INFORMED CONSENT FORM

Official title: Compatibility of triheptanoin (C7) with the Ketogenic Diet in Patients Diagnosed with Glucose Transporter Type 1 Deficiency (G1D)

NCT number: NCT03301532

IRB Approved date: 01-22-2021

The University of Texas Southwestern Medical Center
Children's Medical Center

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	Compatibility of C7 with the Ketogenic Diet in Patients Diagnosed with 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 the study doctor or the research personnel during regular office hours at 214-456-2768. At other times, you may call them 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?
This study is being done to find out whether an investigational dietary agent called triheptanoin (C7 oil; oil) can be safely added to a ketogenic diet. The ketogenic diet is a dietary intervention commonly used in G1D.

The word "investigational" means the triheptanoin is still being tested in research studies. Triheptanoin is not FDA approved.

Why is this considered research?
This is a research study because triheptanoin is overseen by the FDA as part of specific research, and considers it an Investigational New Drug. 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 currently on a ketogenic diet.

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 15 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.

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.

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
- Blood or urine pregnancy testing (if you are female and able to become pregnant)
- Seizure count

Study Medication/Intervention

If you decide to participate in this study, you will take triheptanoin 4 times a day for one 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

Pre-entry assessments consist of clinical assessment, targeted physical exam, including a general standard medical examination of head, chest, abdomen, and limbs, side effect assessment, blood or urine pregnancy testing (if you are female and are able to become pregnant), and a seizure count.

Entry Day 1

You will be admitted for a 48-hour inpatient stay for oil administration and monitoring. Entry evaluations will be done within a day of pre-entry and consist of a blood draw to evaluate blood cell counts, lipid panel, and normal blood chemicals, including a random glucose. 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. A continuous electroencephalogram (EEG), which entails placing wires over the scalp to measure brain electrical activity, will be completed on you over the 48-hour inpatient stay. We will also place an intravenous (IV) line into your arm. It may be used if the study doctors need to give you treatment very quickly while you are in the hospital and may also be used to draw blood samples.

Day 2

You will be given C7 starting on the morning of Day 2. You will be given oil at a rate of 45% of your daily caloric intake, divided into 4 doses (breakfast, lunch, dinner, and before bed). You will receive continuous EEG for the duration of C7 administration. You will have a clinical assessment and will be asked about any side effects. You will receive your final dose in the evening on Day 2. You will have blood drawn to evaluate blood cell counts, lipid panel, and normal blood chemicals. You will undergo a random glucose and beta-hydroxybutyrate level (which is a blood byproduct of the ketogenic diet) in the morning with your first dose of C7 and at bedtime with your last dose of oil. 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 asked about any side effects.

Day 3

You will remain inpatient until approximately noon on Day 3 to ensure no unexpected withdrawal effects from C7. You will undergo a blood draw in the morning and just prior to discharge. 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. The continuous EEG will be stopped just prior to discharge on Day 3. You will have a clinical assessment, be asked about any side effects, and a seizure count will be performed.

Day 4 (Final On-Study Evaluations)
You will return for a discontinuation visit on Day 4. You will complete a medical history, clinical assessment, physical exam, side effect assessment, and seizure count, and have non-fasting blood drawn to evaluate hematology, lipid panel, and chemistry. 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. This visit will complete your participation, and you will be discontinued from the study.

The table below summarizes the study visits and procedures at each visit.

Evaluation	Screen	Day 1 Pre-Entry and Entry	Day 2	Day 3	Day 4
Informed Consent		X			
Documentation of Disease/Disorder	X	X			
Medical/Treatment History	X	X			X
Clinical Assessment		X	X	X	X
Targeted Physical Exam		X			X
Side Effect Assessment		X	X	X	X
Pregnancy Testing		X			
Nutritional Assessment		X			
Seizure Count		X		X	X
Inpatient		Admit: Noon		D/C: Noon	
Continuous EEG		X	X	½ day	
Laboratory Evaluations: Hematology, Chemistry		X	X	X	X
Laboratory Evaluations: Random glucose, Beta-hydroxybutyrate			X AM & PM	X AM & at D/C	
Blood collection to measure C7 ketones[1]		X	X	X	X
Triheptanoin Supplementation			X		

[1]Optional

The side effect assessment, nutritional assessment, 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?
Your participation in this study will be approximately 4 days. You will receive the dietary agent for 24 hours.

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	**Rare**
• mild diarrhea	• none
Occasionally	**Serious but Rare**
• gastric discomfort	• breakthrough seizures (ketogenic diet only; none documented

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 or urine pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick or using about 2 tablespoons of urine), 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 drawing blood from your arm or starting an IV in your arm 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 and 30 cc of urine (about 2 tablespoons) will be 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 EEG 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. If breakthrough seizures occur, you will be treated according to standard of care or best practices for your condition. 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 or may not 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. 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 for completing this study. If you do not complete the final visit on Day 4, you will only be paid for the visits that you have completed.

You will be reimbursed for your parking expenses, transportation to and from the research center (for example, airfare or gasoline), hotel, and car rental costs, up to $1220 for each visit. 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. Compensation will be credited to the card after completion of the study visits. Your name, address, date of birth and social security number will be shared with a third-party solely for the purposes of compensation processing. All information will be stored in a secure fashion.

Please note that if you are on record as owing money to the State of Texas, such as for back child support or a delinquent student loan, the payment may be applied to that debt.

An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year, unless it's a reimbursement.

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."

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, Procedures and Evaluations, or Final On-Study Evaluations 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.

Subjects and/or their insurance will not be paying anything for the first three days of study. All medical tests and the hospitalization are covered by the study for the first 3 days of study. If after Day 3, participants are still hospitalized or need to be admitted back into the hospital for further medical care then, their insurance will be charged for all medical costs in the event they are needed after Day 3.

What will happen if I am harmed as a result of taking part in this study?
The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section "Contact Information" for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being 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.

Whom do I call if I have questions or problems?

For questions about the study, contact Dr. Juan Pascual at 214-456-2768 during regular hours. 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