



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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 17 September 2012 | <p>Amendment 1 included the following important changes:</p> <ul style="list-style-type: none">• 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 | <p>Amendment 2 included the following important changes:</p> <ul style="list-style-type: none">• 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