An open-label randomised cross-over study to evaluate the albuminuria lowering effect of dapagliflozin, exenatide and their combination in patients with type 2 diabetes

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Ethical review	Approved WMO
Status	Completed
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON46820

Source
ToetsingOnline

Brief title
DECADE

Condition

- Diabetic complications

Synonym
diabetes, Diabetes Mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Martini Ziekenhuis
Source(s) of monetary or material Support: Antaros Medical ,Astra Zeneca,Lokale subsidies;Astra Zeneca (beschikbaar stellen studiemedicatie);Antaros Medical (kosten MRI's)

Intervention

Keyword: Albuminuria, Dapagliflozin, Diabetes, Exenatide

Outcome measures

Primary outcome

The main study endpoint is the change in albuminuria from baseline at the end

of each treatment period.

Secondary outcome

* To assess the correlation in albuminuria-lowering response of dapagliflozin

and exenatide within each individual

* To assess the effect of dapagliflozin, exenatide and their combination on

extracellular volume

* To evaluate the correlation between change in extracellular volume and effect

on albuminuria

* To assess the effect of dapagliflozin, exenatide and their combination on

fractional lithium excretion

* To assess the effect of dapagliflozin, exenatide and their combination on

blood pressure

* To assess the effect of dapagliflozin, exenatide and their combination on

weight

* To evaluate the correlation between the pharmacokinetics of dapagliflozin and

exenatide and their albuminuria lowering effect

* To assess the effect of dapagliflozin, exenatide and their combination renal

parameters as measured with MRI

* To assess the effect of dapagliflozin, exenatide and their combination on

liver fat as measured with MRI

Study description

Background summary

Glucagon-like peptide receptor agonists (GLP1-RA) and sodium-glucose co-transporter 2 (SGLT-2) inhibitors are the two latest new drug classes for the management of type 2 diabetes. These drugs lower HbA1c when given as monotherapy or as adjunct to other glucose lowering drugs. Interestingly, both drug classes show beneficial effects on multiple cardiovascular risk factors such as body weight, blood pressure and albuminuria and they have been shown to reduce renal and cardiovascular risk. It is unknown whether the combination of both drug classes confers an even more beneficial effect than either treatment alone.

Study objective

The main objective of the study is to determine the albuminuria lowering effect of the GLP1-RA exenetide, SGLT-2 inhibitor dapagliflozin and their combination in patients with type 2 diabetes and micro- or macroalbuminuria.
Secondary objectives are to assess the correlation in albuminuria-lowering response of dapagliflozin and exenatide within each individual, to assess the effect of dapagliflozin, exenatide and their combination on extracellular volume, to evaluate the correlation between change in extracellular volume and effect on albuminuria, to assess the effect of dapagliflozin, exenatide and their combination on blood pressure and weight, to evaluate the correlation between the pharmacokinetics of dapagliflozin and exenatide and their albuminuria lowering effect, and to assess changes in renal parameters and liver fat as measured with MRI during treatment with dapagliflozin, exenatide and their combination.

Study design

A randomized, prospective, single centre, crossover trial with a total duration of 45 weeks per patient.

Intervention

Patients receive in random order 6 weeks of treatment with the GLP1-RA exenatide 2 mg/week s.c., 6 weeks of treatment with the SGLT-2 inhibitor dapagliflozin 10 mg/day and 6 weeks of treatment with the combination of exenatide and dapagliflozin, with 9-weeks wash-out periods in between.

Study burden and risks

At the beginning and end of each treatment period blood is collected for clinical chemistry. Patients are requested to collect three consecutive first morning void urine samples at the beginning and end of each treatment period, and one additional first morning void urine sample halfway the treatment period. Extracellular volume and total body water will be measured at the beginning and end of each treatment period with a bio-impedance spectrometer. MRI scans of the kidney and the liver are performed at the start and at the end of each treatment periode. There are no direct benefits for the patients to be included and participation is on a free-will base.

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

* Type 2 diabetes
* HbA1c * 6.5% (48 mmol/mol)
* eGFR > 30 ml/min/1.73m2
* Albumin:creatinine ratio >3.5mg/mmol and *100 mg/mmol
* Age * 18 years
* Written informed consent

Exclusion criteria

* Pregnant women and women of child-bearing potential who are not using reliable contraception
* Cardiovascular disease: myocardial infarction, angina pectoris, percutanous transluminal coronary angioplasty, coronary artery bypass grafting, stroke, heart failure (NYHA I-IV) < 6 months before inclusion
* Uncontrolled blood pressure (> 160/ 100 mmHg)
* Active malignancy
* History of autonomic dysfunction (e.g. history of fainting or clinically significant orthostatic hypotension)
* Participation in any clinical investigation within 3 months prior to initial dosing.
* Donation or loss of 400 ml or more of blood within 8 weeks prior to initial dosing
* History of drug or alcohol abuse within the 12 months prior to dosing, or evidence of such abuse as indicated by the laboratory assays conducted during the screening.
* Use of SGLT-2 inhibitor, GLP1-RA or DPP-4 inhibitor.
* Lithium use
* Any medication, surgical or medical condition which might significantly alter the absorption, distribution, metabolism, or excretion of medications
* Any condition when MRI is contraindicated

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	21-01-2019
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bydureon
Generic name:	exenatide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Forxiga
Generic name:	dapagliflozin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	28-03-2018
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	24-04-2018

Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	03-12-2018
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	21-01-2019
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	04-02-2019
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	25-02-2019
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	17-06-2019
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24855
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-004709-42-NL
CCMO	NL63792.099.18
OMON	NL-OMON24855