Rotation for Optimal Targeting of Albuminuria and Treatment Evaluation

No registrations found.

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

Summary

ID

NL-OMON26322

Source
Nationaal Trial Register

Brief title
ROTATE-2

Health condition

Type 2 diabetes and albuminuria

Sponsors and support

Primary sponsor: University Medical Center Groningen
Source(s) of monetary or material Support: PROTON project, Novo Nordisk Foundation

Intervention

Outcome measures

Primary outcome

Albuminuria reduction

Secondary outcome

Glycocalyx thickness

Study description

Background summary

Rationale: Clinical practice guidelines recommend ACE-inhibitors or ARBs to all patients with diabetes and elevated albuminuria. Strikingly, 30 to 40% of patients do not respond to these first choice guideline recommended drugs. Previous cross-over studies showed that uptitrating the dose of the ACEi or ARB or rotation from ACEi to ARB (or vice versa) did not solve therapy resistance. These data suggest that patient factors in stead of drug factors determine individual drug response. Whether rotation to drugs from other drug classes improve drug response to therapy resistant patients is not prospectively investigated, but may be expected given the variable pathogenesis of diabetes and the supposedly different mechanisms of action of different albuminuria lowering drug classes. A better understanding on the individual response to different albuminuria lowering drugs may help to tailor optimal therapy.

Objective: To determine the individual albuminuria lowering response of four different albuminuria lowering drug classes in patients with type 2 diabetes and micro and macroalbuminuria.

Study design: A randomized, prospective, double blind, multicentre, crossover trial with a total duration of 48 weeks.
Study population: Patients with type 2 diabetes of at least 18 years or older and elevated albuminuria (> 50 mg/g).
Intervention (if applicable): Patients receive in random order 4 weeks of treatment with a angiotensin receptor blocker (telmisartan 80 mg/day), SGLT2 inhibitor (empagliflozin; 10 mg/day), DPP4 inhibitor (linagliptin 5 mg/day) and a glycosaminoglycan (sulodexide 200 mg/day) with 4-weeks wash-out periods in between. After the last treatment period patients will be re-reandomized to a 4-week treatment period to the drug that induced the strongest or least strong albuminuria-lowering response for that particular patient.

Main study parameters/endpoints: The main study endpoint is the proportion of patients in whom the drug selected in the fifth treatment period exerts the strongest or least strong albuminuria lowering effect compared to the drugs used in the other treatment periods for each individual.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: At the beginning and end of each treatment period blood is collected for clinical chemistry. Patients are requested to collect first morning void urine samples every 2 weeks throughout the study. Office blood pressure and body weight are monitored every 4 weeks. There are no direct benefits for the patients to be included and participation is on a free-will base.

Study design

Treatment periods last 4 weeks, with 4 weeks of wash-out in between consecutive treatment periods. Blood and urine samples are measured every 4 weeks.

Intervention

-Telmisartan

-Empagliflozin

-Linagliptin

-Sulodexide

Contacts

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Eligibility criteria

Inclusion criteria

• Type 2 diabetes

• eGFR > 45ml/min/1.73m2

• Albumin:creatinine ratio >50mg/g and ≤500 mg/g

• 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 (office bp > 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 or longer if required by local regulations, and for any other limitation of participation based on local regulations.

• 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:

o Major gastrointestinal tract surgery such as gastrectomy, gastroenterostomy, or bowel resection;

o Gastro-intestinal ulcers and/or gastrointestinal or rectal bleeding within last six months;

o Pancreatic injury or pancreatitis within the last six months;

o Evidence of hepatic disease as determined by any one of the following: ALT or AST values exceeding 3x ULN at inclusion visit, a history of hepatic encephalopathy, a history of esophageal varices, or a history of portocaval shunt;

o Evidence of urinary obstruction of difficulty in voiding at screening

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2016
Enrollment:	52
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL5459
NTR-old	NTR5603
Other	: 2015-005113-73

Study results