

# The effectiveness of dapagliflozin versus furosemide in controlling blood pressure in resistant hypertension with subclinical fluid retention in chronic kidney disease

<b>Submission date</b> 28/12/2023	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 12/01/2024	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 06/11/2024	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Chronic kidney disease (CKD) poses a significant health challenge, often accompanied by uncontrolled blood pressure (hypertension) that is difficult to manage. This study aims to address this issue by comparing the effectiveness of two medications, dapagliflozin and furosemide, in individuals with CKD and resistant hypertension. Dapagliflozin is known for its ability to lower blood pressure and promote urine excretion by affecting kidney function. Furosemide, a commonly used diuretic, is also prescribed to manage fluid retention and blood pressure.

### Who can participate?

Patients aged 18 years and over with chronic kidney disease before undergoing kidney replacement therapy, who also have a condition of resistant hypertension.

### What does the study involve?

Participants undergo interviews, echocardiograms and bioimpedance spectroscopy (BIS), and receive dietary advice to limit their salt intake to less than 2 g per day. They are randomly allocated to two groups to be treated with either dapagliflozin or furosemide. Blood samples and data are collected over a 6-month period. Body fluid status is measured using BIS monthly during the first 3 months and at 6 months. Echocardiogram and laboratory tests are carried out at 6 months.

### What are the possible benefits and risks of participating?

The anticipated benefits include potential reductions in blood pressure, slowing the progression of kidney impairment, and lowering the risk of heart disease. However, some participants may experience hypovolemia (low body fluid volume) if the treatment is not followed according to guidelines or if there is an occurrence of drug allergies.

Where is the study run from?  
Bhumibol Adulyadej Hospital (Thailand)

When is the study starting and how long is it expected to run for?  
September 2023 to August 2024

Who is funding the study?  
Bhumibol Adulyadej Hospital (Thailand)

Who is the main contact?  
Natchaya Songsilp, muk.natchaya@gmail.com

## Contact information

**Type(s)**  
Public, Scientific, Principal Investigator

**Contact name**  
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## Additional identifiers

**EudraCT/CTIS number**  
Nil known

**IRAS number**

**ClinicalTrials.gov number**  
Nil known

**Secondary identifying numbers**  
IRB8866

## Study information

**Scientific Title**  
Efficacy of dapagliflozin compared to furosemide for controlling blood pressure in resistant hypertension with subclinical fluid retention in chronic kidney disease

## Study objectives

Current study hypothesis as of 29/10/2024:

There is currently no comparative study of SGLT2i and furosemide use in patients with chronic kidney disease (CKD) and resistant hypertension, so a comparison of both medications for reducing high blood pressure was conducted.

Previous study hypothesis as of 12/04/2024:

There is currently no comparative study of SGLT2i and furosemide use in patients with chronic kidney disease (CKD) and uncontrolled hypertension, so a comparison of both medications for reducing high blood pressure was conducted.

Previous study hypothesis:

There is currently no comparative study of SGLT2i and furosemide use in patients with chronic kidney disease (CKD) and resistant hypertension, so a comparison of both medications for reducing high blood pressure was conducted.

## Ethics approval required

Ethics approval required

## Ethics approval(s)

Approved 19/10/2023, The Institutional Review Board of Bhumibol Adulyadej Hospital, Directorate of Medical Service, Royal Thai Air Force (171 Phaholyothin road, Khlong Thanon, Salmai, Bangkok, 10220, Thailand; +66 25347255; bhumibolhospital@rtaf.mi.th), ref: 8866

## Study design

Single-center non-inferior prospective randomized open-label study

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please use the contact details to request a patient information sheet

## Health condition(s) or problem(s) studied

Resistant hypertension with subclinical fluid retention in chronic kidney disease

## Interventions

1. Select participants for the research based on inclusion and exclusion criteria.
2. Inform patients about the study and obtain their informed consent to participate.
3. Gather baseline data through interviews, echocardiogram, bioimpedance spectroscopy (BIS), and provide dietary advice to limit salt intake to less than 2 g per day.

4. Randomly assign patients into two groups by block of four randomization.
5. Conduct the experiment by administering 10 mg of dapagliflozin per day to the experimental group, and provide an initial dose of 20 mg/day of furosemide to the control group, adjusting the dosage based on BIS assessments.
6. Perform blood sampling, collect variables related to the research outcomes, and record data over a 6-month period.
7. Assess body fluid status using BIS monthly during the first 3 months and at 6 months.
8. Evaluate outcomes at the 6-month mark through Echocardiogram and laboratory tests.
9. Analyze the obtained results statistically.

## **Intervention Type**

Drug

## **Pharmaceutical study type(s)**

Bioequivalence

## **Phase**

Phase IV

## **Drug/device/biological/vaccine name(s)**

Dapagliflozin, furosemide

## **Primary outcome measure**

Blood pressure is measured using sphygmomanometer at baseline and 6 months

## **Secondary outcome measures**

Current secondary outcome measures as of 12/04/2024:

1. Urine volume is measured by patient 24-hour urine volume collection at baseline and 6 months
2. LV mass index is measured using Echocardiogram at baseline and 6 months
3. Total body water is measured using bioimpedance at baseline and 6 months
4. Intracellular water is measured using bioimpedance at baseline and 6 months
5. Extracellular water is measured using bioimpedance at baseline and 6 months
6. Extracellular water/total body water is measured using bioimpedance at baseline and 6 months
7. Hospitalization for heart failure reported outcome using an IPD data at 6 months
8. NT-pro BNP level is measured using laboratory blood test at baseline and 6 months
9. eGFR is measured using laboratory blood test at baseline and 6 months
10. Serum sodium is measured using laboratory blood test at baseline and 6 months
11. Urine albumin creatinine ratio is measured using laboratory urine test at baseline and 6 months
12. Urine sodium is measured using laboratory urine test at baseline and 6 months
12. Body weight is measured using weighing at the hospital at baseline and 6 months

Previous secondary outcome measures:

1. Urine volume is measured by patient 24-hour urine volume collection at baseline and 6 months
2. LV mass index is measured using Echocardiogram at baseline and 6 months
3. Total body water is measured using bioimpedance at baseline and 6 months
4. Intracellular water is measured using bioimpedance at baseline and 6 months
5. Extracellular water is measured using bioimpedance at baseline and 6 months
6. Extracellular water/total body water is measured using bioimpedance at baseline and 6 months

7. Death from any cause reported outcome using an IPD data at 6 months
8. Fatal or nonfatal myocardial infarction reported outcome using an IPD data at 6 months
9. Hospitalization for heart failure reported outcome using an IPD data at 6 months
10. NT-pro BNP level is measured using laboratory blood test at baseline and 6 months
11. eGFR is measured using laboratory blood test at baseline and 6 months
12. Serum sodium is measured using laboratory blood test at baseline and 6 months
13. Serum urine albumin creatinine ratio is measured using laboratory urine test at baseline and 6 months
14. Body weight is measured using weighing at the hospital at baseline and 6 months

**Overall study start date**

01/09/2023

**Completion date**

15/08/2024

## Eligibility

**Key inclusion criteria**

Current inclusion criteria as of 29/10/2024:

1. Age from 18 years old
2. Chronic kidney disease (GFR-EPI 20-60 ml/min/1.73m<sup>2</sup>)
3. Resistant hypertension with fluid retention detected by bioimpedance

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Previous inclusion criteria as of 12/04/2024:

1. Age from 18 years old
2. Chronic kidney disease (GFR-EPI 20-60 ml/min/1.73m<sup>2</sup>)
3. Uncontrolled hypertension with fluid retention detected by bioimpedance

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Previous inclusion criteria:

1. Age from 18 years old
2. Chronic kidney disease (GFR-EPI 20-60 ml/min/1.73m<sup>2</sup>)
3. Resistant hypertension

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Upper age limit**

90 Years

**Sex**

Both

**Target number of participants**

30

**Total final enrolment**

16

**Key exclusion criteria**

Current exclusion criteria as of 29/10/2024:

1. Patient receiving diuretics or SGLT2i
2. Resistant HT with euvolemic status
3. Life expectancy <12 months (principal investigator's judgement)
4. Living-donor transplant scheduled within the next 12 months
5. Cardiovascular disease (dilated cardiomyopathy, valvular heart disease)
6. Active infection
7. Current active malignancy
8. Known HIV or active hepatitis B or C
9. Chronic liver disease and/or screening alanine transaminase or aspartate transaminase above 3 times the upper limit of the normal range
10. Pregnancy or breastfeeding
11. Subject has any kind of disorder that compromises their ability to informed consent and/or to comply with study procedures

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10. Pregnancy or breastfeeding
11. Subject has any kind of disorder that compromises their ability to informed consent and/or to comply with study procedures

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Previous exclusion criteria:

1. Life expectancy less than 12 months
2. Living-donor transplant scheduled within the next 12 months
3. Cardiovascular disease (dilated cardiomyopathy, valvular heart disease)
4. Active infection
5. Current active malignancy
6. Known HIV or active hepatitis B or C
7. Chronic liver disease and/or screening alanine transaminase or aspartate transaminase above 3 times the upper limit of the normal range
8. Pregnancy or breastfeeding
9. Subject has any kind of disorder that compromises their ability to informed consent and/or to comply with study procedures

**Date of first enrolment**

18/01/2024

**Date of final enrolment**

11/02/2024

## Locations

**Countries of recruitment**

Thailand

**Study participating centre**

**Bhumibol Adulyadej Hospital**

171 Phaholyothin Road

Khlong Thanon

Salmai

Bangkok

Thailand

10220

## Sponsor information

**Organisation**

Bhumibol Adulyadej Hospital

**Sponsor details**

171 Phaholyothin road

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Bangkok

Thailand

10220  
+66 25347000  
bhumibolhospital@rtaf.mi.th

**Sponsor type**

Hospital/treatment centre

**Website**

<https://bhumibolhospital.rtaf.mi.th/>

**ROR**

<https://ror.org/041e85345>

## Funder(s)

**Funder type**

Hospital/treatment centre

**Funder Name**

Bhumibol Adulyadej Hospital

## Results and Publications

**Publication and dissemination plan**

Planned publication in a high-impact peer-reviewed journal

**Intention to publish date**

18/04/2025

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request from Natchaya Songsilp (muk.natchaya@gmail.com).

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol file</a>			12/04/2024	No	No
<a href="#">Other unpublished results</a>			06/11/2024	No	No