EMPACT-MI: A streamlined, multicentre, randomised, parallel group, double-blind placebo-controlled superiority trial to evaluate the effect of EMPAgliflozin on hospitalisation for heart failure and mortality in patients with aCuTe Myocardial Infarction

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Myocardial disorders
Study type	Interventional

Summary

ID

NL-OMON56313

Source
ToetsingOnline

Brief title
EMPACT-MI - A study to test empagliflozin in people who had a heart attack

Condition

- Myocardial disorders

Synonym
Myocardial Infarction

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim

Intervention

Keyword: heart failure, mortality, Myocardial Infarction, Phase III

Outcome measures

Primary outcome

Primary endpoint:

• Composite of time to first HHF or all-cause mortality

Secondary outcome

Key secondary endpoints which are part of the testing strategy:

• Total number of HHF or all-cause mortality

• Total number of non-elective CV hospitalization or all-cause mortality

• Total number of non-elective all-cause hospitalisation or all-cause mortality

• Total number of hospitalisation for MI or all-cause mortality

Other secondary endpoints:

• Time to CV mortality

Study description

Background summary

Acute myocardial infarction (MI) affects approximately 7 million individuals every year. Despite advancements in its treatment, a significant unmet need persists with more than one third of all MI patients having either died or developed heart failure (HF) after five years. The observed benefits of

empagliflozin on mortality and hospitalisation for HF (HHF) in patients with T2D and established atherosclerotic CV disease in the EMPA-REG OUTCOME trial appeared independent of glucose control and provided a strong rationale to explore the effects of empagliflozin in populations with established HF. However, as these benefits were consistent in both patients with and without HF, a similarly strong rationale exists for exploring efficacy and safety of empagfliflozin in patients without established but at high risk of developing HF, frequently represented by patients with an acute MI. Further data with empagliflozin from animal studies have given additional support by showing benefits on cardiac remodelling and contractility in the post-acute MI setting. This trial plans to evaluate efficacy and safety of empagliflozin in patients with an acute MI, specifically related to effects on the risk of HHF and mortality. The main hypothesis is that early intervention with empagliflozin vs placebo on top of standard of care in this patient population reduces the subsequent risk of HHF and mortality.

Study objective

The main objective of this event-driven trial is to demonstrate the superiority of empagliflozin 10 mg once daily versus placebo, in addition to standard of care, for the reduction of the composite endpoint of time to first heart failure hospitalisation or all-cause mortality in high-risk patients hospitalised for acute MI.

Study design

A streamlined, randomised, double-blind, parallel group, placebo controlled, multi-national and multicentre trial

Intervention

Patient will receive medication (IP) in addition to the stnadard treatment - tablets to be taken daily.
the study visits are at the hospital, though some are online (via app or computer), for which some questionnaires need to be completed.

Study burden and risks

The main hypothesis is that early intervention with empagliflozin vs placebo on top of standard of care in this patient population reduces the subsequent risk of HHF and mortality.

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

Main Inclusion Criteria:
• Signed and dated written informed consent in accordance with ICH-GCP and local legislation prior to admission to the trial
• Diagnosis of acute MI (type 1 per the Universal Definition of Myocardial Infarction [R20-0005]): STEMI or NSTEMI with randomisation to occur no later than 14 calendar days after hospital admission. For patients with an in-hospital MI as qualifying event, randomisation must still occur within 14 days of hospital admission.
• High risk of HF, defined as EITHER
a) Symptoms (e.g. dyspnea; decreased exercise tolerance; fatigue), or signs of congestion (e.g. pulmonary rales,crackles or crepitations; elevated jugular venous pressure; congestion on chest X-ray), that require treatment (e.g.

augmentation or initiation of oral diuretic therapy; i.v. diuretic therapy; i.v. vasoactive agent; mechanical intervention etc.) at any time during the hospitalisation.
OR
b) Newly developed LVEF < 45% as measured by echocardiography, ventriculography, cardiac CT, MRI or radionuclide imaging during index hospitalisation.

In addition at least one of the following risk factors:
- Age > 65 years
- Newly developed LVEF < 35%
- Prior MI (before index MI) documented in medical records
- eGFR < 60 ml/min/1.73m2 (according to creatinine from most recent local lab during the index hospitalisation and calculated with the CKDEPI formula)
- Atrial fibrillation (persistent or permanent ; if paroxysmal, only valid if associated with index MI)
- Type 2 diabetes mellitus (prior or new diagnosis)
- NTproBNP >1,400 pg/mL for patients in sinus rhythm, >2,800 pg/mL if atrial fibrillation; BNP >350 pg/mL for patients in sinus rhythm, >700 pg/mL if atrial fibrillation, measured at any time during hospitalisation
- Uric acid >7.5 mg/dL (>446 µmol/L), measured at any time during hospitalisation
- Pulmonary Artery Systolic Pressure [or right ventricular systolic pressure] >40 mmHg (non-invasive [usually obtained from clinically indicated post-MI echocardiography] or invasive, at any time during hospitalisation)
- Patient not revascularized (and no planned revascularization) for the index MI (Includes e.g. patients where no angiography is performed, unsuccessful revascularization attempts, diffuse atherosclerosis not amenable for intervention; but does NOT include if revascularization was not performed due to nonobstructive coronary arteries)
- 3-vessel coronary artery disease at time of index MI
- Diagnosis of peripheral artery disease (extracoronary vascular disease, e.g. lower extremity artery disease or carotid artery disease)

Exclusion criteria

Main Exclusion Criteria:
1) Diagnosis of chronic HF prior to index MI
2) Systolic blood pressure < 90 mmHg at randomisation
3) Cardiogenic shock or use of i.v. inotropes in last 24 hours before randomisation
4) Coronary Artery Bypass Grafting planned at time of randomisation
5) Current diagnosis of Takotsubo cardiomyopathy
6) Any current severe (stenotic or regurgitant) valvular heart disease
7) eGFR < 20 ml/min/1.73m2 (using CKD-EPI formula based on most recent

creatinine from local lab during hospitalisation) or on dialysis
8) Type I diabetes mellitus
9) History of ketoacidosis
16) Women who are pregnant, nursing, or who plan to become pregnant while in the trial.

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):	02-07-2021
Enrollment:	298
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:	18-02-2021

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-06-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-06-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-08-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-10-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-12-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-01-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-11-2022

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-12-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-03-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-11-2023
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
EudraCT	EUCTR2019-001037-13-NL
ClinicalTrials.gov	NCT04509674
CCMO	NL75472.042.21