INFORMED CONSENT FORM

Dietary treatment of Glucose Transporter Type 1 Deficiency (G1D).

NCT number: NCT03181399

IRB Approved date: 01-22-21

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System
Children's Medical Center
Retina Foundation of the Southwest
Texas Scottish Rite Hospital for Children
Texas Health Presbyterian Hospital Dallas

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	Dietary treatment of Glucose Transporter Type 1 Deficiency (G1D)
Funding Agency/Sponsor:	National Institutes of Neurological Disorders and Stroke (NINDS)
Study Doctors:	Juan M Pascual, MD, PhD Deepa Sirsi, MD Saima Kayani, MD

You may call these study doctors or research personnel during regular office hours at 214-456-2768. At other times, you may call a doctor on call at the same number and follow the instructions.

Note: If you are a parent or guardian of a minor and have been asked to read and sign this form, the "you" in this document refers to the minor.

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?
The study is being done to find out whether an investigational dietary agent called triheptanoin (C7 oil) can treat your condition (Glucose Transporter Type 1 Deficiency or G1D) better or more safely than standard medication.

The word "investigational" means the triheptanoin is still being tested in research studies and has been approved by the U.S. Food and Drug Administration (FDA) for use in this research.

Why is this considered research?
This is a research study because triheptanoin is not FDA approved for any purpose, and that the study is being done to see if it can treat G1D better or more safely than

standard medication. The FDA has not approved triheptanoin consumption for any other general purpose.

The following definitions may help you understand this study:

- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you have been diagnosed with G1D and are either on a modified Atkins diet or are not currently on dietary 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 center.

How many people will take part in this study?
About 50 people will take part in this study at UT Southwestern or Children's Medical Center.

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.

If you live out-of-state or outside the United States, you will be given the choice to consent to this study over the telephone or in person. This will help minimize your travel time and travel costs.

<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.

You may also have to fill out certain forms or have the following exams, tests or procedures:

- Documentation of Glucose Transporter Type 1 Deficiency (G1D) (including genotyping)
- Medical/Treatment History

- Pregnancy testing (if applicable)
- Seizure diary

Study Medication/Intervention

If you decide to participate in this study you will take triheptanoin 4 times a day, as a replacement for part of the fat in your diet. The amount of oil you will take each day will be determined based on your nutritional consult with the registered dietician.

Procedures and Evaluations during the Research

EEG, Visits 1, 2, and3: Electroencephalogram (EEG) will be performed at visits 1, 2, and 3. This will take place at Children's Medical Center. No sedation, special medications or injections will be used to complete these procedures. We expect that EEG lead placement will take approximately 1 hour. The EEG will remain in place for up to 24 hours. The EEG in this study is designed for research, to evaluate any brain wave abnormalities. You will be told if notice any important changes. You and your regular doctor can decide together whether to follow up with more tests or treatment. Because the EEG and blood studies done in this study are not for medical purposes, only select or no research results will be sent to you or to your regular doctor.

Neuropsychological evaluation will occur at visit 1, visit 2, and visit 3: You will undergo an evaluation to measure your mood, how well you adapt to situations and change, and a standardized test to evaluate how well you think and solve problems. These tests will take approximately 2 hours to complete, and will be completed at every visit.

Screening

Screening and pre-entry evaluations may occur concurrently. All screening activities are consistent with standard of care. Screening includes documentation of diagnosis, medical history, and pregnancy testing if appropriate.

Pre-Entry Day 1

The first day of your visit is Pre-entry Day 1. Pre-entry assessments consist of clinical assessment and a targeted physical exam. Neuropsychological testing will be done on the same day in the afternoon. Neuropsychological testing is questionnaires designed to test intelligence, memory and comprehension.

On day one or day two, you will have a blood draw to evaluate hematology, chemistry, and lipid panel. We will obtain blood that is left over from the blood draws or draw additional blood, if needed, to measure the amount of C7 ketones. Providing this extra blood is optional. You will be started on-intervention the day after screening and pre-entry evaluations. We will also draw additional blood after you take the two doses of C7 oil to measure the amount of C7 ketones. Providing this extra blood is optional also. You will receive your initial doses of triheptanoin under

24 hour inpatient stay to ensure your safety. You will have neuropsychological testing on the day of discharge, in the afternoon.

Each month between Visit 1 and 2, the research coordinator will contact you to evaluate adherence and tolerability. Additionally, you will complete a monthly seizure log. On month two you will complete safety blood work at a local clinical laboratory and have the results returned to Dr. Juan Pascual at UT Southwestern Medical Center. If you do not comply with the month two blood draw you may have the delivery of oil delayed until you return to compliance with the protocol.

6 Month Visit
You will return for a discontinuation visit at 6 months after initiation of treatment. You undergo essentially the same set of evaluations completed at enrollment. You will complete a medical history, clinical visit, physical exam, pregnancy test if appropriate, and neuropsychological testing on the first day of the visit. On day one or day two, you will have a blood draw to evaluate hematology, chemistry, and lipid panel. We will obtain blood that is left over from the blood draws or draw additional blood, if needed, to measure the amount of C7 ketones. Providing this extra blood is optional. You will also have a fasting EEG. You will have one final dose of oil for the purposes of the EEG, at the dose you are accustomed to taking therapeutically. At that point, you will be discontinued from the oil. You will return on day 2 for off-oil neuropsychological testing.

9 month Visit
You will return for a study exit visit 3 months after completing C7 treatment. You will complete a medical history, clinical visit, physical exam, pregnancy test, and neuropsychological testing on the first day of the visit. On day one or day two, you will have a blood draw to evaluate hematology, chemistry, and lipid panel. You will also have a fasting EEG.

The movement scale, clinical global impression scale (CGI), side effect assessment, neuropsychological evaluations, nutritional assessment, genotyping (if necessary), EEG, and metabolite evaluations in this study are designed for research not for medical purposes. They are not useful for finding problems or diseases. Even though the researchers are not looking at the results of these evaluations 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 these evaluations are not for medical purposes, the research results will not be sent to you or to your regular doctor. You may request a copy of the results of the clinical exam and laboratory work to be sent to your doctor at the conclusion of the study.

How long can I expect to be in this study?

		Visit 1* Pre-Entry and Entry		Monthly Phone Calls	Visit 2 (±7 days) 6 mo. on-oil		Visit 3 (±7 days) 3 mo. off-oil	
Evaluation	Screen -1 month	Day 1 Pre-Entry and Entry	Day 2 Entry	Months 1-5	Day 1 On oil	Day 2 Off oil	Day 1	Day 2
Informed Consent		X						
Documentation of Disease/Disorder	X	X			X		X	
Medical/Treatment History	X	X			X		X	
Clinical Assessment		X			X		X	
Targeted Physical Exam		X			X		X	
Ataxia Scale		X			X		X	
Clinical Global Impression		X			X		X	
Side Effect Assessment		X		X	X		X	
Pregnancy Testing		X			X			
Neuropsychological tests		X	X		X	X	X	
Nutritional Assessment		X		X	X		X	
Seizure Count		X		X	X		X	
Inpatient		Admit: Noon	D/C: Noon		Admit: Noon	D/C: Noon	Admit: Noon	D/C: Noon
Continuous EEG		X	X		X	X	X	X
Laboratory Evaluations: Hematology, Chemistry Day 1 or Day 2		X	X	X	X	X	X	X
Blood collection to measure C7 ketones[1]		X	X		X	X		
Triheptanoin Supplementation			Start			End		

[1] Optional

Your participation in this study will be approximately 9 months. You will receive the dietary agent for 6 months, and will then be asked to return at 9 months for a follow up visit.

You can choose to stop participating 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?

Study Procedure/Intervention
Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

Triheptanoin may cause some, all or none of the side-effects listed below.

Frequent
- mild diarrhea

Occasionally
- gastric discomfort
- Weight gain

Rare
- none

Serious but Rare
- none

Psychological Stress
Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

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

Risks to Sperm, Embryo, Fetus or Breast-fed Infant
Males: Being in this research may damage your sperm, which could cause harm to a child that you may father while on this study. If you take part in this study and are sexually active, you must agree to use a medically-acceptable form of birth control. Medically-acceptable forms of birth control include:

(1) surgical sterilization (vasectomy), or
(2) a condom used with a spermicide (a substance that kills sperm).

Females: If you are part of this study while pregnant or breast-feeding an infant, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you can become pregnant, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you participate in this study. If you take part in this study and you are sexually active, you and any person that you have sex with must use medically-acceptable birth control (contraceptives) during the study. Medically-acceptable birth control (contraceptives) includes:

(1) surgical sterilization (such as hysterectomy or “tubes tied”),

(2) approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Implanon),

(3) barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or

(4) an intrauterine device (IUD).

If you do become pregnant during this study, you must tell the researchers immediately.

Risks of Blood Drawing

Risks associated with IV include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely.

You will have approximately 12 tablespoons of blood collected because you are in this research study.

EEG

You may experience mild discomfort due to the electrode gel and cap placed on head or slight itchiness due to the cap.

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?

The researchers will make every effort to keep you comfortable during the scan as well as during blood draws. If you are too uncomfortable at any time, please tell the study doctor and we will stop the study right away. Your standard clinical care will not be affected.

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 or address 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, including any medications you are taking for this study.

What are the possible benefits of this study?
If you agree to take part in this study, there may be direct benefits to you, as prior studies with patients diagnosed with other metabolic disorders taking the triheptanoin diet have noticed a decrease of progression of their illness. However, the researchers cannot guarantee that you will benefit from participation in this research.

We hope the information learned from this study will benefit others with G1D in the future. Information gained from this research could lead to better detection, earlier diagnosis and improved treatment.

What options are available if I decide not to take part in this research study?
You do not have to participate in this research to receive care for your medical problem. Instead of being in this study, you have the following options:

- Ketogenic diet
- Medication treatment for individual symptom management

Please talk to the researchers or your personal doctor about these options.

Will I be paid if I take part in this research study?
Yes. You will be paid $250.00 at each regular study visit (enrollment visit, 6 month follow up, and 9 month follow up). If you stop taking part in this study or are withdrawn by the research team, you will receive payment for only the visits you have completed. For example, if you complete 2 study visits you will be paid $500.00 total.

Your Social Security Number (SSN) will be given to The University of Texas Southwestern Medical Center in order to process your payment as required by law. 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.

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

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 sup-

port 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."

You will be reimbursed for your parking expenses, transportation to and from the research center (for example air fare or gasoline), hotel, and car rental costs, up to $1220 for each visit. You will also be reimbursed for your month two lab draw blood work up to $1750. In order to receive reimbursement, you will need to turn in all your receipts to the research coordinator.

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.

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).

However, 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 at Dallas or Children's Medical Center.

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 you are a clinic patient of Dr. Juan Pascual, , Dr. Saima Kayani, or Dr. Deepa Sirsi, the following statement applies to you: Your doctor is a research investigator in this study. S/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

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?

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.

You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- National Institute for Neurological Disorders and Stroke
- The University of Chicago (Dr. Douglas Nordli). This is another researcher and research facility that is working with UT Southwestern on the Research Project.
- Representatives of government agencies, like the U.S. Food and Drug Administration (FDA), involved in keeping research safe for people; and
- The UT Southwestern Institutional Review Board.

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.

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.

Are there procedures I should follow after stopping participation in this research?

Yes. If you, the researchers, or the sponsor stops your participation in the research, you may be asked to do the following:

- Let the researchers know immediately that you wish to withdraw from the research.
- Return to the research center for tests that may be needed for your safety.
- Return any unused study materials, including empty containers.
- Discuss your future medical care, if any, with the researchers and/or your personal doctor.

If you wish to discontinue the oil before 6 months, we will ask you to come in for a discontinuation visit as soon as feasible and remain on the oil until you return. If you wish to discontinue prior to your exit visit due to intolerable side effects, you will be provided instruction on discontinuation, and you will be asked to come in for a final visit as soon as feasible. You will complete a medical history, clinical visit, physical exam, pregnancy test, and neuropsychological testing on the first day of the exit visit. On day two, you will complete a fasting blood draw to evaluate hematology and chemistry. You will also have a fasting EEG and will be discontinued from the study at this visit.

Whom do I call if I have questions or problems?
For questions about the study, contact Dr. Juan Pascual at 214.456.2768. At other times, you may call a doctor on call at the same number or at 214.456.7000 and follow the instructions.

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

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

_____

Legally Authorized Representative's Name (Printed)

_____ _____ _____ AM / PM

Legally Authorized Representative's Signature Date Time

_____

Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM

Signature of Person Obtaining Consent Date Time

ASSENT OF A MINOR:
I have discussed this research study with my parent or legal guardian and the researchers, and I agree to participate.

_____	_____	_____ AM / PM
Participant's Signature (age 10 through 17)	Date	Time

Interpreter Statement:
I have interpreted this consent form into a language understandable to the participant and the participant has agreed to participate as indicated by their signature on the associated short form.

_____
Name of Interpreter (Printed)

_____	_____	_____ AM / PM
Signature of Interpreter	Date	Time