The RENAL LIFECYCLE trial: A Randomized Controlled Clinical Trial to Assess the Effect of Dapagliflozin on Renal and Cardiovascular Outcomes in Patients with Severe Chronic Kidney Disease

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This study has been transitioned to CTIS with ID 2023-508389-13-00 check the CTIS register for the current data. To determine whether dapagliflozin is superior to placebo in reducing the incidence of the primary composite endpoint of kidney failure...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56031

Source
ToetsingOnline

Brief title
Renal Lifecycle trial

Condition

- Other condition
- Nephropathies

Synonym
severe CKD; renal failure

Health condition

Hemo- and peritoneal dialysis patients; Transplant patients

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Nierstichting,Astra Zeneca

Intervention

Keyword: reno- and cardioprotective effects, severe CKD, SGLT2 inhibitor

Outcome measures

Primary outcome

The primary outcome measure is the incidence of a composite of all-cause mortality, kidney failure, and heart failure hospitalization. This is a clinically relevant outcome measure and previous trials with dapagliflozin in patients with earlier stages of CKD than enrolled in the current trial have shown that dapaglilflozin reduces the incidence of each of these outcomes.

Secondary outcome

1. To determine if dapagliflozin is superior to placebo in reducing the incidence of each of the components of the primary composite endpoint in the overall patient group:

• All-cause mortality

• Kidney failure (chronic dialysis, kidney transplantation or mortality due to kidney failure)

• Hospitalization for heart failure

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2. To determine whether dapagliflozin is superior to placebo in reducing the incidence of the primary composite endpoint of all-cause mortality, kidney failure, or heart failure hospitalization in each of the three subgroups of patients:

• Patients with advanced CKD i.e. an eGFR <=25 mL/min/1.73m2

• Dialysis patients with residual diuresis >=500 mL/24h

• Transplant patients with an eGFR <=45 mL/min/1.73m2

Study description

Background summary

Chronic kidney disease (CKD) affects approximately 10% of the adult population worldwide. The most common causes of CKD are diabetes, hypertension, and chronic glomerulonephritis. Subjects with CKD are at high risk for various complications, among others cardiovascular morbidity and mortality, heart failure, and end-stage kidney disease requiring kidney replacement therapy.Treatment for CKD encompasses tight blood pressure control, preferably with angiotensin converting enzyme inhibitor (ACE-I) or angiotensin II receptor blockers (ARBs) as well as a tight glucose control in diabetic patients to prevent or delay progression of CKD and CVD. These interventions have been proven efficacious, but still the residual risk to develop cardiovascular complications and to reach kidney failure remains high. There is therefore a need for additional interventions.

Study objective

This study has been transitioned to CTIS with ID 2023-508389-13-00 check the CTIS register for the current data.

To determine whether dapagliflozin is superior to placebo in reducing the incidence of the primary composite endpoint of kidney failure, hospitalization for heart failure, and all-cause mortality in the overall patient group, consisting of patients with eGFR <=25 mL/min/1.73m2, dialysis patients with residual diuresis >= 500 mL/24hr , and kidney transplant recipients with eGFR

<=45 mL/min/1.73m2.

Study design

This is a randomized, double-blind, parallel-group study

Intervention

Dapagliflozine 10mg/dag vs placebo

Study burden and risks

The study population chosen for this study is a broad population of patients with severe CKD. Three patient groups will be included: patients with an eGFR <=25 ml/min/1.73 m2 (not on dialysis or undergoing a kidney transplant); common dialysis patients with residual diuresis >=500 ml/24 hours (including hemo- and peritoneal dialysis), and recipients of kidney transplants. These patients are almost always excluded from clinical trials, while they are at very high risk of adverse outcomes and few effective therapies are available for these patients. Phase 2/3 clinical trials have also shown that dapagliflozin reduces albuminuria, an important risk marker for renal and cardiovascular disease progression.

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

In order to be eligible to participate in the randomized controlled double blind trial subject must meet the criteria for one of the three strata:
• Patients with advanced CKD i.e. an eGFR <=25 mL/min/1.73m2
• Hemo- and peritoneal dialysis patients with a residual diuresis >=500 mL/24h (at least 3 months after start of dialysis)
• Transplant patients with an eGFR <=45 mL/min/1.73m2 (at least 6 months after transplantation)

In addition, to be eligible all subjects must meet all criteria below
• Age >18 years
• Willing to sign informed consent
• Pre-dialysis patients with eGFR <=25 mL/min/1.73m2 have to be on a stable dose (no changes in dose or type of drug) of ACEis or ARBs for at least 4 weeks prior to the screening visit to be eligible to proceed to the randomization visit unless there is documented evidence that the patient does not tolerate an ACEi or ARB. These subjects will maintain their stable doses of ACEis or ARBs throughout the trial (when possible and tolerated by the patient). ACEi or ARBs are not required for patients on maintenance dialysis or kidney transplant recipients.

Exclusion criteria

• Mentally incapacitated subjects (i.e. not able to sign informed consent)
• Diagnosis of type 1 diabetes mellitus
• Concurrent treatment with SGLT2 inhibitor
• History of >=2 urinary tract / genital infections during the last six months
• Life expectancy <6 months in the opinion of the treating physician.
• Scheduled start of dialysis within 3 months or scheduled kidney transplantation within 6 months
• In patients with an eGFR <=25 mL/min/1.73m2: kidney disease treated with immunosuppressive agents during the last 6 months

• patients treated during the last 6 months with a course of immunosuppressive agents or intensification of treatment with immunosuppressive agents, such as patients with a kidney transplant and acute rejection or patients with GPA (Morbus Wegener) and a recent flare.
• Active malignancy aside from treated squamous cell or basal cell carcinoma of the skin.
• History of severe hypersensitivity or known severe hepatic impairment (Child-Pugh class C)
• History of severe noncompliance to medical regimens or unwillingness to comply with the study protocol.
• Current pregnancy, lactation or women of child-bearing potential (WOCBP) unless using highly-effective contraceptive measurements until 4 weeks after last intake of the study medication
• Presence of other transplanted organ besides a kidney transplant
• Severe lactose intolerance
• Autosomal Dominant Polycystic Kidney Disease (ADPKD) treated with tolvaptan

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:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-11-2022
Enrollment:	1000
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	16-03-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-06-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-08-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-04-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-04-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-08-2023
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EU-CTR	CTIS2023-508389-13-00
EudraCT	EUCTR2021-005446-15-NL
ClinicalTrials.gov	NCT05374291
CCMO	NL80581.042.22