# Clinical trial results:
# A 6-Month, Open-Label, Multi-Center, Flexible-Dose Extension Study to the B2061032 Study to Evaluate the Safety, Tolerability and Efficacy of Desvenlafaxine Succinate Sustained-Release (DVS SR) Tablets in the Treatment of Children and Adolescent Outpatients with Major Depressive Disorder

## Summary

| | |
|---|---|
| EudraCT number | 2008-001876-67 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 22 April 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 03 November 2016 |
| First version publication date | 03 November 2016 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | B2061030 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01371708 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Alias ID: 3151A6-3344 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Pfizer, Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.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? | Yes |
| 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 | 22 April 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 April 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 April 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

This Phase 3, multi-center, open-label, flexible-dose extension study of desvenlafaxine succinate sustained-release (DVS SR) in the treatment of child (7 to 11 years of age) and adolescent (12 to 17 years of age) outpatients with Major Depressive Disorder (MDD) who completed the preceding double-blind study (B2061032) aimed to evaluate the long-term safety, tolerability and efficacy of DVS SR in the treatment of children and adolescents with MDD.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation Good Clinical Practice Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial participants. The final protocol and any amendments were reviewed and approved by the Institutional Review Board(s) and/or Independent Ethics Committee(s) at each of the investigational centres participating in the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 02 February 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 282 |
| Country: Number of subjects enrolled | Chile: 1 |
| Worldwide total number of subjects | 283 |
| EEA total number of subjects | 0 |

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) | 87 |

| | |
|---|---|
| Adolescents (12-17 years) | 196 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants completing study B2061032 who, in the Investigator's opinion, would benefit from long-term treatment with DVS SR, may have been eligible for this extension study. Of the 304 participants completing study B2061032, 283 transitioned to this study at the Week 8 visit of the preceding double-blind study. Of these, 281 received treatment.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo/DVS-SR |

Arm description:

Participants received placebo tablets in previous study B2061032 and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Desvenlafaxine succinate sustained-release |
| Investigational medicinal product code | |
| Other name | DVS SR |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received placebo in the previous study B2061032, and DVS SR in this extension study B2061030 in a flexible dosing regimen (20, 25, 35, or 50 mg/day as clinically indicated) of up to 26 weeks, followed by a taper phase of up to 2 weeks.

| | |
|---|---|
| **Arm title** | DVS-SR, low dose/DVS-SR |

Arm description:

Participants received DVS-SR in weight-based dosing (20, 25, or 35 mg) in previous study B2061032, and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Desvenlafaxine succinate sustained-release |
| Investigational medicinal product code | |
| Other name | DVS SR |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received DVS SR in weight based dosing (20, 25, or 35 mg) in previous study B2061032, and DVS SR in this extension study B2061030 in a flexible dosing regimen (20, 25, 35, or 50 mg/day as clinically indicated) of up to 26 weeks, followed by a taper phase of up to 2 weeks.

| | |
|---|---|
| **Arm title** | DVS-SR, high dose/DVS-SR |

Arm description:

Participants received DVS-SR in weight-based dosing (25, 35, or 50 mg) in previous study B2061032, and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Desvenlafaxine succinate sustained-release |
| Investigational medicinal product code | |
| Other name | DVS SR |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received DVS SR in weight based dosing (20, 25, or 50 mg) in previous study B2061032, and DVS SR in this extension study B2061030 in a flexible dosing regimen (20, 25, 35, or 50 mg/day as clinically indicated) of up to 26 weeks, followed by a taper phase of up to 2 weeks.

| **Number of subjects in period 1** | Placebo/DVS-SR | DVS-SR, low dose/DVS-SR | DVS-SR, high dose/DVS-SR |
|---|---|---|---|
| Started | 92 | 93 | 98 |
| Received treatment | 91 | 93 | 97 |
| Completed | 66 | 63 | 59 |
| Not completed | 26 | 30 | 39 |
| Adverse event, non-fatal | 5 | 8 | 12 |
| Not specified | 3 | 2 | 4 |
| No longer willing to participate | 7 | 7 | 13 |
| Started study but did not receive study treatment | 1 | - | 1 |
| Lost to follow-up | 5 | 9 | 7 |
| Medication error/not related to AE | - | 1 | - |
| Insufficient clinical response | 3 | 2 | - |
| Protocol deviation | 2 | 1 | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo/DVS-SR |
| Reporting group description: | |
| Participants received placebo tablets in previous study B2061032 and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030. | |
| Reporting group title | DVS-SR, low dose/DVS-SR |
| Reporting group description: | |
| Participants received DVS-SR in weight-based dosing (20, 25, or 35 mg) in previous study B2061032, and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030. | |
| Reporting group title | DVS-SR, high dose/DVS-SR |
| Reporting group description: | |
| Participants received DVS-SR in weight-based dosing (25, 35, or 50 mg) in previous study B2061032, and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030. | |

| Reporting group values | Placebo/DVS-SR | DVS-SR, low dose/DVS-SR | DVS-SR, high dose/DVS-SR |
|---|---|---|---|
| Number of subjects | 92 | 93 | 98 |
| Age, Customized<br>Units: Participants | | | |
| 2 to 11 years | 28 | 26 | 33 |
| 12 to 17 years | 64 | 67 | 65 |
| Gender, Male/Female<br>Units: Participants | | | |
| Female | 43 | 52 | 61 |
| Male | 49 | 41 | 37 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 283 | | |
| Age, Customized<br>Units: Participants | | | |
| 2 to 11 years | 87 | | |
| 12 to 17 years | 196 | | |
| Gender, Male/Female<br>Units: Participants | | | |
| Female | 156 | | |
| Male | 127 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo/DVS-SR |

Reporting group description:

Participants received placebo tablets in previous study B2061032 and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| | |
|---|---|
| Reporting group title | DVS-SR, low dose/DVS-SR |

Reporting group description:

Participants received DVS-SR in weight-based dosing (20, 25, or 35 mg) in previous study B2061032, and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| | |
|---|---|
| Reporting group title | DVS-SR, high dose/DVS-SR |

Reporting group description:

Participants received DVS-SR in weight-based dosing (25, 35, or 50 mg) in previous study B2061032, and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| | |
|---|---|
| Subject analysis set title | Combination Group |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Combination of 3 groups of participants from previous study B2061032 received desvenlafaxine succinate sustained release in flexible dosing ranging from 20 to 50 mg in the current extension study, B2061030.

### Primary: Percentage of Participants With a Treatment-emergent Adverse Event (TEAE)

| | |
|---|---|
| End point title | Percentage of Participants With a Treatment-emergent Adverse Event (TEAE)[1] |

End point description:

A TEAE was defined as an event that was absent before treatment and emerged or worsened during the treatment period.
Analysis population included all participants who received at least 1 dose of study drug in study B2061030.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

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: No statistical analyses was planned for this primary endpoint

| End point values | Placebo/DVS-SR | DVS-SR, low dose/DVS-SR | DVS-SR, high dose/DVS-SR | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 91 | 93 | 97 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 78 | 73.1 | 71.1 | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants With a Treatment-emergent Adverse Event (TEAE) (Combination Group)

| End point title | Percentage of Participants With a Treatment-emergent Adverse Event (TEAE) (Combination Group)[2] |
|---|---|

End point description:

A TEAE was defined as an event that was absent before treatment and emerged or worsened during the treatment period.
Analysis population included all participants who received at least 1 dose of study drug in study B2061030.

| End point type | Primary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

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: No statistical analyses was planned for this primary endpoint

| **End point values** | Combination Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 281 | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 74 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline to Week 26 in Total Score on the Children's Depression Rating Scale, Revised (CDRS-R), Based on Observed Cases

| End point title | Change From Baseline to Week 26 in Total Score on the Children's Depression Rating Scale, Revised (CDRS-R), Based on Observed Cases |
|---|---|

End point description:

The CDRS-R consists of 17 items. The total score is the sum of responses to the 17 items and ranges from 17 to 113. Lower total scores indicate lower intensity of symptoms. Remission on the CDRS-R was defined as a CDRS-R score <=28. It was recommended that the CDRS-R be performed prior to the Clinical Global Impression assessments. Mean change from baseline=score at Week 26 minus score at baseline of study B2061032.
Analysis population included all participants who had a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, and had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| **End point values** | Placebo/DVS-SR | DVS-SR, low dose/DVS-SR | DVS-SR, high dose/DVS-SR | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 63 | 57 | 56 | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -6.79 (± 12.05) | -10.72 (± 10.8) | -8.57 (± 13.01) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline to Week 26 in Total Score on the Children's Depression Rating Scale, Revised (CDRS-R), Based on Observed Cases (Combination Group)

| End point title | Change From Baseline to Week 26 in Total Score on the Children's Depression Rating Scale, Revised (CDRS-R), Based on Observed Cases (Combination Group) |
|---|---|

End point description:

The CDRS-R consists of 17 items. The total score is the sum of responses to the 17 items and ranges from 17 to 113. Lower total scores indicate lower intensity of symptoms. Remission on the CDRS-R was defined as a CDRS-R score <=28. It was recommended that the CDRS-R be performed prior to the Clinical Global Impression assessments. Mean change from baseline=score at Week 26 minus score at baseline of study B2061032.
Analysis population included all participants who had a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030, and were available for evaluation.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| **End point values** | Combination Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 176 | | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -8.63 (± 12.03) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Score From Baseline to Week 26 on the Clinical Global Impression-Severity (CGI-S) Scale, Based on Observed Cases

| End point title | Change in Score From Baseline to Week 26 on the Clinical Global Impression-Severity (CGI-S) Scale, Based on Observed Cases |
|---|---|

End point description:

The Clinical Global Impression (CGI) Scale is a tool that summarizes all available patient data, including history, symptoms, behavior, and the impact of the symptoms on ability to function. The scale consists of 2 measures: the CGI-S, which rates the severity of illness from 1 to 7, and the CGI-Improvement Scale, which assesses improvement in illness since baseline. The CGI-S is a 7-point scale a clinician uses

to rate a patient's severity of illness. Scores range from 1 to 7, with 1 indicating “normal, not at all ill” and 7, “among the most extremely ill patients.” Higher score on the CGI-S indicates greater severity of illness. Mean change from baseline=score at Week 26 minus score at baseline of study B2061032.
Analysis population included all participants who had a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, and had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| **End point values** | Placebo/DVS-SR | DVS-SR, low dose/DVS-SR | DVS-SR, high dose/DVS-SR | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 63 | 57 | 56 | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -1.02 (± 1.18) | -1.44 (± 1.12) | -0.7 (± 1.37) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Score From Baseline to Week 26 on the Clinical Global Impression-Severity (CGI-S) Scale, Based on Observed Cases (Combination Group)

| End point title | Change in Score From Baseline to Week 26 on the Clinical Global Impression-Severity (CGI-S) Scale, Based on Observed Cases (Combination Group) |
|---|---|

End point description:

The CGI Scale is a tool that summarizes all available patient data, including history, symptoms, behavior, and the impact of the symptoms on ability to function. The scale consists of 2 measures: the CGI-S, which rates the severity of illness from 1 to 7, and the CGI-Improvement Scale, which assesses improvement in illness since baseline. The CGI-S is a 7-point scale a clinician uses to rate a patient's severity of illness. Scores range from 1 to 7, with 1 indicating “normal, not at all ill” and 7, “among the most extremely ill patients.” Higher score on the CGI-S indicates greater severity of illness. Mean change from baseline=score at Week 26 minus score at baseline of study B2061032.
Analysis population included all participants who had a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030, and were available for evaluation.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| **End point values** | Combination Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 176 | | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -1.05 (± 1.26) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With a Response of Very Much Improved or Much Improved on the Clinical Global Impression-Improvement (CGI-I) Scale at Week 26, Based on Observed Cases

| End point title | Percentage of Participants With a Response of Very Much Improved or Much Improved on the Clinical Global Impression-Improvement (CGI-I) Scale at Week 26, Based on Observed Cases |
|---|---|

End point description:

The CGI Scale is a tool that summarizes all available patient data, including history, symptoms, behavior, & impact of symptoms on ability to function. The scale consists of 2 measures: the CGI-Severity scale, which rates the severity of illness from 1 to 7, and the CGI-I scale, which assesses improvement in illness since baseline. The CGI-I is a 7-point scale used a clinician uses to assess improvement in a patient's illness relative to baseline. Scores range from 1 ("very much improved") to 7 ("very much worse"); a value of 0 = not assessed. A response on the CGI-I scale is defined as a CGI-I scores of 1 or 2. Mean change from baseline=score at Week 26 minus score at baseline of study B2061032.
Analysis population included all participants who had a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, and had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| **End point values** | Placebo/DVS-SR | DVS-SR, low dose/DVS-SR | DVS-SR, high dose/DVS-SR | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 63 | 57 | 56 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 87.3 | 94.7 | 89.3 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With a Response of Very Much Improved or Much Improved on the Clinical Global Impression-Improvement (CGI-I) Scale at Week 26, Based on Observed Cases (Combination Group)

| End point title | Percentage of Participants With a Response of Very Much Improved or Much Improved on the Clinical Global Impression-Improvement (CGI-I) Scale at Week 26, Based on Observed Cases (Combination Group) |
|---|---|

End point description:

The CGI Scale is a tool that summarizes all available patient data, including history, symptoms, behavior, & impact of symptoms on ability to function. The scale consists of 2 measures: the CGI-Severity scale, which rates the severity of illness from 1 to 7, & the CGI-I scale, which assesses improvement in illness since baseline. The CGI-I is a 7-point scale used a clinician uses to assess improvement in a patient's illness relative to baseline. Scores range from 1 (“very much improved”) to 7 (“very much worse”); a value of 0 = not assessed. A response on the CGI-I scale is defined as a CGI-I scores of 1 or 2. Mean change from baseline=score at Week 26 minus score at baseline of study B2061032.
Analysis population included all participants who had a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030, & were available for evaluation.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| **End point values** | Combination Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 176 | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 90.3 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants by Score on the Clinical Global Impression-Improvement (CGI-I) Scale, Based on Observed Cases

| End point title | Percentage of Participants by Score on the Clinical Global Impression-Improvement (CGI-I) Scale, Based on Observed Cases |
|---|---|

End point description:

The CGI Scale is a tool that summarizes all available patient data, including history, symptoms, behavior, & the impact of the symptoms on ability to function. The scale consists of 2 measures: the CGI-Severity scale, which rates the severity of illness from 1 to 7, and the CGI-I scale, which assesses improvement in illness since baseline. The CGI-I is a 7-point scale used to assess improvement in a patient's illness relative to baseline. Scores range from 1 (“very much improved”) to 7 (“very much worse”); a value of 0 = not assessed. A response on the CGI-I scale is defined as a CGI-I scores of 1 or 2. Mean change from baseline=score at Week 26 minus score at baseline of study B2061032.
Analysis population included all participants who had a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, and had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| End point values | Placebo/DVS-SR | DVS-SR, low dose/DVS-SR | DVS-SR, high dose/DVS-SR | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 63 | 57 | 56 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 26: Very much improved | 54 | 73.7 | 53.6 | |
| Week 26: Much improved | 33.3 | 21.1 | 35.7 | |
| Week 26: Minimally improved | 9.5 | 5.3 | 10.7 | |
| Week 26: No change | 1.6 | 0 | 0 | |
| Week 26: Minimally worse | 1.6 | 0 | 0 | |
| Week 26: Much worse | 0 | 0 | 0 | |
| Week 26: Very much worse | 0 | 0 | 0 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants by Score on the Clinical Global Impression-Improvement (CGI-I) Scale, Based on Observed Cases (Combination Group)

| End point title | Percentage of Participants by Score on the Clinical Global Impression-Improvement (CGI-I) Scale, Based on Observed Cases (Combination Group) |
|---|---|

End point description:

The CGI Scale is a tool that summarizes all available patient data, including history, symptoms, behavior, & the impact of the symptoms on ability to function. The scale consists of 2 measures: the CGI-Severity scale, which rates severity of illness from 1 to 7, and the CGI-I scale, which assesses improvement in illness since baseline. The CGI-I is a 7-point scale used to assess improvement in a patient's illness relative to baseline. Scores range from 1 (“very much improved”) to 7 (“very much worse”); a value of 0 = not assessed. A response on the CGI-I scale is defined as a CGI-I score of 1 or 2. Mean change from baseline=score at Week 26 minus score at baseline of study B2061032.
Analysis population included all participants with a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030, & were available for evaluation.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| End point values | Combination Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 176 | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 26: Very much improved | 60.2 | | | |
| Week 26: Much improved | 30.1 | | | |
| Week 26: Minimally improved | 8.5 | | | |
| Week 26: No change | 0.6 | | | |
| Week 26: Minimally worse | 0.6 | | | |
| Week 26: Much worse | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 26: Very much worse | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Remission at Week 26, Based on Score on the Children's Depression Rating Scale, Revised (CDRS-R), <=28 and on Observed Cases

| End point title | Percentage of Participants With Remission at Week 26, Based on Score on the Children's Depression Rating Scale, Revised (CDRS-R), <=28 and on Observed Cases |
|---|---|

End point description:

Remission on the CDRS-R was defined as a CDRS-R score <=28. The CDRS-R consists of 17 items. The total score is the sum of responses to the 17 items and ranges from 17 to 113. Lower total s cores indicate lower intensity of symptoms.
Analysis population included all participants who had a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, and had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| End point values | Placebo/DVS-SR | DVS-SR, low dose/DVS-SR | DVS-SR, high dose/DVS-SR | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 63 | 57 | 56 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 73 | 89.5 | 75 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Remission at Week 26, Based on a Score on the Children's Depression Rating Scale, Revised (CDRS-R), <=28 and on Observed Cases (Combination Group)

| End point title | Percentage of Participants With Remission at Week 26, Based on a Score on the Children's Depression Rating Scale, Revised (CDRS-R), <=28 and on Observed Cases (Combination Group) |
|---|---|

End point description:

Remission on the CDRS-R was defined as a CDRS-R score <=28. The CDRS-R consists of 17 items. The total score is the sum of responses to the 17 items and ranges from 17 to 113. Lower total s cores indicate lower intensity of symptoms.
Analysis population included all participants who had a CDRS-R evaluation at Baseline of study B2061030 (Week 8 of study B2061032), took at least 1 dose of study drug, had at least 1 CDRS-R evaluation after the first dose of study drug in B2061030, and were available for evaluation.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 8 (B2061032)/Day 1 (B2061030) to Week 26 of B2061030

| **End point values** | Combination Group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 176 | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 79 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From informed consent through Week 30 (adverse events) and Week 32 visit (serious adverse events). For participants who discontinued prior to Week 28 visit: Adverse events collected for 14 days, and serious adverse events for 28 days,

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Placebo/DVS-SR |

Reporting group description:

Participants received placebo tablets in previous study B2061032 and desvenlafaxine succinate sustained-release (DVS-SR) in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| | |
|---|---|
| Reporting group title | Combination Group |

Reporting group description:

Combination of 3 groups of participants from previous study B2061032 received DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| | |
|---|---|
| Reporting group title | DVS-SR, low dose/DVS-SR |

Reporting group description:

Participants received DVS-SR in weight-based dosing(20, 25, or 35 mg) in previous study B2061032, and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| | |
|---|---|
| Reporting group title | DVS-SR, high dose/DVS-SR |

Reporting group description:

Participants received DVS-SR in weight-based dosing (25, 35, or 50 mg) in previous study B2061032, and DVS-SR in flexible dosing ranging from 20 to 50 mg in extension study B2061030.

| Serious adverse events | Placebo/DVS-SR | Combination Group | DVS-SR, low dose/DVS-SR |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 91 (4.40%) | 13 / 281 (4.63%) | 6 / 93 (6.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 281 (0.36%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Generalised tonic-clonic seizure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 281 (0.36%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 281 (0.36%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 1 / 281 (0.36%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Agitation | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 2 / 281 (0.71%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hallucination, auditory | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 281 (0.36%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 281 (0.36%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Major depression | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 1 / 281 (0.36%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyromania | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 281 (0.36%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Suicidal ideation | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 5 / 281 (1.78%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 5 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 3 / 281 (1.07%) | 2 / 93 (2.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide threat | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 1 / 281 (0.36%) | 0 / 93 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Ketoacidosis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 281 (0.36%) | 1 / 93 (1.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | DVS-SR, high dose/DVS-SR | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 97 (3.09%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | | |
|---|---|---|---|---|
| Bronchial hyperreactivity | | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Psychiatric disorders | | | | |
| Aggression | | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Agitation | | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hallucination, auditory | | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Initial insomnia | | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Major depression | | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyromania | | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Suicidal ideation | | | | |
| subjects affected / exposed | 2 / 97 (2.06%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Suicide attempt | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicide threat | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Ketoacidosis | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3 %

| **Non-serious adverse events** | Placebo/DVS-SR | Combination Group | DVS-SR, low dose/DVS-SR |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 60 / 91 (65.93%) | 175 / 281 (62.28%) | 57 / 93 (61.29%) |
| Investigations | | | |
| Weight increased | | | |
| subjects affected / exposed | 5 / 91 (5.49%) | 14 / 281 (4.98%) | 4 / 93 (4.30%) |
| occurrences (all) | 5 | 14 | 4 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 8 / 91 (8.79%) | 20 / 281 (7.12%) | 4 / 93 (4.30%) |
| occurrences (all) | 12 | 29 | 7 |
| Ligament sprain | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 3 / 281 (1.07%) | 0 / 93 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 91 (4.40%) | 15 / 281 (5.34%) | 6 / 93 (6.45%) |
| occurrences (all) | 4 | 18 | 7 |
| Headache | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 12 / 91 (13.19%) | 45 / 281 (16.01%) | 16 / 93 (17.20%) |
| occurrences (all) | 19 | 79 | 29 |
| Psychomotor hyperactivity | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 4 / 281 (1.42%) | 1 / 93 (1.08%) |
| occurrences (all) | 4 | 5 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 10 / 91 (10.99%) | 14 / 281 (4.98%) | 3 / 93 (3.23%) |
| occurrences (all) | 10 | 14 | 3 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 6 / 281 (2.14%) | 0 / 93 (0.00%) |
| occurrences (all) | 3 | 6 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 4 / 91 (4.40%) | 13 / 281 (4.63%) | 1 / 93 (1.08%) |
| occurrences (all) | 4 | 17 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 3 / 281 (1.07%) | 0 / 93 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 8 / 281 (2.85%) | 1 / 93 (1.08%) |
| occurrences (all) | 3 | 9 | 1 |
| Nausea | | | |
| subjects affected / exposed | 4 / 91 (4.40%) | 21 / 281 (7.47%) | 11 / 93 (11.83%) |
| occurrences (all) | 5 | 25 | 11 |
| Vomiting | | | |
| subjects affected / exposed | 6 / 91 (6.59%) | 12 / 281 (4.27%) | 2 / 93 (2.15%) |
| occurrences (all) | 7 | 16 | 2 |
| Reproductive system and breast disorders | | | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 4 / 281 (1.42%) | 0 / 93 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 5 / 281 (1.78%) | 3 / 93 (3.23%) |
| occurrences (all) | 2 | 5 | 3 |

| | | | |
|---|---|---|---|
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 5 / 281 (1.78%) | 2 / 93 (2.15%) |
| occurrences (all) | 0 | 5 | 2 |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 6 / 281 (2.14%) | 1 / 93 (1.08%) |
| occurrences (all) | 3 | 6 | 1 |
| Depression | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 8 / 281 (2.85%) | 3 / 93 (3.23%) |
| occurrences (all) | 1 | 8 | 3 |
| Initial insomnia | | | |
| subjects affected / exposed | 5 / 91 (5.49%) | 6 / 281 (2.14%) | 0 / 93 (0.00%) |
| occurrences (all) | 5 | 6 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 7 / 91 (7.69%) | 17 / 281 (6.05%) | 6 / 93 (6.45%) |
| occurrences (all) | 8 | 18 | 6 |
| Irritability | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 14 / 281 (4.98%) | 4 / 93 (4.30%) |
| occurrences (all) | 3 | 15 | 5 |
| Self injurious behaviour | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 4 / 281 (1.42%) | 3 / 93 (3.23%) |
| occurrences (all) | 0 | 4 | 3 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 7 / 281 (2.49%) | 2 / 93 (2.15%) |
| occurrences (all) | 4 | 10 | 2 |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 6 / 281 (2.14%) | 2 / 93 (2.15%) |
| occurrences (all) | 3 | 6 | 2 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 7 / 91 (7.69%) | 16 / 281 (5.69%) | 3 / 93 (3.23%) |
| occurrences (all) | 7 | 16 | 3 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 9 / 91 (9.89%) | 21 / 281 (7.47%) | 4 / 93 (4.30%) |
| occurrences (all) | 10 | 23 | 5 |

| | | | |
|---|---|---|---|
| Otitis media | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 5 / 281 (1.78%) | 1 / 93 (1.08%) |
| occurrences (all) | 3 | 5 | 1 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 5 / 281 (1.78%) | 1 / 93 (1.08%) |
| occurrences (all) | 1 | 5 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 8 / 281 (2.85%) | 2 / 93 (2.15%) |
| occurrences (all) | 1 | 9 | 2 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 91 (4.40%) | 16 / 281 (5.69%) | 10 / 93 (10.75%) |
| occurrences (all) | 5 | 19 | 11 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 4 / 91 (4.40%) | 7 / 281 (2.49%) | 2 / 93 (2.15%) |
| occurrences (all) | 4 | 7 | 2 |
| Increased appetite | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 4 / 281 (1.42%) | 3 / 93 (3.23%) |
| occurrences (all) | 0 | 4 | 3 |

| **Non-serious adverse events** | DVS-SR, high dose/DVS-SR | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 58 / 97 (59.79%) | | |
| Investigations | | | |
| Weight increased | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | | |
| occurrences (all) | 5 | | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 8 / 97 (8.25%) | | |
| occurrences (all) | 10 | | |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Psychomotor hyperactivity<br>subjects affected / exposed<br>occurrences (all)<br><br>Somnolence<br>subjects affected / exposed<br>occurrences (all) | 5 / 97 (5.15%)<br>7<br><br>17 / 97 (17.53%)<br>31<br><br>0 / 97 (0.00%)<br>0<br><br>1 / 97 (1.03%)<br>1 | | |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all) | <br><br>3 / 97 (3.09%)<br>3 | | |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | <br><br>8 / 97 (8.25%)<br>12<br><br>3 / 97 (3.09%)<br>3<br><br>5 / 97 (5.15%)<br>5<br><br>6 / 97 (6.19%)<br>9<br><br>4 / 97 (4.12%)<br>7 | | |
| Reproductive system and breast disorders<br>Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all) | <br><br>3 / 97 (3.09%)<br>3 | | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---|---|---|
| Rash | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 3 / 97 (3.09%) | | |
| occurrences (all) | 3 | | |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 2 / 97 (2.06%) | | |
| occurrences (all) | 2 | | |
| Depression | | | |
| subjects affected / exposed | 4 / 97 (4.12%) | | |
| occurrences (all) | 4 | | |
| Initial insomnia | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |
| subjects affected / exposed | 4 / 97 (4.12%) | | |
| occurrences (all) | 4 | | |
| Irritability | | | |
| subjects affected / exposed | 7 / 97 (7.22%) | | |
| occurrences (all) | 7 | | |
| Self injurious behaviour | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 2 / 97 (2.06%) | | |
| occurrences (all) | 4 | | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 6 / 97 (6.19%) | | |
| occurrences (all) | 6 | | |

| | | | |
|---|---|---|---|
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 8 / 97 (8.25%)<br>8 | | |
| Otitis media<br>subjects affected / exposed<br>occurrences (all) | 1 / 97 (1.03%)<br>1 | | |
| Pharyngitis streptococcal<br>subjects affected / exposed<br>occurrences (all) | 3 / 97 (3.09%)<br>3 | | |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all) | 5 / 97 (5.15%)<br>6 | | |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 2 / 97 (2.06%)<br>3 | | |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 1 / 97 (1.03%)<br>1 | | |
| Increased appetite<br>subjects affected / exposed<br>occurrences (all) | 1 / 97 (1.03%)<br>1 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 13 July 2011 | Clarified that no repackaging or labeling of the study drug containers that obscured the Pfizer label was permitted at the sites. Deleted investigational procedures from the prohibited treatment list. Text revised to clarify participants who were required to sign an informed consent document were those reaching the age of majority rather than reaching the age of 18 years. Addition of methaqualone to the urine drug screen testing list. Added the 10 mg/day dose blister card to the table in Appendix 1 of the protocol. |
| 22 May 2013 | Updates/clarifications to Schedule of Activities. Adult studies in introduction revised. Combined & clarified efficacy endpoints. Permitted omission of taper& exclusion of extension. Updated study duration. Inclusion criteria: 2: changed "legally acceptable representative" to "legal guardian"; 4, 5 & 6: clarified contraception requirements. Exclusion criteria: 1: deleted "potential child or adolescent"; 2: renamed "study drug" to "investigational product"; 4: clarified exclusion of participants requiring prohibited medication; 6: clarified history of suicide behavior exclusion since last visit, added risk assessment; 7: clarified suicidal ideation exclusion since last visit, added risk assessment. Added sections on sponsor qualified medical personnel, rater qualifications, & medication errors. Revised text for storage requirements. Clarified examples & use of permitted & prohibited concomitant treatments. Clarified review of results prior to randomisation. Clarified participant withdrawal, process for lost to follow-up, & added risk assessment. Clarified assessments for AEs/SAEs, vital signs, pregnancy testing, microscopic analysis, urine drug screen & comprehensive psychiatric evaluation. Revised text on guidance materials & clarified rater requirements/training. Added requirements for risk assessment & discontinuation following C-SSRS; evaluations. Clarified AE follow-up, serious versus non-serious AEs, timeframes for reporting, AE examples, defined significant disability/incapacity, protocol-specific SAEs, Hy's Law criteria, causality assessment definition, reporting of exposures in utero, & source for AE information. Clarified the DMC responsibilities, Pfizer record retention policy, participant de-identification information, informed consent process & Pfizer communication of results. Added vendor information. Deleted End of Trial in a Member State section. Added table of diagnostician & rater requirements. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported