ClinicalTrials.gov PRS
Protocol Registration and Results System

ID: 14178A A Study of Vortioxetine (Lu AA21004) in Comparison to Agomelatine in Adults Suffering From Major Depression With Inadequate Response to Previous Medication NCT01488071

Protocol Registration and Results Preview

Close

A Study of Vortioxetine (Lu AA21004) in Comparison to Agomelatine in Adults Suffering From Major Depression With Inadequate Response to Previous Medication (REVIVE)

This study has been completed.

Sponsor:	H. Lundbeck A/S
Collaborators:	
Information provided by (Responsible Party):	H. Lundbeck A/S
ClinicalTrials.gov Identifier:	NCT01488071

Purpose

The objective of the present study is to evaluate whether vortioxetine (10 or 20 mg/day) is at least as effective as agomelatine (25 to 50 mg/day) in patients with depressive symptoms that showed inadequate response to Serotonin Reuptake Inhibitors (SRI) antidepressants.

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

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

Official Title: A Randomised, Double-blind, Parallel-group, Active-controlled, Flexible Dose Study Evaluating the Effects of [Vortioxetine] Lu AA21004 Versus Agomelatine in Adult Patients Suffering From Major Depressive Disorder With Inadequate Response to Antidepressant Treatment

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

Primary Outcome Measure:

- Change From Baseline in MADRS Total Score at Week 8 [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, thus, a negative change (or decrease) from baseline indicates a reduction (or improvement) in symptoms.

Secondary Outcome Measures:

- Change From Baseline in MADRS Total Score at Week 12 [Time Frame: Baseline and Week 12] [Designated as safety issue: No]

- Change From Baseline in HAM-A Total Score at Week 8 [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; higher score indicates greater anxiety, thus, a negative change (or decrease) from baseline indicates a reduction (or improvement) in symptoms.

- Change From Baseline in HAM-A Total Score at Week 12 [Time Frame: Baseline and Week 12] [Designated as safety issue: No]

- Change From Baseline in CGI-S Score at Week 8 [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. Higher score indicates that the subject is more ill, thus, a negative change (or decrease) from baseline indicates a reduction (or improvement) in symptoms.

- Change From Baseline in CGI-S Score at Week 12 [Time Frame: Baseline and Week 12] [Designated as safety issue: No]

- 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. Higher score = more affected.

- Change in Clinical Status Using CGI-I Score at Week 12 [Time Frame: Week 12] [Designated as safety issue: No]

- Proportion of Patients Who Respond at Week 8 (Response Defined as a >=50% Decrease in the MADRS Total Score From Baseline) [Time Frame: Baseline and Week 8] [Designated as safety issue: No]

- Proportion of Patients Who Respond at Week 12 (Response Defined as a >=50% Decrease in the MADRS Total Score From Baseline) [Time Frame: Baseline and Week

12] [Designated as safety issue: No]

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

- Proportion of Patients Who Are in Remission at Week 12 (Remission is Defined as a MADRS Total Score <=10) [Time Frame: Week 12] [Designated as safety issue: No]

- Change From Baseline in SDS Total Score at Week 8 [Time Frame: Baseline and Week 8] [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, thus, a negative change (or decrease) from baseline indicates a reduction (or improvement) in symptoms.

- Change From Baseline in SDS Total Score at Week 12 [Time Frame: Baseline and Week 12] [Designated as safety issue: No]

Enrollment: 495
Study Start Date: January 2012
Primary Completion Date: December 2012

Arms	Assigned Interventions
Experimental: Vortioxetine 10 mg or 20 mg	Drug: Vortioxetine (Lu AA21004) encapsulated tablets, daily, orally Other Names: • Brintellix®
Active Comparator: Agomelatine 25 mg or 50 mg	Drug: Agomelatine encapsulated tablets, daily, orally Other Names: • Valdoxan®

Eligibility

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

- The patient is being treated with a serotonin reuptake inhibitor (SRI) antidepressant (monotherapy) that was prescribed to treat Major Depressive Episode (DSM-IV-TR criteria)
- The response to the current SRI treatment is inadequate and patient agrees to discontinue the current SRI at the baseline
- Montgomery Åsberg Depression Rating Scale (MADRS) total score ≥22 at the Screening Visit and Baseline

- The patient, if a woman, must: agree not to try to become pregnant during the study, AND use adequate, highly effective contraception

Exclusion Criteria:

- The patient has any current Axis I disorders (DSM-IV criteria) other than Major Depressive Disorder (MDD), General Anxiety Disorder (GAD) and Social Anxiety Disorder (SAD)
- The patient is at significant risk of suicide
- The patient is currently receiving formal psychotherapy or other psychoactive medications

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

Responsible Party: H. Lundbeck A/S
Study ID Numbers: 14178A
2011-002362-21 [EudraCT Number]
Health Authority: Austria: Austrian Medicines and Medical Devices Agency
Belgium: Federal Agency for Medicinal Products and Health Products
Bulgaria: Bulgarian Drug Agency
Czech Republic: State Institute for Drug Control
Estonia: The State Agency of Medicine
Germany: Federal Institute for Drugs and Medical Devices
Italy: The Italian Medicines Agency
Lithuania: State Medicine Control Agency - Ministry of Health
Poland: National Institute of Medicines
Romania: National Agency for Medicines and Medical Devices
Russia: FSI Scientific Center of Expertise of Medical Application
Spain: Spanish Agency of Medicines
Sweden: Medical Products Agency
United Kingdom: Medicines and Healthcare Products Regulatory Agency

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Study Results

Participant Flow

Recruitment Details	In- or outpatients who had been treated with antidepressant selective serotonin reuptake inhibitor (SSRI) or selective noradrenaline reuptake inhibitor (SNRI) monotherapy that was prescribed to treat a single episode of Major Depressive Disorder (MDD) or recurrent MDD.
Pre-Assignment Details	The study will consist of a screening period of 4 to 10 days before the Baseline Visit, followed by a 12-week treatment period with vortioxetine or agomelatine. A safety follow-up will be done approximately 4 weeks after the Completion/Withdrawal Visit.

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg	Total (Not public)
▼ Arm/Group Description	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally	
Period Title: **Overall Study**			
Started	253 [1]	242 [2]	495
Completed	200	179	379
Not Completed	53	63	116
Reason Not Completed			
Adverse Event	15	23	38
Lack of Efficacy	11	17	28
Non-compliance with study drug	2	0	2
Protocol Violation	5	7	12
Withdrawal of Consent	14	12	26
Lost to Follow-up	1	0	1
Administrative or Other Reason(s)	5	4	9
(Not Public)	Not Completed = 53 Total from all reasons = 53	Not Completed = 63 Total from all reasons = 63	

[1] all-patients-treated set (APTS)
[2] APTS

Baseline Characteristics

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg	Total
▼ Arm/Group Description	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally	
Overall Number of Baseline Participants	253	242	**495**
▼ Baseline Analysis Population Description	Age and Gender: All-patients-treated set (APTS) - all patients in the APRS who took at least one dose of investigational medicinal product (IMP). Study Specific Characteristics: Full-analysis set (FAS) - all patients in the APTS who had a valid baseline assessment and at least one valid post-baseline assessment of the MADRS total score.		
Age, Continuous Mean (Standard Deviation) Units: years	47.0 (12.4)	45.6 (12.4)	46.3 (12.4)
Gender, Male/Female Measure Type: Number Units: participants			

Female	195	175	370
Male	58	67	125
MADRS: Baseline Total Score [1] Mean (Standard Deviation) Units: units on a scale	29.1 (4.4)	28.7 (4.0)	28.9 (4.2)
	[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 - 60. The higher the score, the more severe.		
HAM-A: Baseline Total Score [1] Mean (Standard Deviation) Units: units on a scale	21.6 (6.3)	21.4 (6.2)	21.5 (6.2)
	[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; higher score indicates greater anxiety.		
CGI-S Baseline Severity Score [1] Mean (Standard Deviation) Units: units on a scale	4.4 (0.6)	4.4 (0.6)	4.4 (0.6)
	[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. Higher score indicates that the patient is more ill.		
SDS Total Baseline Score [1] Mean (Standard Deviation) Units: units on a scale	19.2 (5.3)	19.3 (5.2)	19.3 (5.3)
	[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:	Change From Baseline in MADRS Total Score at Week 8
▼ 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, thus, a negative change (or decrease) from baseline indicates a reduction (or improvement) in symptoms.
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

full-analysis set (FAS)

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	220	190
Mean (Standard Error) Units: units on a scale	-16.53 (0.48)	-14.38 (0.51)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Mixed model for repeated measurements (MMRM), using all available data, with a freely varying mean and covariance structures and with treatment, week, and site group as fixed factors and the baseline score as a covariate. The model also included interaction between week and baseline score, as

		well as interaction between week and treatment. Non-inferiority, upper limit of Confidence Interval should not exceed 2.
Statistical Test of Hypothesis	P-Value	0.0018
	Comments	Under established non-inferiority the p-value is not adjusted.
	Method	Mixed Models Analysis
	Comments	MMRM
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.16
	Confidence Interval	(2-Sided) 95% -3.51 to -0.81
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.69
	Estimation Comments	[Not specified]

2. Secondary Outcome

Title:	Change From Baseline in MADRS Total Score at Week 12
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description
FAS

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	200	178
Mean (Standard Error) Units: units on a scale	-18.95 (0.50)	-16.92 (0.53)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0054
	Comments	No adjustments for multiple comparisons were made.
	Method	Mixed Models Analysis
	Comments	The same MMRM methodology as for the primary endpoint was used.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.03
	Confidence Interval	(2-Sided) 95% -3.45 to -0.60
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.72
	Estimation Comments	[Not specified]

3. Secondary Outcome

Title:	Change From Baseline in HAM-A Total Score at Week 8
▼ 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; higher score indicates greater anxiety, thus, a negative change (or decrease) from baseline indicates a reduction (or improvement) in symptoms.
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

FAS

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	220	190
Mean (Standard Error) Units: units on a scale	-11.68 (0.39)	-9.79 (0.42)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0008
	Comments	No adjustments for multiple comparisons were made.
	Method	Mixed Models Analysis
	Comments	The same MMRM methodology as for the primary endpoint was used.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.89
	Confidence Interval	(2-Sided) 95% -2.98 to -0.80
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.56
	Estimation Comments	[Not specified]

4. Secondary Outcome

Title:	Change From Baseline in HAM-A Total Score at Week 12
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 12
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	200	178
Mean (Standard Error) Units: units on a scale	-13.52 (0.40)	-11.59 (0.42)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	0.0007

Hypothesis	Comments	No adjustments for multiple comparisons were made.
	Method	Mixed Models Analysis
	Comments	The same MMRM methodology as for the primary endpoint was used.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.93
	Confidence Interval	(2-Sided) 95% -3.04 to -0.81
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.57
	Estimation Comments	[Not specified]

5. Secondary Outcome

Title:	Change From Baseline in CGI-S Score at Week 8
▼ 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. Higher score indicates that the subject is more ill, thus, a negative change (or decrease) from baseline indicates a reduction (or improvement) in symptoms.
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

FAS

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	220	190
Mean (Standard Error) Units: units on a scale	-1.84 (0.07)	-1.55 (0.07)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0023
	Comments	No adjustments for multiple comparisons were made.
	Method	Mixed Models Analysis
	Comments	The same MMRM methodology as for the primary endpoint was used.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.30
	Confidence Interval	(2-Sided) 95% -0.48 to -0.11
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.10
	Estimation Comments	[Not specified]

6. Secondary Outcome

Title:	Change From Baseline in CGI-S Score at Week 12
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description
FAS

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally

Number of Participants Analyzed	200	178
Mean (Standard Error) Units: units on a scale	-2.20 (0.07)	-1.93 (0.07)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0075
	Comments	No adjustments for multiple comparisons were made.
	Method	Mixed Models Analysis
	Comments	The same MMRM methodology as for the primary endpoint was used.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.27
	Confidence Interval	(2-Sided) 95% -0.47 to -0.07

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

7. 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. Higher score = more affected.
Time Frame:	Week 8
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

FAS

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	220	190
Mean (Standard Error) Units: units on a scale	1.97 (0.06)	2.22 (0.07)

Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0048
	Comments	No adjustments for multiple comparisons were made.
	Method	Mixed Models Analysis

	Comments	The same MMRM methodology as for the primary endpoint was used.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.25
	Confidence Interval	(2-Sided) 95% -0.42 to -0.08
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.09
	Estimation Comments	[Not specified]

8. Secondary Outcome

Title:	Change in Clinical Status Using CGI-I Score at Week 12
▼ Description:	[Not specified]
Time Frame:	Week 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description
FAS

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	200	178
Mean (Standard Error) Units: units on a scale	1.74 (0.06)	1.99 (0.07)

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0055
	Comments	No adjustments for multiple comparisons were made.
	Method	Mixed Models Analysis
	Comments	The same MMRM methodology as for the primary endpoint was used.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.25
	Confidence Interval	(2-Sided) 95% -0.42 to -0.07
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.09
	Estimation Comments	[Not specified]

9. Secondary Outcome

Title:	Proportion of Patients Who Respond at Week 8 (Response Defined as a >=50% Decrease in the MADRS Total Score From Baseline)
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

FAS, last observation carried forward (LOCF)

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	252	241
Measure Type: Number Units: percentage of participants	61.5	47.3

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0012
	Comments	Wald's Test. No adjustments for multiple comparisons were made.
	Method	Regression, Logistic
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.81
	Confidence Interval	(2-Sided) 95% 1.26 to 2.60
	Estimation Comments	[Not specified]

10. Secondary Outcome

Title:	Proportion of Patients Who Respond at Week 12 (Response Defined as a >=50% Decrease in the MADRS Total Score From Baseline)
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description
FAS, LOCF

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	252	241
Measure Type: Number	69.8	56.0

Units: percentage of participants		

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0014
	Comments	Wald's Test. No adjustments for multiple comparisons were made.
	Method	Regression, Logistic
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.83
	Confidence Interval	(2-Sided) 95% 1.26 to 2.65

	Estimation Comments	[Not specified]

11. Secondary Outcome

Title:	Proportion of Patients Who Are in Remission at Week 8 (Remission is 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	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	252	241
Measure Type: Number Units: percentage of participants	40.5	29.5

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0054
	Comments	Wald's Test. No adjustments for multiple comparisons were made.
	Method	Regression, Logistic
	Comments	[Not specified]
Method of	Estimation Parameter	Odds Ratio (OR)

Estimation	Estimated Value	1.72
	Confidence Interval	(2-Sided) 95% 1.17 to 2.52
	Estimation Comments	[Not specified]

12. Secondary Outcome

Title:	Proportion of Patients Who Are in Remission at Week 12 (Remission is Defined as a MADRS Total Score <=10)
▼ Description:	[Not specified]
Time Frame:	Week 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description
FAS, LOCF

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	252	241
Measure Type: Number Units: percentage of participants	55.2	39.4

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	Wald's Test. No adjustments for multiple comparisons were made.
	Method	Regression, Logistic

	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	2.01
	Confidence Interval	(2-Sided) 95% 1.39 to 2.90
	Estimation Comments	[Not specified]

13. Secondary Outcome

Title:	Change From Baseline in SDS Total Score at Week 8
▼ 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, thus, a negative change (or decrease) from baseline indicates a reduction (or improvement) in symptoms.
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

FAS

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	162	135
Mean (Standard Error) Units: units on a scale	-9.28 (0.53)	-7.06 (0.55)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0021
	Comments	No adjustments for multiple comparisons were made.
	Method	Mixed Models Analysis
	Comments	The same MMRM methodology as for the primary endpoint was used.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.22
	Confidence Interval	(2-Sided) 95% -3.63 to -0.81
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.72
	Estimation Comments	[Not specified]

14. Secondary Outcome

Title:	Change From Baseline in SDS Total Score at Week 12
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description
FAS

Arm/Group Title	Vortioxetine 10 mg or 20 mg	Agomelatine 25 mg or 50 mg
▼ Arm/Group Description:	encapsulated tablets, daily, orally	encapsulated tablets, daily, orally
Number of Participants Analyzed	148	132
Mean (Standard Error) Units: units on a scale	-10.99 (0.55)	-9.24 (0.58)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Vortioxetine 10 mg or 20 mg, Agomelatine 25 mg or 50 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0209
	Comments	No adjustments for multiple comparisons were made.
	Method	Mixed Models Analysis
	Comments	The same MMRM methodology as for the primary endpoint was used.
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.75
	Confidence Interval	(2-Sided) 95% -3.23 to -0.27
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.75
	Estimation Comments	[Not specified]

Adverse Events

Time Frame		
Additional Description		
Source Vocabulary Name	[Not specified]	
Assessment Type	[Not specified]	
Arm/Group Title	Vortioxetine	Agomelatine
▼ 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.

Serious Adverse Events

	Vortioxetine	Agomelatine
	Affected / at Risk (%)	Affected / at Risk (%)
Total	3/253 (1.19%)	4/242 (1.65%)
Gastrointestinal disorders		
Peptic ulcer perforation [A]	1/253 (0.4%)	0/242 (0%)
General disorders		
Oedema peripheral [A]	1/253 (0.4%)	0/242 (0%)
Investigations		
Gamma-glutamyltransferase increased [A]	0/253 (0%)	1/242 (0.41%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Breast cancer [A]	0/253 (0%)	1/242 (0.41%)
Psychiatric disorders		
Anxiety [A]	1/253 (0.4%)	0/242 (0%)
Depression [A]	1/253 (0.4%)	0/242 (0%)
Reproductive system and breast disorders		
Metrorrhagia [A]	0/195 (0%)	1/175 (0.57%)
Social circumstances		
Social stay hospitalisation [A]	0/253 (0%)	1/242 (0.41%)

Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 15.1

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%

	Vortioxetine	Agomelatine
	Affected / at Risk (%)	Affected / at Risk (%)
Total	82/253 (32.41%)	77/242 (31.82%)
Gastrointestinal disorders		
Nausea [A]	41/253 (16.21%)	22/242 (9.09%)
Nervous system disorders		
Dizziness [A]	18/253 (7.11%)	28/242 (11.57%)
Headache [A]	26/253 (10.28%)	32/242 (13.22%)
Somnolence [A]	10/253 (3.95%)	19/242 (7.85%)

Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 15.1

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 results of this study will be published. Authors of the primary publication based on this study must fulfil the criteria defined by the International Committee of Medical Journal Editors (ICMJE). The primary publication must be published before any secondary publications are submitted for publication.

Results Point of Contact

Name/Official Title:	H. Lundbeck A/S
Organization:	H. Lundbeck A/S
Phone:	+45 36301311
Email:	LundbeckClinicalTrials@lundbeck.com

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