Clinical trial results:
An interventional, randomised, double-blind, parallel-group, placebo-controlled study on the efficacy of vortioxetine on cognitive dysfunction in patients with partial or full remission of major depressive disorder

Summary

EudraCT number	2014-000229-19
Trial protocol	EE DE FI SK
Global end of trial date	25 April 2016

Results information

Result version number	v1 (current)
This version publication date	29 March 2017
First version publication date	29 March 2017

Trial information

Trial identification

Sponsor protocol code	15905A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02279953
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	Lundbeck Clinical Trials, H. Lundbeck A/S, LundbeckClinicalTrials@lundbeck.com
Scientific contact	Lundbeck Clinical Trials, H. Lundbeck A/S, LundbeckClinicalTrials@lundbeck.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?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 April 2016
Global end of trial reached?	Yes
Global end of trial date	25 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of vortioxetine (10 to 20 mg/day) as adjunctive treatment to stable selective serotonin reuptake inhibitor (SSRI) dose versus stable SSRI monotherapy on cognitive performance (focusing on the aspect concerning speed of processing, executive functioning and attention) in patients who are in partial or full remission from their Major Depressive Episode (MDE).

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and ICH Good Clinical Practice (1996)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 October 2014
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	Slovakia: 9
Country: Number of subjects enrolled	Estonia: 31
Country: Number of subjects enrolled	Finland: 79
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Serbia: 9
Worldwide total number of subjects	151
EEA total number of subjects	142

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	150
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In- or out patients who: had achieved either partial or full remission of major depressive disorder (MDD) diagnosed according to DSM-IV-TR™ criteria, had a Hamilton Depression Rating Scale 17-items (HAM-D17) total score ≤10, had received SSRI monotherapy for the current MDD, had a Perceived Deficits Questionnaire – Depression (PDQ-D) total score>25

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Vortioxetine 10-20 mg + placebo

Arm description: -

Arm type	Experimental
Investigational medicinal product name	vortioxetine
Investigational medicinal product code	
Other name	Brintellix
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 or 20mg vortioxetine encapsulated table administered once daily orally. The initial treatment dose of vortioxetine was 10mg/day. Based on the investigator judgement there was a possibility to increase the dose with a 10mg increment to 20mg/day at Week 1.

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

Dosage and administration details:

Powder filled capsule orally once daily

Arm title	SSRI + placebo

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Escitalopram
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Escitalopram 5, 10, 15, or 20mg/day; encapsulated tablets, orally at current stable dose

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Powder filled capsule orally once daily

Investigational medicinal product name	Citalopram
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Citalopram – 10, 20, 30, or 40mg/day; encapsulated tablets, orally at current stable dose

Investigational medicinal product name	Sertraline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Sertraline – 50, 100, 150, or 200mg/day; encapsulated tablets, orally at current stable dose

Arm title	Vortioxetine 10-20 mg + SSRI

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	Brintellix
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 or 20mg vortioxetine encapsulated table administered once daily orally. The initial treatment dose of vortioxetine was 10mg/day. Based on the investigator judgement there was a possibility to increase the dose with a 10mg increment to 20mg/day at Week 1.

Investigational medicinal product name	Escitalopram
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Escitalopram 5, 10, 15, or 20mg/day; encapsulated tablets, orally at current stable dose

Investigational medicinal product name	Citalopram
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Citalopram – 10, 20, 30, or 40mg/day; encapsulated tablets, orally at current stable dose

Investigational medicinal product name	Sertraline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Sertraline – 50, 100, 150, or 200mg/day; encapsulated tablets, orally at current stable dose

Number of subjects in period 1	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI
Started	50	49	52
Completed	47	44	47
Not completed	3	5	5
Adverse event, non-fatal	1	2	3
Lost to follow-up	1	-	-
Administrative reason	1	1	1
Lack of efficacy	-	1	-
Protocol deviation	-	1	-
Non complicance	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Vortioxetine 10-20 mg + placebo
Reporting group description: -	
Reporting group title	SSRI + placebo
Reporting group description: -	
Reporting group title	Vortioxetine 10-20 mg + SSRI
Reporting group description: -	

Reporting group values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI
Number of subjects	50	49	52
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	49	49	52
From 65-84 years	1	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	50.6	47.9	45.9
standard deviation	± 10	± 11.5	± 12.7
Gender categorical Units: Subjects			
Female	34	34	41
Male	16	15	11
Race Units: Subjects			
White	50	49	52

Reporting group values	Total		
Number of subjects	151		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	150		

From 65-84 years	1		
85 years and over	0		

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	109		
Male	42		
Race Units: Subjects			
White	151		

End points

End points reporting groups

Reporting group title	Vortioxetine 10-20 mg + placebo
Reporting group description: -	
Reporting group title	SSRI + placebo
Reporting group description: -	
Reporting group title	Vortioxetine 10-20 mg + SSRI
Reporting group description: -	

Primary: Change from baseline to Week 8 in Digit Symbol Substitution Test (DSST)

End point title	Change from baseline to Week 8 in Digit Symbol Substitution Test (DSST)

End point description:

Digit Symbol Substitution Test (DSST) is a cognitive test designed to assess psychomotor speed of performance requiring visual perception, spatial decision-making, and motor skills. It consists of 133 digits and requires the patient to substitute each digit with a simple symbol in a 90-second period. Each correct symbol is counted, and the total score ranges from 0 (less than normal functioning) to 133 (greater than normal functioning)

End point type	Primary

End point timeframe:

Baseline to Week 8

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	48	
Units: Score				
least squares mean (standard error)	8.1 (± 1.16)	7.94 (± 1.15)	7.9 (± 1.14)	

Statistical analyses

Statistical analysis title	Vortioxetine + SSRI vs SSRI + placebo
Comparison groups	SSRI + placebo v Vortioxetine 10-20 mg + SSRI
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9769
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.17
upper limit	3.08

Statistical analysis title	Vortioxetine + placebo vs SSRI + placebo
Comparison groups	SSRI + placebo v Vortioxetine 10-20 mg + placebo
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9191
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.98
upper limit	3.3

Statistical analysis title	Vortioxetine + placebo vs vortioxetine + SSRI
Comparison groups	Vortioxetine 10-20 mg + placebo v Vortioxetine 10-20 mg + SSRI
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8954
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.91
upper limit	3.32

Secondary: Change from baseline to Week 8 in University of San Diego Performance-based Skills Assessment – Brief (UPSA-B) total score

End point title	Change from baseline to Week 8 in University of San Diego Performance-based Skills Assessment – Brief (UPSA-B) total score

End point description:

The UPSA-B is a role-play based performance test designed to assess functional skills in patients with mental illness. The UPSA-B consists of two subscales: managing finances (for example, counting correct change, writing a check to pay a bill) and communication with others (for example, dialling an emergency telephone number, rescheduling a medical appointment). Raw scores of the two subscales are converted to scaled scores from 0 to 100, where higher scores indicate better functional capacity.

End point type	Secondary

End point timeframe:

Baseline to Week 8

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	48	
Units: Score				
least squares mean (standard error)	5.99 (± 1.06)	4.28 (± 1.02)	5.24 (± 1.03)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Rey Auditory Visual Learning Test (RAVLT) scores: Acquisition

End point title	Change from baseline to Week 8 in Rey Auditory Visual Learning Test (RAVLT) scores: Acquisition

End point description:

Rey Auditory Verbal Learning Task (RAVLT) is a cognitive test designed to assess verbal learning and memory, including immediate memory, efficiency of learning, retroactive and encoding versus retrieval. The RAVLT consists of a number of tasks where the RAVLT acquisition (learning) is the total number of correctly recalled words from three lists of words with a possible score between 0 and 45. The higher score the better performance

End point type	Secondary

End point timeframe:

Baseline to week 8

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	48	
Units: Score				
least squares mean (standard error)	4.29 (± 0.66)	3.45 (± 0.66)	2.75 (± 0.66)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Rey Auditory Visual Learning Test

(RAVLT) scores: Delayed call

End point title	Change from baseline to Week 8 in Rey Auditory Visual Learning Test (RAVLT) scores: Delayed call

End point description:

Rey Auditory Verbal Learning Task (RAVLT) is a cognitive test designed to assess verbal learning and memory, including immediate memory, efficiency of learning, retroactive and encoding versus retrieval. The RAVLT consists of a number of tasks where RAVLT delayed recall (memory) is the number of correctly recalled words at the end of the test battery from one list of words with a possible score between 0 and 15. The higher score the better performance.

End point type	Secondary

End point timeframe:

Baseline to week 8.

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	48	
Units: Score				
least squares mean (standard error)	1.43 (± 0.37)	1.46 (± 0.36)	0.82 (± 0.36)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Trail Making Test A (TMT-A) score

End point title	Change from baseline to Week 8 in Trail Making Test A (TMT-A) score

End point description:

Trail Making Test (TMT) is a cognitive test designed to assess scanning, visuomotor tracking, executive function, and cognitive flexibility. It consists of two parts, A and B. Part A assesses cognitive processing speed. The lower the score the faster the processing speed.

End point type	Secondary

End point timeframe:

Baseline to week 8

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	48	
Units: Score				
least squares mean (standard error)	-5.4 (± 1.42)	-1.86 (± 1.4)	-3.55 (± 1.39)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Trail Making Test B (TMT-B) score

End point title	Change from baseline to Week 8 in Trail Making Test B (TMT-B) score

End point description:

TMT is a cognitive test designed to assess scanning, visuomotor tracking, executive function, and cognitive flexibility. It consists of two parts, A and B. Part B examines executive functioning and ability to shift cognitive set. The lower the score the faster the ability to shift cognitive set.

End point type	Secondary

End point timeframe:

Baseline to Week 8.

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	48	
Units: Score				
least squares mean (standard error)	-12.33 (± 2.54)	-9.55 (± 2.52)	-10.91 (± 2.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Simple Reaction Time (SRT)

End point title	Change from baseline to Week 8 in Simple Reaction Time (SRT)

End point description:

Simple Reaction Time (SRT) is designed to assess psychomotor speed. The patient presses a "yes" button, whenever an onscreen playing card is turned over. The lower score the better performance.

End point type	Secondary

End point timeframe:

Baseline to week 8

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	47	46	
Units: Score				
least squares mean (standard error)	-0.031 (± 0.013)	-0.01 (± 0.013)	-0.019 (± 0.013)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Choice Reaction Time (CRT)

End point title	Change from baseline to Week 8 in Choice Reaction Time (CRT)

End point description:

Choice Reaction Time (CRT) is designed to assess visual attention. The patient presses a "yes" button whenever an onscreen playing card is turned over and is red, or a "no" button if the card is not red. The lower score the better performance.

End point type	Secondary

End point timeframe:

Baseline to week 8

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	47	46	
Units: Score				
least squares mean (standard error)	-0.016 (± 0.011)	-0.014 (± 0.011)	-0.01 (± 0.011)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Stroop Colour Naming Test (STROOP) score: Congruent

End point title	Change from baseline to Week 8 in Stroop Colour Naming Test (STROOP) score: Congruent

End point description:

Stroop Colour Naming Test (STROOP) is a cognitive test designed to assess the ability to inhibit a prepotent response to reading words while performing a task that requires attention control. The STROOP comprises two sheets with 50 words on each, and each word is the name of a colour.
In the Congruent STROOP Sheet, the word and ink colour match. The lower the score the faster the processing speed.

End point type	Secondary

End point timeframe:

Baseline to week 8

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	48	
Units: Score				
least squares mean (standard error)	-6.58 (± 1.24)	-4.52 (± 1.22)	-7.04 (± 1.22)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Stroop Colour Naming Test (STROOP) score : Incongruent

End point title	Change from baseline to Week 8 in Stroop Colour Naming Test (STROOP) score : Incongruent

End point description:

Stroop Colour Naming Test (STROOP) is a cognitive test designed to assess the ability to inhibit a prepotent response to reading words while performing a task that requires attention control. The STROOP comprises two sheets with 50 words on each, and each word is the name of a colour. In the Incongruent STROOP Sheet, the word and ink colour do not match. The lower the score the greater the cognitive flexibility.

End point type	Secondary

End point timeframe:

Baseline to week 8.

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	48	
Units: Score				
least squares mean (standard error)	-8.86 (± 1.83)	-8.69 (± 1.81)	-9.13 (± 1.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Perceived Deficits Questionnaire –Depression (PDQ-D) total score

End point title	Change from baseline to Week 8 in Perceived Deficits Questionnaire –Depression (PDQ-D) total score

End point description:

Patient-reported cognitive function outcome including attention concentration, retrospective memory, prospective memory, and, planning organization. The total score of the 20 items ranges from 0 to 80 with higher scores reflecting greater subjective cognitive dysfunction as perceived by the patient.

End point type	Secondary

End point timeframe:

Baseline to week 8.

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	48	
Units: Score				
least squares mean (standard error)	-15.71 (± 1.63)	-13.11 (± 1.62)	-15.58 (± 1.61)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Hamilton Depression Rating Scale 17 items (HAM-D17) total score

End point title	Change from baseline to Week 8 in Hamilton Depression Rating Scale 17 items (HAM-D17) total score

End point description:

The Hamilton Depression Rating Scale (HAM-D17) is a 17-item rating scale designed to measure the severity of depressive symptoms in patients with primary depressive illness. It includes psychological and somatic depressive symptoms. The rating is based on specific statements, content of the answers, tone, facial expression and gestures of the patient during a clinical interview. Total score from 0-52. The higher the score, the more severe.

End point type	Secondary

End point timeframe:

Baseline to week 8.

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	44	47	
Units: Score				
least squares mean (standard error)	-1.18 (± 0.48)	-0.97 (± 0.48)	-1.8 (± 0.47)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 8 in Clinical Global Impression – Severity of Illness (CGI-S) score

End point title	Change from baseline to Week 8 in Clinical Global Impression – Severity of Illness (CGI-S) score

End point description:

The Clinical Global Impression - Severity of Illness (CGI-S) is a 7-point scale rated from 1 (normal, not at all ill) to 7 (among the most extremely ill patients).

End point type	Secondary

End point timeframe:

Baseline to week 8.

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	44	47	
Units: Score				
least squares mean (standard error)	-0.22 (± 0.1)	-0.13 (± 0.1)	-0.25 (± 0.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression – Global Improvement (CGI-I) score at Week 8

End point title	Clinical Global Impression – Global Improvement (CGI-I) score at Week 8

End point description:

The Clinical Global Impression - Global Improvement (CGI-I) is a 7-point scale rated from 1 (very much improved) to 7 (very much worse).

End point type	Secondary

End point timeframe:

Week 8

End point values	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	44	47	
Units: Score				
least squares mean (standard error)	2.98 (± 0.17)	3.35 (± 0.17)	3.14 (± 0.17)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: First dose to follow-up	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1
Reporting groups	
Reporting group title	Vortioxetine 10-20 mg + placebo
Reporting group description: Vortioxetine 10-20 mg + placebo	
Reporting group title	SSRI + placebo
Reporting group description: SSRI + placebo	
Reporting group title	Vortioxetine 10-20 mg + SSRI
Reporting group description: Vortioxetine10-20 mg + SSRI	

Serious adverse events	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	0 / 52 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Vortioxetine 10-20 mg + placebo	SSRI + placebo	Vortioxetine 10-20 mg + SSRI
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 50 (48.00%)	11 / 49 (22.45%)	29 / 52 (55.77%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 50 (12.00%)	0 / 49 (0.00%)	2 / 52 (3.85%)
occurrences (all)	7	0	2
Headache			
subjects affected / exposed	3 / 50 (6.00%)	5 / 49 (10.20%)	9 / 52 (17.31%)
occurrences (all)	3	5	10
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	3 / 52 (5.77%)
occurrences (all)	1	1	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 50 (8.00%)	0 / 49 (0.00%)	4 / 52 (7.69%)
occurrences (all)	6	0	4
Nausea			
subjects affected / exposed	11 / 50 (22.00%)	1 / 49 (2.04%)	16 / 52 (30.77%)
occurrences (all)	12	1	16
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	1 / 52 (1.92%)
occurrences (all)	3	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 50 (4.00%)	0 / 49 (0.00%)	3 / 52 (5.77%)
occurrences (all)	2	0	3
Restlessness			
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	3 / 52 (5.77%)
occurrences (all)	0	0	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 50 (6.00%)	4 / 49 (8.16%)	3 / 52 (5.77%)
occurrences (all)	3	4	3
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 50 (6.00%)	3 / 49 (6.12%)	1 / 52 (1.92%)
occurrences (all)	3	3	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported