An International, Double-blind, Randomised, Placebo-Controlled Phase III Study to Evaluate the Effect of Dapagliflozin on Reducing CV Death or Worsening Heart Failure in Patients with Heart Failure with Preserved Ejection Fraction (HFpEF) - DELIVER study

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To determine whether dapagliflozin is superior to placebo, when added to standard of care, in reducing the composite of CV death and HF events (hospitalisation for HF or urgent HF visit) in patients with HF and preserved systolic function in* full...

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

Summary

ID

NL-OMON49973

Source
ToetsingOnline

Brief title
DELIVER

Condition

- Heart failures

Synonym
Heart failure, preserved ejection fraction

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Astrazeneca BV

Intervention

Keyword: Dapagliflozin, Heart failure, Preserved ejection fraction, prevention

Outcome measures

Primary outcome

Time to (first occurrence of):

1. CV death.

2. Hospitalisation for HF.

3. Urgent HF visit (e.g., emergency department or outpatient visit).

Secondary outcome

1. Total number of (first and recurrent) hospitalisations for HF and CV death.

2. Change from baseline in the total symptom score (TSS) of the KCCQ at 8

months.

3. Time to the occurrence of CV death

4. Time to the occurrence of death from any cause.

Study description

Background summary

The prevalence of chronic HF continues to increase globally. An estimated 38 million people are affected worldwide. Approximately half of all heart failure patients have HFpEF. Risk of death for HFpEF patients is high, with annualised mortality rate up to 15% in community settings.

However, patients with HFpEF have a particularly significant unmet medical need given that outcome studies hitherto performed have not resulted in any approved pharmacotherapy specifically for this condition. Recent data from cardiovascular (CV) outcome trials of SGLT2 inhibitors (empagliflozin and canagliflozin) indicate that treatment with SGLT2 inhibitors can reduce the risk of CV death and hospitalisation due to HF in patients with T2D overall, and in patients with T2D and concomitant HF.

Dapagliflozin is a potent, highly selective and orally active inhibitor of human renal SGLT2. Dapagliflozin lowers HbA1c with a low risk of inducing hypoglycaemia. In addition, dapagliflozin treatment has also been shown to reduce weight and systolic blood pressure, and to have favourable effects on increased blood uric acid, albuminuria, and arterial elasticity, conditions which are associated with increased CV and renal risk. Dapagliflozin is believed to be nephroprotective through non-glycaemic mechanisms. Dapagliflozin has global marketing approval in approximately 90 countries with the most recent estimate of cumulative post-marketing experience totalling over 1.6 million patient-years.

Study objective

To determine whether dapagliflozin is superior to placebo, when added to standard of care, in reducing the composite of CV death and HF events (hospitalisation for HF or urgent HF visit) in patients with HF and preserved systolic function in
* full study population
* subpopulation with LVEF <60%

Study design

This is an international, multicentre, parallel-group, event-driven,

randomised, phase III, double-blind study in patients with HFpEF

Intervention

Patients will use either dapagliflozin 10 mg or placebo once daily.

Study burden and risks

The patients visit the hospital approximately 10 times over an average of 24 months (depending on when the subject is enrolled in the study). Study participation will vary between approximately 15 - 33 months. The patients are asked to keep in touch with the study doctor throughout the study.
During the study the following study procedures will be performed: physical examination (±3 times), blood draw (±8 times), a pregnancy test is performed (if applicable), (1 time), patients complete several questionnaires (±6 times) and an ECG is taken (1 time). Blood sampling may cause some discomfort or can cause a bruise. The use of study medication can cause side effects.

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. Provision of signed informed consent prior to any study specific procedures.
2. Male or female patients age *40 years.
3. Documented diagnosis of symptomatic heart failure HFpEF
4. LVEF >40%, measured within the last 12 months prior to enrolment and evidence of structural heart disease.
5. NT-pro BNP *300 pg/ml at Visit 1 for patients without ongoing atrial fibrillation/flutter. If ongoing atrial fibrillation/flutter at Visit 1, NT-pro BNP must be
*600 pg/mL.
6. Patients may be ambulatory, or hospitalized; patients must be off intravenous heart
failure therapy (including diuretics)

Exclusion criteria

1. Receiving therapy with an SGLT2 inhibitor within 4 weeks prior to randomisation or
previous intolerance to an SGLT2 inhibitor
2. Type 1 diabetes mellitus (T1D)
3. eGFR <25 mL/min/1.73 m2 (CKD-EPI formula) at Visit 1
4. Systolic blood pressure (BP) <95 mmHg on 2 consecutive measurements
5. Systolic BP*160 mmHg if not on treatment with *3 blood pressure lowering medications
or *180 mmHg irrespective of treatments, on 2 consecutive measurements
6. MI, unstable angina, coronary revascularization within 12 weeks prior to enrolment.
7. Planned coronary revascularization, ablation of atrial flutter/fibrillation and valve
repair/replacement.
8. Stroke or transient ischemic attack (TIA) within 12 weeks prior to enrolment
9. Probable alternative or concomitant diagnoses which in the opinion of the investigator
could account for the patient's HF symptoms and signs (e.g. anaemia, hypothyroidism)
10. Body mass index >50 kg/m2
11. Previous cardiac transplantation, or complex congenital heart disease.

Planned cardiac resynchronisation therapy.

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:	Recruitment stopped
Start date (anticipated):	05-11-2018
Enrollment:	160
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Farxiga
Generic name:	dapagliflozin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	28-06-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	11-10-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-11-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-12-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-02-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-02-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-03-2019

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-08-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-09-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-02-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-02-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-08-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-01-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	12-02-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2018□000802□46-NL
CCMO	NL66182.100.18