IRB# 1618875

University of California Davis Health
Permission to Use Personal Health Information for Research

Study Title (or IRB Approval Number if study title may breach subject's privacy):

UCDCC#289: A Phase Ib/II Study of Selinexor Plus Pembrolizumab in Cisplatin-Ineligible or Cisplatin-Refractory Patients with Advanced Urothelial Carcinoma

Principal Investigator Name:

Mamta Parikh, MD

Sponsor/Funding Agency (if funded):

UCDCCC/ Karyopharm Therapeutics

A. What is the purpose of this form?

State and federal privacy laws protect the use and release of your health information. Under these laws, the University of California or your health care provider cannot release your health information for research purposes unless you give your permission. Your information will be released to the research team which includes the researchers, people hired by the University or the sponsor to do the research and people with authority to oversee the research. If you decide to give your permission and to participate in the study, you must sign this form as well as the Consent Form. This form describes the different ways that UC Davis Health can share your information with the researcher, research team, sponsor and people with oversight responsibility. The research team will use and protect your information as described in the attached Consent Form. However, once your health information is released by UC Davis Health it may not be protected by the privacy laws and might be shared with others. If you have questions, ask a member of the research team.

B. What Personal Health Information will be released?

If you give your permission and sign this form, you are allowing your health care provider to release the following medical records containing your Personal Health Information. Your Personal Health Information includes health information in your medical records, financial records and other information that can identify you.

☑ Entire Medical Record	☐ Lab & Pathology Reports	☐ Emergency Department Records
☐ Ambulatory Clinic Records	☐ Dental Records	☐ Financial records
☐ Progress Notes	☐ Operative Reports	☐ Imaging Reports
☐ Other Test Reports	☐ Discharge Summary	☐ History & Physical Exams
☐ Other (describe)	☐ Consultations	☐ Psychological Tests

C. Do I have to give my permission for certain specific uses?

Yes. The following information will only be released if you give your specific permission by putting your initials on the line(s).

___I agree to the release of information pertaining to drug and alcohol abuse, diagnosis or treatment.
___I agree to the release of HIV/AIDS testing information.
___I agree to the release of genetic testing information.
___I agree to the release of information pertaining to mental health diagnosis or treatment.

D. Who will disclose and/or receive my Personal Health Information??

Your Personal Health Information may be shared with these people for the following purposes:

1. To the research team for the research described in the attached Consent Form;
2. To others at UC with authority to oversee the research
3. To others who are required by law to review the quality and safety of the research, including: U.S. government agencies, such as the Food and Drug Administration or the Office of Human Research Protections, the research sponsor or the sponsor's affiliate organization, or government agencies in other countries.

E. How will my Personal Health Information be shared for the research?

If you agree to be in this study, the research team may share your Personal Health Information in the following ways:

1. To perform the research
2. Share it with researchers in the U.S. or other countries;
3. Use it to improve the design of future studies;
4. Share it with business partners of the sponsor; or
5. File applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

F. Am I required to sign this document?

No, you are not required to sign this document. You will receive the same clinical care if you do not sign this document. However, if you do not sign the document, you will not be able to participate in this research study.

G. Optional research activity

If the research I am agreeing to participate in has additional optional research activity such as the creation of a database, a tissue repository or other activities, as explained to me in the informed consent process, I understand I can choose to agree to have my information shared for those activities or not.

☑ I agree to allow my information to be disclosed for the additional optional research activities explained in the informed consent process.

H. Does my permission expire?

This permission to release your Personal Health Information expires when the research ends and all required study monitoring is over.

I. Can I cancel my permission?

You can cancel your permission at any time. You can do this in two ways. You can write to the researcher or you can ask someone on the research team to give you a form to fill out to cancel your permission. If you cancel your permission, you may no longer be in the research study. You may want to ask someone on the research team if canceling will affect your medical treatment. If you cancel, information that was already collected and disclosed about you may continue to be used for limited purposes. Also, if the law requires it, the sponsor and government agencies may continue to look at your medical records to review the quality or safety of the study.

J. Signature

Subject

If you agree to the use and release of your Personal Health Information, please print your name and sign below. You will be given a signed copy of this form**.**

_____

Subject's Name (print)--*required*

_____ _____

Subject's Signature Date

Parent or Legally Authorized Representative

If you agree to the use and release of the above named subject's Personal Health Information, please print your name and sign below.

_____ _____

Parent or Legally Authorized Representative's Name (print) Relationship to the Subject

_____ _____

Parent or Legally Authorized Representative's Signature Date

Witness

If this form is being read to the subject because s/he cannot read the form, a witness must be present and is required to print his/her name and sign here:

_____

Witness' Name (print)

_____ _____

Witness' Signature Date

UNIVERSITY OF CALIFORNIA, DAVIS
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

STUDY TITLE: UCDCC#289 - A Phase Ib/II Study of Selinexor Plus Pembrolizumab in Cisplatin-Ineligible or Cisplatin-Refractory Patients with Advanced Urothelial Carcinoma (Protocol Dated: 06/03/22)

Principal Investigator: Mamta Parikh, MD
Department: Hematology/Oncology

CALIFORNIA EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a medical research study. As an experimental subject, you have the right to know:

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
  - Any drug or device to be used.
  - Any common or important discomforts and risks.
  - Any benefits you might expect.
  - Other procedures, drugs, or devices that might be helpful, and their risks and benefits compared to this study.
  - Medical treatment, if any, that is available for complications.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document**.**

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at [redacted] If you are unable to the reach the Principal Investigator of this study, Mamta Parikh, M.D., please contact the clinical research coordinator (CRC) responsible for your care. The CRC's contact information will be provided to you. The CRC will assist you in contacting another investigator for this study. For non-emergency issues you can call the UCDMC Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to the medical oncologist on call. In the case of an emergency, dial 911 from any phone.

UC Davis Contact information is summarized below:
Mamta Parikh, M.D. [redacted]
24-hour phone number: (916) 734-2011 **(ask for the medical oncologist on call)**

APPROVED by the Institutional Review Board at the University of California, Davis	
Protocol	APPROVED
1618875	July 25, 2022

This research has been reviewed and approved by an Institutional Review Board ("IRB"). Information to help you understand research is on-line at http://www.research.ucdavis.edu/policiescompliance/irb-admin/ .You may talk to an IRB staff member at (916) 703-9151, hs-IRBAdmin@ucdavis.edu , or at 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817 for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

INTRODUCTION

What is a research study?
A research study is an experiment meant to answer specific questions, such as:

- Does a new medication work better?
- Is a new medication safe?
- Does a new medication work better than what we have now?

You are being invited to take part in a research study because you are more than 17 years old and have cancer of your urinary system (urothelial) that has spread. Your cancer has either spread locally, near where it started, or has spread to other parts of your body. Another factor that makes you potentially eligible for this study is that you are not eligible to receive the chemotherapy drug Cisplatin, or you have been given Cisplatin and your cancer has gotten worse.

This study is being sponsored by UC Davis Comprehensive Cancer Center. This means that UC Davis doctors have developed the rules for the study (study protocol) and UC Davis doctors are in charge of the study. A drug company called Karyopharm makes the study drug Selinexor and is providing money for the study.

In addition to getting information from this consent form, a doctor will explain the study to you. You have the right to know about everything that will happen, or might happen, to you during the study before you decide to participate. This is called "Informed Consent." Please take as long as you wish to make your decision. It may help to discuss the study with your family, friends or your personal doctor. You can also ask more questions of the study staff at any time.

In studies like this, the patients who volunteer to participate are called "subjects." The doctor in charge of the study is called the "study doctor" or "investigator." The study doctors and scientists who run the study are called "researchers", and other people who help run the study are call the "research team."

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to test a combination of two drugs to treat your type of cancer. One of the two drugs is called Pembrolizumab. This drug has already been approved by the Food and Drug Administration (FDA) to treat your type of cancer. The other drug is called Selinexor and it has **not** been FDA approved to treat your type of cancer. In this study, both drugs will be used together. Because this combination has never been tested or approved, it is called "experimental." We want to know if this combination of drugs is both safe and effective. We also want to know if these drugs work better or worse than other treatments for your type of cancer.

This study has two parts called "Phases." The two phases are the Dose Escalation Phase and the Dose Expansion Phase.

Dose Escalation Phase

This first part of this study is called is the "Dose Escalation Phase" (Phase1b). In a dose escalation phase, the researchers determine the right amount of the drug (dose) that should be given to the patients. This is done by first selecting a small number of patients and giving them increasingly larger amounts of a drug. In this study, 6 to 12 patients will be selected to receive different doses of the study drug Selinexor. Each of the patients will also receive the standard dose of the approved drug Pembrolizumab. The first dose of Selinexor will be in an amount that has been given to patients in the past and has not caused any serious side effects. The dose will be increased slowly until the highest safe dose is determined. Patients will receive Selinexor once every week. Selinexor will be given to patients as pills that are swallowed. Patients will receive Pembrolizumab once every three weeks as an injection (shot). Unless a study doctor determines that patients should stop treatment, this phase will last about six weeks.

Dose Expansion Phase

The second phase of the study is called the "Dose Expansion Phase" (Phase 2). After the highest safe dose of the two study drugs combined is determined, 15 to 21 additional patients will be enrolled in the study. These new patients will be added to the patients from the previous phase and all will be treated with the maximum safe amounts of the drug determined during the Dose Escalation Phase. The patients who participated in the Dose Escalation Phase will continue receiving the two study drugs in the same way, and on the same schedule as in the previous phase. The newly enrolled patients will begin receiving the study drugs in the same way, and on the same schedule. Unless a study doctor determines that treatment should be stopped, the patients who participated in the Dose Escalation Phase will be in the study for about 24 months. Those who enroll the Dose Expansion Phase will be in the study for about 22 months.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

We plan to enroll up to 27 people in this study here at UC Davis.

BEFORE YOU BEGIN THE STUDY

Pre-Study Screening Tests

If you agree to participate in the study, you will be asked to sign this consent form and then participate in "Pre-study Screening Tests" to determine if you meet all of the requirements to be enrolled in the study. Many of the tests, procedures or examinations are part of normal cancer care, and you may have already had them. If you have already had any of these tests, procedures or examinations, you might not have to repeat them. This will be up to your study doctor. Any of the pre-study tests that are performed, or need to be repeated, will be done for the sole purpose of the study. Other than the routine blood draws, the only test that might cause discomfort is the tissue biopsy. A tissue biopsy will only be required if a sample has not been collected in the past or is not adequate for study purposes.

The pre-study screening tests are listed below.

- Discussion of this study and review and signing of this Informed Consent Form
- Recording of your demographic information, including your age, sex, and race/ethnicity
- Review of your medical and surgical history, including previous cancer treatments and any medications (including herbal or dietary supplements) you are taking or have taken. If you have medical records from another clinic or hospital, you will be asked to get copies of these records, or your study doctor may be able to request them on your behalf.
- Complete physical examination will be performed that will include measuring your vital signs (blood pressure, breathing rate, pulse, body temperature, oxygen
- saturation), and recording your height and weight
- ECOG performance status/an evaluation of your ability to carry out daily activities
- Imaging CT scans of your internal organs, including chest, abdomen and pelvis (CAP). A CT scan is an X-ray scan that gives off radiation.
- Pre-treatment tissue biopsy only if no tissue previously collected is available and adequate.
- Research blood sample collection
- Blood will be drawn for routine safety laboratory tests (including blood cell counts, liver and kidney functions, and thyroid test).
    - Your blood will be tested for certain types of viral infections, including the human immunodeficiency virus (HIV; the virus that causes acquired immunodeficiency syndrome [AIDS]). Your doctor may ask you to sign a separate Informed Consent Form to ask for your permission to check your blood for HIV. You will not be able to take part in this trial if you are infected with HIV or if you refuse to be tested for HIV

Description of Pre-study Screening Tests:

- **Blood drawing (venipuncture):** Blood sample will be drawn by inserting a needle into a vein in your arm. Each sample will be approximately 2-5 teaspoons. The total amount of blood to be drawn will depend on how long you are in the study.
- **CT Scan:** You will have a computed tomography (CT) scan of your chest, abdomen, and pelvis. CT scans are also called CAT scans (computerized axial tomography). A CT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. You will need to lie still on a table with your body inside a large doughnut shaped machine. The table will move and the machine will make clicking and whirring noises as the pictures are taken. Each CT scan will take about 15 minutes to a half-hour.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

Below is a complete list of tests and procedures that will occur during the study. Some of these tests and procedures will happen only during Pre-study Screening. Others will be repeated several times during your treatment. Those patients enrolled in the Dose Escalation Phase will have more tests and procedures than those who only participate in the Dose Expansion Phase.

If you decide to participate in this study, you will be asked to do the following:

- Physical examination: Pre-study, at the beginning of each treatment, and post treatment
- Performance status (measures how well you are able to carry out ordinary daily activities): Pre-study, prior to the start of each treatment and after the completion of each treatment
- Evaluation for side effects from the treatment and recordings of these side effects: prior to the start of each treatment and after the completion of each treatment
- Review of medications: Pre-study, prior to the start of each treatment and after the completion of each treatment Blood tests to check your blood counts, kidney function, liver function, electrolytes on pre-study, prior to the start of each treatment and after the completion of each treatment
- Blood test to check your thyroid, pre-study, prior to the start of each treatment and after the completion of each treatment Blood test to check for hepatitis and HIV - Pre-study
- Blood draw for research blood evaluation pre-study and prior to the start of each treatment
- Tumor evaluation: Pre-study and as needed on treatment.
- Follow-up: Safety visit, 7 days post treatment discontinuation

Treatment Cycles

Treatment cycles help the doctors and the research team keep track of your health and safety. In this study, a treatment cycle is three weeks long. The Treatment cycles begin when you are enrolled in the study and receive your first dose of the study drugs. During each cycle, you will receive three doses of Selinexor and one dose of Pembrolizumab. At the end of each cycle, you will have exams and tests to monitor your health and safety. These tests and exams appear in the middle column of the chart below.

Safety Visit After Completion of All Study Treatment

After you complete your last dose of the study drugs, you will have a Post-treatment Safety Visit about one week later. A study doctor will examine you and you will have blood tests. This visit is simply to monitor your progress and find out if you are having any problems associated with the medications you received during the study.

The chart/table that follows this section shows all of the test and procedures and when they will happen.

Evaluation	**Prior to enrollment**		**Prior to Treatment** (3-week cycles)	**After Treatment**	**After Completion of All Study Treatment**
Each cycle is 21 Days	**Screening (# days prior to first dose)**		**All Cycles**		**Safety Visit**
Scheduling Window (days)	**≤ 28**	**≤ 14**	**21 days ± 3**		**± 7**
Sign Informed Consent Form	X				
History					
Medical History	X		X		X
Clinical/Laboratory/Assessments					
Physical Exam		X	X		X
Vital Signs		X	X		X
Adverse events and medication collection			Continuously		
Complete Blood Cell Count Collection		X	X		X
Serum Chemistry Blood Collection		X	X		X

Evaluation	Prior to enrollment		Prior to Treatment (3-week cycles)	After Treatment	After Completion of All Study Treatment
Each cycle is 21 Days	**Screening (# days prior to first dose)**		**All Cycles**		**Safety Visit**
Scheduling Window (days)	**≤ 28**	**≤ 14**	**21 days ± 3**		**± 7**
Thyroid Blood Test		X	X		X
Hepatitis B/C and HIV Blood Tests	X				
Pregnancy Test (if applicable)		X			
CT Imaging Scans of Chest, Abdomen/Pelvis[2]	X			X[2]	
Research Samples					
Pre-treatment Tissue Biopsy	X[1]				
Blood Sample for Research[3]		X	X[3]		X[3]
Study Treatment Administration					
Selinexor, every week			X		
Pembrolizumab IV, every 3 weeks			X		

[1] If previously collected tissue is available no biopsy needed
[2]CT assessment will be performed every 6 weeks for the first 4 cycles, then every 12 weeks.
[3] Blood samples for research will be obtained on Day 0, Day 8 (±3 days) and Day 21 (±3 days) of Cycle 1, and when you come off all study treatment (±7 days).

Study location: UC Davis is currently coordinating the enrollment of patients for this study at the sites listed below. We anticipate that your treatment will be administered (given) at the site of your enrollment.

UC Davis Medical Center
2315 Stockton Blvd.
Sacramento, CA 95817

UC Davis Comprehensive Cancer Center
4501 X Street
Sacramento, CA 95817

HOW LONG WILL I BE IN THE STUDY?

The rules of the study (study protocol) call for a maximum of 24 months of treatment. You will be asked to participate for as long as your cancer is not getting worse and you are not having unmanageable side effects. The study doctor may decide to stop treatment if he or she believes it is not in your best intertest to continue. After you finish you last dose of study drugs, you will be asked to return to the office for at least one follow-up visit. Other visits could be scheduled if the study doctor believes it is necessary. After your final visit, study staff will continue to collect information about your cancer and any further treatment you receive for the rest of your life.

CAN I STOP BEING IN THE STUDY?

Yes. You can decide to stop the study at any time and it will not be held against you. Tell your study doctor if you are thinking about stopping or decide to stop. Your doctor will tell you how to stop safely. It is important to tell the study doctor if you are thinking about stopping so any risks from the treatment can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

Your study doctor may stop you from taking part in this study at any time if he or she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

There may be other reasons to stop your participation in this study that are not known at this time. If you stop participating in the study, or the study ends, you will stop receiving the study drug(s) and may be asked to come back for final tests and procedures. If you choose to stop taking the study drug before the study ends, you should discuss the following options with the study doctor:

- You can continue to visit the study doctor for study related procedures or tests.
- You can stop study related visits but allow the study doctor or his/her study staff to obtain information about your health by reviewing your medical records, by contacting you, a family member or a legal representative, or through other means as allowed by local law.
- You can completely leave the study and have no more contact with the study doctor and his/her study staff for study related procedures or questions as of the date of your request.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THE STUDY?

Pembrolizumab

What is known about this study drug?
Pembrolizumab, which is approved in the USA and some other countries, is available by prescription to treat several different cancers, but may not be approved to treat your type of cancer. Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e. causing hospitalization or be life threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

Side effects associated with the use of pembrolizumab

Very Common (> 20%)

- Itching of the skin
- Loose or watery stools
- Cough

Common side effects (≥ 10% to 20%)

- Joint pain
- Fever
- Back pain
- Rash
- Low level of salt in the blood that may cause you to feel tired, confused, have a headache, muscle cramps and/or feel sick to your stomach
- Pain in your belly
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools
- Loss of skin color

Uncommon serious adverse (1% to 5%)

- Inflammation of the lungs, so you may feel short of breath and cough (pneumonitis)
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e. peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection (Severe skin reactions, including Stevens-Johnson syndrome or toxic epidermal necrolysis)
- Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools (hypothyroidism)
- Infusion reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion (anaphylaxis, a serious, potentially life threatening allergic reaction)
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus (colitis)

Side effects associated with the use of pembrolizumab – Continued

Rare, Serious adverse events (≤ 1%)

- Inflammation of the kidney so you may less urine or have cloudy or bloody urine, swelling, and low back pain (nephritis)
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting. (Hypophysitis)
- Adrenal glands (on top of the kidneys) that may not make enough hormone which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan (adrenal insufficiency)
- Type I diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and vomiting that gets worse when you eat (pancreatitis)
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine (hepatitis)
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches (uveitis)
- Inflammation of the muscles so you may feel weak or have pain in your muscles (myositis)
- Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to the legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis (Guillain-Barré syndrome)
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting (myocarditis)
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis)
- A condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing(myasthenic syndrome/myasthenia gravis including exacerbation)
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs (sarcoidosis)
- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness (encephalitis)
-

Side effects associated with the use of pembrolizumab – Continued

Rare, Serious adverse events (≤ 1%) – Continued

- Inflammation of the spinal cord which can disrupt the normal responses from the brain to the rest of the body, and from the rest of the body to the brain, resulting in symptoms such as paralysis and sensory loss. (myelitis)
- Inflammation of the blood vessels (vasculitis). Symptoms will depend on the particular blood vessels that are involved in the inflammatory process, for example, if it is your skin, you may get a rash. If your nerves are not getting enough blood, you could have numbness and weakness. You may also experience fever, weight loss, and fatigue.
- Low levels of parathyroid hormone (a hormone made by 4 tiny glands in your neck) which may result in low blood calcium and cause muscle cramps or spasms; fatigue or weakness; numbness, tingling or burning in your fingertips, toes or lips (hypoparathyroidism)

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis)
- Severe responses of the immune system that cause the body to attack its own blood cells, spleen, liver, lymph nodes, skin and brain. This may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma.(hemophagocytic lymphohistiocytosis)
- Changes in eyesight, eye pain, whitish patches on the skin and hearing loss (Vogt- Koyanagi-Harada syndrome)
- Inflammation and scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver). This can cause symptoms similar to those seen with inflammation of the liver (hepatitis) such as pain in right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis).

In addition:

- Allergic reaction (may include skin swelling and/or swelling of the face or throat and could be severe or life threatening)

If you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GvHD), which may include diarrhea, skin rashes, and liver damage, after receiving pembrolizumab. Sometimes this condition can lead to death.

If you have had a solid organ transplant (for example, if you have received a kidney or heart transplant), you may experience rejection of the transplanted organ. Your doctor will monitor you and should tell you what signs and symptoms you should report depending on the type of organ transplant that you have had.

Patients treated with pembrolizumab BEFORE going on to receive an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), should inform their transplant physicians that they have received pembrolizumab in the past.

In patients with any hematologic malignancy (cancers of the blood like Hodgkin lymphoma, multiple myeloma): there is a potential for an increased risk of severe complications following allogeneic stem cell transplant in patients who previously received pembrolizumab BEFORE an allogeneic stem cell transplant.

Reports of clotting of blood within the liver and severe graft versus host disease (which can include skin, liver and gastrointestinal symptoms), including death, have been received for patients who received pembrolizumab BEFORE an allogeneic stem cell transplant.

Side effects associated with the use of pembrolizumab – Continued

Patients with multiple myeloma who were treated with pembrolizumab in combination with either pomalidomide or lenalidomide (drugs related to thalidomide which affect the body's immune system) and dexamethasone (a steroid) had an increased number of serious side effects and deaths as compared to patients who received only dexamethasone and either pomalidomide or lenalidomide

Side effects associated with the use of selinexor

Uncommon Side Effects (1% to 5%)

- Fever with a decrease in white blood cells (Febrile neutropenia)
- Low levels of blood platelets (Thrombocytopenia)
- Low levels of red blood cells (Anemia)
- Fatigue
- Vomiting
- Nausea
- Diarrhea
- Inflammation of the lungs in which the lungs become heavy (Pneumonia)

Side effects associated with the use of selinexor

Uncommon Side Effects (1% to 5%) Continued

- Dehydration

Rare, Side Effects (≤ 1%)

- Decrease in white blood cells (Neutropenia)
- Clouding of the lens of the eye (Cataracts)
- Blurry vision
- Fever
- General weakness or lack of energy
- Abdominal pain
- Constipation
- Lung infection
- Presence of bacteria in the blood (Bacteremia)
- Coughing and chest discomfort, inflammation of the bronchi (Bronchitis)
- Upper respiratory tract infection
- Inflammation of the stomach (gastroenteritis)
- Urinary tract infection
- Weight loss
- Decreased appetite
- Elevated creatinine in blood
- Fainting
- Dizziness
- Confusion
- Mental status changes
- Difficulty breathing
- Nose bleeds
- Blood infection (sepsis)
- Low sodium levels in the blood
- Delirium
- Septic shock (life-threatening condition that happens when your blood pressure drops to a dangerously low level after an infection)

General Risks:

Blood draw Risks: Routine laboratory tests and the research blood draws may result in bruising, infection and minor pain or discomfort comparable to a needle prick.

Biopsy Risks: Risks of biopsy include infection, bleeding and pain at the biopsy site. Your physician and/or surgeon will explain this procedure and its side effects. You will be asked to sign a separate consent form for this procedure.

General Risks:

CT scan risks: CT scans involve the risks of radiation. In addition, if contrast material (iodine dye) is used, there is a slight risk of developing an allergic reaction, from mild (itching, rash) to severe (difficulty breathing, shock, or rarely, death). Having a CT scan may mean some added discomfort. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner, or by lying in one position for a long time.

HIV testing risks: Being tested for HIV may cause anxiety regardless of the test results. Receiving positive results may make you very upset. If other people learn about the positive test results, you may have trouble obtaining insurance or employment.

IV Inserted in the Vein risks: Inserting a needle into a vein to inject medication may cause inflammation, pain, bruising, bleeding, or infection.

Radiological risks: This study involves a radiation exposure that is higher than most other diagnostic tests using ionizing radiation. The exposure to radiation from this procedure might result in a slight increase in cancer risk in normal healthy individuals. However, since you already have cancer, a risk estimate cannot be accurately determined.

Reproductive Risks: If you become or think you might be pregnant during the study, tell your study doctor immediately.

For female participants who have the potential to become pregnant:
There are/may be risks to a fetus if you become pregnant while participating in this study. The potential risks to a fetus or a nursing child are not known.

If you are pregnant or nursing a child you cannot participate in this trial. You will be tested to see if you are pregnant and you must confirm that you do not intend to become pregnant during the trial. If you become pregnant or suspect being pregnant during study treatment or within 4 months after completing study treatment, you must inform the Study Doctor immediately, and you will need to stop taking the study drug immediately. You will not continue study treatment; however, your study doctor will want to follow your pregnancy. You may be asked to sign another consent form so information can be collected about the outcome of your pregnancy.

Premenopausal females who can become pregnant must agree to either practice total abstinence or use effective contraception before participating in this study. The rhythm method, “natural family planning”, and withdrawal are not acceptable methods of contraception for this trial. Effective contraception for this study includes: male condom, female condom, contraceptive sponge, contraceptive diaphragm, combined oral contraceptive pill, contraceptive patch, contraceptive vaginal ring, progestin-only pill, injectable, hormonal intrauterine device, non-hormonal intrauterine device, contraceptive implant, male sterilization, female sterilization (including hysterectomy).

You must use contraception, at least ***72 hours*** before starting study treatment unless you abstain from sexual intercourse. You must use contraception during study treatment and for at least four months after stopping study treatment.

General Risks:

For male participants with female partners who have the potential to become pregnant:
There may be risks to the fetus if your partner is pregnant or becomes pregnant while you are in this study. You and your partner must either practice total abstinence or use effective contraception before participating in this study. The rhythm method, "natural family planning", and withdrawal are not acceptable methods of contraception for this trial. Effective contraception for this study includes: male condom, female condom, contraceptive sponge, contraceptive diaphragm, combined oral contraceptive pill, contraceptive patch, contraceptive vaginal ring, progestin-only pill, injectable, hormonal intrauterine device, non-hormonal intrauterine device, contraceptive implant, male sterilization, female sterilization (including hysterectomy)

You should also refrain from donating semen during therapy and for ***four months*** after stopping the therapy.

There is theoretical concern that study treatment can result in sperm abnormalities and/or can transmit harmful substances in the semen during sex. Therefore, if you are a male, you must remain abstinent or to use a condom, even if you have undergone vasectomy, and to advise your female partners of childbearing potential to use highly effective contraception while you are receiving study treatment and for four months after you stop study treatment. You must tell your study doctor or study personnel immediately if your partner becomes pregnant during this time.

If your partner becomes pregnant or suspects becoming pregnant during study treatment or within four months after completing study treatment, you must inform the Study Doctor immediately. Your Study Doctor may want to follow the pregnancy and may ask your partner to sign a consent form so he/she can collect information about the outcome of the pregnancy.

Unknown Risks:
The experimental treatments may have side effects that no one knows about yet. The researchers will tell you of new information that might make you change your mind about participating in the study.

For more information about risks and side effects, ask your study doctor.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You may not benefit from taking part in this research. The information we get from this study may help us to learn more about this study treatment, and this may help future cancer patients.

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

Your alternative is not to take part in this study. If you choose not to take part in this study, your future care will not be affected. Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Participating in a different study, if available
- Getting no treatment
- Getting comfort care, also called palliative care
    - This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that your personal information will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law.

If information from the study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your research records for research, quality assurance, and data analysis include:

- The investigators involved in the conduct of this study and their designees
- The funding source of this study Karyopharm and their representatives
- The National Cancer Institute (NCI)/CTEP
- The Food and Drug Administration (FDA)
- The UC Davis Institutional Review Board (IRB)
- The manufacturer of selinexor (Karyopharm)

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 study results. You can search this Web site at any time.

If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission. Your medical records may become part of the research record. If that happens, your medical records may be looked at by the sponsor of this study and government agencies or other groups associated with the study. They may not copy or take your personal health information from your medical records unless permitted or required by law.

If you agree to participate in this research study, a signed copy of this consent document and the privacy authorization form may be filed in your electronic medical record (EMR) and your study participation may be added to your EMR. This information will be used for your care and treatment and for healthcare operations, which may include billing and payment. Federal and state privacy laws give patients the right to access information about their care and treatment contained in their medical record. During this study, you may not be able to access certain information related to this study in your EMR until the study is complete to ensure that the study remains unbiased. By consenting to participate in this study, you are also consenting to this possible temporary withholding of your research records.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (http://www.ucdmc.ucdavis.edu/legal/privacy/) and in an attached document.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

If you are injured or get sick because of this study, medical care is available to you through UC Davis Health, your local provider, or emergency services.

- If it is an emergency, call 911 right away or go to the emergency room.
- For non-emergency issues, you can call the UC Davis Health Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to the Hem/Onc Resident on-call.

It is important that you promptly tell the person in charge of this research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by the University or the study sponsor or may be billed to your insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about compensation, you may call the IRB Administration at (916) 703-9151 or email at hs-IRBAdmin@ucdavis.edu .

If the sponsor pays any of your medical expenses, we may be required to give the sponsor your name, date of birth, and Medicare ID or social security number.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

This research is being funded by Karyopharm also called the funding source. Funding sources may change or be added.

You or your health plan will be billed for the costs of routine medical care you receive during the study. These costs may include operating room fees, pharmacy charges, treatments, hospitalization, scans, etc. You will be expected to pay for the usual deductibles and co-payments, and for any routine care that is not covered. Only the costs of research or experimental procedures will be paid by the study.

Whenever possible, pre-authorization will be obtained. If the costs are not covered, these costs will be discussed prior to proceeding with the study.

For more information about possible costs, please contact the research team. The research team can follow UC Davis Uninsured Non-Emergency Estimate Policy (Policy ID 1883) to work with their department and Decision Support Services to get you a cost estimate.

WILL I BE COMPENSATED FOR BEING IN THIS STUDY?

You will not be compensated for your participation in this study.

Bio-specimens (such as blood, tissue, or saliva) collected from you for this study and/or information obtained from your bio-specimens may be used in this research or other research and shared with other organizations. You will not share in any commercial value or profit derived from the use of your bio-specimens and/or information obtained from them.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or willingness to continue in the study.

DO THE RESEARCHERS HAVE A FINANCIAL INTEREST IN THIS RESEARCH STUDY?

UC Davis is being paid to conduct this study, but the study doctors and research staff have not received any direct income from the study sponsor.

WILL SPECIMENS (tissue, blood, urine or other body materials) TAKEN FROM ME BE USED FOR FUTURE RESEARCH PURPOSES?

You have had a biopsy (or surgery) to see if you have cancer. Your doctor removed some body tissue to do some tests. The results of these tests were given to you by your doctor and are being used to plan your care.

We would like to keep some of the tissue and blood that is left for future research purposes. Your specimen(s) will only be used for research purposes. If you agree, these specimen(s) will be kept and used to learn more about your disease as well as other diseases.

The research that may be done with your specimen(s) will not benefit you directly nor have an effect on your care. It might help people who have your disease and other diseases in the future. Any reports about the research, done with your specimen(s), will not be shared with you or your doctor and the reports will not be put in your health record.

Your name, address, phone number and any other identifying information will be taken off anything associated with your specimen before it is given to the researcher. This would make it very difficult for any research results to be linked to you or your family. To help protect your privacy, people outside the research process will not have access to results about any one person.

The benefits of research using specimens include learning more about what causes diseases, how to prevent them, how to treat them, and how to cure them. There are very few risks to you. The greatest risk is the release of information from your health records which may be necessary for us to obtain along with your specimens. We will protect your records so that your name, address, and phone number will be kept private.

Please read each question below and think about your choice. After reading each question, initial next to "YES" or "NO". If you have any questions, please discuss this with the researcher.

1. My samples such as tissue and blood may be kept for use in future research:

   YES_____ NO_____

2. Someone may contact me in the future to ask me to use my specimens in future research:

   YES_____ NO_____

For further information on the use of specimens for future research purposes and your rights as a research participant, please visit: http://research.ucdavis.edu/IRBAdmin/Participants.

WHERE CAN I GET MORE INFORMATION?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

VOLUNTARY CONSENT:

My signature below will indicate that I have decided to participate in this study as a research subject. I have read and understand the information above. I understand that I will be given a signed and dated copy of this consent form and the Bill of Rights. If you agree to participate in this research study, a signed copy of this consent document will be filed in your electronic medical record (EMR).

Signature of Subject	Printed Name of Subject	Date

Signature of Person Obtaining Consent Printed Name of Person Obtaining Consent Date

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SIGN BELOW ONLY IF A WITNESS WILL OBSERVE THE CONSENT PROCESS (for use with IRB "Short Form")

Signature of Witness to Consent Process Printed Name of Witness Date
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