Clinical trial results:
FTO-genotype dependent weight reduction under treatment with bromocriptin in obese patients

Summary

EudraCT number	2011-005628-16
Trial protocol	DE
Global end of trial date	03 June 2015

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021
Summary attachment (see zip file)	Synopsis (Weight reduction in obesity under bromocriptine therapy.pdf)

Trial information

Trial identification

Sponsor protocol code	Uni-Koeln-1473

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	DRKS-Number: DRKS00003349

Notes:

Sponsors

Sponsor organisation name	University of Cologne
Sponsor organisation address	Kerpener Str. 62, Köln, Germany, 50924
Public contact	Dr. Michael Faust, University of Cologne, 0049 02214784098, michael.faust@uk-koeln.de
Scientific contact	Dr. Michael Faust, University of Cologne, 0049 02214784098, michael.faust@uk-koeln.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	20 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 June 2015
Global end of trial reached?	Yes
Global end of trial date	03 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

reduction of BMI

Protection of trial subjects:

Regular visits (see sketch of study plan) during the study phase with monitoring of general condition, blood pressure measurement, recording of side effects as well as laboratory checks (blood count, kidney- and liver function tests, blood sugar) during the main visits.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2013
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	Germany: 37
Worldwide total number of subjects	37
EEA total number of subjects	37

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)	36
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The subjects of the study were approached through the following procedures:
- Contacting patients of the Polyclinic for Endocrinology, Diabetology and Preventive Medicine of the University Hospital Cologne
-Display and flyer in the rooms of the University Hospital Cologne
-Newspaper advertisement

Thes

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	37
Number of subjects completed	37

Period 1

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

Blinding implementation details:

Computer assisted bock randomization.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo Capsule
Investigational medicinal product code	
Other name	Trade name: P-tablets white 7mm Lichtenstein®
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Starting dose was 1 Capsul. The dose was increased in steps of 1 Capsule to a maximum of 4 Capsules. Ts. The assigned mediation (verum or placebo) was administered in the morning immediately after getting up. From the first dose, the mediation was administered daily for a period of 18 weeks ending with the last dose at final visit

Arm title	Verum

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Bromocriptine mesilate
Investigational medicinal product code	
Other name	Bromocritpin ratiopharm (Tradename)
Pharmaceutical forms	Capsule
Routes of administration	Ocular use

Dosage and administration details:

Each tablet contains 2.87mg bromocriptine mesilate, corresponding to 2.5 mg bromocriptine, for the preparation in the clinical trial half a tablet of bromocriptine was used for the preparation of a capsule used in the clinical trial.
In the trial the content of half a tablet of bromocriptine 2.5mg was used, giving a dosage of 1.25mg per capsule.
Starting dose was 1.25 mg per day (1 Capsule). The dose was increased in steps of 1.25 mg to a maximum of 5 mg per day (4 Capsules) if tolerated. The assigned mediation (verum or placebo) was administered in the morning immediately after getting up. From the first dose, the mediation was administered daily for a period of 18 weeks ending with the last dose at final visit.

Number of subjects in period 1	Placebo	Verum
Started	18	19
Completed	13	12
Not completed	5	7
Adverse event, non-fatal	1	2
Lost to follow-up	-	3
private reasons, lack of time	3	2
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Verum
Reporting group description: -	

Reporting group values	Placebo	Verum	Total
Number of subjects	18	19	37
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	46.3	44.2	
full range (min-max)	20 to 66	28 to 65	-
Gender categorical Units: Subjects			
Female	10	9	19
Male	8	10	18
FTO risk allele status Units: Subjects			
FTO risk allele absent (wild type)	7	6	13
FTO risk allele heterozygous	8	9	17
FTO risk allele homozygous	3	4	7
Body mass index (BMI)			
kg/m2			
Units: kg/m2			
median	37.1	39.1	
full range (min-max)	30.6 to 53.7	30 to 51.6	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Verum
Reporting group description: -	

Primary: Change in Body Mass Index

End point title	Change in Body Mass Index
End point description:	
End point type	Primary
End point timeframe:	
23.09.2013 to 30.12.2014	

End point values	Placebo	Verum		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: kg/m2				
median (standard deviation)	-0.42 (± 0.99)	-0.25 (± 1.26)		

Statistical analyses

Statistical analysis title	Statistic primary endpoint

Statistical analysis description:

The primary outcome variable is the change in BMI (difference) from the beginning to the end of the treatment phase. This is compared between treatment groups using exploratory evaluation techniques and is used to determine an effect for the following confirmatory study. The evaluation of the change within the genotype subgroups, as well as the evaluation of the secondary target parameters, is exploratory.

Giving the number of cases of 15 patients per treatment group, the one-sided significa

Comparison groups	Placebo v Verum
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45
Method	t-test, 1-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

06.05.2013 to 03.06.2015

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Adverse events in whole study population

Reporting group description: -

Serious adverse events	Adverse events in whole study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 37 (8.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fracture of radius	Additional description: Fracture of left radial head		
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Swalloing a medicine blister			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adverse events in whole study population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 37 (40.54%)		
Vascular disorders			
Dizziness postural			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	4		
Hypotension			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 37 (32.43%)		
occurrences (all)	13		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	3		
Dysphagia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	5 / 37 (13.51%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Psychiatric disorders			
Sleeping disorder			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Musculoskeletal and connective tissue			

disorders			
Dorsalgia			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Pain of knee			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 June 2013	Adjustment of an exclusion criterion due to an amendment of the summary of product characteristics to the test substance by the drug manufacturers
04 December 2013	Increasing of cases due to high drop-out rate

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.

The number of cases in the study was small. The prespecified strata with different genotypes could not be completely filled despite an increase in the total number of subjects included.

Notes: