Canagliflozin REnal Distribution Intervention Trial (CREDIT)

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26995

Source
NTR

Brief title
CREDIT

Health condition

Type 2 diabetes mellitus

Sponsors and support

Primary sponsor: University Medical Center Groningen
Source(s) of monetary or material Support: ZonMw and Diabetes Fonds

Intervention

Outcome measures

Primary outcome

The main study parameters are dynamic PET data and images and radiation count measurement, and free plasma concentrations of canagliflozin.

Secondary outcome

The secondary study parameters are (estimated) Glomerular Filtration Rate, plasma glucose and urine glucose excretion

Study description

Background summary

Sodium glucose cotransporter 2 (SGLT2) inhibitors are a novel class of drugs used in the treatment of type 2 diabetes mellitus and they have shown to slow progression of diabetic kidney disease and to have beneficial effects on cardiovascular end points, in particular reduction of heart failure. However, the response of SGLT2 inhibitors on albuminuria and eGFR varies between individuals and about 20% of patients does not respond at all. Consequently, a considerable proportion of patients remain at high risk of progressive renal function loss. We hypothesize that the variability in drug response between individuals is the result of between individual variability in drug disposition to target tissues. To test this hypothesis we have synthesized an 18F PET radiotracer of the SGLT2 inhibitor canagliflozin, retaining the original molecular structure. As a first step, we will evaluate 18F-canagliflozin receptor specific binding, receptor occupancy, and optimal PET scanning time. As such, in this clinical feasibility study, we will generate essential PET data to optimize the design of a future clinical study in subjects with type 2 diabetes and microvascular complications.

Study objective

We hypothesize that the underlying mechanisms of the varying response to a drug in multiple parameters within an individual can be attributed to variability in the causal path between drug administration, drug tissue distribution, and tissue receptor interaction.

In this clinical feasibility study we will assess radiolabeled canagliflozin pharmacokinetic characteristics and determine specific receptor binding, receptor occupancy and optimal scanning time in patients with diabetes. The main objectives are;

To assess canagliflozin target (i.e. receptor) specific binding in vivo

To assess receptor occupancy of canagliflozin in vivo

Study design

During both study days, for all patients, after radiotracer drug administration, arterial plasma samples will be taken obtained by an automated sampler for radioactivity in full blood and plasma. After administration of oral canagliflozin 11 venous blood samples will be obtained for canagliflozin PK assessment. 24-hour urine will be collected for the measurement of 24-h glucose, protein, albumin, sodium, potassium, creatinine, and urea excretion at both study days. Plasma glucose will be measured after oral canagliflozin administration.

Intervention

On the first study day, a non-diagnostic dose CT scan will be performed to optimally position the individual patient for the dynamic PET scan (e.g. with kidney, aorta and part of the liver inside the field of view) and attenuation correction, respectively. At time=0, patients will receive an intravenous diagnostic dose of 200Mbq 18F canagliflozin radiotracer followed by a 90-minute dynamic PET scan. At the second visit patients will receive an oral dose of 50, 100 or 300 mg canagliflozin (3 patients per dose group). At the approximate time of maximal plasma canagliflozin concentration (tmax, t=2.5h) a second intravenous radiotracer dose will be administered immediately followed by a second 90-minute dynamic PET scan. In this second scan, receptor binding sites are occupied by canagliflozin, hence the reduction of radiotracer uptake compared to the baseline scan can be used to determine the receptor occupancy based on the binding potentials obtained from both scans. In all patients arterial plasma samples will be taken after radiotracer administration, to quantify radiation measures of 18F canagliflozin and its metabolites and venous blood samples will be taken after oral canagliflozin administration to obtain plasma concentrations of canagliflozin.

Contacts

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Eligibility criteria

Inclusion criteria

Type 2 diabetes
Age ≥ 40 years <75 years
Written informed consent

Exclusion criteria

• Pregnant women and women of child-bearing potential who are not using reliable contraception
• eGFR < 30 mL/min/1.73 m2
• Subjects on diuretics are allowed to participate but the dose should be stable for at least 4 weeks prior to screening
• Subjects already on a SGLT2 inhibitor are allowed to participate, but the drug should be interrupted 1 week prior to the first study day till the end of the second study day
• Subjects using a sulphonylurea.
• Established peripheral arterial disease
• Cardiovascular disease: myocardial infarction, angina pectoris, percutanous transluminal coronary angioplasty, coronary artery bypass grafting, stroke, heart failure (NYHA I-IV) < 3 months before inclusion
• History of hypersensitivity to canagliflozin or another SGLT2 inhibitor
• Active malignancy
• 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.
• Any medication, surgical or medical condition which might significantly alter the absorption, distribution, metabolism, or excretion of medications including, but not limited to any of the following:

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2020
Enrollment:	9
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable
Application type: Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 50114
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL7707
CCMO	NL70157.042.19
OMON	NL-OMON50114

Study results