



Clinical trial results: Effects on Exercise Hemodynamics of Vasopressin Blockade by Conivaptan Infusion in Heart Failure

Summary

EudraCT number	2012-003219-77
Trial protocol	DK
Global end of trial date	26 June 2016

Results information

Result version number	v1 (current)
This version publication date	25 November 2021
First version publication date	25 November 2021

Trial information

Trial identification

Sponsor protocol code	2012-003219-77
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01752543
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The Heart Centre, Copenhagen University Hospital, Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Finn Gustafsson, Copenhagen University Hospital, Rigshospitalet, 0045 35459743, Finn.Gustafsson@regionh.dk
Scientific contact	Finn Gustafsson, Copenhagen University Hospital, Rigshospitalet, 0045 35459743, Finn.Gustafsson@regionh.dk

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	20 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 May 2015
Global end of trial reached?	Yes
Global end of trial date	26 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To test if infusion of the V1A/V2-receptor blocker conivaptan improves hemodynamics and physical capacity in HF patients on optimal HF medical therapy and to improve understanding of the role of vasopressin in HF.

Protection of trial subjects:

The study was performed according to the Helsinki Declaration and data was anonymized and t

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2012
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	Denmark: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	13
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were included from 13. December 2013 to 20. May 2015
All patients were followed in the outpatient clinic at the University Hospital of Copenhagen, Rigshospitalet, Denmark

Pre-assignment

Screening details:

Patients (> 18 years old) with left ventricular systolic dysfunction evaluated by an ejection fraction < 45 % and with symptomatic HF (NYHA-class II-IV) were eligible for enrollment in the present study. All patients were followed in the outpatient HF clinic at the University Hospital of Copenhagen (Rigshospitalet).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Conivaptan group

Arm description:

Patients who received conivaptan

Arm type	Active comparator
Investigational medicinal product name	Conivaptan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Patients received a 20 mg loading dose followed by a continuous infusion of conivaptan of 0.83 mg/h as recommended in conivaptan treatment guidelines.

Arm title	Placebo group
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Arm description:

Patients who received placebo

Arm type	Placebo
Investigational medicinal product name	saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Patients received a loading noise of 100 ml/30 min followed by an infusion og 4.2 ml/hours corresponding to the infusion rate of the patients in the conivaptan group
Conivaptan/saline was administered by a study nurse

Number of subjects in period 1	Conivaptan group	Placebo group
Started	10	10
Completed	10	10

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
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Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	54.1 ± 12.1	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	18	18	

End points

End points reporting groups

Reporting group title	Conivaptan group
Reporting group description:	
Patients who received conivaptan	
Reporting group title	Placebo group
Reporting group description:	
Patients who received placebo	

Primary: to investigate if treatment with conivaptan leads to a decrease in pulmonary capillary wedge pressure (PCWP) and/or an increase in cardiac output during submaximal exercise (defined as 50 % of the submaximal exercise capacity) compared with placebo.

End point title	to investigate if treatment with conivaptan leads to a decrease in pulmonary capillary wedge pressure (PCWP) and/or an increase in cardiac output during submaximal exercise (defined as 50 % of the submaximal exercise capacity) compared with placebo.
End point description:	
End point type	Primary
End point timeframe:	
Patients were included from 13. December 2013 to 20. May 2015	

End point values	Conivaptan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: mean	10	10		

Statistical analyses

Statistical analysis title	Statistical analyses
Statistical analysis description:	
Within group differences were tested using the paired t-test. Between group differences were tested using two-sided t-test and a general linear ANCOVA model with treatment as a fixed effect and baseline value as a covariate	
Comparison groups	Conivaptan group v Placebo group
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.05
Method	ANCOVA

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Follow-up information regarding hospitalization, death, heart transplantation or implantation of a left ventricular assist device was collected after 60, 90 and 365 days for all patients included in the study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Overall trial
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Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		

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: There were no adverse events during infusion of conivaptan or placebo or at the 1-week or one-month follow-up in either group. Infusion of conivaptan was not associated with electrolyte disturbances, important changes of vital parameters or cardiac arrhythmias. There were no infusion site reactions in the conivaptan or the placebo group. One patient in the conivaptan group and one patient in the placebo group died from worsening HF before the 6 month follow-up visit.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 January 2015	We applied for an amendment to prolongate the inclusion period as were we behind schedule with the inclusion of patients

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported