Approved by IRB:

UF IRB-01 Approved

NCT05120284

UF Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:

_____

Place of employment & position:

_____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this Research Study (this "Research Study")?

Phase IIA Trial of Dichloroacetate (DCA) in Glioblastoma Multiforme (GBM)

3. Who is paying for this Research Study?

The sponsor of this study is the Food and Drug Administration.

4. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research? How long will you be involved?

The purpose of the study is to find out if a drug called sodium dichloroacetate (DCA), which is an investigational drug not approved by the FDA, can change the chemical reactions that help make GBM tumors grow. Participation is for 7-36 months.

b) What is involved with your participation, and what are the procedures to be followed in the research?

Study participation will require travel to your hospital in order to complete study visits. You may receive this investigational medication before your surgery as well as after your surgery. Other study procedures include blood draws from a vein, and taking the study medication as ordered.

c) What are the likely risks or discomforts to you?

Potential discomforts include loss of time related to study visits and study procedures, pain associated with blood draws, and numbness or tingling in the hands or feet related to the study medication.

d) What are the likely benefits to you or to others from the research?

There is no direct benefit to you from participating in this study. Presenting research results generally helps the career of the scientist(s) working on this clinical trial.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

The current treatment for glioblastoma is limited to maximal safe surgical resection, followed by chemotherapy and radiation therapy.

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.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study

Since this research study is being done at several locations, before signing this document, please read the attached "Consent Addendum" that will give you additional information about your location.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

5. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

This study does not affect your normal clinical care. You will continue to receive routine medical care from your usual doctors and medical care providers during study participation.

6. What will be done only because you are in this Research Study?

You will travel to the study site approximately every 28 days (2 times each cycle [Cycle 56 days] for first 3 cycles and then once a cycle, (every 56 days) for the duration of the study. The first visit is called a screening/baseline visit and will occur 7-14 days before surgery. During this visit, a medical history and physical exam will be conducted, as well as a review of study medication. A special genetic test called GSTZ1 haplotype analysis, that uses cheek cells, will also be completed to determine which dose of the study medicine you will be assigned to receive. During this test, a cotton swab will be drawn gently back and forth over your cheek inside your mouth to collect cells, a procedure called a buccal swab. The cells will be sent to Medosome Biotec, a laboratory in Alachua, Florida for genotyping, which will determine how much DCA you will receive.

Each visit will take approximately one hour to complete. During day 1 of each cycle, 6 ml or less than 3 teaspoons of blood will be collected. These samples, labeled with a subject ID, will be sent to Dr. Stacpoole's lab at the University of Florida. These specimens will be stored for the duration of the study and then destroyed. If you decide to take part in this study, you will be sequentially assigned to either begin DCA prior to your surgery or not begin DCA until after your surgery.

Study participants assigned to the pre-surgical DCA arm will receive a one week supply of DCA for dosing prior to your surgery, where the surgeon will try to remove as much tumor as possible. The study team will give participants instructions on how to take the DCA every 12 hours as ordered, every day, leading up to their surgery. The participants will bring their DCA bottle(s) back to the research team on the day of your surgery for a compliance check.

After your surgery, both those who have already started DCA, and those that have not will receive a 1 month supply of DCA at your study visit. The amount of DCA you receive is based on the result of your genotyping test. Based on the result of your test, you will either receive 6.25 mg/kg DCA oral suspension or 12.5 mg/kg DCA oral suspension every 12 hours. Study coordinators will review with you your DCA dosing schedule andthe importance of adherence. In between study visits, the study

coordinator or study team member will complete a visit either by telephone or email to check on your health status and compliance with DCA dosing every 2 weeks for the first cycle and then once every 4 weeks for the remaining cycles. For the first 2 months you will receive enough drug to last you 4 weeks. You will have to come back to the clinic to receive the additional 4 weeks to complete your cycle. After 3 cycles you will receive enough drug to last for 8 weeks. Each time you come to receive more drug you must also return the bottles that you used and bring your drug diary for a compliance check.

Standard of care laboratory results from blood, and brain imaging (such as a CT scan or a MRI) will be obtained from your medical record.

Once this research study is completed, any information that might identify you **will** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed in question 1 of the addendum.

7. What identifiable health information will be collected about you and how will it beused?

The Research Team will collect:

- Name
- Date of birth
- Address
- Results from research related analysis of blood, urine and buccal swabs
- Standard of care test results from blood, urine, and brain imaging (such as aCT scan or MRI) will be obtained from your medical record.
- Date of collection of specimens collected for this study

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals or clinics). The University ofFlorida Institutional Review Board (IRB), may also collect your health information.

The Research Team listed in question 1 of the local addendum will use or share yourhealth information as described below to carry out this research study.

8. With whom will this health information be shared?

This health information may be shared with:

- the study sponsor and their representatives (listed in Question 3 of this form);
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections;
- government agencies which are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments;
- the IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected,
- The Johns Hopkins Central Operations Office.

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

9. How long will you be in this Research Study?

You will be asked to participate in this study for 7 - 36 months

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

10. How many people are expected to take part in this Research Study?

Forty study participants are expected to enroll in this study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

11. What are the possible discomforts and risks from taking part in this Research Study?

Psychological risks to the patients entered into this study include those associated with travel to the clinic visits and the stress of recurrent clinical testing.

The liquid formulation of DCA is mixed with an artificial sweetener (NutraSweet) containing aspartame and strawberry extract. Most people don't find the taste unpleasant.

DCA is not approved by the Food and Drug Administration (FDA). DCA has been given to children and adults with diseases such as congenital lactic acidosis, brain tumors, and other serious conditions. DCA has also been given to healthy volunteers participating in research studies.

DCA is generally well tolerated when given by mouth. Studies in animals and humans have shown that when the drug is given chronically (longer than 2 months), reversible (not permanent) nerve damage (peripheral neuropathy) may occur. Peripheral neuropathy is a kind of nerve damage that may have symptoms like tingling, numbness, and/or weakness of fingers and toes.

The risks of drawing blood from the vein include: discomfort at the site of the insertion; possible bruising and swelling around the insertion site; rarely, infection; and, uncommonly faintness from the procedure.

Pregnancy: Studies to determine the effects of DCA on unborn babies have not been done. Because participation in this study may harm an unborn baby, birth control must be used in any female or male of child-bearing age. If you become pregnant or father a child while you are in this study, you must tell the study doctor at once. To avoid risk to an unborn baby with pregnancy, it is important that you or your sexual partner do not become pregnant while you are participating in this research study.

No method of birth control is 100% effective. However, there are a number of contraceptive methods for both men and women that are highly effective. For men, the most highly effective form of birth control is a vasectomy. For women the most highly effective methods of birth control are surgical sterilization (tubal ligation) hysterectomy, Depo-Provera injections, IUDs (Intrauterine Devices) and contraceptive implants (Implanon). If you or your partner is using one of these methods, the woman will be adequately protected from becoming pregnant during this study.

If you have intercourse during this study, you should understand that even if you and your partner use effective birth control, there is still a small chance that a pregnancy could occur. The risks of taking DCA while pregnant are unknown, and could include potential loss of a pregnancy (a miscarriage) or possible birth defects. If you are female and become pregnant, you will be returned to your pre-study treatment and be withdrawn from the study.

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 1 of the local addendum or theperson reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by Universitypolicy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question1 of the local addendum.

12a. What are the potential benefits to you for taking part in this Research Study?

There are no known benefits of receiving DCA.

12b. How could others possibly benefit from this Research Study?

The benefit to others from your participation relates to the importance of determining whether DCA may be effective in improving the health patients with recurrent glioblastomas.

13. What other choices do you have if you do not want to be in this study?

Participation in this study is completely voluntary. You may choose to continue to receive the standard of care treatment from your physician.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

14a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at anytime. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 1 of the local addendum. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 1 of the local addendum to letthem know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study.No additional health information about you will be collected or disclosed to the ResearchTeam. However, if you take back this Authorization, you may not be able to continue inthis study. Please discuss this with a member of the Research Team listed in question #3.

14b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

- If you do not follow the instructions given to you by the study team
- If your healthcare providers think that DCA may be harming you or if they think it is too great a physical and/or emotional hardship for you to continue in this study; or
- Any reason as determined by the principal investigator

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SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study;the alternative to being in the study; and how the participant's protected health informationwill be collected, used, and shared with others:

_____ _____

Signature of Person Obtaining Consent Authorization — Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

_____ _____

Signature of Person Consenting and Authorizing — Date

_____ _____

Interpreter/Witness to the Consent Procedures (Print Name) (*Witness optional unless IRB or Sponsor required*) — Date/Time