A multicentre randomised, double blind, active controlled, parallel group comparison of Nebivolol plus HCTZ and Irbesartan plus HCTZ in the treatment of isolated systolic hypertension in elderly patients: The NEHIS study.

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To demonstrate the superiority of the combination Nebivolol plus HCTZ versus Irbesartan plus HCTZ in terms of SBP reduction after 12 weeks of treatment in elderly patients with isolated systolic hypertension.

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

Summary

ID

NL-OMON36031

Source
ToetsingOnline

Brief title
The NEHIS study

Condition

- Vascular hypertensive disorders

Synonym
isolated systolic hypertension / isolated elevated systolic bloodpressure

Research involving

Human

Sponsors and support

Primary sponsor: Menarini International Operations Luxembourg S.A : Mr. Alessandro Casini
Source(s) of monetary or material Support: Sponsor: Menarini International Operations Luxembourg S.A

Intervention

Keyword: elderly, irbesartan, isolated systolic hypertension, nebivolol

Outcome measures

Primary outcome

The primary efficacy variable will be the change from baseline (Day 0) to the

end of treatment (Day +84) in systolic blood pressure.

Secondary outcome

Percentage of normalized patients (mean SBP <= 140 mmHg)at the end of treatment

(Day +84);

Percentage of responding patients (decrease of mean SBP >= 20 mmHg)at the end of

treatment (Day +84);

Change from baseline to the end of treatment (Day +84) in the 24-hour mean SBP,

measured by ABPM;

Change from baseline to the end of treatment (Day +84) in the 24-hour mean DBP,

measured by ABPM;

Change from baseline to the end of treatment (Day +84) in SBP in the last six

hours of the 24-hour dose period (as measured by 24-hour ABPM);

Change from baseline to the end of treatment (Day +84) in DBP in the last six

hours of the 24-hour dose period (as measured by 24-hour ABPM);

Change from baseline to the end of treatment (Day +84) in SBP and DBP for other

time intervals [i.e. daytime mean (06:00-00:00), and night-time mean

(00:00-6:00)] (as measured by 24-hour ABPM).

ABPM readings will be read and evaluated centrally.

Study description

Background summary

Isolated Systolic hypertension is a common and particularly poorly controlled form of hypertension and is a strong predictor of cardiovascular morbidity and mortality.
Encouraging long-term data from clinical trials strongly support the usefulness of adequate antihypertensive treatment in elderly patients with isolated systolic hypertension. Indeed most of patients do not reach an adequate blood pressure control with monotherapy and require a combination therapy with two different antihypertensive agents.
Nebivolol is a novel cardio selective beta-1 blocker with vasodilating properties.
Irbesartan is a recent ATII receptor antagonist; clinical data have demonstrated the efficacy of this drug on blood pressure control, especially isolated systolic blood pressure.
The present study aims to demonstrate superiority of the combination Nebivolol + Hydrochlorothiazide as compared to the combination Irbesartan + Hydrochlorothiazide.

Study objective

To demonstrate the superiority of the combination Nebivolol plus HCTZ versus Irbesartan plus HCTZ in terms of SBP reduction after 12 weeks of treatment in elderly patients with isolated systolic hypertension.

Study design

Double-blind randomised 2 parallel groups study

Intervention

Once daily Nebivolol 5 mg/HCTZ 12.5 mg or Irbesartan 150 mg/HCTZ 12.5 mg for 12 weeks.

Study burden and risks

There is a slight risk of pain or bruising and infection when blood is drawn for laboratory tests.
None of the other study procedures are associated with any clinically significant risks.
Subjects may experience a slight discomfort during the 24-h bloodpressure registration, at times the cuff is inflated.

Possible side effects of Irbesartan are tiredness, dizziness, gastro-intestinal complaints (nausea/vomiting and to a much lesser extend diarrhoea, dyspepsia/heartburn).

Possible side effects of Nebivolol: Headache, dizziness, tiredness and paraesthesia are the most common side effect in clinical studies. Up till 10% of the patients experienced the following side effects: dyspnoe, constipation, nausea, diarrhoea and oedema.

The most common side effects of Hydrochlorothiazide are hypokalaemia, dry mouth, tiredness, muscle cramps, dizziness, gout, worsening of pre-existing diabetes, thrombocytopenia.

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 aged at least 60 years;
• Office systolic blood pressure >140 mmHg and office diastolic blood pressure <= 90 mmHg;
• Subjects should have at least 2 additional risk factors
• Willing to give written informed consent.

Exclusion criteria

•Systolic blood pressure equal to or greater than 180 mmHg at the end of washout (visit 2) or run-in period (visit 3b);
•Differences >20mmHg for SBP and >10mmHg for DBP on 3 consecutive readings at baseline
•Current treatment with more than 2 antihypertensive agents within the last 6 months;
•History of stroke, myocardial infarction, PCI or coronary bypass surgery within the last 12 months
•Symptomatic lower limb ischemia i.e. claudicatio intermittens
•Secondary hypertension (i.e.renovascular, adrenal, endocrine, tumor ..);
•Serum creatinine > 150 µmol/L
•Hepatic impairment defined as ASAT or ALAT >2 x upper normal limit;
•Chronic administration of any medication known to affect blood pressure.
•bradycardia (heart rate < 60 bpm prior to start therapy).
•Acute heart failure, cardiogenic shock or episodes of heart failure decompensation requiring i.v. inotropic therapy;
•Clinically significant ECG abnormalities at baseline.
•Any other medical or mental condition or laboratory abnormality that makes the patient unsuitable for the study in the opinion of the investigator.

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):	17-11-2011
Enrollment:	90
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Karvezide
Generic name:	Irbesartan/Hydrochlorothyzide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Nebilet Plus
Generic name:	Nebivolol/Hydrochlorothiazide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-06-2011
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-10-2011
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	21-10-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2010-023104-28-NL
CCMO	NL35854.028.11