A 36-week, randomized, double-blind, multi-center, parallel group, active controlled study to evaluate the efficacy, safety and tolerability of LCZ696 compared to valsartan in patients with chronic heart failure and preserved left-ventricular ejection fraction.

Published: 22-07-2009
Last updated: 06-05-2024

To demonstrate the efficacy of LCZ696 in patients with chronic heart failure with preserved ejection fraction (HF-PEF) by testing the hypothesis that the reduction in NT-proBNP from baseline to study end with LCZ696 is greater than that with...

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

Summary

ID

NL-OMON35586

Source
ToetsingOnline

Brief title
LCZ696B2214

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: chronic heart failure, LCZ696

Outcome measures

Primary outcome

To demonstrate the efficacy of LCZ696 in patients with chronic heart failure with preserved ejection fraction (HF-PEF) by testing the hypothesis that the reduction in NT-proBNP with LCZ696 is greater that that with valsartan after 12 weeks of treatment.

Secondary outcome

To evaluate LCZ696, compared to valsartan on the following parameters:

- BNP, MR-pro-ANP and cGMP

- echocardiographic parameters of diastolic function

- improvement in signs and symptoms of heart failure, changes in quality of life assessments (assessed by total score and individual scores of the sub-domains from the KCCQ) and changes in clinical composite score

- major adverse cardiovasular events

- renal function; eGFR, serum creatinine, proteinuria change

- vascular arterial stiffness, in a subset of patients

- changes in blood pressure

- safety and tolerability

Study description

Background summary

In this trial, we want to assess whether the efficacy, safety and tolerability of LCZ696 as compared to valsartan warrants continuation into the next development phase for HF-PEF (Heart Failure - Preserved Ejection Fraction).

Study objective

To demonstrate the efficacy of LCZ696 in patients with chronic heart failure with preserved ejection fraction (HF-PEF) by testing the hypothesis that the reduction in NT-proBNP from baseline to study end with LCZ696 is greater than that with valsartan after 12 weeks of treatment.

Study design

At visit 1 (screening) patients with chronic heart failure (NYHA-Class II-IV) who meet all in- and exclusion criteria will start in the placebo run in period (1-2 weeks). The patients must discontinue their ACEinhibitors and ARBs 24 hours prior to visit 2.
The patients will be randomised at visit 2 (2 weeks after visit 1), if all in- and exclusion criteria are met. There are 2 randomisations groups: one group of patients will receive valsartan as treatment, the other group LCZ696. In 2-3 weeks time the doses will be titrated to the maximum dose of the particular randomisation group. The total treatment period for a patient is 37-38weeks, there will be 11 study visits performed.

Intervention

- LCZ696 therapy, starts with 50 mg bid at visit 2 (randomisation). Then titration at visit 3 (after 1 week) to 100 mg bid. At visit 4 (after 2-3 weeks) titration to 200 mg bid (maximum dose in this trial). This medication is ongoing until visit 7 (12 weeks after randomisation).
- valsartan therapy, starts with 40 mg bid at visit 2 (randomisation). Then titration at visit 3 (after 1 week) to 80 mg bid. At visit 4 *after 2-3 weeks) titration to 160 mg bid (maximum dose in this trial). This medication is ongoing until visit 7 (12 weeks after randomisation).

Study burden and risks

There is no garantee 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 11 times, regular measurements of pulse and bloodpressure, echocardiography 3 times, ECGs made 3 times. There will be blood taken every visit and patient is asked to fill out quality of life questionnaires 3 times.

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

See protocol for complete criteria (page 21 -22)
2) Male or female outpatients, * 40 years of age
3) Patients with documented stable chronic heart failure (NYHA II - IV) and:
- LVEF * 45% (local measurement, within the past 6 months or after any event that would

effect ejection fraction)
- Plasma NT-proBNP > 400 pg/ml at Visit 1
- Patients must be on diuretic therapy prior to Visit 1 (flexible dose permitted)
4) Patients with at least one of the following symptoms at visit 1:
- Dyspnea on exertion
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Peripheral edema

Exclusion criteria

See protocol for complete criteria pages 22-24
1) Patients with a prior LVEF reading <45%, at any time
2) Patient who require treatment with both an ACE inhibitor and an ARB
3) Isolated right heart failure due to pulmonary disease
4) Dyspnea and/ore edema from non-cardiac causes, such as lung disease, anemia, or severe obesity
7) Presence of hypertrophic obstructive cardiomyopathy
8) Secondary forms of cardiomyopathy such as restrictive cardiomyopathy or infiltrative cardiomyopathy
12) History of MI, unstable angina, coronary bypass surgery or any PCI, stroke or TIA during the past 3 months prior to visit 1

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: Recruitment stopped

Start date (anticipated):	12-10-2010
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Diovan
Generic name:	valsartan
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-07-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-12-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-02-2010
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:	17-06-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-07-2010
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-09-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-01-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-02-2011
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	EUCTR2009-010208-27-NL
CCMO	NL27808.042.09