

# 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

Last updated: 15-04-2024

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.

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Heart failures
<b>Study type</b>	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 heart function has not yet been evaluated extensively. In observational studies a connection was shown between cognitive 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 III 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

Haaksbergweg 16  
Amsterdam 1101 BX  
NL

### Scientific

Novartis

Haaksbergweg 16  
Amsterdam 1101 BX  
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  $\geq 60$  years of age.
  - Chronic heart failure with current symptom(s) (NYHA class II-IV) at Screening visit.
  - LVEF  $\geq 40\%$ 
    - 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.
  - Patients 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