NCT03729411

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

Study Title: CC# 13106: Pilot Study of Safety and Feasibility of Acquiring Hyperpolarized Imaging in Patients with Gliomas.

This is a clinical trial, a type of research study. Your study doctor, Susan Chang, M.D., and her associates from the University of California, San Francisco (UCSF) Department of Neurosurgery 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 brain cancer.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine if a newly developed imaging technique of carbon-13 magnetic resonance spectroscopic imaging (^{13}C MRSI) will be useful to physicians and patients with brain cancer in making treatment decisions and seeing how well various types of treatment work. During your ^{13}C MRSI scan your body will be injected with the investigational agent 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.

Hyperpolarized ^{13}C Pyruvate is a non-radioactive isotope of carbon. The doses of [1-^{13}C] Pyruvate and/or [2-^{13}C] pyruvate that will be used in this study have been shown to be safe and well tolerated in a previous human study.

The National Cancer Institute will be providing funding to support the conduct of the study.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 140 people may participate in the study at UCSF.

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

There are two groups in this study. Your study doctor will tell you which group you will be participating in prior to your enrollment.

Subjects in Group 1 will receive a single examination that includes the acquisition of MR imaging data and the injection of hyperpolarized ^{13}C pyruvate, which is a new imaging agent that can help to define tumor characteristics. The purpose of this part of the study is to determine the most appropriate parameters to use in obtaining such imaging data from the brain. Subjects in Group 2 will receive two examinations with pyruvate injections before and after treatment with radiation therapy and Temozolomide in order to study changes imaging parameters. These are standard treatments for patients with brain cancer.

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

You will need to have the following tests or procedures to find out if you are eligible for the study. These are part of regular clinical care and may be done even if you do not join the study. You will also have some procedures that are only being done because you are in the study. These are called study procedures and are noted as “study test” in the list of procedures below. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

You must complete your screening procedures within 90 days prior to participating in the study. Your screening visit may take up to 2 hours depending on which procedures you have.

- A **medical history**: this will include questions about your health, current medications including natural or herbal products, demographic data, and prior medical history including information about your brain cancer.
- A **physical exam**: This examination will be similar to those done for your regular medical care and will also include measurements of systolic and diastolic blood pressure, heart rate, respiratory rate, body temperature, and blood oxygen saturation (by pulse oximetry).
- **Karnofsky Performance status**: You will be asked about your ability to perform everyday tasks
- **Blood drawing (venipuncture)**: You may be asked to give a blood sample for laboratory tests. Less than 2 teaspoons of blood will be drawn by inserting a needle into a vein in your arm. Blood (approximately 1-2 teaspoons) will be drawn through a vein in your arm for routine safety tests.

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 MR exam will be performed at the UCSF Department of Radiology Imaging Center [redacted]. Your visit including the MR exam will take less than 2 hours.

The following procedures are for all patients.

<u>At Baseline before the Pyruvate Injection:</u>

- Vital signs - systolic and diastolic blood pressure, heart rate, respiratory rate, body temperature, and blood oxygen saturation (by pulse oximetry)
- The site that will be used for the injection will be monitored
- You will be placed in the MR scanner and anatomic images will be acquired to define the most appropriate location for obtaining the MRSI data
- The Pyruvate will be placed in a syringe and brought into the scan room

Following approval by the study pharmacist, you will receive the Pyruvate into a vein over a period of less than one minute. Shortly after the injection has started, the ^{13}C MRSI data will be obtained for a period of 2-3 minutes. A second set of anatomic images may be acquired immediately afterwards. During this time, you will be observed for side effects.

<u>At approximately 10 minutes after Pyruvate injection</u>

- The MR scanner table will be pulled out and the set-up modified in order to obtain standard MR data
- You will be asked if you are experiencing any side effects
- Your injection site will be monitored

You will then receive an abbreviated MR exam to obtain imaging data similar to those used for clinical purposes. You may receive an injection of Gadolinium if it has been requested by your oncologist for diagnostic purposes.

If you are in Group 2 you will have a second imaging examination with pyruvate injection after completion of radiation therapy. You will undergo repeat screening to verify that you still meet eligibility criteria. This will include repeat assessment of Karnofsky performance status, vital signs, physical examination, medication history in addition to monitoring for adverse events and evaluation of the prior injection site. You will then undergo imaging (with associated procedures and monitoring) as per the first imaging examination.

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

HOW LONG WILL I BE IN THE STUDY?

You will participate in the study for a maximum of 4 months.

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 so that they can make arrangements for you to do so.

It is important to tell the study doctor if you are thinking about stopping so that any risks from the pyruvate can be checked. 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 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 (^{13}C) Injection

Likely

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

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

Risks related to Study Procedures

Blood Drawing (venipuncture) risks: Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection.

MRI scan 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 pocketknives 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.

For your MRI/MRSI scan, 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. We may ask you to be repositioned for the acquisition of imaging data after the pyruvate injection. The MRI scan takes approximately an hour and a half to complete.

Contrast agent (gadolinium) risks: As part of your imaging examination you may also receive an injection of the contrast agent gadolinium. This agent is used routinely as part of clinical care for helping to visualize brain tumors. There are 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 agents. The condition is called nephrogenic systemic fibrosis (NSF). It can cause skin to tighten or scar and can damage internal organs. Sometimes it can be life threatening. There are no reports of NSF in patients with normal kidney function. Before you have a MRI scan requiring an injection of gadolinium contrast, you will have a blood test in order to check the function of your kidneys. Based on your medical history and the results of the test, a doctor will decide whether it is safe for you to undergo the MRI scans.

Reproductive risks: You should not father a baby or become pregnant 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. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

Unknown Risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

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

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

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 brain 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
- Taking part in another study
- Getting treatment or care for your cancer without being in a study
- Getting no treatment (observation)
- Getting palliative care
- Alternative medicine and/or therapies or homeopathic remedies

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:

- UCSF Committee on Human Research
- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in overseeing research
- UCSF Helen Diller Family Comprehensive Cancer Center
- The University of California
- Governmental agencies in other countries where the Pyruvate agent 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 THE STUDY?

Pyruvate will be provided free of charge by UCSF. Tests, medications and any other treatment that are considered standard-of-care will be billed to you or your healthcare plan/insurance company. All of the tests and study procedures listed in this consent form are required for this study. You will not be billed for any clinic visits or any of the tests required specifically by the study.

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?

You will not be paid for taking part in this study.

In return for your time and travel expenses, your parking will be covered 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 Susan Chang, MD if you feel that you have been injured because of taking part in this study. You can tell her 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 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?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctor Susan Chang, MD [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 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 an additional research study that is being done with people who are taking part in the main study. You may take part in this additional study if you want to. You can still be a part of the main study even if you say "no" to taking part in the additional study.

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

<u>Second 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 obtain

additional information on ^{13}C-pyruvate metabolism, and/or evaluate the performance of new methods, and/or assess the reproducibility of the metabolism.

Benefits
There will be no direct benefit to you for receiving a second pyruvate injection and MR 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 assessing patients.

Risks
Please see the risks related to Hyperpolarized ^{13}C-Pyruvate injection in the risks section, pages 3, 4 and 5, of this consent form.

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 pyruvate injection and MR scan 15-60 minutes following the 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.

_____
Printed Name of Participant

_____ _____
Date Participant's Signature for Consent

_____
Printed Name of Person Obtaining Consent

_____ _____
Date Person Obtaining Consent

_____ _____
Date Witness-Only (required if the participant is a non-English Speaker)

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

EXPERIMENTAL SUBJECT'S
BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject I have the following rights:

1) To be told what the study is trying to find out,

2) To be told what will happen to me and whether any of the procedures, drugs, or devices is different from what would be used in standard practice,

3) To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to me for research purposes,

4) To be told if I can expect any benefit from participating, and, if so, what the benefit might be,

5) To be told of the other choices I have and how they may be better or worse than being in the study,

6) To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study,

7) To be told what sort of medical treatment is available if any complications arise,

8) To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study,

9) To receive a copy of the signed and dated consent form,

10) To be free of pressure when considering whether I wish to agree to be in the study,

_____
Participants Signature and Date

If I have other questions I should ask the researcher or the research assistant. In addition, I may contact the Committee on Human Research, which is concerned with protection of volunteers in research projects. I may reach the committee office by calling: (415) 476-1814 from 8:00 AM to 5:00 PM, Monday to Friday, or by writing to the Committee on Human Research, Box 0962, University of California, San Francisco, CA 94143. Call 476-1814 for information on translations.