NCT03439891

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

Study Title: CC# 174523 - Multicenter Pilot Study of the Safety, Efficacy, and Immune Cell Profiling in Advanced Hepatocellular Carcinoma (HCC) Patients Treated with the Combination of Sorafenib plus Nivolumab as First-Line of Systemic Therapy

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This is a clinical research study. Your study doctor, R. Kate Kelley MD, or one of her associates at the University of California San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center, will explain the study to you.

Research studies include only people who choose to take part. It is your choice whether or not you want to take part in this study. Please take your time to make your decision about participating. You may discuss your decision with your family, friends, and 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 liver cancer called hepatocellular carcinoma (HCC) that cannot be removed by surgery (including liver transplant) that may or may not have spread to other parts of your body or you have Child Pugh B liver function.

Why is this study being done?

The purpose of this study is to test the safety of sorafenib at different dose levels and dose frequencies when combined with nivolumab and see if adding nivolumab makes sorafenib more effective against HCC or Child Pugh B liver function. The investigators hope to learn more about the side effects and how the body handles this drug combination, as well as about how it works against HCC or Child Pugh B liver function.

Sorafenib, a standard treatment for HCC, works by turning off some of the chemicals in the tumor cells that let the tumor grow new blood vessels. Sorafenib is approved by the United States Food and Drug Administration (FDA) for treating certain types of HCC, renal cell carcinoma, and thyroid cancers.

Nivolumab is an antibody (a type of human protein) that may allow the body's immune system to work against tumor cells. Nivolumab is approved by the FDA for treating certain types of melanoma and lung cancers.

The FDA has not approved the combination of sorafenib and nivolumab for treating HCC or Child Pugh B liver function. Therefore, sorafenib and nivolumab are being used in this study as investigational drugs.

There will be two parts to this study:

- Part 1 – Dose Escalation – This part of the study will be to determine the best dose and frequency for sorafenib when combined with nivolumab in patients with advanced or metastatic HCC.

  Once the best dose and frequency for sorafenib has been found, Part 2 of the study will begin.

- Part 2 – Safety Cohort – This part of the study will be to determine the safety and how well side effects of the combination of these study drugs are tolerated in patients with Child Pugh B liver function and patients with advanced HCC.

Bayer is providing the study drug (sorafenib) and funding to UCSF to conduct this study.

How many people will take part in this study?

About 24 people will take part in this study.

- In Part 1 (Dose Escalation), about 6-12 people (at UCSF) will take part in this study. Once the study team has determined the best dose and frequency for sorafenib, Part 2 of the study will begin.
- In Part 2 (Safety Cohort), about 12 people (at UCSF and UC Davis) will take part in this study.

What will happen if I take part in this research study?

Part 1

Part 1 of the study is the dose escalation phase. If you are enrolled in Part 1 (dose escalation), you will take sorafenib (a pill) at the dose and frequency indicated by your study doctor starting on Day 1 of Cycle 1. The first 6 patients will be treated with sorafenib at a dose of 2 tablets (400 mg) once a day, which is lower than the full starting dose of sorafenib but is a dose with acceptable safety and tolerability when given by itself. If this lower dose does not cause any unacceptable side effects, up to 6 more patients may participate in Part 1, with a higher starting dose of sorafenib of 2 tablets (400 mg) twice a day. The side effects and tolerability of these doses will be evaluated carefully for all patients.

Each cycle is 28 days. You will also come into the clinic every two weeks (Days 1 and Days 15 of every cycle) to receive nivolumab. Nivolumab is given as an infusion into a vein in your arm. One infusion takes about 30 minutes.

Part 2

Part 2 of the study is the safety cohort phase. The safety cohort phase is for patients with Child Pugh B liver function and patients with advanced HCC. This phase of the study starts when the dose escalation phase (Part 1) is complete, and the best dose level and dose frequency for sorafenib is determined.

Patients enrolled in Part 1 will continue to receive study drugs after Part 2 opens, until their disease gets worse, if there are too many bad side effects from the study drugs, if they decide to stop participating in the study, or if the study closes.

All patients in Part 2 will take the same dose level and dose frequency of sorafenib (which was determined in Part 1). If you are enrolled in Part 2 (safety cohort), you will take sorafenib (a pill) at a dose of 2 tablets (400 mg) once a day starting on Cycle 1 Day 1. Each cycle is 28 days.

You will also come into the clinic every two weeks (Days 1 and Days 15 of every cycle) to receive nivolumab. Nivolumab is given as an infusion into a vein in your arm. One infusion takes about 30 minutes. Nivolumab may be switched to a monthly infusion on or after Cycle 4, Day 1 if you do not have any unfavorable side effects. The doses and frequency of drugs may be adjusted by your study doctor if you have any side effects.

Before you begin the main part of the study...

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. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

All procedures must be done within 28 days prior to receiving the study drug (Cycle 1 Day 1), unless otherwise noted.

Screening

These tests and procedures may take up to about 6-9 hours but can be done over several different days.

- You will be asked about the medications you are currently taking and have taken in the past including herbal medications
- You will be asked about personal information (age, gender, ethnic origin, etc.)
- Your medical and disease history will be reviewed from your medical records
- You will be asked about any side effects you're having
- You will have a 12 lead Electrocardiogram (ECG) to assess your heart function
    - An ECG records the electrical activity of your heart. Wires or "leads" will be attached to your chest with an adhesive and you will be asked to lie still while the machine prints out an electrical "record" of your heart activity.

This takes about 15-30 minutes.

- You will have a physical examination including measurement of your height, weight, and vital signs (temperature, blood pressure, respirations, and heart rate)
- You will be asked about your ability to perform daily activities (performance status)
- Your liver function will be assessed by physical exam and the results of serum liver tests
- You will have a computed tomography (CT) scan and/or magnetic resonance imaging (MRI) of the chest, abdomen, and pelvis depending on which scans your doctor believes would be best for your tumors. These are special procedures which use X-rays (CT) or magnetic fields (MRI) to create pictures of the inside of your body. These pictures will allow your doctor to monitor your disease before, during, and after you receive nivolumab and sorafenib and to see if the tumors change in size.
    - 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.
    - An 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.
- Your blood will be collected (about 7-8 teaspoons) by inserting a needle into a vein in your arm. The blood sample will be used for the following:
    - Blood chemistry tests
    - Complete blood count (looking at your red and white blood cells and platelets)

  - Thyroid function testing
  - Checking for hepatitis B (HBV), C (HCV), or D (HDV) infection
  - Blood clotting testing
  - Tumor marker testing
  - Pregnancy test- if you are a woman of childbearing potential and if your urine results could not be confirmed as negative
  - Additional blood samples to study the immune cells and other molecular markers in your blood
  - If you are positive for hepatitis (a viral infection), the study doctor will confirm that you are on an antiviral therapy to treat it
- Your urine will be collected for the following tests:
  - Pregnancy test for women of childbearing potential. Results of the pregnancy test must be negative for you to participate in this study.
  - Kidney and bladder function tests
- Your archival tumor tissue will be collected
  - If available, archival (leftover) tumor tissue samples will be collected from a previous surgery or biopsy.

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 need the following tests and procedures. Some of them are part of routine cancer care and may not need to be repeated if you have had them done recently. This will be up to your study doctor.

If you're participating in Part 1, you will take sorafenib starting on Cycle 1 Day 1. Depending on when you join the study, how frequently you take sorafenib and the dose at which you take sorafenib may be different. You can ask your study doctor how often you should take your dose and how much of the drug you will be taking. You will also receive nivolumab at the standard dose through an infusion to a vein in your arm or port if you have previously had one placed starting on Cycle 1 Day 1. The infusion will take about 30 minutes.

If you're participating in Part 2, you will take sorafenib starting on Cycle 1 Day 1. Everyone in Part 2 will take sorafenib at the same frequency and dose. You will also receive nivolumab at the standard dose through an infusion to a vein in your arm starting on Cycle 1 Day 1. The infusion will take about 30 minutes. Nivolumab may be switched to a monthly infusion on or after Cycle 4 Day 1 if you do not have any unfavorable side effects. The doses and frequency of drugs may be adjusted by your study doctor if you have any side effects.

Cycle 1 Day 1

The following tests and procedures will take about 3-4 hours.

- You will be asked about the medications you are currently taking and have

taken in the past including herbal medications
- **Part 1 (Dose Escalation):**
  - You will begin taking sorafenib
    - Ask your study doctor how often you'll be taking sorafenib
  - Nivolumab will be infused into a vein in your arm or port if you have previously had one placed
- **Part 2 (Safety Cohort):**
  - You will begin taking sorafenib
  - Nivolumab will be infused into a vein in your arm or port if you have previously had one placed
- You will be asked about any side effects you're having
- Your drug diary will be checked
  - The study team will check your drug diary to make sure you're taking sorafenib at the right schedule
- You will have a physical examination including measurement of your height, weight, and vital signs (temperature, blood pressure, respirations, and heart rate)
- You will be asked about your ability to perform daily activities (performance status)
- Your liver function will be assessed by physical exam and the results of serum liver tests
- Your urine will be collected for the following tests:
  - Pregnancy test for women of childbearing potential. Results of the pregnancy test must be negative for you to participate in this study (must be done 24 hours prior to your first dose of nivolumab).
  - Kidney and bladder function tests
- Your blood will be collected (about 6-7 teaspoons) by inserting a needle into a vein in your arm. The blood sample will be used for the following:
  - Blood chemistry tests
  - Complete blood count (looking at your red and white blood cells and platelets)
  - Thyroid function testing
  - Blood clotting testing
  - Tumor marker testing
  - Pregnancy test: if you are a woman of childbearing potential and your urine results could not be confirmed as negative
  - Additional blood samples to study the immune cells and other molecular markers in your blood

Cycle 1 Day 15

The following tests and procedures will take about 3-4 hours.

- You will be asked about the medications you are currently taking and have taken in the past including herbal medications
- **Part 1 (Dose Escalation) only:**

  - You will take your dose of sorafenib (at home or in the clinic)
  - Nivolumab will be infused into a vein in your arm or port if you have previously had one placed
- **Part 2 (Safety Cohort) only:**
  - You will take your dose of sorafenib (at home or in the clinic)
  - Nivolumab will be infused into a vein in your arm or port if you have previously had one placed
- You will be asked about any side effects you're having
- Your drug diary will be checked
  - The study team will check your drug diary to make sure you're taking Sorafenib at the right schedule
- You will have a physical examination including measurement of your height, weight, and vital signs (temperature, blood pressure, respirations, and heart rate)
- You will be asked about your ability to perform daily activities (performance status)
- Your liver function will be assessed by physical exam and the results of serum liver tests
- Your urine will be collected for the following test:
  - Pregnancy test for women of childbearing potential. Results of the pregnancy test must be negative for you to participate in this study (must be done 24 hours prior to receiving your dose of nivolumab).
- Your blood will be collected (about 6 teaspoons) by inserting a needle into a vein in your arm. The blood sample will be used for the following:
  - Blood chemistry tests
  - Complete blood count (looking at your red and white blood cells and platelets)
  - Blood clotting testing
  - Additional blood samples to study the immune cells and other molecular markers in your blood
  - Pregnancy test: if you are a woman of childbearing potential and your urine results could not be confirmed as negative

Cycle 2 Day 1

The following tests and procedures will take about 3-4 hours.

- You will be asked about the medications you are currently taking and have taken in the past including herbal medications
- You will take your dose of sorafenib (at home or in the clinic)
- Nivolumab will be infused into a vein in your arm or port if you have previously had one placed
- You will be asked about any side effects you're having
- Your drug diary will be checked
  - The study team will check your drug diary to make sure you're taking Sorafenib at the right schedule

- You will have a physical examination including measurement of your height, weight, and vital signs (temperature, blood pressure, respirations, and heart rate)
- You will be asked about your ability to perform daily activities (performance status)
- Your liver function will be assessed by physical exam and the results of serum liver tests
- Your urine will be collected for the following tests:
    - Pregnancy test for women of childbearing potential. Results of the pregnancy test must be negative for you to participate in this study (must be done 24 hours prior to receiving your dose of nivolumab).
    - Kidney and bladder function test
- Your blood will be collected (about 5-6 teaspoons) by inserting a needle into a vein in your arm. The blood sample will be used for the following:
    - Blood chemistry testing
    - Complete blood count (looking at your red and white blood cells and platelets)
    - Thyroid function testing
    - Blood clotting ability
    - Pregnancy test: if you are a woman of childbearing potential and your urine results could not be confirmed as negative
    - Additional blood samples to study the immune cells and other molecular markers in your blood

Cycle 2 Day 15

The following tests and procedures will take about 3-4 hours.

- You will be asked about the medications you are currently taking and have taken in the past including herbal medications
- You will take your dose of sorafenib (at home or in the clinic)
- Nivolumab will be infused into a vein in your arm or port if you have previously had one placed
- You will be asked about any side effects you're having
- Your drug diary will be checked
    - The study team will check your drug diary to make sure you're taking Sorafenib at the right schedule
- You will have a physical examination including measurement of your height, weight, and vital signs (temperature, blood pressure, respirations, and heart rate)
- You will be asked about your ability to perform daily activities (performance status)
- Your liver function will be assessed by physical exam and the results of serum liver tests
- Your urine will be collected for the following tests:

    - Pregnancy test for women of childbearing potential. Results of the pregnancy test must be negative for you to participate in this study (must be done 24 hours prior to receiving your dose of nivolumab).
- Your blood will be collected (about 4-5 teaspoons) by inserting a needle into a vein in your arm. The blood sample will be used for the following:
    - Blood chemistry tests
    - Complete blood count (looking at your red and white blood cells and platelets)
    - Blood clotting testing
    - Pregnancy test: if you are a woman of childbearing potential and your urine results could not be confirmed as negative
    - Additional blood samples to study the immune cells and other molecular markers in your blood
- Your drug diary will be checked
    - The study team will check your drug diary to make sure you're taking Sorafenib at the right schedule

Cycle 3 Day 1 and beyond

You will be asked to come into the clinic on day 1 of each Cycle. The following tests and procedures will take about 5-7 hours when including scans, or 3-4 hours without scans.

- You will be asked about the medications you are currently taking and have taken in the past including herbal medications
- You will take your dose of sorafenib (at home or in the clinic)
- Nivolumab will be infused into a vein in your arm or port if you have previously had one placed.
    - **Part 2 (Safety Cohort) only:** Depending on how you respond to nivolumab, your study doctor may change your dosing schedule for nivolumab to a monthly infusion (Cycle 4 Day 1, Cycle 5 Day 1, Cycle 6 Day 1, etc.).
- You will be asked about any side effects you're having
- You will have a physical examination including measurement of your height, weight, and vital signs (temperature, blood pressure, respirations, and heart rate)
- You will be asked about your ability to perform daily activities (performance status)
- Your liver function will be assessed by physical exam and the results of serum liver tests
- Approximately every 8 weeks (or 2 complete cycles), you will have a computed tomography (CT) scan or magnetic resonance imaging (MRI) of the chest, abdomen, and pelvis.
- Your urine will be collected for the following tests:
    - Pregnancy test for women of childbearing potential. Results of the pregnancy test must be negative for you to participate in this study (must be done 24 hours prior to receiving your dose of nivolumab).

    - Kidney and bladder function tests
- Your blood will be collected (about 5-7 teaspoons) by inserting a needle into a vein in your arm. The blood sample will be used for the following:
    - Blood chemistry tests
    - Complete blood count (looking at your red and white blood cells and platelets)
    - Blood clotting testing
    - Thyroid function testing
    - Pregnancy test: if you are a woman of childbearing potential and your urine results could not be confirmed as negative
    - Tumor marker testing
    - **On C3D1 and C7D1 Only:** Additional blood samples to study the immune cells and other molecular markers in your blood

Cycle 3 Day 15 and beyond

You will be asked to come into the clinic on day 15 of each Cycle. The following tests and procedures will take about 1-2 hours.

- You will be asked about the medications you are currently taking and have taken in the past including herbal medications
- You will take your dose of sorafenib (at home or in the clinic)
- Nivolumab will be infused into a vein in your arm or port if you have previously had one placed
- You will be asked about any side effects you're having
- Your vital signs will be taken (temperature, blood pressure, respirations, and heart rate)
- Your urine will be collected for the following test:
    - Pregnancy test for women of childbearing potential. Results of the pregnancy test must be negative for you to participate in this study (must be done 24 hours prior to receiving your dose of nivolumab).
- Your blood will be collected (about 3-4 teaspoons) by inserting a needle into a vein in your arm. The blood sample will be used for the following:
    - Blood chemistry tests
    - Complete blood count (looking at your red and white blood cells and platelets)
    - Blood clotting testing
    - Pregnancy test: if you are a woman of childbearing potential and your urine results could not be confirmed as negative

When you are finished receiving Sorafenib and Nivolumab...

After you are finished taking Sorafenib and Nivolumab, the following tests and procedures will be performed.

Safety Follow Up

These visits will occur once you finish taking your study drugs.

Safety Follow Up Visit 1 (30 days after last dose)

This visit will take about 1-2 hours.

- You will be asked about the medications you are currently taking and have taken in the past including herbal medications
- You will be asked about any side effects you're having
- Your drug diary will be checked
    - The study team will check your drug diary to make sure you're taking sorafenib at the right schedule
- You will have a physical examination including measurement of your height, weight, and vital signs (temperature, blood pressure, respirations, and heart rate)
- You will be asked about your ability to perform daily activities (performance status)
- Your liver function will be assessed by physical exam and the results of serum liver tests
- You will have a computed tomography (CT) scan or magnetic resonance imaging (MRI) of the chest, abdomen, and pelvis. It may not be performed if it was done within 28 days prior to this visit.
- Your urine will be collected for the following tests:
    - Pregnancy test for women of childbearing potential. Results of the pregnancy test must be negative for you to participate in this study.
    - Kidney and bladder function tests
- Your blood will be collected (about 6-7 teaspoons) by inserting a needle into a vein in your arm. The blood sample will be used for the following:
    - Complete blood count (looking at your red and white blood cells and platelets)
    - Blood chemistry tests
    - Blood clotting testing
    - Thyroid function testing
    - Pregnancy test: if you are a woman of childbearing potential and your urine results could not be confirmed as negative
    - Tumor marker testing
    - Additional blood samples to study the immune cells and other molecular markers in your blood

Safety Follow Up Visit 2 (100 days after last dose)

This visit will take about 1-2 hours.

- You will be asked about the medications you are currently taking and have taken in the past including herbal medications
- You will be asked about any side effects you're having
- You will have a physical examination including measurement of your height, weight, and vital signs (temperature, blood pressure, respirations, and heart rate)
- You will be asked about your ability to perform daily activities (performance status)
- Your liver function will be assessed by physical exam and the results of serum liver tests
- You will have a computed tomography (CT) scan or magnetic resonance imaging (MRI) of the chest, abdomen, and pelvis. Having these scans may not be required if the most recent scans were performed within 28 days prior to this visit.
- Your urine will be collected for the following tests:
    - Pregnancy test for women of childbearing potential. Results of the pregnancy test must be negative for you to participate in this study.
    - Kidney and bladder function tests
- Your blood will be collected (about 5-6 teaspoons) by inserting a needle into a vein in your arm. The blood sample will be used for the following:
    - Complete blood count (looking at your red and white blood cells and platelets)
    - Blood chemistry tests
    - Blood clotting testing
    - Thyroid function testing
    - Pregnancy test: if you are a woman of childbearing potential and your urine results could not be confirmed as negative
    - Additional blood samples to study the immune cells and other molecular markers in your blood

Long term Follow up

After your last dose of nivolumab and sorafenib, the study team will check on your health and disease status every 3 months for up to two years. This may be during your routine visits with your doctor, or by telephone.

How long will I be in the study?

You will be asked to take sorafenib and nivolumab until your disease gets worse, if there are too many bad side effects from the study drugs, if you decide you don't want to participate in the study, or if the study closes. After you are finished taking nivolumab and sorafenib, the study team will check on your health and disease status for up to two years after your last dose of the study drugs.

Can I continue study drugs if my disease gets worse?

With most anti-cancer drugs, an increase in the size or number of tumors detected with imaging scans (such as CT/MRI scans) or a physical examination indicates that your disease has gotten worse (progressed). This usually means that you should consider switching to another therapy. However, with cancer immunotherapy drugs, that is not always the case. An early increase in the size or number of tumors may not always be a sign of disease progression. The study drugs are thought to work by stimulating your immune system to attack your tumors. When cells from your immune system fight your tumors, one result can be an apparent increase in the size or number of those tumors. In some patients, an early increase can be followed by a reduction in tumor size later.

Because of this possibility, you will have the option of continuing to receive the study drugs even after a scan early in the course of the study shows an increase in your tumors. A later scan will help to see if the increase was caused by real worsening of your disease or if it was caused by immune cells entering your tumors. This confirmatory scan may be performed sooner than 8 weeks after the original scan that showed your tumor had gotten larger, depending on any symptoms you may be having or other test results. Your study doctor will let you know.

You should carefully discuss with your study doctor the option to continue in spite of an apparent increase in tumor size. There are risks of continuing to receive the study drugs. This is because of the possibility that an increase in your tumor represents true worsening of your disease. In that case, you may be exposed to the potential risk of side effects due to the study drugs or from cancer progression. Also, there may be risk in delaying the start of other treatment options that may stop your cancer from growing. In addition, your cancer may progress to the point that you are no longer able to receive other potentially effective therapies.

After you talk with your study doctor, you will need to decide if you want to continue with study drug infusions in spite of apparent disease progression.

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 drugs can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

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

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 drugs. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

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

Side Effects Associated with Nivolumab

Nivolumab may cause one or more of the side effects listed below. This information is based on data from cancer subjects in other clinical trials with nivolumab. In addition, there may be side effects that are not yet known that may occur. You should tell your doctor or nurse right away about any possible side effects you experience.

Very common side effects of nivolumab include [more than 10% of subjects]:

- Diarrhea
- Fatigue
- Itching
- Rash

Common side effects of nivolumab include [1% to less than 10% of subjects]:

- Abdominal pain
- Allergic reaction/hypersensitivity
- Abnormal liver function tests (such as alkaline phosphatase, ALT, AST, or bilirubin) which can be a sign of liver inflammation or injury and can be associated with abnormal liver function
- Chills
- Constipation
- Cough
- Creatinine increased: lab test result associated with decreased kidney function
- Decreased appetite
- Dizziness
- Dry mouth
- Dry skin
- Fever
- Headache
- Increased blood sugar
- Lipase and/or amylase blood tests increased which are lab tests which can be

associated with pancreas inflammation or pancreatitis
- Inflammation of the colon
- Inflammation of the mouth
- Infusion related reaction
- Loss of color (pigment) from areas of skin
- Lung inflammation (pneumonitis - see details below)
- Musculoskeletal pain
- Nausea
- Redness
- Shortness of breath
- Sodium levels in the blood low
- Swelling, including face, arms, and legs
- Thyroid gland function decreased
- Thyroid gland function increased
- Thyroid stimulating hormone increased: lab test result associated with abnormal thyroid function
- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet
- Vomiting

Uncommon side effects of nivolumab include [0.1% to less than 1% of subjects]:

- Adrenal gland function decreased
- Bilirubin (liver function blood test) increased
- Bronchitis
- Dehydration
- Diabetes which may require treatment with insulin
- Double vision
- Dry eye
- Erythema multiforme: skin inflammatory reaction
- Hair loss
- Heart rate increased
- Heart rhythm abnormal
- High blood pressure
- Hives
- Inflammation of the eye
- Inflammation of the kidney
- Inflammation of the pancreas
- Inflammation of the pituitary gland
- Inflammation of the stomach
- Inflammation of the thyroid gland
- Joint pain or stiffness
- Liver inflammation
- Low blood pressure

- Muscle inflammation
- Pemphigoid: blistering of the skin or mouth caused by the immune system attacking healthy tissue
- Pituitary gland function decreased
- Psoriasis: characterized by patches of abnormal, scaly skin
- Renal (kidney) failure or kidney injury
- Respiratory failure
- Upper respiratory tract infection
- Vision blurred

Rare side effects of nivolumab include [0.01% to less than 0.1% of subjects]:

- Anaphylactic reaction (severe allergic reaction)
- Cranial nerve disorder
- Damage to the protective covering of the nerves in the brain and spinal cord
- Diabetes complications resulting in excess blood acid
- Disease caused by body's immune system attacking healthy organs
- Drug induced liver injury
- Guillain-Barre syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
- Inflammation of blood vessels
- Inflammation of the lining of the brain and spinal cord
- Inflammation of the brain, potentially life-threatening or fatal
- Lung infiltrates, associated with infection or inflammation
- Muscle inflammation
- Myasthenic syndrome (neurologic syndrome characterized by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles.
- Polymyalgia rheumatica, an inflammatory disorder causing muscle pain and stiffness
- Rhabdomyolysis: muscle fiber released into the blood stream which could damage your kidneys
- Rosacea: acne-like skin condition resulting in redness of face
- Rupture of the intestine/hole in the intestine
- Sarcoidosis, a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
- Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin
- Syndrome associated with fever, white blood cell activation and abnormal function (including destruction of other blood cells by certain white blood cells), low blood cell counts, rash, and enlargement of the spleen
- Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn
- Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which causes the lymph nodes to become enlarged, inflamed and

painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains
- Vogt Koyanagi Harada syndrome; a disease that affects the pigmented tissue; this may affect the eye leading to swelling, pain and/or blurred vision; the ear leading to hearing loss, ringing in the ears and /or the skin leading to loss of skin color
- Inflammation of heart muscle or lining (such as myocarditis, pericarditis) which can cause altered heart rhythm or in rare cases heart failure

Lung Inflammation (pneumonitis): In rare cases, nivolumab can cause inflammation of the tissues of the lung. This adverse effect has been reported infrequently in patients treated with nivolumab. While many patients with x-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue.

Your study doctor and nurse will watch you closely for changes in your ability to breathe and for other signs or symptoms that might show you are developing this type of lung inflammation and will perform regular tests including physical exams, measurement of oxygen levels through non- invasive testing (i.e., pulse oximeter), blood tests, chest x-rays and/or CT scans.

People who had prior organ, bone marrow, or stem cell transplant are not eligible to participate in this study. If you have a solid organ transplant after participating in this study, you would be at risk of organ rejection, which can be serious or life threatening, If you have a bone marrow or stem cell transplant after participating in this study, you would be at risk for graft versus host disease or other complications which can be serious or life threatening.

Please inform your study doctor or nurse <u>AT ONCE</u> if you experience any of the following:

- Any new or increased shortness of breath;
- Any new or increased chest pain;
- Any new or increased pain/difficulty while breathing;
- Any new or increased cough or any significant change in your type of cough; for example, any new or increased mucous or blood in your cough;
- Any change in the amount of oxygen you require;
- Any fever, fatigue, or other symptoms that occur at the same time as any changes to your breathing or other lung symptoms.

If you start to develop symptoms, your study doctor will ask you to return to the clinic for additional tests, which could include a physical exam, measurement of oxygen levels, blood tests, chest x-rays, and/or CT scans. You will be monitored very closely for

changes in your overall lung symptoms, monitoring may require hospitalization. You may require specific treatment in order to control pneumonitis. You may also be seen by a special doctor called a pulmonologist, who has special training to be an expert in how your lungs work.

Prolonged treatment with medicines that suppress inflammation, sometimes needed to manage the side effects of nivolumab, may lower your body's ability to fight off certain infections (i.e., opportunistic infections). These infections may require treatment with antibiotic or antifungal medications and may be fatal.

Side Effects Associated with Sorafenib

You might experience some or all of these side effects. It is also possible that you might experience side effects that are unknown at this time. As is true for any experimental drug, there may be unknown and potentially serious or life-threatening side effects that could occur with sorafenib.

Very common side effects of sorafenib are [more than 10% of subjects]:

- Diarrhea
- Feeling sick (nausea)
- Feeling weak or tired (fatigue)
- Pain (including mouth pain, abdominal pain, headache, bone pain, tumor pain)
- Hair loss (alopecia)
- Flushed or painful palms or soles (hand foot skin reaction)
- Itching or rash
- Throwing up (vomiting)
- Bleeding)
- High blood pressure, or increases in blood pressure (hypertension)
- Infections
- Loss of appetite (anorexia)
- Constipation
- Joint pain (arthralgia)
- Fever
- Weight loss
- Dry skin
- Low phosphate levels in the blood (hypophosphatemia)
- Increased levels of pancreatic enzymes (amylase or lipase) in the blood
- Decreased levels of lymphocytes in your blood stream (lymphopenia)
- Reddening of the skin in patches (erythema)

Common side effects of sorafenib include [up to 10% of subjects]:

- Flu-like illness
- Indigestion (dyspepsia)

- Difficulty swallowing (dysphagia)
- Inflamed or dry mouth, tongue pain (stomatitis and mucosal inflammation)
- Low calcium levels in the blood (hypocalcemia)
- Low potassium levels in the blood (hypokalemia)
- Low glucose levels in the blood (hypoglycemia)
- Muscle pain (myalgia)
- Disturbed sensations in fingers and toes, including tingling or numbness (peripheral sensory neuropathy)
- Depression
- Erection problems (impotence)
- Altered voice (dysphonia)
- Acne
- Inflamed, dry, or scaly skin that sheds (dermatitis, skin desquamation)
- Heart failure
- Heart attack (myocardial infarction) or chest pain
- Tinnitus (ringing sound in the ear)
- Kidney failure
- Abnormally high levels of protein in the urine (proteinuria)
- General weakness or loss of strength (asthenia)
- Decrease in the number of white blood cells (leukopenia and neutropenia)
- Decrease in number of red blood cells (anemia)
- Low number of platelets in the blood (thrombocytopenia)
- Inflammation of hair follicles (folliculitis)
- Underactive thyroid gland (hypothyroidism)
- Low sodium levels in the blood (hyponatremia)
- Distortion of the sense of taste (dysgeusia)
- Red in the face and often in other areas of the skin (flushing)
- Runny nose (rhinorrhea)
- Heartburn (gastroesophageal reflux disease)
- Skin cancer (keratoacanthomas/squamous cell cancer of the skin)
- A thickening of the outer layer of the skin (hyperkeratosis)
- A sudden, involuntary contraction of a muscle (muscle spasms)
- Increases in liver enzymes (transaminases)

Uncommon side effects of sorafenib include [up to 1% of subjects]:

- Inflamed stomach lining (gastritis)
- Pain in the tummy (abdomen) caused by pancreatitis, inflammation of the gall bladder and/or bile ducts
- Yellow skin or eyes (jaundice) caused by high levels of bile pigments (hyperbilirubinemia)
- Allergic like reactions (including skin reactions and hives)
- Dehydration
- Enlarged breasts (gynecomastia)

- Breathing difficulty (lung disease)
- Eczema
- Overactive thyroid gland (hyperthyroidism)
- Multiple skin eruptions (erythema multiform)
- Abnormally high blood pressure
- Holes in the gut wall (gastrointestinal perforation)
- Reversible swelling in the rear part of the brain that can be associated with headache, altered consciousness, fits, and visual symptoms including visual loss (reversible posterior leukoencephalopathy)
- A sudden, severe allergic reaction (anaphylactic reaction)
- Transient increase in blood enzymes (alkaline phosphatase)
- Abnormal lab test results reflecting blood clotting (INR, abnormal prothrombin level)
- Serious bleeding (including bleeding in the brain, gut wall, and respiratory tract; hemorrhage)

Rare side effects of sorafenib include: [up to 0.1% of subjects]

- Allergic reaction when swelling of the skin (e.g. face, tongue) that may cause difficulty in breathing or swallowing (angioedema)
- Abnormal heart rhythm (QT prolongation)
- Inflammation of the liver, which may lead to nausea, vomiting, abdominal pain, and jaundice (drug induced hepatitis)
- A sunburn-like rash that may occur on skin that has previously been exposed to radiotherapy and can be severe (radiation recall dermatitis)
- Serious reactions of the skin and/or mucous membranes which may include painful blisters and fever, including extensive detachment of the skin (Stevens-Johnson syndrome and toxic epidermal necrolysis)
- Abnormal muscle breakdown which can lead to kidney problems (rhabdomyolysis)
- Damage of the kidney causing them to leak large amounts of protein (nephrotic syndrome)
- Inflammation of the vessels in the skin which may result in rash (leucocytoclastic vasculitis)

Frequency cannot be estimated from data for the following side effect:

- Impaired brain function that can be associated with drowsiness, behavioral changes, or confusion (encephalopathy)
- Aneurysm and artery dissections

Risks from Study Drug Combination

There may be additional side effects related to the combination of nivolumab and sorafenib that are not yet known. It is possible that this combination of drugs will cause

new or more serious side effects than taking these drugs separately. You will be monitored closely for side effects and your doctor may change your medications if it appears that this combination is causing serious side effects. You should tell your doctor about any side effects you experience while on this study. When additional information about side effects is known, you will be notified of any further study drug related effects.

Risks related to study procedures

- **Blood drawing (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, infection, and fainting.
- **Dose Escalation risks**: Since patients will be assigned to different doses of study drug, some patients may receive a dose of the drug that is too small to be effective while others may receive a higher dose that may cause increased side effects. You can ask your study doctor what dose you will be given.
- **Infusion risks:** As with most intravenous products, you may experience pain, irritation, swelling or bruising, or a slight chance of infection at the site where the intravenous catheter (small tube) is inserted into your vein. These side effects may also be observed at the site where blood is drawn for laboratory tests.
- **Intravenous line risks:** The temporary placement of an intravenous line may cause discomfort when inserting the needle, as well as bruising; bleeding; and rarely, infection.
- **Radiation risks:** This research study involves exposure to radiation. Not all this radiation exposure is necessary for your medical care and is for research purposes only. This amount of radiation may involve a low, lifetime risk of cancer. However, we believe that this risk, given your overall medical condition is not clinically relevant. If you have any questions regarding the use of radiation or the risks involved, please consult your study doctor.
- **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.

  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. 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.
- **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 on 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 a 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, a doctor will decide whether it is safe for you to undergo the MRI scans.

- **Reproductive risks:** You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important to understand that you need to use two methods of birth control while on this study. If you are a woman of child bearing potential, you need to continue using birth control for 5 months after your last dose of each study drug, and if you are a male partner of a woman of child bearing potential, 7 months after your last dose of each study drug. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.
- **Hepatitis test risks**: Being tested for Hepatitis may cause anxiety regardless of the test results. A positive test result means that you have been infected with a virus. Receiving positive results may make you very upset. If other people learn about your positive test results, you may have trouble obtaining insurance or employment. If you receive positive results, the study doctor will discuss your care and treatment options with you. If your test is negative, there is still the possibility that you could be infected with the Hepatitis virus and test positive at some time in the future. There is always the possibility that the test results could be wrong.

- **Electrocardiogram risks:** The ECG involves placing electrodes on the skin. You may experience an allergic reaction to the adhesive used to attach the electrodes to the skin. These symptoms are generally mild and clear up on their own. Please let your doctor know if you are aware of any allergies.
- **Unknown Risks:** The experimental drugs 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 that sorafenib in combination with nivolumab will be more useful against cancer compared to the usual treatment, there is no proof of this. We do know that the information from this study will help doctors learn more about sorafenib and nivolumab as a treatment for cancer. 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 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 and may 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.

California regulations require laboratories to report new cases of hepatitis B and hepatitis C infection to the county public health department. The reports include the patient's name, social security number, and other identifying information. Information about these new infections is used to track these diseases statewide and nationwide. Other than this required reporting, your results will be treated confidentially by the study staff. Personally identifying information will not be reported to other departments or agencies. For a full list of reportable conditions, go to the following link:

https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ReportableDiseases.pdf

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of Bayer
- Representatives of the University of California
- Representatives of the Food and Drug Administration (FDA)
- Representatives of the National Cancer Institute (NCI)

Are there any costs to me for taking part in this study?

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.

If you have questions about what costs you will be responsible for, please talk with the study investigator before deciding to enroll in the study. Depending on the type of study, some of your costs could be substantial.

Bayer will provide sorafenib at no cost to you. Nivolumab will be billed to you or your insurance.

Will I be paid for taking part in this study?

You will not be paid for taking part 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, R. Kate Kelley MD, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her [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. Contact your study doctor R. Kate Kelley at the UCSF GI Oncology clinic, [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 office of the Institutional Review Board at 415-476-1814.

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 PARTICIPATION

This section of the informed consent form is about additional research that is being done using tumor samples after the main research has been completed. You can still be in the main study even if you say "no" to taking part in this additional research.

Optional Research on Leftover Samples (All Subjects)

If you give permission, biomarker studies will also be performed on archival (leftover) tissue collected at any time when you have tumor tissue available from a previous surgery or biopsy.

If you agree, specimens collected during this study would also be saved (“banked”) for future research to learn more about cancer and other diseases.

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

Reports about research done with your tissue 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. Results from the future research may be published but your data will not be reported individually.

Things to Think About

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

Your tissue will be stored in a repository at UCSF. If you decide now that your specimens can be kept for future research, you can change your mind at any time. Just contact the study doctor, R. Kate Kelley, MD, in writing at the address below, and let us know that you do not want us to keep your specimens.

R. Kate Kelley, MD
UCSF GI Medical Oncology Dept.
[redacted]

Any identifiable specimen that remains will no longer be used for research and destroyed. However, if any research has already been done using portions of your specimens, the data will be kept and analyzed as part of those research studies.

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

Your specimen will be used only for research and will not be sold. The research done with your tissue may help to develop new products in the future. You will not be paid for allowing your tumor samples to be used in research even though the research done with your samples may help to develop new products in the future. You will not receive any payment or financial benefit from any products, tests, or discoveries derived from these samples.

Benefits

The benefits of research using tissue and blood include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks

Confidentiality: Donating specimens may involve a loss of privacy, but information about you will be handled as confidentially as possible. The manager of the tissue bank and select tissue bank staff members will have access to information about you but they will not release any identifying information about you to researchers using your specimen. The UCSF IRB and other University of California personnel also may see information about you to check on the tissue bank such as for auditing purposes.

All records will be coded and permanently kept in password protected electronic files or locked files with access limited to the study investigators. All collected specimens will be assigned a corresponding code number by the study investigators and will then be processed without knowledge of your identity. Only the UCSF investigator has access to the records that link this coded ID number to you. In addition, specimens shared with other researchers, and the coded ID number will be used to identify your specimens.

Genetic information about your blood or tumor samples that results from this study does not have medical or treatment importance at this time, so you will not receive the results of this testing. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to employers, health providers, insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a relative) carry a genetic disease or by leading to the denial of employment or insurance for you (or a relative). To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record.

It is also possible that your or your family's privacy could be invaded in ways that are currently not possible but made possible in the future by advances in technology. For instance, some scientists performing research with tissue bank materials may try to determine the code of part or all of your chromosomes. This coding could be a way to

accurately identify the sample as coming from you. If a scientist publishes your coding, the source of that coding could be identified as you if someone else has your code through other means to compare to the published coding. The likelihood of this happening is very small, but future technology developments may increase the possibility of this occurring.

Additionally, due to the rarity of the cancer and the likelihood that the research done with the tissue samples will be published in the future, it may be possible to identify you from publications even though your name will not be used in any published reports.

Making Your Choice

Please read the sentence below and think about your choice. After reading put your initials in the "Yes", or "No" box. If you have any questions, please talk to your doctor or nurse, or call our Institutional Review Board at 415-476-1814.

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

1. Any leftover tissue samples collected for this clinical trial or any leftover samples from other biopsies or surgeries I have had for regular medical care may be used for future research.

YES	NO

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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	Person Obtaining Consent
_____	_____
Date	Witness (only required if the participant is a non-English speaker)