A multi-center, prospective, randomized, double-blind study to assess the impact of sacubitril/valsartan vs. enalapril on daily physical activity using a wrist worn actigraphy device in adult chronic heart failure patients

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Primary:- To elucidate the change in physical activity as assessed by the distance walked in meters during the 6-minute walk test between baseline and 12weeks of study drug treatment in sacubitril/valsartan vs. enalapril patients.- To assess changes...

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

Summary

ID

NL-OMON47666

Source
ToetsingOnline

Brief title
CLCZ696B3301 (OUTSTEP-HF)

Condition

- Heart failures

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: Actigraphy, Chronic heartfailure, Daily activity, Sacubitril/valsartan

Outcome measures

Primary outcome

- Change from baseline in 6-minute walking test.

- To assess changes in daily non-sedentary daytime activity between baseline and after 12 weeks of treatment in sacubitril/valsartan vs. enalapril treated patients.

Secondary outcome

To compare the proportion of patients with improved performance (* 30m in the 6MWT between sacubitril/valsartan vs. enalapril (wks 0 to 12).

To demonstrate that sacubitril/valsartan is superior in improving exercise capacity as assessed by 6MWT at wk 12 in a subset of patients with baseline 6min walk distance equal to or less than 300 meters and in between 100-450 meters

To compare the effects of sacubitril/valsartan vs. enalapril on patients symptom progression by means of the Patient Global Assessment (PGA) questionnaire at week 4, week 8 and week12.

To assess dynamics of changes from baseline1 in daily non-sedentary daytime physical activity in sacubitril/valsartan vs. enalapril treated patients in weekly and two-weekly intervals.

To assess changes from baseline 1 in mean daily non-sedentary daytime physical activity classified by its intensity for sacubitril/valsartan vs. enalapril treated patients after week 4, week 8 and week12.

To assess the difference in non-sedentary daytime physical activity between sacubitril/valsartan vs. enalapril treated patients during the treatment period (weeks 0-12).

To assess changes from baseline1 on M6min (an actigraphy-based measure of the peak six minutes of daytime physical activity) in sacubitril/valsartan vs. enalapril treated patients after week 4; week 8 and week 12.

To assess changes from baseline (week 0) in exercise capacity assessed by means of the 6-minute walking test at weeks 4, 8 and 12.

Study description

Background summary

LCZ696 is a medicine which has been approved for the treatment of people with chronic heart failure (NYHA Class II- IV) and reduced ejection fraction. To date, over 17,000 subjects have taken LCZ696 in studies that have been performed in healthy subjects and patients with hypertension, heart failure

with reduced ejection fraction, and heart failure with preserve ejection fraction.

The other medicine in this study is enalapril which is currently available on the market and approved for the treatment of patients with clinical signs of congestive heart failure. Enalapril belongs to a class of medications called angiotensin-converting enzyme inhibitors, or ACE inhibitors, recommended as standard-of- care to treat the post-AMI patients.

The purpose of this randomized, actively controlled, double-blind study with prospective datacollection is to assess differences between sacubitril/valsartan versus enalapril in increasing non-sedentary daytime physical activity in HFrEF patients.

Study objective

Primary:
- To elucidate the change in physical activity as assessed by the distance walked in meters during the 6-minute walk test between baseline and 12 weeks of study drug treatment in sacubitril/valsartan vs. enalapril patients.
- To assess changes in daily non-sedentary daytime activity between baseline and after12 weeks of treatment in sacubitril/valsartan vs. enalapril treated patients.

Study design

This is an international (European), randomized, actively controlled, double-blind, doubledummy, interventional study with prospective datacollection. The study comprises 6 visits over 14 weeks. Adult patients with symptomatic HFrEF (NYHA classes II or III/IV at a 1:1 ratio, see Section 5.3) managed in an ambulatory setting (i.e. by primary care physicians, office based cardiologists, HF outpatient clinics) will be randomized in a 1:1 allocation to receive sacubitril/valsartan or enalapril during the double-blind period. Actigraphy will be performed during the entire duration of the study by means of a wrist -worn accelerometry device; the device will be worn continuously for two weeks prior to randomization in order to obtain an individual baseline for each patient, and throughout the treatment period of the study (12 weeks).

Intervention

Treatment with LCZ696 (sacubitril/valsartan) or enalapril.

Study burden and risks

Risks: Side effects of study medication and burden assessments.

Total treatment:
- Physical examination 6x
- Vital signs 6x
- Blood tests 6x, when investigator deems necessary.
- Urine examination (pregnancy test) 2x
- Questionnaires 5x
- 6 Minute Walking Test 4x
- Determination NYHAclass 6x
- Measure length/weight 1x
- ECG, in case not doen within 4 months before screening.

Contacts

Public
Novartis

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Written informed consent obtained before any study assessment is performed.
- Ambulatory * 18 years of age with a diagnosis of chronic symptomatic HF (NYHA class * II) with reduced ejection fraction, defined as known LVEF * 40% AND one of the following two criteria:
- Plasma NT-proBNP level of * 300 pg/mL or BNP * 100 pg/mL (measurement may be recorded no longer than past 12 months) OR
- Confirmation of a heart failure hospitalization last 12 months.
- Patients must be on stable HF medication for at least 4 weeks prior to Week - 2, where the minimal daily dose of current evidence based therapies is equivalent to at least 2.5 mg/d enalapril
- Willingness to wear the accelerometer wristband continuously for the duration of the trial.
- Patients must be living in a setting, allowing them to move about freely and where they are primarily self responsible for scheduling their sleep and daily activities.

Exclusion criteria

- History of hypersensitivity to any of the study drugs or their excipients or to drugs of similar chemical classes
- Use of sacubitril/valsartan prior to week - 2.
- Bedridden patients, or patients with significantly impaired/limited physical activity and/or fatigue due to medical conditions other than HF, such as, but not limited to angina (chest pain at exertion), arthritis, gout, peripheral artery occlusive disease, obstructive or restrictive lung disease, malignant disease, neurological disorders (e.g. Parkinson*s or Alzheimer*s disease, central and peripheral neuroinflammatory and degenerative disorders or functional central nervous lesions due to hemodynamic or traumatic incidents), injuries (incl. diabetic foot ulcers) or missing limbs
- Patients with palsy, tremor or rigor affecting the nondominant arm.
- Patients with any skin or other condition of the nondominant arm that would limit the ability to wear the actigraphy device continuously (24h/day) over 14 weeks.
- Patients fully depending on a mobility support system, e.g. wheelchair, scooter or walker. Patients are allowed to use a cane as long as this is not used with the non- dominant arm.

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:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-06-2017
Enrollment:	42
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	14-02-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-04-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	20-04-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-05-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-06-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-06-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-11-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-01-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-03-2018
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-04-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-09-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-10-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2016-003085-32-NL
ClinicalTrials.gov	NCT02900378
CCMO	NL60273.100.17