Clinical trial results:
A Double-Blind, Efficacy and Safety Study of Duloxetine versus Placebo in the Treatment of Children and Adolescents with Major Depressive Disorder

Summary

EudraCT number	2008-006492-71
Trial protocol	FI EE SK DE FR
Global end of trial date	13 October 2011

Results information

Result version number	v2 (current)
This version publication date	22 September 2017
First version publication date	14 December 2016
Version creation reason	
Summary attachment (see zip file)	HMCK-Approved CSR (Duloxxetine-F1J-MC-HMCK.pdf)

Trial information

Trial identification

Sponsor protocol code	F1J-MC-HMCK

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00849901
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 6223

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 October 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess whether duloxetine is superior to placebo in the treatment of children and adolescents with major depressive disorder (MDD)

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 March 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 140
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Slovakia: 6
Country: Number of subjects enrolled	Ukraine: 66
Country: Number of subjects enrolled	Russian Federation: 40
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	South Africa: 67
Worldwide total number of subjects	337
EEA total number of subjects	24

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	135
Adolescents (12-17 years)	202
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:

This study consisted of a 10-week acute treatment phase, and a 6-month extension phase.

Period 1

Period 1 title	Acute Treatment Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Duloxetine

Arm description:

Received duloxetine 60, 90, and/or 120 mg orally (PO), once daily (QD) during acute treatment phase.

Arm type	Experimental
Investigational medicinal product name	Duloxetine
Investigational medicinal product code	
Other name	LY248686; Cymbalta
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

60, 90, and/or 120 milligram (mg) of duloxetine capsules were given orally (PO).

Arm title	Fluoxetine

Arm description:

Received fluoxetine 20 and/or 40 mg PO, QD during acute treatment phase.

Arm type	Active comparator
Investigational medicinal product name	Fluoxetine
Investigational medicinal product code	
Other name	Prozac
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

20 and/or 40 mg of fluoxetine capsules administered orally.

Arm title	Placebo

Arm description:

Received placebo PO, QD during acute treatment phase

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules of placebo was given orally.

Number of subjects in period 1	Duloxetine	Fluoxetine	Placebo
Started	117	117	103
Completed	87	91	87
Not completed	30	26	16
Consent withdrawn by subject	4	10	4
Physician decision	1	1	1
Adverse event, non-fatal	9	1	3
Sponsor Decision	1	-	-
Parent or Caregiver Decision	11	5	4
Lost to follow-up	2	4	1
Lack of efficacy	2	3	2
Protocol deviation	-	2	1

Period 2	
Period 2 title	Extension Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Assessor, Subject

Arms	
Are arms mutually exclusive?	Yes
Arm title	Duloxetine/Duloxetine

Arm description:

Received duloxetine 60, 90, and/or 120 milligram (mg) orally (PO), once daily (QD) during both acute treatment phase and extension phase

Arm type	Experimental
Investigational medicinal product name	Duloxetine
Investigational medicinal product code	
Other name	LY248686; Cymbalta
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

60, 90, and/or 120 milligram (mg) of duloxetine capsules was given orally.

Arm title	Fluoxetine/Fluoxetine

Arm description:

Received fluoxetine 20 and/or 40 mg PO, QD during both acute treatment phase and extension phase

Arm type	Active comparator

Investigational medicinal product name	Fluoxetine
Investigational medicinal product code	
Other name	Prozac
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

20 and/or 40 mg of fluoxetine capsules was given orally.

Arm title	Placebo/Duloxetine

Arm description:

Received placebo PO, QD during acute treatment phase, and duloxetine 60, 90, and/or 120 mg PO, QD during extension phase

Arm type	Placebo
Investigational medicinal product name	Placebo/Duloxetine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo PO, QD was given during acute treatment phase, and duloxetine 60, 90, and/or 120 mg PO, QD during extension phase.

Number of subjects in period 2[1]	Duloxetine/Duloxetine	Fluoxetine/Fluoxetine	Placebo/Duloxetine
Started	83	91	86
Completed	56	65	69
Not completed	27	26	17
Consent withdrawn by subject	7	6	3
Physician decision	1	2	-
Adverse event, non-fatal	2	8	4
Parent or Caregiver Decision	10	4	4
Lost to follow-up	3	-	1
Protocol deviation	2	2	4
Lack of efficacy	2	4	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 4 participants from Duloxetine/Duloxetine group and 1 participant from Placebo/Duloxetine group decided not to enter in to the extension phase.

Baseline characteristics

Reporting groups	
Reporting group title	Duloxetine
Reporting group description:	
Received duloxetine 60, 90, and/or 120 mg orally (PO), once daily (QD) during acute treatment phase.	
Reporting group title	Fluoxetine
Reporting group description:	
Received fluoxetine 20 and/or 40 mg PO, QD during acute treatment phase.	
Reporting group title	Placebo
Reporting group description:	
Received placebo PO, QD during acute treatment phase	

Reporting group values	Duloxetine	Fluoxetine	Placebo
Number of subjects	117	117	103
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	13.14	13.08	13.28
standard deviation	± 3.043	± 3.272	± 3.055
Gender, Male/Female Units:			
Female	64	61	51
Male	53	56	52
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	1	1	1
Asian	0	2	0
Black or African American	17	9	13
White	90	93	79
Multiracial	4	7	5
Not Provided	5	5	5
Region of Enrollment Units: Subjects			
United States	50	45	45
Finland	1	4	0
France	3	2	3
Germany	1	1	2
Slovakia	2	3	1
Ukraine	25	23	18
Russian Federation	13	15	12
Estonia	1	0	0
South Africa	21	24	22
Clinical Global Impressions of Severity (CGI-Severity) score			
CGI-Severity score evaluates the severity of illness at the time of assessment. The score ranges from 1 (normal, not at all ill) to 7 (among the most extremely ill patients).			

Units: Units on a scale			
arithmetic mean	4.5	4.5	4.6
standard deviation	± 0.62	± 0.58	± 0.65
Children's Depression Rating Scale-Revised (CDRS-R) Total Score			
CDRS-R Total score measure the presence and severity of depression in children. The scale consists of 17 items scored on a 1-to-5- or 1-to-7-point scale. A rating of 1 indicates normal functioning. Total scores range from 17 to 113. In general, scores below 20 indicate an absence of depression, scores of 20 to 30 indicate borderline depression, and scores of 40 to 60 indicate moderate depression.			
Units: Units on a scale			
arithmetic mean	59.2	58.8	60.2
standard deviation	± 10.45	± 10.56	± 11.67
CDRS-R Subscale Scores, Mood			
CDRS-R Subscale score include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21.			
Units: Units on a scale			
arithmetic mean	16.3	15.9	16.1
standard deviation	± 3.54	± 3.85	± 3.59
CDRS-R Subscale Scores, Somatic			
CDRS-R Subscale score include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21.			
Units: Units on a scale			
arithmetic mean	19.8	19.7	20
standard deviation	± 4.54	± 4.21	± 4.75
CDRS-R Subscale Scores, Subjective			
CDRS-R Subscale score include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21.			
Units: Units on a scale			
arithmetic mean	10.1	10.4	10.4
standard deviation	± 3.08	± 3.24	± 3.46
CDRS-R Subscale Scores, Behavior			
CDRS-R Subscale score include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21.			
Units: Units on a scale			
arithmetic mean	13	12.8	13.5
standard deviation	± 2.79	± 2.87	± 3

Reporting group values	Total		
Number of subjects	337		
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		

Gender, Male/Female Units:			
Female	176		
Male	161		
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	3		
Asian	2		
Black or African American	39		
White	262		
Multiracial	16		
Not Provided	15		
Region of Enrollment Units: Subjects			
United States	140		
Finland	5		
France	8		
Germany	4		
Slovakia	6		
Ukraine	66		
Russian Federation	40		
Estonia	1		
South Africa	67		
Clinical Global Impressions of Severity (CGI-Severity) score			
CGI-Severity score evaluates the severity of illness at the time of assessment. The score ranges from 1 (normal, not at all ill) to 7 (among the most extremely ill patients).			
Units: Units on a scale arithmetic mean standard deviation	- -		
Children's Depression Rating Scale-Revised (CDRS-R) Total Score			
CDRS-R Total score measure the presence and severity of depression in children. The scale consists of 17 items scored on a 1-to-5- or 1-to-7-point scale. A rating of 1 indicates normal functioning. Total scores range from 17 to 113. In general, scores below 20 indicate an absence of depression, scores of 20 to 30 indicate borderline depression, and scores of 40 to 60 indicate moderate depression.			
Units: Units on a scale arithmetic mean standard deviation	- -		
CDRS-R Subscale Scores, Mood			
CDRS-R Subscale score include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21.			
Units: Units on a scale arithmetic mean standard deviation	- -		
CDRS-R Subscale Scores, Somatic			
CDRS-R Subscale score include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21.			
Units: Units on a scale arithmetic mean standard deviation	- -		

CDRS-R Subscale Scores, Subjective			
CDRS-R Subscale score include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21.			
Units: Units on a scale arithmetic mean standard deviation	- 		
CDRS-R Subscale Scores, Behavior			
CDRS-R Subscale score include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21.			
Units: Units on a scale arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Duloxetine
Reporting group description:	
Received duloxetine 60, 90, and/or 120 mg orally (PO), once daily (QD) during acute treatment phase.	
Reporting group title	Fluoxetine
Reporting group description:	
Received fluoxetine 20 and/or 40 mg PO, QD during acute treatment phase.	
Reporting group title	Placebo
Reporting group description:	
Received placebo PO, QD during acute treatment phase	
Reporting group title	Duloxetine/Duloxetine
Reporting group description:	
Received duloxetine 60, 90, and/or 120 milligram (mg) orally (PO), once daily (QD) during both acute treatment phase and extension phase	
Reporting group title	Fluoxetine/Fluoxetine
Reporting group description:	
Received fluoxetine 20 and/or 40 mg PO, QD during both acute treatment phase and extension phase	
Reporting group title	Placebo/Duloxetine
Reporting group description:	
Received placebo PO, QD during acute treatment phase, and duloxetine 60, 90, and/or 120 mg PO, QD during extension phase	

Primary: Change from baseline in Children's Depression Rating Scale-Revised (CDRS-R) total score at week 10 endpoint

End point title	Change from baseline in Children's Depression Rating Scale-Revised (CDRS-R) total score at week 10 endpoint
End point description:	
CDRS-R Total score measure the presence and severity of depression in children. The scale consists of 17 items scored on a 1-to-5- or 1-to-7-point scale. A rating of 1 indicates normal functioning. Total scores range from 17 to 113. In general, scores below 20 indicate an absence of depression, scores of 20 to 30 indicate borderline depression, and scores of 40 to 60 indicate moderate depression. Least Square (LS) means are adjusted for baseline, pooled investigator, age category, visit, treatment, treatment*visit, age category*visit and baseline*visit. Analysis Population Description: Participants with both a baseline and at least one post-baseline value.	
End point type	Primary
End point timeframe:	
Baseline, Week 10	

End point values	Duloxetine	Fluoxetine	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113	113	103	
Units: units on a scale				
least squares mean (standard error)	-24.3 (± 1.09)	-23.7 (± 1.06)	-24.3 (± 1.11)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Duloxetine
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.999
Method	Mixed models analysis
Confidence interval	
sides	2-sided
lower limit	-3
upper limit	3

Secondary: Change from week 10 in Children's Depression Rating Scale-Revised (CDRS-R) total score at week 36 endpoint

End point title	Change from week 10 in Children's Depression Rating Scale-Revised (CDRS-R) total score at week 36 endpoint

End point description:

CDRS-R Total score measure the presence and severity of depression in children. The scale consists of 17 items scored on a 1-to-5- or 1-to-7-point scale. A rating of 1 indicates normal functioning. Total scores range from 17 to 113. In general, scores below 20 indicate an absence of depression, scores of 20 to 30 indicate borderline depression, and scores of 40 to 60 indicate moderate depression. LS means are adjusted for baseline, pooled investigator, age category, visit, age category*visit and baseline*visit. Analysis Population Description: Participants with value during treatment phase and at least one post-Week 10 value.

End point type	Secondary

End point timeframe:

Week 10, Week 36

End point values	Duloxetine/Duloxetine	Fluoxetine/Fluoxetine	Placebo/Duloxetine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	91	85	
Units: units on a scale				
least squares mean (standard deviation)	-7.2 (± 0.86)	-9.9 (± 0.72)	-9.6 (± 0.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Children's Depression Rating Scale-Revised (CDRS-R) subscale score at week 10 endpoint

End point title	Change from baseline in Children's Depression Rating Scale-Revised (CDRS-R) subscale score at week 10 endpoint

End point description:

CDRS-R Subscale scores include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21. Higher score indicates greater severity of disease. LS means are adjusted for baseline, pooled investigator, age category, visit, treatment, treatment*visit, age category*visit and baseline*visit.
Analysis Population Description: Participants with both a baseline and at least one post-baseline value.

End point type	Secondary

End point timeframe:

Baseline, Week 10

End point values	Duloxetine	Fluoxetine	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113	113	103	
Units: units on a scale				
least squares mean (standard error)				
Mood (N=113, 113, 103)	-7 (± 0.36)	-7.1 (± 0.35)	-7 (± 0.37)	
Somatic (N=113, 113, 103)	-7.7 (± 0.42)	-7.6 (± 0.41)	-7.7 (± 0.42)	
Subjective (N=113, 113, 103)	-4 (± 0.23)	-3.6 (± 0.22)	-4 (± 0.23)	
Behavior (N=113, 112, 103)	-5.6 (± 0.3)	-5.4 (± 0.3)	-5.7 (± 0.31)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Week 10 in Children's Depression Rating Scale-Revised (CDRS-R) Subscale Score at Week 36 Endpoint

End point title	Change From Week 10 in Children's Depression Rating Scale-Revised (CDRS-R) Subscale Score at Week 36 Endpoint

End point description:

CDRS-R Subscale scores include Mood (Sum of items 8, 11, 14, 15), Somatic (Sum of items 4-7, 16, 17), Subjective (Sum of items 9, 10, 12, 13) and Behavior (Sum of items 1-3). Mood and Subjective subscale scores range from 4 to 28; Somatic subscale scores range from 6 to 36; Behavior subscale scores range from 3 to 21. Higher score indicates greater severity of disease. LS means are adjusted for baseline, pooled investigator, age category, visit, age category*visit and baseline*visit.
Analysis Population Description: Participants with value during treatment phase and at least one post-Week 10 value.

End point type	Secondary

End point timeframe:

Week 10, Week 36

End point values	Duloxetine/Duloxetine	Fluoxetine/Fluoxetine	Placebo/Duloxetine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	91	85	
Units: units on a scale				
least squares mean (standard error)				
Mood	-1.9 (± 0.34)	-2.5 (± 0.24)	-2.9 (± 0.29)	
Somatic	-2.8 (± 0.35)	-3.6 (± 0.27)	-3.2 (± 0.33)	
Subjective	-0.3 (± 0.24)	-1.3 (± 0.13)	-1.2 (± 0.17)	
Behavior	-1.9 (± 0.23)	-2.8 (± 0.2)	-2.1 (± 0.36)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Clinical Global Impressions of Severity (CGI-Severity) scale at week 10 endpoint

End point title	Change from baseline in Clinical Global Impressions of Severity (CGI-Severity) scale at week 10 endpoint

End point description:

CGI-Severity evaluates the severity of illness at the time of assessment. The score ranges from 1 (normal, not at all ill) to 7 (among the most extremely ill patients). LS means are adjusted for baseline, pooled investigator, age category, visit, treatment, treatment*visit, age category*visit and baseline*visit.
Analysis Population Description: Participants with both a baseline and at least one post-baseline value.

End point type	Secondary

End point timeframe:

Baseline, Week 10

End point values	Duloxetine	Fluoxetine	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113	113	103	
Units: units on a scale				
least squares mean (standard error)	-1.9 (± 0.11)	-1.8 (± 0.1)	-1.9 (± 0.11)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Week 10 in Clinical Global Impressions of Severity (CGI-Severity) Scale at week 36 endpoint

End point title	Change from Week 10 in Clinical Global Impressions of Severity (CGI-Severity) Scale at week 36 endpoint

End point description:

CGI-Severity evaluates the severity of illness at the time of assessment. The score ranges from 1 (normal, not at all ill) to 7 (among the most extremely ill patients). LS means are adjusted for baseline, pooled investigator, age category, visit, age category*visit and baseline*visit.
Analysis Population Description: Participants with value during treatment phase and at least one post-Week 10 value.

End point type	Secondary

End point timeframe:

Week 10, Week 36

End point values	Duloxetine/Duloxetine	Fluoxetine/Fluoxetine	Placebo/Duloxetine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	91	85	
Units: units on a scale				
least squares mean (standard error)	-0.6 (± 0.12)	-1 (± 0.07)	-1.1 (± 0.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with suicidal ideation or suicidal behavior baseline through week 10

End point title	Number of participants with suicidal ideation or suicidal behavior baseline through week 10

End point description:

Columbia Suicide Rating Scale (C-SSRS) captures occurrence, severity, and frequency of suicide-related thoughts and behaviors. Suicidal behavior: a "yes" answer to any of 5 suicidal behavior questions: preparatory acts or behavior, aborted attempt, interrupted attempt, actual attempt, and completed suicide. Suicidal ideation: a "yes" answer to any one of 5 suicidal ideation questions: wish to be dead, and 4 different categories of active suicidal ideation. Treatment Emergent Suicidal Ideation is worsening or new occurrence of events during treatment compared to lead-in baseline (Week -1 - 0).
Analysis Population Description: Participants with at least one post-baseline C-SSRS suicidal ideation or suicidal behavior score and who are at risk for treatment emergent suicidal ideation or behavior.

End point type	Secondary

End point timeframe:

Baseline through Week 10

End point values	Duloxetine	Fluoxetine	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113	113	103	
Units: participants				
number (not applicable)				
Suicidal Ideation	16	16	15	
Suicidal Behavior	0	1	0	

Treatment Emergent Suicidal Ideation	8	9	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with suicidal ideation or suicidal behavior week 10 through week 36

End point title	Number of participants with suicidal ideation or suicidal behavior week 10 through week 36

End point description:

Columbia Suicide Rating Scale (C-SSRS) captures occurrence, severity, and frequency of suicide-related thoughts and behaviors. Suicidal behavior: a "yes" answer to any of 5 suicidal behavior questions: preparatory acts or behavior, aborted attempt, interrupted attempt, actual attempt, and completed suicide. Suicidal ideation: a "yes" answer to any one of 5 suicidal ideation questions: wish to be dead, and 4 different categories of active suicidal ideation. Treatment Emergent Suicidal Ideation is worsening or new occurrence of events during treatment compared to lead-in baseline (Week 7-10).
Analysis Population Description: Participants with at least one post-baseline C-SSRS suicidal ideation or suicidal behavior score and who are at risk for treatment emergent suicidal ideation or behavior.

End point type	Secondary

End point timeframe:

Week 10 through Week 36

End point values	Duloxetine/Duloxetine	Fluoxetine/Fluoxetine	Placebo/Duloxetine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	91	85	
Units: participants				
number (not applicable)				
Suicidal Ideation	13	13	8	
Suicidal Behavior	1	1	0	
Treatment Emergent Suicidal Ideation	9	13	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with potentially clinically significant hepatic laboratory results any time baseline through week 10

End point title	Number of participants with potentially clinically significant hepatic laboratory results any time baseline through week 10

End point description:

Total number of participants with any abnormal post-baseline value, based on all values at scheduled and unscheduled visits. Potentially clinically significant hepatic laboratory results at any time are defined as alanine transaminase (ALT) ≥3 x upper limit of normal (ULN), ALT ≥5 x ULN and ALT ≥10 x ULN, as

well as ALT ≥3 x ULN and Total Bilirubin ≥2 x ULN.
Analysis Population Description: Participants with normal ALT value (ALT <1 x ULN) at last non-missing baseline visit and at least one non-missing post-baseline value.

End point type	Secondary

End point timeframe:

Baseline through Week 10

End point values	Duloxetine	Fluoxetine	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	102	94	
Units: participants				
number (not applicable)				
ALT≥3 x ULN	0	0	0	
ALT≥5 x ULN	0	0	0	
ALT≥10 x ULN	0	0	0	
ALT≥3 x ULN and Total Bilirubin≥2 x ULN	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with potentially clinically significant hepatic laboratory results any time week 10 through week 36

End point title	Number of participants with potentially clinically significant hepatic laboratory results any time week 10 through week 36

End point description:

Total number of participants with any abnormal post-baseline value, based on all values at scheduled and unscheduled visits. Potentially clinically significant hepatic laboratory results at any time are defined as alanine transaminase (ALT) ≥3 x upper limit of normal (ULN), ALT ≥5 x ULN and ALT ≥10 x ULN, as well as ALT ≥3 x ULN and Total Bilirubin ≥2 x ULN.
Analysis Population Description: Participants with normal ALT value (ALT<1 x ULN) at last non-missing visit before Week 10 and at least one non-missing post-Week 10 value.

End point type	Secondary

End point timeframe:

Week 10 through Week 36

End point values	Duloxetine/Duloxetine	Fluoxetine/Fluoxetine	Placebo/Duloxetine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	77	83	82	
Units: participants				
number (not applicable)				
ALT≥3 x ULN	0	1	0	
ALT≥5 x ULN	0	1	0	
ALT≥10 x ULN	0	0	0	

ALT≥3 x ULN and Total Bilirubin≥2 x ULN	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with potentially clinically significant (PCS) changes in systolic blood pressure (BP), diastolic BP, pulse, and weight any time baseline through week 10

End point title	Percentage of participants with potentially clinically significant (PCS) changes in systolic blood pressure (BP), diastolic BP, pulse, and weight any time baseline through week 10

End point description:

PCS increase in systolic and diastolic BP was defined as increase of ≥5 millimeter mercury (mm Hg) from baseline (BL) high value to a value above the 95th percentile at post-BL; PCS increase of pulse was defined as >140 and increase of ≥15 from BL high value for age 7-11 and >120 and increase of ≥15 from BL high value for age 12-17; PCS decrease of pulse was defined as <60 and a decrease of ≥25 from BL low value for age 7-11 and <50 and a decrease of ≥15 from BL low value for age 12-17; PCS decrease of weight was defined as decrease of at least 3.5% from BL low value.
Analysis Population Description: Participants with normal baseline value and at least one post-baseline value, and who were at risk for the specific PCS criteria.

End point type	Secondary

End point timeframe:

Baseline through Week 10

End point values	Duloxetine	Fluoxetine	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	117	117	103	
Units: percentage of participants				
number (not applicable)				
Diastolic BP Increase (N=102, 106, 93)	8.8	7.5	17.2	
Systolic BP Increase (N=100, 106, 90)	7	5.7	6.7	
Pulse Decrease (N=111, 112, 102)	0.9	0.9	1	
Pulse Increase (N=113, 114, 103)	0	0	1	
Weight Decrease (N=113, 114, 103)	12.4	11.4	4.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with potentially clinically significant (PCS) changes in systolic blood pressure (BP), diastolic BP, pulse, and weight any time week 10 through week 36

End point title	Percentage of participants with potentially clinically significant (PCS) changes in systolic blood pressure (BP), diastolic BP,

	pulse, and weight any time week 10 through week 36

End point description:

PCS increase in systolic and diastolic BP was defined as increase of ≥ 5mm Hg from baseline (BL) high value to a value above the 95th percentile at post-BL; PCS increase of pulse was defined as >140 and increase of ≥15 from BL high value for age 7-11 and >120 and increase of ≥15 from BL high value for age 12-17; PCS decrease of pulse was defined as <60 and a decrease of ≥25 from BL low value for age 7-11 and <50 and a decrease of ≥15 from BL low value for age 12-17; PCS decrease of weight was defined as decrease of at least 3.5% from BL low value.
Analysis Population Description: Participants with normal value at last non-missing visit before Week 10 and at least one non-missing post-Week 10 value, and who are at risk for the specific PCS criteria.

End point type	Secondary

End point timeframe:

Week 10 through Week 36

End point values	Duloxetine/Duloxetine	Fluoxetine/Fluoxetine	Placebo/Duloxetine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	91	86	
Units: percentage of participants				
number (not applicable)				
Diastolic BP Increase (N=65, 76, 61)	16.9	11.8	4.9	
Systolic BP Increase (N=64, 80, 69)	12.5	12.5	10.1	
Pulse Decrease (N=78, 84, 82)	0	0	0	
Pulse Increase (N=81, 91, 84)	0	0	0	
Weight Decrease (N=81, 91, 85)	6.2	3.3	9.4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
38 Weeks	
Adverse event reporting additional description:	
F1J-MC-HMCK	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	Placebo_Acute
Reporting group description:	
Received placebo PO, QD during acute treatment phase	
Reporting group title	Fluoxetine_Acute
Reporting group description:	
Received fluoxetine 20 and/or 40 mg PO, QD during acute treatment phase	
Reporting group title	Duloxetine_Acute
Reporting group description:	
Received duloxetine 60, 90, and/or 120 mg orally (PO), once daily (QD) during acute treatment phase	
Reporting group title	Placebo/Duloxetine_Extension
Reporting group description:	
Received duloxetine 60, 90, and/or 120 mg PO, QD during extension phase	
Reporting group title	Fluoxetine_Extension
Reporting group description:	
Received fluoxetine 20 and/or 40 mg PO, QD during extension phase. One participant had discontinued the acute phase due to an adverse event but was accidentally dispensed drug at the last visit of the acute phase, thus based on intent-to-treat principal, this participant was included in the extension phase analyses for adverse events (AEs) (resulting in one more participant being analyzed for AEs than started the extension phase in the Participant Flow section).	
Reporting group title	Duloxetine_Extension
Reporting group description:	
Received duloxetine 60, 90, and/or 120 mg PO, QD during extension phase	

Serious adverse events	Placebo_Acute	Fluoxetine_Acute	Duloxetine_Acute
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 103 (0.97%)	2 / 117 (1.71%)	3 / 117 (2.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
intentional overdose			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ulna fracture			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	1 / 117 (0.85%)	0 / 117 (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			
convulsion			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
epilepsy			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
lymphadenitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
Gastrointestinal disorders			
gastritis			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 103 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
Psychiatric disorders			
adjustment disorder with disturbance of conduct			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
conversion disorder			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
drug abuse			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypomania			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
major depression			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 103 (0.97%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
panic attack			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
restlessness			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social anxiety disorder			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
suicidal ideation			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
pilonidal cyst			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 103 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo/Duloxetine_Extension	Fluoxetine_Extension	Duloxetine_Extension
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 86 (4.65%)	4 / 92 (4.35%)	1 / 83 (1.20%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
intentional overdose			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	1 / 92 (1.09%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ulna fracture			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
convulsion			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	1 / 92 (1.09%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
epilepsy			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	1 / 92 (1.09%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 86 (0.00%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
lymphadenitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
gastritis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
adjustment disorder with disturbance of conduct			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	1 / 92 (1.09%)	0 / 83 (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
conversion disorder			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 86 (1.16%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
drug abuse			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypomania			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 86 (0.00%)	1 / 92 (1.09%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
major depression			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 86 (1.16%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
panic attack			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
restlessness			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 86 (1.16%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social anxiety disorder			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
suicidal ideation			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 86 (1.16%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	1 / 92 (1.09%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
pilonidal cyst			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 86 (1.16%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	0 / 92 (0.00%)	1 / 83 (1.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Placebo_Acute	Fluoxetine_Acute	Duloxetine_Acute
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 103 (66.02%)	72 / 117 (61.54%)	70 / 117 (59.83%)
Injury, poisoning and procedural complications			
incorrect dose administered			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 103 (2.91%)	4 / 117 (3.42%)	2 / 117 (1.71%)
occurrences (all)	3	5	2
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 103 (2.91%)	4 / 117 (3.42%)	10 / 117 (8.55%)
occurrences (all)	3	4	11
headache			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	9 / 103 (8.74%)	18 / 117 (15.38%)	19 / 117 (16.24%)
occurrences (all)	10	22	23
Somnolence			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	6 / 103 (5.83%)	6 / 117 (5.13%)	7 / 117 (5.98%)
occurrences (all)	6	6	7

General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	5 / 103 (4.85%)	3 / 117 (2.56%)	8 / 117 (6.84%)
occurrences (all)	5	5	8
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	7 / 103 (6.80%)	5 / 117 (4.27%)	4 / 117 (3.42%)
occurrences (all)	8	7	4
diarrhoea			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 103 (1.94%)	2 / 117 (1.71%)	6 / 117 (5.13%)
occurrences (all)	2	2	6
nausea			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	11 / 103 (10.68%)	15 / 117 (12.82%)	20 / 117 (17.09%)
occurrences (all)	14	17	28
vomiting			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 103 (2.91%)	6 / 117 (5.13%)	7 / 117 (5.98%)
occurrences (all)	3	7	7
Abdominal pain			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	5 / 103 (4.85%)	2 / 117 (1.71%)	1 / 117 (0.85%)
occurrences (all)	5	2	1
Psychiatric disorders			
insomnia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 103 (1.94%)	6 / 117 (5.13%)	6 / 117 (5.13%)
occurrences (all)	2	6	8
Infections and infestations			
influenza			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	6 / 103 (5.83%)	3 / 117 (2.56%)	7 / 117 (5.98%)
occurrences (all)	8	3	7
Nasopharyngitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	5 / 103 (4.85%)	4 / 117 (3.42%)	2 / 117 (1.71%)
occurrences (all)	5	4	2
sinusitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 103 (2.91%)	1 / 117 (0.85%)	1 / 117 (0.85%)
occurrences (all)	3	1	1
upper respiratory tract infection			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 103 (0.97%)	3 / 117 (2.56%)	4 / 117 (3.42%)
occurrences (all)	1	3	4
Gastroenteritis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 103 (1.94%)	1 / 117 (0.85%)	0 / 117 (0.00%)
occurrences (all)	2	1	0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	7 / 103 (6.80%)	10 / 117 (8.55%)	10 / 117 (8.55%)
occurrences (all)	7	10	11

Non-serious adverse events	Placebo/Duloxetine_ Extension	Fluoxetine_Extensio n	Duloxetine_Extensio n
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 86 (69.77%)	56 / 92 (60.87%)	53 / 83 (63.86%)
Injury, poisoning and procedural complications			
incorrect dose administered			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 86 (0.00%)	3 / 92 (3.26%)	4 / 83 (4.82%)
occurrences (all)	0	3	5
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	6 / 86 (6.98%)	3 / 92 (3.26%)	3 / 83 (3.61%)
occurrences (all)	6	3	3
headache			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	10 / 86 (11.63%)	9 / 92 (9.78%)	9 / 83 (10.84%)
occurrences (all)	12	10	10
Somnolence			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 86 (3.49%)	4 / 92 (4.35%)	2 / 83 (2.41%)
occurrences (all)	4	5	2
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	4 / 86 (4.65%)	3 / 92 (3.26%)	1 / 83 (1.20%)
occurrences (all)	4	3	1
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	7 / 86 (8.14%)	2 / 92 (2.17%)	1 / 83 (1.20%)
occurrences (all)	7	2	1
diarrhoea			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 86 (2.33%)	4 / 92 (4.35%)	3 / 83 (3.61%)
occurrences (all)	2	4	3
nausea			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	12 / 86 (13.95%)	7 / 92 (7.61%)	3 / 83 (3.61%)
occurrences (all)	17	8	6
vomiting			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	8 / 86 (9.30%)	5 / 92 (5.43%)	4 / 83 (4.82%)
occurrences (all)	9	5	5
Abdominal pain			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	1 / 86 (1.16%)	2 / 92 (2.17%)	1 / 83 (1.20%)
occurrences (all)	1	2	1
Psychiatric disorders			
insomnia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 86 (1.16%)	0 / 92 (0.00%)	0 / 83 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
influenza			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	4 / 86 (4.65%)	3 / 92 (3.26%)	5 / 83 (6.02%)
occurrences (all)	4	3	6
Nasopharyngitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	9 / 86 (10.47%)	8 / 92 (8.70%)	9 / 83 (10.84%)
occurrences (all)	9	12	9
sinusitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 86 (1.16%)	1 / 92 (1.09%)	4 / 83 (4.82%)
occurrences (all)	1	1	4
upper respiratory tract infection			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 86 (3.49%)	5 / 92 (5.43%)	5 / 83 (6.02%)
occurrences (all)	3	7	6
Gastroenteritis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 86 (3.49%)	2 / 92 (2.17%)	4 / 83 (4.82%)
occurrences (all)	3	2	4
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 86 (3.49%)	0 / 92 (0.00%)	2 / 83 (2.41%)
occurrences (all)	3	0	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2010	Changes were made to the statistical analyses sections as agreed upon in consultation with FDA. The parallel changes were made to the Protocol Synopsis and documented in the Amendment Summary.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported