



Clinical trial results:

An interventional, randomised, double-blind, parallel-group, placebo-controlled, active-referenced (paroxetine), fixed-dose study on the efficacy of vortioxetine on cognitive dysfunction in working patients with major depressive disorder

Summary

EudraCT number	2014-000230-34
Trial protocol	EE FI LT DE SK
Global end of trial date	05 February 2016

Results information

Result version number	v1 (current)
This version publication date	19 February 2017
First version publication date	19 February 2017

Trial information

Trial identification

Sponsor protocol code	15906A
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02279966
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	05 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 February 2016
Global end of trial reached?	Yes
Global end of trial date	05 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of acute treatment with 10mg/day vortioxetine versus placebo on cognitive performance (focusing on the aspect concerning speed of processing, executive functioning, and attention) in working patients with major depressive disorder (MDD)

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	Finland: 57
Country: Number of subjects enrolled	Germany: 34
Country: Number of subjects enrolled	Estonia: 29
Country: Number of subjects enrolled	Lithuania: 32
Worldwide total number of subjects	152
EEA total number of subjects	152

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)	152
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Working outpatients with a primary diagnosis of recurrent MDD according to DSM-IV-TR™ (classification 296.3x), as confirmed using the Mini International Neuropsychiatric Interview (MINI), who had a Montgomery-Åsberg Depression Rating Scale (MADRS) total score ≥ 26 at the Screening Visit and at the Baseline Visit

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Placebo
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Arm description: -

Arm type	Experimental
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 capsules, orally. 8 weeks of double-blind treatment

Arm title	Vortioxetine 10 mg/day
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	vortioxetine 10 mg/day
Investigational medicinal product code	
Other name	Brintellix, Trintellix
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg/day; encapsulated tablets, orally. 8 weeks of double-blind treatment

Arm title	Paroxetine 20 mg/day
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Paroxetine 20 mg/day
Investigational medicinal product code	
Other name	Seroxat®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

20 mg/day; encapsulated tablets, orally. 8 weeks of double-blind treatment

Number of subjects in period 1	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day
Started	49	48	55
Completed	46	41	47
Not completed	3	7	8
Adverse event, non-fatal	1	3	3
Other	-	2	3
Lack of efficacy	1	2	1
Not treated	1	-	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Vortioxetine 10 mg/day
Reporting group description: -	
Reporting group title	Paroxetine 20 mg/day
Reporting group description: -	

Reporting group values	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day
Number of subjects	49	48	55
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	48	55
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	45.2	47.3	46
standard deviation	± 12.6	± 12	± 11.6
Gender categorical Units: Subjects			
Female	30	35	37
Male	19	13	18
Race Units: Subjects			
White	48	48	54
Black or African American	1	0	0
Other	0	0	1

Reporting group values	Total		
Number of subjects	152		
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)	152		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	102		
Male	50		
Race			
Units: Subjects			
White	150		
Black or African American	1		
Other	1		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Vortioxetine 10 mg/day
Reporting group description: -	
Reporting group title	Paroxetine 20 mg/day
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:	<p>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)</p>
End point type	Primary
End point timeframe:	
Baseline to Week 8	

End point values	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	48	
Units: Score				
least squares mean (standard error)	7.37 (\pm 1.06)	7.59 (\pm 1.08)	6.61 (\pm 1.05)	

Statistical analyses

Statistical analysis title	Vortioxetine vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8845
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.76
upper limit	3.2

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
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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, dialing 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
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End point timeframe:

Baseline to Week 8

End point values	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	50	
Units: Score				
least squares mean (standard error)	5.33 (± 1.11)	5.75 (± 1.13)	5.95 (± 1.08)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7894
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.69
upper limit	3.54

Variability estimate	Standard error of the mean
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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	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	49	
Units: Score				
least squares mean (standard error)	-5.02 (± 1.24)	-5.73 (± 1.27)	-7.32 (± 1.22)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6886
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.23
upper limit	2.8

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	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	44	45	
Units: Score				
least squares mean (standard error)	-13.98 (\pm 3.7)	-16.2 (\pm 3.74)	-13.88 (\pm 3.64)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6734
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.65
upper limit	8.2

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	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	45	47	
Units: Scores				
least squares mean (standard error)	-0.018 (\pm 0.015)	-0.073 (\pm 0.015)	-0.024 (\pm 0.014)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0107
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.055
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.097
upper limit	-0.013

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	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	46	47	
Units: Score				
least squares mean (standard error)	-0.023 (\pm 0.011)	-0.038 (\pm 0.011)	-0.02 (\pm 0.011)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Placebo v Vortioxetine 10 mg/day
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3193
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.045
upper limit	0.015

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	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	49	
Units: Score				
least squares mean (standard error)	-6.49 (± 1.13)	-8.74 (± 1.14)	-9.11 (± 1.09)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1634
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.42
upper limit	0.93

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
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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
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End point timeframe:

Baseline to Week 8

End point values	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	49	
Units: Score				
least squares mean (standard error)	-11.59 (± 2.14)	-12.44 (± 2.19)	-14.3 (± 2.09)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Placebo v Vortioxetine 10 mg/day
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7814
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	5.2

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
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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
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End point timeframe:

Baseline to Week 8

End point values	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	45	49	
Units: Score				
least squares mean (standard error)	-8.36 (± 1.88)	-15.17 (± 1.91)	-15.26 (± 1.83)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0122
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-6.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.12
upper limit	-1.51

Secondary: Change from baseline to Week 8 in Montgomery-Åsberg Depression Rating Scale (MADRS) total score

End point title	Change from baseline to Week 8 in Montgomery-Åsberg Depression Rating Scale (MADRS) total score
End point description: The Montgomery Åsberg Depression Rating Scale (MADRS) is a depression rating scale consisting of 10 items, each rated 0 (no symptom) to 6 (severe symptom). The 10 items represent the core symptoms of depressive illness. Total score from 0 to 60. The higher the score, the more severe	
End point type	Secondary
End point timeframe: Baseline to Week 8	

End point values	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	42	46	
Units: Score				
least squares mean (standard error)	-8 (± 1.21)	-15.15 (± 1.27)	-15.96 (± 1.19)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Placebo v Vortioxetine 10 mg/day
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-7.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.65
upper limit	-3.65

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	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	42	46	
Units: Score				
least squares mean (standard error)	-0.78 (± 0.17)	-1.69 (± 0.18)	-1.76 (± 0.17)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.41

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	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	42	46	
Units: Score				
least squares mean (standard error)	3 (\pm 0.14)	2.13 (\pm 0.15)	2.04 (\pm 0.14)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	-0.47

Secondary: Change from baseline to Week 8 in Functioning Assessment Short Test (FAST) total score

End point title	Change from baseline to Week 8 in Functioning Assessment Short Test (FAST) total score
End point description:	The FAST is a clinician-rating scale designed to assess difficulty in functioning. The FAST assesses 6 specific areas of functioning: autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, leisure time. The total score of the 24 items ranges from 0 to 72 with higher scores reflecting more serious difficulties
End point type	Secondary
End point timeframe:	
Baseline to Week 8	

End point values	Placebo	Vortioxetine 10 mg/day	Paroxetine 20 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	49	
Units: Score				
least squares mean (standard error)	-8.26 (\pm 1.49)	-12.97 (\pm 1.51)	-10.97 (\pm 1.46)	

Statistical analyses

Statistical analysis title	Vortioxetine 10 mg vs placebo
Comparison groups	Vortioxetine 10 mg/day v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0278
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-4.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.9
upper limit	-0.52

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose to follow-up

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	PLACEBO
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Reporting group description:

PLACEBO

Reporting group title	Paroxetine 20 MG
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Reporting group description:

Paroxetine 20 MG

Reporting group title	Vortioxetine 10 MG
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Reporting group description:

Vortioxetine 10 MG

Serious adverse events	PLACEBO	Paroxetine 20 MG	Vortioxetine 10 MG
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 48 (2.08%)	2 / 54 (3.70%)	0 / 48 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Brain contusion			
subjects affected / exposed	0 / 48 (0.00%)	1 / 54 (1.85%)	0 / 48 (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
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 48 (0.00%)	1 / 54 (1.85%)	0 / 48 (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
Infections and infestations			
Pyelonephritis			

subjects affected / exposed	1 / 48 (2.08%)	0 / 54 (0.00%)	0 / 48 (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

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

Non-serious adverse events	PLACEBO	Paroxetine 20 MG	Vortioxetine 10 MG
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 48 (20.83%)	15 / 54 (27.78%)	21 / 48 (43.75%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 48 (0.00%)	4 / 54 (7.41%)	0 / 48 (0.00%)
occurrences (all)	0	4	0
Headache			
subjects affected / exposed	2 / 48 (4.17%)	3 / 54 (5.56%)	7 / 48 (14.58%)
occurrences (all)	2	3	7
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 48 (2.08%)	9 / 54 (16.67%)	18 / 48 (37.50%)
occurrences (all)	1	10	19
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed ^[1]	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 48 (8.33%)	0 / 54 (0.00%)	1 / 48 (2.08%)
occurrences (all)	4	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 48 (6.25%)	0 / 54 (0.00%)	1 / 48 (2.08%)
occurrences (all)	3	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 48 (0.00%)	3 / 54 (5.56%)	0 / 48 (0.00%)
occurrences (all)	0	3	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: gender specific

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