Informed Consent Form cover page

Official title: Effect of Cardiotoxic Anticancer Chemotherapy on the Metabolism of [1-13C]Pyruvate in Cardiac Mitochondria

NCT number: NCT03685175

IRB Approved date: 02-05-24

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	Effect of Cardiotoxic Anticancer Therapy on the Metabolism of [1-^{13}C]Pyruvate in Cardiac Mitochondria – ***Feasibility Arm***
Funding Agency/Sponsor:	UT Southwestern Medical Center Cancer Prevention and Research Institute of Texas, RP180404 National Institutes of Health
Study Doctor:	Vlad Zaha, MD, PhD

You may call the research personnel at 214-645-6269 or 214-645-9269.

Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
This research study is being done in healthy volunteers and patients to develop a new non-invasive MRI method that may be useful for early detection of heart damage, which is a known side effect of anticancer therapy that patients are receiving as part of standard medical care for breast cancer treatment. Your samples will also undergo genetic testing to answer the research question.

Why is this considered research?
Researchers want to learn if there are early changes in the heart that can be detected after a person has anticancer therapy. To detect these changes, this research uses an investigational MRI technology that includes an investigational agent (pyruvate injection) that has not been commercially approved by the Food and Drug Administration. It is approved for research only. The pyruvate injection has been shown to be safe and well tolerated in previous research.
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.

The following definitions may help you understand this study:
- **AIRC**: is the Advanced Imaging Research Center at UT Southwestern Medical Center.

IRB Approved Date: 2/5/2024

Your MRI will be done in the AIRC.

- **Researchers**: means the study doctor and study personnel at the University of Texas Southwestern Medical Center and its affiliated hospitals.
- **Investigational**: procedures or equipment that is for research and not part of standard medical care.
- **Standard Medical Care**: procedures and tests ordered by your doctor for your regular medical care. Standard medical procedures that may be used by the researchers in this study include results of your medical imaging and/or breast biopsy.
- **Metabolism**: a process that the body uses to make energy from food or from stored substances in the body like sugar or fat.
- **Magnetic Resonance Imaging or MRI**: a method to take pictures or measure metabolism of the inside of the body. The MRI exam in this research is investigational.
- **Investigational Agent, Pyruvate**: The pyruvate is prepared in such a way that when metabolized in the body, researchers can see how it is used by the heart, which may help them understand the effects of anticancer therapy on the heart. The pyruvate used in this study is not radioactive. It will be given through an intravenous catheter (IV), or port, during the MRI.
- **Contrast**: a substance infused into a vein through an intravenous catheter (IV), or port, that is used to enhance the differences in color and light between parts of an image during an MRI. The contrast used in this study is called gadolinium.
- **Glucose Gel**: a sugary drink, which contains about the same amount of sugar that is in a can of Coke.
- **Insulin**: a medication used to lower blood sugar. It may be injected into your IV or port.
- **EKG**: or electrocardiograph is a simple, painless way to record the heart's electrical activity. Wires or "leads" will be attached to your chest and you will be asked to lie still while the machine prints out an electrical "record" of your heart activity.

Why am I being asked to take part in this research study?
You are invited to participate in this study because you are a healthy volunteer or have been diagnosed with breast cancer and will be treated with anticancer therapy (standard of care).

Do I have to take part in this research study?
No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.

If you decide not to take part in this research study, it will not change your legal rights or the quality of health care that you receive at this medical center. You will continue to receive the same standard of care medical treatment at UT Southwestern, or Parkland Health & Hospital System, regardless of whether you decide to participate in this study.

How many people will take part in this study?
About 10 people will take part in the feasibility arm of this study in the Advanced Imaging Research Center at UT Southwestern.

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. Some of the procedures may be part of your standard medical care, but others are being done solely for the purpose of this study.

Screening Procedures
To help decide if you qualify to be in this study, the researchers will ask you questions about your health, including medications you take and any surgical procedures you have had. We will collect the following information:

- Demographic information (age, gender, ethnic origin).
- Medical/Surgical History.
- Family History.
- Height and weight.
- MRI safety screening information.
- Current medications.

Procedures and Evaluations during the MRI Research
As part of the research study, there will two investigational cardiac MRI exam visits for each participant.
Follow up visits may be offered if the protocol cannot be completed as scheduled at visits 1 and 2.

For patients, the exams will be after completing your standard of care anticancer therapy and again 1 to 6 months after anticancer therapy and following medical therapy. During the research, study procedures will be scheduled within a time frame to not delay or interfere with breast cancer treatment.

At each research visit: (Visits 1 & 2)

- Bring a list of your medications, vitamins, and supplements to each visit.
- You will change into scrubs and lock up your valuables for each MRI exam.
- You will have a review of study procedures for that visit.
- You will have your height and weight measured.
- You will have your blood pressure, heart rate, respirations and temperature measured.
- You will be screened for MRI safety.
- You will practice breath-holding for the MRI's.

At the two cardiac MRI research visits with two investigational pyruvate injections:

- You will not eat anything after dinner (except for water) for these visits.
- You will have a breakfast of 1 or 2 bagels with or without jelly, but nothing containing fat. Breakfast has to be eaten between 8:00 – 8:30 am.
- You will have a pre-MRI EKG done.
- You will have an IV started in one arm, or your port will be used.

- You may have a total of up to five ounces of blood drawn from your IV for thyroid, and liver function, blood count, lipids, Insulin, glucose, ketones, iron panel, glucose, DNA, cortisol metabolites, and other metabolites. Some blood tests may not be done if available in your medical record.
- You will also have female or male hormones drawn at Visit 1 only.
- You will have your blood sugar tested and drink a dose of a sugary gel, approximately one hour before receiving the first pyruvate injection.
- If you are to receive contrast and kidney function was not measured as part of your screening labs, you will have approximately 1 teaspoon of blood drawn from your IV or port for kidney function testing.
- 45 minutes after drinking the sugary gel you will again have your blood sugar tested and may be injected with a very small amount of insulin. A doctor will be present.
- You will have a cardiac MRI that takes approximately 1½ hours.
- During the MRI you will receive the pyruvate injection through either your IV or port, two times and blood may be drawn eight times at 5, 10, 15, and 30 minutes after each injection.
- After the MRI you will be observed at most for 1 hour. During observation you will have your temperature, blood pressure and heart rate measured and you may have another EKG.
- You will be provided a sandwich/chips lunch during the observation period.
- Each of these MRI visits will take approximately 4 hours. Your onsite participation will be finished after Visit 2.

For the MRIs, you will lie very still on your back inside a large, doughnut-shaped scanner for approximately one hour while the technologist makes measurements and acquires images of cardiac tissue. The scanner normally makes loud noises during the procedure so you will wear ear protection (earplugs and headphones) during the scan. During the MRIs you will have stick-on heart leads placed on your chest and a clip placed on your finger. During the MRIs, you will be asked to hold your breath for brief periods of time.

During the MRI exams, you will receive two doses of pyruvate through the intravenous catheter or port. You will be monitored for any side effects from the pyruvate injections. Follow up by phone may occur approximately 24 hours after the MRI to ask if you experienced any side effects from the MRI visit.

For patients, administration of anticancer therapy will be standard-of-care by your treating physician and you will be followed by your treating physician in between MRI appointments.

You have the option to undergo two research cardiac MRI scans with the conventional contrast. We will compare these scans with the investigational MRI scans. These scans take approximately 1½ hours. These scans may be done on different days than the other two exams.

The MRI images in this study are designed for research, not for medical purposes. Even though the researchers are not looking at your MRI images to find or treat a medical problem,

you will be told if they notice something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. Because the imaging done in this study is not for standard medical purposes, the research results will not be sent to you or your regular doctor.

You can choose to undergo the optional MRI scans described in this section. Please initial if you agree to take part in this procedure.

_____ I agree to having 2 conventional cardiac MRI scans with contrast.

_____ I do not agree to having 2 conventional cardiac MRI scans with contrast.

How long can I expect to be in this study?
Your participation in the study will consist of:

- Screening in person or by phone.
- Two cardiac MRI with investigational pyruvate injection research visits (one after completing your treatment with anticancer therapy and again 1 to 6 months later). Phone visit about 24 hours after each MRI with injection visits may occur.
-

The research screening will take approximately one hour.

The research MRI with injection visits will take up to 4 hours each.

The 24-hour phone visits will take approximately 5 minutes each.

You may also take part in one or two cardiac function MRI scan with contrast.

The research visits DO NOT replace any of the visits with your doctors for standard of care breast cancer treatment.

You can choose to stop participating in the research study for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

What are the risks of the study?
MRI: There are no known risks from exposure to magnetic fields. You may experience nervousness and/or anxiety due to the loud banging made by the MRI machine while it is taking pictures and from confinement in a tight space (claustrophobia). If you become anxious, you can stop the procedure at any time.

You may also experience some discomfort and fatigue from lying still during imaging.

If you have any metal clips or plates in your body, you should tell the researchers. MRI may not be appropriate if you are pregnant or are trying to become pregnant. MRI may not be

appropriate if you have permanent eyeliner or eyebrows or any pieces of metal in your body, such as the following:

- heart pacemaker, heart valve replacement, or aortic clips
- implants, breast tissue expanders
- non-MR compatible IV port
- metal fragments in your eyes, skin, or elsewhere in your body
- brain clips or pieces of metal used in aneurysm surgery or intracranial bypass venous umbrella
- pieces of metal in the body resulting from work as a sheet-metal worker or welder
- clips placed in an internal organ
- prosthetic devices, such as middle ear, eye, joint, or penile implants
- joint replacement
- hearing aid that cannot be removed
- neurostimulator
- insulin pump
- intrauterine device (IUD)
- shunts or stents
- metal mesh or coil implants
- metal plate, pin, screws, or wires, or any other metal implants

Pyruvate – Investigational Agent: The most commonly occurring side effects are short lasting and mild. They may include flushing, headache, nausea, fatigue, taste change, smell change, and throat discomfort. No serious side effects are anticipated from the injection of pyruvate.

IV Contrast: The contrast you will receive is FDA-approved and used routinely for MRI exams in standard medical care. It contains a material called gadolinium used to highlight organs or tissues during imaging. The injection of gadolinium may cause discomfort like headache, nausea, a warm flushing feeling, strange taste, or coldness at the site of injection. These symptoms occur in less than 1 out of 20 patients receiving gadolinium and go away quickly. There is a small risk of severe allergic reaction that can cause breathing difficulties and/or low blood pressures, and these symptoms are extremely rare (approximately 1 in 10,000 to 1 in 100,000 administrations). In the unlikely event you experience these symptoms, a physician will be available to evaluate and, if necessary, provide treatment.

People with severe kidney failure who receive gadolinium contrast are at risk of developing a disorder called Nephrogenic Systemic Fibrosis (NSF) You will have a blood test to make sure your kidneys are functioning properly. You will not be eligible to participate in this research if you have not had a previous reaction to a contrast agent or if you have Sickle Cell Disease.

Insulin: The most commonly occurring side effects are mild, but low blood sugar may occur, along with headache, feeling sick, shakiness, or sweating. If you receive insulin and have any of these symptoms you will be given crackers and juice.

Glucose drink: The most commonly occurring side effects are mild but you may experience a headache or feeling sick.

Psychological Stress: MRI machines are long narrow, cylindrical tubes, which can cause a feeling of claustrophobia or panic in some patients. Some of the questions we will ask as part of this study may make you feel uncomfortable.

Loss of Confidentiality: Any time information is collected, there is potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks to Embryo or Fetus: If you are part of this study while pregnant, it is possible that you may expose the unborn child to risks. You cannot participate in this research if you are pregnant or breastfeeding. Females of childbearing potential must agree to be tested for pregnancy prior to the MRI exam. Males must be surgically sterile or have a female partner of childbearing potential using an acceptable method of contraception (IUD, implant, and a barrier method such as condom, diaphragm, or cervical cap) during the study and for 6 months after patient discontinuation of cancer treatment. Males must also refrain from sperm donation during the study and for 6 months after discontinuation of treatment.

Risks of Blood Drawing: Risks associated with having your blood drawn include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely. You may have a maximum of less than five ounces (ten table spoons) of blood drawn during each MRI visit. In the event that blood needs to be recollected, the patient will be contacted and the needed amount will be collected.

Risks of Genetic Testing: This research study includes optional genetic testing. Human tissue contains genes that determine many of a person's physical characteristics, such as the color of eyes and hair. In some cases, genetic testing of tissues can be used to indicate a risk for the development of certain diseases. Genetic information is unique to each individual and could potentially be used to discover possible changes in a person's future health status or life expectancy, or that of his/her children and family members.

Releasing genetic information to you could cause psychological distress, anxiety or family problems. Releasing this information to others, such as including it in your medical record, may pose a possible risk of discrimination, or increase difficulty in obtaining or maintaining disability, long-term care, or life insurance.

These risks would occur if your information is released by mistake. The measures being taken to protect your privacy are discussed below and make this possibility unlikely.

Even though the results of genetic testing may not be linked to you, it is possible that people of your ethnic background may be found to be at more risk for certain diseases based on future genetic research and this information might harm you in the future as a member of the group. Also, there may be unknown risks of genetic testing in the future.

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician unless the information indicates that you may be at risk for a serious illness known at the time of testing to be treatable and it can be confirmed by a clinical laboratory. In that case, we will attempt to notify you using the contact information you have provided.

If you do not want to be notified of any of these incidental findings, please initial below.
_____ Please notify me of any incidental findings obtained from this research.
_____ Please do not notify me of any incidental findings obtained from this research.

Other Risks: There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

How will risks be minimized or prevented?
MRI: You will be asked to complete an MRI Screening Form before each MRI exam to make sure it is safe for you to have an MRI.

Pyruvate – Investigational agent: Prior to administration of the pyruvate injection, a nurse will assess your temperature and blood pressure, and you will have an EKG for the measurements of your heart. You will be observed for approximately 1 hour after the completion of each MRI procedure with pyruvate injection. During the observation period a nurse will check your temperature, blood pressure and heart rate. You will have another EKG after the MRI. A study physician will be present during the MRI exams.

Contrast: You will be carefully screened with a blood test to measure kidney function prior to your cardiac MRI with contrast. People with kidney disease cannot participate in this study. After receiving contrast, you will asked to drink extra water for 24 to 48 hours after the contrast, so it can be cleared from your body.

Insulin: If you receive insulin you will have your blood sugar checked and you will be monitored for any side effects. You will be given crackers and juice if you have low blood sugar.

Glucose drink: You will have your blood sugar checked and you will be monitored for any side effects.

Loss of Confidentiality: A record of your research participation will be created and will be kept in a locked office. Any data stored on a computer will not identify you, but will have a code used to protect your privacy. Every effort will be made to keep your information confidential.

What will my responsibilities be during the study?
While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.

- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number, address or email changes.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.
- Report to the researchers any injury or illnesses while you are on study even if you do not think it is related.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.
If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking.

What are the possible benefits of this study?
If you agree to take part in this study, there may not be any direct benefits to you. We hope the information learned from this study will benefit others being treated with anticancer therapy in the future. Information gained from this research could lead to better detection of changes in the heart following those treatments.

What options are available if I decide not to take part in this research study?
This is not a treatment study. You do not have to be part of this study to get treatment for your condition.

Will I be paid if I take part in this research study?
You will be paid $100.00 for the completion of each MRI exam with pyruvate injection, and $50.00 for the completion of each conventional cardiac MRI exam. If you choose not to complete the MRI research visits or are withdrawn by the research team, you will not receive payment. You will also be offered lunch.

How will I be paid?
You will be issued a UT Southwestern Greenphire ClinCard, which can be used as a credit or debit card. You will also receive instructions on how to use the card. In order to receive study payments, your name, address, date of birth and Social Security Number (SSN) will be collected from you by the research staff. All information will be stored in a secure fashion

and will be deleted from the UT Southwestern Greenphire ClinCard system once the study has been completed.

If you are an employee of UT Southwestern, your payment will be added to your regular paycheck and income tax will be deducted.

Important Information about Study Payments

1. Your SSN is needed in order to process your payments. Should you decide not to provide your SSN, your study participation payment will be decreased at the current IRS tax rate. Study payments are considered taxable income and are reportable to the IRS.
2. An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.
3. Your ClinCard payment information will not be shared with any third parties and will be kept completely confidential.

This information will remain confidential unless you give your permission to share it with others, or if we are required by law to release it.

UT Southwestern, as a State agency, will not be able to make any payments to you for your participation in this research if the State Comptroller has issued a "hold" on all State payments to you. Such a "hold" could result from your failure to make child support payments or pay student loans, etc. If this happens, UT Southwestern will be able to pay you for your taking part in this research 1) after you have made the outstanding payments and 2) the State Comptroller has issued a release of the "hold."

A parking voucher will be provided for the valet parking service available at the Clements Imaging building when you are here for the investigational MRI visits. No other parking or transportation compensation is provided.

Will my insurance provider or I be charged for the costs of any part of this research study?

No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above). Expenses for the research MRIs are covered by the Researchers.

However, for patients, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care.

What will happen if I am harmed as a result of taking part in this study?

It is important that you report any illness or injury to the research team listed at the top of this form immediately.

Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center or Parkland Health & Hospital System.

You retain your legal rights during your participation in this research.

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

If I agree to take part in this research study, can I be removed from the study without my consent?
Yes. The researchers may decide to take you off this study if:

- Your medical problem remains unchanged or becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The researchers believe that other treatment may be more helpful.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?
Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

What is Protected Health Information (PHI)?
Protected Health Information is information about a person's health that includes information

that would make it possible to figure out who's it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include:

- medical and surgical history,
- current and previous medications,
- age, gender, race and ethnicity,
- height, weight, and vital signs including temperature, pulse, respirations and blood pressure,
- 12-lead ECG results,
- results of urine pregnancy test,
- results of blood tests (kidney function, blood count, lipids, female hormones), and MRI study images

We will get this information by looking at your chart at UT Southwestern Medical Center and Parkland Health & Hospital System.

How will your PHI be shared?

Because this is a research study, we will be unable to keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- The Sponsor, National Institutes of Health Institute for Biomedical Imaging and Bioengineering, funding the study. The sponsor includes any people, entities, groups or companies working for or with the sponsor or owned by the sponsor. The sponsor will receive written reports about your participation in the research. The sponsor may look at your health information to assure the quality of the information used in the research.
- The members of the local research team,
- The Institutional Review Board, Human Research Protection Program Office and the Compliance Office of the University of Texas Southwestern Medical Center, and other groups that oversee how research studies are carried out.
- The Research offices at the University of Texas Southwestern Medical Center and Parkland Health & Hospital System.
- The Food and Drug Administration (FDA) and other U.S. and international governmental regulatory agencies involved in overseeing drug or device research.
- Representatives of domestic and foreign governmental and regulatory agencies may be granted direct access to your health information for oversight, compliance activities, and determination of approval for new medicines, devices, or procedures.

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

How will your PHI be protected?
In an effort to protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of UT Southwestern Medical Center or Parkland Health & Hospital System for review or testing. If the results of this study are reported in medical journals or at meetings, you will not be identified.

Do you have to allow the use of your health information?
You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties but you will not be allowed to participate in the study.

After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to Vlad Zaha, MD, PhD, 5323 Harry Hines Blvd, Dallas, TX 75390-8568. If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the study staff if you have a need to review your PHI collected for this study.

You will only have access to your PHI until the end of the study.

How long will your PHI be used?
PHI expires at the end of the study.
By signing this form, you agree to let us use and disclose your health information for purposes of the study until 2043. This permission to use your personal health information expires when the research ends and all required study monitoring is over.

Are there procedures I should follow after stopping participation in this research?
Yes. You should continue to be followed by your physician for your regular medical care.

Whom do I call if I have questions or problems?
For questions about the study, contact Vlad Zaha, MD, PhD at 214-645-6269 or 214-645-9269.

For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

There is a possibility that additional study endpoints, and related study visits, will be added to the study in the future. The study team plans to contact you in this case to see if you are willing to participate in these study visits.

The study team also plans to contact you in the future to ask you if you are willing to participate in future, related studies.

_____ I agree to being contacted in the future.

_____ I do not agree to being contacted in the future.

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.
- You understand that a copy of this signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.

_____

Name of Participant (Printed)

_____ _____ _____ AM / PM

Signature of Participant Date Time

_____

Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM

Signature of Person Obtaining Consent Date Time

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research: Effect of Cardiotoxic Anticancer Therapy on the Metabolism of [1-^{13}C]Pyruvate in Cardiac Mitochondria - ***Formal Study***

Funding Agency/Sponsor: UT Southwestern Medical Center
Cancer Prevention and Research Institute of Texas, RP180404
National Institutes of Health

Study Doctor: Vlad Zaha, MD, PhD

You may call the research personnel during regular office hours at 214-645-6269 or 214-645-9269.

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Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
This research study is being done in healthy volunteers and patients to develop a new non-invasive MRI method that may be useful for early detection of heart damage, which is a known side effect of anticancer therapy that patients are receiving as part of standard medical care for breast cancer treatment. Your samples will also undergo genetic testing to answer the research question.

Why is this considered research?
Researchers want to learn if there are early changes in the heart that can be detected after a person has anticancer therapy. To detect these changes, this research uses an investigational MRI technology that includes an investigational agent (pyruvate injection) that has not been commercially approved by the Food and Drug Administration. It is approved for research only. The pyruvate injection has been shown to be safe and well tolerated in previous research.
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.

The following definitions may help you understand this study:

- **AIRC**: is the Advanced Imaging Research Center at UT Southwestern Medical Center. Your MRI will be done in the AIRC.
- **Researchers**: means the study doctor and study personnel at the University of Texas Southwestern Medical Center and its affiliated hospitals.
- **Investigational**: procedures or equipment that is for research and not part of standard medical care.

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- **Standard Medical Care**: procedures and tests ordered by your doctor for your regular medical care. Standard medical procedures that may be used by the researchers in this study include results of your medical imaging and/or breast biopsy.
- **Metabolism**: a process that the body uses to make energy from food or from stored substances in the body like sugar or fat.
- **Magnetic Resonance Imaging or MRI**: a method to take pictures or measure metabolism of the inside of the body. The MRI exam in this research is investigational.
- **Investigational Agent, Pyruvate**: The pyruvate is prepared in such a way that when metabolized in the body, researchers can see how it is used by the heart, which may help them understand the effects of anticancer therapy on the heart. The pyruvate used in this study is not radioactive. It will be given through an intravenous catheter (IV), or port, during the MRI.
- **Contrast**: a substance infused into a vein through an intravenous catheter (IV), or port, that is used to enhance the differences in color and light between parts of an image during an MRI. The contrast used in this study is called gadolinium.
- **Glucose gel**: a sugary drink which contains about the same amount of sugar that is in a can of Coke.
- **Insulin**: a medication used to lower blood sugar. It may be injected into your IV or port.
- **EKG**: or electrocardiograph is a simple, painless way to record the heart's electrical activity. Wires or "leads" will be attached to your chest and you will be asked to lie still while the machine prints out an electrical "record" of your heart activity.

Why am I being asked to take part in this research study?
You are invited to participate in this study because you are a healthy volunteer or have been diagnosed with breast cancer and will be treated with anticancer therapy.

Do I have to take part in this research study?
No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.
If you decide not to take part in this research study, it will not change your legal rights or the quality of health care that you receive at this medical center. You will continue to receive the same standard of care medical treatment at UT Southwestern, or Parkland Health & Hospital System, regardless of whether you decide to participate in this study.

How many people will take part in this study?
About 100 people will take part in this study in the Advanced Imaging Research Center at UT Southwestern.

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. Some of the procedures may be part of your standard medical care, but others are being done solely for the purpose of this study.

<u>Screening Procedures</u>
To help decide if you qualify to be in this study, the researchers will ask you questions about your health, including medications you take and any surgical procedures you have had. We will collect the following information:

- Demographic information (age, gender, ethnic origin).
- Medical/Surgical History.

- Family History.
- Height and weight.
- MRI safety screening information.
- Current medications.

Procedures and Evaluations during the MRI Research

As part of the research study, there will be two investigational cardiac MRI exam visits for each participant.

Follow up visits may be offered if the protocol cannot be completed as scheduled at visits 1 and 2. For patients the exams will be before and after completing standard of care therapy depending on treatment. During the research, study procedures will be scheduled within a time frame to not delay or interfere with breast cancer treatment.

At each research visit: (Visits 1 & 2)

- Bring a list of your medications, vitamins, and supplements to each visit.
- You will change into scrubs and lock up your valuables for each MRI exam.
- You will have a review of study procedures for that visit.
- You will have your height and weight measured.
- You will have your blood pressure, heart rate, respirations and temperature measured.
- You will be screened for MRI safety.
- You will practice breath-holding for the MRI's.

At the two cardiac MRI research visits with two investigational pyruvate injections:
(Visits 1 and 2)

- You will not eat anything after dinner (except for water) for these visits.
- You will have a breakfast of 1 or 2 bagels with jelly, but nothing containing fat. Breakfast has to be eaten between 8:00 – 8:30 am.
- You will have a pre-MRI EKG done.
- You will have an IV started in one arm, or your port will be used.
- You may have a total of up to five ounces of blood drawn from your IV for thyroid, and liver function, blood count, lipids, Insulin, glucose, ketones, iron panel, glucose, DNA, cortisol metabolites, and other metabolites. Some blood tests may not be done if available in your medical record.
- You will also have female or male hormones drawn at Visit 1 only.
- You will have your blood sugar tested and drink a dose of a sugary gel approximately one hour before receiving the first pyruvate injection.
- If you are to receive contrast and kidney function was not measured as part of your screening labs, you will have approximately 1 teaspoon of blood drawn from your IV or port for kidney function testing.
- 45 minutes after drinking the sugary gel you will again have your blood sugar tested and may be injected with a very small amount of insulin. A doctor will be present.
- You will have a cardiac MRI that takes approximately 1 hour.
- During the MRI you will receive the pyruvate injection through either your IV or port, two times and blood may be drawn eight times at 5, 10, 15, and 30 minutes after each injection.
- After the MRI you will be observed at most for 1 hour. During observation you will have your temperature, blood pressure and heart rate measured and you may have another EKG.
- You will be provided a sandwich/chips lunch during the observation period.

- Each of these MRI visits will take approximately 4 hours. Your onsite participation will be finished after Visit 2.

For the MRIs, you will lie very still on your back inside a large, doughnut-shaped scanner for approximately one hour while the technologist makes measurements and acquires images of cardiac tissue. The scanner normally makes loud noises during the procedure so you will wear ear protection (earplugs and headphones) during the scan. During the MRIs you will have stick-on heart leads placed on your chest and a clip placed on your finger. During the MRIs, you will be asked to hold your breath for brief periods of time.

During the MRI exams, you will receive two doses of pyruvate through the intravenous catheter or port. You will be monitored for any side effects from the pyruvate injection. Follow up by phone may occur approximately 24 hours after the MRI to ask if you experienced any side effects from the MRI visit.

For patients, administration of anticancer therapy will be standard-of-care by your treating physician and you will be followed by your treating physician in between MRI appointments.

You have the option to undergo two research cardiac MRI scans with the conventional contrast. We will compare these scans with the investigational MRI scans. These scans take approximately 1½ hours. These scans may be done on different days than the other two exams.

The MRI images in this study are designed for research, not for medical purposes. Even though the researchers are not looking at your MRI images to find or treat a medical problem, you will be told if they notice something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. Because the imaging done in this study is not for standard medical purposes, the research results will not be sent to you or your regular doctor.

You can choose to undergo the optional MRI scans described in this section. Please initial if you agree to take part in this procedure.
_____ I agree to having 2 conventional cardiac MRI scans with contrast.
_____ I do not agree to having 2 conventional cardiac MRI scans with contrast.

How long can I expect to be in this study?

- Your participation in the study will consist of:
- Screening in person or by phone.
- One or two cardiac MRIs with investigational pyruvate injection research visits (one after, or one before and one after your medical treatment with anticancer therapy).
- Phone visit about 24 hours after each MRI with injection visits may occur.

The research screening will take approximately one hour.

The research MRI with injection visits will take up to 4 hours each.

The 24-hour phone visits will take approximately 5 minutes each.

You may also take part in one or two cardiac function MRI scans with contrast.

The research visits DO NOT replace any of the visits with your doctors for standard of care breast cancer treatment.

You can choose to stop participating in the research study for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

What are the risks of the study?

MRI: There are no known risks from exposure to magnetic fields. You may experience nervousness and/or anxiety due to the loud banging made by the MRI machine while it is taking pictures and from confinement in a tight space (claustrophobia). If you become anxious, you can stop the procedure at any time.

You may also experience some discomfort and fatigue from lying still during imaging.
If you have any metal clips or plates in your body, you should tell the researchers. MRI may not be appropriate if you are pregnant or are trying to become pregnant. MRI may not be appropriate if you have permanent eyeliner or eyebrows or any pieces of metal in your body, such as the following:

- heart pacemaker, heart valve replacement, or aortic clips
- implants, breast tissue expanders
- non-MR compatible IV port
- metal fragments in your eyes, skin, or elsewhere in your body
- brain clips or pieces of metal used in aneurysm surgery or intracranial bypass venous umbrella
- pieces of metal in the body resulting from work as a sheet-metal worker or welder
- clips placed in an internal organ
- prosthetic devices, such as middle ear, eye, joint, or penile implants
- joint replacement
- hearing aid that cannot be removed
- neurostimulator
- insulin pump
- intrauterine device (IUD)
- shunts or stents
- metal mesh or coil implants
- metal plate, pin, screws, or wires, or any other metal implants

Pyruvate – Investigational Agent: The most commonly occurring side effects are short lasting and mild. They may include flushing, headache, nausea, fatigue, taste change, smell change, and throat discomfort. No serious side effects are anticipated from the injection of pyruvate.

IV Contrast: The contrast you will receive is FDA-approved and used routinely for MRI exams in standard medical care. It contains a material called gadolinium used to highlight organs or tissues during imaging. The injection of gadolinium may cause discomfort like headache, nausea, a warm flushing feeling, strange taste, or coldness at the site of injection. These symptoms occur in less than 1 out of 20 patients receiving gadolinium and go away quickly. There is a small risk of severe allergic reaction that can cause breathing difficulties and/or low blood pressures, and these symptoms are extremely rare (approximately 1 in 10,000 to 1 in 100,000 administrations). In the unlikely event you experience these symptoms, a physician will be available to evaluate and, if necessary, provide treatment.

People with severe kidney failure who receive gadolinium contrast are at risk of developing a disorder called Nephrogenic Systemic Fibrosis (NSF) You will have a blood test to make sure your kidneys are functioning properly. You will not be eligible to participate in this research if you have not had a previous reaction to a contrast agent or if you have Sickle Cell Disease.

Insulin: The most commonly occurring side effects are mild, but low blood sugar may occur, along with headache, feeling sick, shakiness, or sweating. If you receive insulin and have any of these symptoms you will be given crackers and juice.

Glucose drink: The most commonly occurring side effects are mild but you may experience a headache or feeling sick.

Psychological Stress: MRI machines are long narrow, cylindrical tubes, which can cause a feeling of claustrophobia or panic in some patients. Some of the questions we will ask as part of this study may make you feel uncomfortable.

Loss of Confidentiality: Any time information is collected, there is potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks to Embryo or Fetus: If you are part of this study while pregnant, it is possible that you may expose the unborn child to risks. You cannot participate in this research if you are pregnant or breastfeeding. Females of childbearing potential must agree to be tested for pregnancy prior to the MRI exam. Males must be surgically sterile or have a female partner of childbearing potential using an acceptable method of contraception (IUD, implant, and a barrier method such as condom, diaphragm, or cervical cap) during the study and for 6 months after patient discontinuation of cancer treatment. Males must also refrain from sperm donation during the study and for 6 months after discontinuation of treatment.

Risks of Blood Drawing: Risks associated with having your blood drawn include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely. You may have a maximum of less than five ounces (ten tablespoons) of blood drawn during each MRI visit. In the event that blood needs to be recollected, the patient will be contacted and the needed amount will be collected.

Risks of Genetic Testing: This research study includes genetic testing. Human tissue contains genes that determine many of a person's physical characteristics, such as the color of eyes and hair. In some cases, genetic testing of tissues can be used to indicate a risk for the development of certain diseases. Genetic information is unique to each individual and could potentially be used to discover possible changes in a person's future health status or life expectancy, or that of his/her children and family members.

Releasing genetic information to you could cause psychological distress, anxiety or family problems. Releasing this information to others, such as including it in your medical record, may pose a possible risk of discrimination, or increase difficulty in obtaining or maintaining disability, long-term care, or life insurance.

These risks would occur if your information is released by mistake. The measures being taken to protect your privacy are discussed below and make this possibility unlikely.

Even though the results of genetic testing may not be linked to you, it is possible that people of your ethnic background may be found to be at more risk for certain diseases based on future genetic research and this information might harm you in the future as a member of the group. Also, there may be unknown risks of genetic testing in the future.

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician unless the information indicates that you may be at risk for a serious illness known at the time of testing to be treatable and it can be confirmed by a clinical laboratory. In that case, you can decide whether or not we will attempt to notify you using the contact information you have provided.

If you do not want to be notified of any of these incidental findings, please initial below.
_____ Please notify me of any incidental findings obtained from this research.
_____ Please do not notify me of any incidental findings obtained from this research.

Other Risks: There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

How will risks be minimized or prevented?
MRI: You will be asked to complete an MRI Screening Form before each MRI exam to make sure it is safe for you to have an MRI.

Pyruvate – Investigational agent: Prior to administration of the pyruvate injection, a nurse will assess your temperature and blood pressure, and you will have an EKG for the measurements of your heart. You will be observed for approximately 1 hour after the completion of each MRI procedure with contrast and pyruvate injection. During the observation period a nurse will check your temperature, blood pressure and heart rate. You may have another EKG after the MRI. A study physician will be present during the MRI exams.

Contrast: You will be carefully screened with a blood test to measure kidney function prior to your cardiac MRI with contrast. People with kidney disease cannot participate in this study. After receiving contrast, you will asked to drink extra water for 24 to 48 hours after the contrast, so it can be cleared from your body.

Insulin: If you receive insulin you will have your blood sugar checked and you will be monitored for any side effects. You will be given crackers and juice if you have low blood sugar.

Glucose drink: You will have your blood sugar checked and you will be monitored for any symptoms.

Loss of Confidentiality: A record of your research participation will be created and will be kept in a locked office. Any data stored on a computer will not identify you, but will have a code used to protect your privacy. Every effort will be made to keep your information confidential.

What will my responsibilities be during the study?
While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.

- Let the researchers know if your telephone number, address or email changes.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.
- Report to the researchers any injury or illnesses while you are on study even if you do not think it is related.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking.

What are the possible benefits of this study?
If you agree to take part in this study, there may not be any direct benefits to you. We hope the information learned from this study will benefit others being treated with anticancer therapy in the future. Information gained from this research could lead to better detection of changes in the heart following those treatments.

What options are available if I decide not to take part in this research study?
This is not a treatment study. You do not have to be part of it to get treatment for your condition.

Will I be paid if I take part in this research study?
You will be paid $100.00 for the completion of each MRI exam with pyruvate injection, and $50.00 for the completion of each conventional cardiac MRI exam. If you choose not to complete the MRI research visits or are withdrawn by the research team, you will not receive payment.

How will I be paid?
You will be issued a UT Southwestern Greenphire ClinCard, which can be used as a credit or debit card. You will also receive instructions on how to use the card. In order to receive study payments, your name, address, date of birth and Social Security Number (SSN) will be collected from you by the research staff. All information will be stored in a secure fashion and will be deleted from the UT Southwestern Greenphire ClinCard system once the study has been completed.

If you are an employee of UT Southwestern, your payment will be added to your regular paycheck and income tax will be deducted.

Important Information about Study Payments
1. Your SSN is needed in order to process your payments. Should you decide not to provide your SSN, your study participation payment will be decreased at the current IRS tax rate. Study payments are considered taxable income and are reportable to the IRS.

2. An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.
3. Your ClinCard payment information will not be shared with any third parties and will be kept completely confidential.

This information will remain confidential unless you give your permission to share it with others, or if we are required by law to release it.

UT Southwestern, as a State agency, will not be able to make any payments to you for your participation in this research if the State Comptroller has issued a "hold" on all State payments to you. Such a "hold" could result from your failure to make child support payments or pay student loans, etc. If this happens, UT Southwestern will be able to pay you for your taking part in this research 1) after you have made the outstanding payments and 2) the State Comptroller has issued a release of the "hold."

A parking voucher will be provided for the valet parking service available at the Clements Imaging building when you are here for the investigational MRI visits. No other parking or transportation compensation is provided.

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above). Expenses for the research MRIs are covered by the Researchers.

However, for patients, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care.

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately.

Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center, or Parkland Health & Hospital System.

You retain your legal rights during your participation in this research.

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

If I agree to take part in this research study, can I be removed from the study without my consent?
Yes. The researchers may decide to take you off this study if:

- Your medical problem remains unchanged or becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The researchers believe that other treatment may be more helpful.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?
Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

What is Protected Health Information (PHI)?
Protected Health Information is information about a person's health that includes information that would make it possible to figure out who's it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include:

- medical and surgical history,
- current and previous medications,
- age, gender, race and ethnicity,
- height, weight, and vital signs including temperature, pulse, respirations and blood pressure,
- 12-lead ECG results,
- results of urine pregnancy test,
- results of blood tests (kidney function, blood count, lipids, female hormones), and MRI study images

We will get this information by looking at your chart at UT Southwestern Medical Center and Parkland Health & Hospital System.

How will your PHI be shared?
Because this is a research study, we will be unable to keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- The Sponsor, National Institutes of Health Institute for Biomedical Imaging and Bioengineering, funding the study. The sponsor includes any people, entities, groups or

companies working for or with the sponsor or owned by the sponsor. The sponsor will receive written reports about your participation in the research. The sponsor may look at your health information to assure the quality of the information used in the research.

- The members of the local research team,
- The Institutional Review Board, Human Research Protection Program Office and the Compliance Office of the University of Texas Southwestern Medical Center, and other groups that oversee how research studies are carried out.
- The Research offices at the University of Texas Southwestern Medical Center and Parkland Health & Hospital System.
- The Food and Drug Administration (FDA) and other U.S. and international governmental regulatory agencies involved in overseeing drug or device research.
- Representatives of domestic and foreign governmental and regulatory agencies may be granted direct access to your health information for oversight, compliance activities, and determination of approval for new medicines, devices, or procedures.

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

How will your PHI be protected?

In an effort to protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of UT Southwestern Medical Center or Parkland Health & Hospital System for review or testing. If the results of this study are reported in medical journals or at meetings, you will not be identified.

Do you have to allow the use of your health information?

You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties but you will not be allowed to participate in the study.

After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to Vlad Zaha, MD, PhD, 5323 Harry Hines Blvd, Dallas, TX 75390-8568. If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the study staff if you have a need to review your PHI collected for this study.

You will only have access to your PHI until the end of this study.

How long will your PHI be used?
PHI expires at the end of the study.

By signing this form, you agree to let us use and disclose your health information for purposes of the study until 2043. This permission to use your personal health information expires when the research ends and all required study monitoring is over.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Are there procedures I should follow after stopping participation in this research?
Yes. You should continue to be followed by your physician for your regular medical care.

Whom do I call if I have questions or problems?
For questions about the study, contact Vlad Zaha, MD, PhD at 214-645-6269 or 214-6459269.

For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

There is a possibility that additional study endpoints, and related study visits, will be added to the study in the future. The study team plans to contact you in this case to see if you are willing to participate in these study visits.

The study team also plans to contact you in the future to ask you if you are willing to participate in future, related studies.

_____ I agree to being contacted in the future.
_____ I do not agree to being contacted in the future.

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.
- You understand that a copy of this signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.

_____

Name of Participant (Printed)

_____ _____ _____ AM / PM

Signature of Participant Date Time

_____ Name

of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM

Signature of Person Obtaining Consent Date Time