Study Title: Pharmacokinetics Study of Oral 2-Deoxy-D-Glucose (2DG) in Subjects With a Confirmed Diagnosis of Epilepsy

NCT05605301

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Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____ Medical Record # _____

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study. Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a copy of this form.

Who is funding this study?

This study is being funded by the Epilepsy Foundation.

Key Information About This Research Study

Principal Investigator:	Mark Quigg, MD University of Virginia Ivy Translational Research Building 560 Ray C. Hunt Drive Charlottesville, VA 22903 (434) 243-2672
Sponsor:	Dr. Tom Sutula, University of Wisconsin-Madison

You are being asked to take part in a research study. You do not have to take part in this study.
You should only agree to take part in this study after reading this consent form and discussing it with the study team. You may also discuss this with your family, friends, health care providers, or others before you make a decision.

What problem is this study trying to solve?

Currently, many patients continue to suffer from seizures that are not controlled with medications that are currently available and approved by the Food and Drug Administration (FDA). There are also patients who suffer from a severe, life-threatening seizure called status epilepticus in which they experience one long seizure or multiple seizures without stopping.

The purpose of this study is to assess the safety and tolerability of an investigational drug called 2-Deoxy-D-Glucose (2DG) for the treatment of seizures and status epilepticus in patients with epilepsy. We will refer to 2DG as the study drug throughout this consent.

Specifically, this will evaluate how this investigational drug is metabolized by humans. 2DG inhibits or interferes with the body's normal use of sugar as an energy source (it inhibits glucose metabolism. 2DG has

not been approved by the FDA for the treatment of seizures and status epilepticus. It has not been proven to be safe or helpful. So far, 2-deoxyglucose has been given to more than 106 people who have brain cancer.

This is a 3-level 2DG dose escalation study. This means that after 3 subjects have completed enrollment at Dose Level 1 or Cohort 1, the results will be reviewed. The Study Committee will determine if the next cohort should be enrolled at Dose Level 2 or Cohort 2. The same procedure will be repeated after each cohort to review data to determine if the subsequently higher Dose Level should be enrolled. If the Study Committee determines that the most recent dose is not tolerated or that there are significant adverse events, the subsequent Dose Level will not be enrolled.

Why would you want to take part in this study?
You will not be helped by being in this study, but the information gained by doing this study may help you or others in the future with epilepsy.

Why would you NOT want to take part in this study?
You might not want to take part in this study because you will need to be admitted to UVA hospital for 24 hours and have blood drawn after taking this investigational medication.

What will I have to do if I take part in this study?
Full details of all the procedures are found later in this form. Briefly, if you take part in this study, you will:

- be admitted to UVA hospital for 24 hours
- receive one or more of the study drug doses depending on when you enter the study (Cohort 1: 40mg, Cohort 2 60mg, Cohort 3 60 mg twice over one day)
- have blood drawn
- give a urine sample
- undergo additional testing, including an electrocardiogram (EKG) and transthoracic echocardiogram (TTE) to evaluate your heart
- have one follow up phone call after you are released home

We may ask you to participate in 2 additional dosage trials of this investigational drug/study drug. Each of these additional dosage trials are referred to as cohorts. If you choose to participate in multiple dosage trials, you will undergo the same procedure for each dosage trial. You will be asked to indicate whether you wish to participate or not prior to any additional dose level.

What is the difference between being in this study and getting usual care?
If you take part in this study, the following things will be done differently than if you do not take part in this study.

- Multiple electrocardiograms (EKG) – a heart rhythm test
- Minimum of two speckle echocardiograms - a sound wave test of your heart after intravenous (IV) bubbles are injected.
- Placement and maintenance of at least two IVs, from which multiple blood draws (totaling less than 2.5 tablespoons of blood) will be taken and for the speckle echocardiogram. An IV is a small flexible

tube that is inserted into a vein guided by a needle. Once the tube is in place the needle is removed and replaced with cap that allows blood to be withdraw or fluids or medications to be given. This catheter will be placed the first day you arrive in the hospital.
- Multiple urine samples
- Complete scale to assess suicidality multiple times. The study team will ask you questions about previous suicide attempts, suicidal thoughts or plans to determine if you are at risk for suicide. Please be honest with your study document when answering these questions.

You are being asked to be in this study because you are a person with epilepsy.

Up to 9 people will be in this study at UVA.

How long will this study take?

Your participation in this study will require one 24-hour hospital admission to draw blood and 1 follow up phone call for participation in cohort 1 or 2 and one 36-hour hospitalization and 1 follow up phone call for participation in cohort 3. If you participate in more than one cohort, at least 4 weeks will occur between enrollment in each cohort.

What will happen if you are in this study?

There will be 3 cohorts in the study. You may be asked to participate in 1, 2, or all 3 cohorts. You will be told which cohort you belong to when you enter the study.

Note: All assessments and procedures as outlined in this consent are being done solely for research purposes

SCREENING (visit will last about 2 hours, including the time for the echocardiogram)
Visit 1, Day Up to 14 days before the hospitalization:

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have tests and procedures during this time to make sure you are eligible, and it is safe for you to participate. These include the following:

- Review of your medical history
- Physical exam and vital signs, including blood pressure and heart rate
- Neurological exam
- Blood collected for laboratory testing
- EKG
- Urine pregnancy test that must be negative to continue study participation
- Pregnancy testing-must be negative to continue study participation
- Review current medications. There are certain medications that you cannot take while you are participating in this study. The study team will review this list with you.
- Columbia-Suicide Severity Rating Scale
- Echocardiogram to see your heart function

If these tests show you are eligible, we will arrange for you to return to stay overnight in a hotel room provided to you. The next morning, you will come to the UVA hospital to be admitted and receive the medication.

STUDY PROCEDURES

Visit 2, Day 1 (Each visit will last about **24-48 hours)**

You should present to the hospital in a fasted state with nothing by mouth after midnight the previous evening. You will be admitted to the hospital early in the morning at approximately 7 am. You will stay 1 night in the hospital and be discharged the following day.

You will be admitted to the regular hospital unit on the 6th floor (6C) at UVA:

- The University of Virginia Hospital is located at 1215 Lee Street, Charlottesville, Virginia 22903.
- **You will not be allowed to eat after midnight before hospitalization.**
- You will arrive to the unit at 7:00 a.m.

During the morning after admission to the hospital, you will:

- Have urine tests to check for infection or pregnancy
- Have an IV catheter placed to allow easy blood draws.

The admission morning, you will:

- Have blood tests (1 tablespoon of blood) to check sugars, salts, your liver, heart, and kidney function, and your blood counts
- Urine pregnancy test and urine analysis
- Receive the specific dose of 2DG to be taken by mouth
- Have repeat blood draws (1.5tablespoons of blood) through the IV at pre-determined time points to monitor the medication in your blood, with the last blood draw occurring 24 hours after the medication dose is given (see below under “Blood collection for pharmacokinetic analysis”)
- Have an EKG (electrocardiogram) at every blood draw
- Vital signs at every pharmacokinetic analysis

The day after admission, you will have:

- Blood drawn
- Vital signs taken
- EKG
- Echocardiogram (except Cohort 3, Cohort 3 patients will have the echocardiogram the 2nd day after admission

Blood collection for pharmacokinetic analysis:

Blood for pharmacokinetic analysis (how the drug is being metabolized in the body) will be drawn at time 0

(prior to drug administration), and then at 15, 30, 45, and 60 minutes and at 2, 4, 6, 12, and 24 hours after single dose 2DG administration and after the last dose of Dose Level 3.

For patients enrolled in Cohort 3, you will be given an extra dose of study medication the evening of Day 1. You will be required to spend an additional night in the hospital. The 2nd day after your admission you will have the following performed:

- Blood drawn
- Vital signs taken
- EKG
- Echocardiogram

FOLLOW UP:

Visit 3, Day 29

After you are discharged from the hospital, you will have a follow up phone call 2 weeks later. The phone call will last approximately 20 minutes. You will be asked if you have had any problems after discharge from the hospital.

Study Schedule

	Visit 1 (Screening)	**Visit 2 (Admission)**	**Visit 3 (Follow up)**
Study Day	Up to 14 days before admission	1	29
Informed Consent	x		
Review study eligibility	x	x	
Medical History	x		
Vital signs	x	x	
Physical Exam	x	x	
Neurological Exam	x	x	
Suicidality scale	x		
Urine		x	
Blood draw (for laboratory testing)		x	
EKG (electrocardiogram)	x	x	
Study Medication Dispensed		x	
Heart ultrasound (echocardiogram)	x	x	
Overnight hospitalization		X*	
Side effects assessed		x	x
Follow up phone visit			x

*an additional overnight hospitalization for Cohort 3

Note: This study schedule would apply for each of the admissions should you be asked and/or choose to repeat the study procedures within a different cohort.

END OF STUDY:

After you have completed the study admission, you will no longer receive the study drug. You will continue taking any medications you were taking prior to the study.

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety. These responsibilities are listed below:

- You must attend each study visit.
- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Ensure that the study drug is taken as instructed.
- Ensure that the study drug is taken only by you, the person for whom it has been prescribed.
- Answer all of the study-related questions completely.
- You must not eat grapefruit or drink grapefruit juice during the course hospitalization during this study.
- Inform the study doctor or study staff as soon as possible if you have to take any new medications, including anything prescribed by a doctor or those that you can buy without a prescription (over-the-counter), including herbal supplements and vitamins. The study doctor will let you know if you can take these medications.
- You must participate by taking the study drug, allowing for blood draws, and participating in the additional testing required for the study (EKG and heart ultrasound).

Blood Testing

We will take (or "draw") up to 1 tablespoon at each clinic visit and up to 2.5tablespoons of blood during each hospitalization. The total amount of blood we will take will be up to 3.5 tablespoons for each cohort. If you enroll in all three cohorts, we may draw a total of up to 10.5 tablespoons during the course of the study. The blood we take will be tested to check sugars, salts, your liver, heart, and kidney function, your blood counts, and study drug levels.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

Risks and side effects related to 2-Deoxy-D-Glucose (2DG) include:

Less Likely

- Sweating, feeling warm, flushing, hypothermia (low temperature), hunger, confusion, weakness, dizziness, thirst, palpitations, restlessness, nausea, vomiting and drowsiness similar to insulin induced low blood sugar because 2DG inhibits glucose metabolism.

- Reversible heart muscle changes seen under the microscope are possible because they occurred in rat studies of high dose 2DG given for 28 days. However, the changes went away when the drug was stopped, did not occur when given for less than 8 days or at lower doses, and have not been reported in people given 2DG.

- ECG changes (QT prolongation) without any symptoms are possible because some cancer patients given doses of 2DG much higher than the current dose had these changes. However, the changes went away when the drug was stopped, and the changes were not seen at lower doses.

Rare but serious

- Bleeding esophageal and gastric ulcers occurred in one patient while receiving 2DG for brain cancer.

Blood Donation

If you participate in this study, it may affect your ability to donate blood. If you have any questions call the organization where you donate blood and talk to one of their nurses.

Risks from Completing Questionnaires

- Some of the questions asked may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you may skip it and move to the next question.
- Some of the questions asked may make you angry, emotionally upset or stressed out now or at a later time. If you do not wish to answer a question, you may skip it and move on to the next question.
- There could be a risk of discomfort and harm (to psyche, reputation, employability, insurability, social status, criminal or civil liability) that may occur as a result of participation. If you do not wish to answer a question, you may skip it and go to the next question.

During the research, if we learn you are having thoughts about suicide or hurting yourself or others, the research staff will ask you more questions about your thoughts. Based on your response, the staff may provide you with help to get treatment. This may include: working with you to contact your doctor or therapist, referral to a therapist to discuss your thoughts, contact a trusted family member, significant other or clergy, or work with you on a plan that may include getting you to a hospital for safety and treatment.

Risks of having your blood drawn:

Having blood drawn may cause:

- ✓ pain (common),
- ✓ a bruise (sometimes),

- ✓ fainting or passing out (not very often), and
- ✓ infection (rare).

If the people doing the study are exposed to your blood or body fluids in a way that could give them a disease, your blood may be tested. The tests might check for:

- ✓ hepatitis,
- ✓ HIV (Human Immunodeficiency Virus), or
- ✓ other infections.

You and the person exposed would be told the test results. However, your name would be kept private. If your test is positive for hepatitis or HIV or any other infection that may affect your clinical care, we will tell you the results and help you understand what the results mean for you.

Risks of taking blood from an IV catheter:

Risk of Repeated Sticks

Sometimes the catheter stops working. In order to get the blood we need, we may have to stick you again with another needle.

Risks for women:

Pregnancy and Contraception

The drug(s) used in this study can harm an unborn or nursing baby. Therefore, you cannot be in this study if you are pregnant or nursing a baby. A pregnancy blood test will be done 1 day before starting this study if you are a woman able to become pregnant. You MUST NOT become pregnant while on this study or for up to ***1 month*** after your last dose of study drug.

You and your partner must use an approved form of birth control during this study. Examples of birth control you may use are:

- Norplant
- IUD (intrauterine device)
- Depo-Provera
- Birth Control Pills
- Birth Control Patch
- Sterilization

The birth control methods listed below are less effective. They may be used if combined with other birth control methods

- Condoms
- Jellies or foam
- Withdrawal
- Sponge
- Diaphragm
- Rhythm
- Cervical cap

Ask your doctor for more details about the proper birth control method for you. If you become pregnant during this study, you must tell your doctor right away. Your doctor will discuss your treatment and the effect on the pregnancy.

Risks for men:

We also do not know the effects of these drugs on male sperm. If you are a male, you should not father a baby while you are in this study ***or for 1 month*** after your last dose of the study drug. You should also not donate to a sperm bank during this time. To do so may hurt your unborn baby. Use an effective method of birth control during this time. Effective forms of birth control are listed above.

If your partner becomes pregnant during this study, you must tell your doctor right away.

Other unexpected risks:
You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

You will not benefit from being in this study. However, the information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include:

- Standard anti-seizure medications
- Ongoing clinical care
- Consideration of surgical procedures as indicated by your type of epilepsy

If you are an employee of UVA your job will not be affected if you decide not to participate in this study.
If you are a student at UVA, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will be paid $800 for completing each cohort. . If you complete three inpatient dose trials and the required outpatient visits, you will receive a maximum of $2400.00.

You should get your payment about 10 – 14 days after finishing the study. The income may be reported to the IRS as income.

If you do not finish the study, you will be paid $50 per outpatient visit completed and $750.00 per each hospital day completed.

By agreeing to be in this study, you are donating your blood for research, and giving up any property rights you may have in them. The results of this research using your donated materials may have commercial value. However, you will not receive any payments.

Will being in this study cost you any money?

The following procedures/tests, which are being done for research purposes, will be provided at no cost to you or your health insurance: lab tests (urine and blood), study drug, EKG, heart ultrasound (echocardiogram), hospitalization, physician visit, follow up phone call.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask your insurance company for an estimate of what these costs might be or if pre-approval is required.

You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

You do not give up any legal rights, such as seeking compensation for injury, by signing this form. If you feel you have been injured as a result of this study you may contact the Principal Investigator or the IRB (phone numbers are located near the end of this form). If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health
b) You do not follow your doctor's instructions
c) The study sponsor closes the study for safety, administrative or other reasons

If you decide to stop being in the study, we will ask you to complete the final telephone follow up visit, which is to monitor your safety.

Any data collected about you up until the time you leave the study must be kept in order to determine the results of the study.

How will your personal information be shared?

The UVA researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address, and date of birth
- Social Security number ONLY IF you are being paid to be in this study
- Your health information if required for this study. This may include a review of your medical records and test results from before, during, and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The sponsor(s) of this study, and the people or groups it hires to help perform or review this research
- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.
- If you tell us that someone is hurting you, or that you might hurt yourself or someone else, the law may require us to let people in authority know so they can protect you and others.

Information about you and/or samples from you may be given to other researchers outside of the University of Virginia after all identifiers such as name, address, phone # have been removed.

Some of the people outside of UVA who will see your information may not have to follow the same privacy laws that we follow. They may release your information to others, and it may no longer be protected by those laws.
The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

Information and samples obtained from you during this study will not be used in future 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.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form or complete the "Leaving the Study Early" part of this form and return it to the researchers. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your medical records will be able to find out that you are in this study. This is done so your regular doctors will know what you receive as part of this study. If you have other health problems during the study, they will be able to treat you properly.

Please contact the Principal Investigator listed earlier in this form to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Mark Quigg, MD
University of Virginia
Ivy Translational Research Building
560 Ray C. Hunt Drive
Charlottesville, VA 22903
(434) 243-2672

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908 Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the UVA Study Tracking Number (at the bottom of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name. You may also report a concern anonymously by calling the UVA Compliance Hotline phone number at 1-800-235-8700.

Would you like the study team to communicate with you by email or text message?

If you choose to communicate with the study team by unsecure email (email that is not encrypted) or text message to your personal phone, there is some risk that your health information could be read or accessed by someone else while the information is sent or saved by your email or phone provider.

Your personal email or phone provider may also share or release your information because they do not have to follow the privacy laws that UVA follows. Sometimes email and phone providers release information to marketing companies for use in direct advertising. If you choose to communicate by email or text messaging, UVA cannot control this potential loss of privacy, but we want to tell you about this possible risk.

You do not have to agree to communicate with the study team by email or text message to be in this study. If you agree to texting or emailing, the study team will collect your phone and /or email address from you that you would like them to use to contact you. Please note, if you agree to text messaging, charges may apply depending on your data/text plan with your phone provider.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT(PRINT)	DATE

Signature of Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):

☐ Subject

_____	_____	_____
IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Notification of My Health Care Provider

Your health care provider will be notified of your participation in this study.

Leaving the Study Early

Signatures should be obtained in this section if the subject decides to leave the study early.

If you leave the study early the study leader will keep the data collected about you up until the time you leave the study to help determine the results of the study.

Check one option below:

____ I am withdrawing my consent from the intervention or treatment part of this study but agree to continue to have follow up information about me collected by the study team.
The follow up information will be collected by:

- Obtaining information from my medical records
- Phone call 1 week after hospitalization

____ I am withdrawing my consent for this study. No additional information may be collected about me including follow up information from my medical records.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below, you confirm that you have fully explained the implications of withdrawing from the study to the subject and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT(PRINT)	DATE