Version Date: 6-5-17

Northwestern University
Department of Medicine

Consent Form and HIPAA Authorization for Research

PROTOCOL TITLE: Liver Function Measured by HepQuant-SHUNT in the Prediction of Outcomes in Patients with Passive Hepatic Congestion Secondary to Congenital Heart Disease (CHD) or Cardiomyopathy

PRINCIPAL INVESTIGATOR: Daniel Ganger, MD.

SUPPORTED BY: Northwestern University, Division of Gastroenterology and Hepatology

Introduction

You are being asked to take part in a research study. This document has important information about the reason for the study, what you will do if you choose to be in this research study, and the way we would like to use information about you and your health.

Conflict of Interest Disclosure

The following disclosure is made to give you an opportunity to decide if this relationship will affect your willingness to participate in this research study:

If your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before making your decision whether or not to be in the study.

What is the reason for doing this study?

This study will evaluate Cholate Testing as a diagnostic test to measure liver function (how well your liver is working) in patients with liver disease due to cardiomyopathy or congenital heart disease before they undergo heart surgery (heart transplant or Fontan Revision) and to measure liver function improvement after surgery. We will also include patients that have already undergone the Fontan Revision. Cholate Testing is still undergoing clinical research and is not yet an FDA approved diagnostic test. We will measure the liver function by using a test called HepQuant-SHUNT (study test).

There are tests and procedures being done for this study that are research-related and others that are considered standard of care. Standard of care is the regular care you would receive if you did not choose to participate in this study. The study staff can provide you with more information regarding what tests and procedures are research-related and what is standard of care treatment.

You are being asked to take part in this study because you are in need of a heart transplant or extensive heart surgery or have already undergone a Fontan Revision.

Information About The Study

We plan to enroll 20 subjects here at Northwestern. Your participation in this study will last approximately 2 years. For patients that have already undergone surgery their participation in this study be a one-time visit.

What will you do if you choose to be in this study?

Prior to enrollment, you will be seen in the Northwestern University Feinberg School of Medicine, Hepatology Clinic for a regular standard of care visit. The Hepatology Clinic is located on the 16th

floor in the Northwestern Memorial Hospital Lavin Pavilion, 675 N. St. 259 E. Erie, Chicago, IL 60611. While at your clinic visit you will hear about the study from a study doctor. If you agree to participate in the study, you will be asked to come to the Clinical Research Unit (CRU) of Northwestern Memorial Hospital for the first study visit, which will occur within 30 TO 60 days before your scheduled heart surgery. Your contact information will also be recorded. The CRU is located on the 10th floor of Feinberg Pavilion of Northwestern Memorial Hospital, 251 E. Huron, Chicago, IL 60611.

Study Visit Procedures

Once you have been enrolled, you will come to the CRU where you will undergo the study test to determine your liver function. Study staff will call you to schedule these appointments and ask you questions about the drugs you are currently taking. If any of the drugs are a beta blocker or ACE inhibitor you will be asked not to take this medicine on the morning of your study visit. After the study tests are performed you will be given the opportunity to take this medicine while at your study visit.

You will be required to fast (not eat anything) for all study visits. These tests are done for research purposes.

You will come to the Northwestern CRU for a study visit that will include your vital signs including weight and height will be taken and if you are a woman of who could become pregnant you will be asked to provide a urine sample to confirm you are not pregnant. If the urine pregnancy test is positive we will not proceed with the Hep Quant test.

The following information will also be collected at each study visit:

- information regarding any medical problems you are having
- any hospitalizations that have occurred and the reason
- any changes to your medications and the reason

All study visits will include the Study Test (HepQuant Shunt Test):

1. Placement of an intravenous catheter: At the start of testing an intravenous catheter will be placed in your arm. The catheter will be used for administering Cholate Testing compounds and removing blood samples. The catheter will stay in place for approximately 2 hours.
2. Administration of Cholate Testing compounds: Cholate is a natural substance produced by your liver to help absorb food and small amounts are normally present in your blood. You will be given one form of cholate mixed in juice for you to drink. At the same time another form of cholate will be given through the catheter in your arm. Cholate Testing is an experimental procedure.
3. Cholate Testing blood draws: blood will be removed from the catheter in your arm and analyzed to see how well your liver absorbs the two forms of cholate you were given. This will tell us how well your liver is working. Blood (5 mls or 1 teaspoon) will be drawn before you receive the Cholate testing compounds. Then blood (10 mls or 2 teaspoons) will again be drawn 5 minutes after you receive the Cholate testing compounds. Blood (10 mls or 2 teaspoons) will be drawn 4 more times, at 20 minutes, 45 minutes, 60 minutes, and 90 minutes, after you receive the Cholate Testing compounds. The total amount of blood drawn for Cholate Testing will be about 11 teaspoons (55 mls) at each testing visit.

If you are a woman who is able to become pregnant, you will have a urine pregnancy test at each visit. If pregnant you will not be allowed to continue in the study.

Study Visit #1 – within 30 days prior to your scheduled heart surgery or for patients with Fontan Revision this will be a one time visit
Your vital signs including weight and height will be taken and if you are a woman of child bearing potential (woman able to get pregnant) you will be asked to provide a urine sample to confirm you are not pregnant. If the urine pregnancy test is positive we will not proceed with the HepQuant-SHUNT.

The following information will also be collected at this visit:
- information regarding any medical problems you are having
- any hospitalizations that have occurred and the reason
- any changes to your medications and the reason

Study test will be performed
This visit will take approximately 2.5-3 hours.

Study visit #2-5, post surgery visits (2.5 -3 hours)
You will also be required to have visits on: 1 month, 6 months, 1 year and two years post-surgery.

At these visits, the following evaluations will be done:
- Body Weight
- Vital signs taken (Blood pressure, heart rate, respiration and temperature)
- If female of child-bearing potential: you will be asked to provide a urine sample for urine pregnancy test
- Blood samples will be taken for your standard of care labs.
- Study test will be performed

The following information will also be collected at this visit:
- information regarding any medical problems you are having
- any hospitalizations that have occurred and the reason
- any changes to your medications and the reason

These visits will take approximately 2.5-3 hours.

The total blood volume collected for the Study tests (HepQuant-SHUNT) will be 55mLs or about 11 teaspoons for each test, or 275mLs for each patient over the 2 years of the study. For subjects that will only have the test one-time the blood collected will be about 55 mls.

What are some of the possible risks and discomforts?
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.

Risks from test compounds
The HepQuant-SHUNT tests done for this study will use compounds called Cholates. They are labeled with stable (not radio-active) isotopes. Stable isotopes are naturally occurring heavy atoms that are everywhere and in everything, including our bodies. Stable isotopes do not decay like radioactive isotopes and do not produce any radioactivity so they are safe to ingest. The cholate forms used in this study have been enriched in these stable heavy atoms so the cholate forms can be measured in blood. These cholate forms have been registered with the FDA since 2002, and their use in humans has been monitored since that time. To date, the cholate forms used in this study have not been associated with any complaints or side effects. However, they are still considered experimental and there may be unknown risks.

Risks from Albumin

The cholate form that is given intravenously is mixed with albumin for test administration. Albumin is a protein which is a normal part of your blood. In rare cases, hypersensitivity reactions to intravenous albumin have been reported in the literature. No hypersensitivity reactions have yet been reported when using the amounts of albumin administered in the cholate test.

Risks of Placing Catheter in Vein

Risks associated with placing a catheter in a vein in your arm will include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely.

Risks of Other Medications

Beta blockers or ACE inhibitors could affect the blood flow to the liver, so subjects who are currently taking either a beta blocker or an ACE inhibitor will be asked to delay taking their normal dose the morning of their testing and until their test is completed. Delaying these medications could cause a temporary elevation in blood pressure but the risk would be minimal, similar to that of subjects that miss doses of medications in everyday life. To minimize risk, subjects taking both a beta blocker and an ACE inhibitor will not be asked to participate in this study.

Loss of Confidentiality

Anytime 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.

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.

What do I need to know about reproductive health/sexual activity if I am in this study?

The effect of the compounds used in the study procedure called “HepQuant-SHUNT” on human sperm and eggs has not been studied. The effects on the developing fetus using the study drug during pregnancy and the risk of birth defects are also unknown or may be unforeseeable. Therefore, both men and women should not attempt pregnancy and women should not be pregnant or breast-feeding while taking part in this study.

If sexually active, both men and women should use an effective method of birth control while taking the study drug. Barrier contraceptives (condoms or diaphragm) with spermicide, intrauterine devices (IUD’s), hormonal contraceptives, oral contraceptive pills, surgical sterilization, and complete abstinence are examples of effective methods. If you or your partner become pregnant while taking the study drug, it is important that you tell your study nurse/doctor immediately. You may have to stop the study drug. Other treatment options will be discussed with you if you stop the study drug.

What are the Possible Benefits for Me or Others?

You may or may not receive any benefit from being in the study. If you take part in this study, other people with liver disease secondary to heart disease may benefit in the future.

What other procedures or courses of treatment might be available to me?

You do not have to take part in this research study. You have the alternative to choose not to give consent to participate in this study. If you do not wish to participate in this study, you will receive the usual care that patients with your condition receive from doctors, nurses and healthcare professionals in the hospital, and may include heart transplant or other heart surgery.

Are there any financial costs to being in this study*?*

There will be no costs to you for being in this study.

Will I receive payment for participation in this study?
You will not be paid for your participation in this study.

If you use the Northwestern Memorial Hospital parking garage at 222 E. Huron, Chicago, IL 60611 for your Study visit, you will be given a parking voucher at your visit to cover your parking expenses.

What should I do if I am injured as a result of being in this study?
If you become ill or get an injury or illness as a result of study medications or procedures, you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

The hospital [university, researchers] will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.

If I have questions or concerns about this research study, whom can I call?
Any questions you may have about this study may be directed to the study doctor, Daniel Ganger, MD., at (312) 695-4496. Questions about research subjects' rights may be directed to The Office for the Protection of Research Subjects of Northwestern University at (312) 503-9338. If problems arise evenings or weekends you may call (312) 695-5624.

What are my rights as a research subject?
If you choose to be in this study, you have the right to be treated with respect, including respect for your decision whether or not you wish to continue or stop being in the study. You are free to choose to stop being in the study at any time.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment.
Any new findings developed during the course of this research that may affect your willingness to continue in this study will be shared with you.

If you want to speak with someone who is not directly involved in this research, or have questions about your rights as a research subject, please contact the Northwestern University Institutional Review Board (IRB) Office. You can call them at 312-503-9338.

What about my confidentiality and privacy rights?
We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

- All information in a medical record
- Results of physical examinations
- Medical history
- Lab tests, or certain health information indicating or relating to your liver function
- Records about the heart surgery or heart transplant procedure you are to undergo
- Records of liver imaging tests looking to measure how stiff your liver is

The following groups of people may give the researchers information about you:

- All current and previous health care providers, including but not limited to the Northwestern Medical Group (NMG) and Northwestern Memorial Hospital (NMH).

Once we have the health information listed above, we may share some of this information with the following people. Please note that any research information shared with people outside of Northwestern University and its clinical partners (or affiliates) will not contain your name, address, telephone or social security number or any other direct personal identifier unless disclosure of the direct identifier is required by law [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigators office]

- Authorized members of the Northwestern University workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board (a committee which is responsible for the ethical oversight of the study),

- Clinical affiliates, including but not limited the Rehabilitation Institute of Chicago (RIC), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and the Ann & Robert H. Lurie Children's Hospital of Chicago (Lurie Children's). Your participation in this clinical trial will be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers.

- Other University research centers and University contractors who are also working on the study,

- Study monitors and auditors who make sure that the study is being done properly,

- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).

Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.

The results of this study may also be used for teaching, publications, or presentations at scientific meetings.

ClinicalTrials.gov

A description of this clinical trial is 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.

Please note that:

- You do not have to sign this consent form. If you do not, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits. However, you will not be allowed to take part in this research study.
- You may change your mind and "take back" (revoke) this consent at any time. Even if you revoke this consent, the Principal Investigator may still use or share health information that was obtained about you before you revoked your consent as needed for the purpose of this study. To revoke your consent for the use of your health information, you must do so in writing to:

Daniel Ganger, MD.

Northwestern Memorial Hospital

Department of Medicine, 676 N. St. Clair Street, Suite 1900

Chicago, IL. 60611

- Unless you revoke your consent, it will not expire.

- If you “take back” (revoke) your consent to use any blood taken for the study, the Principal Investigator will make sure that these specimens are destroyed or will make sure that all information that could identify you is removed from these samples.

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Consent Summary:

I have read this consent form and the research study has been explained to me. I have been given time to ask questions, and have been told whom to contact if I have more questions. I agree to be in the research study described above. A copy of the consent form will be provided to me after I sign it. A copy of this signed consent document, information about this study and the results of any test or procedure done may be included in my medical record and may be seen by my insurance company.

_____ _____

Subject's Name (printed) and Signature Date

_____ _____

Name (printed) and Signature of Person Obtaining Consent Date