CONSENT TO PARTICIPATE IN A RESEARCH STUDY

University of Mississippi Medical Center

STUDY TITLE: Empagliflozin in ESRD – A Feasibility Study

PRINCIPAL INVESTIGATOR: Yoshitsugu Obi, MD, PhD

Key information

We are doing this study to learn more about how the drug empagliflozin works in people with end-stage kidney disease. If you are in the study, you will be given empagliflozin for four months and have regular study visits. Empagliflozin is FDA approved for the treatment of diabetes and heart failure but is not approved if patients have end-stage kidney disease. At the study visits, you will have lab tests, physical examinations, a heart echocardiogram, and answer questions related to health and wellness. The side effects of empagliflozin include bladder pain, needing to go to the bathroom more often, difficult, burning or painful urination, blood colored or cloudy urine. Women may have vaginal itching stinging or redness, change in the color, amount or odor of vaginal discharge, and pain when having sex. Taking Empagliflozin may protect your heart health. If you have questions, call Dr. Yoshitsugu Obi, MD, PhD at 601-984-5670.

Introduction

You are being asked to join in a research study because you are on dialysis. Please ask us about anything in this document or that you do not understand. It is your choice to participate in this study, and you can change your mind later.

Purpose

We are doing this study to learn about empagliflozin and its possible kidney and heart benefits in patients on dialysis.

If you agree to participate in this study and are on peritoneal dialysis (dialysis using the abdominal lining), you will take empagliflozin 10 mg each morning between 8:30 and 9:30 AM for three months. If you are on hemodialysis (cleaning your blood with a machine) on Mondays, Wednesdays, and Fridays, you will take empagliflozin 25 mg when you complete dialysis, which will be three times a week. If you are on hemodialysis on Tuesdays, Thursdays, and Saturdays, you will take empagliflozin 10 mg each morning between 8:30 and 9:30 AM.

During the Run-in-visit period, you will have blood drawn for lab work, provide a 12-hour urine sample if you still make urine, and wear a continuous glucose monitor for up to 14 days. You may have an echocardiogram. You may perform and record your blood pressure in the morning and at night for 48 hours using a study BP machine that will measure your blood

pressure once a minute for three minutes. The run-in period lab tests will take about 1 ½ teaspoons to 1 tablespoon of blood that will be used to evaluate how your liver and heart are functioning. Women of childbearing are will have a test that takes about 1 teaspoon of blood to see if you are pregnant.

During the baseline (Month 0) and three monthly study visits you will answer questions about your quality of life the by completing the KDQOL-36 Kidney Disease and Quality of Life questionnaire. You will have lab tests to find out how your liver is functioning. Women of childbearing age will have blood tests to see if you are pregnant at Month 1 and Month 3. At the monthly visits lab tests will take 1½ teaspoons to 1 tablespoon of blood, and at the Run-in, Month 1, 3, and 4 visits you will provide a 12-hour urine sample if you still make urine. At the Run-in and Month 3 visits you may have an echocardiogram. You will wear a continuous glucose monitor for up to 14 days; provide a 12-hour urine sample, after the baseline, Month 1, and Month 3 visits. You may perform and record your blood pressure in the morning and at night for 48 hours using a study BP machine that will measure your blood pressure once a minute for three minutes after the baseline and Month 3 visits. You will have tests to determine how your body is processing the empagliflozin at Months 1, 2, and 3.

Participants on PD will provide blood samples to help us learn about how empagliflozin moves through and is used by the body. You will have an IV tube put in your arm or hand that will be used to draw less than ½ teaspoon of blood just before you take the first dose of empagliflozin and then every half hour for 2 hours, followed by every hour for 2 hours, and then every 4 hours for 12 hours.

Study Activities

Study visit	Run-in	Month 0	Month 1	Month 2	Month 3
Blood AST/ALT, total bilirubin, beta hydroxybutyrate, Blood Empagliflozin level Blood Cystatin C, beta-2 macroglobulin	1 ½ teaspoons	1 ½ teaspoons	1 Tablespoon	1 ½ teaspoons	1 Tablespoon
Blood pregnancy test (if female aged <50 years)	1 ½ teaspoons		1 ½ teaspoons		1 ½ teaspoons
Empagliflozin Peritoneal Dialysis fluid level					X
urinalysis, urine culture if symptomatic		X	X	X	X
Timed urine collection (volume, urea, creatinine)	X		X		X
Transthoracic echocardiogram	X				X
KDQOL-36	X				X
Home BP monitoring	X	X			X
Continuous glucose monitoring	X	X		X	

*You will get the device and instructions for using it at the Month 2 visit, and the data will be collected at the Month 3 visit when the device is returned.
**Dr. Obi will determine whether you have an echocardiogram.

Length of Participation

Your participation will last up to four (4) months with a total of 5 visits.

Number of Participants

We expect 24 participants to enroll in this study here.

Risks & Discomforts

Empagliflozin

Common Side Effects

- Urinating more often
- Difficult, painful or burning while urinating
- Cloudy or blood-tinged urine
- For Women
- Vaginal itching stinging or redness,
- Change in the color of vaginal discharge
- Change in the amount or odor of vaginal discharge
- Pain when having sex

Less common Side Effects

- Skin rash
- Itchiness
- Warm red skin (flushing)
- Pain in the sides of the back
- Fever or chills
- Nausea
- Vomiting
- Joint pain

Less Common but Serious Side Effects

- High blood sugar
- Extreme thirst
- Frequent urination
- Belly pain
- Fruity-smelling breath
- Rapid breathing
- Coma

- Low blood pressure
- Lightheadedness
- Feeling dizzy or falling when you stand up
- Sweaty skin
- Fainting
- Swelling of face, eyelids, tongue, mouth lips, throat, hands or feet
- Trouble breathing
- Depression
- Decreased urination swelling in legs and ankle
- Confusion
- Tiredness
- Pain redness or swelling near the genitals or rectum
- Fever or chills
- Overall feeling of discomfort

Blood samples may cause

- temporary discomfort
- Pain
- Dizziness
- Bruising
- Swelling
- In rare circumstances, infection, at the catheter site.

Echocardiogram may cause

- Temporary discomfort from cool gel
- Temporary discomfort from the pressure of the probe rolling over your abdomen

We do not know how your body might respond to the empagliflozin used in this study. If you experience discomfort during the echocardiogram, let the person performing the procedure know so that appropriate steps may be taken. We will discuss the risks identified above with you and the chances that they will happen. There may be risks that we do not know about at this time. Unknown problems ranging from a mild inconvenience to some severe enough to result in death may occur. If you experience any problems, you should report them immediately to the study doctor, Yoshitsugu Obi MD, Ph.D. at 601-984-5670.

Females of Reproductive Potential and or Lactating Women

The risks of empagliflozin to an unborn child are unknown. You may not be pregnant or trying to become pregnant or breastfeeding while taking part in this research study. Blood pregnancy tests will be done on all women of childbearing potential before beginning the study, Month 1 and Month 3. All women of childbearing potential must use an acceptable method of birth control, such as an implant, intra-uterine device, birth control shot, vaginal ring, or birth control patch/pill, while being treated on this study.

Benefits
You may or may not receive a direct benefit from being in this research study. Empagliflozin may lower your risk of having heart failure or help your body continue to use your own kidneys.

We hope to learn information that may help others in the future.

Alternatives
You do not have to participate in this study. The health care provided at UMMC will not be affected if you do or do not participate in the study. The alternative to participating is not to participate.

The study treatment is experimental. This means that you can only receive it by enrolling in this study. If you choose not to participate in this study, you will receive your usual medical care.

Costs
There will not be additional costs to you if you participate in this study. These costs do not include any costs related to treatment for research-related injury.

The empagliflozin will be supplied by us at no cost to you. Any tests, examinations, or other procedures that are done solely for research purposes, including: blood and urine collections, and echocardiograms as previously described will be paid for by this study. Insurance companies and other third-party payers will not be billed for research procedures. Research related injuries information is available in the Research-Related Injury section.

The rest of the medical care that you will receive in this study is considered standard care for your condition and would be recommended whether or not you participate in this study. These costs will be billed to you or your insurance carrier.

Compensation
A $75 check will be mailed to you for each study visit you complete. If you are on peritoneal dialysis a $200 check will be mailed to you for participating in the additional blood draws as previously described.

Research- Related Injury
In the case of injury or illness resulting from your participation in this study, medical treatment is available to you at the University of Mississippi Medical Center. You will be charged the usual and customary charges for any such treatment you receive.

The sponsor of this research is the Mississippi Center for Clinical and Translational Research. If you develop, an illness or an injury happens because you are in this research study the sponsor will not pay for any medical care. There are no plans to pay you for any lost wages or

other expenses unrelated to the cost of medical treatment resulting from research-related injury.

New Information
You will be told of any information we learn during your participation in this study that may affect your willingness to participate.

Voluntary Participation
Your participation is voluntary. If you decide not to participate in this study, you will not suffer a penalty or loss of benefits to which you are otherwise entitled.

Withdrawal
You may choose to stop your participation in this study at any time. If you decide to withdraw from the study, the information already collected about you may still be used in this study but additional information will not be collected. Your decision to stop your participation will have no effect on the quality of medical care you receive at the University of Mississippi Medical Center.
The study doctor can also remove you from this study without your approval. Possible reasons for removal include:

- It is best for you
- The research is canceled
- You are not able to keep your scheduled appointments or procedures.

Confidentiality
Every effort will be made to keep the information we learn about you private; however, complete, total confidentiality cannot possibly be guaranteed. Study personnel, the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), and the University of Mississippi Medical Center's Office of Research and Sponsored Programs, Office of Clinical Trials, Institutional Review Board (IRB), and Office of Integrity and Compliance may review the study records. If study results are published your name will not be used.

A copy of this informed consent document will be filed in your medical record because the experimental research you are agreeing to participate in involves your care, diagnosis, or treatment.

Protected Health Information
Protected health information is any personal health information through which you can be identified. The information collected in this study includes: age; sex; race; insurance status; the history and diagnosis of your disease; current and previous treatment; laboratory and radiology test results; follow-up information about your general health; the status of your disease and late effects from treatment; and other general information from your medical records including follow- up information about your general health. A decision to participate in this research means that you agree to using your health information for the study described in this form.

This information will not be released beyond the purposes of conducting this study. The information collected for this study will be kept for six years or the time period required by the FDA if that is longer. While this study is ongoing, you may not have access to the research information, but you may request it after the research is completed.

Dr. Obi and The Mississippi Center for Clinical and Translational Research will use your information to determine the effectiveness of treatment in this study. Your medical information and records, once disclosed, may be re-disclosed by any of the recipients identified above and may no longer be protected by the Privacy Standards of the Health Insurance Portability and Accountability Act (HIPAA), which is a federal regulation designed to protect medical information, including medical information and records created through research.

You have the right to cancel this authorization at any time by providing the study doctor, Yoshitsugu Obi, MD, Ph.D. with a written request to cancel the authorization. If you cancel this authorization, medical information and records about you that were created before the authorization was cancelled will be used and de-identified.

Questions

If you have questions about this study or need to report any problems, side effects, or injuries, please call the research team at 601-984-5670. After hours and on weekends, please call 601 984-5670 and ask an operator to connect you to a nephrology fellow on call.

You may discuss your rights as a research participant with the Chairman of the University of Mississippi Medical Center's Institutional Review Board, 2500 North State Street, Jackson, Mississippi 39216; telephone 601 984-2815; facsimile, 601 984-2961. The Institutional Review Board is a group of people not involved with this study who have reviewed the study to protect your rights.

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.

Upon request, we will give you a copy of this consent document to review before you sign. If you choose to participate in this study, you will receive a signed copy of this document.

Statement of Participation

I have been told about this study, including the experimental treatment I may receive and possible risks and benefits. I agree to participate in this study, to follow instructions, and to report any side effects to my study doctor. My participation is voluntary, and I may withdraw at any time without any penalty or loss of benefits to which I am entitled, including medical care at the University of Mississippi Medical Center.

By signing this form, I am not giving up any legal rights I may have.

_____
Participant's Printed Name

_____ _____
Participant's Signature Date

_____
Printed Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date

I acknowledge that the participant identified above has been entered into this study, with properly obtained informed consent.

_____ _____
Signature of Investigator Date