Clinical trial results:
EFFECT OF BROMOCRIPTINE ON LEFT VENTRICULAR FUNCTION IN WOMEN WITH PERIPARTUM CARDIOMYOPATHY

Summary

EudraCT number	2007-003710-34
Trial protocol	DE
Global end of trial date	04 March 2016

Results information

Result version number	v1 (current)
This version publication date	04 January 2024
First version publication date	04 January 2024

Trial information

Trial identification

Sponsor protocol code	PPCM

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00998556
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hannover Medical School
Sponsor organisation address	Carl-Neuberg-Str. 1, Hannover, Germany, 30625
Public contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de
Scientific contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de

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	13 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 March 2016
Global end of trial reached?	Yes
Global end of trial date	04 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of bromocriptine for improvement of the left ventricular function in women with peripartum cardiomyopathy (PPCM).

Protection of trial subjects:

The clinical trial was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with the standards of International Conference on Harmonisation (ICH) Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 63
Worldwide total number of subjects	63
EEA total number of subjects	63

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)	63
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Female subjects in the first 5 months postpartum with new onset of left ventricular (LV) dysfunction (LV ejection fraction ≤35% as assessed by echocardiography) using the internationally accepted criteria for PPCM.

Pre-assignment

Screening details:

Eligibility will be determined based upon the inclusion and exclusion criteria.

Period 1

Period 1 title	overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Long-term intervention

Arm description:

The treatment group received standard heart failure therapy (ACE-inhibitors, diuretica, beta-blockers) and bromocriptine for 8 weeks (5 mg per day for the first 2 weeks, and 2.5 mg per day for the remaining 6 weeks).

Arm type	Experimental
Investigational medicinal product name	Bromocriptine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg per day for the first twwo weeks and 2.5 mg per day for the remaining 6 weeks

Arm title	Short-term/ control intervention

Arm description:

The control group received standard medical therapy as per current clinical practice and bromocriptine 2.5mg/day for up to one week

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

Dosage and administration details:

2.5 mg per day for one week

Number of subjects in period 1	Long-term intervention	Short-term/ control intervention
Started	31	32
Completed	31	31
Not completed	0	1
Physician decision	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Long-term intervention
Reporting group description:	
The treatment group received standard heart failure therapy (ACE-inhibitors, diuretica, beta-blockers) and bromocriptine for 8 weeks (5 mg per day for the first 2 weeks, and 2.5 mg per day for the remaining 6 weeks).	
Reporting group title	Short-term/ control intervention
Reporting group description:	
The control group received standard medical therapy as per current clinical practice and bromocriptine 2.5mg/day for up to one week	

Reporting group values	Long-term intervention	Short-term/ control intervention	Total
Number of subjects	31	32	63
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
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults (18-65)	31	32	63
Age continuous Units: years			
arithmetic mean	34	33.8	
standard deviation	± 4.5	± 5.8	-
Gender categorical Units: Subjects			
Female	31	32	63
Male	0	0	0
Gravida			
number of previous pregnancies			
Units: Subjects			
1 Gravida	10	16	26
2 Gravida	8	3	11
3 Gravida	7	7	14
4 Gravida	4	2	6
5 Gravida	2	1	3
6 Gravida	0	1	1
7 Gravida	0	2	2
Para			
number of previous live births			
Units: Subjects			
1 Para	12	16	28

2 Para	10	6	16
3 Para	7	6	13
4 Para	1	2	3
6 Para	1	1	2
7 Para	0	1	1
NYHA class Units: Subjects			
NYHA 1	1	0	1
NYHA 2	4	4	8
NYHA 3	9	10	19
NYHA 4	17	18	35

End points

End points reporting groups

Reporting group title	Long-term intervention
Reporting group description:	
The treatment group received standard heart failure therapy (ACE-inhibitors, diuretica, beta-blockers) and bromocriptine for 8 weeks (5 mg per day for the first 2 weeks, and 2.5 mg per day for the remaining 6 weeks).	
Reporting group title	Short-term/ control intervention
Reporting group description:	
The control group received standard medical therapy as per current clinical practice and bromocriptine 2.5mg/day for up to one week	

Primary: LVEF change [in %; 6 months FU minus BL]

End point title	LVEF change [in %; 6 months FU minus BL]
End point description:	
LVEF at 6 months; pEP4(MRT/ 2x Echo/ 1xEcho&CEC decision) minus LVEF at BL; Covar. for pEP (MRT/ 2x Echo/1xEcho&CEC decision)	
End point type	Primary
End point timeframe:	
6 months follow up	

End point values	Long-term intervention	Short-term/ control intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	23		
Units: LVEF				
arithmetic mean (standard deviation)	24.1 (± 11.3)	21.2 (± 10.5)		

Statistical analyses

Statistical analysis title	Confirmatory analysis
Comparison groups	Long-term intervention v Short-term/ control intervention
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.381
Method	confirmatory analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AE and SAE were documented up to one month after end of treatment	
Adverse event reporting additional description:	
Only number of affected subjects available, not number of events.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	long-term group
Reporting group description: -	
Reporting group title	short-term group
Reporting group description: -	

Serious adverse events	long-term group	short-term group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)	4 / 32 (12.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery occlusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	long-term group	short-term group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 31 (38.71%)	16 / 32 (50.00%)	
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Coronary artery occlusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Embolism			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Extravasation			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Appendicectomy			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Pregnancy, puerperium and perinatal conditions			

Lactation puerperal increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Dizziness			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	
occurrences (all)	1	1	
Dysgeusia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
General physical health deterioration			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Impaired healing			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	3 / 31 (9.68%)	0 / 32 (0.00%)	
occurrences (all)	3	0	
Presyncope			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 31 (6.45%)	2 / 32 (6.25%)	
occurrences (all)	2	2	
Cyanosis			

subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Psychiatric disorders			
Acute stress disorder			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	
occurrences (all)	1	1	
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	
occurrences (all)	1	2	
Oedema peripheral			

subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Sinus bradycardia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Ventricular fibrillation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Ventricular tachycardia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Haemoglobin decreased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Iron deficiency			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 31 (3.23%)	2 / 32 (6.25%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Gastroenteritis			

subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Gastrointestinal infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
dry skin			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Endocrine disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Hypercalcaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue			

disorders			
Asthenia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Muscle tightness			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Blood urea increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 February 2010	Amendment No.1 including but not limited to Change of coordinating investigator, change of exclusion criteria, change of sample size (50 to 60), six further trial sites
12 July 2011	Amendment No.2 including but not limited to new coordinating Investigator and principal investigator, Time frame for completion of the baseline MRI examination, Addition of the questionnaire for quality of life at visit 5, Clarification of the procedure in case that an MRI is not possible in a patient at baseline and 6 months follow up, Reporting of SAEs directly to the ZKS Leipzig, Bromocriptine will be given to all patients of the control group for 7 days 2.5 mg/day, Stratification determined by LVEF determined by MRI at baseline is not correct and is replaced by ECHO at baseline
12 September 2012	Amendment No.3 including but not limited to addition of an observation phase, clarification of therapy, tolerated deviations from planned visits
28 February 2014	Amendment No.4

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26026286