EFFECTS OF ANGIOTENSIN-RECEPTOR BLOCKADE WITH OLMESARTAN ON CAROTID ATHEROSCLEROSIS IN PATIENTS WITH HYPERTENSION: THE CONFIRMATORY OLMESARTAN PLAQUE REGRESSION STUDY (CONFIRM)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON34922

Source
ToetsingOnline

Brief title
CONFIRM

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerosis, hardening of the arteries

Research involving

Human

Sponsors and support

Primary sponsor: Daiichi Pharmaceutical
Source(s) of monetary or material Support: Daiichi Sankyo

Intervention

Keyword: atherosclerosis, hypertension, olmesartan

Outcome measures

Primary outcome

The primary efficacy variable is the change in PV from baseline as assessed by 3 D ultrasonography after 78 weeks of double-blind treatment with OM 20-40 mg daily compared to ATE 50-100 mg daily.

Secondary outcome

Secondary efficacy variables:

Change from baseline PV at Week 52.

Percent change from baseline PV at Week 52 and at Week 78.

Change from baseline SeDBP and SeSBP at Week 52 and at Week 78.

Change from baseline PV after adjustment for change in SeDBP and SeSBP at Week 52 and at Week 78.

Study description

Background summary

Anti-hypertensive therapy only is not sufficient in the treatment of cardiovasculair diseases. A combination of anti-hypertensive therapy and prevention or retard of atherosclerosis is considered more effective. OM is a drug that lowers bloodpressure, but also has shown in experimental models that it is effective against atherosclerosis. These experimental findings have to be confirmed in humans.
The hypothesis of this study is: Is OM superior compared to ATE in regard to the change from baseline in carotid plaque volume after 78 weeks of treatment.

Study objective

The primary efficacy variable is the change in PV from baseline as assessed by 3 D ultrasonography after 78 weeks of double-blind treatment with OM 20-40 mg daily compared to ATE 50-100 mg daily.
Secondary efficacy variables:
Change from baseline PV at Week 52.
Percent change from baseline PV at Week 52 and at Week 78.
Change from baseline SeDBP and SeSBP at Week 52 and at Week 78.
Change from baseline PV after adjustment for change in SeDBP and SeSBP at Week 52 and at Week 78.

Study design

A randomised, double-blind, double-dummy, parallel-group, multi-national, multi-centre trial.

Intervention

Subjects will be assigned to double-blind treatment groups with OM 20 mg tablets o.d. or ATE
50 mg tablets o.d. (low dose) taken orally in the mornings with the option to increase the dose to
OM 40 mg or ATE 100 mg (high dose) for subjects not achieving blood pressure goal.

Study burden and risks

Medical history and background. Physical exam, bloed and urinetests at the beginning and at the end of the study (2x). women with childbearing potential need to underg a pregnancy test at the start and at the end of the study (2x). Bloodpressure, heartrate and adverse event information will be done at every visit (13x). Waist, bodyweight, 3 D ultrasonography and ECG will be done 3x. All medication used in this trial are marketed products and the safety profile

is documented in the SmPCs.

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. Male and female Caucasian outpatients aged > 40 years.
2. High BP defined as mean SeSBP/SeDBP * 140/90 mmHg.
3. One or more of the following additional risk factors:
* Smoking;
* Dyslipidaemia (high-density lipoprotein (HDL)-cholesterol < 0.9 mmol/L or low-density lipoprotein (LDL)-cholesterol > 2.6 mmol/L, or triglycerides > 1.7 mmol/L);
* Left ventricular hypertrophy;
* Cardiocerebrovascular events > 6 months ago;
* Presence of target organ damage.

4. Non-calcified (not marked shadowing) plaque in the CC artery, in the internal carotid artery or the carotid bulb with a PV * 0.040 cm^3 (* 40 µL) according to the measurements of EUTARC.

Exclusion criteria

1. Secondary or high grade hypertension including grade III hypertension (SeSBP of > 180 mmHg or SeDBP of > 105 mmHg).
2. Stroke, myocardial infarction within the previous 6 months.
3. Interventional or surgical vascular treatment within the previous 3 months.
4. Presence of significant narrowing of the aortic or bicuspid valve and severe obstruction of cardiac outflow (hypertrophic cardiomyopathy).
5. Symptomatic heart failure.
6. Diabetes.
7. Chronic obstructive pulmonary disease (COPD) or asthma.
8. Claudicatio intermittens stage II b or higher.
9. Clinical evidence of severe renal disease [including renovascular occlusive disease, nephrectomy and/or renal transplant, creatinine clearance of < 30 mL/min), macroalbuminuria (> 300 mg albumin/24 hours or 300 µg albumin/mg creatinine)].
10. Treatment with angiotensin converting enzyme (ACE)-inhibitors or angiotensin-receptor blockers (ARBs) during last 3 months.
11. Start of treatment with a lipid-lowering agent or modification of dosage within last 3 months.
12. Electrocardiographic (ECG) evidence of 2nd or 3rd degree atrioventricular (AV) block, atrial fibrillation, cardiac arrhythmia (requiring therapy) or bradycardia (< 50 beats/min at rest).
13. Known intolerance to study drugs.
14. Impaired liver function tests suggesting severe liver disorder.
15. Any life threatening disease.
16. Duplexsonographically determined stenosis of the common or internal carotid artery > 75%.
17. Plaque with marked shadowing from calcification.
18. Target plaques in CC artery extending into both internal and external arteries.
19. Pregnant or lactating female subjects.
20. Female subjects of childbearing potential without adequate contraception: intra-uterine devices, hormonal contraceptives, either oral, depot, patch or injectable and double barrier methods such as condoms or diaphragms with spermicidal gel or foam. If a female becomes pregnant during the trial, she has to be withdrawn immediately (see section 9.4).
21. Subject is currently enrolled in or has not yet completed at least 30 days since ending another investigational device or drug study or is receiving other investigational agents.
22. Subject has previously entered this study.
23. Subjects who have received ATE within 30 days prior to entering the active treatment phase.
24. Subjects who are unwilling or unable to provide informed consent or to participate satisfactorily for the entire trial period.

25. Subjects with history of alcohol and or drug abuse.
26. Subjects with known malabsorption syndrome.
27. Subjects who had donated or lost 450 mL or more blood during the last three months before screening.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-10-2010
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Atenolol
Generic name:	Atenolol
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Doxazosin mesylate
Generic name:	Doxazosin mesylate
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	Hydrochlorothiazide
Generic name:	Hydrochlorothiazide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Olmetec
Generic name:	Olmesartan medoxomil
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-12-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-07-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-07-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-09-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-09-2010
Application type:	Amendment
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	EUCTR2009-013342-92-NL
CCMO	NL30204.068.09
Other	Registratie is nog niet voltooid