Clinical trial results:
Evaluation of the effect of double inhibition of angiotensin II AT1 receptor and neprilysin activity on sympatic nervous system activity in patient with heart failure (B2AN-SNS)

Summary

EudraCT number	2016-001124-66
Trial protocol	FR
Global end of trial date	11 January 2019

Results information

Result version number	v1 (current)
This version publication date	13 July 2022
First version publication date	13 July 2022

Trial information

Trial identification

Sponsor protocol code	15774603

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02787798
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU de Toulouse
Sponsor organisation address	2 rue de Viguerie, Toulouse, France, 31500
Public contact	Caroline PEYROT (chef de projet), CHU de Toulouse, +33 056177078486, peyrot.c@chu-toulouse.fr
Scientific contact	Michel GALINIER, University Hospital Toulouse, +33 0561323661, galinier.m@chu-toulouse.fr

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2018
Global end of trial reached?	Yes
Global end of trial date	11 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This biomedical study will compare the effect of Entresto® and angiotensin-converting-enzyme inhibitor or AT1 receptor of angiotensin II inhibitor on sympathic nervous system activity.

Protection of trial subjects:

A research oversight committee composed of the principal investigator and the head of the ANSM registration laboratory is planned.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 4
Worldwide total number of subjects	4
EEA total number of subjects	4

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients will be recruited from the Cardiology Department of the University Hospital.

Pre-assignment

Screening details:

During the patient follow-up the investigating physician informs the patient and answers all his or her questions concerning the objective, the nature of the constraints, the foreseeable risks and the expected benefits of the research. He also specifies the patient's rights in the context of biomedical research and verifies the eligibility criteria

Period 1

Period 1 title	overall period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

Patients are randomized and only the investigator in charge of recording sympathetic activity by MSNA (primary endpoint) will be blinded to the treatment received. Patients will also be blinded to the study arm in which they will be placed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Entresto group

Arm description:

Patients in this group receive Enteresto treatment.

Arm type	Experimental
Investigational medicinal product name	PR1 (ENTRESTO)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

The initial dosage (100 mg: 49 mg sacubitril and 51 mg valsartan twice daily) will be valsartan twice daily) will be doubled and the patient will be reviewed at V3, 4-8 weeks after initiation of initiation of treatment.

Arm title	Control group

Arm description:

Patients receiving an active comparator instead of Enteresto. Sympathetic activity will be recorded by MSNA after 14 days of stable treatment with the active comparator, whose dosage is the same as for the experimental group.

Arm type	Active comparator
Investigational medicinal product name	PR2 (C09)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

no comment about that

Number of subjects in period 1	Entresto group	Control group
Started	2	2
Completed	0	0
Not completed	2	2
Physician decision	2	-
Lack of efficacy	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Entresto group
Reporting group description:	
Patients in this group receive Enteresto treatment.	

Reporting group title	Control group
Reporting group description:	
Patients receiving an active comparator instead of Enteresto. Sympathetic activity will be recorded by MSNA after 14 days of stable treatment with the active comparator, whose dosage is the same as for the experimental group.	

Reporting group values	Entresto group	Control group	Total
Number of subjects	2	2	4
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	2	4
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	1	1	2
Male	1	1	2

End points

End points reporting groups

Reporting group title	Entresto group

Reporting group description:

Patients in this group receive Enteresto treatment.

Reporting group title	Control group

Reporting group description:

Patients receiving an active comparator instead of Enteresto. Sympathetic activity will be recorded by MSNA after 14 days of stable treatment with the active comparator, whose dosage is the same as for the experimental group.

Primary: Muscle destined sympathetic activity (MSNA)

End point title	Muscle destined sympathetic activity (MSNA)[1]

End point description:

The primary endpoint is muscle destined sympathetic activity (MSNA) measured by microneurography. The recording is made with a tungsten microelectrode (200 µm in diameter), inserted in contact with the efferent orthosympathetic fibers that run around the
fibular nerve. A reference microelectrode is inserted subcutaneously at a distance of 2-3 cm from the measuring microelectrode.
measurement microelectrode.

End point type	Primary

End point timeframe:

During all the study.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Lack of inclusion

End point values	Entresto group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: NA				

Notes:

[2] - no results analysable

[3] - no results analysable

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
From patient consent signature until 7 days after the end of the participation of the patient.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	NA

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: no adverse events reported

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 January 2017	- Removal of the non-inclusion criterion "Patient treated with a statin". - Elimination of plasma catecholamines during blood tests. - Extension of the duration of inclusions. - Modification of the information notice.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

no results avaiblable in this study.

Notes: