An exploratory open-label PET-observer-blinded pilot study to evaluate the effect of 3 and 12 months treatment with Aliskeren-based versus amlodipin-based antihypertensive treatment in patients with a small abdominal aortic aneurysm and mild to moderate hypertension on aneurysmal FDG-uptake as measured with FDG PET

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Main objective: * To evaluate the effect and variation of 3 and 12 months treatment with Aliskeren-based versus amlodipine-based antihypertensive treatment on aneurismal FDG-uptakeExploratory objectives: * To explore the effect of 3 and 12 months...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Aneurysms and artery dissections
Study type	Observational invasive

Summary

ID

NL-OMON35808

Source
ToetsingOnline

Brief title
Aliskiren_AAA_PET

Condition

- Aneurysms and artery dissections

Synonym
dilatation of the abdominal aorta

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: (1) Novartis - bloeddrukregistratie; (2) Eigen researchstichting (extra PET/CTs)

Intervention

Keyword: abdominal aortic aneurysm, FDG-PET, hypertension

Outcome measures

Primary outcome

- Change from baseline in aneurismal FDG-uptake as measured with PET-CT after 3

and 12 months

Secondary outcome

- Variation of aneurismal FDG-uptake as measured with PET-CT after 3 and 12

months

- Change from baseline in aneurismal diameter after 12 months

- Change from baseline in FDG-uptake in other large blood vessels after 3 and

12 months

Study description

Background summary

Standard therapy of small AAAs currently consists of *watchful waiting* strategy with aggressive blood pressure (BP) control. This includes a Ultrasound (more recently CT or MRI scan) every 12 months (for AAAs between 3.5 * 4.4 cm) or every 6 months (for AAAs between 4.5 and 5.5 cm) to observe whether the AAA is growing in diameter. AAAs with a diameter > 5.5 cm (fulfilling the definition of large AAAs) are generally considered eligible for repair (exclusion from the circulation) using open abdominal surgery or endovascular aneurysm repair (EVAR) to prevent fatal rupture. For patients with small AAAs, the risk of surgery is generally considered higher than the risk of rupture. Recent publications have shown that evaluation of AAAs using FDG-uptake with PET-scan may identify small AAAs that are more prone to grow and/or rupture as these AAAs as compared to normal aorta*s show increased inflammatory activity which is considered the major pathophysiological pathway. Evaluation of FDG-uptake is also sensitive enough to observe the short-term effects of endovascular intervention of large AAAs, as unpublished data show a statistically significant reduction in aneurismal FDG-uptake only 6 weeks after endovascular repair of large AAAs. Therefore, the change in aneurismal FDG-uptake may also be a very promising and sensitive method to evaluate treatment effects of medical interventions within a relatively short period of time (3 months).

Study objective

Main objective:
* To evaluate the effect and variation of 3 and 12 months treatment with Aliskeren-based versus amlodipine-based antihypertensive treatment on aneurismal FDG- uptake

Exploratory objectives:
* To explore the effect of 3 and 12 months treatment with Aliskeren-based versus amlodipine-based antihypertensive treatment on aneurismal growth (diameter), to explore any relationships between aneurismal FDG-uptake, aneurismal diameter, and medical intervention, and to explore the change in FDG-uptake in other large blood vessels (ascending thoracic aorta, descending thoracic aorta, suprarenal abdominal aorta, iliac, and femoral arteries)

Study design

This study is designed to explore the effect of 3 and 12 months treatment with Aliskeren-based versus amlodipine-based antihypertensive treatment on aneurismal FDG-uptake, by performing a first PET scan pre-treatment, a second PET scan after 3 months treatment, and the last PET scan after 12 months treatment. As mentioned previously, significant changes in aneurismal FDG-uptake were observed 6 weeks after endovascular intervention.
As the effects of medical intervention may take longer to observe, the second PET scan is to be performed after 3 months of treatment. An interim analysis on

the changes on FDG-uptake after 3 months will be performed after all patients have undergone their 2nd PET scan after 3 months of treatment.
In order to compare changes in aneurismal FDG-uptake with aneurismal growth (observable after 12 months), the last PET scan is to be performed after 12 months of treatment.
In order to compare the effects of Aliskeren-based versus amlodipine-based antihypertensive treatment on FDG-uptake, an open label parallel group design is considered the most appropriate. To minimize observer-bias for the primary endpoint, PET-observers will be blinded for the treatment of the patients.

Study burden and risks

Burden/risks:
The burden that accompanies participation in this study consists of 1 extra and 2 prolonged visits to our medical center. Furthermore patients will have to measure their blood pressure daily and have to wear a blood pressure cuff for 24 hours once every 4 months. Finally patients are exposed to radiation when undergoing PET/CT scanning, i.e. 12,5 mSv of extra radiation exposure in a period of 1 year.

Potential benefits:
In patients with a small AAA, aggressive BP control is an important part of the treatment in delaying aneurysm growth. After administration of aliskiren, good BP lowering results have been obtained in previous studies. If insufficient BP lowering is achieved, addition of hydrochlorothiazide is allowed, in order to obtain good BP control. Therefore, patients in the aliskiren-based arm will benefit from the BP lowering effects of aliskiren with or without hydrochlorothiazide. Similarly, after administration of amlodipine, good BP lowering results have been published. If insufficient BP lowering is achieved, addition of hydrochlorothiazide is allowed, in order to obtain good BP control. Therefore, patients in the amlodipine-based arm will benefit from the BP lowering effects of amlodipine with or without hydrochlorothiazide.

Risk Benefit assessment:
The use of the Home BP monitoring device, the inclusion- and exclusion criteria (especially concerning lab values, vital signs, and abnormal blood pressure), the safety assessments (regarding vital signs, blood pressure, clinical lab, and AEs), and the discontinuation criteria (regarding unacceptably high blood pressures, hypotension, and clinically significant safety assessments/lab values) are considered sufficient to minimize the potential risks to the patients.

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

1. Patients with a proven AAA of >30 mm and < 55 mm
2. Age: as of 18 years old
3. Weight > 50 kg
4. Mild to moderate hypertension (defined as 130 < msSBP < 180 or 85 < msDBP <110), at screening and/or baseline, without current antihypertensive medication.

Exclusion criteria

1. Patients without an AAA, or with an AAA * 55 mm, or * 30 mm
2. Patients with an AAA who are eligible for surgical repair for any reason
3. Diabetes mellitus

4. Inability of the subjects to switch from all prior antihypertensive medications safely as required by the protocol and need for drugs other than study drugs at the time of baseline
5. Severe hypertension (msSBP *180 mmHg and/or msDBP *110 mmHg) at screening and/or baseline
6. Pregnant or nursing (lactating) women
7. Known or suspected contraindications, including history of allergy or hypersensitivity (such as angioedema) to DRIs, CCBs, ACEIs, statins or diuretics in general (for example, to aliskiren / amlodipine / hydrochlorothiazide / statins)
8. Concomitant drugs that are strong inhibitors of CYP3A4 or P-glycoprotein inhibitors (ketoconazole, itraconazole, nefazodone, rolandeomycin, clarithromycin, ritonavir, nelfinavir, cyclosporine, verapamil, quinidine)
9. Previous or current diagnosis of heart failure (NYHA Class II-IV)
10. Second or third degree heart block without a pacemaker, or potentially life-threatening arrhythmia during the 12 months prior to screening
11. Clinically symptomatic valvular heart disease at screening visit
12. A past medical history of clinically significant ECG abnormalities
13. Confirmed serum potassium *5.3 mEq/L (mmol/L) at screening or baseline.
14. Impaired renal function, defined as eGFR < 45 mL/min/1.73 m2 MDRD
15. Donation or loss of 400 ml or more of blood within eight (8) weeks prior to initial dosing, or longer if required by local regulation
16. Participation in any clinical investigation within four (4) weeks prior to first dose or longer if required by local regulations, and for any other limitation of participation based on local regulations.
17. Patients who have undergone prior radionuclide treatment or examinations or X-ray examinations with a cumulative radiation exposure, which added to the radation exposure of the current study, would exceed local limits.

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-12-2011
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	amlodipine
Registration:	Yes - NL intended use
Product type:	Medicine
Generic name:	hydrochlorothiazide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	rasilez
Generic name:	aliskiren
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	10-05-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-01-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2011-000538-12-NL
CCMO	NL35683.029.11