Clinical trial results:
Interventional, Open-label Study Of Flexible Doses Of Vortioxetine On Depressive Symptoms In Patients With Major Depressive Disorder And Early Dementia

Summary

EudraCT number	2019-001326-10
Trial protocol	ES IT
Global end of trial date	20 July 2022

Results information

Result version number	v1 (current)
This version publication date	05 August 2023
First version publication date	05 August 2023

Trial information

Trial identification

Sponsor protocol code	18315A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04294654
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	H. Lundbeck A/S, LundbeckClinicalTrials@lundbeck.com, +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	20 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 July 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the effectiveness of 12-week acute treatment with flexible doses of 5-20 milligrams (mg) per day vortioxetine on depressive symptoms in participants with Major Depressive Disorder (MDD) and early dementia.

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	19 February 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	Spain: 23
Country: Number of subjects enrolled	Estonia: 11
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Poland: 37
Worldwide total number of subjects	83
EEA total number of subjects	83

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)	20

From 65 to 84 years	62
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 83 participants were screened. 82 participants received at least 1 dose of vortioxetine.

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 daily for 12 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:

Participants received vortioxetine daily for 12 weeks

Number of subjects in period 1[1]	Vortioxetine
Started	82
Received at least 1 dose of study drug	82
Completed	69
Not completed	13
Consent withdrawn by subject	2
Adverse event, non-fatal	5
Unspecified	3
Non-compliance with IMP	1
Lack of efficacy	1
Protocol deviation	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 83 participants were screened. 82 participants received at least 1 dose of vortioxetine.

Baseline characteristics

Reporting groups	
Reporting group title	Vortioxetine
Reporting group description:	
Participants received vortioxetine daily for 12 weeks.	

Reporting group values	Vortioxetine	Total	
Number of subjects	82	82	
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)	20	20	
From 65-84 years	61	61	
85 years and over	1	1	
Age Continuous Units: years			
arithmetic mean	70.3		
standard deviation	± 7.25	-	
Gender Categorical Units: Subjects			
Female	54	54	
Male	28	28	
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. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at two-point intervals. The total score of the 10 items ranges from 0 to 60.			
Units: score on a scale			
arithmetic mean	30.4		
standard deviation	± 3.85	-	

End points

End points reporting groups

Reporting group title	Vortioxetine
Reporting group description:	
Participants received vortioxetine daily for 12 weeks.	

Primary: Change from Baseline to Week 12 in Montgomery and Åsberg Depression Rating Scale (MADRS) Total Score

End point title	Change from Baseline to Week 12 in Montgomery and Åsberg Depression Rating Scale (MADRS) Total Score[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. 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 two-point intervals. The total score of the 10 items ranges from 0 to 60.

The within-group p-value from Baseline to Week 12 was <0.0001 based on Mixed Model for Repeated Measures.

The full-analysis set (FAS) included all participants who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score. Here, 'Overall number of subjects analyzed' signifies participants evaluable for this outcome measure

End point type	Primary

End point timeframe:

Baseline, Week 12

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: Statistical analysis was entered in Description due to EudraCT system limitations for reporting on single-group studies.

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: score on a scale				
least squares mean (standard error)	-12.4 (± 0.780)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Digit-Symbol Substitution Test (DSST) Total Score

End point title	Change from Baseline to Week 12 in Digit-Symbol Substitution Test (DSST) Total Score

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).

The FAS included all participants who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score. Here, 'Overall number of subjects analyzed' signifies participants evaluable for this outcome measure

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: score on a scale				
least squares mean (standard error)	4.9 (± 0.898)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Rey Auditory Verbal Learning Test (RAVLT) score

End point title	Change from Baseline to Week 12 in Rey Auditory Verbal Learning Test (RAVLT) score

End point description:

The RAVLT is a cognitive test intended to measure a participant's learning and memory. In this test, 2 lists of 15 nouns (List A and List B) are used. The maximum score is 15 per trial and is based on the number of words correctly recalled (0 to 15) for each trial.

The FAS included all participants who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score. Here, 'Overall number of subjects analyzed' signifies participants evaluable for this outcome measure

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: score on a scale				
least squares mean (standard error)	2.1 (± 0.897)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Instrumental Activities of Daily Living (IADL) Total Score

End point title	Change from Baseline to Week 12 in Instrumental Activities of Daily Living (IADL) Total Score

End point description:

The IADL is a clinician-rated scale of a participant's daily functioning. The scale covers 8 functions: the participant's ability to use the telephone, do the shopping, prepare food, do the housekeeping, laundry, take responsibility for their own medications and handle their own finances, and their mode of transportation. The scores for each function are then summed to yield a total score ranging from 0 (low function, dependent) to 8 (high function, independent). The rater assigns scores 1 to 3, 1 to 4, or 1 to 5, depending on the number of items in each function, and this yields a polytomous score ranging from 8 (high function, independent) to 31 (low function, dependent).

The FAS included all participants who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score. Here, 'Overall number of subjects analyzed' signifies participants evaluable for this outcome measure

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: score on a scale				
least squares mean (standard error)	0.1 (± 0.123)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Clinical Global Impression – Severity of Illness (CGI-S) Score

End point title	Change from Baseline to Week 12 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 used his or her clinical experience of this participant's 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 patients).

The FAS included all participants who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score. Here, 'Overall number of subjects analyzed' signifies participants evaluable for this outcome measure

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: score on a scale				
least squares mean (standard error)	-1.0 (± 0.106)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Demonstrating Response (Defined as a ≥50% Decrease From Baseline in MADRS Total Score) at Week 12

End point title	Number of Participants Demonstrating Response (Defined as a ≥50% Decrease From Baseline in MADRS Total Score) at Week 12

End point description:

The FAS included all participants who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score.

End point type	Secondary

End point timeframe:

Week 12

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	82			
Units: Percentage of participants				
number (confidence interval 95%)	35.7 (24.6 to 48.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression – Improvement (CGI-I) Score at Week 12

End point title	Clinical Global Impression – Improvement (CGI-I) Score at Week 12

End point description:

The CGI-I provides the clinician’s impression of the participant's improvement (or worsening). The clinician assessed 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.

The FAS included all participants who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score. Here, 'Overall number of subjects analyzed' signifies participants evaluable for this outcome measure

End point type	Secondary

End point timeframe:

Week 12

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: score on a scale				
least squares mean (standard error)	2.8 (± 0.107)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Bath Assessment of Subjective Quality of Life in Dementia (BASQID) Total Score

End point title	Change from Baseline to Week 12 in Bath Assessment of Subjective Quality of Life in Dementia (BASQID) Total Score

End point description:

The BASQID is a clinician-rated scale designed to assess subjective quality of life (QoL) in participants with dementia. The BASQID contains 14 core questions (Life Satisfaction and Feelings of Positive QoL), which are scored from 0 to 4, with 4 indicating a better QoL.

The FAS included all participants who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score. Here, 'Overall number of subjects analyzed' signifies participants evaluable for this outcome measure

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: score on a scale				
least squares mean (standard error)	5.7 (± 0.699)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Remission (Defined as a MADRS Total Score ≤10) at Week 12

End point title	Number of Participants with Remission (Defined as a MADRS Total Score ≤10) at Week 12

End point description:

The FAS included all participants who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score.

End point type	Secondary

End point timeframe:

Week 12

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	82			
Units: Percentage of participants				
number (confidence interval 95%)	17.1 (9.2 to 28.0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From date of study drug administration (Day 1) up to Week 16	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0
Reporting groups	
Reporting group title	Vortioxetine
Reporting group description:	
Participants received vortioxetine daily for 12 weeks.	

Serious adverse events	Vortioxetine		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 82 (1.22%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Vortioxetine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 82 (46.34%)		
Injury, poisoning and procedural complications			
Accidental overdose			

subjects affected / exposed occurrences (all)	1 / 82 (1.22%) 1		
Cardiac disorders Cardiac failure subjects affected / exposed occurrences (all)	 1 / 82 (1.22%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Psychomotor hyperactivity subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	 6 / 82 (7.32%) 7 3 / 82 (3.66%) 3 2 / 82 (2.44%) 2 2 / 82 (2.44%) 2		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 1 / 82 (1.22%) 1		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	 1 / 82 (1.22%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Diarrhoea	 9 / 82 (10.98%) 9 9 / 82 (10.98%) 9		

subjects affected / exposed	3 / 82 (3.66%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 82 (3.66%)		
occurrences (all)	3		
Psychiatric disorders			
Tension			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences (all)	1		
Thinking abnormal			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	2 / 82 (2.44%)		
occurrences (all)	2		
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed occurrences (all)	3 / 82 (3.66%) 3		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all) Decreased appetite subjects affected / exposed occurrences (all)	 1 / 82 (1.22%) 1 1 / 82 (1.22%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported