A Phase III, randomised, double blind, placebo-controlled, parallel group, efficacy, safety and tolerability trial of once daily, oral doses of Empagliflozin as Adjunctive to inSulin thErapy over 52 weeks in patients with Type 1 diabetes mellitus (EASE-2)

Published: 27-05-2015
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The objective of this study is to assess the efficacy, safety, tolerability and pharmacokinetics (PK) of once daily oral doses of empagliflozin 10 in patients with Type 1 diabetes mellitus (T1DM) as adjunctive to insulin therapy. Empagliflozin is...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON44884

Source
ToetsingOnline

Brief title
EASE-2

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes, Diabetes Mellitus Type 1

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Diabetes Mellitus Type 1, Empagliflozin, SGLT-2 inhibitor

Outcome measures

Primary outcome

The change from baseline in HbA1c after 26 weeks of treatment.

Secondary outcome

- Incidence rate of symptomatic hypoglycaemic AEs with confirmed plasma glucose < 54 mg/dL (< 3.0 mmol/L) and/or severe hypoglycaemic AEs per patient-year from week 5 to week 26.

- Incidence rate of symptomatic hypoglycaemic AEs with confirmed plasma glucose < 54 mg/dL (< 3.0 mmol/L) and/or severe hypoglycaemic AEs per patient-year from week 1 to week 26.

- Change from baseline in body weight (kg) after 26 weeks.

- Change from baseline in total daily insulin dose (TDID), U/kg, after 26 weeks.

- Change from baseline in the percentage of time spent in target glucose range of 70-180 mg/dL (3.9-10.0 mmol/L) as determined by continuous glucose monitoring (CGM) in weeks 23 to 26.

- Change from baseline in systolic blood pressure (SBP) after 26 weeks.

- Change from baseline in diastolic blood pressure (DBP) after 26 weeks.

Study description

Background summary

Type 1 diabetes mellitus (T1DM) accounts for 5 to 10% of all cases of diabetes mellitus. This disease is a complex disorder that requires constant attention to diet, exercise, glucose monitoring, and insulin therapy to achieve good glycaemic control.
Most bodies recommend that adult patients with T1DM should obtain glycated haemoglobin (HbA1c) <= 7.0%. However, most patients generally achieve HbA1c levels no lower than 8.0%. Hence, with the currently available treatment options, patients with T1DM often fail to maintain adequate blood glucose control. This may lead to acute conditions and debilitating secondary complications including heart disease, blindness and kidney failure.
Empagliflozin has the potential to provide a novel approach to the treatment of T1DM, as adjunctive therapy to insulin which may lead to a reduction of plasma glucose levels.

Study objective

The objective of this study is to assess the efficacy, safety, tolerability and pharmacokinetics (PK) of once daily oral doses of empagliflozin 10 in patients with Type 1 diabetes mellitus (T1DM) as adjunctive to insulin therapy. Empagliflozin is being compared to placebo.

Study design

In total, 720 patients with T1DM who meet the entry criteria will be entered (randomised) in the trial.
This multi-national, randomised, placebo-controlled, double-blind, parallel group study compares 2 doses of empagliflozin (10 mg and 25 mg) to placebo in patients with T1DM as adjunctive to insulin therapy.
Patients will be enrolled (screened) in the trial once they have signed the informed consent. All patients who are suitable after screening will undergo a 6 week T1DM therapy optimisation period, followed by a 2 week open-label placebo run-in period before randomisation. Patients who successfully complete both of these periods will be randomised into the 52 week double-blind treatment period. After the treament periode, the study will be completed by a three week follow-up period.

Intervention

Patients will start a two week placebo run-in period at visit 5.
Patients will be randomized to either Empagliflozin 10 mg, Empagliflozine 25 mg

of matching placebo (ratio 1:1:1) at visit 6.

Study burden and risks

Assuming a patients completes the trial, the following procedures will be performed:
Hight:1x
Weight: 9x
Waist circumference: 5x
Vital signs (blood pressure and heart rate): 15x
Standard physical exam: 4x
ECG: 3x
Blood- and urine analysis: 10x
8-point plasma glucose profile (the patient should measure the glucose at least 8 times within a 24 hour period): 5x
Management of diet and physical activity: continuous throughout the study
Glucose home monitoring: starting at visit 2 and up to visit 17, the patient needs to measure his glucose at least 4 times a day. Measurements need to be recorded in the e-diary. At day 1 - 5, the patient needs to measure the glucose at least 8 to 10 times a day including 1 measurement during the night.
Continuous Glucose Monitoring: 1 period of two weeks and 2 periods of four weeks.
Completing the e-diary: at least once a day
DTSQ questionnaire: at visit 2, 6, 12 and 16
EQ-5D-5L questionnaire: at visit 6, 12 and 16
HFS-W questionnaire: at visit 2, 6, 12 and 16
HCRU questionnaire: at visit 6, 12 and 16

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

- Male or female patient receiving insulin for the treatment of documented diagnosis of T1DM for at least 1 year at the time of Visit 1;- Fasting C-peptide value of 0.7 ng/mL (0.23 nmol/L) at Visit 2 measured by the central laboratory ;- Use of, and be willing, based on the Investigator's judgement, to continue throughout the duration of the trial, either:;--MDI of insulin consisting of at least one basal insulin injection and at least three daily bolus injections OR ;--CSII of any insulin type, with at least 5 months experience of using CSII prior to Visit 1;- HbA1c >= 7.5% en <= 10.0% at Visit 5 measured by the central laboratory;- Age >= 18 years at Visit 1;Additional inclusion criteria may apply

Exclusion criteria

- History of T2DM, maturity onset diabetes of the young (MODY), pancreatic surgery or chronic pancreatitis;- Pancreas, pancreatic islet cells or renal transplant recipient;- T1DM treatment with any other antihyperglycaemic drug (e.g. metformin, alpha-glucosidase inhibitors, GLP-1 analogues, SGLT-2 inhibitors, pramlintide, inhaled insulin, pre-mixed insulins etc.) except subcutaneous basal and bolus insulin within 3 months prior to Visit 1 ;- Occurrence of severe hypoglycaemia involving coma and/or seizure that required hospitalisation or hypoglycaemia-related treatment by an emergency physician or paramedic within 3 months prior to Visit 1;- Occurence of severe DKA (i.e a pH < 7.0 or prolonged Intensive Care Unit admission exceeding two days) requiring hospitalisation within 3 months prior to Visit 1;Additional exclusion criteria may apply

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:	Recruitment stopped
Start date (anticipated):	27-07-2015
Enrollment:	40
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:	27-05-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2015

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2016

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2014-001922-14-NL
ClinicalTrials.gov	NCT02414958
CCMO	NL52670.018.15