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Protocol Registration and Results System

ID: 11985A Efficacy of Vortioxetine (Lu AA21004) in the Prevention of Relapse of Major Depressive Episodes NCT00596817

Protocol Registration and Results Preview

Close

Efficacy of Vortioxetine (Lu AA21004) in the Prevention of Relapse of Major Depressive Episodes

This study has been completed.

Sponsor:	H. Lundbeck A/S
Collaborators:	
Information provided by (Responsible Party):	H. Lundbeck A/S
ClinicalTrials.gov Identifier:	NCT00596817

Purpose

This study will evaluate the efficacy of Vortioxetine in the prevention of relapse of major depressive episodes in patients who responded to open-label treatment with Vortioxetine.

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

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

Official Title: A Double-blind, Randomised, Placebo-controlled, Multicentre, Relapse-prevention Study With Two Doses of [Vortioxetine] Lu AA21004 in Patients With Major Depressive Disorder

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

Primary Outcome Measure:

- Relapse Within First 24 Weeks of the Double-blind Period Based on a MADRS Total Score >=22 or an Unsatisfactory Treatment Effect (Lack of Efficacy) as Judged by the Investigator [Time Frame: Within first 24 weeks of the double-blind period] [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.

Secondary Outcome Measures:

- Relapse During the Entire Double-blind Period Based on a MADRS Total Score >=22 or an Unsatisfactory Treatment Effect (Lack of Efficacy) as Judged by the Investigator [Time Frame: Within 64 weeks of the double-blind period] [Designated as safety issue: No]

- Change From Double-blind Baseline in MADRS Total Score After 24 Weeks of Double-blind Treatment [Time Frame: Double-blind Baseline and Week 24 of the double-blind period] [Designated as safety issue: No]

- Change From Double-blind Baseline in HAM-D-17 Total Score After 24 Weeks of Double-blind Treatment [Time Frame: Double-blind Baseline and Week 24 of the double-blind period] [Designated as safety issue: No]

  The Hamilton Depression Scale - 17 items (HAM-D-17) 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 52. The higher the score, the more severe.

- Change From Double-blind Baseline in HAM-A Total Score After 24 Weeks of Double-blind Treatment [Time Frame: Double-blind Baseline and Week 24 of the double-blind period] [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 Double-blind Baseline in CGI-S Score After 24 Weeks of Double-blind Treatment [Time Frame: Double-blind Baseline and Week 24 of the double-blind period] [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.

- Proportion of Responders at Week 24 of the Double-blind Period (Response Defined as a >=50% Reduction in MADRS Total Score From Open-label Baseline) [Time Frame: Week 24 of the double-blind period (Counted From Open-label Baseline)] [Designated as safety issue: No]

- Proportion of Remitters at Week 24 of the Double-blind Period (Remission Defined as a MADRS Total Score <=10) [Time Frame: Week 24 of the double-blind period] [Designated as safety issue: No]

- Change From Double-blind Baseline in SDS Total Score at Week 24 of the Double-blind Period [Time Frame: Week 24 of the double-blind period (Counted From Double-blind Baseline)] [Designated as safety issue: No]

  The Sheehan Disability Scale (SDS) comprises self-rated items designed to measure impairment. The patient rates the extent to which his or her (1) work, (2) social life or leisure activities and (3) home life or family responsibilities are impaired on a 10-point

visual analogue scales, on which 0 = normal functioning and 10 = severe functional impairment. The three items may be summed into a single dimensional measure of global functional impairment that ranges from 0 (unimpaired) to 30 (highly impaired). The higher the score, the more severe.

Enrollment: 639
Study Start Date: December 2007
Study Completion Date: October 2009
Primary Completion Date: September 2009

Arms	Assigned Interventions
Placebo Comparator: Placebo	Drug: Placebo capsules, daily, orally
Experimental: Vortioxetine: 5 or 10 mg	Drug: Vortioxetine (Lu AA21004) encapsulated tablets, daily, orally Other Names: • Brintellix

Eligibility

Ages Eligible for Study: 18 Years to 75 Years
Genders Eligible for Study: Both
Inclusion Criteria:

- Major Depressive Episode (MDE) as the primary diagnosis according to DSM-IV TR criteria
- At least one other MDE before the current one
- Moderate to severe depression

Exclusion Criteria:

- Any current psychiatric disorder other than Major Depressive Disorder (MDD) as defined in the DSM-IV TR
- Any substance disorder within the previous 6 months
- Female patients of childbearing potential who are not using effective contraception
- Use of any psychoactive medication 2 weeks prior to screening and during the study

Randomisation Criteria: Patients in remission (MADRS total score <=10) at both Week 10 and Week 12

Other protocol-defined 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:

Boulenger JP, Loft H, Florea I. A randomized clinical study of Lu AA21004 in the prevention of relapse in patients with major depressive disorder. J Psychopharmacol. 2012 Nov;26(11):1408-16. doi: 10.1177/0269881112441866. Epub 2012 Apr 9.

Responsible Party: H. Lundbeck A/S
Study ID Numbers: 11985A
2007-001871-13 [EudraCT Number]
Health Authority: Australia: Department of Health and Ageing Therapeutic Goods Administration
Austria: Federal Office for Safety in Health Care
Belgium: The Federal Public Service (FPS) Health, Food Chain Safety and Environment
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
India: Ministry of Health
Korea: Food and Drug Administration
Norway: Norwegian Medicines Agency
Poland: The Central Register of Clinical Trials
Sweden: Medical Products Agency
Taiwan: National Bureau of Controlled Drugs
Thailand: Food and Drug Administration
Turkey: Ministry of Health
United Kingdom: Medicines and Healthcare Products Regulatory Agency
South Africa: Medicines Control Council

Study Results

Participant Flow

Recruitment Details	Patients were in- and outpatients from psychiatric settings.
Pre-Assignment Details	The study consisted of two consecutive periods: a 12-week open-label treatment period with Vortioxetine and a double-blind, fixed-dose, placebo-controlled treatment period of at least 24 weeks.

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg	Total (Not public)
Arm/Group Description	Placebo : capsules, daily, orally	Vortioxetine (Lu AA21004) : encapsulated tablets, daily, orally	
Period Title: **Open-label Period**			
Started	0	639	639
Completed	0	492	492
Not Completed	0	147	147
Reason Not Completed			
Adverse Event	0	49	49
Lack of Efficacy	0	33	33

Other Reasons	0	65	65
(Not Public)	Not Completed = 0 Total from all reasons = 0	Not Completed = 147 Total from all reasons = 147	

Period Title: **Open-label Period to Double-blind Period**

Started	0	492	492
Completed	0	400	400
Not Completed	0	92	92
Reason Not Completed			
Adverse Event	0	5	5
Lack of Efficacy	0	24	24
Not Eligible	0	49	49
Other Reasons	0	14	14
(Not Public)	Not Completed = 0 Total from all reasons = 0	Not Completed = 92 Total from all reasons = 92	

Period Title: **Double-blind Period**

Started	192 [1] NOTE : The number of participants to start a Period is not equal to the number who completed previous Period.	204 [2] NOTE : The number of participants to start a Period is not equal to the number who completed previous Period.	396
Completed	104	125	229
Not Completed	88	79	167
Reason Not Completed			
Adverse Event	5	16	21
Lack of Efficacy	52	28	80
Non-compliance With Study Product	3	4	7
Protocol Violation	11	8	19
Withdrawal of Consent	7	3	10
Lost to Follow-up	0	2	2
Other Reasons	10	18	28
(Not Public)	Not Completed = 88 Total from all reasons = 88	Not Completed = 79 Total from all reasons = 79	

[1] 194 patients were randomised. 2 did not receive study medication. 192 is full-analysis set (FAS).

[2] 206 patients were randomised. 2 did not receive study medication. 204 is FAS.

Baseline Characteristics

Arm/Group Title	Open-label Period (APTS)	Placebo - Double-blind Period (FAS)	Vortioxetine: 5 or 10 mg - Double-blind Period (FAS)	Total

▼ Arm/Group Description	[Not specified] NOTE : An entry in Arm/Group Description is recommended.	Placebo : capsules, daily, orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	Vortioxetine (Lu AA21004) : encapsulated tablets, daily, orally	
Overall Number of Baseline Participants	639	192	204	**1035**
▼ Baseline Analysis Population Description	The total number of patients under Baseline Measures is not 1035 as automatically calculated, but 639 as stated in the "Open-label Period (APTS)" column and 396 in the "Double-blind Period (FAS)". The "Total" column of each Baseline Measure is Double-blind Period (FAS).			
Age, Continuous Mean (Standard Deviation) Units: years	44.6 (12.4)	45.1 (12.1)	44.8 (12.4)	45.0 (12.3)
Gender, Customized Measure Type: Number Units: participants				
Female (Open-label Period)	397	NA [1]	NA [2]	NA [3]
Male (Open-label Period)	242	NA [4]	NA [5]	NA [6]
Female (Double-blind Period)	0	120	130	250
Male (Double-blind Period)	0	72	74	146
	[1] Only data for Open-label Period **[2]** Only data for Open-label Period **[3]** Total not calculated because data are not available (NA) in one or more arms. **[4]** Only data for Open-label Period **[5]** Only data for Open-label Period **[6]** Total not calculated because data are not available (NA) in one or more arms.			
MADRS [1] Mean (Standard Deviation) Units: units on a scale	32.3 (4.1)	4.66 (3.16)	4.89 (3.00)	4.78 (3.08)
	[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-D-17 [1] Mean (Standard Deviation) Units: units on a scale	22.8 (4.5)	3.96 (3.15)	4.46 (3.27)	4.21 (3.21)
	[1] The Hamilton Depression Scale - 17 items (HAM-D-17) 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 52. The higher the score, the more severe.			
HAM-A [1] Mean (Standard Deviation) Units: units on a scale	22.6 (6.6)	4.60 (3.60)	5.09 (3.83)	4.85 (3.72)
	[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	4.8 (0.7)	1.54 (0.69)	1.56 (0.68)	1.55 (0.69)
	[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.			
SDS [1] Mean (Standard Deviation) Units: units on a scale	20.8 (5.7)	8.37 (7.44)	8.95 (7.09)	8.66 (7.27)
	[1] The Sheehan Disability Scale (SDS) comprises self-rated items designed to measure impairment. The patient rates the extent to which his or her (1) work, (2) social life or leisure activities and (3) home life or family responsibilities are impaired on a 10-point visual analogue scales, on which 0 = normal functioning and 10 = severe functional impairment. The three items may be summed into a single dimensional measure of global functional impairment that ranges from 0 (unimpaired) to 30 (highly impaired). The higher the score, the more severe.			

Outcome Measures

1. Primary Outcome

Title:	Relapse Within First 24 Weeks of the Double-blind Period Based on a MADRS Total Score >=22 or an Unsatisfactory Treatment Effect (Lack of Efficacy) as Judged by the Investigator
▼ 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:	Within first 24 weeks of the double-blind period
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg
▼ Arm/Group Description:	capsules, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	192	204
Measure Type: Number Units: percentage of patients who relapsed	26.0	13.2

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine: 5 or 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0035
	Comments	[Not specified]
	Method	Other [Cox-model]
	Comments	Cox-model using an exact method to handle ties

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	2.01
	Confidence Interval	(2-Sided) 95% 1.26 to 3.21
	Estimation Comments	[Not specified]

2. Secondary Outcome

Title:	Relapse During the Entire Double-blind Period Based on a MADRS Total Score >=22 or an Unsatisfactory Treatment Effect (Lack of Efficacy) as Judged by the Investigator
▼ Description:	[Not specified]
Time Frame:	Within 64 weeks of the double-blind period
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg
▼ Arm/Group Description:	capsules, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	192	204
Measure Type: Number Units: percentage of patients who relapsed	30.2	15.2

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine: 5 or 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0010
	Comments	A nominal p-value is provided.
	Method	Other [Cox-Model]

	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	2.09
	Confidence Interval	(2-Sided) 95% 1.35 to 3.23
	Estimation Comments	[Not specified]

3. Secondary Outcome

Title:	Change From Double-blind Baseline in MADRS Total Score After 24 Weeks of Double-blind Treatment
▼ Description:	[Not specified]
Time Frame:	Double-blind Baseline and Week 24 of the double-blind period
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; observed cases (OC)

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg
▼ Arm/Group Description:	capsules, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	132	151
Mean (Standard Error) Units: units on a scale	1.45 (0.55)	-0.62 (0.51)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine: 5 or 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0020
	Comments	A nominal p-value is provided.
	Method	ANCOVA

	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.06
	Confidence Interval	(2-Sided) 95% -3.36 to -0.77
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.66
	Estimation Comments	[Not specified]

4. Secondary Outcome

Title:	Change From Double-blind Baseline in HAM-D-17 Total Score After 24 Weeks of Double-blind Treatment
▼ Description:	The Hamilton Depression Scale - 17 items (HAM-D-17) 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 52. The higher the score, the more severe.
Time Frame:	Double-blind Baseline and Week 24 of the double-blind period
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

FAS; OC

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg
▼ Arm/Group Description:	capsules, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	136	158
Mean (Standard Error) Units: units on a scale	1.61 (0.46)	0.30 (0.42)

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine: 5 or 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0171
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.31
	Confidence Interval	(2-Sided) 95% -2.39 to -0.24
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.55
	Estimation Comments	[Not specified]

5. Secondary Outcome

Title:	Change From Double-blind Baseline in HAM-A Total Score After 24 Weeks of Double-blind 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:	Double-blind Baseline and Week 24 of the double-blind period
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; OC

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg
▼ Arm/Group Description:	capsules, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	136	158
Mean (Standard Error) Units: units on a scale	0.89 (0.50)	-0.23 (0.46)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine: 5 or 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0612
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.12
	Confidence Interval	(2-Sided) 95% -2.30 to 0.05
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.60
	Estimation Comments	[Not specified]

6. Secondary Outcome

Title:	Change From Double-blind Baseline in CGI-S Score After 24 Weeks of Double-blind 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:	Double-blind Baseline and Week 24 of the double-blind period
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

FAS; OC

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg
▼ Arm/Group Description:	capsules, daily, orally	encapsulated tablets, daily, orally

Number of Participants Analyzed	132	151
Mean (Standard Error) Units: units on a scale	0.24 (0.08)	-0.14 (0.08)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine: 5 or 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.38
	Confidence Interval	(2-Sided) 95% -0.57 to -0.18

	Parameter Dispersion	Type: Standard Error of the mean Value: 0.10
	Estimation Comments	[Not specified]

7. Secondary Outcome

Title:	Proportion of Responders at Week 24 of the Double-blind Period (Response Defined as a >=50% Reduction in MADRS Total Score From Open-label Baseline)
▼ Description:	[Not specified]
Time Frame:	Week 24 of the double-blind period (Counted From Open-label Baseline)
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

FAS; OC

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg
▼ Arm/Group Description:	capsules, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	132	151
Measure Type: Number Units: percentage of patients	91.7	98.0

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine: 5 or 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.025
	Comments	A nominal p-value is provided.
	Method	Fisher Exact
	Comments	[Not specified]
Method of	Estimation Parameter	Other[Difference]

Estimation	Estimated Value	6.35
	Confidence Interval	(2-Sided) 95% 1.13 to 11.56
	Estimation Comments	[Not specified]

8. Secondary Outcome

Title:	Proportion of Remitters at Week 24 of the Double-blind Period (Remission Defined as a MADRS Total Score <=10)
▼ Description:	[Not specified]
Time Frame:	Week 24 of the double-blind period
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

FAS; OC

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg
▼ Arm/Group Description:	capsules, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	132	151
Measure Type: Number Units: percentage of patients	82.6	94.7

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine: 5 or 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.002
	Comments	A nominal p-value is provided.
	Method	Fisher Exact
	Comments	[Not specified]
	Estimation Parameter	

Method of Estimation		Other[Difference]
	Estimated Value	12.13
	Confidence Interval	(2-Sided) 95% 4.73 to 19.52
	Estimation Comments	[Not specified]

9. Secondary Outcome

Title:	Change From Double-blind Baseline in SDS Total Score at Week 24 of the Double-blind Period
▼ Description:	The Sheehan Disability Scale (SDS) comprises self-rated items designed to measure impairment. The patient rates the extent to which his or her (1) work, (2) social life or leisure activities and (3) home life or family responsibilities are impaired on a 10-point visual analogue scales, on which 0 = normal functioning and 10 = severe functional impairment. The three items may be summed into a single dimensional measure of global functional impairment that ranges from 0 (unimpaired) to 30 (highly impaired). The higher the score, the more severe.
Time Frame:	Week 24 of the double-blind period (Counted From Double-blind Baseline)
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

FAS; OC

Arm/Group Title	Placebo	Vortioxetine: 5 or 10 mg
▼ Arm/Group Description:	capsules, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	118	135
Mean (Standard Error) Units: units on a scale	0.14 (0.58)	-0.53 (0.57)

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine: 5 or 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3642
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.67
	Confidence Interval	(2-Sided) 95% -2.12 to 0.78
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.73
	Estimation Comments	[Not specified]

Adverse Events

Time Frame	Serious Adverse Events: 12-week open-label period, 24-week double-blind period and 4-week safety follow-up period. Other Adverse Events: 12-week open-label period and 24-week double-blind 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	Open-label Period (APTS)	Placebo - Double-blind Period (FAS)	Vortioxetine: 5 or 10 mg - Double-blind Period (FAS)
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

	Open-label Period (APTS)	Placebo - Double-blind Period (FAS)	Vortioxetine: 5 or 10 mg - Double-blind Period (FAS)
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	14/639 (2.19%)	6/192 (3.12%)	7/204 (3.43%)

Cardiac disorders			
Stress cardiomyopathy [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Gastrointestinal disorders			
Abdominal pain [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Gastritis [A]	0/639 (0%)	0/192 (0%)	1/204 (0.49%)
General disorders			
Non-cardiac chest pain [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Hepatobiliary disorders			
Cholelithiasis [A]	0/639 (0%)	1/192 (0.52%)	0/204 (0%)
Infections and infestations			
Bronchitis [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Cystitis [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Influenza [A]	0/639 (0%)	1/192 (0.52%)	0/204 (0%)
Nasopharyngitis [A]	0/639 (0%)	1/192 (0.52%)	0/204 (0%)
Pneumonia [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Streptococcal infection [A]	0/639 (0%)	0/192 (0%)	1/204 (0.49%)
Upper respiratory tract infection [A]	0/639 (0%)	1/192 (0.52%)	0/204 (0%)
Injury, poisoning and procedural complications			
Accidental overdose [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Alcohol poisoning [A]	0/639 (0%)	1/192 (0.52%)	1/204 (0.49%)
Joint dislocation [A]	0/639 (0%)	1/192 (0.52%)	0/204 (0%)
Road traffic accident [A]	0/639 (0%)	0/192 (0%)	2/204 (0.98%)
Upper limb fracture [A]	0/639 (0%)	1/192 (0.52%)	0/204 (0%)
Metabolism and nutrition disorders			
Hypoglycaemia [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Neoplasms benign,			

malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Sebaceous carcinoma [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Nervous system disorders			
Loss of consciousness [A]	0/639 (0%)	1/192 (0.52%)	0/204 (0%)
Serotonin syndrome [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Pregnancy, puerperium and perinatal conditions			
Abortion incomplete [A]	0/397 (0%)	0/120 (0%)	1/130 (0.77%)
Psychiatric disorders			
Alcohol abuse [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Depression [A]	2/639 (0.31%)	1/192 (0.52%)	0/204 (0%)
Suicide attempt [A]	1/639 (0.16%)	0/192 (0%)	0/204 (0%)
Social circumstances			
Social stay hospitalisation [A]	0/639 (0%)	0/192 (0%)	1/204 (0.49%)

Indicates events were collected by non-systematic methods.

A Term from vocabulary, MEDDRA12_0

▼ Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%		
	Open-label Period (APTS)	**Placebo - Double-blind Period (FAS)**	**Vortioxetine: 5 or 10 mg - Double-blind Period (FAS)**
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	337/639 (52.74%)	73/192 (38.02%)	79/204 (38.73%)
Gastrointestinal disorders			
Dry mouth [A]	41/639 (6.42%)	0/192 (0%)	4/204 (1.96%)
Nausea [A]	164/639 (25.67%)	6/192 (3.12%)	18/204 (8.82%)
General disorders			
Fatigue [A]	32/639 (5.01%)	4/192 (2.08%)	4/204 (1.96%)
Infections and infestations			

Gastroenteritis A	12/639 (1.88%)	6/192 (3.12%)	11/204 (5.39%)
Influenza A	7/639 (1.1%)	9/192 (4.69%)	14/204 (6.86%)
Nasopharyngitis A	52/639 (8.14%)	26/192 (13.54%)	22/204 (10.78%)
Injury, poisoning and procedural complications			
Accidental overdose [1] A	36/639 (5.63%)	15/192 (7.81%)	16/204 (7.84%)
Nervous system disorders			
Dizziness A	44/639 (6.89%)	7/192 (3.65%)	6/204 (2.94%)
Headache A	117/639 (18.31%)	25/192 (13.02%)	25/204 (12.25%)
Psychiatric disorders			
Insomnia A	36/639 (5.63%)	3/192 (1.56%)	5/204 (2.45%)

Indicates events were collected by non-systematic methods.
A Term from vocabulary, MEDDRA12_0

[1] Everything beyond the prescribed dose, for instance one extra tablet, is counted as an overdose.

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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