DAPARHT: DAPAgliflozin for Renal protection in Heart Transplant recipients

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Ethical review	Approved WMO
Status	Pending
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON51463

Source
ToetsingOnline

Brief title
DAPARHT

Condition

- Heart failures
- Renal disorders (excl nephropathies)

Synonym
Cardiac Failure, Renal dysfunction

Research involving
Human

Sponsors and support

Primary sponsor: Oslo University Hospital
Source(s) of monetary or material Support: Astra Zeneca,AstraZeneca Nordics;Nationalforeningen for folkehelsen;etc.

Intervention

Keyword: Dapagliflozin, Heart transplant, Renal protection

Outcome measures

Primary outcome

Primary endpoint: The chronic slope of the eGFR from 2 weeks to

end-of-treatment (12 months).

Secondary outcome

Secondary endpoints:

1. Change in body weight

2. The change in the albumin/creatinine ratio in the urine from baseline to

end-of-treatment in patients with a baseline ratio > 30 mg/g at baseline

3. The change in the blood level of glycated haemoglobin (HbA1c) in patients

with diabetes mellitus

Study description

Background summary

Kidney failure is common in heart transplant recipients and is a major cause of morbidity and mortality. Sodium glucose transporter 2 (SGLT2) inhibitors were developed as antidiabetics but were subsequently shown to reduce the incidence of adverse cardiovascular outcomes and protect renal function in non-diabetics as well as diabetics. However, SGLT2 inhibitors have not been tested in clinical trials in heart transplant recipients.

Study objective

The DAPARHT trial is designed to assess effect of the SGLT2 inhibitor dapagliflozin to prevent deteriorating renal function in heart transplant recipients. Secondary objectives are to assess the impact of treatment on: i) weight, ii) glucose homeostasis, and iii) proteinuria, iv) the number of rejections, and (v) safety and tolerability. As exploratory outcomes, we will

assess the effect of treatment on renal outcomes, clinical events (death, myocardial infarction, cerebral stroke, cancer, and end-stage renal disease), cardiac function, quality of life, and new-onset diabetes.

Study design

This is a phase 3, double-blind, randomised, placebo-controlled trial. Participants will be randomised in a 1:1 fashion to receive 10 mg of oral dapagliflozin or a matching placebo once daily for one year. The study is designed to show superiority regarding the primary endpoint in patients assigned to active treatment versus patients allocated to the placebo arm. In the open-label phase, patients who were originally assigned to active treatment will receive open-label dapagliflozin, whereas patients originally assigned to placebo will not receive study-specific treatment.

Study Period
Estimated date of first patient enrolled (study start) January 1st, 2022
Anticipated recruitment period: January 1st, 2022 - June 30th, 2023
Estimated date of last patient completed blinded treatment phase: June 30th, 2024
Estimated date of last patient completed open-label treatment phase: June 30th, 2026
Estimated date of last patient completed (last patient, last visit: Study end): July 31st, 2026
Treatment Duration: 12 months blinded treatment + 24 months open label
Follow-up: 37 months

Intervention

After the participant has provided informed consent, he or she will be randomised to receive oral dapagliflozin or a matching placebo. The randomisation process will be performed online via the commercially available electronic case report form (eCRF) system called Viedoc®. The investigational drug, dapagliflozin 10 mg/placebo is taken orally, once daily, for the duration of the blinded treatment phase (12 months). There will be no dose titration. At the end of the blinded treatment phase, the efficacy measurements will be performed, stored, and locked, and all adverse events will be recorded before the study drug allocation is revealed in the eCRF. Patients allocated to dapagliflozin will be invited to continue treatment throughout the open-label phase (24 months); whereas patients allocated to placebo will enter the open-label phase without treatment beyond the standard of care. Both groups will be followed-up for safety and efficacy as specified in the study procedure overview.

The investigational medicinal products will be administered once daily for one year. No other study-specific intervention will be provided. Beyond the first

year, the patients are invited to enter the open-label follow-up phase, where the code for the individual patient is opened, and patients who were originally allocated to dapagliflozin will be encouraged to continue treatment; whereas patients assigned to placebo will continue standard-of-care treatment.

The patients will self-administer the investigational drug.

Study burden and risks

There are several studies on diabetes, chronic kidney disease and chronic heart failure using the study medication without major risks being reported. In addition, urinary tract infections, genital infections and ketoacidosis (diabetic patients only) are increased have been reported, but the figures are low and not a major clinical issue for not using it.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1. Heart transplant recipient >= 1 year after heart transplant.
2. Age >= 18 years

Exclusion criteria

1. Contraindications to study medication.
2. Estimated GFR < 25 ml/min/m2
3. Type I diabetes
4. Severe liver failure (Child-Pugh*s score C)
5. Life expectancy reduced to < 2 years as judged by the investigator
6. Unresolved malignant disease
7. Failure to obtain written informed consent
8. SGL2 inhibitor treatment over the last month
9. Pregnancy
10. Breast-feeding
11. Woman of child-bearing potential who is not willing to use a highly effective method of birth control

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2023

Enrollment:	70
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Dapagliflozin
Generic name:	Forxiga
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-10-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-01-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-003175-34-NL
ClinicalTrials.gov	NCT05321706
CCMO	NL81652.078.22