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 Units: Participants			
2 to 11 years	28	26	33
12 to 17 years	64	67	65
Gender, Male/Female Units: Participants			
Female	43	52	61
Male	49	41	37

Reporting group values	Total		
Number of subjects	283		
Age, Customized Units: Participants			
2 to 11 years	87		
12 to 17 years	196		
Gender, Male/Female 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 occurrences (all) Headache subjects affected / exposed occurrences (all) Psychomotor hyperactivity subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	5 / 97 (5.15%) 7 17 / 97 (17.53%) 31 0 / 97 (0.00%) 0 1 / 97 (1.03%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 3 / 97 (3.09%) 3		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 8 / 97 (8.25%) 12 3 / 97 (3.09%) 3 5 / 97 (5.15%) 5 6 / 97 (6.19%) 9 4 / 97 (4.12%) 7		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	 3 / 97 (3.09%) 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 subjects affected / exposed occurrences (all)	8 / 97 (8.25%) 8		
Otitis media subjects affected / exposed occurrences (all)	1 / 97 (1.03%) 1		
Pharyngitis streptococcal subjects affected / exposed occurrences (all)	3 / 97 (3.09%) 3		
Sinusitis subjects affected / exposed occurrences (all)	5 / 97 (5.15%) 6		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 97 (2.06%) 3		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 97 (1.03%) 1		
Increased appetite subjects affected / exposed occurrences (all)	1 / 97 (1.03%) 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