NT-proBNP Selected PreventiOn of cardiac eveNts in a populaTion of dIabetic patients without A history of Cardiac disease a prospective randomized trial

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

Summary

ID

NL-OMON47526

Source
ToetsingOnline

Brief title
Prevention of cardiac events by T2DM patients

Condition

- Diabetic complications

Synonym
diabetes cardiac disease, diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Medical university of Vienna
Source(s) of monetary or material Support: sponsor

Intervention

Keyword: Prevention cardiac events T2DM

Outcome measures

Primary outcome

Superiority of high dose treatment with RAS-antagonists and beta-blockers compared to conventional therapy regarding the reduction of unplanned hospitalization or death due to a cardiac event in T2DM patients with a NT-proBNP > 125pg/ml.

Co-primary objective

Superiority of high dose treatment with RAS-antagonists and beta-blockers compared to conventional therapy regarding the reduction of unplanned hospitalization or death due to a cardiac event in T2DM patients in the whole study population

Secondary outcome

Dependency of treatment efficacy (reduction of unplanned hospitalization or death due to a cardiac event in T2DM patients) on the NT-proBNP concentration (interaction effect between NT-proBNP concentrations and treatment).

Study description

Background summary

PONTIAC was designed as a proof of concept study. The number of patients

included was low and accordingly confirmation in a larger cohort is mandatory. Secondly, the hypothesis that the treatment effect is restricted to patients with high NT-proBNP levels cannot be deduced from the data. In this context a concordant relationship between risk and treatment efficacy can be assumed. This would result in an increasing number needed to treat up to a point of ineffectiveness, depending on underlying risk. But, also a discordant relationship is possible as side effects or over-suppression of neurohumoral systems can lead to a preponderance of side effects over small or non-existing treatment effects. Such a discordant treatment effect is called *interaction effect* in statistical methodology. A cohort of patients without any evidence of a cardiac disease, independent of NT-proBNP is mandatory to test for such interactions. All these populations have to be evaluated in regard to safety and efficacy. As both investigated groups of drugs are registered, the design for a further study will be a post-authorization efficacy study (PAES) and a post-authorization safety study (PASS) in distinct populations.

Study objective

The purpose of this study is to evaluate the effect of high dose RAS-antagonists and beta-blocker treatment for the primary prevention of cardiac events in a population of patients with Type 2 diabetes mellitus (T2DM) with no evidence of a preexisting cardiac disease. This will be done in patients with NT-proBNP concentrations > 125pg/ml and the whole study population. An additional aim is to demonstrate the dependency of the treatment efficacy on the level of amino-terminal pro-B type natriuretic peptide (NT proBNP) as a surrogate of imminent cardiac risk (so called interaction between NT proBNP and treatment). A health economic analysis will objectify the impact on health care costs in accordance to the endpoints.

Study design

This study is a randomized parallel group, active-controlled, two-arm, long-term morbidity and mortality trial to evaluate the efficacy and safety of high dose RAS-antagonist and beta-blocker therapy compared to standard diabetes therapy in patients with diabetes without any history or sign of a cardiac disease.

Intervention

Echocardiography, ECG, bloodsamples and EuroQOL

Study burden and risks

Burden:
The time involved in this study, in the clinic is approximately 5 hours

Risk:
patiënt can not tolerate the full dose of the medication with signs of bradycardia, clinically significant hypotension (symptomatic, increase of serum Creatinine, hyperkalemia.
Potentiallly there are risks related to the insertion of a needle for the bloodsamples, those are bruising, pain, dizziness and bleeding

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 mellitus for at least six months
>18 years of age men or female
written informed consent to participate in the study and ability to comply with

all requirements

Exclusion criteria

maximum dose of RAS-antagonists or beta-blocker
symptomatic hypotension and/or systolic blood pressure < 100 mgHG at visit 1
symptomatic bradycardia and/or heart rate < 60 bpm at visit 1
history of hypersensivity to any of the drugs investigated as well as known or suspected contraindications to the study drug of previous history of intolerance to high dose of RAAS antagonists or beta-blocker in the absence of any other bloddpressure lowering drugs
Creatinin > 2.5 mg/dl

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-03-2018
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	bisoprolol, metprololsuccinat, carvedilol, nebivolol...Zie sectie J opmerkingen
Generic name:	Beta-blockers

Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	enalapril, ramipril,lisinopril,cilazapril,perindopril, etcZie sectie J opmerkingen
Generic name:	RAS-Antagonists
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	28-06-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-08-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2015-000239-34-NL
ClinicalTrials.gov	NCT02817360

Register	ID
CCMO	NL58644.068.16