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

CC#159517: Hyperpolarized C-13 Pyruvate as a Biomarker of PI3K/mTOR Pathway Inhibition in Patients with Advanced Solid Tumor Malignancies

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 been diagnosed with an advanced solid tumor that has spread to your liver or other location within your abdomen.

WHY IS THIS STUDY BEING DONE?

This study has two parts; Part A and Part B. You are being asked to participate in Part A of the study.

The main purpose of part A is to determine if a new imaging technique – **hyperpolarized C-13 pyruvate magnetic resonance spectroscopic imaging (MRSI)** – can reliably detect and characterize advanced solid tumors that have spread to the liver or other sites within the abdomen.

A **solid tumor** is an abnormal mass of tissue that usually does not contain cysts or liquid areas. Different types of solid tumors are named for the type of cells that form them. Examples of solid tumors are sarcomas, carcinomas, and lymphomas.

During your MRSI scan your body will be injected with the investigational agent C-13 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 50 people will participate in part A of this study at UCSF.

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

If you agree to participate in this study, you will be asked to undergo a Magnetic Resonance (MR) scan using C-13 pyruvate injection(s).

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.

These reasons will be discussed with you by your study doctor or the clinic staff. If the tests show you are not eligible, we will explain why.

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. 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 (unless noted otherwise as "for research purposes"). 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 6 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.

- Medical history - You will be asked about your health, any current and past illnesses, and medications you are taking and those you have taken
- Physical exam, vital signs, height, and weight
- ECOG performance status (Questions about how your disease is affecting your daily life)
- Tumor assessment by standard CT/MRI scan of the chest, abdomen and pelvis
- Blood tests (approximately 2 tablespoons) for:
    - Complete blood count (CBC) with differential and platelet count
    - Blood chemistry assessments
- Review of your medications (both prescription and over-the-counter) and side effects
- Electrocardiogram (ECG/EKG)

MRI/MRSI Scan
If the exams, tests and procedures show that you can proceed with MRI/MRSI part of the study, then you will need the following tests and procedures. This clinic visit will take approximately 2 to 3 hours to complete.

- **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 [redacted]. 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.

- **C-13 Pyruvate injection and MRSI:**
  - 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 will be monitored and your vital signs collected for 30 minutes following completion of the scan.
- **(OPTIONAL) Additional Pyruvate Injection and MRSI scan:**
  - You will be asked if you would like to receive an optional, second pyruvate injection and MRSI scan at the end of this consent form. The second injection will provide additional information on how well your tumor works, and how well your tumor takes up pyruvate injection and to confirm the results of your first injection and scan.

Study location: All study procedures will be done at the UCSF [redacted].

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 the 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 (C-13) Injection

Less Likely

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

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.

No radiation risk beyond routine clinical care: This study involves radiation exposure as part of routine clinical care. You will not receive additional radiation as a result of participating in this study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.

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.

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 diagnosed with a solid tumor that has spread to the liver.

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.

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?

The sponsor will provide the pyruvate injection and MRSI imaging at no cost to you.

Some of the services you will receive are being done only because you are participating in this research study. Examples of these 'research only' services include: ECG/EKG, the research MRI/MRSI scans, and the pyruvate injection. Those services will be paid for by the study and will not be billed to you or your health insurance company. If you believe you have received a bill for a research related procedure contact the study team and the UCSF Medical Center office that sent the bill.

In addition, some of the services you will receive during this research study are considered to be "routine clinical services" that you would have received even if you were not participating in the research study. Examples are complete physical exam, tumor imaging (MRI and CT), and routine blood collection. These services will be billed to your health insurance company, and you will be responsible for paying any deductibles, co-payments or co-insurance that are a normal part of your health insurance plan. If you do not have health insurance, you will be responsible for those costs.

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 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?

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 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.

Please Note: This section of the informed consent form is about the optional parts of this research study. You may take part in these optional parts of the study if you want to. You can still be part of the main study even if you say "no" to take part in any of these additional studies. No matter what you decide to do, it will not affect your care. If you have any questions, please talk to the researchers, or call our research review board at 415-476-1814.

As described earlier in the 'What Will Happen If I Take Part in This Research Study?' section of the consent form, the researchers are asking if you would agree to an additional pyruvate inject and MRSI scan which will occur 15 – 60 minutes following my first scan. This additional injection and scan will provide additional information on how well your tumor works, and how well your tumor takes up pyruvate injection and to confirm the results of your first injection and scan.

Benefits
There will be no direct benefit to you for receiving a second pyruvate injection and MRSI scan. Information from this scan will be used by the researchers to see whether the imaging results are reproducible, and better evaluate the use of this imaging method for treating patients.

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

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.

Please indicate your response below by putting your initials in the "Yes" or "No" box:

I agree to an additional pyruvate injection and MRSI scan, which will occur 15 – 60 minutes following my first scan.

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.

_____ _____
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