A double blind, randomized, parallel, study to assess the effects of aliskiren/amlodipine and amlodipine monotherapy on ankle foot volume (AFV) in patients naïve to trial drugs with mild to moderate hypertension.

Published: 16-12-2009
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Primary objective:To assess and compare the effects of aliskiren/amlodipine and amlodipine on pedal edema after 4 weeks of treatment as measured by ankle foot volume (AFV) (water displacement method) in patients with mild to moderate hypertension....

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Vascular hypertensive disorders
Study type	Interventional

Summary

ID

NL-OMON35085

Source
ToetsingOnline

Brief title
Effect of SPA on AFV

Condition

- Vascular hypertensive disorders

Synonym
high blood pressure, hypertension

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: - hypertension, - pedal edema

Outcome measures

Primary outcome

Difference in ankle foot volume (AFV) between baseline and after 4 weeks

treatment.

Secondary outcome

Blood pressure at different time points, ECG evaluations and standard clinical

laboratory evaluations (hematology, blood chemistry, urinalysis).

Study description

Background summary

The renin-angiotensin system (RAS) plays a major role in the regulation of arterial blood pressure and the pathogenesis of hypertension. Aliskiren is the first in a new class of antihypertensives, direct renin inhibitor. Amlodipine is a long-acting dihydropyridine calcium channel blocker and the most commonly prescribed drug in this class. It has demonstrated clinical efficacy in a wide range of the hypertensive patient population in reducing blood pressure. Ankle edema is one of the most frequent side effects of antihypertensive therapy with calcium channel blockers.

Study objective

Primary objective:
To assess and compare the effects of aliskiren/amlodipine and amlodipine on pedal edema after 4 weeks of treatment as measured by ankle foot volume (AFV) (water displacement method) in patients with mild to moderate hypertension.

Secondary objective:
To assess the safety and tolerability of aliskiren/amlodipine and amlodipine in patients with mild to moderate hypertension.

Study design

The study is planned as a multi-center, double blind, randomized, parallel study with blinded 2-week placebo run-in phase in patients with mild to moderate hypertension.

A total of 88 hypertensive male and female subjects will be enrolled and randomized in equal numbers to 2 treatments. Each subject will participate in a screening period (up to 14 days), a 2-week washout period, a 2-week blinded run-in period, followed by one 4-week treatment period, and an end of study evaluation.

During the washout period and during the single blinded placebo run-in period, all patients will check blood pressure using a home blood pressure monitoring device once daily in the morning. Patients must discontinue the washout period or the run-in period if the blood pressure rises to unacceptable levels.

During each treatment period, the subject will receive one of the treatments at a lower dose for 1 week on an out patient basis. The subject will then be force up-titrated to the study dose which will continue for 3 more weeks.

Subjects will be instructed to return to the clinics at specified time for safety and PK/PD assessments. Pharmacodynamic assessments (ankle foot volume) will be assessed at the beginning, and after 4 weeks of treatment.

Similarly, safety assessments will be performed at screening, baseline, end of week 1, end of week 4 and end of study. These will include physical examinations, ECGs, vital signs, standard clinical laboratory evaluations (hematology, blood chemistry, urinalysis), adverse event and serious adverse event monitoring.

Intervention

SPA100 arm: Aliskiren/amlopdipine 150/5 mg/day and placebo to amlodipine for the first week and then up-titrated to aliskiren/amlodipine 300/10 mg/day (2x150/5 mg) and placebo to amlodipine for the next 3 weeks.

Amlodipine arm: Amlodipine 5 mg/day and placebo to 150/5 mg aliskiren/amlodipine for the first week and then up-titrated to amlodipine 10 mg/day and placebo to 300/10 mg (2x150/5 mg) Aliskiren/amlodipine for the next 3 weeks.

Study burden and risks

Burden:
Each subject will participate in a ascreening period (up to 14 days), a 1 to 3-week wash-out period, a 2-week blinded placebo run-in period, followed by one 4 week treatment period, and an end of study evaluation. At the screening visit, if the subject meets all inclusion/exclusion criteria the subject will be asked to discontinue or taper-off all current antihypertensive therapy during the washout period and will then enter in a single-blind run-in phase with placebo for 2 weeks. During each treatment period, the subject will receive one of the treatments at a lower dose for 1 week on an out patient basis. The subject will then be force up-titrated to the study dose which will continue for 3 more weeks. Subjects will be instructed to return to the clinics at specified time for safety and PK/PD assessments.
Safety assessments will include physical examinations, ECGs, vital signs, standard clinical laboratory evaluations (hematology, blood chemistry, urinalysis), adverse event and serious adverse event monitoring.

Potential risks:
Single dose and multiple dose administration of the fixed-dose combination in healthy subjects and patients with hypertension was well tolerated and safe. The most frequent AEs were peripheral edema, headaches, diarrhea, dizziness, cough. Similar AEs can be expected for the current study.

Potential benefits:
This study is designed to evaluate whether the addition of aliskiren to amlodipine can attenuate ankle edema formation in hypertensive patients treated for 4 weeks. The combination of aliskiren/amlodipine (300/10 mg) has been proven to be efficacious in decreasing blood pressure. Blood pressure reduction may therefore be the main benefit for the subjects to participate in this study. For subjects in the SPA group, there may be less side-effect in the form of pedal edema.

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

- Male or female 18-75 yrs old
- Mild to moderate hypertension
- Amlopdipine naïve
- Body mass index (BMI) must be 18-32 kg/m2

Exclusion criteria

- Inability of the subjects to switch from all prior antihypertensive medications
- Severe hypertension at screening or baseline.
- Heart failure
- T1DM / T2DM

Study design

Design

Study phase:	2
Study type:	Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-03-2010
Enrollment:	88
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Norvasc
Generic name:	amlodipine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	SPA100
Generic name:	aliskiren/amlodipine

Ethics review

Approved WMO

Date:	16-12-2009
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

Approved WMO

Date:	21-01-2010
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

Approved WMO

Date:	16-02-2010
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	02-03-2010
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	08-07-2010
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	24-08-2010
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	30-08-2010
Application type:	Amendment
Review commission:	STEG: Stichting Therapeutische Evaluatie Geneesmiddelen (Almere)

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	EUCTR2009-014359-63-NL
CCMO	NL30462.040.09