ClinicalTrials.gov PRS
Protocol Registration and Results System

ID: 11984B Open-label Safety Extension Study of 2.5, 5 and 10 mg of Vortioxetine (Lu AA21004) in Long-term Treatment of Major Depressive Disorder in Adults NCT00694304

Protocol Registration and Results Preview

Close

Open-label Safety Extension Study of 2.5, 5 and 10 mg of Vortioxetine (Lu AA21004) in Long-term Treatment of Major Depressive Disorder in Adults

This study has been completed.

Sponsor:	H. Lundbeck A/S
Collaborators:	
Information provided by (Responsible Party):	H. Lundbeck A/S
ClinicalTrials.gov Identifier:	NCT00694304

Purpose

The purpose of the study is to evaluate long-term safety and tolerability of Vortioxetine over a period of 52 weeks in patients with Major Depressive Disorder (MDD) having completed 8-week acute treatment.

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

Study Type: Interventional
Study Design: Treatment, Single Group Assignment, Open Label, N/A, Safety Study

Official Title: A Long-term, Open-label, Flexible-dose, Extension Study Evaluating the Safety and Tolerability of [Vortioxetine] Lu AA21004 in Patients With Major Depressive Disorder

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

Primary Outcome Measure:

- Number of Patients With Adverse Events (AEs) [Time Frame: Baseline to end of the 4-week safety follow-up period] [Designated as safety issue: Yes]

- Percentage of Patients Who Withdrew Due to Intolerance to Treatment [Time Frame: Baseline to Week 52] [Designated as safety issue: Yes]

Secondary Outcome Measures:

- Change From Baseline in MADRS Total Score After 52 Weeks of Treatment [Time Frame: Baseline and Week 52] [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-D-24 Total Score After 52 Weeks of Treatment [Time Frame: Baseline and Week 52] [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.

- Change From Baseline in HAM-A Total Score After 52 Weeks of Treatment [Time Frame: Baseline and Week 52] [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 52 Weeks of Treatment [Time Frame: Baseline and Week 52] [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 52 (Response Defined as a >=50% Decrease in MADRS Total Score) [Time Frame: Week 52] [Designated as safety issue: No]

- Proportion of Remitters at Week 52 (Remission Defined as a MADRS Total Score <=10) [Time Frame: Week 52] [Designated as safety issue: No]

- Proportion of Patients With a MADRS Total Score >=22 After 52 Weeks of Treatment [Time Frame: Baseline and Week 52] [Designated as safety issue: No]

- Change From Baseline in SDS Total Score After 52 Weeks of Treatment [Time Frame: Baseline and Week 52] [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: 535
Study Start Date: May 2008
Study Completion Date: April 2010
Primary Completion Date: March 2010

Arms	Assigned Interventions
Experimental: Vortioxetine	Drug: Vortioxetine (Lu AA21004) 2.5, 5, or 10 mg/day; tablets; orally Other Names: • Brintellix

Eligibility

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

- Patients who completed 8-week short-term treatment study for Major Depressive Episode, NCT00635219 / 11984A

Exclusion Criteria:

- Any current psychiatric disorder other than MDD as defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Ed., Text revision (DSM-IV TR)
- Female patients of childbearing potential who are not using effective contraception
- Use of any psychoactive medication

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:

Baldwin DS, Hansen T, Florea I. Vortioxetine (Lu AA21004) in the long-term open-label treatment of major depressive disorder. Curr Med Res Opin. 2012 Oct;28(10):1717-24. doi: 10.1185/03007995.2012.725035. Epub 2012 Sep 17.

Responsible Party: H. Lundbeck A/S
Study ID Numbers: 11984B
EudraCT 2007-004992-21 [Registry ID: EudraCT]
Health Authority: Australia: Department of Health and Ageing Therapeutic Goods Administration
Bulgaria: Bulgarian Drug Agency
Canada: Health Canada
Czech Republic: State Institute for Drug Control
Estonia: The State Agency of Medicine
Finland: Finnish National Agency for Medicines
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)

Hong Kong: Department of Health
India: Drugs Controller General of India
Korea: Food and Drug Administration
Latvia: State Agency of Medicines
Lithuania: State Medicine Control Agency - Ministry of Health
Malaysia: Ministry of Health
Philippines: Bureau of Food and Drugs
Romania: National Agency for Medicines and Medical Devices
Slovenia: Agency for Medicinal Products - Ministry of Health
Spain: Spanish Agency of Medicines
Taiwan: National Bureau of Controlled Drugs
Turkey: Ministry of Health
Ukraine: Ministry of Health

Study Results

Participant Flow

Recruitment Details	Patients eligible to participate in Study 11984B were patients who had completed lead-in Study NCT00635219 / 11984A immediately prior to inclusion into Study 11984B.
Pre-Assignment Details	The study consisted of a 52-week open-label period and a 4-week Safety Follow-up Period.

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day	Total (Not public)
Arm/Group Description	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.	
Period Title: **Overall Study**		
Started	535	535
Completed	328	328
Not Completed	207	207
Reason Not Completed		
Adverse Event	42	42
Lack of Efficacy	35	35
Non-compliance With Study Product	16	16
Protocol Violation	6	6
Withdrawal of Consent	61	61
Lost to Follow-up	15	15
Administrative or Other Reasons	32	32
(Not Public)	Not Completed = 207 Total from all reasons = 207	

Baseline Characteristics

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Overall Number of Baseline Participants	535
Baseline Analysis Population Description	Age and Sex: all-patients-treated set (APTS) - all patients who took at least one dose of Vortioxetine after Baseline; MADRS, HAM-D-24, HAM-A, CGI-S and SDS: full-analysis set (FAS) - all patients in the APTS who had at least one valid post-Baseline assessment of the MADRS total score.
Age, Continuous Mean (Standard Deviation) Units: years	45.7 (12.3)
Gender, Male/Female Measure Type: Number Units: participants	
Female	366
Male	169
MADRS [1] Mean (Standard Deviation) Units: units on a scale	13.5 (8.7)
	[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-24 [1] Mean (Standard Deviation) Units: units on a scale	13.4 (8.7)
	[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.

HAM-A [1] Mean (Standard Deviation) Units: units on a scale	11.0 (7.2)
	[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. The higher the score, the more severe.
CGI-S [1] Mean (Standard Deviation) Units: units on a scale	2.7 (1.2)
	[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	12.42 (8.13)
	[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:	Number of Patients With Adverse Events (AEs)
Description:	[Not specified]
Time Frame:	Baseline to end of the 4-week safety follow-up period
Safety Issue?	Yes

Outcome Measure Data 1 Note

Analysis Population Description
APTS

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Number of Participants Analyzed	535
Measure Type: Number Units: participants	
Patients With AEs	391
Patients With SAEs	18
Patients With AEs Leading to Withdrawal	42

2. Primary Outcome

Title:	Percentage of Patients Who Withdrew Due to Intolerance to Treatment
Description:	[Not specified]
Time Frame:	Baseline to Week 52
Safety Issue?	Yes

Outcome Measure Data 1 Note

Analysis Population Description
APTS

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Number of Participants Analyzed	535

Measure Type: Number Units: percentage of patients	7.7

3. Secondary Outcome

Title:	Change From Baseline in MADRS Total Score After 52 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 52
Safety Issue?	No

Outcome Measure Data 1 Note

Analysis Population Description
FAS; observed cases (OC)

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the

	Arm/Group Title.
Number of Participants Analyzed	329
Mean (Standard Deviation) Units: units on a scale	-7.35 (8.21)

4. Secondary Outcome

Title:	Change From Baseline in HAM-D-24 Total Score After 52 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 52
Safety Issue?	No

Outcome Measure Data 1 Note

Analysis Population Description
FAS; OC

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Number of Participants Analyzed	342
Mean (Standard Deviation) Units: units on a scale	-6.86 (8.45)

5. Secondary Outcome

Title:	Change From Baseline in HAM-A Total Score After 52 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 52
Safety Issue?	No

Outcome Measure Data 1 Note

Analysis Population Description
FAS; OC

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Number of Participants Analyzed	342
Mean (Standard Deviation) Units: units on a scale	-5.44 (7.08)

6. Secondary Outcome

Title:	Change From Baseline in CGI-S Score After 52 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 52
Safety Issue?	No

Outcome Measure Data 1 Note

Analysis Population Description
FAS; OC

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Number of Participants Analyzed	342
Mean (Standard Deviation) Units: units on a scale	-1.00 (1.22)

7. Secondary Outcome

Title:	Proportion of Responders at Week 52 (Response Defined as a >=50% Decrease in MADRS Total Score)
Description:	[Not specified]
Time Frame:	Week 52
Safety Issue?	No

Outcome Measure Data 1 Note

Analysis Population Description
FAS; OC; Baseline from lead-in study NCT00635219 / 11984A

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Number of Participants	329

Analyzed	
Mean (Standard Deviation) Units: percentage of patients	94.2 (23.4)

8. Secondary Outcome

Title:	Proportion of Remitters at Week 52 (Remission Defined as a MADRS Total Score <=10)
Description:	[Not specified]
Time Frame:	Week 52
Safety Issue?	No

Outcome Measure Data 1 Note

Analysis Population Description
FAS; OC; Baseline from lead-in study NCT00635219 / 11984A

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Number of Participants Analyzed	329
Mean (Standard Deviation) Units: percentage of patients	83.0 (37.6)

9. Secondary Outcome

Title:	Proportion of Patients With a MADRS Total Score >=22 After 52 Weeks of Treatment
Description:	[Not specified]
Time Frame:	Baseline and Week 52
Safety Issue?	No

Outcome Measure Data 1 Note

Analysis Population Description
FAS; OC

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the Arm/Group Title.
Number of Participants Analyzed	329
Measure Type: Number Units: percentage of patients	2.74

10. Secondary Outcome

Title:	Change From Baseline in SDS Total Score After 52 Weeks of Treatment
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:	Baseline and Week 52
Safety Issue?	No

Outcome Measure Data 1 Note

Analysis Population Description
FAS; OC

Arm/Group Title	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description:	tablets; orally NOTE : An Arm/Group Description is shorter than the

	Arm/Group Title.
Number of Participants Analyzed	285
Mean (Standard Deviation) Units: units on a scale	-5.60 (6.91)

Adverse Events

Time Frame	Serious Adverse Events: 52-week open label period and 4-week safety follow-up period Other Adverse Events: 52-week open label 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	Vortioxetine 2.5, 5, or 10 mg/Day
Arm/Group Description	[Not specified] NOTE : An entry in Arm/Group Description

	is recommended.

Serious Adverse Events

		Vortioxetine 2.5, 5, or 10 mg/Day
		Affected / at Risk (%)
Total		18/535 (3.36%)
General disorders		
Chest pain	A	1/535 (0.19%)
Infections and infestations		
Appendicitis	A	1/535 (0.19%)
Pneumonia	A	1/535 (0.19%)
Injury, poisoning and procedural complications		
Intentional overdose	A	1/535 (0.19%)
Road traffic accident	A	1/535 (0.19%)
Musculoskeletal and connective tissue disorders		
Back pain	A	1/535 (0.19%)
Muscle spasms	A	1/535 (0.19%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Benign salivary gland neoplasm	A	1/535 (0.19%)
Psychiatric disorders		
Adjustment disorder with mixed anxiety and depressed mood	A	1/535 (0.19%)
Depression	A	3/535 (0.56%)
Suicidal ideation	A	3/535 (0.56%)
Suicide attempt	A	1/535 (0.19%)
Renal and urinary disorders		
Nephrolithiasis	A	1/535 (0.19%)
Reproductive system and breast disorders		
Menorrhagia	A	1/366 (0.27%)
Skin and subcutaneous tissue disorders		
Dermatitis herpetiformis	A	1/535 (0.19%)

Indicates events were collected by non-systematic methods.

A Term from vocabulary, 12.1

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%
	Vortioxetine 2.5, 5, or 10 mg/Day
	Affected / at Risk (%)

Total		256/535 (47.85%)
Gastrointestinal disorders		
Nausea	A	106/535 (19.81%)
Infections and infestations		
Influenza	A	27/535 (5.05%)
Nasopharyngitis	A	56/535 (10.47%)
Injury, poisoning and procedural complications		
Accidental overdose	A	29/535 (5.42%)
Investigations		
Weight increased	A	31/535 (5.79%)
Nervous system disorders		
Dizziness	A	34/535 (6.36%)
Headache	A	82/535 (15.33%)
Psychiatric disorders		
Insomnia	A	38/535 (7.1%)

Indicates events were collected by non-systematic methods.

A Term from vocabulary, 12.1

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.

Results Point of Contact

Name/Official Title:	H. Lundbeck A/S
Organization:	H. Lundbeck A/S
Phone:	+45 3630 1311
Email:	LundbeckClinicalTrials@lundbeck.com

Close

U.S. National Library of Medicine | U.S. National Institutes of Health | U.S. Department of Health & Human Services