ClinicalTrials.gov PRS
Protocol Registration and Results System

ID: 12541A Randomised Placebo-controlled Duloxetine-referenced Study of Efficacy and Safety of 5 mg of Vortioxetine (Lu AA21004) in Acute Treatment of Major Depressive Disorder in Elderly Patients NCT00811252

Protocol Registration and Results Preview

Close

Randomised Placebo-controlled Duloxetine-referenced Study of Efficacy and Safety of 5 mg of Vortioxetine (Lu AA21004) in Acute Treatment of Major Depressive Disorder in Elderly Patients

This study has been completed.

Sponsor:	H. Lundbeck A/S
Collaborators:	
Information provided by (Responsible Party):	H. Lundbeck A/S
ClinicalTrials.gov Identifier:	NCT00811252

Purpose

To assess the efficacy of Vortioxetine (5 mg daily) versus placebo in the acute treatment of depression by means of the change from baseline in the 24-item Hamilton Depression Scale (HAM-D24) total score after 8 weeks of double-blind treatment in elderly patients.

Condition	Intervention	Phase
Major Depressive Disorder	Drug: Placebo Drug: Vortioxetine (Lu AA21004) Drug: Duloxetine	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Efficacy Study

Official Title: Randomised, Double-blind, Parallel-group, Placebo-controlled, Duloxetine-referenced, Fixed Dose Study Comparing the Efficacy and Safety of [Vortioxetine] Lu AA21004 in Acute Treatment of Major Depressive Disorder in Elderly Patients

Further study details as provided by H. Lundbeck A/S:

Primary Outcome Measure:

- Change From Baseline in HAM-D-24 Total Score After 8 Weeks of Treatment [Time Frame: Baseline and Week 8] [Designated as safety issue: No]
  The Hamilton Depression Scale - 24 Items (HAM-D-24) measures depression severity. Items are rated on a scale from 0 (symptoms not present) to a maximum of 2 to 4 (symptom extremely severe) for a total score range of 0 to 76. The higher the score, the more severe.

Secondary Outcome Measures:

- Change From Baseline in HAM-D-24 Total Score After 6 Weeks of Treatment [Time Frame: Baseline and Week 6] [Designated as safety issue: No]
- Change From Baseline in HAM-D-24 Total Score After 4 Weeks of Treatment [Time Frame: Baseline and Week 4] [Designated as safety issue: No]
- Change From Baseline in HAM-D-24 Total Score After 2 Weeks of Treatment [Time Frame: Baseline and Week 2] [Designated as safety issue: No]
- Change From Baseline in HAM-D-24 Total Score After 1 Week of Treatment [Time Frame: Baseline and Week 1] [Designated as safety issue: No]

- Change From Baseline in MADRS Total Score After 8 Weeks of Treatment [Time Frame: Baseline and Week 8] [Designated as safety issue: No]
  The Montgomery Åsberg Depression Rating Scale (MADRS) is a depression rating scale consisting of 10 items, each rated 0 (no symptom) to 6 (severe symptom). The 10 items represent the core symptoms of depressive illness. The rating should be based on a clinical interview with the patient, moving from broadly phrased questions about symptoms to more detailed ones, which allow a precise rating of severity, covering the last 7 days. Total score from 0 to 60. The higher the score, the more severe.

- Change From Baseline in HAM-A Total Score After 8 Weeks of Treatment [Time Frame: Baseline and Week 8] [Designated as safety issue: No]
  The Hamilton Anxiety Rating Scale (HAM-A) consists of 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 is rated from 0 (absent) to 4 (maximum severity). Total score from 0 to 56. The higher the score, the more severe.

- Change From Baseline in CGI-S Score After 8 Weeks of Treatment [Time Frame: Baseline and Week 8] [Designated as safety issue: No]
  The Clinical Global Impression - Severity of Illness (CGI-S) is a 7-point scale rated from 1 (normal, not at all ill) to 7 (among the most extremely ill patients). The investigator should use his/her total clinical experience with this patient population to judge how mentally ill the patient is at the time of rating.

- Change in Clinical Status Using CGI-I Score at Week 8 [Time Frame: Week 8] [Designated as safety issue: No]
  The Clinical Global Impression - Global Improvement (CGI-I) is a 7-point scale rated from 1 (very much improved) to 7 (very much worse). The investigator rated the patient's overall improvement relative to baseline, whether or not, in the opinion of the investigator, this was entirely due to the drug treatment.

- Change From Baseline in GDS Total Score After 8 Weeks of Treatment [Time Frame: Baseline and Week 8] [Designated as safety issue: No]
  The Geriatric Depression Scale (GDS) is a patient self-rating scale designed for the screening of depression in the elderly. It has also been validated as a measure of depression severity. The original version consists of 30 questions with a yes/no answer. In this study, the short 15-item version was used. The total score ranges from 0 to 15, with 15 representing maximum severity.

- Proportion of Responders at Week 8 (Response Defined as a >=50% Reduction in the HAM-D-24 Total Score) [Time Frame: Week 8] [Designated as safety issue: No]

- Proportion of Remitters at Week 8 (Remission Defined as a MADRS Total Score <=10) [Time Frame: Week 8] [Designated as safety issue: No]

- Risk of Suicidality Using C-SSRS Scores [Time Frame: Up to 8 weeks] [Designated as safety issue: Yes]
  The Columbia-Suicide Severity Rating Scale (C-SSRS) was developed by researchers at Columbia University as a tool to systematically assess suicidal ideation and behaviour in patients during participation in a clinical study. The C-SSRS is composed of questions that address suicidal behaviour and questions that address suicidal ideation, with sub-questions that assess severity. The tool was administered via an interview with the patient.

Enrollment: 453
Study Start Date: January 2009
Study Completion Date: March 2010
Primary Completion Date: February 2010

Arms	Assigned Interventions
Placebo Comparator: Placebo	Drug: Placebo capsules; daily; orally
Experimental: Vortioxetine 5 mg	Drug: Vortioxetine (Lu AA21004) encapsulated tablets; daily; orally

	Other Names: • Brintellix
Duloxetine 60 mg Active reference	Drug: Duloxetine encapsulated tablets; daily; orally Other Names: • Cymbalta®

Eligibility

Ages Eligible for Study: 65 Years and older
Genders Eligible for Study: Both
Inclusion Criteria:

Clinical Diagnosis of recurrent Major Depressive Episode (MDE) according the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) criteria with:

- Reported duration of the current episode of at least 4 weeks
- MADRS total score >=26
- At least one previous MDE before the age of 60 years

Exclusion Criteria:

- Mini Mental State Exam (MMSE) <24
- Any current anxiety disorder as defined in the DSM-IV-TR
- Current or past history of manic or hypomanic episode, schizophrenia, or any other psychotic disorder, including major depression with psychotic features, mental retardation, organic mental disorders, or mental disorders due to a general medical condition as defined in the DSM-IV-TR
- Any substance disorder (except nicotine and caffeine) within the previous 6 months as defined in the DSM-IV-TR
- Presence or history of a clinically significant neurological disorder (including epilepsy)
- Neurodegenerative disorder (Alzheimer's disease, Parkinson disease, multiple sclerosis, Huntington disease, etc)
- Any Axis II disorder that might compromise the study
- Significant risk of suicide according to the investigator's opinion, or has a score >=5 on item 10 of the MADRS or has made a suicide attempt in the previous 6 months

Other inclusion and exclusion criteria may apply.

Contacts and Locations

Investigators

Study Director: Email contact via H. Lundbeck A/S LundbeckClinicalTrials@lundbeck.com

More Information

Results Publications:

Katona C, Hansen T, Olsen CK. A randomized, double-blind, placebo-controlled, duloxetine-referenced, fixed-dose study comparing the efficacy and safety of Lu AA21004 in elderly patients with major depressive disorder. Int Clin Psychopharmacol. 2012 Jul;27(4):215-23. doi: 10.1097/YIC.0b013e3283542457.

Responsible Party: H. Lundbeck A/S
Study ID Numbers: 12541A
2008-002901-38 [EudraCT Number]
Health Authority: Canada: Health Canada
Finland: Finnish Medicines Agency
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Germany: Federal Institute for Drugs and Medical Devices
Sweden: Medical Products Agency
Ukraine: Ministry of Health
United States: Food and Drug Administration

Study Results

Participant Flow

Recruitment Details	Patients were mainly recruited via psychiatric, psycho-geriatric, and geriatric inpatient or outpatient settings.
Pre-Assignment Details	The study consisted of a Screening Period; an 8-week Core Treatment Period; a 1-week double-blind down-taper period (Week 9); and a 4-week Safety Follow-up Period after completion/withdrawal (Weeks 8 to 12).

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg	Total (Not public)
Arm/Group Description	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally	
Period Title: **Overall Study**				
Started	145	156	151	452
Completed	128	136	128	392
Not Completed	17	20	23	60
Reason Not Completed				
Adverse Event	6	10	15	31
Lack of Efficacy	7	2	0	9
Protocol Violation	3	3	2	8
Withdrawal of Consent	1	2	2	5
Lost to Follow-up	0	0	2	2
Administrative or Other Reasons	0	3	2	5
(Not Public)	Not Completed = 17 Total from all reasons = 17	Not Completed = 20 Total from all reasons = 20	Not Completed = 23 Total from all reasons = 23	

Baseline Characteristics

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg	Total
Arm/Group Description	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally	
Overall Number of Baseline Participants	145	156	151	**452**
Baseline Analysis Population Description	Full-analysis set (FAS) - all patients in the all-patients-treated set (APTS) who had at least one valid post-baseline assessment of the primary efficacy variable			
Age, Continuous Mean (Standard Deviation) Units: years	70.3 (4.4)	70.5 (4.8)	70.9 (5.5)	70.6 (4.9)
Gender, Male/Female Measure Type: Number Units: participants				
Female	90	107	100	297
Male	55	49	51	155
HAM-D-24 [1] Mean (Standard Deviation) Units: units on a scale	29.4 (5.1)	29.2 (5.0)	28.5 (4.9)	29.0 (5.0)
	[1] The Hamilton Depression Scale - 24 Items (HAM-D-24) measures depression severity. Items are rated on a scale from 0 (symptoms not present) to a maximum of 2 to 4 (symptom extremely severe) for a total score range of 0 to 76. The higher the score, the more severe.			
MADRS [1] Mean (Standard Deviation) Units: units on a scale	30.3 (3.2)	30.7 (3.6)	30.4 (3.1)	30.5 (3.3)

	[1] The Montgomery Åsberg Depression Rating Scale (MADRS) is a depression rating scale consisting of 10 items, each rated 0 (no symptom) to 6 (severe symptom). The 10 items represent the core symptoms of depressive illness. The rating should be based on a clinical interview with the patient, moving from broadly phrased questions about symptoms to more detailed ones, which allow a precise rating of severity, covering the last 7 days. Total score from 0 to 60. The higher the score, the more severe.			
HAM-A [1] Mean (Standard Deviation) Units: units on a scale	19.5 (5.7)	19.9 (5.8)	19.2 (6.5)	19.5 (6.0)
	[1] The Hamilton Anxiety Rating Scale (HAM-A) consists of 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 is rated from 0 (absent) to 4 (maximum severity). Total score from 0 to 56. The higher the score, the more severe.			
CGI-S [1] Mean (Standard Deviation) Units: units on a scale	4.7 (0.7)	4.8 (0.7)	4.7 (0.8)	4.7 (0.7)
	[1] The Clinical Global Impression - Severity of Illness (CGI-S) is a 7-point scale rated from 1 (normal, not at all ill) to 7 (among the most extremely ill patients). The investigator should use his/her total clinical experience with this patient population to judge how mentally ill the patient is at the time of rating.			
GDS [1] Mean (Standard Deviation) Units: units on a scale	7.7 (2.0)	7.4 (2.2)	7.7 (2.3)	7.6 (2.2)
	[1] The Geriatric Depression Scale (GDS) is a patient self-rating scale designed for the screening of depression in the elderly. It has also been validated as a measure of depression severity. The original version consists of 30 questions with a yes/no answer. In this study, the short 15-item version was used. The total score ranges from 0 to 15, with 15 representing maximum severity.			

Outcome Measures

1. Primary Outcome

Title:	Change From Baseline in HAM-D-24 Total Score After 8 Weeks of Treatment
Description:	The Hamilton Depression Scale - 24 Items (HAM-D-24) measures depression severity. Items are rated on a scale from 0 (symptoms not present) to a maximum of 2 to 4 (symptom extremely severe) for a total score range of 0 to 76. The higher the score, the more severe.
Time Frame:	Baseline and Week 8
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

Full-analysis set (FAS) - all patients in the all-patients-treated set (APTS) who had at least one valid post-baseline assessment of the primary efficacy variable; last observation carried forward (LOCF); analysis of covariance (ANCOVA)

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Mean (Standard Error) Units: units on a scale	-10.3 (0.76)	-13.7 (0.74)	-15.8 (0.75)

Statistical Analysis 1

Statistical	Comparison Groups	Placebo, Vortioxetine 5 mg

Analysis Overview	Comments	As soon as an endpoint was non-significant at the 0.05 level of significance, the testing procedure was stopped for all subsequent endpoints.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0011
	Comments	Since p-value <0.05, hierarchically testing continued
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-3.32
	Confidence Interval	(2-Sided) 95% -5.31 to -1.34
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.01
	Estimation Comments	A statistical testing strategy was defined a priori for a single dose of vortioxetine that was tested versus placebo in the primary and key secondary efficacy analyses.

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Duloxetine 60 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	This treatment arm was not in the testing sequence. A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-5.48
	Confidence Interval	(2-Sided) 95% -7.50 to -3.46
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.03
	Estimation Comments	[Not specified]

2. Secondary Outcome

Title:	Change From Baseline in HAM-D-24 Total Score After 6 Weeks of Treatment
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 6
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; LOCF, ANCOVA

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Mean (Standard Error) Units: units on a scale	-10.2 (0.71)	-12.3 (0.69)	-14.4 (0.70)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	As soon as an endpoint was non-significant at the 0.05 level of significance, the testing procedure was stopped for all subsequent endpoints.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0240
	Comments	Since p-value <0.05, hierarchically testing continued
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.13
	Confidence Interval	(2-Sided) 95% -3.98 to -0.28
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.94
	Estimation Comments	A statistical testing strategy was defined a priori for a single dose of vortioxetine that was tested versus placebo in the primary and key secondary efficacy analyses.

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Duloxetine 60 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	This treatment arm was not in the testing sequence. A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-4.22
	Confidence Interval	(2-Sided) 95% -6.10 to -2.34
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.96
	Estimation Comments	[Not specified]

3. Secondary Outcome

Title:	Change From Baseline in HAM-D-24 Total Score After 4 Weeks of Treatment
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 4
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Mean (Standard Error) Units: units on a scale	-8.99 (0.64)	-10.1 (0.62)	-12.3 (0.63)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2134
	Comments	Since p-value >0.05, hierarchically testing stopped here.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.06
	Confidence Interval	(2-Sided) 95% -2.72 to 0.61
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.85
	Estimation Comments	[Not specified]

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Duloxetine 60 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	This treatment arm was not in the testing sequence. A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-3.30
	Confidence Interval	(2-Sided) 95% -4.99 to -1.60
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.86
	Estimation Comments	[Not specified]

4. Secondary Outcome

Title:	Change From Baseline in HAM-D-24 Total Score After 2 Weeks of Treatment
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 2
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Mean (Standard Error) Units: units on a scale	-6.66 (0.53)	-6.95 (0.51)	-7.91 (0.52)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6879
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.28
	Confidence Interval	(2-Sided) 95% -1.67 to 1.10
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.70
	Estimation Comments	[Not specified]

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Duloxetine 60 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0827
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.25
	Confidence Interval	(2-Sided) 95% -2.65 to 0.16
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.72
	Estimation Comments	[Not specified]

5. Secondary Outcome

Title:	Change From Baseline in HAM-D-24 Total Score After 1 Week of Treatment
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 1
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	154	147
Mean (Standard Error) Units: units on a scale	-3.62 (0.41)	-4.04 (0.40)	-3.48 (0.41)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4482
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.42
	Confidence Interval	(2-Sided) 95% -1.49 to 0.66
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.55
	Estimation Comments	[Not specified]

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Duloxetine 60 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7971
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.14
	Confidence Interval	(2-Sided) 95% -0.95 to 1.24
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.56
	Estimation Comments	[Not specified]

6. Secondary Outcome

Title:	Change From Baseline in MADRS Total Score After 8 Weeks of Treatment
▼ Description:	The Montgomery Åsberg Depression Rating Scale (MADRS) is a depression rating scale consisting of 10 items, each rated 0 (no symptom) to 6 (severe symptom). The 10 items represent the core symptoms of depressive illness. The rating should be based on a clinical interview with the patient, moving from broadly phrased questions about symptoms to more detailed ones, which allow a precise rating of severity, covering the last 7 days. Total score from 0 to 60. The higher the score, the more severe.
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg

▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Mean (Standard Error) Units: units on a scale	-11.2 (0.77)	-15.5 (0.75)	-18.0 (0.76)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	A nominal p-value is provided. No correction for multiplicity was made.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-4.29
	Confidence Interval	(2-Sided) 95% -6.32 to -2.26
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.03
	Estimation Comments	[Not specified]

7. Secondary Outcome

Title:	Change From Baseline in HAM-A Total Score After 8 Weeks of Treatment
▼ Description:	The Hamilton Anxiety Rating Scale (HAM-A) consists of 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 is rated from 0 (absent) to 4 (maximum severity). Total score from 0 to 56. The higher the score, the more severe.
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Mean (Standard Error) Units: units on a scale	-5.74 (0.55)	-8.09 (0.54)	-9.28 (0.54)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0015
	Comments	A nominal p-value is provided. No correction for multiplicity was made.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.35
	Confidence Interval	(2-Sided) 95% -3.80 to -0.91
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.74
	Estimation Comments	[Not specified]

8. Secondary Outcome

Title:	Change From Baseline in CGI-S Score After 8 Weeks of Treatment

▼ Description:	The Clinical Global Impression - Severity of Illness (CGI-S) is a 7-point scale rated from 1 (normal, not at all ill) to 7 (among the most extremely ill patients). The investigator should use his/her total clinical experience with this patient population to judge how mentally ill the patient is at the time of rating.
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Mean (Standard Error) Units: units on a scale	-1.03 (0.11)	-1.63 (0.10)	-2.05 (0.11)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	A nominal p-value is provided. No correction for multiplicity was made.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.60
	Confidence Interval	(2-Sided) 95% -0.88 to -0.32
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.14
	Estimation Comments	[Not specified]

9. Secondary Outcome

Title:	Change in Clinical Status Using CGI-I Score at Week 8
▼ Description:	The Clinical Global Impression - Global Improvement (CGI-I) is a 7-point scale rated from 1 (very

	much improved) to 7 (very much worse). The investigator rated the patient's overall improvement relative to baseline, whether or not, in the opinion of the investigator, this was entirely due to the drug treatment.
Time Frame:	Week 8
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Mean (Standard Error) Units: units on a scale	2.91 (0.10)	2.35 (0.09)	2.07 (0.10)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	A nominal p-value is provided. No correction for multiplicity was made.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.56
	Confidence Interval	(2-Sided) 95% -0.82 to -0.31
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.13
	Estimation Comments	[Not specified]

10. Secondary Outcome

Title:	Change From Baseline in GDS Total Score After 8 Weeks of Treatment
▼ Description:	The Geriatric Depression Scale (GDS) is a patient self-rating scale designed for the screening of

	depression in the elderly. It has also been validated as a measure of depression severity. The original version consists of 30 questions with a yes/no answer. In this study, the short 15-item version was used. The total score ranges from 0 to 15, with 15 representing maximum severity.
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; observed cases (OC); ANCOVA

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	144	154	142
Mean (Standard Error) Units: units on a scale	-0.65 (0.17)	-1.08 (0.17)	-1.32 (0.17)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0552
	Comments	A nominal p-value is provided. No correction for multiplicity was made.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.44
	Confidence Interval	(2-Sided) 95% -0.88 to 0.01
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.23
	Estimation Comments	[Not specified]

11. Secondary Outcome

Title:	Proportion of Responders at Week 8 (Response Defined as a >=50% Reduction in the HAM-D-24 Total Score)

▼ Description:	[Not specified]
Time Frame:	Week 8
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description
FAS; LOCF

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Measure Type: Number Units: percentage of patients	35	53	63

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0008
	Comments	A nominal p-value is provided. No correction for multiplicity was made.
	Method	Regression, Logistic
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	0.43
	Confidence Interval	(2-Sided) 95% 0.26 to 0.70
	Estimation Comments	[Not specified]

12. Secondary Outcome

Title:	Proportion of Remitters at Week 8 (Remission Defined as a MADRS Total Score <=10)
▼ Description:	[Not specified]
Time Frame:	Week 8
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description
FAS; LOCF

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	145	155	148
Measure Type: Number Units: percentage of patients	21	34	47

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0090
	Comments	A nominal p-value is provided. No correction for multiplicity was made.
	Method	Regression, Logistic
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	0.47
	Confidence Interval	(2-Sided) 95% 0.27 to 0.83
	Estimation Comments	[Not specified]

13. Secondary Outcome

Title:	Risk of Suicidality Using C-SSRS Scores
▼ Description:	The Columbia-Suicide Severity Rating Scale (C-SSRS) was developed by researchers at Columbia University as a tool to systematically assess suicidal ideation and behaviour in patients during participation in a clinical study. The C-SSRS is composed of questions that address suicidal behaviour and questions that address suicidal ideation, with sub-questions that assess severity. The tool was administered via an interview with the patient.
Time Frame:	Up to 8 weeks

Safety Issue?	Yes

▼ Outcome Measure Data ✓

▼ Analysis Population Description

C-SSRS Data by Columbia Classification Algorithm for Suicide Assessment (C-CASA) Category (APTS)

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; daily; orally	encapsulated tablets; daily; orally
Number of Participants Analyzed	114	121	114
Measure Type: Number Units: participants			
No ideation or behavior	103	107	106
Completed Suicide	0	0	0
Suicide Attempt	0	0	1
Preparatory Actions Toward Imminent Suicidal Behav	0	0	0
Suicidal Ideation: Passive	8	14	7
Suicidal Ideation: Active / Nonspecific	3	0	0
Suicidal Ideation: Active / Method, but no intent	0	0	0
Suicidal Ideation: Active / Method and intent, but	0	0	0
Suicidal Ideation: Active / Method, intent, and pl	0	0	0
Self-Injurious Behavior Without Suicidal Intent	0	0	0

Adverse Events

Time Frame	Serious Adverse Events: 8-week double-blind treatment period and 4-week safety follow-up period Other Adverse Events: 8-week double-blind treatment period
Additional Description	
Source Vocabulary Name	[Not specified]
Assessment Type	[Not specified] NOTE : An Assessment Type for Table Default has not been specified.

Arm/Group Title	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg

▼ Arm/Group Description	[Not specified] NOTE : An entry in Arm/Group Description is recommended.	[Not specified] NOTE : An entry in Arm/Group Description is recommended.	[Not specified] NOTE : An entry in Arm/Group Description is recommended.

▼ **Serious Adverse Events**

	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	4/145 (2.76%)	1/156 (0.64%)	1/151 (0.66%)
Injury, poisoning and procedural complications			
Hip fracture [A]	1/145 (0.69%)	0/156 (0%)	0/151 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bile duct cancer [A]	1/145 (0.69%)	0/156 (0%)	0/151 (0%)
Prostate cancer [A]	0/55 (0%)	0/49 (0%)	1/51 (1.96%)
Nervous system disorders			
Transient ischaemic attack [A]	1/145 (0.69%)	0/156 (0%)	0/151 (0%)
Psychiatric disorders			
Depression [A]	1/145 (0.69%)	0/156 (0%)	0/151 (0%)
Major depression [A]	0/145 (0%)	1/156 (0.64%)	0/151 (0%)

Indicates events were collected by non-systematic methods.
A Term from vocabulary, MEDDRA12_1

▼ **Other (Not Including Serious) Adverse Events**

Frequency Threshold for Reporting Other Adverse Events	5%

	Placebo	Vortioxetine 5 mg	Duloxetine 60 mg
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	63/145 (43.45%)	72/156 (46.15%)	104/151 (68.87%)
Gastrointestinal disorders			
Constipation [A]	6/145 (4.14%)	10/156 (6.41%)	21/151 (13.91%)
Diarrhoea [A]	10/145 (6.9%)	8/156 (5.13%)	14/151 (9.27%)
Dry mouth [A]	7/145 (4.83%)	10/156 (6.41%)	33/151 (21.85%)
Nausea [A]	12/145 (8.28%)	34/156 (21.79%)	50/151 (33.11%)
General disorders			
Fatigue [A]	5/145 (3.45%)	11/156 (7.05%)	16/151 (10.6%)
Metabolism and nutrition disorders			
Decreased appetite [A]	2/145 (1.38%)	7/156 (4.49%)	8/151 (5.3%)
Nervous system disorders			
Dizziness [A]	10/145 (6.9%)	14/156 (8.97%)	14/151 (9.27%)
Headache [A]	25/145 (17.24%)	18/156 (11.54%)	18/151 (11.92%)
Somnolence [A]	3/145 (2.07%)	4/156 (2.56%)	16/151 (10.6%)
Reproductive system and breast disorders			
Ejaculation delayed [A]	0/55 (0%)	0/49 (0%)	3/51 (5.88%)
Erectile dysfunction [A]	0/55 (0%)	0/49 (0%)	3/51 (5.88%)
Skin and subcutaneous			

tissue disorders			
Hyperhidrosis [A]	4/145 (2.76%)	6/156 (3.85%)	16/151 (10.6%)

Indicates events were collected by non-systematic methods.
A Term from vocabulary, MEDDRA12_1

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The main publication has to be published before any sub-publications. H. Lundbeck A/S follows the Vancouver declaration with respect to authorship.

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