Clinical trial results:
Interventional, Open-Label Effectiveness Study of Flexible Doses of Vortioxetine on Depressive Symptoms in Patients With Major Depressive Disorder Comorbid With Generalized Anxiety Disorder

Summary

EudraCT number	2019-001325-27
Trial protocol	ES IT
Global end of trial date	09 March 2021

Results information

Result version number	v1 (current)
This version publication date	17 March 2022
First version publication date	17 March 2022

Trial information

Trial identification

Sponsor protocol code	18314A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04220996
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
Scientific contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, 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	09 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2021
Global end of trial reached?	Yes
Global end of trial date	09 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to assess the effectiveness of 8-week acute treatment with 10 to 20 milligrams (mg)/day vortioxetine on depressive symptoms in participants with major depressive disorder comorbid with generalized anxiety disorder.

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	27 December 2019
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	Estonia: 19
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Poland: 55
Country: Number of subjects enrolled	Spain: 6
Worldwide total number of subjects	102
EEA total number of subjects	96

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)	101

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 102 enrolled participants, 100 participants were treated with vortioxetine, out of which 23 participants received vortioxetine as a first-treatment for the current major depressive episode (MDE) and 77 participants switched to vortioxetine due to inadequate response to the current antidepressant medication treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Vortioxetine

Arm description:

Participants received vortioxetine tablets 10 mg/day orally at Week 0. At Week 1, the dose was to be increased to 20 mg/day for all participants. The dose could be adjusted to 10 or 20 mg/day at scheduled or unscheduled visits, depending on the participants' response as per the investigator's judgement. The treatment was continued for a total of 8 weeks.

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

Dosage and administration details:

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

Number of subjects in period 1	Vortioxetine
Started	102
Received at least 1 dose of study drug	100
Completed	97
Not completed	5
Consent withdrawn by subject	1
Adverse event, non-fatal	2
Enrolled but not treated	2

Baseline characteristics

Reporting groups	
Reporting group title	Vortioxetine

Reporting group description:

Participants received vortioxetine tablets 10 mg/day orally at Week 0. At Week 1, the dose was to be increased to 20 mg/day for all participants. The dose could be adjusted to 10 or 20 mg/day at scheduled or unscheduled visits, depending on the participants' response as per the investigator's judgement. The treatment was continued for a total of 8 weeks.

Reporting group values	Vortioxetine	Total	
Number of subjects	102	102	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	101	101	
From 65-84 years	1	1	
85 years and over	0	0	
Gender Categorical Units: Subjects			
Female	64	64	
Male	38	38	

End points

End points reporting groups

Reporting group title	Vortioxetine

Reporting group description:

Participants received vortioxetine tablets 10 mg/day orally at Week 0. At Week 1, the dose was to be increased to 20 mg/day for all participants. The dose could be adjusted to 10 or 20 mg/day at scheduled or unscheduled visits, depending on the participants' response as per the investigator's judgement. The treatment was continued for a total of 8 weeks.

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

End point title	Change From Baseline in Montgomery and Åsberg Depression Rating Scale (MADRS) Total Score at Week 8[1]

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. The items in the scale are designed to assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Symptoms were rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). The total score of the 10 items ranged from 0 to 60, with higher scores reflecting more severe symptoms. The analysis was performed using a mixed model for repeated measurements (MMRM). Full analysis set (FAS) included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 8

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical comparison between 2 groups was not done.

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: units on a scale				
least squares mean (standard error)	-16.8 (± 0.800)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With MADRS Response (Defined as a ≥50% Decrease From Baseline in MADRS Total Score) at Week 8

End point title	Percentage of Participants With MADRS Response (Defined as a ≥50% Decrease From Baseline in MADRS Total Score) at Week 8

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. The items in the scale are designed to assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Symptoms were rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). The total score of the 10 items ranged from 0 to 60, with higher scores reflecting more severe symptoms. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score.

End point type	Secondary

End point timeframe:

Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: percentage of participants				
number (confidence interval 95%)	60.8 (50.4 to 70.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With MADRS Remission (Defined as a MADRS Total Score ≤10) at Week 8

End point title	Percentage of Participants With MADRS Remission (Defined as a MADRS Total Score ≤10) at Week 8

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. The items in the scale are designed to assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Symptoms were rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). The total score of the 10 items ranged from 0 to 60, with higher scores reflecting more severe symptoms. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score.

End point type	Secondary

End point timeframe:

Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: percentage of participants				
number (confidence interval 95%)	35.1 (25.6 to 45.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hamilton Anxiety Rating Scale (HAM-A) Total Score at Week 8

End point title	Change From Baseline in Hamilton Anxiety Rating Scale (HAM-A) Total Score at Week 8

End point description:

The HAM-A is a 14-item rating scale designed to assess the global anxiety. It includes 14 items that assess anxious mood, tension, fear, insomnia, intellectual (cognitive) symptoms, depressed mood, behaviour at interview, somatic (sensory), cardiovascular, respiratory, gastrointestinal, genitourinary, autonomic, and somatic (muscular) symptoms. Each symptom was rated from 0 (absent) to 4 (maximum severity). The total score of the 14 items ranged from 0 to 56, with higher scores reflecting more severity. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: units on a scale				
least squares mean (standard error)	-16.1 (± 0.861)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hospital Anxiety and Depression Scale (HADS) HADS-Anxiety (HADS-A) Subscales Score at Week 8

End point title	Change From Baseline in Hospital Anxiety and Depression Scale (HADS) HADS-Anxiety (HADS-A) Subscales Score at Week 8

End point description:

The HADS is a patient-rated scale designed to screen for anxiety and depressive states in participants. The HADS consists of two subscales: the D-scale measures depression, and the A-scale measures anxiety. Each subscale contains 7 items, and each item was rated from 0 (absent) to 3 (maximum severity). The score of each subscale ranged from 0 to 21, with higher scores reflecting more severity. The A-scale score has been reported in this endpoint. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of

participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: units on a scale				
least squares mean (standard error)	-7.2 (± 0.486)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hospital Anxiety and Depression Scale (HADS) HADS-Depression (HADS-D) Subscales Score at Week 8

End point title	Change From Baseline in Hospital Anxiety and Depression Scale (HADS) HADS-Depression (HADS-D) Subscales Score at Week 8

End point description:

The HADS is a patient-rated scale designed to screen for anxiety and depressive states in participants. The HADS consists of two subscales: the D-scale measures depression, and the A-scale measures anxiety. Each subscale contains 7 items, and each item was rated from 0 (absent) to 3 (maximum severity). The score of each subscale ranged from 0 to 21, with higher scores reflecting more severity. The D-scale score has been reported in this endpoint. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: units on a scale				
least squares mean (standard error)	-8.2 (± 0.534)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functioning Assessment Short Test (FAST) Total Score Week 8

End point title	Change From Baseline in Functioning Assessment Short Test (FAST) Total Score Week 8

End point description:

The FAST is a clinician-rated scale 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, and leisure time. Each item was rated on a 4-point scale from 0 (no difficulty) to 3 (severe difficulty). The items were summed to yield a total score ranging from 0 to 72, with higher scores reflecting more serious difficulties. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: units on a scale				
least squares mean (standard error)	-23.0 (± 1.625)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FAST Autonomy Score Week 8

End point title	Change From Baseline in FAST Autonomy Score Week 8

End point description:

The FAST is a clinician-rated scale 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, and leisure time. Each item was rated on a 4-point scale from 0 (no difficulty) to 3 (severe difficulty). The FAST autonomy score has been reported in this endpoint. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: units on a scale				
least squares mean (standard error)	-3.4 (± 0.283)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FAST Occupational Functioning Score Week 8

End point title	Change From Baseline in FAST Occupational Functioning Score Week 8

End point description:

The FAST is a clinician-rated scale 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, and leisure time. Each item was rated on a 4-point scale from 0 (no difficulty) to 3 (severe difficulty). The FAST occupational functioning score has been reported in this endpoint. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: units on a scale				
least squares mean (standard error)	-5.3 (± 0.422)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FAST Cognitive Functioning Score at Week 8

End point title	Change From Baseline in FAST Cognitive Functioning Score at Week 8

End point description:

The FAST is a clinician-rated scale 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, and leisure time. Each item was rated on a 4-point scale from 0 (no difficulty) to 3 (severe difficulty). The FAST cognitive functioning score has been reported in this endpoint. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: units on a scale				
least squares mean (standard error)	-5.7 (± 0.413)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FAST Financial Issues Score at Week 8

End point title	Change From Baseline in FAST Financial Issues Score at Week 8

End point description:

The FAST is a clinician-rated scale 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, and leisure time. Each item was rated on a 4-point scale from 0 (no difficulty) to 3 (severe difficulty). The FAST financial issues score has been reported in this endpoint. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: units on a scale				
least squares mean (standard error)	-1.1 (± 0.133)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FAST Interpersonal Relationships Score at Week 8

End point title	Change From Baseline in FAST Interpersonal Relationships

	Score at Week 8

End point description:

The FAST is a clinician-rated scale 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, and leisure time. Each item was rated on a 4-point scale from 0 (no difficulty) to 3 (severe difficulty). The FAST interpersonal relationships score has been reported in this endpoint. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: units on a scale				
least squares mean (standard error)	-5.3 (± 0.535)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FAST Leisure Time Score at Week 8

End point title	Change From Baseline in FAST Leisure Time Score at Week 8

End point description:

The FAST is a clinician-rated scale 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, and leisure time. Each item was rated on a 4-point scale from 0 (no difficulty) to 3 (severe difficulty). The FAST leisure time score has been reported in this endpoint. The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: units on a scale				
least squares mean (standard error)	-2.2 (± 0.200)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression - Severity of Illness (CGI-S) Score at Week 8

End point title	Change From Baseline in Clinical Global Impression - Severity of Illness (CGI-S) Score at Week 8

End point description:

The CGI was developed to provide global measures of the severity of a participant's clinical condition and improvement or worsening during clinical studies. The CGI consist of 2 clinician-rated subscales: severity of illness (CGI-S) and global improvement (CGI-I). The CGI-S provides the clinician's impression of the participant's current state of mental illness. The clinician used their 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). The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: units on a scale				
least squares mean (standard error)	-2.1 (± 0.127)			

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 was developed to provide global measures of the severity of a participant's clinical condition and improvement or worsening during clinical studies. The CGI consist of 2 clinician-rated subscales: severity of illness (CGI-S) and global improvement (CGI-I). The CGI-I provides the clinician's impression of the participant's improvement (or worsening). The clinician assessed the participant's condition relative to baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). The analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS

total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: units on a scale				
least squares mean (standard error)	1.9 (± 0.106)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quality of Life Enjoyment and Satisfaction Questionnaire Long Form (Q-LES-Q LF) Physical Health Activity Score at Week 8

End point title	Change From Baseline in Quality of Life Enjoyment and Satisfaction Questionnaire Long Form (Q-LES-Q LF) Physical Health Activity Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF physical health activity score converted to percentage has been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: percent score				
least squares mean (standard error)	28.0 (± 2.903)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Q-LES-Q LF Feelings Score at Week 8

End point title	Change From Baseline in Q-LES-Q LF Feelings Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF feeling score covnerted to percentage has been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: percent score				
least squares mean (standard error)	28.0 (± 2.625)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Q-LES-Q LF Work Score at Week 8

End point title	Change From Baseline in Q-LES-Q LF Work Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF work score converted to percentage has been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	71			
Units: percent score				
least squares mean (standard error)	29.3 (± 3.701)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Q-LES-Q LF Household Duties Score at Week 8

End point title	Change From Baseline in Q-LES-Q LF Household Duties Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF household duties score converted to percentage has been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percent score				
least squares mean (standard error)	28.2 (± 2.645)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Q-LES-Q LF School Course Work Score at Week 8

End point title	Change From Baseline in Q-LES-Q LF School Course Work Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF school course work score converted to percentage has been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: percent score				
least squares mean (standard error)	38.3 (± 24.325)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Q-LES-Q LF Leisure Time Activities Score at Week 8

End point title	Change From Baseline in Q-LES-Q LF Leisure Time Activities Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF leisure time activities score converted to percent has been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: percent score				
least squares mean (standard error)	34.8 (± 2.726)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Q-LES-Q LF Social Relations Score at Week 8

End point title	Change From Baseline in Q-LES-Q LF Social Relations Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF social relations score converted to percentage has been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: percent score				
least squares mean (standard error)	26.2 (± 2.611)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Q-LES-Q LF Satisfaction With Medication Score at Week 8

End point title	Change From Baseline in Q-LES-Q LF Satisfaction With Medication Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF satisfaction with medication score converted to percentage has been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: percent score				
least squares mean (standard error)	33.1 (± 3.477)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Q-LES-Q LF General Activities Score at Week 8

End point title	Change From Baseline in Q-LES-Q LF General Activities Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF general activities score converted to percentage has been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: percent score				
least squares mean (standard error)	25.7 (± 2.515)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Q-LES-Q LF Overall Satisfaction and Contentment Score at Week 8

End point title	Change From Baseline in Q-LES-Q LF Overall Satisfaction and Contentment Score at Week 8

End point description:

The original Q-LES-Q LF 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 was rated on a 5-point scale ranging from 1 (very poor) to 5 (very good). The Q-LES-Q LF overall satisfaction and contentment score converted to percentage has

been reported in this endpoint. Analysis was performed using MMRM. FAS included all enrolled participants who received at least 1 dose of the study drug and had a valid baseline and at least 1 valid post-baseline assessment of the MADRS total score. Here, overall number of participants analyzed = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: percent score				
least squares mean (standard error)	38.3 (± 3.425)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose date up to Week 12	
Adverse event reporting additional description:	
All-patients-treated set included all enrolled participants who took at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Vortioxetine
Reporting group description:	
Participants received vortioxetine tablets 10 mg/day orally at Week 0. At Week 1, the dose was to be increased to 20 mg/day for all participants. The dose could be adjusted to 10 or 20 mg/day at scheduled or unscheduled visits, depending on the participants' response as per the investigator's judgement. The treatment was continued for a total of 8 weeks.	

Serious adverse events	Vortioxetine		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Vortioxetine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 100 (27.00%)		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	21 / 100 (21.00%)		
occurrences (all)	23		
Abdominal pain			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	6		

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