Cover Page: Informed Consent

Protocol Title: Comparison of furosemide alone versus the combination of furosemide and albumin for diuresis in cirrhotic patients with fluid retention

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RUSH

CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH STUDY

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Protocol Title: Comparison of furosemide alone versus the combination of furosemide and albumin for diuresis in cirrhotic patients with fluid retention

Name of Participant: _____

Key Information:

You are being invited to participate in a research study. Research studies answer important questions that might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Taking part in this research study is voluntary. You do not have to participate in this study and may choose to leave the study at any time. If you decide not to participate in this study or leave the study at a later time, your health care, benefits, or relationship with Rush University Medical Center will not change or be affected.

The purpose of this study is to assess the difference between two methods of increasing fluid removal in patients with liver disease. The study will involve the use of furosemide (Lasix ®) and albumin. Furosemide is approved for use by the United States Food and Drug Administration (FDA) for edema (fluid retention) and cirrhotic ascites (fluid retention in the abdomen). Albumin is approved for use by the United States FDA but does not carry the indication for edema and cirrhotic ascites.

If you agree to participate in this study, your participation may last up to 7 days during your hospital stay. There will be no additional study visits once you have been discharged from the hospital.

There are risks to you for participating in this study. In this study, there is a risk of decreased kidney function and potentially experiencing side effects of the medications used in the study.

The most common side effects of furosemide include low blood pressure, dizziness and/or headache and irritation of the skin at the site of injection. The most common side effects of albumin are high blood pressure, headache, nausea/vomiting, and irritation of the skin at the site of injection. However, your physician will be monitoring you daily during the study and will take precautions to prevent these from happening. In addition, there is a risk of loss of confidentiality if your medical information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening.

There may be no benefit to you from taking part in this study, which is why we are doing this research to compare the different options available. Our hope is that it will possibly help you or benefit other people in the future. Because individuals respond differently to therapy, no one can know in advance if it will be helpful for you. If the therapy that is chosen for you is not believed to be helpful for you by your doctor, the doctor will start an alternative standard of care treatment.

You also have the option to not participate in this study. If you choose not to participate in this study, the physician will determine your treatment plan, which typically includes the drugs furosemide (Lasix ®) and albumin. You should discuss this with your study doctor.

Detailed Information: Please review the rest of this document for details about the above topics and additional information you should know before making a decision about whether or not you will participate in this study.

Why are you being invited to participate in this study?

You are being asked to participate in this study because you have liver disease that is causing an buildup of fluid. In order to treat this condition, your provider will give you medications to help you urinate and remove some of the fluid.

How many participants will take part in this study?

Approximately 150 participants at Rush University Medical Center are expected to take part in this study.

What are the activities you will be doing if you participate in this study?

If you agree to participate in this study, you must first sign this informed consent form. Afterwards, you will be able to take part in the study activities. The study activities will either begin the day you sign the consent form or the day after.

Before you begin the study:

- You will be randomized to 1 of 2 groups and you will have a 50% chance of being in each group. Randomization means that you will be assigned by chance (like flipping a coin) to see which group (heads/tails) you will be put into.
    - Group 1 will receive the standard of care with furosemide (Lasix ®) intravenously (into the vein) between 40 to 80 mg twice a day for at least 2 days.
    - Group 2 will receive the standard of care with furosemide (Lasix ®) intravenously between 40 to 80 mg twice a day with albumin 12.5 grams intravenously twice a day for at least 2 days.
- On the first day of your study participation, you will be administered the medications mentioned above based on your group assignment.

During the study:

- Once you have been randomized, your healthcare provider will monitor your daily response to the medications you received and obtain daily blood draws from your vein for labs. You will also be asked to urinate in a urine collection cylinder to measure how much urine you are making and your weight will be recorded daily by the nurse. The monitoring by your healthcare provider is standard of care.
- Depending on your response to the medications on day 3 of your study participation, your healthcare provider may change your treatment plan.
- If you are not improving on the medications and you have been randomized into Group 1, your healthcare provider may switch your medications to the alternative standard of care treatment that is assigned to Group 2.
- If you are not improving on the medications and you have been randomized into Group 2, your healthcare provider may switch your medications to the alternative standard of care treatment that is assigned to Group 1.

After you have completed treatment

- Your healthcare provider will continue to monitor your labs through daily blood draws from your vein. This is standard of care regardless of which treatment group you are randomized into.

What are the risks and discomforts of participating in this study?

Side effects, risks, and/or discomforts from participation in this study may include:

- The most common side effects of furosemide:
    - Low blood pressure
    - Dizziness
    - Headache
    - Irritation of the skin at the site of injection

- The most common side effects of albumin:
    - High blood pressure
    - Headache
    - Nausea/vomiting
    - Irritation of the skin at the site of injection

There may be other risks that may happen that we cannot predict. The study doctor or staff can discuss any questions you have about these medications.

Can you leave or be removed from this study?

You have the right to leave a study at any time without penalty. For your safety, however, you should consider the study doctor's advice about how to leave this study. If you choose to withdraw from the study, you will be able to withdraw the same day you make your decision and there will be no consequences associated with your decision. Your study doctor will adjust your treatment plan according to where you are in your treatment course when you exit the study.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interests;
- You do not follow the instructions of study staff;
- The study is cancelled for any reason.

What about confidentiality of your medical information?

This authorization is voluntary. Rush University Medical Center and its affiliates ("Rush") will not withhold or refuse your treatment, payment, enrollment, or eligibility for benefits if you sign this authorization. You do not have to sign this authorization, but that means that you cannot be in the study or receive study-related treatment.

By signing this document, you voluntarily authorize (give permission to) Dr. Nicole Alvey, PharmD and her study team, and other Rush personnel involved with the conduct and review of this study to use or disclose (release) health information that identifies you for the study described in this document.

During the study, Dr. Nicole Alvey, PharmD and her study team will collect Protected Health Information (PHI) about you for the purposes of this research. PHI is your health information that includes your medical history and new information obtained as a result of this study. Some of this information will come from your medical record. The health information that Rush may used or disclosed for this research includes:

- Weight
- Results of lab tests
- Urine output

Dr. Nicole Alvey, PharmD and her study team may share your health information and the results of your study-related procedures and tests with people outside of Rush who assist with the conduct and review of this study. The persons who receive your health information may not be

required by Federal privacy laws to protect it and may share your information with others without your permission, but only if permitted by the laws governing them. Your health information described above may be used or disclosed to:

- To the Researchers: Rush University Medical Center (RUMC) Transplant Surgery Attendings, RUMC Hepatology Attendings and Transplant Pharmacists
- Monitoring agencies such as the Food and Drug Administration (FDA), the National Institutes of Health and the Rush Institutional Review Board (IRB).

While you participate in the study you will have access to your medical record, but Dr. Nicole Alvey, PharmD is not required to release your study information that is not part of your medical record. Rush is required by law to protect your health information, and study records that identify you will be kept confidential. The results of study tests/procedures performed as part of this study may become part of your medical record. Any study information in your medical record will be kept indefinitely. Your identity will not be revealed on any report, publication, or at scientific meetings.

You have a right to inspect and copy the information to be disclosed with this authorization and you may obtain a copy of the information by contacting the office listed above.

If you no longer want to be in the study and do not want your future health information to be used, you may change your mind and revoke (take back) this authorization at any time by writing to Dr. Alvey at 1653 West Congress Parkway, Chicago, IL 60612.If the authorization is revoked, you will no longer be allowed to participate in the study and previously authorized individuals/entities may still use or disclose health information that they have already obtained about you as necessary to maintain the integrity or reliability of the current study.

This authorization is valid for the entirety of this research study. It will expire upon completion of the study or if you revoke (take back) the authorization.

If you withdraw from this study, the data already collected from you may not be removed from the study records. The study doctor and/or study team may ask you whether they can continue to collect follow-up data on you. If follow-up information will be requested, you will be asked to sign a separate consent form before this information can be collected.

Records of participation in this study will be maintained and kept confidential as required by law. All identifying information will be de-identified. Data collected from your medical record will be recorded in a secure, password protected database.

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews new and ongoing human research studies to check that the rules and regulations are followed regarding the protection of the rights and welfare of human participants.

What are the costs to participate in this study?

You or your insurance will be responsible for paying the cost of the hospital visit. Participation in this study puts you in one of two standard of care treatment groups which is included in your

hospital bill at discharge. If you have health insurance the insurance may or may not pay for the costs associated with your participation in this study. You will have to pay for any co-payments, deductibles or co-insurance amounts that your insurance coverage requires.

Will you be paid for your participation in this study?

You will not be paid for being in this study.

What if you are injured as a result of your participation in this study?

If you get ill or injured from being in the study, Rush University Medical Center will help you get medical treatment. You should let the study doctor know right away that you are ill or injured. If you believe you have become ill or injured from this study, you should contact, attending physician Dr. Chan, who is a transplant surgery attending assisting with enrollment in this study, at 312-942-4252.

You should let any health care provider who treats you know that you are in this study. If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact your study doctor.

You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. Costs not covered by insurance could be substantial.

Rush University Medical Center has no program for financial compensation or other forms of compensation for injuries which you may incur as a result of participation in this study.

By signing this form, you are not giving up any legal rights to seek compensation of injury.

What other information should you know about?
Investigator Dual-Role
Your health care provider is an investigator on this research study, and as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from a clinician who is not associated with this study. You are not obligated to participate in any research study offered by your clinician. The decision to not participate will not affect your clinical care now or in the future.

Who can you contact for more information about this study?
Questions are encouraged. If you have further questions about this study, you may e-mail Dr. Nicole Alvey, PharmD at her e-mail address: Nicole_Alvey@ rush.edu

Who can you contact if you have concerns about your rights as a study participant?
Questions about the rights of research participants may be addressed to the Rush University

Medical Center Office of Research Affairs at 1-800-876-0772.

What are your rights as a study participant?
Taking part in this study is voluntary. If you choose not to participate in this study or to leave the study at any time, your health care, benefits or relationship at Rush University Medical Center will not change or be affected.

If you choose to leave this study and you do not want any of your information to be used, you must inform Dr. Alvey in writing at the address on the first page. Dr. Alvey may still use your information that was collected prior to your written notice.

SIGNATURE BY THE PARTICIPANT:
By signing below, you are consenting to participate in this research study. You have read the information given or someone has read it to you. You have had the opportunity to ask questions, which have been answered satisfactorily to you by the study staff. You do not waive any of your legal rights by signing this consent form. You will be given a signed copy of this consent.

Name of Participant	Signature of Participant	Date of Signature

SIGNATURE BY THE INDIVIDUAL OBTAINING CONSENT:
I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge.

Signature of Individual Obtaining Consent	Date of Signature

SIGNATURE OF THE PRINCIPAL INVESTIGATOR:
I attest that I am aware of the enrollment of this subject in the study discussed in this consent document.

Signature of the Principal Investigator	Date of Signature