Clinical trial results:
Multicenter double-blind randomized clinical trial assessing efficacy and safety of exenatide in the treatment of hypothalamic obesity after craniopharyngioma therapy.

Summary

EudraCT number	2013-004755-21
Trial protocol	FR
Global end of trial date	25 September 2018

Results information

Result version number	v1 (current)
This version publication date	20 September 2026
First version publication date	20 September 2026

Trial information

Trial identification

Sponsor protocol code	CHUBX2012/17

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02860923
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU de Bordeaux
Sponsor organisation address	12 rue dubernat, talence, France,
Public contact	Clinical trials manager, CHU de Bordeaux, 33 557820329, celine.bairras-martin@chu-bordeaux.fr
Scientific contact	Clinical trials manager, CHU de Bordeaux, 33 557820329, celine.bairras-martin@chu-bordeaux.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	15 March 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Compare the change of body weight at month 6 after a lifestyle intervention + exenatide compare to the one after the same lifestyle intervention+ placebo in adults patients suffering from a hypothalamic obesity due to treatment of craniopharyngioma.

Protection of trial subjects:

Procédure simplifiée (MR001)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 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: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	38
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Date of first inclusion: 30/01/2017
Date of last inclusion: 22/02/2018
12 centres in France participated in the study

Pre-assignment

Screening details:

-Age between 18 and 70 years
-History of craniopharyngioma treated by surgery associated or not with radiotherapy, with no sign of recurrence in the last 12 months as attested by an MRI of the hypothalamo-hypophyseal region less than 12 months old
-BMI > 30kg/m² with verified weight gain since treatment of the craniopharyngioma

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	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Exenatide group

Arm description:

Treatment with exenatide at the initial dose of 5 µg x 2/day (subcutaneously administered) increased after 4 weeks to 10 µg x 2/day

Arm type	Experimental
Investigational medicinal product name	exenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Treatment with exenatide at the initial dose of 5 µg x 2/day (subcutaneously administered) increased after 4 weeks to 10 µg x 2/day

Arm title	Placebo group

Arm description:

Patients will be maintained on placebo (injected subcutaneously, twice a day)

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients will be maintained on placebo (injected subcutaneously, twice a day)

Number of subjects in period 1	Exenatide group	Placebo group
Started	20	20
Completed	20	20

Baseline characteristics

Reporting groups	
Reporting group title	Exenatide group
Reporting group description:	
Treatment with exenatide at the initial dose of 5 µg x 2/day (subcutaneously administered) increased after 4 weeks to 10 µg x 2/day	
Reporting group title	Placebo group
Reporting group description:	
Patients will be maintained on placebo (injected subcutaneously, twice a day)	

Reporting group values	Exenatide group	Placebo group	Total
Number of subjects	20	20	40
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			
arithmetic mean	40.4	40.4	
standard deviation	± 14.8	± 12.4	-
Gender categorical			
Units: Subjects			
Female	8	9	17
Male	12	11	23
Weight			
Units: kilogram(s)			
arithmetic mean	108.8	106.5	
standard deviation	± 18.7	± 18.0	-

End points

End points reporting groups

Reporting group title	Exenatide group
Reporting group description:	
Treatment with exenatide at the initial dose of 5 µg x 2/day (subcutaneously administered) increased after 4 weeks to 10 µg x 2/day	
Reporting group title	Placebo group
Reporting group description:	
Patients will be maintained on placebo (injected subcutaneously, twice a day)	

Primary: Weight difference 6 months after the start of treatment compared to the value at inclusion (M0)

End point title	Weight difference 6 months after the start of treatment compared to the value at inclusion (M0)
End point description:	
The weight is measured in the morning on an empty stomach, in a patient in underwear with a scale having a range of 200kg and a 100g scale	
End point type	Primary
End point timeframe:	
Between inclusion and 6 months after the start of treatment	

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: kilogram(s)				
arithmetic mean (standard deviation)	-2.3 (± 5.9)	0.8 (± 5.9)		

Statistical analyses

Statistical analysis title	Description of weights between M0 and M6
Statistical analysis description:	
For the main analysis, missing data on the primary endpoint are treated with the "missing=failure" strategy	
Comparison groups	Exenatide group v Placebo group
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1127
Method	Wilcoxon (Mann-Whitney)

Secondary: Evolution of the cardio-metabolic risk factors between the beginning and the end of the study taken individually - evolution of abdominal perimeter

End point title	Evolution of the cardio-metabolic risk factors between the beginning and the end of the study taken individually - evolution of abdominal perimeter

End point description:

End point type	Secondary

End point timeframe:

At 6 months

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	15		
Units: centimeter				
arithmetic mean (standard deviation)	-11.0 (± 19.3)	3.3 (± 18.4)		

Statistical analyses

Statistical analysis title	Linear modelling of the evolution of waist

Statistical analysis description:

Model adjusted on waist circumference at M0

Comparison groups	Exenatide group v Placebo group
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	-8.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.12
upper limit	4.88

Secondary: Evolution of the cardio-metabolic risk factors between the beginning and the end of the study taken individually - evolution of the Body Mass Index (BMI)

End point title	Evolution of the cardio-metabolic risk factors between the beginning and the end of the study taken individually - evolution of the Body Mass Index (BMI)

End point description:

End point type	Secondary

End point timeframe:

At 6 months

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	15		
Units: kilogram(s)/square meter				
arithmetic mean (standard deviation)	-1.2 (± 1.4)	-0.5 (± 1.4)		

Statistical analyses

Statistical analysis title	Linear modelling of BMI change
Statistical analysis description: Model adjusted on BMI at M0	
Comparison groups	Exenatide group v Placebo group
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	0.25

Secondary: Evolution of the cardio-metabolic risk factors between the beginning and the end of the study taken individually - Evolution of triglycerides

End point title	Evolution of the cardio-metabolic risk factors between the beginning and the end of the study taken individually - Evolution of triglycerides
End point description:	
End point type	Secondary
End point timeframe: At 6 months	

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	-0.16 (± 0.66)	0.08 (± 0.75)		

Statistical analyses

Statistical analysis title	Linear modelling of the evolution of triglycerides
Statistical analysis description: Model adjusted on triglycerides at M0	
Comparison groups	Placebo group v Exenatide group
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	0.24

Secondary: Evolution of cardio-metabolic risk factors between the beginning and the end of the study taken individually - Evolution of HDL cholesterol

End point title	Evolution of cardio-metabolic risk factors between the beginning and the end of the study taken individually - Evolution of HDL cholesterol
End point description:	
End point type	Secondary
End point timeframe: At 6 months	

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	0.04 (± 0.25)	0.05 (± 0.30)		

Statistical analyses

Statistical analysis title	Linear modelling of the evolution of HDL cholester
Statistical analysis description: Model adjusted on HDL at M0	
Comparison groups	Exenatide group v Placebo group
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.15

Secondary: Evolution of cardio-metabolic risk factors between the beginning and the end of the study taken individually - Evolution of LDL cholesterol

End point title	Evolution of cardio-metabolic risk factors between the beginning and the end of the study taken individually - Evolution of LDL cholesterol
End point description:	
End point type	Secondary
End point timeframe: At 6 months	

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	-0.34 (± 1.10)	0.17 (± 0.70)		

Statistical analyses

Statistical analysis title	Linear modelling of the evolution of LDL cholester
Statistical analysis description: Model adjusted on LDL at M0	
Comparison groups	Exenatide group v Placebo group

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	0.11

Secondary: Evolution of cardio-metabolic risk factors between the beginning and the end of the study taken individually - Evolution of fat mass

End point title	Evolution of cardio-metabolic risk factors between the beginning and the end of the study taken individually - Evolution of fat mass
End point description:	
End point type	Secondary
End point timeframe:	
At 6 months	

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	14		
Units: percent				
arithmetic mean (standard deviation)	-0.7 (± 1.4)	-2.8 (± 5.9)		

Statistical analyses

Statistical analysis title	Linear modelling of the evolution of fat mass
Statistical analysis description:	
Model adjusted on fat mass at M0	
Comparison groups	Exenatide group v Placebo group
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	2.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	5.03

Secondary: Evolution of glycaemic control - Evolution of fasting blood glucose between M0 and M6

End point title	Evolution of glycaemic control - Evolution of fasting blood glucose between M0 and M6

End point description:

End point type	Secondary

End point timeframe:

At 6 months

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	13		
Units: millimole(s)/litre				
arithmetic mean (standard deviation)	-0.2 (± 0.8)	-0.1 (± 0.4)		

Statistical analyses

Statistical analysis title	Linear modelling of the evolution of fasting blood

Statistical analysis description:

Model adjusted on fasting blood glucose at M0

Comparison groups	Exenatide group v Placebo group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	0.35

Secondary: Evolution of glycaemic control - Evolution of fasting insulin levels between M0 and M6

End point title	Evolution of glycaemic control - Evolution of fasting insulin levels between M0 and M6

End point description:

End point type	Secondary

End point timeframe:

At 6 months

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	10		
Units: thousand of an international unit/litre				
arithmetic mean (standard deviation)	0.3 (± 7.0)	1.1 (± 5.0)		

Statistical analyses

Statistical analysis title	Linear modelling of the evolution of fasting insul
Statistical analysis description:	
Model adjusted on fasting insulin level at M0	
Comparison groups	Exenatide group v Placebo group
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	-0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.75
upper limit	4.92

Secondary: Evolution of glycemic control - Evolution of the percentage of HbA1C percentage between M0 and M6

End point title	Evolution of glycemic control - Evolution of the percentage of HbA1C percentage between M0 and M6
End point description:	
End point type	Secondary
End point timeframe:	
At 6 months	

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	10		
Units: percent				
arithmetic mean (standard deviation)	-0.1 (± 0.3)	0.2 (± 0.3)		

Statistical analyses

Statistical analysis title	Linear modelling of the evolution of the HbA1C
Statistical analysis description:	
Model adjusted on HbA1C percentage at M0	
Comparison groups	Exenatide group v Placebo group
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	-0.02

Secondary: Evolution of energy expenditure between the beginning and the end of the study

End point title	Evolution of energy expenditure between the beginning and the end of the study
End point description:	
The evolution of energy expenditure is calculated by the evolution of the average number of steps per day since the last visit visit, between M0 and M6	
End point type	Secondary
End point timeframe:	
At 6 months	

End point values	Exenatide group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	12		
Units: steps/day				
median (standard deviation)	-615.8 (± 3028.5)	-198.2 (± 3319.1)		

Statistical analyses

Statistical analysis title	Evolution of the average number of steps per day
Statistical analysis description: Model fitted to the average number of steps per day since the last visit at M0	
Comparison groups	Exenatide group v Placebo group
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Slope
Point estimate	-417.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2893.95
upper limit	2058.78

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall study	
Adverse event reporting additional description:	
These averse events are described by Preferred terms (PT)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

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

Serious adverse events	Placebo group	Exenatide group	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 20 (25.00%)	5 / 20 (25.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression (10061309)			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose (10000381)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture (10037802)			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cataract operation (10063797)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine polyp (10046811)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting (10047700)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury (10069339)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Erysipelas (10015145)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral (10017918)			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperlipasaemia (10067725)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypernatraemia (10020679)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo group	Exenatide group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 20 (65.00%)	19 / 20 (95.00%)	
Vascular disorders			
Haematoma (10018852)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	3 / 20 (15.00%)	
occurrences (all)	1	4	
Hypertension (10020772)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Phlebitis (10034879)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	

Surgical and medical procedures			
Artificial crown procedure (10058456)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Dental prosthesis placement (10052944)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Endodontic procedure (10051085)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia (10003549)			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 20 (10.00%)	8 / 20 (40.00%)	
occurrences (all)	2	8	
Injection site inflammation (10022078)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Injection site pruritus (10022093)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Malaise (10025482)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	3 / 20 (15.00%)	
occurrences (all)	1	4	
Pyrexia (10037660)			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy (10048908)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Obstructive airways disorder (10061877)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anorexia nervosa (10002649)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Depression (10012378)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall (10016173)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Incision site inflammation (10064903)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Tooth fracture (10062544)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

Cardiac disorders			
Palpitations (10033557)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness (10013573)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Headache (10019211)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	7 / 20 (35.00%)	
occurrences (all)	1	8	
Blood and lymphatic system disorders			
Polycythaemia (10036051)			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Ear and labyrinth disorders			
Vertigo (10047340)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Eye disorders			
Vision blurred (10047513)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Visual impairment (10047571)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain (10000081)			
alternative assessment type: Non-systematic			

subjects affected / exposed	4 / 20 (20.00%)	6 / 20 (30.00%)	
occurrences (all)	4	6	
Abdominal pain lower (10000084)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Constipation (10010774)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Diarrhoea (10012735)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Eructation (10015137)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Flatulence (10016766)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Gastrooesophageal reflux disease (10017885)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Nausea (10028813)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	10 / 20 (50.00%)	
occurrences (all)	1	11	
Toothache (10044055)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

Vomiting (10047700)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	4	
Hepatobiliary disorders			
Cholelithiasis (10008629)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hepatocellular injury (10019837)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hepatic steatosis (10019708)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Polymorphic light eruption (10036087)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Pruritus (10037087)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Trichorrhexis (10044625)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Urticaria (10046735)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Endocrine disorders			

Diabetes insipidus (10012599)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia (10003239)			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Back pain (10003988)			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 20 (15.00%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Bone pain (10006002)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Coccydynia (10009829)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Muscle fatigue (10049565)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Muscle spasms (10028334)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Neck pain (10028836)			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			

Breast abscess (10006171)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Bronchitis (10006451)			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Cystitis (10011781)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis (10017888)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hand-foot-and-mouth disease (10019113)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Influenza (10022000)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Laryngitis (10023874)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis (10028810)			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 20 (15.00%)	4 / 20 (20.00%)	
occurrences (all)	3	5	
Rhinitis (10039083)			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Sialoadenitis (10040628)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Sinusitis (10040753)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Tonsillitis (10044008)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	4	
Tooth abscess (10044016)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Tracheitis (10044302)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Urinary tract infection (10046571)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite (10061428)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Dyslipidaemia (10058108)			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Glucose tolerance impaired (10018429)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Glucose tolerance impaired in pregnancy (10018430)			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Hyperlipasaemia (10067725)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Hypernatraemia (10020679)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hypoglycaemia (10020993)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Type 2 diabetes mellitus (10067585)			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2016	1. Update of the inclusions criterias. 2. Update of the non-inclusions criterias. 3. Changes in the strategic part of the study. 4. Adjustment of secondary judgment criteria. 5. Corrections of the research timeline. 6. Adjustment of the participant tracking summary table. 8. Added the coordinates of the coordinating CRA to the list of key contacts. 9. Update of the investigations centers.
05 October 2016	1. Update of the investigations centers
01 December 2016	1. Protocol update and harmonization: update of the vigilance unit and pharmacy liaisons, addition of the Clinical Trials number, harmonization of the treatment name in the protocol. 2. Product flow update. 3. Clarification of the blinding procedure. 4. Change to the quality of life questionnaire and modification of the Three Factor Eating Questionnaire version. 5. Update of the participant follow-up summary table. 6. Update of the consent collection procedure. 7. Update of the visit schedule. 8. Correction of the scientific advisory board composition 9. Update of the information and informed consent form. 10. Addition of the Patient Booklet
05 April 2017	1. Update of secondary objectives 2. Update of inclusion criteria 3. Update of non inclusion criteria 4. Update of the study strategy 5. Update of the benefit/risk ratio and secondary endpoints 6. Modification of the participant follow-up summary table 7. Update of the research process 8. modifications of the procedure for returning used products 9. Update of the appendices 10. Update of the information sheet and informed consent
06 September 2017	1. Added centre 12. 2. Change of the number of the sent treatment boxes to the centers.

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/38450721