual disturbances, blurred vision
- A tear or hole in the bowels which may cause pain or that may require surgery
- Heartburn
- Numbness and tingling of the arms, legs and upper body
- Muscle weakness
- Non-healing wound

Rare but serious side effects (less than 4% of patients) of dexamethasone are:

- Bleeding from sores in stomach
- Broken bones

Radiation risks

Some of the tests that you will have in this research study will expose you to radiation. Everyone receives a small amount of radiation every day called "background radiation". This radiation is natural and comes from space, air, water, soil, and the food you eat. Each year you are exposed to about 3 milliSieverts (mSv) of this background radiation. A milliSievert is a unit of radiation dose. For comparison, the estimated radiation dose from each of these tests is listed below. The risk to your health from this level of radiation exposure is too low to be detectable and may be nonexistent.

18-FDG PET/CT: 19 mSv
Osseous Survey: 1 mSv
Whole-Body CT: 20 mSv

Reproductive risks

Chemotherapy and radiation treatments could cause sterility (unable to have children).

Taking isatuximab and KPd may involve unknown risks to an embryo, fetus (unborn baby) or nursing infant. Therefore, you could not join this study if you are pregnant, if you are planning to become pregnant, or if you are breast-feeding.

If you join this study, you would have to use at least 2 effective methods of birth control or abstain from heterosexual intercourse from the time this form is signed until at least 6 months after the last dose of carfilzomib. If you are already using 2 methods of birth control, you would have to check with the study doctor or a member of the study staff to make sure it is acceptable.

If you became pregnant after joining this study, you would have to notify the study doctor immediately. Participation in this study would end, and you would receive counseling and follow-up throughout the pregnancy and for about 6 months after the child is born.

The effects of isatuximab and KPd on fathering a child are also unknown. Men who join this study must also agree to use 2 or more forms of effective and acceptable birth control or abstain from heterosexual intercourse from the time this form is signed until at least 3 months after the last dose of carfilzomib.

If you are a man and your partner becomes pregnant while you are participating in this study, you would have to notify the study doctor immediately. You would receive counseling and be asked to sign a separate consent form to allow the research team to follow up throughout the pregnancy and for about 6 months after the child is born.

Other possible side effects

Blood Draws
Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or get an infection. Infection rarely happens. There may be redness and irritation at the place where the needle enters your vein.

Non-physical risks

If you join this study, non-physical risks are:

- You might not be able to work.

What are the benefits?

We do not know if this study would help you. We are testing isatuximab combined with KPd to see its effects on people with multiple myeloma. You might get better if you receive isatuximab and KPd, but your condition could stay the same or even get worse. We hope the information from this study will help other people with multiple myeloma in the future.

You have other choices besides this study.

You do not have to join this study. You are free to say “yes” or “no”. Your regular medical care would not change if you decide to say “no”.

You have other choices for treatment. Each of these choices has risks and benefits. You should talk to your doctor or healthcare provider about these choices.

Other choices include: standard chemotherapy, another research study, no treatment, or comfort care.

Enrollment in this study may exclude you from other research studies.

Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Center and University of Washington.
- Genzyme Corporation, the funding source and provider of isatuximab for this study, and its agents.
- Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.

We will do our best to keep personal information confidential. But we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

How is my genetic information protected?

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies.

GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevents health insurance companies or group health plans from:

•Asking for genetic information obtained in research studies, or

•Using genetic information when making decisions regarding your eligibility or premiums

GINA does not help or protect against genetic discrimination by companies that sell life, disability or long-term care insurance.

Would we pay you if you join this study?

There is no payment for being in this study.

Would you have extra costs if you join this study?

If you join this study, you would **not** be billed for:

- Cost of isatuximab
- Cost of research lab tests

What if you get sick or hurt after you join this study?

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact your study doctor. They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You would not lose any legal right to seek payment for treatment if you sign this form.

What will my information and/or tissue samples be used for?

Your information and tissue samples (such as blood and tumor cells) will be used for the purposes of this study.

Your tissue samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your tissue samples.

During this study, if the researchers learn new information that could possibly be important to your general health or to your disease or condition, they will not be able to share that information with you because the tests are investigational.

In addition, be aware that by agreeing to participate in this study, your information or tissue samples could be used for future research studies or sent to other investigators for future research studies without additional consent from you. These future research studies will be reviewed by an oversight group known as an institutional review board

if required by law. The information that identifies you will first be removed from your information or tissue samples. If you do not want your information or tissue samples to be used for future research studies without your consent, you should not participate in this study.

Your rights

- You do not have to join this study. You are free to say "yes" or "no".
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we might learn new information that you need to know. For example, some information may affect your health or well-being. Other information might make you change your mind about being in this study. If we learn these kinds of information, we would tell you.
- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). Your regular medical care would not change. You would have no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.
- If you decide to drop out, we would want you to tell the study doctor. The doctor could tell you about the effects of stopping isatuximab and KPd. You and the doctor could talk about the follow-up care and testing that would help the most.
- Before you leave the study, the doctor might ask you to continue in the long term follow-up part of the study.

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.

Your responsibilities

If you join this study, you would have some responsibilities.

- Follow the schedule of study visits and procedures.
- Take study medications as directed.
- Prevent pregnancy.
- Tell us about side effects.

For more information

If you have questions or concerns about this study, you can talk to your doctor anytime. Other people you could talk to are listed below.

If you have questions about:	**Call:**
This study (including complaints and requests for information)	(206) 606-7348 (Dr. Andrew Cowan)
If you get sick or hurt in this study	(206) 606-7348 (Dr. Cowan)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	(206) 606-1377 (Patient Financial Services, Fred Hutchinson Cancer Center)

Emergency number (24 hours): (206) 598-6190

Read each question and think about your choice. When you decide on each question, please circle **YES** or **NO**.

Do you agree to donate your blood samples, tissue, and information to study this treatment regimen, while on this trial?

(circle one)

YES **NO**

Signatures

Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask any questions you have;
- had the opportunity to discuss the research with the person obtaining consent; and
- agree to participate in this study.

Participant (age 18+):

_____	_____	_____
Printed Name	Signature	Date

Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent signature:

_____	_____	_____
Printed Name	Signature	Date

If you served as an interpreter or impartial witness during the consent process, sign below to indicate you attest to the accuracy of the presentation and the participant's apparent understanding of and willingness to participate in the research.

Impartial Witness or Interpreter:

_____	_____	_____
Printed Name	Signature	Date

Protocol: RG1121154
Current consent version date: 04/22/2024
Previous consent version date: 02/20/2024
Copies to: Researcher's file
Subject
Subject's medical record