INFORMED CONSENT FORM

Part 1：STUDY INFORMATION

Title of study: Dapagliflozin Delays the Loss of Residual Renal Function in Patients Undergoing Peritoneal Dialysis: A Single-Center Randomized Open-Label Study

Dear Sir/Madam,

You are invited to take part in this study because you have chronic kidney disease and underwent peritoneal dialysis. Participation requires your written consent. Before you decide whether you want to participate in this study, you will be given an explanation about what the study involves.

The overall description of this study (including the collection, storage and use of your data and biosamples as well as this document) has been reviewed by an independent Ethics Committee to ensure that the rights, safety and well-being of study patients are protected.

Your condition may or may not improve if you join the study, but the information we get from this study might help other patients with the same condition in the future.

Why is this study about?

We are doing this study to learn more about a new treatment (Dapagliflozin) in peritoneal dialysis patients and also to better understand the studied disease and associated health problems.

Residual renal function represents the functional capacity of remaining nephron units in dialysis patients, helping to clear fluids and metabolic wastes to maintain the internal environment of the body as stable as possible. Numerous studies have demonstrated that preserving residual renal function in peritoneal dialysis patients can reduce complications, improve dialysis adequacy, and lower mortality rates. Methods to protect residual renal function include controlling blood pressure, managing blood sugar, adjusting dialysis prescriptions, and using renin-angiotensin system antagonists. However, the effectiveness of these methods is limited. Dapagliflozin, a medication for treating type 2 diabetes, has been proven in various studies to protect residual renal function in non-dialysis chronic kidney disease patients. Additionally, this class of drugs has been shown to improve heart function. Pharmacological studies suggest that this drug is well-tolerated in peritoneal dialysis patients, with safety profiles similar to those in non-dialysis patients.

About 70 people will take part in this study. Half of the participants will receive Dapagliflozin (Dapagliflozin group) and half will not use any medication other than the basic treatment (control group). The total duration is 24 weeks.

To make the comparison between Dapagliflozin group and control group as fair as possible, the study is a randomize open-label study. This means that neither you nor the

study doctor will know if you receive Dapagliflozin or not before the randomize. After randomization, you and your study doctor will know that you are receiving Dapagliflozin.

All study participants will also receive peritoneal dialysis and basic medication treatment (chronic kidney disease complication treatment drugs, RAAS inhibitor and antidiabetic drugs for diabetic patients). Your doctor will check if you can continue with your current medications or if you need to change any of your current treatments.

Do I have to take part?

You have a choice whether or not you would like to participate.

Please take as much time as you need to make a decision about whether or not you would like to participate in this study. It may be helpful to talk with your friends and family as you make this decision.

If you join the study, you can leave at any time. Leaving will not affect your care. If you choose to leave the study, please let your study doctor know as soon as possible. Please consider the study time commitments and responsibilities as a research patient when you are deciding to take part.

If you don't join the study, you will continue to receive care from peritoneal dialysis center. Your study doctor or treating physician will talk to you about other possible treatments, their risks and benefits.

What will happen if I join the study?

You will be in the study for 30 weeks. The study includes a Screening Period, a Treatment Period, and a Follow-up Period:

- Screening Period: will last for up to one week and includes 1 study visit (or more visits if needed) to check if the study is right for you.

- Screening Period: will last for up to one week and includes 1 study visit (or more visits if needed) to check if the study is right for you.
- Treatment Period of up to 24 weeks: You will receive your randomly assigned study drug (Dapagliflozin or Not) every month. This part of the treatment period is "open-label", which means that both you and your study doctor know that you are receiving Dapagliflozin.
- Follow-up Period: will last up to 4 weeks and includes 1 additional visit after you have stopped taking Dapagliflozin (for Dapagliflozin group) or completed the study observation (for control group).

Before you can start the study, you will undergo a series of tests. This is called screening. If you meet the screening criteria you will be randomly assigned a study treatment. “Randomly assigned” means that what treatment you get will be by chance, like flipping a coin. You have a 1 in 2 chance of being given Dapagliflozin during the the study. If the study is not right for you the reasons will be explained. Your study doctor or treating physician will talk to you about other possible treatments.

You will take basic medication treatment (chronic kidney disease complication treatment drugs, RAAS inhibitor for hypertension patients, and antidiabetic drugs for diabetic patients) throughout the study. You must follow these instructions and not take any other drugs without discussing with your study doctor first.

You will have around approximately 5 visits that will last up to 1 hours.

If you participate in this study, you are required to come to the peritoneal dialysis center for study visits. If you cannot come to a visit, you must tell your study doctor. During these visits, tests and procedures will be performed (see Part III for more details) and study treatment will be given. All patients will be monitored closely, and side effects will be reviewed.

You will only be given Dapagliflozin or not while the study is going on but not after it has ended. The study drug will be given via oral once a day by yourself.

Please note that the study, and your participation in the study, may be stopped earlier than expected, for example for scientific or safety reasons.

What are the required tests and procedures?

To conduct the study, some tests and procedures will have to be performed on you. The following tests and procedures will be included:

- Physical examination, including blood pressure, pulse rate, height and weight.
- 24-hour Urine samples: You will be given instructions on how to collect your urine and it is very important that you follow these instructions. All urine your body produces in a 24-hour period will be collected in a single container. The urine output will be measured continuously for 2 days, and the average volume will be calculated, with the unit being milliliters. The sample will be measured the concentrations of sodium, glucose, urea, Dapagliflozin 3-O-glycosyl glucuronide.
- Blood collection:
  - to ensure that your organs are functioning properly.
  - to measure concentrations of brain natriuretic peptide.
  - to measure the blood levels of glycosylated Hemoglobin.
  - to measure concentrations of sodium.

- to measure concentrations of sodium.
- to measure concentrations of glucose.
- to measure the blood levels of Dapagliflozin 3-O-glycosyl glucuronide.

- Dialysate samples:
  - 24-hour dialysate to calculate the clearance of urea.
  - 2-hour dialysate to calculate the peritoneal equilibration test.
- Echocardiogram to assess the cardiac systolic function at baseline and the ending of research.

A total of approximately 11 mL (approximately 1 tablespoons) of blood will be required for all screening tests. No more than approximately 8 mL (approximately 1 tablespoons) of blood will be drawn on any visit day after screening. The total volume to be collected during the study will be approximately 38 mL (approximately 4 tablespoons)

The complete list of tests and procedures, including their detailed schedule is available in “Part III: Additional Information for Patients.”

What are the risks of joining the study?

There is a risk that your disease will not get better, or even get worse during the study.

It is possible that some patients could have side effects that we do not know about yet.

If you have severe side effects from the study drug, the study doctor may ask you not to continue in the study.

As of October 2023, 20 peritoneal dialysis patients have received the study drug for a month in a clinical study.

It is possible for some patients to have side effects that are not yet known.

The following are side effects known to be related to treatment with Dapagliflozin:

- *Hypoglycemia:* Although previous studies have shown that Dapagliflozin does not cause hypoglycemia in non-diabetic patients, regular follow-up to monitor blood sugar is recommended. Diabetic patients who join the study group need to monitor their blood sugar and adjust the dosage of other antidiabetic drugs accordingly. It's also recommended to carry sugar-containing food to correct hypoglycemia.

- *Infections:* Urinary tract infections and genital infections may occur, with daily external genitalia cleaning recommended as a preventive measure.

- *Ketoacidosis* This is a very rare complication, characterized by symptoms such as excessive thirst, delayed gastric emptying, nausea, and vomiting. Ensuring daily carbohydrate intake is a preventive measure.

- Risks associated with venepuncture include pain and/or bruising; fainting, infection at the puncture site, and self-healing are rare.

We will observe any side effects/adverse reactions that may be caused by the treatment with Dapagliflozin through regular check-ups and follow-ups, and take preventive measures to manage them. If you experience any discomfort or adverse reactions, please contact the research doctor immediately. Additionally, there is always a possibility that the treatment may not be effective, and your condition may continue to progress due to ineffective treatment or other concurrent diseases.

What are the possible benefits of taking part?

There is no certainty that you will have any benefit from the study drug. However, it is expected that the study treatment will help you.

The information the study Sponsor receives from this study may help to better treat patients with peritoneal dialysis.

It is not certain that you will directly benefit from the participation in the study. Your participation may, however, help other patients in the future by improving the knowledge of diseases and improving medical care.

What happens if something changes while I am in the study?

Changes may happen in the study that could make you change your mind about continuing to take part. If something changes, we will tell you as soon as possible.
You can choose to leave the study at any time. The study doctor can also choose to take you out of the study if they believe that it is best for you. Your participation in the study also stops when the Sponsor, health authorities, the ethics or regulatory agencies decide that the study must be stopped.

What happens if I am harmed or injured during the study?

If there is an emergency, call 120 right away or go to the emergency room and contact your study doctor as soon as you can. If you become ill or are injured while you are in this research study, you must tell your study doctor straight away. If trial-related harm occurs, treatment and compensation will be provided in accordance with national medical insurance.

What will happen to my data and biosamples gathered in the study?

In order to conduct the study, the Study site will have to collect and register information such as your name, address, telephone number, medical conditions, and medical history. This information will be used to confirm your identity and to assess your health conditions. Some of this information will be obtained from your physicians/available in your medical records and might include details of your life style, your demographics (age, gender, and ethnic), your images (eg, X-rays and scans), and data generated from the images. Your medical records will be kept at the hospital, and researchers, research supervisory departments. The ethics committees will be allowed to access your medical records. Any public report about the results of this study will not disclose your personal identity.

In addition, the study site will collect biosamples from you (such as blood, urine, and dialysate). All samples will be disposed of harmlessly after use, and reports for all tests except for Dapagliflozin 3-O-glycosyl glucuronide will be provided for review. These will be analyzed, and the data derived from the analysis will be part of your coded data.

What other options are available if you choose not to participate in this study?

If you decide not to participate in this study, or if you choose to withdraw from the study at any point, there are other options available. These include use angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, dialysis prescription adjustments.

Should you have any questions regarding your personal rights, you can contact the ethics committee of our institution at the following phone number: 028-87393449.

Part II: CONSENT FORM

Participant Statement:
I confirm that:

- The study doctor has explained the study to me comprehensively.
- I have had the opportunity to discuss the study with the study doctor and all my questions were answered.
- I have had an adequate amount of time to consider the study.
- I have read and understood all the above information related to the study.
- I understand that I will receive a copy of this document once I have signed it.
- I understand that my decision to take part in the study is entirely voluntary. If I decide not to participate in the study or to stop my participation during the study, this will not affect my standard medical care.
- I have truthfully answered all questions about my medical history and will follow all rules listed in the document.

I consent to take part in the clinical study and study procedures described herein.
I understand that my participation also entails:

- My name and contact details being collected during the study as described to me, and accessed and reviewed by listed authorized people;
- My coded data being used by the Sponsor or by people or companies acting on its behalf or working with the Sponsor;
- My coded data being used by persons or organizations located in countries that do not have data protection rules equivalent to those of my country. I understand that the Sponsor monitors these uses and takes all possible measures to protect my privacy;

I further understand that I can make a choice about the topics listed below and that by ticking "Yes" I do give consent and that by ticking "No" I do not give consent:

I agree to use my personal data in order to contact me either during or after the Study, to ask about my opinion on the provided Clinical Trial Transparency materials.	Yes	No
The study doctor may notify your physician of your participation in the study and may share relevant medical information with him/her if necessary, for managing your health and safety throughout. If you agree, please indicate name and contact details of your physician here:		

	STUDY PARTICIPANT
FULL NAME	
DATE (dd-Mmm-Year)	
SIGNATURE	

	Signature of person conducting the informed consent discussion
FULL NAME	
DATE (dd-Mmm-Year)	
SIGNATURE	

	Legally accepted representative
FULL NAME	
DATE (dd-Mmm-Year)	
SIGNATURE	
Relationship to participant	

Part III: ADITTIONAL INFORMATION FOR PATIENTS

1 Contact details

Study Doctor	
Phone No.	
Address	
Email	
Ethics Committee:	
Phone No.	
Address	
Email Address	

2 Detailed list of visits and Test/Procedures

Table 1 Screening Period

Study Period	Screening (Day -30 to Day -1)
Read and sign the informed consent	X
Information about your medical history will be obtained	X
You will be asked about previous and current medications that you are taking	X
Physical examination including weight and height	X
Questionnaires	X
Vital signs	X
Echocardiogram	X
Blood and urine tests	X
Pregnancy test (if applicable)	X
You will be asked about any problems that you may be experiencing	X

Table 2 Treatment Period

Study Visit	V1	V2	V3	V4
Visit windows (day)	±7	±7	±7	±7
Study week	2	12	24	28
You will be asked about current medications that you are taking	X	X	X	X
Physical examination including weight, blood pressure	X	X	X	X
You will be asked about any problems or side effects that you may be experiencing	X	X	X	X
24-hour urine collection starting 2 days before visit	X	X	X	X
Blood and urine tests	X	X	X	X
Kt/V_{urea}	X	X	X	X
Peritoneal equilibration test	X	X	X	X
Echocardiogram	X			X
Study drug administration	X	X	X	X
Pregnancy test (if applicable)	X	X	X	X

Table 3 Follow-up Period

Study Period	**4 weeks post last treatment visit ± 7d**
Physical examination including weight	
Vital signs	
Blood and urine tests	
Urine pregnancy test (if applicable)	
You will be asked about any problems or side effects that you may be experiencing	
You will be asked about current medications that you are taking	