A multi-center, randomized, double-blind, parallel-group dose-finding study to assess the effect of 3 doses of LIK066 compared to placebo or empagliflozin in type 2 diabetes mellitus patients with heart failure

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Main study objective is to find out which dose among three different doses of LIK066 is the most efficacious, safe and well tolerated in type 2 diabetes patients with heart failure. We will also learn which medication is better at managing patients...

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

Summary

ID

NL-OMON45545

Source
ToetsingOnline

Brief title
CLIK066B2204

Condition

- Cardiac disorders, signs and symptoms NEC
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
decompensatio cordis, Diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (verrichter/sponsor van het onderzoek)

Intervention

Keyword: efficacy, Heart failure, SGLT1 & SGLT2 inhibitors, Type 2 Diabetes

Outcome measures

Primary outcome

To determine the dose-response signal and assess the dose-response relationship

of 3 doses of LIK066 as measured by the change from baseline in NT-proBNP

relative to placebo after 12 weeks of treatment in T2DM patients with HF.

Secondary outcome

1. To evaluate the effect of all LIK066 doses vs placebo at 12 weeks and 36

weeks on:

- Change from BL in glycated hemoglobin (HbA1c)

- Change from BL in fasting plasma glucose (FPG)

- Change from BL in weight

- Change from BL in body composition (bio-impedance in all patients where

appropriate and dual-energy x-ray absorptiometry (DXA) in a subset of patients)

- Change from BL in sitting systolic blood pressure (SBP) and diastolic blood

pressure (DBP)

- Change from BL in the fasting lipid profile and hsCRP

- Change from BL in 24h urinary glucose and sodium excretion,in a subset of

patients

- Change from BL in left atrial size and volume assessed by echocardiography

- Change from BL in NYHA class

2. To evaluate the effect of all LIK066 doses vs empagliflozin at 12 weeks and 36 weeks on:

- Change from BL in HbA1c

- Change from BL in FPG

- Change from BL in weight

- Change from BL in body composition (bio-impedance in all patients where appropriate and DXA in a subset of patients)

- Change from BL in sitting SBP and DBP

- Change from BL in the fasting lipid profile and hsCRP

- Change from BL in 24h urinary glucose and sodium excretion, in a subset of patients

3. To evaluate the change from BL to 36 weeks in all LIK066 doses vs placebo on NT-proBNP.

4. To evaluate safety (adverse events (AEs) and lab parameters) and tolerability of LIK066 over 12 weeks and over 36 weeks for all patients

5. To evaluate 24h urinary calcium and phosphate excretion after 12 weeks and after 36 weeks in a subset of patients

6. To evaluate bone mineral density in a subset of patients

Study description

Background summary

Diabetes type 2 is a severe condition with increased risk of cardiovascular conditions and its complications such as heart failure. SGLT2 inhibitors are approved for the treatment of type2 diabetes. Since LIK066 is a SGLT1 as well as a SGLT2 inhibitor, it has a double mode of action on kidneys as well as intestines. Moreover, SGLT1 receptors are also located in the heart, where the mode of action is not clear yet. This study will investigatore the effect of SGLT1/2 inhibitor LIK066 on heart failure biomarker NT-proBNP in a population with type 2 diabetes and reduced cardiac function. Also, the glucose-lowering potential of LIK066 will be studied.

Study objective

Main study objective is to find out which dose among three different doses of LIK066 is the most efficacious, safe and well tolerated in type 2 diabetes patients with heart failure. We will also learn which medication is better at managing patients` blood sugar and heart failure, compared to either empagliflozin or placebo.

Study design

This is a multi-center, randomized, double-blind, double-dummy, parallel-group study evaluating the efficacy, safety and tolerability of 3 doses of LIK066 vs placebo and vs empagliflozin in type 2 diabetes patients with heart failure.
After the screenings visit, eligible patients will enter the run-in period.
After completion of the run-in period, eligible patients will be randomized and treated during 36 weeks. The total duration of the study is max. 40 weeks.

Intervention

Treatment with LIK066, Empagliflozine or placebo.

Study burden and risks

Risks: Side effects of study medication and burden assessments.

Burden:
- Physical exam: 9x

- Length: 1x
- Vital signs: 9x
- Blood tests (fasting): 4x
- Blood tests (non-fasting): 2x
- Daily measurement of blood sugar at home
- Pregnancy test: 4x (if applicable)
- Urine testsk: 6x
- Bioimpedance: 3x
- ECG: 3x
- Echocardiogram: 3x
- Questionnaires (5 items): 5x
- Optional blood- and urine tests: 3x
- Optional DEXA test: 3x

Contacts

Public
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL
Scientific
Novartis

Raapopseweg 1
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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* BMI * 22kg/m2
* Type 2 diabetes with HbA1c between 6.5% and 10.0%
* Documented symptomatic chronic heart failure (NYHA II-IV)
* Plasma NT-proBNP > 300pg/ml
* eGFR * 45ml/min/1.73m2 (MDRD)

Exclusion criteria

* Pregnant or nursing (lactating) women
* Type 1 diabetes, monogenic diabetes, diabetes resulting from pancreatic injury, or secondary forms of diabetes
* History of ketoacidosis, lactic acidosis, or hyperosmolar coma
* Symptomatic genital infection or UTI within 4 weeks of screening
* Myocardial infarction, stroke, surgery for heart disease, percutaneous coronary intervention within 3 months of screening
* Unstable angina within 3 months of screening
* Isolated right HF due to pulmonary disease
* Patients with a mean sitting systolic blood pressure * 100mmHg, at randomization

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):	08-01-2018

Enrollment:	22
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Jardiance
Generic name:	Empagliflozin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	LIK066
Generic name:	LIK066

Ethics review

Approved WMO Date:	25-04-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-07-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-08-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-09-2017

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-10-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-10-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-11-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-01-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-03-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-05-2018
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	EUCTR2016-003084-19-NL
ClinicalTrials.gov	NCT03152552
CCMO	NL60488.100.17