NCT03858530

# PARENTAL PERMISSION AND CHILD ASSENT TO PARTICIPATE IN A RESEARCH STUDY AT CHILDREN'S MERCY HOSPITALS

## Using Ultrasound Elastography to Predict Development of Sinusoidal Obstruction Syndrome

**SUMMARY** (Details of this information are in the sections below)

We are asking your child to be in this research study. Being in a research study is completely voluntary, and your choice will not affect your child's regular medical care. This research study is done to determine if ultrasound elastography and contrast enhanced ultrasound can detect a complication from sinusoidal obstruction syndrome (SOS) also known as veno occlusive disease (VOD) earlier than clinical symptoms, such as an enlarged liver or changes in liver function blood work, to determine which patients need the medication to help treat this condition. The following things are part of this study: ultrasound elastography, contrast enhanced ultrasound and limited abdominal ultrasound examinations. Being in this study will require an initial ultrasound examination within two weeks prior to your child's admission for the start of his/her conditioning regimen and then throughout your child's inpatient stay for your child's hematopoietic cell transplant (HCT) and up to 100 days after your child's HCT (which may be inpatient or outpatient). The biggest risk from being in this study is a slight loss of confidentiality. Ultrasound elastography or contrast enhanced ultrasound have no documented health risks separate from traditional diagnostic ultrasound. The use of the contrast agent, Lumason, is FDA approved for the use in children and adults, to look for liver problems, and has been used in other research studies to look at the heart in adults and has been well tolerated. There may not be any direct benefit to your child for being in this study. The physicians taking care of your child will not know the results of the ultrasound examinations. Instead of being in this study, your child can continue to get regular medical care.

## WHO IS DOING THIS STUDY?

A study team led by Dr. Sherwin Chan is doing this study. Other health care professionals may help them.

We are asking your child to be a part of this research study. Please read the information below and ask questions about anything that you do not understand before you make a choice.

## WHY IS THIS STUDY BEING DONE?

Hepatic sinusoidal obstruction syndrome (SOS) or veno-occlusive disease (VOD) is disease that can affect the liver of children and adults following hematopoietic cell transplant (HCT), which is also known as blood and marrow transplant (BMT). SOS/VOD is believed to be caused by damage to the veins in the liver during chemotherapy and/or radiation before HCT/BMT. However, symptoms of the disease typically do not show up until several days after HCT/BMT. This damage can lead to blockage of these veins, which can cause weight gain from fluid buildup and/or changes in liver function lab work. We think that when the damage to the veins happens, it will cause the liver to get stiffer because it is not able to move blood through the liver back to the heart correctly. The disease can be separated into mild, moderate, and severe forms and there are treatments available for this disease if diagnosed early. However, we have been studying the use of a new type of ultrasound called, ultrasound elastography, to help detect when these changes in the liver occur.

Traditional ultrasound pictures are created by using sound waves that are sent through the body. These sound waves bounce off of internal organs and structures and return to the ultrasound machine. These sound waves help create a picture of what the internal organs such as the liver and other structures look like. Ultrasound elastography imaging is a new tool that uses ultrasound pressure and sound waves to provide an estimate of tissue stiffness. By determining

how stiff the liver tissue is, we can predict the presence of disease, such as SOS/VOD. Ultrasound elastography does not have any increased risks over traditional ultrasound imaging.

The use of contrast enhanced ultrasound examinations are also being used in the detection of SOS. The contrast that will be used with ultrasound in this study is called Lumason (manufactured by Bracco Diagnostics). Lumason is approved by the Food and Drug Administration (FDA) for detecting and characterizing liver lesions and has also been used to help diagnosis blood clots in the liver. The value of contrast-enhanced ultrasound is still evolving, but findings from case reports suggest that the use of contrast could help facilitate an early diagnosis and clinical follow-up for SOS. Thus, this makes the use of Lumason contrast in this research study an experiment. Lumason uses microbubbles that are injected through an IV or central line, which you will already have in place as part of your clinical care.

The purpose of this research study is to determine if ultrasound elastography and contrast-enhanced ultrasound can be used as an early diagnostic tool for detecting SOS after BMT. We did a preliminary study on a similar patient population and found that ultrasound elastography is able to detect changes in the liver five days after transplant in patients that developed SOS. This is about nine to 11 days sooner than when clinical symptoms start to show up. The purpose of this study is to test our results in a larger patient population and perform more ultrasound elastography examinations to determine if our preliminary results hold true and to see if we are able to detect changes in liver stiffness even earlier than in our previous trial. If we are able detect the presence of SOS earlier, then we can begin available treatments that can slow progression or stop the disease.

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**WHO CAN BE IN THIS STUDY?**

We are asking your child to be a part of this research study because your child is undergoing an HCT.

Up to 80 Children and adults, ages 1 month through 21 years, will be asked to be in this study at Children's Mercy Hospitals.

If your child has any of the following issues he/she will not be unable to participate in the study:

- A heart abnormality
- A lung abnormality
- Allergies to the ingredients of the study drug, which include:
    - Sulfur hexafluoride
    - Polyethylene glycol 4000
    - Distearoylphosphatidylcholine (DSPC)
    - Dipalmitoylphosphatidylglycerol sodium (DPPG-Na)
    - Palmitic acid
- If your child is not unable to roll over
- If your child is pregnant
- If your child is breastfeeding

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**WHAT WILL HAPPEN TO ME IN THIS STUDY?**

Being in this study involves having ultrasounds at specific time points outlined below based on your child's disease course. Limited abdomen and limited abdominal Doppler ultrasound, contrast-enhanced ultrasound and ultrasound elastography examinations will take approximately one hour to complete. All exams will either occur in your child's room or within the Radiology department at Children's Mercy Hospital Adele Hall.

If you decide for your child to be in this study, the following things will happen:

- The study team will collect information from your child's medical record. The information collected will include the following:

    - Information about your child's imaging results
    - Information about your child's medical history and the course of HCT
    - Information about your child's HCT and conditioning regimen
    - Laboratory results

- If your child consents for the CIBMTR Research Database (IRB#11120281), as part of that consent your child agrees to allow the researchers to use the data entered as part of that database for future research. The information collected from the CIBMTR database for this study will include the following:

    - Information about your child's HCT and conditioning regimen
    - Information regarding your child's medical history and current health
    - Date of birth
    - Race/Ethnicity
    - Gender/height/weight
    - Laboratory results
    - Vital signs

    If your child does not consent for the CIBMTR Research Database, the study team will collect the above information from your medical record.

- The study team will get into your child's medical record from time to time to update the information collected. This will happen because researchers may need to know how your child's health has changed over time.

Your child will undergo US examinations based on disease course as outlined below:

1. All Patients: Patients will undergo limited abdominal US with Doppler, Contrast-enhanced ultrasound and SWE once a week upon admission for conditioning until the patient day +30 BMT or discharge, whichever comes first.

2. Inpatient SOS: patients will undergo limited abdominal US with Doppler, Contrast-enhanced ultrasound and SWE once a week upon admission for conditioning until resolution of SOS.

3. Late Onset SOS: patients will undergo limited abdominal US with Doppler, Contrast-enhanced ultrasound and SWE once a week upon admission for conditioning until resolution of SOS.

| | **ALL PATIENTS** | | **INPATIENT SOS** | **LATE ONSET SOS** |
|---|---|---|---|---|
| | **Prior to Conditioning** | **Start of Conditioning through Day +30** | **Through Resolution of SOS** | **Through Resolution of SOS** |
| | **Screening** | **Once per Week** | **Once per Week** | **Once per Week** |
| **Limited Abdomen and Limited Abdominal Doppler Ultrasound** | **X** | **X** | **X** | **X** |
| **Contrast Enhanced Ultrasound** | **X** | **X** | **X** | **X** |

| | | | | |
|---|---|---|---|---|
| **Ultrasound Elastography** | **X** | **X** | **X** | **X** |

## WHAT ARE THE RISKS OF THE STUDY?

There are certain risks in this study. These risks may include a slight risk of loss of confidentiality. your child's confidentiality will be protected to the greatest extent possible.

Ultrasound Elastography risks:

Ultrasound elastography has no documented health risks separate from traditional diagnostic ultrasound. Ultrasound imaging has some theoretical risks. It introduces energy into the body, which can heat body tissues slightly. It also can produce small pockets of gas in body fluids or tissues. These theoretical risks are proportional to the strength of the ultrasound waves. In the study procedures, we will be using weak ultrasound waves that do not generate enough energy to be significant. A large World Health Organization (WHO) study of diagnostic ultrasound using similar energy showed that there were no harmful effects from ultrasound imaging.

Contrast-Enhanced Ultrasound Risks:

Contrast-enhanced ultrasound uses microbubbles that will be injected through an existing IV or central line. The ultrasound imaging itself does not have any known health risks separate from traditional diagnostic ultrasound. The use of the contrast agent, Lumason, is FDA approved for use in children and adults, to look for liver problems, and has been used in other research studies to look at the heart in adults and has been well tolerated. We will monitor and record any Lumason side effects that we see.

Possible Side Effects: Each side effect happens to less than 5 children out of every 100 (<5%)

| Adverse Reaction | Number | (%) |
|---|---|---|
| Any Adverse Reaction | 340 | 5 |
| Headache | 65 | 1 |
| Nausea | 37 | 0.5 |
| Dysgeusia | 29 | 0.4 |
| Injection site pain | 23 | 0.3 |
| Feeling hot | 18 | 0.3 |
| Chest discomfort | 17 | 0.2 |
| Chest pain | 12 | 0.2 |
| Dizziness | 11 | 0.2 |
| Injection site warmth | 11 | 0.2 |

Hypersensitivity reactions such as skin erythema, rash, urticaria, flushing, throat tightness, dyspnea, or anaphylactic shock have uncommonly been observed following the injection of Lumason.

There have been very rare instances of an allergic reaction to Lumason. If your child has a known allergy, your child will not be enrolled in the study. There have also been very rare instances of serious heart reactions to Lumason when given to adults. If your child has a known heart problem, your child will not be enrolled in the study. Trained personnel and resuscitation equipment will be present during the entire study procedure in case there are any reactions.

If your child has any of these problems or changes in the way you feel, you should tell the investigator or other study personnel as soon as possible.

There may be risks we don't know about right now. We will tell you and your child about any new information that might change your decision to stay in the study.

**WHAT ARE THE BENEFITS OF BEING IN THIS STUDY?**

There may not be direct benefit to your child's from being in this research study. By being in this study, your child may help researchers find better diagnostic tools for detecting SOS/VOD in children and adults in the future.

**WHAT ABOUT EXTRA COSTS?**

There is no cost to you for your child participating in this study. Basic expenses such as transportation and the personal time it will take to come to all study visits will be your responsibility. Your child's research visit may be combined with a routine care visit. You or your child's insurance company will still be required to pay for all of your child's routine care that would have occurred if your child was not part of this research study.

**WHAT ABOUT CONFIDENTIALITY?**

Your child has rights regarding the privacy and confidentiality of his or her health information. When health information includes identifiers (like names, addresses, phone numbers and social security or individual taxpayer identification (ITIN) numbers) that link it directly to an individual, it is called protected health information (PHI). Federal laws require that PHI be kept secure and private. In certain situations, federal law also requires that you approve how your child's PHI is used or disclosed. A research study is one of those situations.

By signing this permission/assent form, you are permitting the following people to have access to your child's medical record and use your child's PHI for the research purposes described in this form. You are also permitting your child's PHI to be shared with everyone listed below:

- The research team, which includes persons involved in this study at Children's Mercy Hospitals and University of Washington, Seattle.
- The Institutional Review Board at Children's Mercy Hospitals and University of Washington, Seattle.
- People from organizations that provide independent accreditation and oversight of hospitals and research;
- Government/regulatory agencies (both US and international), such as the Office for Human Research Protections whose job it is to protect human subjects and oversee the conduct of research

The research record is separate from your child's medical record. Information about your child that is obtained during this study will be recorded in a research record and may also be recorded in your child's medical record. A research record will be created and kept in the Department of Radiology research office. The research record may include documents that have your child's name, assigned study ID number, medical record number, hospital account number, date of birth, and dates of service. All research records will be maintained in a confidential manner.

There will be a separate database, in which all study information is collected. This database will be used to analyze the study information and find out the study results. Information in this database will include your child's assigned study ID number, medical record number, date of birth, and dates of service.

By signing this permission/assent form, you are allowing your child's health information to be recorded in the research record. You are also permitting your child's research record and medical record to be shared with everyone listed above.

Some people or groups who get your child's identifiable health information might not have to follow the same privacy rules that we follow. We will share your child's health information only when we must, will only share the information that is needed, and will ask anyone who receives it from us to protect your child's privacy. However, once your child's information is shared outside of CMH, we cannot promise that it will remain private.

You may choose not to sign this permission/assent form and not have your child be in the study. You may cancel your permission to use and share your child's PHI at any time by contacting the study personnel listed on this form. You may also contact Children's Mercy Hospitals Health Information Management (HIM) in writing or Dr. Sherwin Chan, Children's Mercy Hospital, 2401 Gillham Road, Kansas City, MO 64108 in writing. If you cancel your permission, your child may no longer participate in this study. Your child's PHI that has already been collected for the study may still be used; however, no new information will be collected except information related to adverse events or other safety issues.

If you do not cancel your permission, your child's PHI may continue to be recorded until the entire study is finished. This may take years. Any study information recorded in your child's medical record will be kept forever. Unless stated elsewhere in this form, you may not have access to your child's research record or research test results.

Results of this study may be made public. If made public, your child will not be identified in any publications or presentations.

In addition to the use of data described above, 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 your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

## WHAT ARE THE ALTERNATIVES TO BEING IN THIS STUDY?

Instead of being in this study, you or your child may choose for your child not to be in the study.

## WHAT ARE MY RIGHTS AS A STUDY PARTICIPANT?

Being in a research study is voluntary. Your child does not have to be in this study to receive medical care. If you choose for your child not to be in this study or withdraw your child from this study, there will be no penalty or loss of benefits to which your child is otherwise entitled.

We will inform you and your child of any new information that we find out during this study. This information may affect your decision to keep your child in the study. If you choose to withdraw your child from (quit) the study or if you are asked by your child's personal doctor to withdraw your child from the study, you must tell the study team as soon as possible.

If you withdraw your child from the study early for any reason, the information that already has been collected will be kept in the research study and included in the data analysis.

Dr. Sherwin Chan, the Institutional Review Board or the FDA may stop the study at any time. The investigator(s) or your doctor may remove you from the study at any time without your permission.

## WHO SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

Dr. Sherwin Chan is in charge of this research study. You may call Dr. Chan at 816-234-3273 with questions at any time during the study. You may also call Amie Robinson, the study coordinator, at 816-302-8311 with any questions you may have.

You should call Dr. Chan if you believe that you are sicker or have suffered injury of any kind as a result of being in this research study.

You may also call Children's Mercy Hospitals' Pediatric Institutional Review Board (IRB) at (816) 701-4358 with questions or complaints about this study. The IRB is a committee of physicians, statisticians, researchers, community advocates, and others that ensures that a research study is ethical and that the rights of study participants are protected.

**SPONSOR AND INSTITUTIONAL RESPONSIBILITIES**

In the case of illness or injury resulting from this study, treatment is available at Children's Mercy Hospitals, but will be provided at the usual charge. Payment for this treatment will be your responsibility. The hospital may not bill insurance or other third-party payers for this care. Children's Mercy Hospitals does not have funds set aside to pay research participants if the research results in injury. By signing this form, you are not giving up any legal rights to seek compensation for injury.

**PERMISSION OF PARENT OR LEGALLY AUTHORIZED REPRESENTATIVE**

The purposes, procedures, and risks of this research study have been explained to me. I have had a chance to read this form and ask questions about the study. Any questions I had have been answered to my satisfaction. I give permission for _____ to participate in this research study. A copy of this signed form will be given to me.

_____ _____ _____
Signature of Parent/Legally Authorized Representative Date Relationship to Participant

__ Parent signing above has court-issued documentation showing sole legal responsibility for the care and custody of the child

__ Second parent is deceased

__ Second parent is unknown

__ Second parent lacks legal capacity to sign

__ Second parent is not reasonably available (document at least 3 attempts to locate and contact second parent)

_____ _____ _____
Signature of Parent/Legally Authorized Representative Date Relationship to Participant

**ASSENT OF MINOR**

I have been told that if I am in this study I will have ultrasound elastography examinations done at different time points before, during and after my HCT (transplant). I have been told that I don't have to be in this study. I may quit the study at any time, and no one will be mad at me. I have had a chance to discuss the study and ask questions. My questions have been answered. I agree to be in the study and do what I am asked to do as long as I continue in the study.

_____ _____

Signature of Minor Date

**STUDY PERSONNEL**

I have explained the purposes, procedures, and risks involved in this study in detail to:

_____
Print name(s) of Parents/ Legally Authorized Representative, and

_____, who in my opinion ___ IS / ___ IS NOT capable of assenting to participate in this study.
Print child's name.

If child IS NOT capable of assenting, please state reason why:

__ Age of child:_____ (insert age)

__ Limitation in understanding based on child's condition

__ Other, please explain_____

_____ _____ _____
Signature of Person Obtaining Permission/Assent Date Time

Print Name of Person Obtaining Permission/Assent _____

**WITNESS**

Witness signature is only required in the following circumstances:

- Consent obtained via telephone/telemedicine;
- Enrolling non-English speaking participant via the short form method;
- Subject or LAR cannot read or write or is visually impaired; OR
- IRB has required a witness or patient advocate to be present.

I have witnessed the consent process and signature(s) for this research study:

_____ _____
Signature of Witness Date

Print Name of Witness_____
(Must also sign the translated document)

**INTERPRETER**

☐ Interpreter Used ☐ Qualified Bilingual Study Staff Used

I was present and provided interpretation services during the signing of this document.

_____ _____

Signature of Interpreter Date

Printed Name of Interpreter: _____
(Must also sign the translated document)
Relationship of Interpreter to Subject:_____