Randomized, double blind, placebo controlled, multicenter pilot study on the effects of empagliflozin on clinical outcomes in patients with acute decompensated heart failure

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Primary:The primary objective of this trial is to evaluate whether empagliflozin 10mg/day will relieve dyspnea, improves diuretic response, decreases length of initial hospital stay and NT-proBNP compared to placebo during hospital admission for...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON46516

Source
ToetsingOnline

Brief title
EMPA-RESPONSE-AHF

Condition

- Cardiac disorders, signs and symptoms NEC

Synonym
'Acute Heart Failure'

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Boehringer Ingelheim,Grant van Fabrikant van Empagliflozine voor de uitvoering van de studie

Intervention

Keyword: Diuretic Response, Empagliflozin, Heart failure, SGLT2 inhibition

Outcome measures

Primary outcome

a) Dyspnea relief, assessed by VAS at baseline to day 4 (or discharge if

earlier);

b) Diuretic response (defined as * weight kg/[(total i.v. dose)/40mg]+[(total

oral dose)/80mg)] furosemide (or equivalent loop diuretic dose) up to day 4) c)

Length of initial hospital stay;

d) Change in NT-proBNP from baseline to day 4 (or discharge if earlier)

Secondary outcome

Death and/or heart failure re-admission through day 60

Change in plasma values of renal function, including creatinine, eGFR,

cystatin C, BUN, renal biomarkers and hemoglobin, hematocrit, albumin from

baseline to day 4 (or discharge if earlier) or day 30

Change in urinary renal biomarkers to day 4 or day 30

Study description

Background summary

Acute decompensated heart failure is one of the fastest growing diseases in the world and athe leading cause of hospital admissions worldwide. Short term

mortality and rehospitalization are extremely high (20-30% within 3-6 months). There is no therapy available that improves clinical outcome of these patients. Therefore, there is a very high unmet need to find effective treatments in patients with acute decompensated heart failure. Despite treatment with loop diuretics, many patients are discharged with residual congestion, which is related to a higher risk of early rehospitalization and death. Renal Failure and worsening renal function in patients with AHF is common and related to an impaired outcome. Empagliflozin is a selective inhibitor of sodium glucose co-transporter with diuretic and renal protective properties. Recently, empagliflozin reduced the risk of cardiovascular outcome and of death from any cause in patients with type 2 diabetes at high risk for cardiovascular events. Interestingly, hospitalization for heart failure was reduced by 35% and risk of progression of nephropathy by 44 %. We hypothesize that the reduction in the risk of hospitalization for heart failure was caused by the diuretic and renal protective properties of empagliflozin and that empagliflozin is therefore beneficial for the treatment of patients who are hospitalized for acute decompensated heart failure.

Study objective

Primary:
The primary objective of this trial is to evaluate whether empagliflozin 10mg/day will relieve dyspnea, improves diuretic response, decreases length of initial hospital stay and NT-proBNP compared to placebo during hospital admission for acute decompensated heart failure.

Secondary Objective:
The secondary objectives of this trial are to evaluate the effects of empagliflozin on change in dyspnea, renal function, and NT-proBNP and on 30-day death and/or heart failure hospital.

Safety Objectives: The safety objectives of this trial are to evaluate whether empagliflozin is well tolerated, and does not cause an excess number of (serious) adverse events. Specific attention will be paid to hypotension, renal dysfunction, keto-acidosis and/ or hyperosmolar hyperglyaecemic syndrome.

Study design

Multicenter, prospective, double-blind, placebo controlled, parallel design, interventional, pilot study

Intervention

Empagliflozine 1 dd 10 mg versus placebo (matching) for 30 days

Study burden and risks

Patients need to take the study medication and come to one research visit after hospitalisation
Side effects include hypoglycemia, itching, olguria, blood pressure drop and genital infections. Rare cases of (severe) diabetic keto-acidosis have been reported. Additionally, possible (extra) venapunctures for blood sampling

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. Male or female >18 years of age;
2. Hospitalized for AHF; AHF is defined as including all of the followings measured at any time between presentation (including the emergency department) and the end of screening:
a. Dyspnea at rest or with minimal exertion
b. Signs of congestion, such as edema, rales, and/or congestion on chest radiograph

c. BNP *350 pg/mL or NT-proBNP *1,400 pg/mL (for patients with AF: BNP*500 pg/mL or NT-proBNP *2,000 pg/mL)
d. Treated with loop diuretics at screening
3. Able to be randomized within 24 hours from presentation to the hospital
4. Able and willing to provide freely given written informed consent
5. eGFR (CKD-EPI) *30 ml/min/1.73m2 between presentation and randomization

Exclusion criteria

1. Diabetes Mellitus Type I
2. Dyspnea primarily due to non-cardiac causes
3. Cardiogenic shock
4. Acute coronary syndrome within 30 days prior to randomization
5. Planned or recent percutaneous or surgical coronary intervention within 30 days prior to randomization
6. Signs of keto-acidosis and/or hyperosmolar hyperglaecemic syndrome (pH>7.30 and glucose >15 mmol/L and HCO3>18 mmol/L)
7. Pregnant or nursing (lactating) women
8. Current participation in any interventional study
9. Inability to follow instructions or comply with follow-up procedures
10. Any other medical conditions that may put the patient at risk or influence study results in the investigator*s opinion, or that the investigator deems unsuitable for the study.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	02-01-2018
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Jardiance
Generic name:	Empagliflozin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-09-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-10-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-09-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-10-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-03-2019
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
Other	2017-001679-22
EudraCT	EUCTR2017-001679-22-NL
CCMO	NL62419.042.17

Study results

Date completed:	16-09-2019
Actual enrolment:	80