ICF Cover Page

Official Title: The Hemodynamic Effects of Sodium-Glucose Co-Transporter 2 Inhibitors in Acute Decompensated Heart Failure

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The UNIVERSITY OF CHICAGO
The Division of the Biological Sciences • The University of Chicago Medical Center

CONSENT/AUTHORIZATION FOR PARTICIPATION IN A RESEARCH PROTOCOL

Protocol Number: IRB22-0346

Name of Subject: _____

Medical History Number: _____

STUDY TITLE: The Hemodynamic Effects of Sodium-Glucose Co-Transporter 2 Inhibitors in Acute Decompensated Heart Failure

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KEY INFORMATION

We are asking you to choose whether or not to volunteer for a research study about a Sodium-Glucose Co-Transporter 2 Inhibitor (SGLT2i) drug called dapagliflozin in people who have been admitted to the intensive care unit (ICU) after a right heart catheterization procedure. The purpose of this section is to give you key information to help you decide whether to participate. We have included detailed information after this section. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is above.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

You are being asked to take part in this study because you have heart failure, you are scheduled for a right heart catheterization procedure as part of your routine care, and your doctor thinks you may need to be admitted to the ICU after the procedure. Heart failure occurs when the heart muscle does not pump blood as well as it should. A right heart catheterization procedure is a test done to see how well your heart is pumping. After a right heart catheterization procedure, some patients may need to be admitted to the ICU for more tests and treatment if the pressure in their heart or lungs is very high or if the heart is not pumping enough blood. During the ICU stay, doctors closely monitor the condition of their patients and may give them medications for their heart failure care and other related conditions. One example of a type of medication that may be given is a SGLT2i drug called dapagliflozin.

The SGLT2i used in this study, dapagliflozin, is approved by the Food and Drug Administration to reduce the risk of hospitalization and death in patients with certain types of heart failure. This includes

patients with your type of heart failure; however, more information is needed to better understand how patients admitted to the ICU might benefit from SGLT2i. By doing this study, we hope to learn more about the possible benefits.

If your treating physician does not admit you to the ICU after your right heart catheterization procedure, you will not be able to join this study.

In this study, we will compare patients in the ICU who are given a SGLT2i to patients who are not given SGLT2i. Normally, the decision to give a SGLT2i or not is up to the individual doctor. Both scenarios are considered within routine care for ICU patients. If you join this study, the decision will be made by a computer program. You will be randomly assigned (like the flip of a coin) to one of the two study groups:

1) SGLT2i
2) No SGLT2i

You will have an equal chance of being in either group. This assignment process is called randomization. We will tell you and your doctor which study group you get assigned to. If your doctor believes that your group assignment is not the best treatment option for your medical condition, their treatment decision will override your group assignment, and you will be changed to the group your doctor thinks you should be in.

If you are in the SGLT2i group, you will be given dapagliflozin during your ICU stay. For all subjects, after randomization, heart failure care and SGLT2i (if applicable) will be managed according to routine care. We will collect information from your medical records for this study. Your participation in this research will last about four days.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

Being in this study may not help you directly. We hope that your participation in the study will benefit other people in the future by helping us learn more about treatments for heart failure. For a complete description of benefits, refer to the Detailed Consent Section below.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You may choose not to participate in this study if you have concerns about the risks involved. The main risk of participation is loss of confidentiality. The research team will take care to protect your confidentiality throughout the study.

If you are assigned to the SGLT2i study group, the most serious side effects associated with dapagliflozin include the following. You may be at risk for the same side effects if you are prescribed dapagliflozin outside of the study.

- Ketoacidosis (increased ketones in your blood or urine)
    - Ketoacidosis has happened in people with diabetes. Ketoacidosis is a serious condition, which needs to be treated in a hospital. Ketoacidosis **may lead to death**.
- Necrotizing fasciitis of the perineum [a rare but serious bacterial infection that causes damage to the tissue under the skin (necrotizing fasciitis) in the area between and around the

anus and genitals (perineum)]

- Necrotizing fasciitis of the perineum may lead to hospitalization, may require multiple surgeries, and **may lead to death**.
- Signs and symptoms may include fever, feeling very weak, tired or uncomfortable (malaise), and you develop any of the following symptoms in the area between and around your anus and genitals: pain or tenderness, swelling, redness of skin (erythema).

For a complete description of risks, refer to the Detailed Consent Section below.

Instead of being in this study, you may choose not to participate. You do not need to participate in this study to receive treatment with a SGLT2i. Outside of the study, the decision whether or not you receive a SGLT2i or not would be up to your treating physician. For a complete description of alternate treatments, refer to the Detailed Consent Section below.

DO YOU HAVE TO TAKE PART IN THE STUDY?

Taking part in this study is voluntary. If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

You may choose not to participate at any time during the study. You will not lose any services, benefits, or rights you would normally have if you choose to leave the study. The University of Chicago/University of Chicago Medical Center will not condition (withhold or refuse) treating you on whether you sign this Authorization or revoke your authorization at a later time. If you do not sign this form, you will not receive the research-related intervention(s).

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS, OR CONCERNS?

The person in charge of the study is Dr. Grinstein of the University of Chicago. If you have questions, suggestions, or concerns regarding this study, or if you want to withdraw from the study, his contact information is: (773) 702-9396.

If you have a research-related injury, you should immediately contact Dr. Grinstein at (773) 702-9396. In case of emergency, call (773) 702-6800 and ask for pager # 4016.

For questions about your rights as a research subject, please contact the University of Chicago BSD IRB at 773-702-6505.

DETAILED CONSENT

WHAT IS INVOLVED IN THE STUDY?

About 40 people will take part in this study at the University of Chicago.

If you agree to participate in this research study, you will be asked to sign this consent form. If you sign the consent form, but your treating physician does not admit you to the ICU after your right heart catheterization procedure, you will not be able to join this study.

Randomization
Normally, the decision to give a SGLT2i or not is up to the individual doctor. Both scenarios are considered within routine care for ICU patients. If you join this study, the decision will be made by a computer program instead. If your treating physician decides to admit you to the ICU, you will be randomly assigned (like the flip of a coin) to one of the two study groups:

1) SGLT2i
2) No SGLT2i

You will have an equal chance of being in either group. We will tell you and your doctor which study group you get assigned to. If your doctor believes that your group assignment is not the best treatment option for your medical condition, their treatment decision will override your group assignment, and you will be changed to the group your doctor thinks you should be in. If this happens, we will still collect your medical data as described below.

SGLT2i Group
If you are in this group, you will be given dapagliflozin during your ICU stay. You will be given dapagliflozin once a day for up to 4 days or until you are transferred out of the ICU. After randomization, your SGLT2i and heart failure care will be managed according to routine care, and we will collect your medical data for this study as described below. After you finish taking dapagliflozin for this study, your doctor will discuss your ongoing treatment plan with you.

No SGLT2i Group
If you are in this group, you will <u>not</u> be given dapagliflozin. After randomization, your heart failure care will be managed according to routine care. We will collect your medical data for this study as described below.

Data Collection
We will collect the following information from your medical records about your right heart catheterization procedure and ICU stay:

- Information about your health status
- Information about your medications
- Right heart catheterization results
- Laboratory test results
- Hemodynamic measurements (measurements of the pressures in your heart and lungs)

Other Information
In the future, identifiers associated with your data could be removed from the data. The de-identified data could then be used for future research by our research team or other researchers without notifying you or asking your permission for this use.

The results from this study will not be shared with you.

Dr. Grinstein may decide to take you off of the study without your consent if:
- You are unable to meet the requirements of the study or your medical condition changes;
- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

During your participation in this study, you are at risk for the following. You should discuss these with the study doctor. There may also be other risks that we cannot predict.

Loss of Confidentiality
Any time information is collected about you there is a potential risk for loss of confidentiality. However, the researchers will make every effort to keep your information confidential. Please see the "What about Confidentiality?" section below for more information.

Risks of dapagliflozin (SGLT2i group only)
There are known side effects associated with taking the SGLT2i drug dapagliflozin. The following side effects are taken from the FDA Medication Guide. You may be at risk for the same side effects if you are prescribed dapagliflozin outside of the study.

The most common side effects of include:
- Vaginal yeast infections and yeast infections of the penis
- Stuffy or runny nose and sore throat
- Changes in urination, including urgent need to urinate more often, in larger amounts, or at night

Serious side effects include:
- Dehydration (a dangerous loss of body fluid)
    - Dehydration may cause you to feel dizzy, faint, light-headed, or weak, especially when you stand up (orthostatic hypotension).
    - There have been reports of sudden kidney injury in people with Type 2 diabetes who are taking this medication.
- Vaginal yeast infection
    - Symptoms include vaginal odor, white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese), vaginal itching.
- Yeast infection of the penis (balanitis)
    - Certain men who are not circumcised may have swelling of the penis that makes it difficult to pull back the skin around the tip of the penis. Other symptoms of yeast infection of the penis include redness, itching, or swelling of the penis; rash of the penis; foul smelling discharge from the penis; pain in the skin around the penis.

- Ketoacidosis (increased ketones in your blood or urine)
  - Ketoacidosis has happened in people with diabetes. Ketoacidosis is a serious condition, which needs to be treated in a hospital. Ketoacidosis **may lead to death**.
  - Symptoms may include nausea, tiredness, vomiting, trouble breathing. stomach area (abdominal) pain.
- Serious urinary tract infections
  - Signs or symptoms of a urinary tract infection include a burning feeling when passing urine, a need to urinate often, the need to urinate right away, pain in the lower part of your stomach (pelvis), or blood in the urine. Sometimes people also may have a fever, back pain, nausea or vomiting.
  - Serious urinary tract infections that may lead to hospitalization have happened in people who are taking this medication.
- Low blood sugar (hypoglycemia)
  - If you take this medication with another medicine that can cause low blood sugar, your risk of getting low blood sugar is higher.
  - Signs and symptoms may include headache, irritability, confusion, dizziness, drowsiness, hunger, shaking or feeling jittery, sweating, weakness, and fast heartbeat.
- Necrotizing fasciitis of the perineum [a rare but serious bacterial infection that causes damage to the tissue under the skin (necrotizing fasciitis) in the area between and around the anus and genitals (perineum)]
  - Necrotizing fasciitis of the perineum may lead to hospitalization, may require multiple surgeries, and **may lead to death**.
  - Signs and symptoms may include fever, feeling very weak, tired or uncomfortable (malaise), and you develop any of the following symptoms in the area between and around your anus and genitals: pain or tenderness, swelling, redness of skin (erythema).

Unknown Risks

There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could influence your willingness to continue, this new information will be discussed with you.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

Being in this study may not help you directly. We hope that your participation in the study will benefit other people in the future by helping us learn more about treatments for heart failure.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you may choose not to participate. You do not need to participate in this study to receive treatment with a SGLT2i. Outside of the study, the decision whether or not you receive a SGLT2i or not would be up to your treating physician.

WHAT ARE THE COSTS?

There will be no costs to you or your insurance company resulting from your participation in this research study. However, you or your insurance company will be responsible for costs related to your

usual medical care, such as your overnight hospital stays, because these are happening as part of your routine care. If you are in the SGLT2i group, you or your insurance company will also be responsible for costs related to your SGLT2i treatment and treatment for the known side effects you may experience, because these are happening as part of your routine care.

WHAT HAPPENS IF I HAVE AN INJURY?

If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, the University of Chicago Medical Center will provide such treatment at the University of Chicago Medical Center at no cost to you. You must notify Dr. Grinstein as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure, and is not the result of your disease or condition. The costs of any non-emergency care for such an injury will be billed to you or your insurance in the ordinary manner. If you think that you have suffered a research related injury, you must let Dr. Grinstein know right away.

WILL I BE PAID FOR MY PARTICIPATION?

You will not be paid to participate in this study.

WHAT ABOUT CONFIDENTIALITY?

There is a risk of potential loss of confidentiality. To minimize this risk, study records that identify you will be kept confidential. Data will be stored in a locked drawer in a locked office and/or entered on a password-protected, HIPAA-compliant computer. Only the research team will have access to the data.

During this study, Dr. Grinstein and his research team will collect protected health information (PHI) about you for the purposes of this research. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago. Protected Health Information (PHI) consists of any health information that is collected about you, which could include your medical history and new information collected as a result of this study. Most of this information will come from your medical record. The information to be used on this study includes your name, medical record number, and dates (including date of birth and dates related to your heart failure care). This information will be used to collect data for the study, and some of it will be collected as data for study analysis.

Your records may be reviewed by federal agencies whose responsibility is to protect human subjects in research including the Office of Human Research Protections (OHRP). Representatives of the University of Chicago, including the Institutional Review Board (a committee that oversees the research) and the Office of Clinical Research may also view the records of the research. If your research record is reviewed by any of these groups, they may also need to review your entire medical record.

Once information is shared outside the University of Chicago, please note that your identifiable health information may be shared with someone else. The same laws that the University of Chicago must obey may not protect your health information.

During your participation in this study, you will have access to your medical record. Dr. Grinstein is not required to release to you research information that is not part of your medical record.

This consent form will be kept by the research team for at least six years. The study results will be kept in your research record and be used by the research team until completion of this study. At the time of study completion, either the research information not already in your medical record will be destroyed or information identifying you will be removed from study results.

Data from this study may be used in medical publications or presentations. Your name and any other identifying information will be removed before this data is used. If we wish to use identifying information in publications, we will ask for your approval at that time. We may also share de-identified data with collaborators or others for research purposes.

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.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

If you choose to no longer be in the study and you do not want any of your future health information to be used, you must inform Dr. Grinstein in writing at the address on the first page. Dr. Grinstein may still use your information that was collected prior to your written notice.

We will tell you about significant new information that may affect your willingness to stay in this study.

You will be given a signed copy of this document. Your authorization to use and disclose your health information does not have an expiration date.

CONSENT

SUBJECT

The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____

Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT

I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of Person Obtaining Consent: _____

Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:

Signature of Investigator/Physician: _____

Date: _____ Time: _____ AM/PM (Circle)