Official Title: Use of a Fish Oil-Based Intravenous Lipid Emulsion (Omegaven®) in the Treatment of Parenteral Nutrition (PN) Induced Liver Injury
IRB-Approved Date: 7/21/2010
NCT01845116

CAROLINAS HEALTHCARE SYSTEM
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Use of a Fish Oil-Based Intravenous Lipid Emulsion (Omegaven®) in the Treatment of Parenteral Nutrition (PN) Induced Liver Injury

INTRODUCTION

Dr. Caicedo and his associates are asking you/your child to participate in the Omegaven study at Levine Children's Hospital (LCH) and Carolinas HealthCare System (CHS). You are asked to enroll or enroll your child in this study due to liver damage from being fed by an IV (intravenously, meaning by a vein), and the study team believes that you or your child may benefit from this medication. We anticipate that you/your child will be enrolled in the study for at least six months, and that you/your child will be one of approximately five patients enrolled each year at CHS.

HOW THE STUDY WORKS

You are being asked to enroll or enroll your child in a study. You/your child has intestinal failure, meaning you/your child's intestine cannot absorb enough nutrients to grow. Therefore, you/your child has required special nutrition ("TPN" or PN) that is given by an IV. This IV nutrition is necessary and life saving, but it can result in severe liver disease. You/your child was chosen for this study because you/your child has developed chronic liver disease that is getting worse. Research studies have shown that the IV fat mixture (called Intralipid®), which is part of your/your child's IV nutrition, may be contributing to the liver disease. An alternative form of the IV fat mixture, called Omegaven®, could be used in place of Intralipid® for you/your child. Omegaven® has 10% fish oil, which is different from Intralipid®, which contains soybean oils. In studies performed in Europe, Canada and the U.S., infants and children treated with Omegaven® showed reversal in the signs of liver damage from being fed through a vein.

Currently, Omegaven® is not approved for use in the U.S. and is considered investigational. This means that the drug has not been approved by the Food and Drug Administration (FDA). However, due to your/your child's condition, we have received permission through the FDA to make Omegaven® available to you/your child.

Omegaven® is given IV through a small tube placed in a small vein or larger vein deep within the body. Omegaven® is given along with other solutions that have dextrose (sugar) and amino acids (protein). No other fat mixtures will be given during the time Omegaven® is being given, since we believe the other mixtures are contributing to your/your child's liver disease.

Omegaven® can be given either in the hospital or as a home infusion, but the first dose will be given in the hospital. If Omegaven® is given on an outpatient basis, you/your child will be required to return to Levine Children's Specialty Center once a month or other mutually agreed upon schedule for evaluation and follow-up. Per the study, your home health care agency will make arrangements for the required weekly or monthly blood draws you/your child will need while at home in order to remain on Omegaven®. The lab results will then be faxed to the Pediatric Nutrition Support Clinic at the Levine Children's Specialty Center at [redacted].

RISKS AND DISCOMFORTS

Previous studies have shown no special risks of using this drug in humans. As with all medications, side effects may include allergic reaction. Allergic reaction may range from minor itching or rash to major reactions which can result in death. The manufacturer has indicated that there may be increased risk of an allergic reaction to this product in patients with egg or shellfish allergies. Omegaven® is not recommended for patients with impaired lipid metabolism (break down of fat in the body), severe hemorrhagic (bleeding) disorders, or unstable diabetes mellitus when blood sugars are not well controlled.

Due to lack of experience in certain life threatening situations, the manufacturer does not recommend the use of Omegaven® in patients with severe liver or renal insufficiency (liver or kidney problems/disorders). Therefore, the risk associated with using Omegaven® in you/your child, given that you/your child has severe liver injury, is not known.

Risks seen while **Omegaven®** is given include:

Likely:

- There may be an association with essential fatty acid deficiency, or elevated free fatty acids or triglycerides (other types of fat in the blood)

Less Likely:

- Fishy taste

Rare but Serious:

- Prolonged bleeding time
- Infections
- Sharp increases in blood sugar levels

Undesirable effects that are seen while Omegaven® is given, that may also occur with conventional fat (for example: Intralipid®) include:

Likely:

- Slight rise in body temperature
- Heat sensation and/or cold sensation
- Feeling of heat sensation of face/neck
- Allergic reactions/redness to skin

Less Likely:

- Chills
- Lack of appetitie, nause, vomiting
- Headache, pain in the chest, bone pain

Rare but Serious:

- Difficulty breathing
- Increase/decrease in blood pressure
- Painful erection of the penis that can last for more than one hour

The long term side effects of Omegaven® are not known, and there is a risk that the drug may cause bleeding to occur on its own, meaning there are no other reasons for bleeding to happen. Because of this, blood tests will be performed regularly (about every 2 weeks) to monitor how you/your child is handling the treatment (how the blood clots and the level of fatty acids in the blood). The amount of blood that is collected will not be more than 3 milliliters (less than 1 teaspoon), in addition to the standard lab work that is used to help follow you/your child. Risks associated with blood drawing may include pain, bruising, and infection. Rarely, a person faints. If we determine that there are significant changes in any lab tests or the way in which you/your child can handle the lipids, we may choose to stop the study. We will discuss these decisions with you.

Other side effects may exist which are not known yet. If any new information is learned during the study, it will be shared with all participants.

Reproductive Risks

The effects of Omegaven® on the reproductive system (sperm, eggs) or to a developing unborn baby are not known. Because of this, patients who are on Omegaven® should not

become pregnant. For entry into this study, we require that all participants who are of appropriate age, agree to abstain from sexual intercourse (cannot have sex while on Omegaven®) or use a reliable, effective contraception (such as condoms or birth control pills) while on Omegaven®.

If of appropriate age and sex, before your child starts on the study, a confidential pregnancy test will be performed. Results will be given to the child by one of the study doctors or investigators. Every effort will be made to maintain confidentiality regarding a positive pregnancy test. Our policy is that we would not tell parent(s) or guardian(s) without the child's permission. However, under certain circumstances, we may have to share this information. For example, if your child's life or someone elses's life was at risk or if abuse was suspected, then it may be necessary to tell you as parent(s) or guardian(s) of a positive pregnancy test.

If we feel that it is necessary to tell a parent or guardian of a positive pregnancy test, we would meet privately with your child first to discuss our concerns before sharing any information regarding the pregnancy. If your child becomes pregnant while receiving Omegaven®, we will need to withdraw your child from the study. This means that even if we do not share results, parent(s) or guardian(s) may suspect pregnancy despite our best efforts to maintain confidentiality. If your child becomes pregnant or if there is any chance that your child is pregnant (late menstrual period), please contact the study team immediately so we may provide medical assistance and counseling.

BENEFITS

This study may or may not improve your/your child's condition. The information gained from your/your child's case may benefit others with your/your child's condition.

EXCLUSION CRITERIA

- Pregnancy
- Other causes of chronic liver disease (cystic fibrosis, biliary atresia, alpha-1 antitrypsin deficiency**)**
- Signs of advanced liver disease including cirrhosis on biopsy (where the liver has lost its ability to function normally due to chronic injury), varices (swollen veins in the lining of the stomach due to liver disease), ascites (abnormal collection of fluid in the abdomen due to liver disease)
- Known allergy to fish or egg protein
- Inability to properly break down fat in the body
- Severe bleeding disorders

- Unstable diabetes mellitus where blood sugars are not well controlled
- Low blood pressure that causes the body's organs not to get good blood flow and oxygen
- Stroke
- Recent heart attack
- Undefined coma (unconsciousness) status
- Enrolled in any other clinical trial involving an investigational agent (unless approved first by Dr. Caicedo, the clinical study investigator)

ALTERNATIVE PROCEDURE/TREATMENT

Participation to use Omegaven® is entirely voluntary. If you choose not to use Omegaven®, the alternative treatment is to continue the current treatment you/your child is receiving. This includes the use of soy based fats in the nutrition by vein. The use of the soy based fats have been standard practice for the past 25 years.

ADDITIONAL COST

The FDA has approved charging for the cost of Omegaven®. The cost of Omegaven® is the same as the cost of the fats given now by vein. Your insurance company may not pay for research treatments. If the insurance plan does not pay, then CHS *Healthy @ Home*, *LLC*, will cover all of the costs of the infusion of Omegaven®.

COMPENSATION

You will not be compensated in any way for participation in this study.

In the event that you/your child are harmed as a result of your participation in this study protocol, we will provide or arrange for treatment as necessary. This treatment, as well as other medical expenses, will be billed to you or your insurance company in the usual manner.

WITHDRAWAL

Your participation in this study is completely voluntary. You should feel under no pressure to be in this Omegaven® study. If you decide not to be in this study, you will not in any way harm your relations with your doctors or with LCH or CHS. You are free to stop your child or yourself from being in the study if you change your mind after entering it. This would not harm your relations with your doctors or with LCH or CHS.

We will tell you about new medical findings that may affect your willingness to continue in the study.

CONFIDENTIALITY:
The records of this study will be kept private. In any sort of report we might publish, we will not include any information that will make it possible to identify a patient. Your/your child's record for this study protocol may, however, be reviewed and/or photocopied by Carolinas HealthCare System, or by representatives of the Food and Drug Administration or other government agencies. To that extent, confidentiality is not absolute.

AUTHORIZATION:
If you wish to have your child/yourself take part in this clinical study protocol, you will be asked to sign this consent form. It allows the study investigator to collect, process and pass on any relevant personal health information collected from your/your child during the study. These are the activities routinely carried out during all clinical studies:

You have been told that personal information about you/your child (including sensitive personal health information, such as your/your child's medical history and your/your child's racial/ethnic origin if relevant to the study) will be reviewed, collected on a computer database, stored in electronic or manual files, audited, and/or otherwise processed by:

- The clinical study investigator, Dr. Caicedo and research staff,
- regulatory or other governmental authorities of the United States and other countries,
- Carolinas HealthCare System employees,
- other persons or agencies as required by law or allowed by federal regulations.

You have been told that your/your child's personal data will be collected and processed to:

- Check your/your child's suitability to take part in the study,
- monitor your/your child's treatment with the study medication,
- compare and pool treatment results with those of other subjects in clinical studies,
- support the development of the study medication,
- support the licensing application for regulatory approval of Omegaven® in the world,
- support the marketing, distribution, sale and use of Omegaven® anwhere in the world.

FINANCIAL INTEREST OF INVESTIGATOR

The doctors will receive no financial benefit in any form by asking you to participate in this study.

QUESTIONS

The physicians offering this study at Levine Children's Hospital and Carolinas HealthCare System are Dr. Ricardo Caicedo at [redacted]; Dr. Michelle Chiu and Dr. Karen Lessaris at [redacted]. You may ask them any questions you have now. If you have questions later, you may contact:

Dr. Caicedo at:
Department of Pediatric Gastroenterology
[redacted]

Drs. Chiu and Lessaris at:
Department of Neonatology
[redacted]

The Institutional Review Board is a group of people who review the research to protect your/your child's rights. If you have questions about the conduct of this study or about your/your child's rights as a reasearch subject, you may call the chairperson of the Institutional Review Board of Carolinas HealthCare System for information regarding patients' rights in a reserarch study. You can obtain the name and number of this person by calling [redacted].

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CONSENT

I have read the above information. I have asked any questions I had, and those questions have been answered. I agree for myself/my child to be in this study and authorize the use of my/my child's personal health information. If of childbearing age, I will us or I agree for my child to use birth control during the time that I am/she is receiving Omegaven®. Dr. Caicedo or one of his associates will give me a copy of this form.

_____	_____	_____
Patient (guardian) Print Name	Date	Time
_____	_____	_____
Patient (guardian) Print Name	Date	Time
_____	_____	_____
Signature of Person Obtaining Consent	Date	Time
_____	_____	_____
Investigator Signature	Date	Time

Identity of representative
___Next of Kin
___Parent/Guardian
___Healthcare Power of Attorney