A multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II - IV)

Published: 05-02-2009
Last updated: 06-05-2024

The primary objectives of this study are to test if aliskiren monotherapy is superior or at least non-inferior to enalapril monotherapy (in the entire study population) and/or to test if aliskiren/enalapril combination is superior to enalapril...

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

Summary

ID

NL-OMON39821

Source
ToetsingOnline

Brief title
Atmosphere

Condition

- Heart failures

Synonym
Chronic heart failure

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Aliskiren, Chronic heart failure

Outcome measures

Primary outcome

The primary objectives of this study are to test if aliskiren monotherapy is superior or at least non-inferior to enalapril monotherapy (in the entire study population) and/or to test if aliskiren/enalapril combination is superior to enalapril monotherapy (in the entire study population and/or in the non-diabetic population), in delaying time to first occurrence of either cardiovascular death or heart failure hospitalization in patients with chronic heart failure (NYHA Class II - IV).

Secondary outcome

To evaluate whether, aliskiren monotherapy and/or the combination of aliskiren/enalapril is superior to enalapril monotherapy in improving the clinical summary score (assessed by KCCQ) from baseline to month 12.

Study description

Background summary

The purpose of this study is to evaluate the effect of aliskiren monotherapy (in the entire study population) and aliskiren/enalapril combination therapy (in the entire study population and/or in the non-diabetic population), compared to enalapril monotherapy, on top of conventional CHF treatment (except for ACEi that will be substituted with study treatment), in delaying time to first occurrence of either cardiovascular (CV) death or heart failure hospitalization events in patients with stable chronic heart failure (NYHA Class II - IV). Data from this study is intended to be used to support a supplemental worldwide registration submission of aliskiren for treatment to improve CV death and heart failure hospitalization outcomes in patients with chronic heart failure (NYHA Class II * IV).

Study objective

The primary objectives of this study are to test if aliskiren monotherapy is superior or at least non-inferior to enalapril monotherapy (in the entire study population) and/or to test if aliskiren/enalapril combination is superior to enalapril monotherapy (in the entire study population and/or in the non-diabetic population), in delaying time to first occurrence of either cardiovascular death or heart failure hospitalization in patients with chronic heart failure (NYHA Class II - IV).

Study design

At Visit 1 (screening), patients with chronic heart failure (NYHA Class II * IV) on stable pharmacological treatment for heart failure for at least four weeks prior to visit (except for diuretics) and meeting all inclusion criteria, will enter a stabilization active run-in period (3-12 weeks), during which the tolerability to enalapril and aliskiren on top of the pre-existing drugs and all laboratory eligibility criteria will be evaluated.

Patient randomization will occur after completion of the active run-in period (Visit 4), once the safety monitoring results are available at the site and the patient has met all inclusion criteria and none of the exclusion criteria. Patients will be allocated to one of the two stratification groups, according to the tolerated dose of enalapril, and be randomized in a 1:1:1 ratio to one of the three treatment arms (aliskiren monotherapy, enalapril monotherapy, or aliskiren/enalapril combination therapy). After randomization, patients will be up-titrated to the maximum dose of the corresponding therapies.

The trial will be event driven and all randomized patients will remain in the trial until the number of primary events have been reached. It is planned that the total trial duration will be approximately 6,5 years, with a recruitment period of 4 years and a target double-blind treatment period of 18-74 months.

Intervention

The patients will be equally randomized to one of the following 3 treatment:
* Aliskiren-enalapril combination therapy
* Enalapril monotherapy
* Aliskiren monotherapy

Study burden and risks

There is no garantuee that one will personally benefit from participation in this study other than free study medication and regular check ups.
Possible burdens of the study may be: coming to the clinic 14-20 times, regular measurement of pulse and bloodpressure. Furthermore, EKG's will be made en there will be blood taken several times.

Contacts

Public
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL
Scientific
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

See protocol for complete criteria (page34)
1. Out patients * 18 years of age, male or female.
2. Patients with a diagnosis of chronic heart failure (NYHA Class II * IV):
* LVEF * 35% at visit 1 (local measurement, within the past 6 months).
* Elevated BNP at visit 1: BNP * 150 pg/ml (according to local measurement).
OR BNP * 100 pg/ml (according to local measurement) and unplanned hospitalization with HF within the last 12 months prior visit 1.
OR
Elevated NT-proBNP at visit 1: BNP * 600 pg/ml (according to local measurement).
OR NT-proBNP * 400 pg/ml (according to local measurement) and unplanned hospitalization with HF within the last 12 months prior visit 1.;3. Patients must be treated with an ACE inhibitor at a stable dose (enalapril 10 mg
daily at least or any other ACE inhibitor based on equivalent doses described in Table 4-1: Dose equivalence guidance table of ACEi's) for at least 4 weeks prior to visit 1.
4. Patients must be treated with a beta blocker, unless contraindicated or not tolerated, at a stable dose for at least 4 weeks prior to visit 1 (for patients not on target dose, according to local guidelines, or in absence of that medication, the reason should be documented).

Exclusion criteria

See protocol for complete criteria (page34-36)
2. Patients treated concomitantly with both ARB and aldosterone antagonist in addition to study drug at visit 1.
4. Symptomatic hypotension and/or less than 95 mmHg SBP at Visit 1 and/ or less than 90 mmHg SBP at Visits 4.
5. Acute coronary syndrome, stroke, transient ischemic attack, cardiac, carotid or major vascular surgery, percutaneous coronary intervention (PCI) or carotid angioplasty, within the past 3 months prior to visit 1.
6. Coronary or carotid artery disease likely to require surgical or percutaneous intervention within the 6 months after visit 1.
18. Serum potassium * 5.0 mmol/L at Visit 1 or * 5.2 mmol/L at Visit 4.
29. Patients with diabetes mellitus

Study design

Design

Study phase:	3
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):	29-07-2009
Enrollment:	150
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet geregistreerd
Generic name:	aliskiren/ enalapril combination
Product type:	Medicine
Brand name:	Rasilez
Generic name:	aliskiren
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Renitec
Generic name:	enalapril
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	05-02-2009
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-04-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-07-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-10-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-11-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-05-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-10-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-12-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-12-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-01-2011
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-01-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-03-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-04-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-09-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-10-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-11-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-11-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-11-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-01-2012
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-02-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-12-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-02-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-05-2013
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-06-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-07-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-08-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-09-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-07-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-09-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-10-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-10-2014
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-10-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-12-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-11-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2008-004104-31-NL
ClinicalTrials.gov	NCT00853658
CCMO	NL26299.042.09