A multicenter, randomized, double-blind, active-controlled study to evaluate the effects of LCZ696 compared to valsartan on cognitive function in patients with chronic heart failure and preserved ejection fraction

Published: 01-05-2017
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To evaluate the effects of LCZ696 compared to valsartan on cognitive function over 3 years in patients with HFpEF as assessed by the CogState cognitive assessment battery.

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

Summary

ID

NL-OMON50528

Source
ToetsingOnline

Brief title
CLCZ696B2320 (PERSPECTIVE)

Condition

- Heart failures
- Structural brain disorders

Synonym
heart failure

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: cognitive function, heart failure, LCZ696, preserved ejection fraction

Outcome measures

Primary outcome

To evaluate the effects of LCZ696 compared to valsartan on cognitive function over 3 years in patients with HFpEF as assessed by the CogState cognitive assessment battery.

Secondary outcome

To evaluate the effect of LCZ696 compared to valsartan on amyloid deposition in the brain in a subset of patients using positron emission Tomography amyloid (PET) imaging over 3 years.

To evaluate the effects of LCZ696 compared to valsartan on individual cognitive domains (memory, executive function, and attention) as assessed by the individual components of the CogState battery over 3 years

To compare LCZ696 to valsartan in evaluating changes in instrumental activities of daily living (IADL) as assessed with Functional Activity Questionnaire (FAQ) over 3 years.

Study description

Background summary

Cognitive impairment has been reported in patients with heart failure in several studies. Prevalence observed ranged from 25-75% within these studies. Changes in cognition due to improved hart function has not yet been evaluated extensively. In observational studies a connection was shown between congitive impairment and elevated blood pressure. Also correlation between cognitive impairment at the age of 70 and the development of dementia 10-20 years later was shown.
It would be possible that improvement of the heart function and blood pressure, due to a long term treatment of LCZ696 can result in a improvement of the cognition.

Also, in this study the effect of the NEP-inhibitor component to the existence of Amyloid-beta, which might be a factor in developing Alzheimers' disease. This has not been found in the Paradigm-HFstudy.

In this study beta-amyloid plaquea will be investigated by MRI/PETscans.

Study objective

To evaluate the effects of LCZ696 compared to valsartan on cognitive function over 3 years in patients with HFpEF as assessed by the CogState cognitive assessment battery.

Study design

Multi-center, randomized, double-blind, parallel group phase Ill study with active comparator.
Screening period of up to 2 weeks. Single-blind, run-in period 3-8 weeks (treatment with LCZ696 and valsartan separately).
Thereafter randomization (1:1) to:
1. LCZ696 200 mg bid,
2. Valsartan 160 mg bid.
Back-titration if dose is not tolerated.
Continuation of regular treatment against heart failure (except ACE-, angiotensin - and renin inhibitors).
Total study duration 38 months (including screening/run-in).

Intervention

Treatment with LCZ696 or valsartan.

Study burden and risks

Risks are the radiation (3x natural radiation amount), possible AEs due to the

IMP and burden study procedures.

- Physical examination: 10 x
- Vital signs: 12 x
- Weight: 8 x
- Bloodtests: 11 x
- Echocardiogram: 1 x
- MRI: max 3 x
- PET scan: 3 x
- Cogstate: 9 x
- Completion of PROs: 9 x

During study, forbidden co-medication.

Contacts

Public
Novartis

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Scientific
Novartis

Haaksbergweg 16
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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male or female patients aged >= 60 years of age.
- Chronic heart failure with current symptom(s) (NYHA class II-IV) at Screening visit.
- LVEF >= 40%
a. By any method using most recent assessment within 6 months prior to screening visit OR
b. By an echocardiogram performed during the screening visit, if previous assessment is not available.
- Patiens with at least 1 of the following:
- prior HF hospitalisation in 12 months prior to screening visit
- NT-proBNP > 125 pg/ml at screening visit.
- Patient with evidence of adequate functioning (e.g.: intellectual, motor, visual and auditory) to complete the study assessments and has elementary education or 6 years of sustained employment.
See protocol for more details.

Exclusion criteria

- Current acute decompensated HF requiring therapy
- Acute coronary syndrome, cardiac surgery, other major CV surgery, urgent PCI, carotid surgery/angioplasty, history of stroke or transient ischemic attack within the 3 months prior to Screening visit or an elective PCI within 30 days prior to Screening visit.
- Patients who require treatment with 2 or more of the following: an ACEi, an ARB or a renin inhibitor.
- MMSE score < 24 at Screening visit
- Patients with a clinical diagnosis of Alzheimer*s disease or other dementia syndromes or any indication for or current treatment with cholinesterase inhibitors and/or another prescription Alzheimer*s Disease (AD) treatment (e.g., memantine).
- Inability to perform tests based on significant motor or sensory skill.
See protocol for details and more exclusion criteria

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):	25-09-2017
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Diovan
Generic name:	valsartan
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Entresto
Generic name:	sacubitril/valsartan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	01-05-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	17-08-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	27-09-2017

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2019

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-01-2021

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2016-001254-17-NL
ClinicalTrials.gov	NCT02884206
CCMO	NL60363.029.17