Clinical trial results:
The effect of metoprolol on myocardial function, hemodynamics and heart failure symptoms in patients with hypertrophic obstructive cardiomyopathy

Summary

EudraCT number	2017-004478-32
Trial protocol	DK
Global end of trial date	01 September 2020

Results information

Result version number	v1 (current)
This version publication date	17 November 2021
First version publication date	17 November 2021

Trial information

Trial identification

Sponsor protocol code	03-11-2017

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensen Blvd. 99, Aarhus N, Denmark, 8200
Public contact	Steen Hvitfeldt Poulsen, Aarhus University Hospital, steepoul@rm.dk
Scientific contact	Steen Hvitfeldt Poulsen, Aarhus University Hospital, steepoul@rm.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	29 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2020
Global end of trial reached?	Yes
Global end of trial date	01 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We want to quantify the effect of metoprololsuccinat on myocardial function, hemodynamics and symptoms in patients with hypertrophic obstructive cardiomyopathy.

Protection of trial subjects:

The study was conducted in accordance with the protocol, consistent to ICH-GCP and applicable local regulatory requirements. The written informed consent with a declaration of data privacy was signed and dated by the subject. The study was monitored externally by the Good Clinical Practice Unit at Aarhus University.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2018
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: 29
Worldwide total number of subjects	29
EEA total number of subjects	29

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)	16
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: May 1, 2018, and September 1, 2020.

Pre-assignment

Screening details:

73 patients were screened.

Period 1

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

Blinding implementation details:

For blinding of the tablets, both metoprolol and placebo was capsulated in gelatin for an identical apperance.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo First

Arm description:

Subjects were randomised to Placebo first and Metoprolol second

Arm type	Crossover
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

three tablets once daily

Arm title	Metoprolol First

Arm description:

Subjects were randomised to Metoprolol first and Placebo second.

Arm type	Active comparator
Investigational medicinal product name	Metoprololsuccinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

three tablets once daily, corrresponding to 150 mg

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Three tablet once daily

Number of subjects in period 1	Placebo First	Metoprolol First
Started	14	15
Completed	14	15

Baseline characteristics

Reporting groups	
Reporting group title	1 Period

Reporting group description: -

Reporting group values	1 Period	Total	
Number of subjects	29	29	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	16	16	
From 65-84 years	13	13	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	60		
standard deviation	± 11	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	18	18	

End points

End points reporting groups	
Reporting group title	Placebo First
Reporting group description: Subjects were randomised to Placebo first and Metoprolol second	
Reporting group title	Metoprolol First
Reporting group description: Subjects were randomised to Metoprolol first and Placebo second.	

Primary: delta PCWP	
End point title	delta PCWP
End point description: delta (exercise - rest) change in pulmonary capillary wedge pressure (PCWP)	
End point type	Primary
End point timeframe: two weeks in each arm	

End point values	Placebo First	Metoprolol First		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: mmHg				
arithmetic mean (standard deviation)	23 (± 9)	21 (± 9)		

Statistical analyses

Statistical analysis title	Paired students t-test
Statistical analysis description: Within patient difference.	
Comparison groups	Placebo First v Metoprolol First
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
6 weeks	
Adverse event reporting additional description:	
Information about adverse events were collected both during routinely scheduled visits as well when subjects opportunistically contacted the researchers.	
Assessment type	Systematic

Dictionary used	
Dictionary name	none
Dictionary version	0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo	
Reporting group title	Metoprolol
Reporting group description:	
Metoprolol	

Serious adverse events	Placebo	Metoprolol	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 17 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Placebo	Metoprolol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	17 / 17 (100.00%)	
Vascular disorders			
Freezing phenomenon	Additional description: cold hands and feet		
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 15 (13.33%)	3 / 17 (17.65%)	
occurrences (all)	2	3	
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	2 / 15 (13.33%)	3 / 17 (17.65%)	
occurrences (all)	2	3	
Dizziness			
subjects affected / exposed	2 / 15 (13.33%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Restless legs syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 15 (20.00%)	2 / 17 (11.76%)	
occurrences (all)	3	2	
Respiratory, thoracic and mediastinal disorders			
Non-cardiac chest pain			
subjects affected / exposed	2 / 15 (13.33%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
Infection			
subjects affected / exposed	0 / 15 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Infections and infestations			
Cough			
subjects affected / exposed	3 / 15 (20.00%)	2 / 17 (11.76%)	
occurrences (all)	3	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported