Clinical trial results:
A Phase 3, Multicenter, Open-label, 12-month Extension Safety and Tolerability Study of SPD489 in the Treatment of Adults with Binge Eating Disorder

Summary

EudraCT number	2012-003313-34
Trial protocol	SE DE IT ES
Global end of trial date	21 October 2014

Results information

Result version number	v1 (current)
This version publication date	21 February 2016
First version publication date	21 February 2016

Trial information

Trial identification

Sponsor protocol code	SPD489-345

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01657019
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire Development, LLC
Sponsor organisation address	725 Chesterbrook Boulevard, Wayne, United States, 19087
Public contact	Study Physician, Shire Development, LLC, +1 866 842 5335,
Scientific contact	Study Physician, Shire Development, LLC, +1 866 842 5335,

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	21 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of SPD489 (50 and 70mg/day) for the treatment of BED in adults 18-55 years of age (inclusive at the time of consent for the respective antecedent SPD489 BED trial). Long-term safety will be described using:
1. Occurrence of TEAEs.
2. Response to the Columbia Suicide Severity Rating Scale (C-SSRS).
3. Specific evaluation of blood pressure and pulse, weight and waist circumference, clinical laboratory evaluations, and ECG results.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation of Good Clinical Practice, the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 August 2012
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	Spain: 8
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	United States: 580
Worldwide total number of subjects	604
EEA total number of subjects	24

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)	604
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was an open-label extension study to evaluate the long-term safety of SPD489 in adults aged 18-55 years with binge eating disorder (BED) who completed 1 of 3 antecedent studies, all of which tested SPD489 for BED (SPD489-208, SPD489-343, or SPD489-344).

Pre-assignment

Screening details:

Subjects were screened for eligibility over a period of 2 weeks.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All participants

Arm description:

Subjects initially received lisdexamfetamine dimesylate, 30 mg, during the dose optimization phase, regardless of their treatment assignment in the antecedent study. The dose was increased to an optimal dose of either 50 or 70 mg. Subjects received treatment for a total of 52 weeks, then were followed for 1 week.

Arm type	Experimental
Investigational medicinal product name	lisdexamfetamine dimesylate
Investigational medicinal product code	
Other name	Vyvanse, SPD489, LDX
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects initially received lisdexamfetamine dimesylate as a 30 mg capsule administered orally, once daily during the dose optimization phase, regardless of their treatment assignment in the antecedent study. The dose was increased to an optimal dose of either a 50 or 70 mg capsule administered orally, once daily.

Number of subjects in period 1	All participants
Started	604
Completed	369
Not completed	235
Protocol violation	6
Not specified	58
Adverse event	55
Lost to follow-up	48
Withdrawal by subject	65
Lack of efficacy	3

Baseline characteristics

Reporting groups	
Reporting group title	All participants

Reporting group description:

Subjects initially received lisdexamfetamine dimesylate, 30 mg, during the dose optimization phase, regardless of their treatment assignment in the antecedent study. The dose was increased to an optimal dose of either 50 or 70 mg. Subjects received treatment for a total of 52 weeks, then were followed for 1 week.

Reporting group values	All participants	Total	
Number of subjects	604	604	
Age categorical Units: Subjects			
< 40 years	302	302	
>/= 40 years	302	302	
Age continuous Units: years			
arithmetic mean	39.1		
standard deviation	± 9.99	-	
Gender categorical Units: Subjects			
Female	525	525	
Male	79	79	

End points

End points reporting groups

Reporting group title	All participants

Reporting group description:

Subjects initially received lisdexamfetamine dimesylate, 30 mg, during the dose optimization phase, regardless of their treatment assignment in the antecedent study. The dose was increased to an optimal dose of either 50 or 70 mg. Subjects received treatment for a total of 52 weeks, then were followed for 1 week.

Primary: Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs) as a Measure of Safety

End point title	Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs) as a Measure of Safety[1]

End point description:

This endpoint analyzed the Safety Analysis Set (SAS), defined as all subjects who took at least 1 dose of investigational product and who had at least 1 post-Visit 0 safety assessment in the study.

End point type	Primary

End point timeframe:

52 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this open label study was focused on continued safety, no formal analysis was performed as only descriptive statistics were used.

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	599			
Units: percentage of subjects				
number (not applicable)				
Any TEAE	84.5			
Serious TEAEs	2.8			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With a Positive Response on The Columbia Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Subjects With a Positive Response on The Columbia Suicide Severity Rating Scale (C-SSRS)[2]

End point description:

Suicidality was assessed by using the C-SSRS, a semi-structured interview designed to capture the occurrence, severity, and frequency of suicide-related thoughts and behaviors. The interview and rating for the C-SSRS was completed by a clinician who had been successfully trained. The interview was initiated with 5 (yes/no) questions, presented in ascending order of severity, about suicidal ideation. The most severe type of ideation was rated for frequency, duration, controllability, deterrents, and reason. If the answers to the first 2 ideation questions were "yes," the clinician asked questions 3-5. Active suicidal ideation included any subject who answered "yes" to questions 2-5. If the answers to ideation

questions 1 and 2 were "no," then the clinician proceeded to 5 (yes/no) questions that addressed suicidal behavior, which was categorized as actual attempt, interrupted attempt, aborted attempt, preparatory acts or behaviors, and completed suicide.
This endpoint analysed the SAS.

End point type	Primary

End point timeframe:

53 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this open label study was focused on continued safety, no formal analysis was performed as only descriptive statistics were used.

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	597			
Units: subjects				
Suicidal behavior	0			
Active suicidal ideation	2			
Non-suicidal self-injurious behavior	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With an Improved Response on The Clinical Global Impressions of Improvement (CGI-I) Scale

End point title	Percentage of Subjects With an Improved Response on The Clinical Global Impressions of Improvement (CGI-I) Scale

End point description:

The CGI rating scales permitted the global evaluation of a subject's condition severity and improvement over time. The CGI-I was performed to rate the improvement of a subject's condition on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse) and included a 'not assessed' option. The responses were dichotomized into 2 categories (improved or not improved). Improved included very much improved and much improved; not improved included minimally improved, no change, minimally worse, much worse, and very much worse. Not assessed and missing values were excluded from the percentage calculation.
This endpoint analyzed the Full Analysis Set (FAS), defined as all subjects in the SAS who had at least 1 post-Visit 0 clinical experience outcome assessment in this study.

End point type	Secondary

End point timeframe:

Weeks 1, 4, 24, and 52, and end of treatment (either Visit 16 [Week 52] or Early Termination)

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	597			
Units: percentage of subjects				
number (confidence interval 95%)				
Visit 1 (Week 1), n=589	53.7 (49.6 to 57.7)			

Visit 4 (Week 4), n=572	88.5 (85.8 to 91.1)			
Visit 9 (Week 24), n=466	92.7 (90.3 to 95.1)			
Visit 16 (Week 52), n=369	95.4 (93.2 to 97.5)			
End of Treatment, n=597	89.9 (87.5 to 92.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in The Global Score for The Eating Disorder Examination Questionnaire (EDE-Q)

End point title	Change From Baseline in The Global Score for The Eating Disorder Examination Questionnaire (EDE-Q)

End point description:

The EDE-Q is a 28-item questionnaire measuring eating pathology and is derived directly from the Eating Disorder Examination Interview. The EDE-Q focuses on the past 28 days to assess the main behavioral (eating and purging) and attitudinal features of eating disorders. The 28 items are rated by the subject on a 7-point scale (ranging from 0 to 6), with higher scores indicating increased pathology. The EDE-Q includes 4 subscales: Restraint, Eating Concern, Weight Concern, and Shape Concern. The global score is the average of all 28 items, with a range of 0 to 6. A negative value indicates a favorable result. The values presented are the mean change from baseline.
This endpoint analyzed the FAS.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 24, and 52, and end of treatment (either Visit 16 [Week 52] or Early Termination)

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	597			
Units: units on a scale				
arithmetic mean (standard deviation)				
Visit 4 (Week 4), n=483	-1.66 (± 1.156)			
Visit 9 (Week 24), n=391	-1.95 (± 1.271)			
Visit 16 (Week 52), n=314	-1.95 (± 1.261)			
End of Treatment, n=503	-1.9 (± 1.284)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Response to The EuroQoL Group 5

Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Mobility

End point title	Percentage of Subjects With a Response to The EuroQoL Group 5 Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Mobility

End point description:

The EQ-5D-5L is one of the most widely used generic index measures of health-related quality of life. It consists of a 5-item descriptive system that measures 5 dimensions of health, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is represented by a single item with 5 levels of responses, from poor health to good health. The percentages of subjects with various responses to the mobility questionnaire are reported. Percentages are based on all subjects in the Full Analysis Set with a valid result at the given visit.
This endpoint analyzed the FAS.

End point type	Secondary

End point timeframe:

End of Treatment (ET; either Visit 16 [Week 52] or Early Termination)

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	555			
Units: percentage of subjects at ET				
number (not applicable)				
I have no problems in walking about	91.2			
I have slight problems in walking about	6.8			
I have moderate problems in walking about	1.4			
I have severe problems in walking about	0.4			
I am unable to walk about	0.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Response to The EuroQoL Group 5 Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Self Care

End point title	Percentage of Subjects With a Response to The EuroQoL Group 5 Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Self Care

End point description:

The EQ-5D-5L is one of the most widely used generic index measures of health-related quality of life. It consists of a 5-item descriptive system that measures 5 dimensions of health, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is represented by a single item with 5 levels of responses, from poor health to good health. The percentages of subjects with various responses to the self care questionnaire are reported. Percentages are based on all subjects in the Full Analysis Set with a valid result at the given visit.
This endpoint analyzed the FAS

End point type	Secondary

End point timeframe:

End of Treatment (ET; either Visit 16 [Week 52] or Early Termination)

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	555			
Units: percentage of subjects at ET				
number (not applicable)				
I have no problems washing or dressing myself	97.1			
I have slight problems washing or dressing myself	1.8			
Moderate problems washing or dressing myself	0.7			
I have severe problems washing or dressing myself	0.2			
I am unable to wash or dress myself	0.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Response to The EuroQoL Group 5 Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Usual Activities

End point title	Percentage of Subjects With a Response to The EuroQoL Group 5 Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Usual Activities

End point description:

The EQ-5D-5L is one of the most widely used generic index measures of health-related quality of life. It consists of a 5-item descriptive system that measures 5 dimensions of health, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is represented by a single item with 5 levels of responses, from poor health to good health. The percentages of subjects with various responses to the usual activities questionnaire are reported. Percentages are based on all subjects in the Full Analysis Set with a valid result at the given visit.
This endpoint analyzed the FAS.

End point type	Secondary

End point timeframe:

End of Treatment (ET; either Visit 16 [Week 52] or Early Termination)

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	555			
Units: percentage of subjects at ET				
number (not applicable)				
I have no problems doing my usual activities	88.5			
I have slight problems doing my usual activities	8.3			
Moderate problems doing my usual activities	2.2			

I have severe problems doing my usual activities	0.9			
I am unable to do my usual activities	0.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Response to The EuroQoL Group 5 Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Pain and Discomfort

End point title	Percentage of Subjects With a Response to The EuroQoL Group 5 Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Pain and Discomfort

End point description:

The EQ-5D-5L is one of the most widely used generic index measures of health-related quality of life. It consists of a 5-item descriptive system that measures 5 dimensions of health, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is represented by a single item with 5 levels of responses, from poor health to good health. The percentages of subjects with various responses to the pain/discomfort questionnaire are reported. Percentages are based on all subjects in the Full Analysis Set with a valid result at the given visit.
This endpoint analyzed the FAS.

End point type	Secondary

End point timeframe:

End of Treatment (ET; either Visit 16 [Week 52] or Early Termination)

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	555			
Units: percentage of subjects at ET				
number (not applicable)				
I have no pain or discomfort	71.2			
I have slight pain or discomfort	20.9			
I have moderate pain or discomfort	7			
I have severe pain or discomfort	0.9			
I have extreme pain or discomfort	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Response to The EuroQoL Group 5 Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Anxiety or Depression

End point title	Percentage of Subjects With a Response to The EuroQoL Group 5 Dimension 5-Level Self-Report Questionnaire (EQ-5D-5L) For Anxiety or Depression

End point description:

The EQ-5D-5L is one of the most widely used generic index measures of health-related quality of life. It

consists of a 5-item descriptive system that measures 5 dimensions of health, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is represented by a single item with 5 levels of responses, from poor health to good health. The percentages of subjects with various responses to the anxiety/depression questionnaire are reported. Percentages are based on all subjects in the Full Analysis Set with a valid result at the given visit.
This endpoint analyzed the FAS.

End point type	Secondary

End point timeframe:

End of Treatment (ET; either Visit 16 [Week 52] or Early Termination)

End point values	All participants			
Subject group type	Reporting group			
Number of subjects analysed	555			
Units: percentage of subjects at ET				
number (not applicable)				
I am not anxious or depressed	75.9			
I am slightly anxious or depressed	18.7			
I am moderately anxious or depressed	4.5			
I am severely anxious or depressed	0.9			
I am extremely anxious or depressed	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

53 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	All participants

Reporting group description:

Subjects initially received lisdexamfetamine dimesylate, 30 mg, during the dose optimization phase, regardless of their treatment assignment in the antecedent study. The dose was increased to an optimal dose of either 50 or 70 mg. Subjects received treatment for a total of 52 weeks, then were followed for 1 week.

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 599 (2.84%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			

subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 599 (0.17%)		
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 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intestinal perforation			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	2 / 599 (0.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Adjustment disorder with anxiety			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anxiety			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Helicobacter infection			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 599 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	447 / 599 (74.62%)		
Investigations			
Blood pressure increased			
subjects affected / exposed	26 / 599 (4.34%)		
occurrences (all)	29		
Heart rate increased			
subjects affected / exposed	15 / 599 (2.50%)		
occurrences (all)	17		
Weight decreased			
subjects affected / exposed	19 / 599 (3.17%)		
occurrences (all)	21		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	14 / 599 (2.34%)		
occurrences (all)	16		
Nervous system disorders			
Dizziness			
subjects affected / exposed	21 / 599 (3.51%)		
occurrences (all)	23		
Headache			
subjects affected / exposed	79 / 599 (13.19%)		
occurrences (all)	103		
Hypoaesthesia			

subjects affected / exposed	15 / 599 (2.50%)		
occurrences (all)	21		
Paraesthesia			
subjects affected / exposed	14 / 599 (2.34%)		
occurrences (all)	15		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	28 / 599 (4.67%)		
occurrences (all)	29		
Feeling jittery			
subjects affected / exposed	30 / 599 (5.01%)		
occurrences (all)	33		
Irritability			
subjects affected / exposed	36 / 599 (6.01%)		
occurrences (all)	47		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	41 / 599 (6.84%)		
occurrences (all)	42		
Diarrhoea			
subjects affected / exposed	26 / 599 (4.34%)		
occurrences (all)	29		
Dry mouth			
subjects affected / exposed	163 / 599 (27.21%)		
occurrences (all)	175		
Nausea			
subjects affected / exposed	41 / 599 (6.84%)		
occurrences (all)	45		
Toothache			
subjects affected / exposed	12 / 599 (2.00%)		
occurrences (all)	12		
Vomiting			
subjects affected / exposed	15 / 599 (2.50%)		
occurrences (all)	17		
Skin and subcutaneous tissue disorders			

Hyperhidrosis subjects affected / exposed occurrences (all)	16 / 599 (2.67%) 16		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Bruxism subjects affected / exposed occurrences (all) Initial insomnia subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 30 / 599 (5.01%) 36 35 / 599 (5.84%) 35 25 / 599 (4.17%) 26 74 / 599 (12.35%) 80		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 16 / 599 (2.67%) 17 16 / 599 (2.67%) 18		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Gastroenteritis viral subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 14 / 599 (2.34%) 14 18 / 599 (3.01%) 19 16 / 599 (2.67%) 16 53 / 599 (8.85%) 65		

Sinusitis subjects affected / exposed occurrences (all)	35 / 599 (5.84%) 38		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	68 / 599 (11.35%) 81		
Urinary tract infection subjects affected / exposed occurrences (all)	27 / 599 (4.51%) 28		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	36 / 599 (6.01%) 37		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2012	Amendment 1 included the following important changes: • Clarified pregnancy testing requirements in the inclusion criteria • Clarified inclusion criteria to state that a subject must have a BED diagnosis as confirmed by the eating disorder module of the SCID-I and EDE-Q from the antecedent study • Clarified exclusion criteria to state that if a subject had any clinically significant ECG or laboratory abnormality at the Screening Visit (Visit -1), if applicable or Visit 0, the subject would be excluded • Clarified exclusion criteria to state that pregnant or nursing females would be excluded • Clarified that female subjects must have had a negative serum pregnancy test at study entry (Visit 0) and a negative urine pregnancy test at Visit 0, and added that contraception requirements were to be reviewed at every study visit and recorded in the source documents • Added monthly urine pregnancy tests to the planned study procedures • Added assessment of the suitability of the subject to remain in the study, which was to be conducted at all visits • Added details clarifying fasting laboratory procedures • Clarified that demographic information was to be taken from the antecedent study database for subjects completing the Screening Visit • Added that no psychoactive medication use would be permitted during the study, and that use within 5 times the half-life of the medication before study entry would be exclusionary • Clarified various details related to commonly excluded prior and concomitant medications.
22 May 2013	Amendment 2 included the following important changes: • Updated emergency reporting time. • Clarified pregnancy testing requirements in the inclusion criteria • Clarified the state that a current diagnosis rather than concurrent symptoms of bulimia nervosa or anorexia nervosa is exclusionary. • Removed distribute daily diary at Visit 3 in Table 1. • Added suitability to remain in the study to Visit 16(ET) in Table 1 and Table 2 • Added an Overall Risk/Benefit Assessment to Section 1. • Clarified that the time frame subjects were permitted to receive psychotherapy intervention for binge eating disorder (BED). • Clarified that the Mini International Neuropsychiatric Interview Plus (MINI-Plus) will be completed to exclude comorbid Axis I disorders. • Clarified that a urine drug screen will be conducted at the Screening Visit (Visit -1) only for subjects who enroll 30 days from completion of the antecedent study. • Added Suitability to Remain in the Study. • Added adverse event (AE) reporting requirements for a change in vital signs and electrocardiogram (ECG) results. • Added protocol history appendix.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported