UCSF University of California San Francisco
IRB NUMBER: 18-25747
IRB APPROVAL DATE: 11/05/2021
IRB EXPIRATION DATE: 07/12/2022

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

CC# 185511: Immunogenic Priming with 177Lu-PSMA Targeted Therapy in Advanced Prostate Cancer: A Phase 1b Study

This is a clinical trial, a type of research study. Your study doctor, Rahul Aggarwal, MD, or one of his associates from the UCSF Helen Diller Family Comprehensive Cancer Center will explain the clinical trial to you.

Clinical trials include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you have a type of prostate cancer which is called metastatic castration-resistant prostate cancer (mCRPC) that has come back (recurred) or is spreading (metastatic).

Why Is This Study Being Done?

The purpose of this study is to find out what effects, good and/or bad, that the investigational therapy ^{177}Lu-PSMA-617 in combination with pembrolizumab has on you and your metastatic castrate-resistant prostate cancer (mCRPC). This study is divided into two parts: Part A and B. The purpose of Part A is to determine the dose and schedule that will be investigated in Part B. In Part A, there are three different dosing schedules and you will receive ^{177}Lu-PSMA-617 and Pembrolizumab based on when you enter the study. You and your study doctor will know which dose and schedule you will be assigned. Once a dose for ^{177}Lu-PSMA-617 has been set and a schedule has been determined, Part B will open to enrollment. In Part B, all eligible patients will receive ^{177}Lu-PSMA-617 and Pembrolizumab at the same dose and on the same schedule.

Radioligand Therapy (RLT) uses a small molecule (in this case 177Lu-PSMA-617), which carries a radioactive component to destroys tumor cells. When 177Lu-PSMA-617 is injected into the body, it attaches to the Prostate-Specific Membrane Antigen (PSMA) receptor found on your tumor cells. After 177Lu-PSMA-617 attaches to the PSMA receptor, its radiation component destroys the tumor cell.

^{177}Lu-PSMA-617 is considered investigational, which means it has not been approved by the U.S. Food and Drug Administration (FDA).

Pembrolizumab is approved by the FDA for the treatment of certain types of skin cancer, lung cancer, and head and neck cancer, but it is not approved for patients with metastatic castrate-resistant prostate cancer. Therefore, the use of pembrolizumab and its combination with ^{177}Lu-PSMA-617, in this study is considered investigational.

The test used to find genetic mutations (changes in your genes) in this study is called the Strata

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next-generation sequencing (StrataNGS) test. This test has not been approved by the Food and Drug Administration (FDA) and is considered investigational. The testing laboratory (e.g. Strata Oncology) that will perform the StrataNGS test is CLIA-approved so while the laboratory itself meets CLIA standards, the test results may not be conclusive and would need to be validated in subsequent testing.

This trial is being funded by the Prostate Cancer Foundation and the National Cancer Institute. Merck, the company that makes Pembrolizumab and Endocyte, the company that makes ^{177}Lu-PSMA-617, will only be providing the study drugs. The investigators do not have any financial or proprietary interests in the companies.

How Many People Will Take Part In This Study?

At UCSF, about 18 patients will take part in Part A and 25 patients will take part in Part B.

What Will Happen If I Take Part In This Research Study?

Before you begin the main part of the study:

Screening Visit:

You will need to have the following exams, tests, or procedures to find out if you can be in the main part of the study. Most of these exams, tests, or procedures are part of your routine cancer care and may be done even if you do not participate in this study. If you have had some of these exams done recently, they may not need to be repeated. This will be up to your study doctor to determine. These exams, tests, or procedures must be completed within 28 days (Schedules 1 and 2) or within 21 - 49 days (Schedule 3) before starting study drugs, unless stated otherwise below.

The total time to complete the screening exams, tests, and procedures is about 6 - 8 hours.

The study will be explained to you by the study doctor and study staff and you will be asked to sign this consent form before any study-related procedures are done.

- You will have a physical examination, including height and weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- Your complete medical history will be reviewed (includes review of medications, assessment of your disease, past procedures, past treatments, and current baseline medical conditions)
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 8 teaspoons) will be used for the following:
    - Routine safety tests
    - Check your thyroid function (TSH)

- Check your hormone levels and how well your prostate is working (PSA)

- You will have a biopsy that will be done at the site where we can most easily get a piece of the tumor and the biopsy can involve the bone, lymph node, or other sites. The tumor tissue collected from the biopsy will be used for biomarker testing and genetic sequencing test. Biomarkers are substances in your tissues that may provide information on any changes to your proteins, how your cancer cells are responding to study treatment and whether your cells are becoming resistant (no longer responding) to the study treatment. Genetic sequencing test looks for mutations (changes in your genes) that may have occurred. The tumor biopsy will be performed within 12 weeks of your screening visit. The type of biopsy you have will either be a core biopsy, punch biopsy, or excisional biopsy.
  - Core Biopsy: The doctor will use a local anesthesia on the skin to numb the area where a hollow needle (about the size of the tip of a ballpoint pen) will be inserted. Then the doctor will make a cut through the skin into the area of the tumor. The doctor will remove a piece of the tumor using a hallow needle one or more times into the tumor to collect a sample.
  - Punch Biopsy: The doctor will use a local anesthesia on the skin to numb the area where a rounded knife will be used to cut through the skin. The doctor will then remove a piece of the tumor by inserting the hollow needle one or more times into the tumor. The doctor will then close the area of the biopsy with stitches. This will take 30 minutes. If needed, your doctor may use CT-scan technology to help guide the biopsy. If this is done, you may be asked to stay in the clinic for up to 4 hours after the biopsy for observation. Your doctor will let you know if the biopsy will use CT technology and if observation is needed.
  - Excisional Biopsy: The doctor will use a local anesthesia on the skin to numb the area, and then the doctor will remove 4 small pieces of skin (approximately the size of a pencil eraser). After the procedure, you may get stitches in the area where the biopsies are taken from.
- You will have a ^{68}Ga-PSMA-11 PET/CT or a ^{68}Ga-PSMA-11 PET/MR of the face, neck, chest, abdomen, and pelvis to take detailed pictures of any tumors that express a special protein, PSMA, found on your tumor. The ^{68}Ga-PSMA-11 PET/CT scan will be performed within 12 weeks of your screening visit.
  - ^{68}Ga-PSMA-11 PET/CT scan: For this procedure, an IV is started in the hand. A small amount of radioactive chemical (^{68}Ga-PSMA-11) is injected into the bloodstream. Once the ^{68}Ga-PSMA-11is injected, you will be asked to wait for about an hour to allow for ^{68}Ga-PSMA-11 to distribute in the body. Then you will be asked to lie down on a table and the body is scanned. The total time for this procedure is about 2-3 hours.
  - ^{68}Ga-PSMA-11 PET/MR scan: For this procedure, an IV is started in the arm. A small amount of radioactive chemical (^{68}Ga-PSMA-11) is injected into the bloodstream. Once the ^{68}Ga-PSMA-11is injected, you will be asked to wait for about an hour to allow for ^{68}Ga-PSMA-11 to distribute in the body. Then you will be asked to lie down on a table and the body is scanned. The total time for this procedure is about 2-3 hours.
- You will have a bone scan, MRI, contrast-enhanced CT, or PET/CT imaging of the face, neck, chest, abdomen, and pelvis 28 days before your first dose.

- Bone scan: A bone scan is a test that makes detailed images of your bones and any tumors on them. Before the bone scan, a small amount of radioactive substance is injected into your vein. About 3 hours later, you will lie on a table under a machine, which will make an image of your bones. The test itself will take about 1 hour, but the whole process takes up to 4 hours.
- MRI scan: A Magnetic Resonance Imaging (MRI) scan takes an image of your head or body to observe the location and size of your tumor. For the MRI scan, you may be given a 'contrast material' (a special dye that makes it easier for doctors to see different tissues in your body). Gadolinium is contrast material that causes some tumors to appear much brighter than normal tissue on MRI scans (these tumors may not be visible without gadolinium). The contrast material may be given to you in your arm through an intravenous catheter (a tiny tube inserted into a vein). You will then lie down on a narrow bed, which will be placed in a tunnel that is 6 feet long by 22 inches wide and open at each end. You will lie there quietly for about one hour, during which time you will hear a loud machine-like noise. The MRI scan is done in the Radiology Department and takes approximately an hour and a half to complete.
- CT scan: A CT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. For the CT scan, you may be given a "contrast material" (a special dye that makes it easier for doctors to see different tissues in your body). The contrast material may be given orally, intravenously, or rectally (less likely). Oral contrast material is given to you to drink and is used to help outline the stomach and intestines. Intravenous (IV) contrast material is given to you by injecting the contrast material into a line, which is attached to a needle in your arm and is used to get clearer pictures of your body cavity. A rectal contrast fills up the loops of your lower bowel so the doctors can see your tumor better. After you have been given the contrast material (either by mouth, by vein, or rectum), you will lie flat on a table that will move you into the CT scan machine. You will be asked to lie still and may be asked to hold your breath for a few seconds. The CT scan is done in the Radiology Department and takes about half an hour.
- PET/CT scan: A PET/CT scan takes an image of your head or body to observe the location and size of your tumor. For this procedure, an IV is started in the hand. A small amount of radioactive chemical (glucose) is injected into the bloodstream. Once the glucose is injected, you will be asked to wait for about an hour to allow glucose to distribute in the body. Then you will be asked to lie down on a table and the body is scanned. The total time for this procedure is about 2-3 hours.

During the main part of the study:

If the exams, tests, and procedures show that you can be in the main part of the study, and you choose to take part, then you will have the following tests and procedures done.

^{177}Lu-PSMA-617: will be injected as a 30-minute IV infusion. 30 minutes prior to your infusion, you will start a 4-hour saline infusion and you may receive medicine to help ease the feeling of nausea and vomiting.

Pembrolizumab: Pembrolizumab will be administered by a 30-minute IV infusion at a dose of 200 mg every 3 weeks.

You will be given written instructions about your radiation treatment and how to reduce the risk of radiation exposure to those around you. If you have any questions about these instructions, please ask your study doctor or nurse.

For Part A, only:

If you enter the study and are assigned to Schedule 1:

- On Cycle 1, Day 1, you will receive ^{177}Lu-PSMA-617 through an IV with saline.
  - Your study doctor may also give you medicine through your IV to help ease the feeling of nausea and vomiting if needed.
- On Day 1 of Cycles 2 and beyond, you will receive Pembrolizumab through an IV.

If you enter the study and are assigned to Schedule 2:

- On Day 1 of Cycle 1, you will receive ^{177}Lu-PSMA-617 and Pembrolizumab through an IV with saline.
  - Your study doctor may also give you medicine through your IV to help ease the feeling of nausea and vomiting if needed.
- On Day 1 of Cycle

If you enter the study and are assigned to Schedule 3:

- 21 Days prior to Cycle 1, you will receive Pembrolizumab through an IV.

- On Day 1, Cycle 1, you will receive ^{177}Lu-PSMA-617 through an IV with saline.
  - Your study doctor may also give you medicine through your IV to help ease the feeling of nausea and vomiting if needed.

21 Days Before Cycle 1 (Schedule 3, only)

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
  - Routine safety tests
  - Check your thyroid function (TSH)

  - Check your hormone levels and how well your prostate is working (PSA)
  - Researchers would like to perform an analysis of how well your body's immune (protective) system, works.
- You will talk to your doctor about any side effects you had since your last visit.

For Part A and Part B:

Day 1 of Cycle 1

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
  - Routine safety tests
  - Check your thyroid function (TSH)
  - Check your hormone levels and how well your prostate is working (PSA)
  - Researchers would like to perform an analysis of how well your body's immune (protective) system, works.
- You will talk to your doctor about any side effects you had since your last visit.

Day 2 of Cycle 1

- You will have a SPECT-CT scan of the face, neck, chest, abdomen, and pelvis **(OPTIONAL).**
  - A SPECT-CT scan is a special type of CT scan that combines two different diagnostic scans into one for a more complete view of certain area of your body. The SPECT scan uses small amounts of radiation to lets your doctor analyze the function of some of your internal organs, whereas the CT scan may be able to help narrow down specifically where the problem is occurring, such as in the bone or nearby tissue. This takes around 20-30 minutes. There is no requirement to drink anything or be injected with anything for this part of the test.

Day 8 and 15 of Cycle 1

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.

- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 8 teaspoons) will be used for the following:
    - Routine safety tests
- You will talk to your doctor about any side effects you had since your last visit.

Day 1 of Cycles 2 and beyond

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
    - Routine safety tests
    - Check your thyroid function (TSH)
    - Check your hormone levels and how well your prostate is working (PSA)
    - Researchers would like to perform an analysis of how well your body's immune (protective) system, works.
- You will have a bone scan, MRI, contrast-enhanced CT, or PET/CT imaging of the face, neck, chest, abdomen, and pelvis
- You will have a biopsy (Cycle 2, Day 1, only). The tumor tissue collected from your biopsy will be sent for biomarker testing and genetic sequencing test.
- You will talk to your doctor about any side effects you had since your last visit.

Day 8 and 15 of Cycle 2

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 8 teaspoons) will be used for the following:
    - Routine safety tests
- You will talk to your doctor about any side effects you had since your last visit.

When you are finished receiving ^{177}Lu-PSMA-617 and Pembrolizumab:

End of Treatment (EOT) Study Visit

After having received the last dose in this study, you will remain in the study to be followed for safety until the EOT visit. The EOT visit will happen 30 days after the last dose of ^{177}Lu-PSMA-617 and Pembrolizumab. The following tests and procedures will be performed at this visit:

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
    - Routine safety tests
    - Check your thyroid function (TSH)
    - Check your hormone levels and how well your prostate is working (PSA)
    - Researchers would like to perform an analysis of how well your body's immune (protective) system, works.
- You will have a PET/CT or PET/MR using 68Ga-PSMA-11 (**OPTIONAL**)
- You will have a bone scan, MRI, contrast-enhanced CT, or PET/CT imaging of the face, neck, chest, abdomen, and pelvis
- You will talk to your doctor about any side effects you had since your last visit.

30-Day Follow-Up

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
    - Routine safety tests
    - Check your thyroid function (TSH)
    - Check your hormone levels and how well your prostate is working (PSA)
- You will talk to your doctor about any side effects you had since your last visit.

Study location: All study procedures will be done at UCSF.

How Long Will I Be In The Study?

The exact length of time that you participate in this study will depend on your response to treatment. After completing all study treatments or after you are withdrawn from treatment, you will be asked to complete one final follow-up visit to ask about your side effects or potential benefits you may be experiencing from study treatment, as described above. Your total participation in this study from the time you have signed the informed consent to your last visit, including follow-up visits, may be two years (depending on how your cancer responds to treatment and how well you tolerate the treatment).

Can I Stop Being In The Study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the study drug can be evaluated by the study doctor. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

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

If you decide to stop study treatments, your study doctor will not presume that you have withdrawn from the study but will assume that you will continue to participate in any follow-up activities described above. If you do not want to participate in any or all follow-up activities, you must inform your study doctor in writing at the address below and clearly identify the activities you do not want.

Rahul Aggarwal, MD
UCSF Helen Diller Family Comprehensive Cancer Center
[redacted]

Please note that any information collected before you withdraw will be kept and used to complete the research. Even if you withdraw consent for further follow-up or contacts, if the investigator becomes aware of additional safety information this will be reported to the sponsor in order to comply with legal or regulatory requirements.

Your Responsibilities:

If you participate in this study, you will be expected to:

- Keep all study appointments and follow all instructions given to you by your study doctor and study staff.
- Describe how you feel and discuss possible side effects.

- Tell the study doctor about all medications you are taking including prescriptions, herbal supplements and over-the-counter medications.
- Discuss any medication (prescription or over the counter) that you wish to start taking with your study doctor before you start taking it.
- Tell the study doctor about any changes in your health.
- Certain medications cannot be taken while you are participating in this trial. Your study doctor will explain what these medications are. If you need treatment with any medications that are not allowed during your participation in this trial, you must inform the study doctor or the study staff. You will not be denied medications required to treat an illness you may have, but you may be required to stop taking the study medication. This is for your safety, since some medications may not work well with the study treatment, and you might have physical problems.

- Tell your study doctor about <u>any</u> medical treatments that you plan to receive during the study (such as elective surgery or radiation).
- Tell your study doctor or study staff if you change your address, telephone number, or other contact information

What Will Happen To My Blood and Tissue Samples If I Take Part?

Biological samples (blood and tumor samples) will be used for the scientific evaluation of this study, including testing performed by outside laboratories (including Strata Oncology). Samples sent to outside laboratories for research testing will be labeled with your personal information (name, date of birth, medical record number, and clinical information). Only laboratory personnel staff involved with the research testing will have access to your samples and information.

Any remaining samples that are available after the study-specific tests are completed will be known as leftover samples. Any samples that are taken from you for use outside of the study-specific tests will be known as new samples. Leftover and new samples may be used for other current or future research involving the same drug(s), the same or related therapeutic area, or for other relevant health research, except where prohibited by local laws or regulations. This research may involve tests that reveal genetic information.

All requests for research on leftover and/or new samples that are volunteered under this consent will be reviewed by a committee of the research leaders involved with this study to ensure the research supports appropriate and well-defined needs of our scientific research activities and efforts to develop new therapies.

Samples may be transferred to the research sponsor, its collaborators, research partners, designees, or other relevant third parties who may analyze the samples in connection with this study or other current or future research involving the same drug(s), the same or related therapeutic area, or other relevant health research. These samples may be transferred to individuals or companies located outside of the country/region in which they were taken when determined by the study leaders to be important for our scientific research and development of therapies. However, the samples and data will be kept confidential and secure in accordance with

applicable laws regarding privacy and security. Your samples will not be sold to any other people or companies.

Each sample of biological material is deemed to be a "donation" and you will not receive any financial or in kind benefit associated with the development of any new therapies derived from the use of your donation, which may be of commercial value.

If you withdraw your consent to take part in the study, you may contact the investigator and have your samples destroyed if they have not yet been used. You may also choose to withdraw your consent to the use of your samples for other current or future research involving the same drug(s), the same or related therapeutic area, or for other relevant health research. Any use of your samples that occurs before you withdraw your consent remains the property of the study sponsor.

Please see the "Optional Research" section of this consent form to read more on donating your samples for future research and to consent by answering a few 'yes' or 'no' questions, if you choose to participate.

What Side Effects Or Risks Can I Expect From Being In The Study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study drug. In some cases, side effects can be serious, life-threatening, long lasting, or may never go away.

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

^{177}Lu-PSMA-617

- **Radiation risk summary**: This research study involves exposure to a significant amount of radiation. While this amount of radiation is intended to treat your condition, it does involve a risk of a secondary cancer. However, the UCSF Radiation Safety Committee has reviewed the use of radiation in this research study and has designated this use as acceptable to obtain the benefits provided by the results of the study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.
- **Salivary gland toxicity**: ^{177}Lu-PSMA-617 can collect in the salivary glands and so can cause damage to the salivary glands. This radiation can cause dry mouth when there is not enough saliva to keep your mouth wet, although it is believed that this can be temporary, patients have been reported to have long-term effect on saliva production. Dry mouth can cause your lips to feel dry or crack. Your tongue may feel rough and dry and it may be difficult to chew and swallow your food.
- **Bone marrow effects**: Radiation can kill bone marrow cells than lead to low levels of red blood cells, platelets (a special cell which helps the blood to clot), and other blood

cells such as white blood cells (helps to fight infection). A decrease in the various blood cell types may put you at risk for bleeding, fatigue, shortness of breath, and infection. This happens in many patients and is frequently temporary. If this does occur to you, there will be longer intervals between administrations in order to let your body rest and to allow the blood cells to return to normal levels. However, the decreased blood cells may be long-standing and/or permanent resulting in your discontinuation from this therapeutic study. Your blood counts will be checked between administrations to make sure you have not developed significant bone marrow injury.

- **Renal effects**: ^{177}Lu-PSMA-617 is cleared from the body through the kidneys, which results in high levels of radiation exposure to the kidneys. This increases the chance that you may develop a temporary chronic kidney injury. You will receive an infusion throughout the administration of the study drug that contains amino acids. This fluid is given in order to minimize the dose to your kidneys. Your kidney function will be checked between therapies to make sure you have not developed significant kidney injury.
- **Secondary cancers**: The high dose of radiation associated with this therapy increases the risk of developing cancers later in your life. In particular, hematopoietic malignancies (such as leukemia) are at increased risk, although rare.

Pembrolizumab

Pembrolizumab is approved for treatment of certain cancers in the USA and some other countries. However pembrolizumab and its combination with ^{177}Lu-PSMA-617 is considered investigational for patients with metastatic castrate-resistant prostate 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.

Very Common

Out of 100 people who receive pembrolizumab, 20 or more people may have the following:

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

Common

Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

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

Uncommon

Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:

- Inflammation of the lungs, so you may feel short of breath and cough (pneumonitis)
- Too much thyroid hormone, so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools (hyperthyroidism)
- 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 infusion at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion
- 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)
- 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)

Rare

Out of 100 people who receive pembrolizumab, less than 1 person may have the following:

- Inflammation of the nerves that may cause pain, weakness, or tingling in your hands and feet, and may spread to your legs, arms, and upper body, leading to severe muscle weakness and possible temporary paralysis (Guillain-Barré syndrome)
- Inflammation of the muscles, so you may feel weak or have pain in your muscles (myositis)
- 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 have vomiting that gets worse when you eat (pancreatitis)
- 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 liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, a pain in the right side of your belly, yellow eyes and skin, and dark urine (hepatitis)
- 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 (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, having 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 1 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 kidney, so you may pass less urine or have cloudy or bloody urine, swelling, and low back pain (nephritis)
- 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. Sometimes this condition can lead to death (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 may cause 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)
- Inflammation of the spinal cord with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, and constipation (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.

Additionally, since pembrolizumab was approved (for melanoma) 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 the right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis).

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.

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 that may become serious or life threatening, and in some cases, may 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.

Risks from study procedures

Risks of Venipuncture/Intravenous Needle Insertion: The collection of a blood sample may cause some discomfort. Obtaining blood may sometimes cause pain/discomfort at the site where the blood is drawn, bruising, bleeding, occasional light-headedness and, rarely, infection or fainting.

Bone scan risks: Bone scan side effects are not common, and when encountered are usually mild, such as nausea and vomiting, or you may become uncomfortable lying still for the duration of the examination. The bone scan involves an injection, in the vein of your arm, of a radiotracer (radioactive compound that localizes in the bone). The injection of the radiotracer may feel like a small sting and there may be possible bruising at the injection site. You will be exposed to a limited and medically acceptable dose of radiation during the procedure. There is always a slight risk of damage from being exposed to any radiation.

CT scan risks: CT scans involve the risks of radiation (see above). 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). The contrast material may also cause kidney problems, especially if you are dehydrated or have poor kidney function. The study doctors will ask you about any allergies or related conditions before the procedure. If you have any of these problems, you may not be allowed to have a CT scan with contrast.

Having a CT scan may mean some added discomfort for you. 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. If contrast material is used, you may feel discomfort when it is injected by vein. You may feel warm and flushed and get a metallic taste in your mouth.

Rarely, the contrast material may cause nausea, vomiting or a headache.

PET/CT scan risks: The PET/CT scan exposes your body to radiation, see radiation risk above. The radiation levels come from a tracer, which is a radioactive chemical, injected into a vein in your arm. The tracer lets the doctor see how your cells are functioning and the radiation levels are very low. You may have an allergic reaction to the chemical used in the scan. For some patients, having to lie still on the scanning table for the length of the procedure may cause some discomfort or pain. After the scan, your arm may be a little bit sore or have some redness where the IV was placed in your arm. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

Radiation risks: This research study involves exposure to a significant amount of radiation. Most of the radiation is from the study drugs. The target of this radiation is the tumor, however, for all administrations, other organs are exposed as follows: Bone marrow (0.1 Gy), Kidneys (5 Gy), Liver (1 Gy), Salivary glands (10 Gy), Spleen (1 Gy). While this amount of radiation is intended to treat your condition, it does involve a risk of a secondary cancer. However, the UCSF Radiation Safety Committee has reviewed the use of radiation in this research study and has designated this use as acceptable to obtain the objectives of the study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.

MRI risks: Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which in the process could possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI.

Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear earplugs. At

times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

Because the risks to a fetus from MRI are unknown, pregnant women must not participate in this study.

Contrast agent (gadolinium) risks: A few side effects of gadolinium injection such as mild headache, nausea, and local pain may occur. Rarely (less than 1% of the time) low blood pressure and lightheadedness occurs. This can be treated immediately with intravenous fluids. Very rarely (less than one in one thousand), patients are allergic to gadolinium. These effects are most commonly hives and itchy eyes, but more severe reactions have been seen which result in shortness of breath.

Patients with severe kidney disease sometimes have a bad reaction to gadolinium contrast. The condition is called nephrogenic systemic fibrosis (NSF). It can cause skin to tighten or scar and can damage internal organs. Sometimes it can be life threatening. There are no reports of NSF in patients with normal kidney function. Before you have an MRI scan requiring an injection of gadolinium contrast, you will have a blood test in order to check the function of your kidneys. Based on your medical history and the results of the test, either your treating doctor or the study doctor will decide whether it is safe for you to undergo the MRI scans.

Gadolinium can build up in the brain; however, it is unknown how this will impact your health. Some types of gadolinium are more strongly linked to buildup in the brain. UCSF prefers to use gadobutrol, which is less likely to build up in the brain, compared to other types of gadolinium. However, for some types of liver imaging, a less stable agent called gadoxetate is sometimes required.

Gadolinium as an MRI imaging agent will only be used when medically necessary for your care. When it is medically necessary, the study doctors believe that the clear benefits of using gadolinium for imaging outweigh the unknown risks, which is minimized by using gadobutrol.

Tumor biopsy risks: The general risks associated with this procedure are pain, discomfort, infection, bleeding and injury to organs nearby.

Genetic Testing Confidentiality Risks: There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

Reproductive risks: ^{177}Lu-PSMA-617 and/or pembrolizumab may have harmful effects on a fetus. Also, it is not known if ^{177}Lu-PSMA-617 and/or pembrolizumab has any harmful effects on sperm. To avoid risk of drug exposure to your partner through the semen, even in men with vasectomies (tubes that carry semen from the testicles have been cut), you must use a condom

and another effective method of birth control when you have sex with a woman of child-bearing potential, while on the study drug and for 2 months following your last dose. The type of birth control you use must be discussed with and approved by the study doctor before you begin the study. This is done to prevent pregnancy.

Donation of sperm is also not allowed during the study and for 2 months following the last dose of study drug.

You should advise your study doctor if you father a child while on the study drug and/or during the 2 months following your last dose. The doctor will advise you on any appropriate medical attention for your partner should this be necessary. The study doctor may ask you and your partner to allow him/her to collect information about her pregnancy and the health of the baby.

Unknown Risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything 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?

Taking part in this study may or may not make your health better. While doctors hope treatment with ^{177}Lu-PSMA-61 and pembrolizumab will be more useful against metastatic castration-resistant prostate cancer (mCRPC) there is no proof of this. We do know that the information from this study will help doctors learn more about ^{177}Lu-PSMA-61 and pembrolizumab as a treatment for metastatic castration-resistant prostate cancer (mCRPC). This information could help future cancer patients.

What Other Choices Do I Have If I Do Not Take Part In This Study?

Your other choices may include:

- Getting treatment or care for your cancer without being in a study.
- Taking part in another study.
- 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.

Please talk to your study doctor about your choices before deciding if you will take part in this study.

How Will Information About Me Be Kept Confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this 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 medical records for research, quality assurance, and data analysis include:

- University of California
- The study doctor and study staff,
- Merck, Endocyte, and its current or future research partners, collaborators, assignees, licensees or designees and their affiliates, agents, and employees
- Food and Drug Administration (FDA), National Cancer Institute (NCI), or other government agencies involved in keeping research safe for people
- Other persons required by law
- Strata Oncology, or other outside laboratory facility, performing research testing on blood or tissue samples.

What Are The Costs Of Taking Part In This Study?

Endocyte, the company that makes ^{177}Lu-PSMA-617, and Merck, the company that makes Pembrolizumab will provide both drugs at no cost to you. Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover all standard medical care costs if you are receiving medical services out-of-network. Any procedures done only for research will not be charged to you or your insurer.

Strata Oncology or outside laboratory facility will perform research testing on blood or tissue samples at no cost to you/your insurance company.

Will I Be Paid For Taking Part In This Study?

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

What Happens If I Am Injured Because I Took Part In This Study?

It is important that you tell your Study Doctor or the Study Chair, Dr. Rahul Aggarwal, if you feel that you have been injured because of taking part in this study. You can tell your treating physician in person or call Dr. Aggarwal's office [redacted].

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415-476-1814.

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 your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who Can Answer My Questions About The Study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. You may also contact the Principal Investigator, Rahul Aggarwal, MD's office [redacted].

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Institutional Review Board at 415-476-1814.

ClinicalTrials.gov is a website that provides information about clinical trials. 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.

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OPTIONAL RESEARCH

This section of the informed consent is about additional research studies that are being done with people who are taking part in the study. You may take part in these additional studies only if you want to. Everyone who is taking part in the main study is being asked to take part in this optional study.

Optional SPECT-CT Scan

As described earlier in the 'During the main part of the study' section of the consent form, the researchers are asking if you would be willing to undergo a SPECT-CT scan on Day 2 of Cycle 1. Researchers would like to analyze how well you r dose response by samples will be analyzed to see how well your body is responding to the treatment and how the treatment effects different parts of your body. Please indicate your response below by putting your initials in the "Yes" or "No" box:

1. I agree to have a SPECT-CT scan on Day 2 of Cycle 1.

YES	NO

Things to Think About

The choice to let us perform a SPECT-CT scan is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that you want to undergo the additional scan, you can change your mind at any time. Just contact us and let us know that you do not want to have the additional optional scan. We may not be able to destroy any data that we have already collected, if analysis has already begun.

Benefits

The benefits of the SPECT-CT scan is that this may help in understanding your disease and other cancers, how to prevent them, how to treat them and how your body responses to the treatments.

Risks

Having an additional scan will expose you to more radiation (from the SPECT-CT imaging agent). Talk to your study doctor about the risks of having a SPECT-CT scan before you make your choice.

Optional PET/CT or PET/MRI using 68Ga-PSMA-11

As described earlier in the 'During the main part of the study' section of the consent form, the researchers are asking if you would be willing to undergo a PET/CT or PET/MRI using 68Ga-PSMA-11 at the end of treatment. Researchers would like to collect more information about how Ga-68-PSMA is absorbed in your body. Please indicate your response below by putting your initials in the "Yes" or "No" box:

2. I agree to have a PET/CT or PET/MRI using 68Ga-PSMA-11 at the end of treatment.

YES	NO

Things to Think About

The choice to let us perform an additional PET/CT or PET/MRI using 68Ga-PSMA-11 is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that you want to undergo the additional scan, you can change your mind at any time. Just contact us and let us know that you do not want to have the additional optional scan. We may not be able to destroy any data that we have already collected, if analysis has already begun.

Benefits

The end of treatment scan may help the study doctors gather more information about how 68Ga-PSMA-11 is absorbed in your body, and if it is more effective than other scans used to detect prostate cancer metastasis. There may be no direct benefit to you.

Risks

Having an additional scan will expose you to more radiation (from the 68Ga-PSMA-11 imaging agent). Talk to your study doctor about the risks of having an additional PET/CT or PET/MRI using 68Ga-PSMA-11, before you make your choice.

Storing Leftover Blood and Tissue Samples for Future Research

If there is any leftover blood or tissue from the blood draws and tissue biopsies required in this study after the study tests are done, we are asking if you are willing to donate those left over samples for future research. If you do not want to take part in this optional portion of this study, you may still take part in the main study as described above.

If you agree, your samples and information about you may be made available to use for future research. Reports about research done with your samples will not be given to you or your doctor.

These reports will not be put in your health record. The research will not have an effect on your care.

The research that may be done with your samples is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

Things to Think About

The choice to let us keep the leftover samples for future research is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that your samples can be kept for research, you can change your mind at any time. Just call or write to us and let us know that you do not want us to use your samples.

Any samples that remain will no longer be used for research. However, if any research has already been done using portions of your samples, the data will be kept and analyzed as part of those research studies. We also cannot retract any data that has been shared with other researchers.

In the future, people who do research may need to know more about your health. While we may give them reports about your health, we will not give them your name, address, phone number, or any other information that would let the researchers know who you are.

Sometimes tissue and blood are used for genetic research (about diseases that are passed on in families). Even if your tissue is used for this kind of research, the results will not be put in your health records.

Your samples will be used only for research and will not be sold. The research done with your samples may help to develop new products in the future. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

Benefits

The benefits of research using blood and/or tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them. Your samples will be used only for research and will not be sold. The research done with your samples may help to develop new products in the future. New products may have commercial value but you will not receive any compensation for the development or sale of these products.

Risks

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

How will my genetic information be shared?

Genetic information (also known as genotype data) and the medical record data (also known as phenotype data) may be shared broadly in a coded form for future genetic research or analysis. We may give certain medical information about you (for example, diagnosis, blood pressure, age if less than 85) to other scientists or companies not at UCSF, including to a (public or controlled access) government health research database, but we will not give them your name, address, phone number, or any other identifiable information. Research results from these studies will not be returned to you.

Donating data may involve a loss of privacy, but information about you will be handled as confidentially as possible. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. Taking part in a genetic study may also have a negative impact or unintended consequences on family or other relationships. It is possible that future research could one day help people of the same race, ethnicity, or sex as you. However, it is also possible through these kinds of studies that genetic traits might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

There will be no direct benefit to you from allowing your data to be kept and used for future research. However, we hope we will learn something that will contribute to the advancement of science and understanding of health and disease. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits. If you decide later that you do not want your information to be used for future research, you can notify the investigator in writing at:

Rahul Aggarwal, MD
UCSF Helen Diller Family Comprehensive Cancer Center
[redacted]

, and any remaining data will be destroyed. However, we cannot retract any data has been shared with other researchers.

Will I be contacted in the future about this or other research?

We, the local site study team, may want to contact you in the future. You can decide now whether or not you want to be contacted. You can also change your mind later.

If you agree, we may contact you for several reasons. For example, over time, stored samples may be used up or decrease in quality, so we may contact you to ask for more samples. We may also contact you to update basic information or request information about your health.

Additionally, we may want to contact you to see if you want to participate in other research. We

will not notify you every time your samples and information are used. However, some researchers might apply to do a study for which they would need to contact you. For example, they might want to ask you to give another sample or to fill out a survey, or they might ask you to do a phone interview or come in to be seen by a researcher or doctor. If a study like this is approved, someone from this project will contact you. They will tell you about the study so you can decide if you want to receive more information. There will be a new consent process just for that study. You can decide then to take part or not take part. If at any time, you decide you no longer want to be contacted about future studies, please tell us.

Can I change my mind after I agree to let my samples be used?

You have the right to change your mind about the future use of your leftover blood and tissue samples and information at any time. If you want to leave the project, let us know. Just contact the study doctor, Rahul Aggarwal, MD, in writing at the address below, and let us know that you do not want us to keep your samples.

Rahul Aggarwal, MD
UCSF Helen Diller Family Comprehensive Cancer Center
[redacted]

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, put your initials in the "Yes" or "No" box. If you have any questions, please talk to your doctor or nurse, or call our research review board at IRB's phone number.

No matter what you decide to do, it will not affect your care.

3. My excess tissue may be kept for use in research to learn about, prevent, or treat cancer.

YES	NO

4. My excess blood may be kept for use in research to learn about, prevent, or treat cancer.

YES	NO

5. Someone may contact me in the future to ask me to take part in more research.

YES	NO

6. My genetic information and associated data may be kept for use in future research.

YES	NO

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Participant's name (print)
Date	Person Obtaining Consent
Date	Witness – Only required if the participant is a non-English speaker

next-generation sequencing (StrataNGS) test. This test has not been approved by the Food and Drug Administration (FDA) and is considered investigational. The testing laboratory (e.g. Strata Oncology) that will perform the StrataNGS test is CLIA-approved so while the laboratory itself meets CLIA standards, the test results may not be conclusive and would need to be validated in subsequent testing.

This trial is being funded by the Prostate Cancer Foundation and the National Cancer Institute. Merck, the company that makes Pembrolizumab and Endocyte, the company that makes ^{177}Lu-PSMA-617, will only be providing the study drugs. The investigators do not have any financial or proprietary interests in the companies.

How Many People Will Take Part In This Study?

At UCSF, about 18 patients will take part in Part A and 25 patients will take part in Part B.

What Will Happen If I Take Part In This Research Study?

Before you begin the main part of the study:

Screening Visit:

You will need to have the following exams, tests, or procedures to find out if you can be in the main part of the study. Most of these exams, tests, or procedures are part of your routine cancer care and may be done even if you do not participate in this study. If you have had some of these exams done recently, they may not need to be repeated. This will be up to your study doctor to determine. These exams, tests, or procedures must be completed within 28 days (Schedules 1 and 2) or within 21 - 49 days (Schedule 3) before starting study drugs, unless stated otherwise below.

The total time to complete the screening exams, tests, and procedures is about 6 - 8 hours.

The study will be explained to you by the study doctor and study staff and you will be asked to sign this consent form before any study-related procedures are done.

- You will have a physical examination, including height and weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- Your complete medical history will be reviewed (includes review of medications, assessment of your disease, past procedures, past treatments, and current baseline medical conditions)
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 8 teaspoons) will be used for the following:
    - Routine safety tests
    - Check your thyroid function (TSH)

  - Check your hormone levels and how well your prostate is working (PSA)
- You will have a biopsy that will be done at the site where we can most easily get a piece of the tumor and the biopsy can involve the bone, lymph node, or other sites. The tumor tissue collected from the biopsy will be used for biomarker testing and genetic sequencing test. Biomarkers are substances in your tissues that may provide information on any changes to your proteins, how your cancer cells are responding to study treatment and whether your cells are becoming resistant (no longer responding) to the study treatment. Genetic sequencing test looks for mutations (changes in your genes) that may have occurred. The tumor biopsy will be performed within 12 weeks of your screening visit. The type of biopsy you have will either be a core biopsy, punch biopsy, or excisional biopsy.
  - Core Biopsy: The doctor will use a local anesthesia on the skin to numb the area where a hollow needle (about the size of the tip of a ballpoint pen) will be inserted. Then the doctor will make a cut through the skin into the area of the tumor. The doctor will remove a piece of the tumor using a hallow needle one or more times into the tumor to collect a sample.
  - Punch Biopsy: The doctor will use a local anesthesia on the skin to numb the area where a rounded knife will be used to cut through the skin. The doctor will then remove a piece of the tumor by inserting the hollow needle one or more times into the tumor. The doctor will then close the area of the biopsy with stitches. This will take 30 minutes. If needed, your doctor may use CT-scan technology to help guide the biopsy. If this is done, you may be asked to stay in the clinic for up to 4 hours after the biopsy for observation. Your doctor will let you know if the biopsy will use CT technology and if observation is needed.
  - Excisional Biopsy: The doctor will use a local anesthesia on the skin to numb the area, and then the doctor will remove 4 small pieces of skin (approximately the size of a pencil eraser). After the procedure, you may get stitches in the area where the biopsies are taken from.
- You will have a ^{68}Ga-PSMA-11 PET/CT or a ^{68}Ga-PSMA-11 PET/MR of the face, neck, chest, abdomen, and pelvis to take detailed pictures of any tumors that express a special protein, PSMA, found on your tumor. The ^{68}Ga-PSMA-11 PET/CT scan will be performed within 12 weeks of your screening visit.
  - ^{68}Ga-PSMA-11 PET/CT scan: For this procedure, an IV is started in the hand. A small amount of radioactive chemical (^{68}Ga-PSMA-11) is injected into the bloodstream. Once the ^{68}Ga-PSMA-11is injected, you will be asked to wait for about an hour to allow for ^{68}Ga-PSMA-11 to distribute in the body. Then you will be asked to lie down on a table and the body is scanned. The total time for this procedure is about 2-3 hours.
  - ^{68}Ga-PSMA-11 PET/MR scan: For this procedure, an IV is started in the arm. A small amount of radioactive chemical (^{68}Ga-PSMA-11) is injected into the bloodstream. Once the ^{68}Ga-PSMA-11is injected, you will be asked to wait for about an hour to allow for ^{68}Ga-PSMA-11 to distribute in the body. Then you will be asked to lie down on a table and the body is scanned. The total time for this procedure is about 2-3 hours.
- You will have a bone scan, MRI, contrast-enhanced CT, or PET/CT imaging of the face, neck, chest, abdomen, and pelvis 28 days before your first dose.

- Bone scan: A bone scan is a test that makes detailed images of your bones and any tumors on them. Before the bone scan, a small amount of radioactive substance is injected into your vein. About 3 hours later, you will lie on a table under a machine, which will make an image of your bones. The test itself will take about 1 hour, but the whole process takes up to 4 hours.
- MRI scan: A Magnetic Resonance Imaging (MRI) scan takes an image of your head or body to observe the location and size of your tumor. For the MRI scan, you may be given a 'contrast material' (a special dye that makes it easier for doctors to see different tissues in your body). Gadolinium is contrast material that causes some tumors to appear much brighter than normal tissue on MRI scans (these tumors may not be visible without gadolinium). The contrast material may be given to you in your arm through an intravenous catheter (a tiny tube inserted into a vein). You will then lie down on a narrow bed, which will be placed in a tunnel that is 6 feet long by 22 inches wide and open at each end. You will lie there quietly for about one hour, during which time you will hear a loud machine-like noise. The MRI scan is done in the Radiology Department and takes approximately an hour and a half to complete.
- CT scan: A CT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. For the CT scan, you may be given a "contrast material" (a special dye that makes it easier for doctors to see different tissues in your body). The contrast material may be given orally, intravenously, or rectally (less likely). Oral contrast material is given to you to drink and is used to help outline the stomach and intestines. Intravenous (IV) contrast material is given to you by injecting the contrast material into a line, which is attached to a needle in your arm and is used to get clearer pictures of your body cavity. A rectal contrast fills up the loops of your lower bowel so the doctors can see your tumor better. After you have been given the contrast material (either by mouth, by vein, or rectum), you will lie flat on a table that will move you into the CT scan machine. You will be asked to lie still and may be asked to hold your breath for a few seconds. The CT scan is done in the Radiology Department and takes about half an hour.
- PET/CT scan: A PET/CT scan takes an image of your head or body to observe the location and size of your tumor. For this procedure, an IV is started in the hand. A small amount of radioactive chemical (glucose) is injected into the bloodstream. Once the glucose is injected, you will be asked to wait for about an hour to allow glucose to distribute in the body. Then you will be asked to lie down on a table and the body is scanned. The total time for this procedure is about 2-3 hours.

During the main part of the study:

If the exams, tests, and procedures show that you can be in the main part of the study, and you choose to take part, then you will have the following tests and procedures done.

^{177}Lu-PSMA-617: will be injected as a 30-minute IV infusion. 30 minutes prior to your infusion, you will start a 4-hour saline infusion and you may receive medicine to help ease the feeling of nausea and vomiting.

Pembrolizumab: Pembrolizumab will be administered by a 30-minute IV infusion at a dose of 200 mg every 3 weeks.

You will be given written instructions about your radiation treatment and how to reduce the risk of radiation exposure to those around you. If you have any questions about these instructions, please ask your study doctor or nurse.

For Part A, only:

If you enter the study and are assigned to Schedule 1:

- On Cycle 1, Day 1, you will receive ^{177}Lu-PSMA-617 through an IV with saline.
  - Your study doctor may also give you medicine through your IV to help ease the feeling of nausea and vomiting if needed.
- On Day 1 of Cycles 2 and beyond, you will receive Pembrolizumab through an IV.

If you enter the study and are assigned to Schedule 2:

- On Day 1 of Cycle 1, you will receive ^{177}Lu-PSMA-617 and Pembrolizumab through an IV with saline.
  - Your study doctor may also give you medicine through your IV to help ease the feeling of nausea and vomiting if needed.
- On Day 1 of Cycle

If you enter the study and are assigned to Schedule 3:

- 21 Days prior to Cycle 1, you will receive Pembrolizumab through an IV.

- On Day 1, Cycle 1, you will receive ^{177}Lu-PSMA-617 through an IV with saline.
  - Your study doctor may also give you medicine through your IV to help ease the feeling of nausea and vomiting if needed.

21 Days Before Cycle 1 (Schedule 3, only)

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
  - Routine safety tests
  - Check your thyroid function (TSH)

- Check your hormone levels and how well your prostate is working (PSA)
- Researchers would like to perform an analysis of how well your body's immune (protective) system, works.

- You will talk to your doctor about any side effects you had since your last visit.

For Part A and Part B:

Day 1 of Cycle 1

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
  - Routine safety tests
  - Check your thyroid function (TSH)
  - Check your hormone levels and how well your prostate is working (PSA)
  - Researchers would like to perform an analysis of how well your body's immune (protective) system, works.
- You will talk to your doctor about any side effects you had since your last visit.

Day 2 of Cycle 1

- You will have a SPECT-CT scan of the face, neck, chest, abdomen, and pelvis **(OPTIONAL).**
  - A SPECT-CT scan is a special type of CT scan that combines two different diagnostic scans into one for a more complete view of certain area of your body. The SPECT scan uses small amounts of radiation to lets your doctor analyze the function of some of your internal organs, whereas the CT scan may be able to help narrow down specifically where the problem is occurring, such as in the bone or nearby tissue. This takes around 20-30 minutes. There is no requirement to drink anything or be injected with anything for this part of the test.

Day 8 and 15 of Cycle 1

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.

- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 8 teaspoons) will be used for the following:
    - Routine safety tests
- You will talk to your doctor about any side effects you had since your last visit.

Day 1 of Cycles 2 and beyond

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
    - Routine safety tests
    - Check your thyroid function (TSH)
    - Check your hormone levels and how well your prostate is working (PSA)
    - Researchers would like to perform an analysis of how well your body's immune (protective) system, works.
- You will have a bone scan, MRI, contrast-enhanced CT, or PET/CT imaging of the face, neck, chest, abdomen, and pelvis
- You will have a biopsy (Cycle 2, Day 1, only). The tumor tissue collected from your biopsy will be sent for biomarker testing and genetic sequencing test.
- You will talk to your doctor about any side effects you had since your last visit.

Day 8 and 15 of Cycle 2

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 8 teaspoons) will be used for the following:
    - Routine safety tests
- You will talk to your doctor about any side effects you had since your last visit.

When you are finished receiving ^{177}Lu-PSMA-617 and Pembrolizumab:

End of Treatment (EOT) Study Visit

After having received the last dose in this study, you will remain in the study to be followed for safety until the EOT visit. The EOT visit will happen 30 days after the last dose of ^{177}Lu-PSMA-617 and Pembrolizumab. The following tests and procedures will be performed at this visit:

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
    - Routine safety tests
    - Check your thyroid function (TSH)
    - Check your hormone levels and how well your prostate is working (PSA)
    - Researchers would like to perform an analysis of how well your body's immune (protective) system, works.
- You will have a PET/CT or PET/MR using 68Ga-PSMA-11 **(OPTIONAL)**
- You will have a bone scan, MRI, contrast-enhanced CT, or PET/CT imaging of the face, neck, chest, abdomen, and pelvis
- You will talk to your doctor about any side effects you had since your last visit.

30-Day Follow-Up

- You will have a physical examination, including weight.
- You will have your vital signs checked (temperature, blood pressure, pulse, and breathing rate).
- You will be asked about your basic daily activities to determine your general health, how you have been feeling, and about your daily activities (performance status).
- Your current medications will be reviewed, as well as any treatments you had since your last visit or will have in the future.
- Your blood will be collected by inserting a needle into a vein in your arm. The blood sample (about 16 teaspoons) will be used for the following:
    - Routine safety tests
    - Check your thyroid function (TSH)
    - Check your hormone levels and how well your prostate is working (PSA)
- You will talk to your doctor about any side effects you had since your last visit.

Study location: All study procedures will be done at UCSF.

How Long Will I Be In The Study?

The exact length of time that you participate in this study will depend on your response to treatment. After completing all study treatments or after you are withdrawn from treatment, you will be asked to complete one final follow-up visit to ask about your side effects or potential benefits you may be experiencing from study treatment, as described above. Your total participation in this study from the time you have signed the informed consent to your last visit, including follow-up visits, may be two years (depending on how your cancer responds to treatment and how well you tolerate the treatment).

Can I Stop Being In The Study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the study drug can be evaluated by the study doctor. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

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

If you decide to stop study treatments, your study doctor will not presume that you have withdrawn from the study but will assume that you will continue to participate in any follow-up activities described above. If you do not want to participate in any or all follow-up activities, you must inform your study doctor in writing at the address below and clearly identify the activities you do not want.

Rahul Aggarwal, MD
UCSF Helen Diller Family Comprehensive Cancer Center
[redacted]

Please note that any information collected before you withdraw will be kept and used to complete the research. Even if you withdraw consent for further follow-up or contacts, if the investigator becomes aware of additional safety information this will be reported to the sponsor in order to comply with legal or regulatory requirements.

Your Responsibilities:

If you participate in this study, you will be expected to:

- Keep all study appointments and follow all instructions given to you by your study doctor and study staff.
- Describe how you feel and discuss possible side effects.

- Tell the study doctor about all medications you are taking including prescriptions, herbal supplements and over-the-counter medications.
- Discuss any medication (prescription or over the counter) that you wish to start taking with your study doctor before you start taking it.
- Tell the study doctor about any changes in your health.
- Certain medications cannot be taken while you are participating in this trial. Your study doctor will explain what these medications are. If you need treatment with any medications that are not allowed during your participation in this trial, you must inform the study doctor or the study staff. You will not be denied medications required to treat an illness you may have, but you may be required to stop taking the study medication. This is for your safety, since some medications may not work well with the study treatment, and you might have physical problems.

- Tell your study doctor about <u>any</u> medical treatments that you plan to receive during the study (such as elective surgery or radiation).
- Tell your study doctor or study staff if you change your address, telephone number, or other contact information

What Will Happen To My Blood and Tissue Samples If I Take Part?

Biological samples (blood and tumor samples) will be used for the scientific evaluation of this study, including testing performed by outside laboratories (including Strata Oncology). Samples sent to outside laboratories for research testing will be labeled with your personal information (name, date of birth, medical record number, and clinical information). Only laboratory personnel staff involved with the research testing will have access to your samples and information.

Any remaining samples that are available after the study-specific tests are completed will be known as leftover samples. Any samples that are taken from you for use outside of the study-specific tests will be known as new samples. Leftover and new samples may be used for other current or future research involving the same drug(s), the same or related therapeutic area, or for other relevant health research, except where prohibited by local laws or regulations. This research may involve tests that reveal genetic information.

All requests for research on leftover and/or new samples that are volunteered under this consent will be reviewed by a committee of the research leaders involved with this study to ensure the research supports appropriate and well-defined needs of our scientific research activities and efforts to develop new therapies.

Samples may be transferred to the research sponsor, its collaborators, research partners, designees, or other relevant third parties who may analyze the samples in connection with this study or other current or future research involving the same drug(s), the same or related therapeutic area, or other relevant health research. These samples may be transferred to individuals or companies located outside of the country/region in which they were taken when determined by the study leaders to be important for our scientific research and development of therapies. However, the samples and data will be kept confidential and secure in accordance with

applicable laws regarding privacy and security. Your samples will not be sold to any other people or companies.

Each sample of biological material is deemed to be a "donation" and you will not receive any financial or in kind benefit associated with the development of any new therapies derived from the use of your donation, which may be of commercial value.

If you withdraw your consent to take part in the study, you may contact the investigator and have your samples destroyed if they have not yet been used. You may also choose to withdraw your consent to the use of your samples for other current or future research involving the same drug(s), the same or related therapeutic area, or for other relevant health research. Any use of your samples that occurs before you withdraw your consent remains the property of the study sponsor.

Please see the "Optional Research" section of this consent form to read more on donating your samples for future research and to consent by answering a few 'yes' or 'no' questions, if you choose to participate.

What Side Effects Or Risks Can I Expect From Being In The Study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study drug. In some cases, side effects can be serious, life-threatening, long lasting, or may never go away.

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

^{177}Lu-PSMA-617

- **Radiation risk summary**: This research study involves exposure to a significant amount of radiation. While this amount of radiation is intended to treat your condition, it does involve a risk of a secondary cancer. However, the UCSF Radiation Safety Committee has reviewed the use of radiation in this research study and has designated this use as acceptable to obtain the benefits provided by the results of the study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.
- **Salivary gland toxicity**: ^{177}Lu-PSMA-617 can collect in the salivary glands and so can cause damage to the salivary glands. This radiation can cause dry mouth when there is not enough saliva to keep your mouth wet, although it is believed that this can be temporary, patients have been reported to have long-term effect on saliva production. Dry mouth can cause your lips to feel dry or crack. Your tongue may feel rough and dry and it may be difficult to chew and swallow your food.
- **Bone marrow effects**: Radiation can kill bone marrow cells than lead to low levels of red blood cells, platelets (a special cell which helps the blood to clot), and other blood

cells such as white blood cells (helps to fight infection). A decrease in the various blood cell types may put you at risk for bleeding, fatigue, shortness of breath, and infection. This happens in many patients and is frequently temporary. If this does occur to you, there will be longer intervals between administrations in order to let your body rest and to allow the blood cells to return to normal levels. However, the decreased blood cells may be long-standing and/or permanent resulting in your discontinuation from this therapeutic study. Your blood counts will be checked between administrations to make sure you have not developed significant bone marrow injury.

- **Renal effects**: ^{177}Lu-PSMA-617 is cleared from the body through the kidneys, which results in high levels of radiation exposure to the kidneys. This increases the chance that you may develop a temporary chronic kidney injury. You will receive an infusion throughout the administration of the study drug that contains amino acids. This fluid is given in order to minimize the dose to your kidneys. Your kidney function will be checked between therapies to make sure you have not developed significant kidney injury.
- **Secondary cancers**: The high dose of radiation associated with this therapy increases the risk of developing cancers later in your life. In particular, hematopoietic malignancies (such as leukemia) are at increased risk, although rare.

Pembrolizumab

Pembrolizumab is approved for treatment of certain cancers in the USA and some other countries. However pembrolizumab and its combination with ^{177}Lu-PSMA-617 is considered investigational for patients with metastatic castrate-resistant prostate 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.

Very Common

Out of 100 people who receive pembrolizumab, 20 or more people may have the following:

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

Common

Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

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

Uncommon

Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:

- Inflammation of the lungs, so you may feel short of breath and cough (pneumonitis)
- Too much thyroid hormone, so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools (hyperthyroidism)
- 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 infusion at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion
- 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)
- 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)

Rare

Out of 100 people who receive pembrolizumab, less than 1 person may have the following:

- Inflammation of the nerves that may cause pain, weakness, or tingling in your hands and feet, and may spread to your legs, arms, and upper body, leading to severe muscle weakness and possible temporary paralysis (Guillain-Barré syndrome)
- Inflammation of the muscles, so you may feel weak or have pain in your muscles (myositis)
- 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 have vomiting that gets worse when you eat (pancreatitis)
- 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 liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, a pain in the right side of your belly, yellow eyes and skin, and dark urine (hepatitis)
- 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 (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, having 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 1 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 kidney, so you may pass less urine or have cloudy or bloody urine, swelling, and low back pain (nephritis)
- 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. Sometimes this condition can lead to death (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 may cause 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)
- Inflammation of the spinal cord with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, and constipation (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.

Additionally, since pembrolizumab was approved (for melanoma) 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 the right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis).

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.

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 that may become serious or life threatening, and in some cases, may 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.

Risks from study procedures

Risks of Venipuncture/Intravenous Needle Insertion: The collection of a blood sample may cause some discomfort. Obtaining blood may sometimes cause pain/discomfort at the site where the blood is drawn, bruising, bleeding, occasional light-headedness and, rarely, infection or fainting.

Bone scan risks: Bone scan side effects are not common, and when encountered are usually mild, such as nausea and vomiting, or you may become uncomfortable lying still for the duration of the examination. The bone scan involves an injection, in the vein of your arm, of a radiotracer (radioactive compound that localizes in the bone). The injection of the radiotracer may feel like a small sting and there may be possible bruising at the injection site. You will be exposed to a limited and medically acceptable dose of radiation during the procedure. There is always a slight risk of damage from being exposed to any radiation.

CT scan risks: CT scans involve the risks of radiation (see above). 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). The contrast material may also cause kidney problems, especially if you are dehydrated or have poor kidney function. The study doctors will ask you about any allergies or related conditions before the procedure. If you have any of these problems, you may not be allowed to have a CT scan with contrast.

Having a CT scan may mean some added discomfort for you. 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. If contrast material is used, you may feel discomfort when it is injected by vein. You may feel warm and flushed and get a metallic taste in your mouth.

Rarely, the contrast material may cause nausea, vomiting or a headache.

PET/CT scan risks: The PET/CT scan exposes your body to radiation, see radiation risk above. The radiation levels come from a tracer, which is a radioactive chemical, injected into a vein in your arm. The tracer lets the doctor see how your cells are functioning and the radiation levels are very low. You may have an allergic reaction to the chemical used in the scan. For some patients, having to lie still on the scanning table for the length of the procedure may cause some discomfort or pain. After the scan, your arm may be a little bit sore or have some redness where the IV was placed in your arm. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

Radiation risks: This research study involves exposure to a significant amount of radiation. Most of the radiation is from the study drugs. The target of this radiation is the tumor, however, for all administrations, other organs are exposed as follows: Bone marrow (0.1 Gy), Kidneys (5 Gy), Liver (1 Gy), Salivary glands (10 Gy), Spleen (1 Gy). While this amount of radiation is intended to treat your condition, it does involve a risk of a secondary cancer. However, the UCSF Radiation Safety Committee has reviewed the use of radiation in this research study and has designated this use as acceptable to obtain the objectives of the study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.

MRI risks: Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which in the process could possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI.

Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear earplugs. At

times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

Because the risks to a fetus from MRI are unknown, pregnant women must not participate in this study.

Contrast agent (gadolinium) risks: A few side effects of gadolinium injection such as mild headache, nausea, and local pain may occur. Rarely (less than 1% of the time) low blood pressure and lightheadedness occurs. This can be treated immediately with intravenous fluids. Very rarely (less than one in one thousand), patients are allergic to gadolinium. These effects are most commonly hives and itchy eyes, but more severe reactions have been seen which result in shortness of breath.

Patients with severe kidney disease sometimes have a bad reaction to gadolinium contrast. The condition is called nephrogenic systemic fibrosis (NSF). It can cause skin to tighten or scar and can damage internal organs. Sometimes it can be life threatening. There are no reports of NSF in patients with normal kidney function. Before you have an MRI scan requiring an injection of gadolinium contrast, you will have a blood test in order to check the function of your kidneys. Based on your medical history and the results of the test, either your treating doctor or the study doctor will decide whether it is safe for you to undergo the MRI scans.

Gadolinium can build up in the brain; however, it is unknown how this will impact your health. Some types of gadolinium are more strongly linked to buildup in the brain. UCSF prefers to use gadobutrol, which is less likely to build up in the brain, compared to other types of gadolinium. However, for some types of liver imaging, a less stable agent called gadoxetate is sometimes required.

Gadolinium as an MRI imaging agent will only be used when medically necessary for your care. When it is medically necessary, the study doctors believe that the clear benefits of using gadolinium for imaging outweigh the unknown risks, which is minimized by using gadobutrol.

Tumor biopsy risks: The general risks associated with this procedure are pain, discomfort, infection, bleeding and injury to organs nearby.

Genetic Testing Confidentiality Risks: There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

Reproductive risks: ^{177}Lu-PSMA-617 and/or pembrolizumab may have harmful effects on a fetus. Also, it is not known if ^{177}Lu-PSMA-617 and/or pembrolizumab has any harmful effects on sperm. To avoid risk of drug exposure to your partner through the semen, even in men with vasectomies (tubes that carry semen from the testicles have been cut), you must use a condom

and another effective method of birth control when you have sex with a woman of child-bearing potential, while on the study drug and for 2 months following your last dose. The type of birth control you use must be discussed with and approved by the study doctor before you begin the study. This is done to prevent pregnancy.

Donation of sperm is also not allowed during the study and for 2 months following the last dose of study drug.

You should advise your study doctor if you father a child while on the study drug and/or during the 2 months following your last dose. The doctor will advise you on any appropriate medical attention for your partner should this be necessary. The study doctor may ask you and your partner to allow him/her to collect information about her pregnancy and the health of the baby.

Unknown Risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything 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?

Taking part in this study may or may not make your health better. While doctors hope treatment with ^{177}Lu-PSMA-61 and pembrolizumab will be more useful against metastatic castration-resistant prostate cancer (mCRPC) there is no proof of this. We do know that the information from this study will help doctors learn more about ^{177}Lu-PSMA-61 and pembrolizumab as a treatment for metastatic castration-resistant prostate cancer (mCRPC). This information could help future cancer patients.

What Other Choices Do I Have If I Do Not Take Part In This Study?

Your other choices may include:

- Getting treatment or care for your cancer without being in a study.
- Taking part in another study.
- 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.

Please talk to your study doctor about your choices before deciding if you will take part in this study.

How Will Information About Me Be Kept Confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this 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 medical records for research, quality assurance, and data analysis include:

- University of California
- The study doctor and study staff,
- Merck, Endocyte, and its current or future research partners, collaborators, assignees, licensees or designees and their affiliates, agents, and employees
- Food and Drug Administration (FDA), National Cancer Institute (NCI), or other government agencies involved in keeping research safe for people
- Other persons required by law
- Strata Oncology, or other outside laboratory facility, performing research testing on blood or tissue samples.

What Are The Costs Of Taking Part In This Study?

Endocyte, the company that makes ^{177}Lu-PSMA-617, and Merck, the company that makes Pembrolizumab will provide both drugs at no cost to you. Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover all standard medical care costs if you are receiving medical services out-of-network. Any procedures done only for research will not be charged to you or your insurer.

Strata Oncology or outside laboratory facility will perform research testing on blood or tissue samples at no cost to you/your insurance company.

Will I Be Paid For Taking Part In This Study?

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

What Happens If I Am Injured Because I Took Part In This Study?

It is important that you tell your Study Doctor or the Study Chair, Dr. Rahul Aggarwal, if you feel that you have been injured because of taking part in this study. You can tell your treating physician in person or call Dr. Aggarwal's office [redacted].

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415-476-1814.

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 your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who Can Answer My Questions About The Study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. You may also contact the Principal Investigator, Rahul Aggarwal, MD's office [redacted].

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Institutional Review Board at 415-476-1814.

ClinicalTrials.gov is a website that provides information about clinical trials. 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.

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OPTIONAL RESEARCH

This section of the informed consent is about additional research studies that are being done with people who are taking part in the study. You may take part in these additional studies only if you want to. Everyone who is taking part in the main study is being asked to take part in this optional study.

Optional SPECT-CT Scan

As described earlier in the 'During the main part of the study' section of the consent form, the researchers are asking if you would be willing to undergo a SPECT-CT scan on Day 2 of Cycle 1. Researchers would like to analyze how well you r dose response by samples will be analyzed to see how well your body is responding to the treatment and how the treatment effects different parts of your body. Please indicate your response below by putting your initials in the "Yes" or "No" box:

1. I agree to have a SPECT-CT scan on Day 2 of Cycle 1.

YES	NO

Things to Think About

The choice to let us perform a SPECT-CT scan is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that you want to undergo the additional scan, you can change your mind at any time. Just contact us and let us know that you do not want to have the additional optional scan. We may not be able to destroy any data that we have already collected, if analysis has already begun.

Benefits

The benefits of the SPECT-CT scan is that this may help in understanding your disease and other cancers, how to prevent them, how to treat them and how your body responses to the treatments.

Risks

Having an additional scan will expose you to more radiation (from the SPECT-CT imaging agent). Talk to your study doctor about the risks of having a SPECT-CT scan before you make your choice.

Optional PET/CT or PET/MRI using 68Ga-PSMA-11

As described earlier in the 'During the main part of the study' section of the consent form, the researchers are asking if you would be willing to undergo a PET/CT or PET/MRI using 68Ga-PSMA-11 at the end of treatment. Researchers would like to collect more information about how Ga-68-PSMA is absorbed in your body. Please indicate your response below by putting your initials in the "Yes" or "No" box:

2. I agree to have a PET/CT or PET/MRI using 68Ga-PSMA-11 at the end of treatment.

YES	NO

Things to Think About

The choice to let us perform an additional PET/CT or PET/MRI using 68Ga-PSMA-11 is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that you want to undergo the additional scan, you can change your mind at any time. Just contact us and let us know that you do not want to have the additional optional scan. We may not be able to destroy any data that we have already collected, if analysis has already begun.

Benefits

The end of treatment scan may help the study doctors gather more information about how 68Ga-PSMA-11 is absorbed in your body, and if it is more effective than other scans used to detect prostate cancer metastasis. There may be no direct benefit to you.

Risks

Having an additional scan will expose you to more radiation (from the 68Ga-PSMA-11 imaging agent). Talk to your study doctor about the risks of having an additional PET/CT or PET/MRI using 68Ga-PSMA-11, before you make your choice.

Storing Leftover Blood and Tissue Samples for Future Research

If there is any leftover blood or tissue from the blood draws and tissue biopsies required in this study after the study tests are done, we are asking if you are willing to donate those left over samples for future research. If you do not want to take part in this optional portion of this study, you may still take part in the main study as described above.

If you agree, your samples and information about you may be made available to use for future research. Reports about research done with your samples will not be given to you or your doctor.

These reports will not be put in your health record. The research will not have an effect on your care.

The research that may be done with your samples is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

Things to Think About

The choice to let us keep the leftover samples for future research is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that your samples can be kept for research, you can change your mind at any time. Just call or write to us and let us know that you do not want us to use your samples.

Any samples that remain will no longer be used for research. However, if any research has already been done using portions of your samples, the data will be kept and analyzed as part of those research studies. We also cannot retract any data that has been shared with other researchers.

In the future, people who do research may need to know more about your health. While we may give them reports about your health, we will not give them your name, address, phone number, or any other information that would let the researchers know who you are.

Sometimes tissue and blood are used for genetic research (about diseases that are passed on in families). Even if your tissue is used for this kind of research, the results will not be put in your health records.

Your samples will be used only for research and will not be sold. The research done with your samples may help to develop new products in the future. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

Benefits

The benefits of research using blood and/or tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them. Your samples will be used only for research and will not be sold. The research done with your samples may help to develop new products in the future. New products may have commercial value but you will not receive any compensation for the development or sale of these products.

Risks

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

How will my genetic information be shared?

Genetic information (also known as genotype data) and the medical record data (also known as phenotype data) may be shared broadly in a coded form for future genetic research or analysis. We may give certain medical information about you (for example, diagnosis, blood pressure, age if less than 85) to other scientists or companies not at UCSF, including to a (public or controlled access) government health research database, but we will not give them your name, address, phone number, or any other identifiable information. Research results from these studies will not be returned to you.

Donating data may involve a loss of privacy, but information about you will be handled as confidentially as possible. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. Taking part in a genetic study may also have a negative impact or unintended consequences on family or other relationships. It is possible that future research could one day help people of the same race, ethnicity, or sex as you. However, it is also possible through these kinds of studies that genetic traits might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

There will be no direct benefit to you from allowing your data to be kept and used for future research. However, we hope we will learn something that will contribute to the advancement of science and understanding of health and disease. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits. If you decide later that you do not want your information to be used for future research, you can notify the investigator in writing at:

Rahul Aggarwal, MD
UCSF Helen Diller Family Comprehensive Cancer Center
[redacted]

, and any remaining data will be destroyed. However, we cannot retract any data has been shared with other researchers.

Will I be contacted in the future about this or other research?

We, the local site study team, may want to contact you in the future. You can decide now whether or not you want to be contacted. You can also change your mind later.

If you agree, we may contact you for several reasons. For example, over time, stored samples may be used up or decrease in quality, so we may contact you to ask for more samples. We may also contact you to update basic information or request information about your health.

Additionally, we may want to contact you to see if you want to participate in other research. We

will not notify you every time your samples and information are used. However, some researchers might apply to do a study for which they would need to contact you. For example, they might want to ask you to give another sample or to fill out a survey, or they might ask you to do a phone interview or come in to be seen by a researcher or doctor. If a study like this is approved, someone from this project will contact you. They will tell you about the study so you can decide if you want to receive more information. There will be a new consent process just for that study. You can decide then to take part or not take part. If at any time, you decide you no longer want to be contacted about future studies, please tell us.

Can I change my mind after I agree to let my samples be used?

You have the right to change your mind about the future use of your leftover blood and tissue samples and information at any time. If you want to leave the project, let us know. Just contact the study doctor, Rahul Aggarwal, MD, in writing at the address below, and let us know that you do not want us to keep your samples.

Rahul Aggarwal, MD
UCSF Helen Diller Family Comprehensive Cancer Center
[redacted]

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, put your initials in the "Yes" or "No" box. If you have any questions, please talk to your doctor or nurse, or call our research review board at IRB's phone number.

No matter what you decide to do, it will not affect your care.

3. My excess tissue may be kept for use in research to learn about, prevent, or treat cancer.

YES	NO

4. My excess blood may be kept for use in research to learn about, prevent, or treat cancer.

YES	NO

5. Someone may contact me in the future to ask me to take part in more research.

YES	NO

6. My genetic information and associated data may be kept for use in future research.

YES	NO

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Participant's name (print)
Date	Person Obtaining Consent
Date	Witness – Only required if the participant is a non-English speaker