Clinical trial results:
Randomised, double-blind, placebo controlled trial evaluating the effects of naloxone hydrochloride nasal spray on eating behaviours in bulimia nervosa

Summary

EudraCT number	2016-003107-65
Trial protocol	GB
Global end of trial date	02 November 2018

Results information

Result version number	v1 (current)
This version publication date	17 February 2020
First version publication date	17 February 2020
Summary attachment (see zip file)	OPNT001-BN-001 Summary CSR (Summary CSR OPI001_Version 1.0_20191101_SIGNED.pdf)

Trial information

Trial identification

Sponsor protocol code	OPNT001-BN-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Opiant Pharmaceuticals Inc
Sponsor organisation address	233 Wilshire Blvd., Suite 280, Santa Monica, United States, CA90401
Public contact	Opiant Pharmaceutcials Development, Opiant Pharmaceuticals UK Ltd, 0044 2034023098, jherry@opiant.com
Scientific contact	Opiant Pharmaceutcials Development, Opiant Pharmaceuticals UK Ltd, 0044 2034023098, jherry@opiant.com

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	02 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 November 2018
Global end of trial reached?	Yes
Global end of trial date	02 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess if treatment with naloxone hydrochloride nasal spray reduces the binging behaviour in bulimia nervosa.

Protection of trial subjects:

Study was conducted in compliance with ICH GCP and relevant data protection regulations.
Research Ethics committee favourable option was obtained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 April 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	United Kingdom: 86
Worldwide total number of subjects	86
EEA total number of subjects	86

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)	86
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient's first visit in the study (first patient screened) was on 26th April 2017, the first patient was randomised/treated on 17th May 2017. The last patient was randomised 28th August 2018. The recruitment period was 16 months.
All patients were recruited in the UK.

Pre-assignment

Screening details:

Eligibility criteria were reviewed at a screening visit. Subjects were also asked to complete a daily diary about their condition for two weeks.

Period 1

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

Blinding implementation details:

The nasal spray bottles were identified by a unique numerical code and were otherwise identical. Sites issued the lowest available bottle number to the patients as they were randomised. The site team and monitors had no way to know the contents of the nasal spray.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

Treatment Naloxone Hydrochloride 40mg/ml nasal spray

Arm type	Experimental
Investigational medicinal product name	Naloxone hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Intranasal use

Dosage and administration details:

Naloxone hydrochloride was dosed at 4mg (one spray of 0.1ml of the 40mg/ml formulation in one nostril) once daily as needed plus one additional dose as needed at least 2 hours after the first dose in response to a binging urge (within 24 hours from 6am each day). At baseline and the Week 8 visits, subjects self-administered one dose at the visit.

Arm title	Placebo

Arm description:

Treatment with placebo nasal spray

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Intranasal use

Dosage and administration details:

One dose (one spray of 0.1ml of the placebo formulation) in one nostril once daily as needed plus one additional dose as needed at least 2 hours after the first dose in response to a binging urge (within 24 hours from 6am each day). At baseline and the Week 8 visits, subjects self-administered one dose at the visit.

Number of subjects in period 1	Active	Placebo
Started	44	42
Completed	31	29
Not completed	13	13
Consent withdrawn by subject	8	4
Physician decision	-	1
Non specific	-	2
Adverse event, non-fatal	1	2
Lost to follow-up	2	4
Protocol deviation	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Active
Reporting group description: Treatment Naloxone Hydrochloride 40mg/ml nasal spray	
Reporting group title	Placebo
Reporting group description: Treatment with placebo nasal spray	

Reporting group values	Active	Placebo	Total
Number of subjects	44	42	86
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
Adults (18-64 years)	44	42	86
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	44	42	86
Male	0	0	0
Race Units: Subjects			
Asian	1	2	3
White	42	38	80
Other	1	1	2
Multiple	0	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	42	42	84
Unknown	1	0	1
Height Units: cm			
arithmetic mean	165.8	166.6	
standard deviation	± 6.7	± 6.2	-
Weight Units: kg			
arithmetic mean	71.28	70.9	
standard deviation	± 19.26	± 20.93	-
BMI			

Units: kg/m²			
arithmetic mean	25.89	25.15	
standard deviation	± 6.81	± 6.69	-

End points

End points reporting groups	
Reporting group title	Active
Reporting group description:	
Treatment Naloxone Hydrochloride 40mg/ml nasal spray	
Reporting group title	Placebo
Reporting group description:	
Treatment with placebo nasal spray	

Primary: Binging Days from Baseline to Week 8	
End point title	Binging Days from Baseline to Week 8
End point description:	
End point type	Primary
End point timeframe:	
The 2 weeks prior to Week 8	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Days				
arithmetic mean (standard deviation)	14.8 (± 13.8)	13.8 (± 12.9)		

Statistical analyses

Statistical analysis title	Comparison of number of binging days from baseline
Statistical analysis description:	
Treatment group comparison of number of binging days from baseline to Week 8 imputing missing eDiary days using moving averages (ITT analysis set)	
Comparison groups	Active v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7756
Method	generalized estimating equation
Parameter estimate	Likelihood Ratio
Point estimate	0.957
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.706
upper limit	1.297

Secondary: Number of binging episodes from baseline to Week 8

End point title	Number of binging episodes from baseline to Week 8

End point description:

End point type	Secondary

End point timeframe:

The 2 weeks prior to Week 8

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Binging episodes				
arithmetic mean (standard deviation)	36.7 (± 123.8)	18.9 (± 20.6)		

Statistical analyses

Statistical analysis title	Comparison of number of binging episodes

Statistical analysis description:

Treatment group comparison of number of binging episodes from baseline to Week 8 (ITT analysis set)

Comparison groups	Active v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8431
Method	Generalised Estimating Equations
Parameter estimate	Likelihood Ratio
Point estimate	0.964
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.674
upper limit	1.381

Secondary: Purging behaviour at Week 8

End point title	Purging behaviour at Week 8

End point description:

End point type	Secondary

End point timeframe:

The two weeks prior to Week 8

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Purging Episodes				
arithmetic mean (standard deviation)	35.4 (± 122.5)	25.6 (± 26.6)		

Statistical analyses

Statistical analysis title	Comparison of number of purging episodes
Statistical analysis description:	
Treatment group comparison of number of purging episodes from baseline to Week 8 (ITT analysis set)	
Comparison groups	Active v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0452
Method	negative binomial model
Parameter estimate	Likelihood Ratio
Point estimate	0.674
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.458
upper limit	0.992

Secondary: Total number of calories in the taste test at Week 8

End point title	Total number of calories in the taste test at Week 8
End point description:	
End point type	Secondary
End point timeframe:	
The two weeks prior to Week 8	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Calories				
arithmetic mean (standard deviation)	395.72 (± 299.3)	341.05 (± 375.96)		

Statistical analyses

Statistical analysis title	Total number of calories - Week 8
Statistical analysis description: Treatment group comparison of total number of calories in the taste test at Week 8 (ITT analysis set)	
Comparison groups	Active v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7191
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.77

Secondary: Total number of calories in the taste test at baseline	
End point title	Total number of calories in the taste test at baseline
End point description:	
End point type	Secondary
End point timeframe: The two weeks prior to Baseline	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Calories				
arithmetic mean (standard deviation)	392.39 (± 348.08)	309.24 (± 264.92)		

Statistical analyses

Statistical analysis title	Total number of calories - Baseline
Statistical analysis description:	
Treatment group comparison of total number of calories in the taste test at baseline (ITT analysis set)	
Comparison groups	Active v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.699
Method	ANOVA
Parameter estimate	Ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.73

Secondary: Eating disorder questionnaire (EDE-Q) at Week 8	
End point title	Eating disorder questionnaire (EDE-Q) at Week 8
End point description:	
End point type	Secondary
End point timeframe:	
At Week 8	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Score				
arithmetic mean (standard deviation)	4.0 (± 1.2)	3.7 (± 1.3)		

Statistical analyses

Statistical analysis title	Comparison of eating disorder questionnaire
Statistical analysis description:	
Treatment group comparison of eating disorder questionnaire (ITT analysis set)	
Comparison groups	Active v Placebo

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2108
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	0.22

Secondary: Visual analogue scale (VAS) on mood at Week 8

End point title	Visual analogue scale (VAS) on mood at Week 8

End point description:

End point type	Secondary

End point timeframe:

At Week 8

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Score				
arithmetic mean (standard deviation)	0.05 (± 14.3)	-0.76 (± 15.26)		

Statistical analyses

Statistical analysis title	VAS mood difference

Statistical analysis description:

Treatment group comparison of VAS mood difference before and after dosing (ITT analysis set)

Comparison groups	Active v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0197
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	8.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.33
upper limit	14.76

Secondary: Visual analogue scale (VAS) on craving at Week 8

End point title	Visual analogue scale (VAS) on craving at Week 8
End point description:	

End point type	Secondary
End point timeframe:	
At week 8	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: Score				
arithmetic mean (standard deviation)	-3.39 (± 31.90)	2.07 (± 22.73)		

Statistical analyses

Statistical analysis title	VAS craving difference
Statistical analysis description:	
Treatment group comparison of VAS craving difference before and after dosing (ITT analysis set)	
Comparison groups	Active v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8306
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	-1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.38
upper limit	12.4

Secondary: Visual analogue scale (VAS) on hunger at Week 8

End point title	Visual analogue scale (VAS) on hunger at Week 8

End point description:

End point type	Secondary

End point timeframe:

At Week 8

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: Score				
arithmetic mean (standard deviation)	11.68 (± 25.65)	-5.75 (± 20.14)		

Statistical analyses

Statistical analysis title	VAS hunger difference

Statistical analysis description:

Treatment group comparison of VAS difference before and after dosing (ITT analysis set)

Comparison groups	Active v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.357
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	-5.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.92
upper limit	6.57

Secondary: Visual analogue scale (VAS) on anxiety at Week 8

End point title	Visual analogue scale (VAS) on anxiety at Week 8

End point description:

End point type	Secondary

End point timeframe:

At Week 8

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: Score				
arithmetic mean (standard deviation)	2.13 (± 20.43)	-0.54 (± 19.49)		

Statistical analyses

Statistical analysis title	VAS anxiety difference
Statistical analysis description: Treatment group comparison of VAS anxiety difference before and after dosing (ITT analysis set)	
Comparison groups	Active v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2037
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	5.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	14.2

Secondary: Visual analogue scale (VAS) purging at Week 8

End point title	Visual analogue scale (VAS) purging at Week 8
End point description:	
End point type	Secondary
End point timeframe: At Week 8	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: Score				
arithmetic mean (standard deviation)	5.1 (± 16.54)	10.82 (± 26.24)		

Statistical analyses

Statistical analysis title	VAS purging difference
Statistical analysis description:	
Treatment group comparison of VAS purging difference before and after dosing (ITT analysis set)	
Comparison groups	Active v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.886
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	-0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.33
upper limit	8.95

Secondary: Visual analogue scale (VAS) on feeling full at Week 8

End point title	Visual analogue scale (VAS) on feeling full at Week 8
End point description:	
End point type	Secondary
End point timeframe:	
At Week 8	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: Score				
arithmetic mean (standard deviation)	15.77 (± 30.96)	10.18 (± 31.54)		

Statistical analyses

Statistical analysis title	VAS feeling full
Statistical analysis description:	
Treatment group comparison of VAS feeling full difference before and after dosing (ITT analysis set)	
Comparison groups	Active v Placebo

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4943
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	5.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.74
upper limit	21.98

Secondary: Food craving questionnaire (FCQ) at Week 8

End point title	Food craving questionnaire (FCQ) at Week 8
End point description:	

End point type	Secondary
End point timeframe:	
At Week 8	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: Score				
arithmetic mean (standard deviation)	151.4 (± 27.4)	157.7 (± 31.4)		

Statistical analyses

Statistical analysis title	Comparison of food craving questionnaire
Statistical analysis description:	
Treatment group comparison of food craving questionnaire (ITT analysis set)	
Comparison groups	Active v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2077
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	-9.79

Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.18
upper limit	5.6

Secondary: Abstinence of binging at Week 8 for at least a 2-week period

End point title	Abstinence of binging at Week 8 for at least a 2-week period
End point description:	

End point type	Secondary
End point timeframe:	
At week 8	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Subjects				
Yes	7	8		
No	24	21		

Statistical analyses

Statistical analysis title	Comparison of abstinence of binging at Week 8
Statistical analysis description:	
Treatment group comparison of abstinence of binging at Week 8 for at least a two weeks period. Only subjects who have performed Week 8 visit (ITT analysis set)	
Comparison groups	Active v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.784
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.845
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.253
upper limit	2.823

Other pre-specified: Treatment emergent adverse events (event)

End point title	Treatment emergent adverse events (event)

End point description:

End point type	Other pre-specified

End point timeframe:

From informed consent until end of study

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	42		
Units: Events	188	131		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Treatment Emergent Adverse Events (Subject)

End point title	Treatment Emergent Adverse Events (Subject)

End point description:

End point type	Other pre-specified

End point timeframe:

From informed consent until end of study

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	42		
Units: Subjects	37	38		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment Emergent Adverse Events (From Baseline until Week 10 follow-up)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	Active
Reporting group description:	
Treatment Naloxone Hydrochloride 40mg/ml nasal spray	
Reporting group title	Placebo
Reporting group description:	
Treatment with placebo nasal spray	

Serious adverse events	Active	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Mood altered			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (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: 5 %

Non-serious adverse events	Active	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 44 (84.09%)	38 / 42 (90.48%)	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 44 (29.55%)	11 / 42 (26.19%)	
occurrences (all)	16	14	
Dizziness			
subjects affected / exposed	5 / 44 (11.36%)	6 / 42 (14.29%)	
occurrences (all)	5	6	
Dysgeusia			
subjects affected / exposed	5 / 44 (11.36%)	0 / 42 (0.00%)	
occurrences (all)	5	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 44 (11.36%)	3 / 42 (7.14%)	
occurrences (all)	9	5	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	11 / 44 (25.00%)	6 / 42 (14.29%)	
occurrences (all)	14	8	
Diarrhoea			
subjects affected / exposed	3 / 44 (6.82%)	4 / 42 (9.52%)	
occurrences (all)	3	4	
Abdominal pain			
subjects affected / exposed	0 / 44 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	3	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	5 / 44 (11.36%)	3 / 42 (7.14%)	
occurrences (all)	5	3	
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain			
subjects affected / exposed	5 / 44 (11.36%)	5 / 42 (11.90%)	
occurrences (all)	5	6	
Nasal inflammation			
subjects affected / exposed	7 / 44 (15.91%)	0 / 42 (0.00%)	
occurrences (all)	9	0	
Rhinalgia			
subjects affected / exposed	4 / 44 (9.09%)	3 / 42 (7.14%)	
occurrences (all)	4	3	
Epistaxis			
subjects affected / exposed	3 / 44 (6.82%)	1 / 42 (2.38%)	
occurrences (all)	4	1	
Nasal congestion			
subjects affected / exposed	3 / 44 (6.82%)	2 / 42 (4.76%)	
occurrences (all)	3	2	
Nasal discomfort			
subjects affected / exposed	6 / 44 (13.64%)	0 / 42 (0.00%)	
occurrences (all)	6	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 44 (9.09%)	5 / 42 (11.90%)	
occurrences (all)	6	5	
Depressed mood			
subjects affected / exposed	7 / 44 (15.91%)	2 / 42 (4.76%)	
occurrences (all)	8	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 44 (6.82%)	0 / 42 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 44 (11.36%)	5 / 42 (11.90%)	
occurrences (all)	5	5	
Gastroenteritis			
subjects affected / exposed	0 / 44 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	3	

Rhinitis subjects affected / exposed occurrences (all)	3 / 44 (6.82%) 3	0 / 42 (0.00%) 0	
Product issues Product taste abnormal subjects affected / exposed occurrences (all)	7 / 44 (15.91%) 7	1 / 42 (2.38%) 1	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	3 / 44 (6.82%) 3	1 / 42 (2.38%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 January 2017	Updated exclusion criteria: Addition of other behavioural therapies besides CBT in the exclusion criteria ... Removal of exclusion of > 5 cigarettes a day to removed recruitment barrier … Addition of morning diary to ensure overnight activity isn't missed … Addition of timing of taste test. … Addition of post dosing VAS and post dosing nasal mucosa exam when IMP is likely to have optimal effect … Addition of IMP priming to ensure accurate dosing … Removal of the sustained attention to response test (SART) and the balloon analogue risk task (BART), to improve patient visit time … Removal of taste test from screening as not necessary
24 November 2017	Update of exclusion criteria to include all antidepressant treatments besides fluoxetine and to increase the alcohol intake limit from 21 units per week to 32 units per week. Updated patient eDiary to permit recording of AE and concomitant medications

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported