



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 |
| Scientific contact | H. Lundbeck A/S, LundbeckClinicalTrials@lundbeck.com, +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 | 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 (\pm 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 (\pm 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 (\pm 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 (\pm 0.106) | | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|------------------------|---|
| End point title | Number of Participants Demonstrating Response (Defined as a \geq 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 (\pm 0.107) | | | |

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

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 |
|-----------------|---|

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 (\pm 0.699) | | | |

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 | | |

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

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