Clinical trial results:
A Randomized, Double-blind, Parallel-group, Active-controlled Study Evaluating the Efficacy of Vortioxetine Versus Desvenlafaxine in Adult Patients Suffering from Major Depressive Disorder with Partial Response to SSRI Treatment

Summary

EudraCT number	2019-002704-41
Trial protocol	CZ EE LV BG SK BE ES
Global end of trial date	04 February 2022

Results information

Result version number	v1 (current)
This version publication date	22 February 2023
First version publication date	22 February 2023

Trial information

Trial identification

Sponsor protocol code	18498A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04448431
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com
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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	04 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to compare the efficacy of vortioxetine versus desvenlafaxine after 8 weeks of treatment, on depressive symptoms in participants with major depressive disorder (MDD) who have responded partially to monotherapy with a selective serotonin reuptake inhibitor (SSRI).

Protection of trial subjects:

This study was conducted in compliance with Good Clinical Practice and in accordance with the ethical principles described in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2020
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	Argentina: 132
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 32
Country: Number of subjects enrolled	Czechia: 73
Country: Number of subjects enrolled	Estonia: 20
Country: Number of subjects enrolled	Latvia: 10
Country: Number of subjects enrolled	Mexico: 27
Country: Number of subjects enrolled	Russian Federation: 150
Country: Number of subjects enrolled	Slovakia: 53
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Sweden: 16
Country: Number of subjects enrolled	Ukraine: 83
Worldwide total number of subjects	605
EEA total number of subjects	213

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)	598
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

605 participants were enrolled in the study. 603 participants received at least one dose of study treatment.

Period 1

Period 1 title	Overall study (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
Arm title	Vortioxetine

Arm description:

Participants received 10 milligrams (mg) vortioxetine once daily for the first week. At the end of Week 1 (Day 7), the dose was increased to 20mg/day. The dose may have been adjusted (10 or 20mg/day) at unscheduled visits or at the end of Week 4 (Day 28) (only once) based on the participant's response and the investigator’s clinical judgement. No dose changes were permitted after Week 4. The dose remained fixed until the end of the treatment period (Week 8, Day 56). From Week 8, participants received placebo once daily for one week.

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:

Placebo was administered per dose and schedule specified in the arm description.

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

Dosage and administration details:

Vortioxetine was administered per dose and schedule specified in the arm description.

Arm title	Desvenlafaxine

Arm description:

Participants received a fixed dose of 50mg once daily during the treatment period. In order to maintain the blind, a dose adjustment could have been requested based on the participant’s response and the investigator’s clinical judgement, however, the dose of desvenlafaxine remained fixed. From Week 8, participants received 50mg desvenlafaxine or placebo every other day for one week.

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

Dosage and administration details: Placebo was administered per dose and schedule specified in the arm description.	
Investigational medicinal product name	Desvenlafaxine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Desvenlafaxine was administered per dose and schedule specified in the arm description.

Number of subjects in period 1	Vortioxetine	Desvenlafaxine
Started	312	293
Received at least 1 dose of study drug	310	293
Completed	295	284
Not completed	17	9
Consent withdrawn by subject	5	3
Adverse event, non-fatal	6	3
Not specified	2	2
Lost to follow-up	1	-
Lack of efficacy	1	1
Not treated	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Vortioxetine
Reporting group description:	
Participants received 10 milligrams (mg) vortioxetine once daily for the first week. At the end of Week 1 (Day 7), the dose was increased to 20mg/day. The dose may have been adjusted (10 or 20mg/day) at unscheduled visits or at the end of Week 4 (Day 28) (only once) based on the participant's response and the investigator's clinical judgement. No dose changes were permitted after Week 4. The dose remained fixed until the end of the treatment period (Week 8, Day 56). From Week 8, participants received placebo once daily for one week.	
Reporting group title	Desvenlafaxine
Reporting group description:	
Participants received a fixed dose of 50mg once daily during the treatment period. In order to maintain the blind, a dose adjustment could have been requested based on the participant's response and the investigator's clinical judgement, however, the dose of desvenlafaxine remained fixed. From Week 8, participants received 50mg desvenlafaxine or placebo every other day for one week.	

Reporting group values	Vortioxetine	Desvenlafaxine	Total
Number of subjects	312	293	605
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)	307	291	598
From 65-84 years	5	2	7
85 years and over	0	0	0
Gender Categorical Units: Subjects			
Female	216	212	428
Male	96	81	177
Race Units: Subjects			
Asian	3	0	3
Black	0	1	1
Not reported	10	6	16
Other	14	14	28
White	285	272	557
Montgomery and Åsberg Depression Rating Scale (MADRS) Total Score			
The MADRS is a 10-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. The total score of the 10 items ranges from 0 (no symptoms) to 60 (severe symptoms), with higher scores indicating more severe symptoms. Participants with valid baseline scores are presented here (Vortioxetine n=309; Desvenlafaxine n=293)			
Units: Score on a scale			

arithmetic mean	30.65	30.69	
standard deviation	± 3.702	± 3.922	-

End points

End points reporting groups

Reporting group title	Vortioxetine

Reporting group description:

Participants received 10 milligrams (mg) vortioxetine once daily for the first week. At the end of Week 1 (Day 7), the dose was increased to 20mg/day. The dose may have been adjusted (10 or 20mg/day) at unscheduled visits or at the end of Week 4 (Day 28) (only once) based on the participant's response and the investigator's clinical judgement. No dose changes were permitted after Week 4. The dose remained fixed until the end of the treatment period (Week 8, Day 56). From Week 8, participants received placebo once daily for one week.

Reporting group title	Desvenlafaxine

Reporting group description:

Participants received a fixed dose of 50mg once daily during the treatment period. In order to maintain the blind, a dose adjustment could have been requested based on the participant's response and the investigator's clinical judgement, however, the dose of desvenlafaxine remained fixed. From Week 8, participants received 50mg desvenlafaxine or placebo every other day for one week.

Primary: Change from Baseline to Week 8 in Montgomery and Åsberg Depression Rating Scale (MADRS) Total Score

End point title	Change from Baseline to Week 8 in Montgomery and Åsberg Depression Rating Scale (MADRS) Total Score

End point description:

The MADRS is a 10-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at 2-point intervals. The total score of the 10 items ranges from 0 (no symptoms) to 60 (severe symptoms), with higher scores indicating more severe symptoms.

Analysis was performed on the Full-analysis set (FAS) – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	286		
Units: Score on a scale				
least squares mean (standard error)	-13.61 (± 0.51)	-13.14 (± 0.52)		

Statistical analyses

Statistical analysis title	Vortioxetine vs. Desvenlafaxine
Comparison groups	Vortioxetine v Desvenlafaxine
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.4196
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	Mean difference (final values)
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	0.67
Variability estimate	Standard error of the mean
Dispersion value	0.58

Secondary: Percentage of MADRS Responders at Week 8

End point title	Percentage of MADRS Responders at Week 8

End point description:

Response was defined as a ≥50% decrease in MADRS total score from baseline. The MADRS is a 10-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. The total score of the 10 items ranges from 0 (no symptoms) to 60 (severe symptoms), with higher scores indicating more severe symptoms.

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	286		
Units: Percentage of participants				
number (not applicable)	43.4	36.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With MADRS Remission at Week 8

End point title	Percentage of Participants With MADRS Remission at Week 8

End point description:

Remission was defined as a MADRS total score ≤10. The MADRS is a 10-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. The total score of the 10 items ranges from 0 (no symptoms) to 60 (severe symptoms), with higher scores indicating more severe symptoms.

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	286		
Units: Percentage of participants				
number (not applicable)	18.0	20.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 8 in MADRS Anhedonia Factor Score

End point title	Change from Baseline to Week 8 in MADRS Anhedonia Factor Score

End point description:

The MADRS is a 10-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. The anhedonia factor score is based on 5 items (apparent sadness, reported sadness, concentration difficulties, lassitude, and inability to feel) and ranges from 0 to 30 with higher scores representing more severe symptoms.

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	286		
Units: Score on a scale				
least squares mean (standard error)	-8.11 (± 0.32)	-7.80 (± 0.33)		

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 CGI-I provides the clinician’s impression of the participant's improvement (or worsening). The clinician assesses the participant's condition relative to a Baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). In all cases, the assessment was made independent of whether the rater believed the improvement was drug-related.

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	286		
Units: Score on a scale				
least squares mean (standard error)	2.31 (± 0.07)	2.40 (± 0.07)		

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 CGI-S provides the clinician’s impression of the participant’s current state of mental illness. The clinician uses his or her clinical experience of this participant population to rate the severity of the participant's current mental illness on a 7-point scale ranging from 1 (Normal - not at all ill) to 7 (among the most extremely ill participants).

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	286		
Units: Score on a scale				
least squares mean (standard error)	-1.54 (± 0.06)	-1.41 (± 0.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Digital Symbol Substitution Test (DSST) Total Score to Week 8

End point title	Change from Baseline in Digital Symbol Substitution Test (DSST) Total Score to Week 8

End point description:

The DSST is a cognitive test designed to assess psychomotor speed of performance requiring visual perception, spatial decision-making, and motor skills. The DSST is sensitive to cognitive impairments affecting attention, processing speed, and executive function (including working memory). The DSST consists of 133 digits and requires the participant 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).

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	285		
Units: Score on a scale				
least squares mean (standard error)	9.72 (± 0.89)	9.53 (± 0.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Participant's Probability of Choosing Hard Task For Each Effort Expenditure for Rewards Task (EEfRT) Trial at Week 8

End point title	Participant's Probability of Choosing Hard Task For Each Effort Expenditure for Rewards Task (EEfRT) Trial at Week 8

End point description:

The EEfRT is a neuropsychological task to assess willingness to make efforts to obtain a monetary reward under different conditions of reward probability and magnitude. The participant is given an opportunity to choose between two tasks with different levels of difficulty: a "hard task" and an "easy task" option, which require different amounts of repeated manual button pressing. For easy-task choices, the participant is eligible to win a fixed amount of monetary reward on each trial if he/she successfully completes the task. For hard-task choices, the participant is eligible to win higher amounts that vary per trial within a range ("reward magnitude").

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	276		
Units: Probability				
number (not applicable)	0.31	0.32		

Statistical analyses

No statistical analyses for this end point

Secondary: EEfRT: Proportion of Hard Choice Tasks at Week 8

End point title	EEfRT: Proportion of Hard Choice Tasks at Week 8

End point description:

The EEfRT is a neuropsychological task to assess willingness to make efforts to obtain a monetary reward under different conditions of reward probability and magnitude. The participant is given an opportunity to choose between two tasks with different levels of difficulty: a "hard task" and an "easy task" option, which require different amounts of repeated manual button pressing. For easy-task choices, the participant is eligible to win a fixed amount of monetary reward on each trial if he/she successfully completes the task. For hard-task choices, the participant is eligible to win higher amounts that vary per trial within a range ("reward magnitude").

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	276		
Units: Proportion				
arithmetic mean (standard error)	0.33 (± 0.01)	0.34 (± 0.01)		

Statistical analyses

No statistical analyses for this end point

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-rated clinical outcome assessment tool designed to assess difficulty in functioning. The FAST consists of 24 items in 6 specific areas of functioning: autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, leisure time. Each item is rated on a 4-point scale from 0 (no difficulty) to 3 (severe difficulty). The items are summed to yield a total score ranging from 0 (no difficulty) to 72 (severe difficulty), with higher scores reflecting more serious difficulties.

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	296	288		
Units: Score on a scale				
least squares mean (standard error)	-15.79 (± 0.85)	-14.15 (± 0.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 8 in FAST Sub-domain Scores

End point title	Change from Baseline to Week 8 in FAST Sub-domain Scores

End point description:

The FAST is a clinician-rated clinical outcome assessment tool designed to assess difficulty in functioning. The FAST consists of 24 items in 6 specific areas of functioning: autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, leisure time. Each item is rated on a 4-point scale from 0 (no difficulty) to 3 (severe difficulty).

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301	290		
Units: Score on a scale				
least squares mean (standard error)				
Autonomy (n= 300, 290)	-2.52 (± 0.23)	-2.05 (± 0.24)		
Occupational Functioning (n= 295, 288)	-2.91 (± 0.25)	-2.49 (± 0.25)		
Cognitive Functioning (n= 301, 290)	-3.17 (± 0.32)	-2.74 (± 0.33)		
Financial Issues (n= 301, 290)	-0.61 (± 0.13)	-0.60 (± 0.14)		
Interpersonal Relationships (n= 301, 290)	-3.77 (± 0.36)	-3.22 (± 0.37)		
Leisure Time (n= 301, 290)	-1.40 (± 0.17)	-1.47 (± 0.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 8 in the Quality of Life, Enjoyment, and Satisfaction Questionnaire (Q-LES-Q) Long Form Subscales

End point title	Change From Baseline to Week 8 in the Quality of Life, Enjoyment, and Satisfaction Questionnaire (Q-LES-Q) Long Form Subscales

End point description:

The Q-LES-Q Long Form is a participant self-rated scale designed to measure the degree of enjoyment and satisfaction experienced by participants in various areas of daily life. It consists of 93 items to measure: physical health, feelings, work, household duties, school, leisure time activities, social relations, and general activities. Each item is rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). Raw scores for each category are converted to a 1 to 100 scale with higher scores representing higher quality of life.

Analysis was performed on the FAS – all randomized participants who took at least 1 dose of double-blind study drug and had a valid baseline and at least 1 valid post-baseline assessment of the primary efficacy variable (MADRS). Here, 'number of subjects analyzed' signifies participants evaluable for this endpoint. ‘n’ signifies participants evaluable for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine	Desvenlafaxine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301	290		
Units: Score on a scale				
least squares mean (standard error)				
Work (n= 195, 195)	17.70 (± 1.81)	16.83 (± 1.84)		
Household Duties (n= 287, 276)	14.29 (± 1.84)	14.22 (± 1.89)		
School (n= 33, 36)	11.12 (± 6.41)	18.73 (± 5.84)		
Leisure Time (n= 301, 290)	20.78 (± 2.05)	20.92 (± 2.10)		
Social Relations (n= 301, 290)	16.10 (± 1.69)	15.56 (± 1.73)		
Physical Health (n= 301, 290)	17.79 (± 1.70)	16.63 (± 1.74)		
Feelings (n= 301, 289)	17.20 (± 1.73)	16.46 (± 1.78)		
General Activities (n= 301, 290)	17.99 (± 1.57)	17.12 (± 1.61)		
Satisfaction with Medication (n= 246, 222)	27.46 (± 1.66)	23.81 (± 1.72)		
Overall Satisfaction and Contentment (n= 301, 290)	24.96 (± 2.24)	23.63 (± 2.30)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug (Day 1) up to Week 12. Adverse Events were not reported after Day 56 (Visit 5) unless they were Serious Adverse Events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Desvenlafaxine

Reporting group description:

Participants received a fixed dose of 50mg once daily during the treatment period. In order to maintain the blind, a dose adjustment could have been requested based on the participant's response and the investigator's clinical judgement, however, the dose of desvenlafaxine remained fixed. From Week 8, participants received 50mg desvenlafaxine or placebo every other day for one week.

Reporting group title	Vortioxetine

Reporting group description:

Participants received 10 milligrams (mg) vortioxetine once daily for the first week. At the end of Week 1 (Day 7), the dose was increased to 20mg/day. The dose may have been adjusted (10 or 20mg/day) at unscheduled visits or at the end of Week 4 (Day 28) (only once) based on the participant's response and the investigator's clinical judgement. No dose changes were permitted after Week 4. The dose remained fixed until the end of the treatment period (Week 8, Day 56). From Week 8, participants received placebo once daily for one week.

Serious adverse events	Desvenlafaxine	Vortioxetine	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 293 (0.34%)	0 / 310 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 293 (0.34%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Desvenlafaxine	Vortioxetine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 293 (20.82%)	85 / 310 (27.42%)	
Nervous system disorders			

Headache			
subjects affected / exposed	25 / 293 (8.53%)	30 / 310 (9.68%)	
occurrences (all)	29	34	
Dizziness			
subjects affected / exposed	16 / 293 (5.46%)	16 / 310 (5.16%)	
occurrences (all)	18	16	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	27 / 293 (9.22%)	62 / 310 (20.00%)	
occurrences (all)	29	75	

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