NCT# 02911467

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

CC#15559: Magnetic Resonance (MR) Imaging with Hyperpolarized Pyruvate (^{13}C) as a Predictive Biomarker of Response in Castration-Resistant Prostate Cancer

This is a clinical trial, a type of research study. Your study doctor, Rahul Aggarwal, M.D., and his associates from the University of California, San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center will explain the clinical trial to you.

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

You are being asked to take part in this study because you have prostate cancer.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine if a newly developed imaging technique – C-13 magnetic resonance spectroscopic imaging (MRSI) -- will be useful to patients diagnosed with metastatic prostate cancer resistant to testosterone-lowering medication, by allowing physicians to see how well they respond to further androgen signaling inhibitor (ASI) treatment, or other types of prostate cancer therapies. Examples of androgen signaling inhibitors used in prostate cancer include abiraterone acetate, enzalutamide, and others.

During your magnetic resonance spectroscopic imaging (MRSI) scan, your body will be injected with the investigational agent C-13 labeled pyruvate. An investigational agent is one that has not been approved for use by the Food and Drug Administration (FDA) and is available for research only.

The National Institutes of Health (NIH) will be providing funding to support the conduct of the study.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 75 men will take part in this study at UCSF.

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

If you agree to participate on this study, you will be asked to participate in a Magnetic Resonance (MR) scan using C-13 pyruvate injection(s) prior to initiating treatment for your

prostate cancer as recommended by your treating physician. This will be your "baseline scan". After you start your treatment with an androgen signaling inhibitor or other systemic therapy (such as chemotherapy), you will undergo a second MR scan with C-13 pyruvate injection(s) (2 to 12 weeks after your first MR scan). If you initially respond to therapy and then your disease begins to grow, you will undergo a third MR scan with C-13 pyruvate injection at the time of disease progression.

If you give your consent to be in this study by signing this form, you will have tests and procedures (called "screening") done. These are done to reduce the risks of taking part in this study and to make sure it is okay for you to be in the study.

It is possible that after these tests are reviewed, you will not be able to be in the study. There may be other reasons why you cannot be in this study. These reasons will be discussed with you by your study doctor or the clinic staff.

Screening (before you begin the main part of the study):

After you have signed this consent, the screening tests listed below will be done within 28 days before you receive the imaging scan. You will need to have the following exams, tests or procedures to find out if you can be in the main part of the study. Most of these exams, tests or procedures are part of your regular cancer care. 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 hours. The screening procedures do not have to be completed in one day and you are allowed to take breaks if you have multiple procedures in one day.

- A complete medical history and your current medical condition will be collected including information about your current health status
- Physical Examination including assessment of performance status, a measure of how healthy you are
- Vital signs (blood pressure, heart rate, temperature), height and weight
- CT/MRI scan of the abdomen and pelvis (can be done within 12 weeks of your baseline MR scan)
- Whole body bone scan (can be done within 12 weeks of your baseline MR scan)
- Blood tests, approximately 2 tablespoons of blood will be obtained:
    - Complete blood count (CBC) with differential and platelet count
    - Blood chemistry testing
    - Prostate Specific Antigen (PSA) testing
- A review of medications that you are taking (including over-the-counter medications and supplements)
- Electrocardiogram (ECG/EKG)

During the main part of the study:

If the exams, tests and procedures show that you can be in the main part of the study, and you choose to take part, then you will need the following tests and procedures. Your clinic visit including the MRI/MRSI exam will take approximately 3 hours.

Baseline Pyruvate Injection(s) and Scans

Before the pyruvate injection(s):

- Vital signs - blood pressure, heart rate, breathing rate, temperature
- You will have a blood test (approximately 1 tablespoon of blood will be drawn) for:
  - Lactate Dehydrogenase (LDH) testing
- MRI
  - You will undergo a high spatial resolution MRI to visualize a target tumor lesion. The imaging exam will be performed at the UCSF Department of Radiology Imaging Center located at the Mission Bay campus in Byers Hall. For your MRI, you will lie down on a narrow bed, which will then be placed in a tunnel, which is 6 feet long by 2 feet wide. Your participation may mean some discomfort for you. You may receive gadolinium (a contrast agent) through a vein in your arm. Gadolinium is an agent that causes some tumors to appear much brighter than normal tissue on MRI scans; before gadolinium is injected the tumor may not be visible. You will lie there quietly for about one hour, during which time you will hear a loud machine-like noise. The MRI scan takes approximately an hour and a half to complete.

Pyruvate injection(s) and MRSI(s)

- You will receive the pyruvate into a vein over a period of less than one minute. About 1-2 minutes after you receive the pyruvate, you will undergo a MRSI exam while remaining in the MR scanner. The scan will take less than 5 minutes. During this time you will be observed for any side effects.
- You then may receive an optional second pyruvate injection and MR scan within 15 to 60 minutes following your first scan. The purpose of performing a second scan is to test whether this imaging method produces the same results when repeated. You will be asked whether you would like to receive this optional, second pyruvate injection and MR scan at the end of the consent form.

At 30 minutes after each pyruvate injection

- We will measure your vital signs - blood pressure and heart rate.
- Your injection site will be monitored
- We will review any side effects you may be experiencing

Optional tumor biopsy for research purposes
After the pyruvate injection and MRI/MRSI imaging, you may undergo an optional tumor biopsy of the pre-selected tumor site after this baseline MRI scan and again at a later time point if your cancer worsens (does not respond to treatment). You will be asked to complete the optional consent section of this form that will allow the study doctors to collect tissue from this procedure. Your tissue sample will be analyzed for specific protein levels. More information can be found under the ***About Using Tissue for Research*** section on page 10 of this consent form.

Following your baseline measures, you will begin treatment with an androgen signaling inhibitor (ASI) or other type of prostate cancer therapy (treatment may be given as part of routine care or as part of a clinical trial)

2-12 weeks after your baseline pyruvate injection(s) and scan(s)

- You will undergo another pyruvate injection and MRSI
- You will have a blood test (approximately 1 tablespoon of blood will be drawn) for: LDH testing
- You will undergo the same examination as that outlined above prior to start of treatment.

Every 4 weeks (+/- 14 days)

- You will have blood tests (approximately 1 tablespoon of blood will be drawn) for:
  o PSA testing

Every 12 weeks (+/- 4 weeks)

- You will have the following scans:
  - CT or MRI of the abdomen/pelvis
  - Whole body bone scan

If your tumor initially responds to therapy and then starts growing:

- You may undergo another pyruvate injection and MRSI
  - The same target from the first biopsy will be re-evaluated, or another target tumor will be selected if the first can no longer be evaluated
- You will have a blood test (approximately 1 tablespoon of blood will be drawn) for: LDH testing
- You may have an optional tumor biopsy

Study location: All study procedures will be done at the UCSF Mission Bay campus.

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, and they will tell you how to stop safely.

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

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

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

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your healthcare team may give you medicines to help lessen side effects. Many side effects go away soon after the Pyruvate injection is completed. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

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

Risks and side effects related to Hyperpolarized Pyruvate (13C)

Injection <u>Likely</u>

- Bruising at the injection site
- Pain at the injection site

<u>Less Likely</u>

- Fatigue
- Dizziness
- Decreased sensitivity to touch
- Increased heart rate
- Low blood pressure
- Headache
- Feeling hot/flushing
- Taste disturbance
- Smell disturbance
- Dry mouth
- Urgency to use the bathroom
- Throat pain

Other Risks Related to Study Procedures

Blood drawing and injection (venipuncture) risks: Injection can cause temporary discomfort from the needle stick, bruising, and infection.

Intravenous line: The temporary placement of an intravenous line may cause discomfort when inserting the needle, as well as bruising; bleeding; and rarely, infection.

Radiation (x-ray) risks: The amount of radiation you will be exposed to is relatively small. Such doses of radiation may be potentially harmful, but the risks are so small that they are difficult to measure. If you have had many x-rays, you should discuss this with the researchers before agreeing to be in this study.

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

ECG risks: The adhesive on the leads may cause skin irritation including redness, itching, swelling or rash. These symptoms are generally mild and clear up on their own.

CT scan risks: CT scans will expose you to radiation. Some people may experience feelings of anxiety or claustrophobia while undergoing a CT scan. The CT scan may require that a dye (contrast material) be injected into your vein through an intravenous (i.v.) line. There is a risk of an allergic reaction to the dye, although this is rare. Allergic reactions may include nausea, flushing, a 'pins and needles' sensation, mild headache, skin rash, itchy eyes, shortness of breath, and lightheadedness or low blood pressure (which can be treated with intravenous fluids).

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 ear plugs. At times during the test, you may be asked to not swallow for a while, which can be 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 occurs. This can be treated immediately with intravenous fluids. Very rarely (less than one in one thousand), patients are allergic to gadolinium. These effects are most commonly hives and itchy eyes, but more severe reactions have been seen which result in shortness of breath.

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

Tumor Biopsy risks: Depending on the site of tumors on your baseline scans, you will undergo either a CT-guided biopsy of a metastatic lesion or a prostate biopsy. The biopsy has small but serious risks. While we make every effort to minimize the pain related to the procedure, the procedure is usually uncomfortable and sometimes painful. Where the biopsy is done in your body, it can lead to bleeding in that area, damage of organs near where the biopsy is done, or infection. While it is uncommon, sometimes bleeding or pain from the biopsy will require you to stay overnight in the hospital or require you to go to the operating room to control any bleeding. We check your laboratory values before the biopsy to make sure that the procedure is as safe as possible and to minimize your chance of having a complication. We try to take as little tissue as possible when we do the biopsy, and this means that sometimes the biopsy procedure can be unsuccessful and require a repeat biopsy to get enough tissue. Biopsies of the prostate can lead to inflammation causing pain or difficulty with urination, blood in the urine, painful ejaculation, and/or infection in rare circumstances. Other potential risks will be described to you and discussed with you by doctors who conduct these biopsies.

Unknown Risks: The experimental imaging agent may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study. Additionally, if the study doctors observe any abnormal findings during the research images, they will inform your primary physician.

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

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There will be no direct benefit to you from participating in this study. However, this study will help doctors learn more about and gather more information about magnetic resonance (MR) imaging to develop future clinical trials, and it is hoped that this information will help in the treatment of future patients with prostate cancer.

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

Your other choices may include:

- Choosing to have a regular MRI scan that does not use the Pyruvate agent
- Choosing not to have an MRI scan
- Taking part in another study
- Not participating in this study

Your physician will discuss these other options with you. Please talk to your doctor about your choices before deciding if you will take part in this study.

HOW WILL MY SPECIMENS AND INFORMATION BE USED?

Researchers will use your specimens and information to conduct this study. Once the study is done using your specimens and information, we may share them with other researchers so they can use them for other studies in the future. We will not share your name or any other personal information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information.

Genetic Testing: Researchers may use your specimens (for example, blood, tissue, saliva, etc.) to look at all of your DNA (this is called "whole genome sequencing. DNA contains information that determines things like eye color, height, or disease risk that are passed on from parent to child.

How will my genetic information be shared?

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

Donating data may involve a loss of privacy, but information about you will be handled as confidentially as possible. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Genetic information that results from this study does not have medical or treatment importance at this

time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. Taking part in a genetic study may also have a negative impact or unintended consequences on family or other relationships. It is possible that future research could one day help people of the same race, ethnicity, or sex as you. However, it is also possible through these kinds of studies that genetic traits might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

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

Commercial Use: Your specimens may be used for commercial use. If this happens, you will not share in any profits.

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:

- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in overseeing research
- National Institutes of Health (NIH) their authorized representatives
- The University of California

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?

You and your insurance will not be billed for the pyruvate injection or MRSI imaging.

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.

Before you agree to be in this study, you may want to contact your healthcare payer/insurer to see if your plan will cover the costs required as part of your participation. You may request more information about the costs of participating in this study and discuss this with the study team.

If you have any questions, your doctor and the study team will be able to provide you with answers.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

There will be no payment for taking part of 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, MD if you feel that you have been injured because of taking part in this study. You can tell him in person or call him [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 or the study sponsor, depending on a number of factors. The University does not normally provide any other form of compensation for

injury. For further information about this, you may call the UCSF Institutional Review Board at 415- 476-1814.

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

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

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

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

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

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 UCSF Institutional Review Board at 415-476- 1814

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

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Please note: This section of the informed consent form is about additional research studies that are being done with people who are taking part in the main study. You may take part in these additional studies if you want to. You can still be a part of the main study even if you say "no" to taking part in any of these additional studies.

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

About Using Tissue for Research

You will be asked to undergo optional tumor biopsies to collect samples from the target tumor lesion. If you agree, we would like to take additional tumor biopsies after the first MRI scan and again if your cancer worsens (does not respond to treatment). We want to collect the biopsy tissues to analyze specific protein levels.

There will be no direct benefit to you from allowing your specimens to be collected. However, we hope we will learn something that will contribute to the advancement of science and understanding of health and disease.

Results from this analysis may be published but your data will not be reported individually. Reports about research done with your leftover tissue will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Things to Think About

The choice to donate your specimen is optional and is up to you. No matter what you decide to do, it will not affect your care.

Your tissue specimen will be stored in a repository at UCSF. If you decide now that your tissue can be collected for research, you can change your mind at any time. Just contact the study doctor, Rahul Aggarwal, MD, in writing at the address below, and let us know that you do not want us to collect or use your tissue. Any identifiable tissue that remains will no longer be used for research and destroyed. However, if any research has already been done using portions of your specimens, the data will be kept and analyzed as part of those research studies.

Rahul Aggarwal, MD
University of California San Francisco
[redacted]

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

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

Benefits

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

Risks

The greatest risk to your privacy is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small. To further safeguard your privacy, information obtained in this part of the study will not be placed in your medical record.

Making Your Choice

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

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

1. I agree to undergo optional tumor biopsies at baseline and if my cancer worsens.

YES	NO

<u>Second C-13 pyruvate injection and MR scan</u>

The study doctor would like your permission to perform an optional, second pyruvate injection and MR scan within 15 to 60 minutes following your first scan. The purpose of a second scan is to see if it will provide additional information on tumor metabolism, and/or expand the region of coverage (i.e. identify the metabolism of lesions previously missed on the first scan), and/or provide information on reproducibility of pyruvate metabolism that can be used to identify significant changes in metabolism with disease progression or response to therapy.

Benefits

There will be no direct benefit to you for receiving a second pyruvate injection and MR scan. The purpose of performing a second scan is to test whether this imaging method produces the same results when repeated.

Risks

There are currently several studies across the country using multiple pyruvate injections and MR scans. To date, patients in these studies have not experienced any adverse side effects of a second pyruvate injection.

Making Your Choice

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

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

1. *I agree to receive a second C-13 pyruvate injection and MR scan 15-60 minutes following the first scan.*

YES	NO

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CONSENT

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

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

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

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

_____ _____
Participant Date

_____
Participant name (print)

_____ _____
Person obtaining consent Date

_____
Person obtaining consent (print)

_____ _____
Witness – Only required if the participant is a non-English speaker Date