Effect of Aliskiren on Muscle Sympathetic Nerve Activity (MSNA) in hypertensive patients with chronic kidney disease

Published: 10-06-2008
Last updated: 10-05-2024

The central hypothesis of this project is that Aliskiren causes a substantial decrease in MSNA in hypertensive patients with CKD.

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

Summary

ID

NL-OMON31722

Source
ToetsingOnline

Brief title
Aliskiren and MSNA in hypertensive patients with chronic renal disease

Condition

- Other condition
- Nephropathies

Synonym
chronic kidney disease, Chronic renal diseases

Health condition

Hypertensie

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Afdeling nefrologie UMC Utrecht

Intervention

Keyword: Chronic Kidney Disease, Hypertension, Muscle Sympathetic Nerve Activity (MSNA), Renin inhibitor

Outcome measures

Primary outcome

Primary endpoint

- the effect of Aliskiren 300mg on MSNA

Primay outcome:

- a substantial decrease in MSNA after 6 weeks treatment with Aliskiren

Secondary outcome

Secondary study parameters

- Assessment whether normalization of MSNA is obtained after treatment with

Aliskiren 300mg/day

- Comparison of the effect on MSNA after treatment with aliskiren with the

effects on ACEi and ARB as comared to the previous studies

- Effect of aliskiren on blood pressure, heart rate, PRA and kidney function.

Secondary outcome:

- Normalization of MSNA will be obtained after treatment with Aliskiren 300mg

- Treatment with Aliskiren 300mg will result in more inhibition of MSNA than

treatment with ACEi and ARB

-We expect a substantial blood pressure decrease, no or little effect on heart

rate, inhibition of PRA and no effect on kidney function.

Study description

Background summary

Cardiovascular (CV) morbidity and mortality are frequently occurring problems in chronic kidney disease (CKD) patients. Apart from the so called traditional risk factors, also risk factors more or less specific to CKD contribute in the pathogenesis of these problems. There is strong evidence that the sympathetic hyperactivity, which often characterizes CKD, is one such factor. Previously, we have shown that angiotensin converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARB) reduce but not normalize this sympathetic hyperactivity. We re-analysed the cohort of patients who were investigated in the past and subsequently treated according to present guidelines. The results show that, despite of treatment, the unfavourable relation between sympathetic hyperactivity and clinical outcome still exits. This might mean that treatment is insufficient. In present study, we want to study the effect of Aliskiren 300mg on sympathetic nerve activity.

Study objective

The central hypothesis of this project is that Aliskiren causes a substantial decrease in MSNA in hypertensive patients with CKD.

Study design

This study is designed as a randomized trial. We collect data on activity of MSNA at two different conditions:

1. At baseline when participants are taken off antihypertensive medication while other medications will be continued.
2. After 6 weeks treatment of participants with Aliskiren 300mg/day and no ACE inhibitor or ARB is given. Other medication, including phosphate binders, vitamine D derivatives, erythropoietine etc will be continued during the whole study. Importantly, also diuretics are continued throughout the study in order to maintain normovolemia, which is evidenced by extracellular volume assessment (bromide distribution).

During the first visit the patient will be randomized into two groups:

o Group 1: Take off ACE inhibitor and ARB for 4 weeks AND after 4 weeks "off-treatment" start with Aliskiren 300mg/day for 6 weeks

o Group 2: Take off ACE inhibitor and ARB and start directly with Aliskiren 300mg/day for 6 weeks. After 6 weeks of Aliskiren the participants will be put in "off-treatment" period i.e. no ACE inhibitor or ARB and no Aliskiren

See Protocol, the FLOWCHART on page 19, for an overview of the study design.

Intervention

Patients will be asked to take off ACE inhibitors and ARB and start directly with Aliskiren 300mg/day for 6 weeks. The first MSNA measurement will be done. After 6 weeks of treatment with only Aliskiren patients will be place in "off-treatment" period i.e. no ACE inhibitor, no ARB and no Aliskiren for 4 weeks. The second MSNA measurement will be done.

OR

The order of treatment will be randomized:

Patients will be put in "off-treatment" period first, the first MSNA measurement will be done. Then patients will start with Aliskiren 300mg/day and

still no ACE inhibitor or ARB. The second MSNA measurement will be done.

Study burden and risks

The risks associated with participation in this study are very limited.

Microneurography: there are no risks associated with this procedure. Usually, nerve recordings cause minimal discomfort and negligible, transient after-effects, when studies are done by an experienced technician.

Aliskiren: de safety of Aliskiren 300mg is studied among 7.800 patients. The incidence of side effects was comparable to the placebo group. In general the side effects were mild and spontanously disapeared. The most common side effects are diarrhea and skin rash. See our study protocol "SUMMARY OF KNOWN AND POTENTIAL RISKS" for more information.

Contacts

Public
Academisch Medisch Centrum

Heemraadweg 523
1382HV Weesp
NL
Scientific
Academisch Medisch Centrum

Heemraadweg 523
1382HV Weesp
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients with stable chronic kidney disease and hypertension: i.e. using antihypertensive drugs and/or blood pressure >145/90mmHg when off medication.;- patients on ACE inhibitor or ARB

Exclusion criteria

Patients with diabetes mellitus
Patients on renal replacement therapy
Pregnant patients
Using of antihypertensive which cannot be stopped
Patients on immunossuppressive therapy and active nephrotic syndrome

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-07-2008
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Rasilez 300 mg
Generic name:	Aliskiren 300mg
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	10-06-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-02-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2007-005401-22-NL
CCMO	NL19926.041.07