THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Mitochondrial Cofactors for the Treatment of Hyperbilirubinemia Due to PEG-asparaginase and or Inotuzumab Ozogamicin in Patients with Acute Lymphoblastic Leukemia (ALL)

2017-0978

Study Chair: Elias Jabbour

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed by an Institutional Review Board (IRB – a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn if a combination of levocarnitine and Vitamin B complex capsules can help control treatment-related hyperbilirubinemia (a liver side effect) in patients with acute lymphoblastic leukemia (ALL). Hyperbilirubinemia may cause yellowing of the skin and/or eyes.

The safety of this combination will also be studied.

This is an investigational study. Levocarnitine is FDA approved and commercially available for the treatment of carnitine deficiency, a decreased ability to turn fats to energy. Vitamin B complex is commercially available. As a dietary supplement, Vitamin B complex does not require approval by the FDA.

Combining levocarnitine and Vitamin B complex to help control abnormal liver tests in ALL is considered investigational. The study doctor can explain how the study drug and supplement are designed to work.

The study drug/supplement may help to control hyperbilirubinemia. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You may receive levocarnitine and Vitamin B complex until the hyperbilirubinemia has improved or for up to 30 days after your last dose of PEG asparaginase or inotuzumab. However, if the hyperbilirubinemia improves and then later comes back during follow-up, you may receive levocarnitine and Vitamin B again at the previous dose level and continue until the hyperbilirubinemia has improved.

You and/or your insurance provider will be responsible for the cost of levocarnitine and Vitamin B complex.

You may choose to receive other investigational therapy, if available. The study doctor will explain the options available to you, including their risks and benefits. You may choose not to have treatment to control hyperbilirubinemia at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- Blood (about 2 tablespoons) will be drawn for routine tests.
- If you can become pregnant, either part of the above routine blood draw or a urine sample will be collected for a pregnancy test. To take part in this study, you must not be pregnant.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Up to 78 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug/Supplement Administration

If you are found to be eligible to take part in this study, and your blood tests show that you have hyperbilirubinemia, you will start taking levocarnitine and Vitamin B complex.

- You will receive **levocarnitine** by vein over about 30-60 minutes 4 times a day (every 6 hours). Your dose of levocarnitine may be increased, depending on how you respond to treatment.
- You will take **Vitamin B complex** capsules by mouth 2 times a day.

If you miss or vomit any doses of taking levocarnitine or Vitamin B complex by mouth, do not make up the doses. Just wait until your next scheduled dose.

The study drug/supplement may be given to you as an inpatient in the hospital (preferred) or as an outpatient.

However, if your doctor thinks it is appropriate for you to leave the hospital, you may continue to receive levocarnitine by vein and Vitamin B complex by mouth as an outpatient. Vitamin B complex taken by mouth would be any commercially available Vitamin B complex product.

If you are unable to continue levocarnitine by vein, you may take levocarnitine by mouth 3 times a day until the liver test has improved.

Study Visits

At least 1 time each week, blood (about 2-3 tablespoons) will be drawn for routine tests.

If it is more convenient for you, you may have some of the blood tests performed at your local doctor's office or clinic. Your local doctor will tell the study doctor at MD Anderson the test results. The study doctor and/or study staff will discuss this option with you.

You will no longer be able to take the study drug/supplement if intolerable side effects occur, or if you are unable to follow study directions.

Your participation on the study will be over when the hyperbilirubenemia has improved.

Follow-Up

About 30 days after your last dose of the study drug/supplement, you may be called by a member of the study staff and asked how you are doing and if you have started any new medications. This call should last about 10 minutes.

Other Information

While taking part in this study, you should not take part in any other research study without checking with the study doctors of each study.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug/supplement and procedures.

Levocarnitine Side Effects

Common (occurring in more than 20% of patients)

• high blood pressure • headache	• diarrhea • vomiting	• abdominal pain

Occasional (occurring in 3-20% of patients)

• swelling (arm/leg) • chest pain • fast/irregular heartbeat • abnormal EKG • blood vessel disorder (possible tissue death) • dizziness • weakness • fever • abnormal sensation (such as pins and needles)	• skin rash • high blood levels of calcium (possible altered mental status, weakness, and/or kidney damage) • nausea • depression • drug dependence • loss of appetite • weight loss • weight gain	• abnormal taste • tarry stool • bleeding • lazy eye • changes in eyesight • kidney failure • lung inflammation • cough • runny nose • allergic reaction

Levocarnitine may occasionally cause low blood cell counts (red blood cells). A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.

Rare but serious (occurring in fewer than 3% of patients)

• seizure • low blood levels of Vitamin K (possible increased risk of bleeding and/or bruising)	• low blood sugar • increased risk of bleeding	• breakdown of muscle tissue (possible kidney failure)

It is not well known how often the following side effect of levocarnitine may occur.

• inflammation of the stomach and/or intestines

Vitamin B Complex

It is not well known how often the following side effects of vitamin B complex may occur.

• swelling • headache • dizziness • fatigue • weakness	• sweating • abdominal swelling • abnormal sensation (such as burning, numbness, or tingling)	• joint pain/swelling • difficulty breathing • allergic reaction

Using the study drug and supplement together may cause side effects that are not seen when each is given alone. The study drug/supplement combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality.** All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant or breastfeed a baby while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you can become pregnant, you must use acceptable birth control methods while on study, such as birth control pills or injections, intrauterine devices (IUDs), or double-barrier methods (for example, a condom in combination with spermicide).

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant may result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Elias Jabbour, at 713-792-4764) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you will be removed from the study drugs and you may be asked to come to the clinic for safety tests. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can collect data from your routine medical care. If you agree, this data will be handled the same as

research data.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson. Possible reasons for study removal may include not following study directions, the disease not responding to the drug(s), or intolerable side effects.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and/or shared with other researchers and/or institutions for use in future research.

Future research with your data is required for this study. You cannot take part in this study without allowing your data to be used for future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data is used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data.

Samples

Samples (such as blood and/or tissue) are being collected from you during this study, but all samples will be collected as part of your standard of care. None of your samples collected during this study will be used for future research.

Genetic Research

Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s).

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

   Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2017-0978.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____

SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR) DATE

_____

PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION