NCT# 02494921

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

CC# 145515: A Phase 1b Study of the Oral CDK4/6 Inhibitor Ribociclib in Combination with Docetaxel Plus Prednisone in Metastatic Castration-Resistant Prostate Cancer

Informed Consent Form

This is a clinical trial, a type of research study. Your study doctor Rahul Aggarwal, M.D. 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 research study because you are a patient with metastatic prostate cancer whose tumor has grown despite hormonal therapy.

Why is this study being done?

The purpose of this study is to learn whether ribociclib (LEE011), when added to a treatment (docetaxel plus prednisone) approved for your type of prostate cancer, helps to stabilize or stop progression of your cancer.

We want to test the safety of ribociclib in combination with docetaxel plus prednisone at different dose levels. We want to find out what effects, good and/or bad, it has on you and your type of cancer.

Ribociclib is a drug designed to block certain proteins called cyclin-dependent protein kinases that are required for cells to divide. These proteins may also control the ability of certain cancers to grow.

Ribociclib is a drug that has not been approved by U.S. Food and Drug Administration (FDA) or any other health authorities for the treatment of people with your medical condition. Ribociclib is currently not "on the market" (available for you to buy) in any country. As of the last update, ribociclib has been administered to 179 patients as a single agent.

Docetaxel is a type of chemotherapy that blocks cells from dividing. Docetaxel, in combination with a low dose of a steroid called prednisone, has been shown to be an effective treatment for your type of prostate cancer and has been approved by the U.S. Food and Drug Administration.

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This will be the first time that all three drugs, ribociclib, docetaxel, and prednisone are used in combination to treat patients.

Novartis Pharmaceuticals, Inc. which manufacturers ribociclib is supplying the study drug free-of-charge and is providing support to the investigator and the institution to conduct the study. The Prostate Cancer Foundation is also providing funding for this study.

How many people will take part in this study?

There are two parts to this study; a dose-finding part (phase Ib) and a dose expansion/phase II part, you will only be participating in the dose-finding part (phase Ib). Approximately 9-18 patients will participate in the dose-finding part (phase Ib) at UCSF.

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

You will receive one of three dosages of ribociclib, in combination with a standard dose of docetaxel and prednisone. Groups of three to six patients will receive treatment at a given dosage level of ribociclib. If, during the first 28 days of treatment, few serious side effects are observed, a new group of three to six patients will join the study. Each group of patients will be treated with the standard dose of docetaxel and prednisone, given together with increasing doses of ribociclib, until the highest tolerable doses are identified.

You will be treated with the combination of ribociclib plus docetaxel + prednisone for up to 9 cycles. If there is no evidence of progression after 9 cycles, you may continue on single agent maintenance ribociclib until the time of disease progression. The dose of ribociclib used during maintenance will be the same dose as that immediately preceding cessation of docetaxel treatment.

Which dose of ribociclib you receive will depend on the progress of the study and the side effects seen with other patients on the study. You will not be able to choose which dose of ribociclib you receive.

You will be asked if you allow further research to be performed on leftover tumor samples. Whether or not you agree to this optional research will not affect your ability to participate in the main portion of the study. Please refer to the end of this consent form for any information about optional research.

Dosing administration instructions:

- Docetaxel will be administered through one of your veins on the first day of each 3-week treatment cycle.
- Prednisone will be taken orally twice daily every day of each 3-week cycle.

- Ribociclib will be taken orally once daily on days 1-4 and 8-15 of each 3-week cycle.
- Filgrastim (also called Neupogen) will be administered under the skin on days 5-7 of each 3-week cycle as well as additional doses as needed.
- On most days, you will take study drugs at home. On the days you come to clinic, you will wait to take the study drugs during the visit once you are instructed to do so.
- You should swallow ribociclib capsules with a large glass of water at the same time each morning.
- You should swallow the ribociclib capsules whole and not chew, crush, or open them.
- You should take prednisone tablets in the morning and mid-afternoon with food.
- If you vomit after taking a dose, do not repeat the dose.
- Do not miss any doses. If you forget to take your study drugs but remember within six hours of when you were supposed to take them, you should take the drugs. If it is more than six hours, you should skip them.
- The study doctor will instruct you on how many capsules or tablets of each drug you should take.
- Avoid consumption of grapefruit, Seville oranges, pomelos, and star fruit or products containing the juice of each (including jams and marmalades) during the study and for 7 days prior to the first dose of ribociclib. Regular orange juice is allowed.

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. Many of these exams, tests or procedures are part of regular routine 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. The total time to complete the screening tests and procedures is about 8-12 hours. The following procedures will be done:

- **A complete medical history and your current medical condition** will be collected including information about your current health status
- Physical Examination
- **Vital signs** (blood pressure, heart rate, temperature), height and weight
- **Blood samples:** A blood sample will be drawn by inserting a needle into a vein in your arm (~4 tablespoons of blood):
    - Complete blood count (CBC) with differential and platelet count
    - Blood chemistry assessment
    - PSA
    - Testosterone
- To measure your disease, you will have one or more of the following tests done (these will be done within 42 days of registration):
- CT and/or MRI scan of the chest, abdomen, and pelvis:

- **A CT scan** is a radiological test that 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 or through one of your veins. 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. After you have been given the contrast material (either by mouth, by vein), 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. Each CT scan will take about 15 minutes to a half hour.

  If a CT scan cannot be performed, an **MRI scan** will be performed. An MRI scan takes an image of your 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 a 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.

- **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.
- **Electrocardiogram (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. The procedure is done in the Cardiology Department and takes about 15-30 minutes.
- You will be asked about any medicines you are taking including over-the-counter medicines, vitamins, or herbal treatments.
- **Performance status** to assess how your disease is affecting your daily activities.
- Either a MUGA (multiple-gated acquisition) scan or an ECHO (echocardiogram), non-invasive tests which take moving pictures of your heart will also be done. These will be done within 42 of registration.
  - **MUGA scan**: A MUGA scan is a test that makes a motion picture that shows how well your heart pumps blood. The scan is performed by taking a small sample of

your own blood that is then "labeled" with a radioactive substance. The labeled blood sample is then re-injected into a vein in your arm and allowed to circulate in your body. Once the labeled blood has circulated around your body, a series of images (similar to a movie) are taken of your heart. You will be asked to lie flat on a table and remain still for about 10-20 minutes while the pictures of your heart are being taken. This test is done in the Nuclear Medicine department and takes about 90 minutes.

- **ECHO**: This examination uses sound waves to make pictures of your heart, which helps determine how well your heart squeezes blood. You will be asked to lie on your left side while a technician places a probe with gel on your chest to create images of your heart to determine the function and size. The procedure is done in the Cardiology Department and will take approximately 45-60 minutes.

During the main part of the study:

If the exams, tests, and procedures show that meet the criteria to be in the research study and you choose to take part, you will then be enrolled in the research study. Each cycle of treatment will last 21 days.

Cycle 1, Day 1 (this visit will take about 4 hours)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature), height, and weight
- Blood samples (~2 tablespoons of blood):
  - Blood counts
  - Routine tests for safety
  - PSA
- Administration of docetaxel through one of your veins
- Start taking oral prednisone twice daily
- Review of side effects
- Performance status
- Concurrent medications
- First oral dose of ribociclib
- Blood samples (~1 tablespoon of blood):
  - Pharmacokinetics – These are blood tests that will help determine the levels of study drug in your blood at different time points.

Cycle 1, Day 2 (this visit will take about 30 minutes)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature)
- Review of side effects

- Performance status
- Blood samples (~1 tablespoon of blood):
    - Pharmacokinetics – These are blood tests that will help determine the levels of study drug in your blood at different time points.

Cycle 1, Days 5-7 (this visit should take about 15 minutes)

- Neupogen administration – given under the skin daily on Days 5-7. These injections will be administered either at home or in the clinic.

Cycle 1, Day 8 (this visit will take about 1 hour)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature)
- Blood samples (~2 tablespoons of blood):
    - Blood counts
    - Routine tests for safety
- Review of side effects
- Performance status
- Concurrent medications

Cycle 1, Day 15 (this visit will take about 1 hour)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature)
- Electrocardiogram (ECG)
- Blood samples (~1 tablespoon of blood):
    - Blood counts
- Review of side effects
- Performance status
- Concurrent medications

Cycle 2, Day 1 (this visit will take about 1 – 1 1/2 hours)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature), height, and weight
- Electrocardiogram (ECG)
- Blood samples (~2 tablespoons of blood):
    - Blood counts

  - Routine tests for safety
  - PSA
- Administration of docetaxel through one of your veins
- Review of side effects
- Performance status
- Concurrent medications

Cycle 2, Days 5-7 (this visit should take about 15 minutes)

Neupogen administration – given under the skin daily on Days 5-7. These injections will be administered either at home or in the clinic.

Day 1 of Every Cycle Thereafter (this visit will take about 4 hours)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature), height, and weight
- Blood samples (~2 tablespoons of blood):
  - Blood counts
  - Routine tests for safety
  - PSA
- Administration of docetaxel through one of your veins
- Review of side effects
- Electrocardiogram (ECG)
- Performance status
- Concurrent medications

Days 5-7 of Every Cycle Thereafter (this visit should take about 15 minutes)

- Neupogen administration – given under the skin daily on Days 5-7. These injections will be administered either at home or in the clinic.

Starting Cycle 4 and Every 3 Treatment Cycles (this visit will take about 5 hours)

The following will be done as part of your routine care:

- CT or MRI of the chest/abdomen/pelvis
- Bone scan

End of Treatment Visit (this visit will take between 1 hour and 5 hours)

During this visit, you will have the following exams, tests, or procedures at the time, as specified. The visit will be done within 30 days of the last treatment.

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature), height, and weight
- Blood samples (~2 tablespoons of blood):
  - Blood counts
  - Routine tests for safety
  - PSA
- Review of side effects
- Performance status
- Concurrent medications
- CT or MRI of the chest/abdomen/pelvis (if not already completed within past 28 days)
- Bone scan (if not already completed within past 28 days)

You will be contacted 30 days after the last dose of study treatment. You will be asked how you are feeling and what medications you have been taking.

If you withdraw from the study, and your disease has not progressed, you may be contacted via a phone call, and asked to have a CT/MRI scan done every two months to measure your disease since stopping study treatment. This will be done for research purposes if this scan is done at a time point other than your routine restaging time point.

Withdrawal of your consent to participate in this study

You may decide that you not only want to stop study treatment but also do not want to come to any further visits, and do not want to have any further assessments or contact by the study staff.

This is considered as withdrawal of your consent from participation in this study. It is important that you inform your Study Doctor.

UCSF will continue to retain and use any research-related results that have already been collected for the study evaluation. No further study-related activities will take place.

You can discuss further regular medical care with your Study Doctor. The choice to withdraw from research participation will not affect your medical care.

Study location: All study procedures will be done at UCSF Helen Diller Family Comprehensive Cancer Center.

What Will I Be Asked to Do While Participating In The Study?

In order for this study to provide good information about how the drugs work, you will be asked to do the following:

- Comply with your study doctor's instructions. Please note: It is very important that you take the medicine given to you just as the doctor tells you to. Do not miss any doses and do not try to double the dose if you miss a dose.
- Notify your study doctor immediately of any injury or unusual symptoms during your participation in this study.
- Review all the health food supplements, over-the-counter and prescription medications with your study doctor before taking them.
- With the exception of emergencies, you should not take other drugs while you are participating in the study without having consulted your study doctor. In case of an emergency treatment, your study doctor should be informed immediately.
- Bring all of your extra study drug medication and empty pill bottles back to the study doctor.
- Do not eat or drink grapefruit, Seville (sour/blood) oranges or products containing the juice of each during the study, as these fruits and their juice can interfere with the blood levels of the drugs. Regular orange juice is okay.
- On the days that you come to clinic visits, you will take the study drug there. Afterward, you will be provided with enough study medication until your next planned clinic visit.
- You will be asked to record the date and time you took the study medication and any side effects you may experience in a diary. This diary must be returned to your study doctor at your next visit.
- During the whole duration of treatment on this study, you are not allowed to participate in another clinical study that may interfere with this study. If you are interested in participating in another study, you must speak to your study doctor about it.

How long will I be in the study?

You will continue study treatment until you experience disease progression, discontinue treatment due to intolerable toxicity, investigator decision, or withdraw consent, whichever occurs first. You will be treated with the combination of ribociclib plus docetaxel + prednisone for up to 9 cycles. If there is no evidence of disease progression after 9 cycles of protocol therapy, patients may continue on single agent maintenance ribociclib until the time of disease progression.

Your doctor can also decide to withdraw you from the study if he/she feels that this is best for you.

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. 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 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 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?

Risks are possible side effects of study medicine, or undergoing tests, such as imaging scans and blood or tumor sample collection.

The potential side effects described below for ribociclib are based on tests in animals and experience in cancer subjects. It is possible that you may experience side effects that are unexpected and unforeseen. Everyone taking part in the study will be watched carefully for any side effects. Preventing side effects, when possible, is an important part of all cancer care.

The potential side effects described below for ribociclib and BYL719 are based on tests in animals and experience in cancer patients. The potential side effects described below for letrozole are based on extensive experience in cancer patients. It is possible that you may experience side effects that are totally unexpected and unforeseen. Everyone taking part in the study will be watched carefully for any side effects, and trying to prevent them, when possible, is an important part of all cancer care.

Risks related to ribociclib

Ribociclib is an investigational drug and not all of the side effects are known. Serious side effects, including death, are a possibility. The long-term effects of ribociclib are also unknown. Risks are possible side effects of study medicine given alone or in combination with other medication(s), and those of taking blood. Based on the data from ongoing studies in cancer patients, the following are the possible risks with taking ribociclib.

Very common side effects (*may affect more than 10% of people*)

- Low white blood cell count which increases the risk of infections (neutropenia or leukopenia)
- Infections (including urinary tract infections, respiratory infections, gastroenteritis and severe, potentially life-threatening infections [sepsis; this is uncommon])
- Low red blood cell count which can lead to tiredness and weakness (anemia)

- Nausea
- Diarrhea
- Vomiting
- Constipation
- Mouth sores, or pain, inflammation and/ or infection of the mouth
- Abdominal pain
- Tiredness or generalized weakness (fatigue or asthenia)
- Swelling of the arms or legs (peripheral oedema)
- Fever (pyrexia)
- Increase in the blood levels of liver parameters as indicated by liver tests (such as transaminases and/or bilirubin)
- Decreased appetite
- Back pain
- Headache
- Dizziness
- Shortness of breath (dyspnea)
- Cough
- Hair thinning or loss (alopecia)
- Skin rash
- Itching of the skin (pruritus)

Common side effects (*may affect up to 10% of people*)

- Low platelet count which can lead to easy bruising and bleeding (thrombocytopenia)
- Low white blood cell count with fever (febrile neutropenia)
- Low lymphocyte count in the blood that can predispose to infections (lymphopenia)
- Fainting episodes/transient loss of consciousness and postural posture (syncope)
- Excessive tearing of the eye (increased lacrimation)
- Dry eye
- Taste alteration (dysgeusia)
- Dry mouth
- Sore throat (oropharyngeal pain)
- Indigestion heartburn (dyspepsia)
- Liver toxicity (hepatotoxicity: injury of the liver due to liver cell damage, including liver failure [the latter is uncommon])
- Increase in creatinine (a waste product in the blood) and a decrease in the kidney's ability to handle the body's waste (blood creatinine increased)
- Changes in the electrical activity of the heart called QTc prolongation. This is an abnormality of the heart rhythm and may cause dizziness, palpitations, fainting, and in severe cases loss of consciousness and even death
- Decreased blood calcium levels (hypocalcaemia)
- Decreased blood potassium levels (hypokalemia)

- Decreased blood phosphorus levels (hypophosphatemia)
- Redness of the skin or reddening of the skin (erythema)
- Dry skin
- Loss of skin coloration/whitening, usually in patches (vitiligo)
- Sensation of losing balance (vertigo)

Rare but Important (*may affect less than 5% of people*):

- Potential accumulation of ribociclib in the thyroid gland. In rats, ribociclib was found to accumulate in the thyroid gland, but there was no evidence of damage to the thyroid gland. There have been no reports of abnormal thyroid function in any patient so far.
- One patient participating in a trial with ribociclib and MEK162 died from bleeding in the brain, which was considered related to ribociclib and MEK162 by the treating physician.
- One patient participating in a trial was diagnosed with acute lymphoblastic leukemia (ALL), which the treating physician considered possibly related to ribociclib.
- One patient participating in a trial was diagnosed with acute respiratory failure, which was considered possibly related to ribociclib
- Four participant deaths occurred on a breast cancer study, which were considered to be related to ribociclib. Two deaths were due to acute respiratory failure, and the other causes of death were pneumonia and sudden death.
- One patient participating in a trial with ribociclib and letrozole was diagnosed with myelodysplastic syndrome, which was considered possibly related to ribociclib. Myelodysplastic syndrome happens when the bone marrow, the material inside your bones where your blood cells are made, no longer works normally, which can lead to feeling tired, short of breath or having small red spots under your skin caused by bleeding or infections.
- On patient participating in a trial with ribociclib and letrozole experienced decreased sodium levels. You may feel tired, have a headache, feel nausea or vomit, or have cramps.
- One patient participating in a trial with ribociclib and letrozole was diagnosed with heart failure. You might feel short of breath, weakness, swelling in your legs, ankles or feet, or an irregular or rapid heartbeat.

Risks and side effects related to **docetaxel** and **prednisone** include those listed below:

Likely

- Rash
- Hair loss
- Fluid retention/swelling
- Fatigue
- Upset stomach
- Soreness and/or weakness of muscles and/or joints

- Increased blood sugar levels, which may cause increased thirst, urination, and fatigue
- Lowered white blood cell count that may lead to increased risk of infection
- Lowered platelet count that may lead to increased bruising or bleeding
- Lowered red blood cell count that may cause tiredness or shortness of breath (if the count gets too low you may need a transfusion)

Less Likely

- Diarrhea
- Nausea and vomiting
- Mouth and throat sores
- Loss of appetite
- Loss of reflexes
- Darkening or lightening of fingernail beds
- Peeling skin on hands and feet
- Insomnia
- Numbness and/or tingling of the fingers and toes

Rare, but serious

- Stomach ulcers and/or bleeding
- Severe allergic reaction (life-threatening breathing problems)
- Abnormal function of the adrenal gland which can cause weakness and fatigue, low blood pressure, nausea, vomiting, diarrhea, irritability and/or restlessness, loss of bone density
- Low blood pressure
- Abnormal changes in personality

In addition, you should **never** stop the prednisone suddenly. If you need to stop the prednisone, your doctor will advise you on how to slowly stop the drug (called a "taper"). If you were to stop taking prednisone suddenly, you could become very weak and tired, develop very low blood pressure, very low blood sugar, and abnormalities of the minerals in your bloodstream. While usually not severe, if not treated, these abnormalities are potentially fatal. If you have a serious illness, infection, or trauma, it will be necessary to increase your dose of prednisone. Anytime you see a doctor for any reason, you should tell him/her that you are taking prednisone.

We do not know the side effects of ribociclib, docetaxel, and prednisone when given alone or in combination with other drugs. A combination of drugs might result in serious or even life-threatening side effects. Some over-the-counter and prescription medications can reduce the effectiveness or increase the side effects of the study treatments. Likewise, the study treatments can increase the side effects or lessen the effectiveness of some medications. This might result in serious or even life-threatening side effects. You should always discuss the use of any drugs (over-the-counter drugs, prescription, or illegal drugs or health food supplements) with your doctor while you are participating in this study. The study protocol describes which medicines are prohibited during the study, and which ones can be taken with caution.

There could be additional unexpected side effects when ribociclib is taken in combination with docetaxel and prednisone.

Risks related to Neupogen (G-CSF):

G-CSF causes bone pain in many people. This pain may occur immediately or several days after receiving G-CSF. The pain may feel like an aching sensation in the bones of the back, hips, pelvis, or breastbone. Pain relievers, such as acetaminophen (Tylenol®) or ibuprofen (Advil®, Nuprin®) may be used to lessen this discomfort.

Occasionally, G-CSF may cause flu-like symptoms. If you already have inflammation of certain blood vessels, arthritis, eczema or psoriasis, G-CSF may cause these conditions to get worse. Other occasional side effects include headaches, muscle aches, tiredness, nausea and vomiting, and trouble sleeping. These symptoms usually go away within 2 or 3 days after stopping G-CSF.

The following side effects are rare and are not generally serious problems:

- Burning, swelling, and redness at the injection site
- Allergic reactions (hives/skin rash, itching, wheezing, fever, rapid heart rate, shortness of breath, dizziness)
- Lowering of blood pressure
- Changes in blood chemistry levels
- Enlargement of the spleen (seen in some patients treated with G-CSF for an extended period of time)

Rare but serious:

- Severe reactions to G-CSF in patients with sickle cell anemia and related sickle cell diseases.
- Pain and bleeding from the spleen, which may require surgery. If you feel pain in your upper left side just below the rib cage, contact your doctor immediately.

Other risks related to this study include:

Blood drawing (venipuncture) risks: Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection. In rare instances where a nurse, a doctor, or a laboratory technician sustains an exposure to your blood, tissue or body fluids by needle stick, cut or splash to mucosa or damaged skin, it may be necessary to test your blood, tissue, or body fluid sample for certain viral infections including Hepatitis B and C and HIV on the sample already available. This is to enable that person to receive appropriate counseling, monitoring, and treatment if necessary. In this instance, the Study Doctor will offer you the information relevant to your health and advise you on the next steps. Confidentiality of your data will be respected at all times.

CT scan risks: CT scans involve the risks of radiation. In addition, if contrast material (iodine dye) is used, there is a slight risk of developing an allergic reaction. The allergic reaction can be 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 you may have before the procedure is done. If you have any of these allergies or conditions, you may not be allowed to have a CT scan in the study.

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 a still position for a long time. If contrast material is used, you may feel discomfort when it is injected into your body. You may feel warm and flushed and/or 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 feel uncomfortable.

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 may occur. This can be treated immediately with fluids given through one of your veins. Very rarely, (less than one in one thousand), patients are allergic to gadolinium. These allergic effects most commonly include hives and itchy eyes, but more severe reactions, including shortness of breath, have been seen.

Patients with severe kidney disease sometimes have a bad reaction to the gadolinium contrast material. This 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 need to have a blood test in order to check the function of your kidneys. Based on your medical history and the results of this test, a doctor will decide whether it is safe for you to undergo the MRI scans.

Bone scan risk: A bone scan involves exposure to radiation. (See Radiation Risks below). Some people may have a closed-in feeling while under the camera. As in any injection, you may have swelling or bruising at the injection site.

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 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 the physician conducting the study.

Electrocardiogram (EKG/ECG) 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.

Echocardiogram (ECHO): The cardiac echogram might cause you to be uncomfortable from the pressure of the probe on your chest or lying still for the examination.

MUGA scan risks: MUGA scans involve the risks of radiation (See Radiation Risks above). You may develop bruising where the needle is placed in your veins to administer the radioactive substance. You may be uncomfortable lying flat.

Safe Handling of Medications: Handling ribociclib and having contact with any urine, feces, or vomit from patients receiving ribociclib may pose some risk to you and your caregivers. To avoid exposure to ribociclib and any associated risks, you and your family members/caregivers will be educated by a member of the study team on how to safely handle, properly dispose of, and clean products that may be contaminated with ribociclib.

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.

Reproductive Risks: You should not father a baby while on this study because the drugs in this study can affect an unborn baby. It is important to understand that you need to use birth control while on this study. You must always wear a condom during intercourse (even if you have had a vasectomy), and if fertile you must also use spermicide. You must continue to wear a condom while taking the drug and for 30 days after stopping treatment. For more information regarding contraception please speak to your study doctor.

Unknown Risks: The experimental treatments may have side effects that no one knows about. 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 the combination of ribociclib with docetaxel plus prednisone will be more useful against cancer compared to the usual treatment, there is no proof of this. Your condition may even get worse during the study. We do know that the information from this study will help doctors learn more about theses study drug combinations as a treatment for cancer. This information could help future cancer patients. However, there is no guarantee that this will happen.

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.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. 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:

- Novartis (the drug supplier) and its authorized agents
- Prostate Cancer Foundation
- The University of California
- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in keeping research safe for people. Governmental agencies in other countries where the study drug may be considered for approval.

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be

included in this record. Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

What are the costs of taking part in this study?

Study drug (ribociclib) will be provided by Novartis and will not cost you any money. You and/or your health plan/insurance company will need to pay for docetaxel and prednisone.

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.

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, Rahul Aggarwal, M.D., if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call [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 and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research 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 Rahul Aggarwal, M.D. [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 Committee on Human Research at 415-476-1814.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US 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

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Please note: This section of the informed consent form is about additional research studies that are being done.

You can say "yes" or "no" to each of the following studies. Please mark your choice for each study.

Biomarker Study: (optional for Phase Ib dose escalation patients)

- What: Biomarkers are important biological indicators, which can be measured from blood samples.
- When: Biomarker samples may be collected before you start your study treatment
- Why: So that the researchers can learn more about your cancer

About Using Samples for Research

Subjects taking part in this clinical study are being invited to take part in this optional research study. This study will use any remaining blood samples for additional research related to the ribociclib, docetaxel, prednisone, and/or cancer.

Any data generated from the additional research studies will belong to UCSF and will not become part of your medical record.

You can choose not to have your samples stored for additional use and still be a part of the study.

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 (describe any rare instances that this may occur).

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
University of California San Francisco
[redacted]

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

Things to Think About

The choice to allow UCSF to use the leftover blood 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 blood samples can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your samples. Then any sample that remains will no longer be used for research.

In the future, people who do research may need to know more about your health.

While UCSF 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 samples will be used only for research and will not be sold.

The research done with your blood samples may help to develop new products in the future.

Benefits

The research that may be done with your blood sample is not designed specifically to help you. It might help people who have cancer and other diseases in the future. The benefits of research using blood sample include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

UCSF will be the exclusive owner of any data and discoveries resulting from this research.

Any commercial product developed at UCSF as a result of these studies would be from the analysis of all samples collected in this study, not from an individual subject's sample.

Overall Risk

There is some risk from a breach of confidentiality. 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.

If this information were released to you, your family, or third parties, it could potentially be misused. Such misuse could lead to adverse psychological effects or undesired effects on the ability of you or your family members to obtain a job or insurance.

The types of medical information that could be collected are your previous medical history, laboratory values, type of cancer, and tumor staging.

In order to minimize these potential risks, all research information obtained for your blood sample and medical records will be kept confidential as described above.

Making Your Choice

Please read the sentences below and think about your choice. After reading the sentence, please 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 415-476-1814.

1. **I agree to allow UCSF to store and use my leftover blood and/or tumor samples for additional research tests related to ribociclib, docetaxel, prednisone and/or cancer.**

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 Printed Name
Date	Person Obtaining Consent
Date	Witness – Only required if the participant is a non-English speaker

LIST OF PROHIBITED MEDICATIONS

Category	Drug Name
Strong CYP3A4/5 inhibitors	Atazanavir/ritonavir, boceprevir, clarithromycin, cobicistat, conivaptan, danoprevir/ritonavir, darunavir/ritonavir, elvitegravir/ritonavir, grapefruit juice, idelalisib, indinavir, indinavir/ritonavir, itraconazole, ketoconazole, lopinavir/ritonavir, mibefradil, nefazodone, nelfinavir,ombitasvir/paritaprevir/dasabuvir/ritonavir (VIEKIRA PAK), posaconazole, ritonavir, saquinavir/ritonavir, telaprevir, telithromycin, tipranavir/ritonavir, troleandomycinvoriconazole
Strong CYP3A4/5 inducers	carbamazepine, enzalutamide, lumacaftor, mitotane, phenobarbital, phenytoin, rifabutin, rifampin (rifampicin), St. John's wort (hypericum perforatum)
Medications with a known risk for QT prolongation	Amiodarone, anagrelide, arsenic trioxide, astemizole, azithromycin, chloroquine, chlorpromazine, cilostazol, ciprofloxacin, cisapride, citalopram, clarithromycin, disopyramide, dofetilide, domperidone, donepezil, dronedarone, droperidol, erythromycin, escitalopram, flecainide, fluconazole, gatifloxacine, grepafloxacin, halofantrine, haloperidol, ibutilide, levofloxacin, levomepromazine, levosulpiride, methadone, moxifloxacin, ondansetron, oxaliplatin, papaverine HCl (intra-coronary), pentamidine, pimozide, procainamide, propofol, quinidine, roxithromycin, sevoflurane, sotalol, sulpiride, sultopride, terlipressin, terodiline, thioridazine, vandetanib
CYP3A4/5 substrates with NTI	Alfentanil, astemizole, cisapride, cyclosporine, diergotamine (dihydroergotamine), ergotamine, fentanyl, pimozide, quinidine, sirolimus, tacrolimus
Other investigational and antineoplastic therapies not part of the study	Other investigational therapies must not be used while the patient is on the study. Anticancer therapy (chemotherapy, all SERMS (including raloxifene) biologic or radiation therapy, and surgery) other than the study treatments must not be given to patients while the patient is on the study medication. If such agents are required for a patient, then the patient must be discontinued from the study.
Herbal preparations/ medications	Herbal preparations/medications are prohibited throughout the study. These herbal medications include, but are not limited to black cohosh, St. John's Wort, Kava, ephedra (ma huang), gingko biloba, dehydroepiandrosterone (DHEA), yohimbe, saw palmetto, and ginseng. Patients should stop using these herbal medications 7 days prior to first dose of study drug.

LIST OF MEDICATIONS TO BE USED WITH CAUTION

Category	Drug Name
Moderate CYP3A4/5 inhibitors	Aprepitant, amprenavir, asafoetida resin (Ferula asafoetida) cimetidine, crizotinib, diltiazem, faldaprevir, imatinib, isavuconazole, netupitant, nilotinib, tofisopam, Schisandra sphenanthera (nan wu wei zi), verapamil
Moderate CYP3A4/5 inducers	Bosentan, dabrafenib, efavirenz, etravirine, genistein,lopinavir[5], modafinil, nafcillin, telotristat
Sensitive CYP3A4/5 substrates	Alpha-dihydroergocryptine, aprepitant, atorvastatin, avanafil, bosutinib,brotizolam, budesonide, buspirone, cobimetinib, darifenacin, dasatininb, ebastine, eletriptan, eplerenone, everolimus, felodipine, fluticasone, grazoprevir, ibrutnib, isavuconazole, ivabradine, ivacaftor, , levomethadyl (LAAM), lomitapide, lovastatin, lumefantrine, lurasidone, maraviroc, midazolam, midostaurin, naloxegol, neratinib, nisoldipine, perospirone, quetiapine, ridaforolimus, sildenafil, simeprevir, simvastatin, ticagrelor, tilidine, tolvaptan, triazolam, ulipristal, vardenafil, venetoclax, vicriviroc, voclosporin
BSEP inhibitors	Alectinib, atorvastatin, bromocriptine, candesartan, clobetasol, clofaziminie, dabigatran, dipyridamole, glyburide, grazoprevir, ledipasvir, mifepristone,pioglitazone, reserpine,rifamycin, simeprevir, telmisartan,timcodar, troglitazone, valinomycin, velpatasvir
MATE1 and OCT2 substrates	Acyclovir, cephalexin, cimetidine, fexofenadine, ganciclovir, glycopyrronium, metformin, pindolol, plisicainide, ranitidine, topotecan, varenicline
OCT1/2 substrates	Amantadine, 6-beta-hydroxycortisol, carboplatin, cisplatin, cephalexin, cephradine, ipratropium, lamivudine, linagliptin, metformin, oxyplatin, oxybutynin, phenformin, picoplatin, pilsicainide, pindolol, ranitidine, sorafenib, tropisetron, trospium, umeclidinium, and zidovudine
BCRP substrates	Daunorubicin, dolutegravir, doxorubicin, hematoporphyrin, imatinib, methotrexate, mitoxantrone, pitavastatin, rosuvastatin, irinotecan, ethinyl estradiol, simvastatin, sulfasalazine, sofosbuvir, tenofovir, topotecan, venetoclax
Medications that carry a possible risk for QT prolongation	Alfuzosin, apomorphine, aripiprazole, artenimol+piperaquine , asenapine, atomoxetine, bedaquiline, bendamustine, bortezomib, bosutinib, buprenorphine, cabozantinib, capecitabine, ceritinib, clomipramine, crizotinib,clozapine, cyamemazine (cyamepromazine), dabrafenib, dasatinib, degarilix, delamanid, desipramine, dexmedetomidine, dolasetron, efavirenz, eliglustat, epirubicin, eribulin mesylate, ezogabine(retigabine), famotidine, felbamate, fingolimod, flupentixol, gemifloxacin, granisetron, hydrocodone-ER, iloperidone, imipramine (melipramine), isradipine, ketanserin, lapatinib, lenvatinib, leuprolide, lithium, melperone, midostaurin, mifepristone, mirabegron, mirtazapine, moexipril/HCTZ, necitumumab, nicardipine, nilotinib, norfloxacin, nortriptyline, nusinersen, ofloxacin, osimertinib, oxytocin, paliperidone, palonosetron, panabinostat, pasireotide, pazopanib, perflutren lipid microspheres, perphenazine, pilsicainide, pimavanserin, pipamperone, promethazine, prothipendyl, rilpivirine, risperidone, romidepsin, sertindole, sorafenib, sunitinib, tamoxifen, tipiracil/trifluridine, tizanidine, tolterodine, toremifene,trimipramine, tropisetron, vardenafil, vemurafenib, venlafaxine, vorinostat, ziprasidone

This will be the first time that all three drugs, ribociclib, docetaxel, and prednisone are used in combination to treat patients.

Novartis Pharmaceuticals, Inc. which manufacturers ribociclib is supplying the study drug free-of-charge and is providing support to the investigator and the institution to conduct the study. The Prostate Cancer Foundation is also providing funding for this study.

How many people will take part in this study?

There are two parts to this study; a dose-finding part (phase Ib) and a dose expansion/phase II part, you will only be participating in the dose-finding part (phase Ib). Approximately 9-18 patients will participate in the dose-finding part (phase Ib) at UCSF.

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

You will receive one of three dosages of ribociclib, in combination with a standard dose of docetaxel and prednisone. Groups of three to six patients will receive treatment at a given dosage level of ribociclib. If, during the first 28 days of treatment, few serious side effects are observed, a new group of three to six patients will join the study. Each group of patients will be treated with the standard dose of docetaxel and prednisone, given together with increasing doses of ribociclib, until the highest tolerable doses are identified.

You will be treated with the combination of ribociclib plus docetaxel + prednisone for up to 9 cycles. If there is no evidence of progression after 9 cycles, you may continue on single agent maintenance ribociclib until the time of disease progression. The dose of ribociclib used during maintenance will be the same dose as that immediately preceding cessation of docetaxel treatment.

Which dose of ribociclib you receive will depend on the progress of the study and the side effects seen with other patients on the study. You will not be able to choose which dose of ribociclib you receive.

You will be asked if you allow further research to be performed on leftover tumor samples. Whether or not you agree to this optional research will not affect your ability to participate in the main portion of the study. Please refer to the end of this consent form for any information about optional research.

Dosing administration instructions:

- Docetaxel will be administered through one of your veins on the first day of each 3-week treatment cycle.
- Prednisone will be taken orally twice daily every day of each 3-week cycle.

- Ribociclib will be taken orally once daily on days 1-4 and 8-15 of each 3-week cycle.
- Filgrastim (also called Neupogen) will be administered under the skin on days 5-7 of each 3-week cycle as well as additional doses as needed.
- On most days, you will take study drugs at home. On the days you come to clinic, you will wait to take the study drugs during the visit once you are instructed to do so.
- You should swallow ribociclib capsules with a large glass of water at the same time each morning.
- You should swallow the ribociclib capsules whole and not chew, crush, or open them.
- You should take prednisone tablets in the morning and mid-afternoon with food.
- If you vomit after taking a dose, do not repeat the dose.
- Do not miss any doses. If you forget to take your study drugs but remember within six hours of when you were supposed to take them, you should take the drugs. If it is more than six hours, you should skip them.
- The study doctor will instruct you on how many capsules or tablets of each drug you should take.
- Avoid consumption of grapefruit, Seville oranges, pomelos, and star fruit or products containing the juice of each (including jams and marmalades) during the study and for 7 days prior to the first dose of ribociclib. Regular orange juice is allowed.

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. Many of these exams, tests or procedures are part of regular routine 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. The total time to complete the screening tests and procedures is about 8-12 hours. The following procedures will be done:

- **A complete medical history and your current medical condition** will be collected including information about your current health status
- Physical Examination
- **Vital signs** (blood pressure, heart rate, temperature), height and weight
- **Blood samples:** A blood sample will be drawn by inserting a needle into a vein in your arm (~4 tablespoons of blood):
    - Complete blood count (CBC) with differential and platelet count
    - Blood chemistry assessment
    - PSA
    - Testosterone
- To measure your disease, you will have one or more of the following tests done (these will be done within 42 days of registration):
- CT and/or MRI scan of the chest, abdomen, and pelvis:

- **A CT scan** is a radiological test that 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 or through one of your veins. 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. After you have been given the contrast material (either by mouth, by vein), 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. Each CT scan will take about 15 minutes to a half hour.

  If a CT scan cannot be performed, an **MRI scan** will be performed. An MRI scan takes an image of your 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 a 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.

- **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.
- **Electrocardiogram (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. The procedure is done in the Cardiology Department and takes about 15-30 minutes.
- You will be asked about any medicines you are taking including over-the-counter medicines, vitamins, or herbal treatments.
- **Performance status** to assess how your disease is affecting your daily activities.
- Either a MUGA (multiple-gated acquisition) scan or an ECHO (echocardiogram), non-invasive tests which take moving pictures of your heart will also be done. These will be done within 42 of registration.
  - **MUGA scan**: A MUGA scan is a test that makes a motion picture that shows how well your heart pumps blood. The scan is performed by taking a small sample of

your own blood that is then "labeled" with a radioactive substance. The labeled blood sample is then re-injected into a vein in your arm and allowed to circulate in your body. Once the labeled blood has circulated around your body, a series of images (similar to a movie) are taken of your heart. You will be asked to lie flat on a table and remain still for about 10-20 minutes while the pictures of your heart are being taken. This test is done in the Nuclear Medicine department and takes about 90 minutes.

- **ECHO**: This examination uses sound waves to make pictures of your heart, which helps determine how well your heart squeezes blood. You will be asked to lie on your left side while a technician places a probe with gel on your chest to create images of your heart to determine the function and size. The procedure is done in the Cardiology Department and will take approximately 45-60 minutes.

During the main part of the study:

If the exams, tests, and procedures show that meet the criteria to be in the research study and you choose to take part, you will then be enrolled in the research study. Each cycle of treatment will last 21 days.

Cycle 1, Day 1 (this visit will take about 4 hours)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature), height, and weight
- Blood samples (~2 tablespoons of blood):
  - Blood counts
  - Routine tests for safety
  - PSA
- Administration of docetaxel through one of your veins
- Start taking oral prednisone twice daily
- Review of side effects
- Performance status
- Concurrent medications
- First oral dose of ribociclib
- Blood samples (~1 tablespoon of blood):
  - Pharmacokinetics – These are blood tests that will help determine the levels of study drug in your blood at different time points.

Cycle 1, Day 2 (this visit will take about 30 minutes)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature)
- Review of side effects

- Performance status
- Blood samples (~1 tablespoon of blood):
    - Pharmacokinetics – These are blood tests that will help determine the levels of study drug in your blood at different time points.

Cycle 1, Days 5-7 (this visit should take about 15 minutes)

- Neupogen administration – given under the skin daily on Days 5-7. These injections will be administered either at home or in the clinic.

Cycle 1, Day 8 (this visit will take about 1 hour)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature)
- Blood samples (~2 tablespoons of blood):
    - Blood counts
    - Routine tests for safety
- Review of side effects
- Performance status
- Concurrent medications

Cycle 1, Day 15 (this visit will take about 1 hour)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature)
- Electrocardiogram (ECG)
- Blood samples (~1 tablespoon of blood):
    - Blood counts
- Review of side effects
- Performance status
- Concurrent medications

Cycle 2, Day 1 (this visit will take about 1 – 1 1/2 hours)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature), height, and weight
- Electrocardiogram (ECG)
- Blood samples (~2 tablespoons of blood):
    - Blood counts

  - Routine tests for safety
  - PSA
- Administration of docetaxel through one of your veins
- Review of side effects
- Performance status
- Concurrent medications

Cycle 2, Days 5-7 (this visit should take about 15 minutes)

Neupogen administration – given under the skin daily on Days 5-7. These injections will be administered either at home or in the clinic.

Day 1 of Every Cycle Thereafter (this visit will take about 4 hours)

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature), height, and weight
- Blood samples (~2 tablespoons of blood):
  - Blood counts
  - Routine tests for safety
  - PSA
- Administration of docetaxel through one of your veins
- Review of side effects
- Electrocardiogram (ECG)
- Performance status
- Concurrent medications

Days 5-7 of Every Cycle Thereafter (this visit should take about 15 minutes)

- Neupogen administration – given under the skin daily on Days 5-7. These injections will be administered either at home or in the clinic.

Starting Cycle 4 and Every 3 Treatment Cycles (this visit will take about 5 hours)

The following will be done as part of your routine care:

- CT or MRI of the chest/abdomen/pelvis
- Bone scan

End of Treatment Visit (this visit will take between 1 hour and 5 hours)

During this visit, you will have the following exams, tests, or procedures at the time, as specified. The visit will be done within 30 days of the last treatment.

- Physical Examination
- Vital signs (blood pressure, heart rate, temperature), height, and weight
- Blood samples (~2 tablespoons of blood):
  - Blood counts
  - Routine tests for safety
  - PSA
- Review of side effects
- Performance status
- Concurrent medications
- CT or MRI of the chest/abdomen/pelvis (if not already completed within past 28 days)
- Bone scan (if not already completed within past 28 days)

You will be contacted 30 days after the last dose of study treatment. You will be asked how you are feeling and what medications you have been taking.

If you withdraw from the study, and your disease has not progressed, you may be contacted via a phone call, and asked to have a CT/MRI scan done every two months to measure your disease since stopping study treatment. This will be done for research purposes if this scan is done at a time point other than your routine restaging time point.

Withdrawal of your consent to participate in this study

You may decide that you not only want to stop study treatment but also do not want to come to any further visits, and do not want to have any further assessments or contact by the study staff.

This is considered as withdrawal of your consent from participation in this study. It is important that you inform your Study Doctor.

UCSF will continue to retain and use any research-related results that have already been collected for the study evaluation. No further study-related activities will take place.

You can discuss further regular medical care with your Study Doctor. The choice to withdraw from research participation will not affect your medical care.

Study location: All study procedures will be done at UCSF Helen Diller Family Comprehensive Cancer Center.

What Will I Be Asked to Do While Participating In The Study?

In order for this study to provide good information about how the drugs work, you will be asked to do the following:

- Comply with your study doctor's instructions. Please note: It is very important that you take the medicine given to you just as the doctor tells you to. Do not miss any doses and do not try to double the dose if you miss a dose.
- Notify your study doctor immediately of any injury or unusual symptoms during your participation in this study.
- Review all the health food supplements, over-the-counter and prescription medications with your study doctor before taking them.
- With the exception of emergencies, you should not take other drugs while you are participating in the study without having consulted your study doctor. In case of an emergency treatment, your study doctor should be informed immediately.
- Bring all of your extra study drug medication and empty pill bottles back to the study doctor.
- Do not eat or drink grapefruit, Seville (sour/blood) oranges or products containing the juice of each during the study, as these fruits and their juice can interfere with the blood levels of the drugs. Regular orange juice is okay.
- On the days that you come to clinic visits, you will take the study drug there. Afterward, you will be provided with enough study medication until your next planned clinic visit.
- You will be asked to record the date and time you took the study medication and any side effects you may experience in a diary. This diary must be returned to your study doctor at your next visit.
- During the whole duration of treatment on this study, you are not allowed to participate in another clinical study that may interfere with this study. If you are interested in participating in another study, you must speak to your study doctor about it.

How long will I be in the study?

You will continue study treatment until you experience disease progression, discontinue treatment due to intolerable toxicity, investigator decision, or withdraw consent, whichever occurs first. You will be treated with the combination of ribociclib plus docetaxel + prednisone for up to 9 cycles. If there is no evidence of disease progression after 9 cycles of protocol therapy, patients may continue on single agent maintenance ribociclib until the time of disease progression.

Your doctor can also decide to withdraw you from the study if he/she feels that this is best for you.

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. 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 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 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?

Risks are possible side effects of study medicine, or undergoing tests, such as imaging scans and blood or tumor sample collection.

The potential side effects described below for ribociclib are based on tests in animals and experience in cancer subjects. It is possible that you may experience side effects that are unexpected and unforeseen. Everyone taking part in the study will be watched carefully for any side effects. Preventing side effects, when possible, is an important part of all cancer care.

The potential side effects described below for ribociclib and BYL719 are based on tests in animals and experience in cancer patients. The potential side effects described below for letrozole are based on extensive experience in cancer patients. It is possible that you may experience side effects that are totally unexpected and unforeseen. Everyone taking part in the study will be watched carefully for any side effects, and trying to prevent them, when possible, is an important part of all cancer care.

Risks related to ribociclib

Ribociclib is an investigational drug and not all of the side effects are known. Serious side effects, including death, are a possibility. The long-term effects of ribociclib are also unknown. Risks are possible side effects of study medicine given alone or in combination with other medication(s), and those of taking blood. Based on the data from ongoing studies in cancer patients, the following are the possible risks with taking ribociclib.

Very common side effects (*may affect more than 10% of people*)

- Low white blood cell count which increases the risk of infections (neutropenia or leukopenia)
- Infections (including urinary tract infections, respiratory infections, gastroenteritis and severe, potentially life-threatening infections [sepsis; this is uncommon])
- Low red blood cell count which can lead to tiredness and weakness (anemia)

- Nausea
- Diarrhea
- Vomiting
- Constipation
- Mouth sores, or pain, inflammation and/ or infection of the mouth
- Abdominal pain
- Tiredness or generalized weakness (fatigue or asthenia)
- Swelling of the arms or legs (peripheral oedema)
- Fever (pyrexia)
- Increase in the blood levels of liver parameters as indicated by liver tests (such as transaminases and/or bilirubin)
- Decreased appetite
- Back pain
- Headache
- Dizziness
- Shortness of breath (dyspnea)
- Cough
- Hair thinning or loss (alopecia)
- Skin rash
- Itching of the skin (pruritus)

Common side effects (*may affect up to 10% of people*)

- Low platelet count which can lead to easy bruising and bleeding (thrombocytopenia)
- Low white blood cell count with fever (febrile neutropenia)
- Low lymphocyte count in the blood that can predispose to infections (lymphopenia)
- Fainting episodes/transient loss of consciousness and postural posture (syncope)
- Excessive tearing of the eye (increased lacrimation)
- Dry eye
- Taste alteration (dysgeusia)
- Dry mouth
- Sore throat (oropharyngeal pain)
- Indigestion heartburn (dyspepsia)
- Liver toxicity (hepatotoxicity: injury of the liver due to liver cell damage, including liver failure [the latter is uncommon])
- Increase in creatinine (a waste product in the blood) and a decrease in the kidney's ability to handle the body's waste (blood creatinine increased)
- Changes in the electrical activity of the heart called QTc prolongation. This is an abnormality of the heart rhythm and may cause dizziness, palpitations, fainting, and in severe cases loss of consciousness and even death
- Decreased blood calcium levels (hypocalcaemia)
- Decreased blood potassium levels (hypokalemia)

- Decreased blood phosphorus levels (hypophosphatemia)
- Redness of the skin or reddening of the skin (erythema)
- Dry skin
- Loss of skin coloration/whitening, usually in patches (vitiligo)
- Sensation of losing balance (vertigo)

Rare but Important (*may affect less than 5% of people*):

- Potential accumulation of ribociclib in the thyroid gland. In rats, ribociclib was found to accumulate in the thyroid gland, but there was no evidence of damage to the thyroid gland. There have been no reports of abnormal thyroid function in any patient so far.
- One patient participating in a trial with ribociclib and MEK162 died from bleeding in the brain, which was considered related to ribociclib and MEK162 by the treating physician.
- One patient participating in a trial was diagnosed with acute lymphoblastic leukemia (ALL), which the treating physician considered possibly related to ribociclib.
- One patient participating in a trial was diagnosed with acute respiratory failure, which was considered possibly related to ribociclib
- Four participant deaths occurred on a breast cancer study, which were considered to be related to ribociclib. Two deaths were due to acute respiratory failure, and the other causes of death were pneumonia and sudden death.
- One patient participating in a trial with ribociclib and letrozole was diagnosed with myelodysplastic syndrome, which was considered possibly related to ribociclib. Myelodysplastic syndrome happens when the bone marrow, the material inside your bones where your blood cells are made, no longer works normally, which can lead to feeling tired, short of breath or having small red spots under your skin caused by bleeding or infections.
- On patient participating in a trial with ribociclib and letrozole experienced decreased sodium levels. You may feel tired, have a headache, feel nausea or vomit, or have cramps.
- One patient participating in a trial with ribociclib and letrozole was diagnosed with heart failure. You might feel short of breath, weakness, swelling in your legs, ankles or feet, or an irregular or rapid heartbeat.

Risks and side effects related to **docetaxel** and **prednisone** include those listed below:

Likely

- Rash
- Hair loss
- Fluid retention/swelling
- Fatigue
- Upset stomach
- Soreness and/or weakness of muscles and/or joints

- Increased blood sugar levels, which may cause increased thirst, urination, and fatigue
- Lowered white blood cell count that may lead to increased risk of infection
- Lowered platelet count that may lead to increased bruising or bleeding
- Lowered red blood cell count that may cause tiredness or shortness of breath (if the count gets too low you may need a transfusion)

Less Likely

- Diarrhea
- Nausea and vomiting
- Mouth and throat sores
- Loss of appetite
- Loss of reflexes
- Darkening or lightening of fingernail beds
- Peeling skin on hands and feet
- Insomnia
- Numbness and/or tingling of the fingers and toes

Rare, but serious

- Stomach ulcers and/or bleeding
- Severe allergic reaction (life-threatening breathing problems)
- Abnormal function of the adrenal gland which can cause weakness and fatigue, low blood pressure, nausea, vomiting, diarrhea, irritability and/or restlessness, loss of bone density
- Low blood pressure
- Abnormal changes in personality

In addition, you should **never** stop the prednisone suddenly. If you need to stop the prednisone, your doctor will advise you on how to slowly stop the drug (called a "taper"). If you were to stop taking prednisone suddenly, you could become very weak and tired, develop very low blood pressure, very low blood sugar, and abnormalities of the minerals in your bloodstream. While usually not severe, if not treated, these abnormalities are potentially fatal. If you have a serious illness, infection, or trauma, it will be necessary to increase your dose of prednisone. Anytime you see a doctor for any reason, you should tell him/her that you are taking prednisone.

We do not know the side effects of ribociclib, docetaxel, and prednisone when given alone or in combination with other drugs. A combination of drugs might result in serious or even life-threatening side effects. Some over-the-counter and prescription medications can reduce the effectiveness or increase the side effects of the study treatments. Likewise, the study treatments can increase the side effects or lessen the effectiveness of some medications. This might result in serious or even life-threatening side effects. You should always discuss the use of any drugs (over-the-counter drugs, prescription, or illegal drugs or health food supplements) with your doctor while you are participating in this study. The study protocol describes which medicines are prohibited during the study, and which ones can be taken with caution.

There could be additional unexpected side effects when ribociclib is taken in combination with docetaxel and prednisone.

Risks related to Neupogen (G-CSF):

G-CSF causes bone pain in many people. This pain may occur immediately or several days after receiving G-CSF. The pain may feel like an aching sensation in the bones of the back, hips, pelvis, or breastbone. Pain relievers, such as acetaminophen (Tylenol®) or ibuprofen (Advil®, Nuprin®) may be used to lessen this discomfort.

Occasionally, G-CSF may cause flu-like symptoms. If you already have inflammation of certain blood vessels, arthritis, eczema or psoriasis, G-CSF may cause these conditions to get worse. Other occasional side effects include headaches, muscle aches, tiredness, nausea and vomiting, and trouble sleeping. These symptoms usually go away within 2 or 3 days after stopping G-CSF.

The following side effects are rare and are not generally serious problems:

- Burning, swelling, and redness at the injection site
- Allergic reactions (hives/skin rash, itching, wheezing, fever, rapid heart rate, shortness of breath, dizziness)
- Lowering of blood pressure
- Changes in blood chemistry levels
- Enlargement of the spleen (seen in some patients treated with G-CSF for an extended period of time)

Rare but serious:

- Severe reactions to G-CSF in patients with sickle cell anemia and related sickle cell diseases.
- Pain and bleeding from the spleen, which may require surgery. If you feel pain in your upper left side just below the rib cage, contact your doctor immediately.

Other risks related to this study include:

Blood drawing (venipuncture) risks: Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection. In rare instances where a nurse, a doctor, or a laboratory technician sustains an exposure to your blood, tissue or body fluids by needle stick, cut or splash to mucosa or damaged skin, it may be necessary to test your blood, tissue, or body fluid sample for certain viral infections including Hepatitis B and C and HIV on the sample already available. This is to enable that person to receive appropriate counseling, monitoring, and treatment if necessary. In this instance, the Study Doctor will offer you the information relevant to your health and advise you on the next steps. Confidentiality of your data will be respected at all times.

CT scan risks: CT scans involve the risks of radiation. In addition, if contrast material (iodine dye) is used, there is a slight risk of developing an allergic reaction. The allergic reaction can be 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 you may have before the procedure is done. If you have any of these allergies or conditions, you may not be allowed to have a CT scan in the study.

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 a still position for a long time. If contrast material is used, you may feel discomfort when it is injected into your body. You may feel warm and flushed and/or 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 feel uncomfortable.

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 may occur. This can be treated immediately with fluids given through one of your veins. Very rarely, (less than one in one thousand), patients are allergic to gadolinium. These allergic effects most commonly include hives and itchy eyes, but more severe reactions, including shortness of breath, have been seen.

Patients with severe kidney disease sometimes have a bad reaction to the gadolinium contrast material. This 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 need to have a blood test in order to check the function of your kidneys. Based on your medical history and the results of this test, a doctor will decide whether it is safe for you to undergo the MRI scans.

Bone scan risk: A bone scan involves exposure to radiation. (See Radiation Risks below). Some people may have a closed-in feeling while under the camera. As in any injection, you may have swelling or bruising at the injection site.

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 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 the physician conducting the study.

Electrocardiogram (EKG/ECG) 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.

Echocardiogram (ECHO): The cardiac echogram might cause you to be uncomfortable from the pressure of the probe on your chest or lying still for the examination.

MUGA scan risks: MUGA scans involve the risks of radiation (See Radiation Risks above). You may develop bruising where the needle is placed in your veins to administer the radioactive substance. You may be uncomfortable lying flat.

Safe Handling of Medications: Handling ribociclib and having contact with any urine, feces, or vomit from patients receiving ribociclib may pose some risk to you and your caregivers. To avoid exposure to ribociclib and any associated risks, you and your family members/caregivers will be educated by a member of the study team on how to safely handle, properly dispose of, and clean products that may be contaminated with ribociclib.

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.

Reproductive Risks: You should not father a baby while on this study because the drugs in this study can affect an unborn baby. It is important to understand that you need to use birth control while on this study. You must always wear a condom during intercourse (even if you have had a vasectomy), and if fertile you must also use spermicide. You must continue to wear a condom while taking the drug and for 30 days after stopping treatment. For more information regarding contraception please speak to your study doctor.

Unknown Risks: The experimental treatments may have side effects that no one knows about. 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 the combination of ribociclib with docetaxel plus prednisone will be more useful against cancer compared to the usual treatment, there is no proof of this. Your condition may even get worse during the study. We do know that the information from this study will help doctors learn more about theses study drug combinations as a treatment for cancer. This information could help future cancer patients. However, there is no guarantee that this will happen.

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.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. 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:

- Novartis (the drug supplier) and its authorized agents
- Prostate Cancer Foundation
- The University of California
- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in keeping research safe for people. Governmental agencies in other countries where the study drug may be considered for approval.

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be

included in this record. Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

What are the costs of taking part in this study?

Study drug (ribociclib) will be provided by Novartis and will not cost you any money. You and/or your health plan/insurance company will need to pay for docetaxel and prednisone.

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.

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, Rahul Aggarwal, M.D., if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call [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 and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research 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 Rahul Aggarwal, M.D. [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 Committee on Human Research at 415-476-1814.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US 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

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Please note: This section of the informed consent form is about additional research studies that are being done.

You can say "yes" or "no" to each of the following studies. Please mark your choice for each study.

Biomarker Study: (optional for Phase Ib dose escalation patients)

- What: Biomarkers are important biological indicators, which can be measured from blood samples.
- When: Biomarker samples may be collected before you start your study treatment
- Why: So that the researchers can learn more about your cancer

About Using Samples for Research

Subjects taking part in this clinical study are being invited to take part in this optional research study. This study will use any remaining blood samples for additional research related to the ribociclib, docetaxel, prednisone, and/or cancer.

Any data generated from the additional research studies will belong to UCSF and will not become part of your medical record.

You can choose not to have your samples stored for additional use and still be a part of the study.

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 (describe any rare instances that this may occur).

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
University of California San Francisco


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

Things to Think About

The choice to allow UCSF to use the leftover blood 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 blood samples can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your samples. Then any sample that remains will no longer be used for research.

In the future, people who do research may need to know more about your health.

While UCSF 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 samples will be used only for research and will not be sold.

The research done with your blood samples may help to develop new products in the future.

Benefits

The research that may be done with your blood sample is not designed specifically to help you. It might help people who have cancer and other diseases in the future. The benefits of research using blood sample include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

UCSF will be the exclusive owner of any data and discoveries resulting from this research.

Any commercial product developed at UCSF as a result of these studies would be from the analysis of all samples collected in this study, not from an individual subject's sample.

Overall Risk

There is some risk from a breach of confidentiality. 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.

If this information were released to you, your family, or third parties, it could potentially be misused. Such misuse could lead to adverse psychological effects or undesired effects on the ability of you or your family members to obtain a job or insurance.

The types of medical information that could be collected are your previous medical history, laboratory values, type of cancer, and tumor staging.

In order to minimize these potential risks, all research information obtained for your blood sample and medical records will be kept confidential as described above.

Making Your Choice

Please read the sentences below and think about your choice. After reading the sentence, please 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 415-476-1814.

1. **I agree to allow UCSF to store and use my leftover blood and/or tumor samples for additional research tests related to ribociclib, docetaxel, prednisone and/or cancer.**

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 Printed Name
Date	Person Obtaining Consent
Date	Witness – Only required if the participant is a non-English speaker

LIST OF PROHIBITED MEDICATIONS

Category	Drug Name
Strong CYP3A4/5 inhibitors	Atazanavir/ritonavir, boceprevir, clarithromycin, cobicistat, conivaptan, danoprevir/ritonavir, darunavir/ritonavir, elvitegravir/ritonavir, grapefruit juice, idelalisib, indinavir, indinavir/ritonavir, itraconazole, ketoconazole, lopinavir/ritonavir, mibefradil, nefazodone, nelfinavir,ombitasvir/paritaprevir/dasabuvir/ritonavir (VIEKIRA PAK), posaconazole, ritonavir, saquinavir/ritonavir, telaprevir, telithromycin, tipranavir/ritonavir, troleandomycinvoriconazole
Strong CYP3A4/5 inducers	carbamazepine, enzalutamide, lumacaftor, mitotane, phenobarbital, phenytoin, rifabutin, rifampin (rifampicin), St. John's wort (hypericum perforatum)
Medications with a known risk for QT prolongation	Amiodarone, anagrelide, arsenic trioxide, astemizole, azithromycin, chloroquine, chlorpromazine, cilostazol, ciprofloxacin, cisapride, citalopram, clarithromycin, disopyramide, dofetilide, domperidone, donepezil, dronedarone, droperidol, erythromycin, escitalopram, flecainide, fluconazole, gatifloxacine, grepafloxacin, halofantrine, haloperidol, ibutilide, levofloxacin, levomepromazine, levosulpiride, methadone, moxifloxacin, ondansetron, oxaliplatin, papaverine HCl (intra-coronary), pentamidine, pimozide, procainamide, propofol, quinidine, roxithromycin, sevoflurane, sotalol, sulpiride, sultopride, terlipressin, terodiline, thioridazine, vandetanib
CYP3A4/5 substrates with NTI	Alfentanil, astemizole, cisapride, cyclosporine, diergotamine (dihydroergotamine), ergotamine, fentanyl, pimozide, quinidine, sirolimus, tacrolimus
Other investigational and antineoplastic therapies not part of the study	Other investigational therapies must not be used while the patient is on the study. Anticancer therapy (chemotherapy, all SERMS (including raloxifene) biologic or radiation therapy, and surgery) other than the study treatments must not be given to patients while the patient is on the study medication. If such agents are required for a patient, then the patient must be discontinued from the study.
Herbal preparations/ medications	Herbal preparations/medications are prohibited throughout the study. These herbal medications include, but are not limited to black cohosh, St. John's Wort, Kava, ephedra (ma huang), gingko biloba, dehydroepiandrosterone (DHEA), yohimbe, saw palmetto, and ginseng. Patients should stop using these herbal medications 7 days prior to first dose of study drug.

LIST OF MEDICATIONS TO BE USED WITH CAUTION

Category	Drug Name
Moderate CYP3A4/5 inhibitors	Aprepitant, amprenavir, asafoetida resin (Ferula asafoetida) cimetidine, crizotinib, diltiazem, faldaprevir, imatinib, isavuconazole, netupitant, nilotinib, tofisopam, Schisandra sphenanthera (nan wu wei zi), verapamil
Moderate CYP3A4/5 inducers	Bosentan, dabrafenib, efavirenz, etravirine, genistein,lopinavir[5], modafinil, nafcillin, telotristat
Sensitive CYP3A4/5 substrates	Alpha-dihydroergocryptine, aprepitant, atorvastatin, avanafil, bosutinib,brotizolam, budesonide, buspirone, cobimetinib, darifenacin, dasatininb, ebastine, eletriptan, eplerenone, everolimus, felodipine, fluticasone, grazoprevir, ibrutnib, isavuconazole, ivabradine, ivacaftor, , levomethadyl (LAAM), lomitapide, lovastatin, lumefantrine, lurasidone, maraviroc, midazolam, midostaurin, naloxegol, neratinib, nisoldipine, perospirone, quetiapine, ridaforolimus, sildenafil, simeprevir, simvastatin, ticagrelor, tilidine, tolvaptan, triazolam, ulipristal, vardenafil, venetoclax, vicriviroc, voclosporin
BSEP inhibitors	Alectinib, atorvastatin, bromocriptine, candesartan, clobetasol, clofaziminie, dabigatran, dipyridamole, glyburide, grazoprevir, ledipasvir, mifepristone,pioglitazone, reserpine,rifamycin, simeprevir, telmisartan,timcodar, troglitazone, valinomycin, velpatasvir
MATE1 and OCT2 substrates	Acyclovir, cephalexin, cimetidine, fexofenadine, ganciclovir, glycopyrronium, metformin, pindolol, plisicainide, ranitidine, topotecan, varenicline
OCT1/2 substrates	Amantadine, 6-beta-hydroxycortisol, carboplatin, cisplatin, cephalexin, cephradine, ipratropium, lamivudine, linagliptin, metformin, oxyplatin, oxybutynin, phenformin, picoplatin, pilsicainide, pindolol, ranitidine, sorafenib, tropisetron, trospium, umeclidinium, and zidovudine
BCRP substrates	Daunorubicin, dolutegravir, doxorubicin, hematoporphyrin, imatinib, methotrexate, mitoxantrone, pitavastatin, rosuvastatin, irinotecan, ethinyl estradiol, simvastatin, sulfasalazine, sofosbuvir, tenofovir, topotecan, venetoclax
Medications that carry a possible risk for QT prolongation	Alfuzosin, apomorphine, aripiprazole, artenimol+piperaquine , asenapine, atomoxetine, bedaquiline, bendamustine, bortezomib, bosutinib, buprenorphine, cabozantinib, capecitabine, ceritinib, clomipramine, crizotinib,clozapine, cyamemazine (cyamepromazine), dabrafenib, dasatinib, degarilix, delamanid, desipramine, dexmedetomidine, dolasetron, efavirenz, eliglustat, epirubicin, eribulin mesylate, ezogabine(retigabine), famotidine, felbamate, fingolimod, flupentixol, gemifloxacin, granisetron, hydrocodone-ER, iloperidone, imipramine (melipramine), isradipine, ketanserin, lapatinib, lenvatinib, leuprolide, lithium, melperone, midostaurin, mifepristone, mirabegron, mirtazapine, moexipril/HCTZ, necitumumab, nicardipine, nilotinib, norfloxacin, nortriptyline, nusinersen, ofloxacin, osimertinib, oxytocin, paliperidone, palonosetron, panabinostat, pasireotide, pazopanib, perflutren lipid microspheres, perphenazine, pilsicainide, pimavanserin, pipamperone, promethazine, prothipendyl, rilpivirine, risperidone, romidepsin, sertindole, sorafenib, sunitinib, tamoxifen, tipiracil/trifluridine, tizanidine, tolterodine, toremifene,trimipramine, tropisetron, vardenafil, vemurafenib, venlafaxine, vorinostat, ziprasidone