ClinicalTrials.gov PRS
Protocol Registration and Results System

ID: 11984A Randomised Placebo-controlled Duloxetine-referenced Efficacy and Safety Study of 2.5, 5 and 10 mg of Vortioxetine (Lu AA21004) in Acute Treatment of Major Depressive Disorder NCT00635219

Protocol Registration and Results Preview

Close

Randomised Placebo-controlled Duloxetine-referenced Efficacy and Safety Study of 2.5, 5 and 10 mg of Vortioxetine (Lu AA21004) in Acute Treatment of Major Depressive Disorder

This study has been completed.

Sponsor:	H. Lundbeck A/S
Collaborators:	
Information provided by (Responsible Party):	H. Lundbeck A/S
ClinicalTrials.gov Identifier:	NCT00635219

Purpose

The purpose of the study is to evaluate the efficacy and the tolerability of three fixed doses of Vortioxetine in order to establish the appropriate clinical effective dose range in the treatment of Major Depressive Disorder (MDD).

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: A Randomised, Double-blind, Parallel-group, Placebo-controlled, Duloxetine-referenced, Fixed-dose Study Evaluating the Efficacy and Safety of Three Dosages of [Vortioxetine] Lu AA21004, in Acute Treatment of Major Depressive Disorder

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

Primary Outcome Measure:

- 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.

Secondary Outcome Measures:

- 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.

- Proportion of Responders at Week 8 (Response Defined as a >=50% Decrease in the MADRS Total Score From Baseline) [Time Frame: Week 8] [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.

- Change From Baseline in HAM-D-24 Total Score After 8 Weeks of Treatment in Patients With Baseline HAM-A Total Score >=20 [Time Frame: Baseline and Week 8] [Designated as safety issue: No]

- Change From Baseline in SDS Total Score After 8 Weeks of Treatment [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.

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

- 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 From Baseline in ASEX Total Score After 8 Weeks of Treatment [Time Frame: Baseline and Week 8] [Designated as safety issue: Yes]
  The Arizona Sexual Experience Scale (ASEX) is a 5-item, patient self-rated scale that evaluates a patient's recent sexual experience. Patients are asked to assess their own experience over the last week (for example, "How strong is your sex drive?", "Are your orgasms satisfying?") and respond on a 6-point scale for each item. The ASEX is used to identify individuals with sexual dysfunction. Possible total score ranges from 5 to 30, with the higher score indicating more patient sexual dysfunction. A negative change indicates a lower sexual dysfunction.

Enrollment: 766
Study Start Date: February 2008
Study Completion Date: April 2009
Primary Completion Date: April 2009

Arms	Assigned Interventions
Placebo Comparator: Placebo	Drug: Placebo capsules; daily; orally
Experimental: Vortioxetine: 2.5 mg	Drug: Vortioxetine (Lu AA21004) 2.5 mg/day; encapsulated tablets; orally Other Names: • Brintellix
Experimental: Vortioxetine: 5 mg	Drug: Vortioxetine (Lu AA21004) 5 mg/day; encapsulated tablets; orally Other Names: • Brintellix
Experimental: Vortioxetine: 10 mg	Drug: Vortioxetine (Lu AA21004) 10 mg/day; encapsulated tablets; orally Other Names: • Brintellix
Duloxetine: 60 mg	Drug: Duloxetine

Active reference	60 mg/day; encapsulated capsules; orally Other Names: • Cymbalta®

Eligibility

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

- MDE as primary diagnosis according to DSM-IV-TR criteria (classification code 296.xx)
- Moderate to severe depression
- Current MDE duration of at least 3 months

Exclusion Criteria:

- Any current psychiatric disorder other than 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

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, Loft H, Dragheim M. A randomised, double-blind, placebo controlled, duloxetine-referenced, fixed-dose study of three dosages of Lu AA21004 in acute treatment of major depressive disorder (MDD). Eur Neuropsychopharmacol. 2012 Jul;22(7):482-91. doi: 10.1016/j.euroneuro.2011.11.008. Epub 2011 Dec 30.

Responsible Party: H. Lundbeck A/S
Study ID Numbers: 11984A
EudraCT 2007-001870-95 [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
Luxembourg: Ministère de la Santé
Malaysia: Ministry of Health
Philippines: Bureau of Food and Drugs
Romania: National Medicines Agency
Slovakia: State Institute for Drug Control
South Korea: Korea Food and Drug Administration (KFDA)
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	The patients were recruited from psychiatric settings.
Pre-Assignment Details	The study consisted of a Screening Period; an 8-week Core Treatment Period; a 1-week double-blind downtaper period (Week 9); and a 4-week Safety Follow-up Period - the 4-week period after completion/withdrawal (Weeks 9 to 12).

Arm/Group Title	Placebo	Vortioxetine 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg	Total (Not public)
▼ Arm/Group Description	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally	
Period Title: **Overall Study**						
Started	148	155	157	151	155	766
Completed	123	130	122	117	113	605
Not Completed	25	25	35	34	42	161
Reason Not Completed						
Adverse Event	12	10	18	15	19	74
Lack of Efficacy	5	6	3	4	6	24
Non-compliance With Study Product	0	0	0	2	1	3
Protocol Violation	0	2	3	2	4	11
Withdrawal of Consent	8	6	8	11	8	41
Lost to Follow-up	0	0	2	0	3	5
Administrative or Other Reasons	0	1	1	0	1	3
(Not Public)	Not Completed = 25 Total from all reasons = 25	Not Completed = 25 Total from all reasons = 25	Not Completed = 35 Total from all reasons = 35	Not Completed = 34 Total from all reasons = 34	Not Completed = 42 Total from all reasons = 42	

Baseline Characteristics

Arm/Group Title	Placebo	Vortioxetine 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg	Total
▼ Arm/Group Description	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally	
Overall Number of Baseline Participants	148	155	157	151	155	**766**
▼ Baseline Analysis Population Description	Full-analysis set (FAS) - all patients in the all-patients-treated set (APTS) who had at least one valid postbaseline assessment of the primary efficacy variable					
Age, Continuous Mean (Standard Deviation) Units: years	43.4 (12.5)	46.0 (12.5)	44.7 (13.1)	45.2 (13.1)	45.3 (12.0)	44.9 (12.7)
Gender, Male/Female Measure Type: Number Units: participants						
Female	103	110	104	100	105	522
Male	45	45	53	51	50	244

MADRS [1] Mean (Standard Deviation) Units: units on a scale	31.7 (4.3)	31.6 (4.0)	32.7 (4.8)	31.8 (3.9)	31.4 (4.2)	31.9 (4.3)
	[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-D-24 [1] Mean (Standard Deviation) Units: units on a scale	29.8 (5.1)	29.6 (5.8)	31.3 (5.8)	30.4 (5.4)	29.9 (5.8)	30.2 (5.6)
	[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.					
CGI-S [1] Mean (Standard Deviation) Units: units on a scale	4.8 (0.7)	4.8 (0.7)	4.8 (0.7)	4.7 (0.7)	4.7 (0.7)	4.8 (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.					
SDS [1] Mean (Standard Deviation) Units: units on a scale	19.9 (5.8)	19.4 (6.5)	19.6 (6.2)	19.6 (6.5)	19.2 (5.9)	19.6 (6.2)
	[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.					
HAM-A [1] Mean (Standard Deviation) Units: units on a scale	23.1 (5.6)	22.2 (6.7)	23.5 (6.2)	23.4 (6.3)	22.8 (6.4)	23.0 (6.3)
	[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.					

Outcome Measures

1. Primary 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

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 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg

Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally
Number of Participants Analyzed	145	155	155	151	149
Mean (Standard Error) Units: units on a scale	-14.8 (0.82)	-16.2 (0.79)	-16.5 (0.80)	-16.3 (0.80)	-16.8 (0.81)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	As soon as an endpoint was non-significant at the 0.025 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	0.1321
	Comments	Since p-value >0.025, hierarchically testing stopped here.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.70
	Confidence Interval	(2-Sided) 95% -3.92 to 0.51
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.13
	Estimation Comments	To adjust for multiplicity the two doses of vortioxetine were tested separately versus placebo in

		the primary and key secondary efficacy analyses at a Bonferroni-corrected significance level of 0.025.

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 10 mg
	Comments	As soon as an endpoint was non-significant at the 0.025 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	0.1847
	Comments	Since p-value >0.025, hierarchically testing stopped here.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.50
	Confidence Interval	(2-Sided) 95% -3.73 to 0.72
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.13
	Estimation Comments	To adjust for multiplicity the two doses of vortioxetine were tested separately versus placebo in the primary and key secondary efficacy analyses at a Bonferroni-corrected significance level of 0.025.

▼ Statistical Analysis 3 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2187
	Comments	This dose 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	-1.38

	Confidence Interval	(2-Sided) 95% -3.59 to 0.82
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.12
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4 ✓

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	0.0741
	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	-2.04
	Confidence Interval	(2-Sided) 95% -4.27 to 0.20
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.14
	Estimation Comments	[Not specified]

2. Secondary 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

FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally

Number of Participants Analyzed	145	155	155	151	149
Mean (Standard Error) Units: units on a scale	-13.3 (0.82)	-14.4 (0.79)	-15.0 (0.80)	-14.9 (0.80)	-15.7 (0.81)

▼ 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	0.1120
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.79
	Confidence Interval	(2-Sided) 95% -4.01 to 0.42
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.13
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 2 ✔

Statistical	Comparison Groups	Placebo, Vortioxetine 10 mg

Analysis Overview	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1487
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.63
	Confidence Interval	(2-Sided) 95% -3.85 to 0.59
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.13
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3246
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.11
	Confidence Interval	(2-Sided) 95% -3.31 to 1.10
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.12
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 4 ✓

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	0.0298
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.47
	Confidence Interval	(2-Sided) 95% -4.70 to -0.24
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.13
	Estimation Comments	No correction for multiplicity was made.

3. Secondary Outcome

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

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; LOCF; Logistic Regression

Arm/Group Title	Placebo	Vortioxetine 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally
Number of Participants Analyzed	145	155	155	151	149
Measure Type: Number Units: percentage of patients	46.9	54.2	56.1	57.6	57.1

▼ Statistical Analysis 1 ✓

Statistical Analysis	Comparison Groups	Placebo, Vortioxetine 5 mg
	Comments	[Not specified]

Overview		
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1370
	Comments	A nominal p-value is provided.
	Method	Other [Adjusting for Baseline]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.41
	Confidence Interval	(2-Sided) 95% 0.90 to 2.23
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0664
	Comments	A nominal p-value is provided.
	Method	Other [Adjusting for Baseline]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.54
	Confidence Interval	(2-Sided) 95% 0.97 to 2.43
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2023
	Comments	A nominal p-value is provided.
	Method	Other [Adjusting for Baseline]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.34
	Confidence Interval	(2-Sided) 95% 0.85 to 2.12
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 4 ✔

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	0.0765
	Comments	A nominal p-value is provided.
	Method	Other [Adjusting for Baseline]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.52
	Confidence Interval	(2-Sided) 95% 0.96 to 2.40
	Estimation Comments	No correction for multiplicity was made.

4. 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 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally
Number of Participants Analyzed	145	155	154	151	149
Mean (Standard Error) Units: units on a scale	2.52 (0.10)	2.32 (0.10)	2.32 (0.10)	2.35 (0.10)	2.31 (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	0.1436
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.20
	Confidence Interval	(2-Sided) 95% -0.47 to 0.07
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.14
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2114
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.17
	Confidence Interval	(2-Sided) 95% -0.44 to 0.10
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.14
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1389
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.20
	Confidence Interval	(2-Sided) 95% -0.47 to 0.07
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.14
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 4 ✓

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	0.1271
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.21
	Confidence Interval	(2-Sided) 95% -0.48 to 0.06
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.14
	Estimation Comments	No correction for multiplicity was made.

5. Secondary Outcome

Title:	Change From Baseline in HAM-D-24 Total Score After 8 Weeks of Treatment in Patients With Baseline HAM-A Total Score >=20
▼ Description:	[Not specified]
Time Frame:	Baseline and Week 8
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

Patients With Baseline HAM-A Total Score >=20: FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally
Number of Participants Analyzed	97	91	100	101	92
Mean (Standard Error) Units: units on a scale	-14.7 (1.10)	-14.3 (1.15)	-15.8 (1.09)	-15.8 (1.07)	-17.3 (1.14)

▼ Statistical Analysis 1 ✓

Statistical	Comparison Groups	Placebo, Vortioxetine 5 mg

Analysis Overview	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4421
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.15
	Confidence Interval	(2-Sided) 95% -4.08 to 1.79
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.49
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4399
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.15
	Confidence Interval	(2-Sided) 95% -4.07 to 1.77
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.49
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 3 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8093
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.37
	Confidence Interval	(2-Sided) 95% -2.65 to 3.40
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.54
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 4 ✔

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	0.0897
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.60
	Confidence Interval	(2-Sided) 95% -5.61 to 0.41
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.53
	Estimation Comments	No correction for multiplicity was made.

6. Secondary Outcome

Title:	Change From Baseline in SDS Total Score After 8 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 8
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

SDS is a patient-reported outcome. The SDS Total Score is the sum of work, social life, or leisure activities, and home life or family responsibilities. FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg
Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally
Number of Participants Analyzed	116	115	119	115	108
Mean (Standard Error) Units: units on a scale	-6.11 (0.72)	-7.10 (0.74)	-6.52 (0.73)	-7.81 (0.74)	-7.91 (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	0.6748
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.41
	Confidence Interval	(2-Sided) 95% -2.35 to 1.52
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.98
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0871
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.70
	Confidence Interval	(2-Sided) 95% -3.64 to 0.25
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.99
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 3 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3186
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.99
	Confidence Interval	(2-Sided) 95% -2.94 to 0.96
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.99

	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 4 ✓

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	0.0768
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.80
	Confidence Interval	(2-Sided) 95% -3.79 to 0.19
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.01
	Estimation Comments	No correction for multiplicity was made.

7. 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; Logistic Regression

Arm/Group Title	Placebo	Vortioxetine 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally
Number of Participants Analyzed	145	155	155	151	149
Measure Type: Number Units: percentage of patients	33.8	32.9	36.1	35.8	34.9

▼ 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	0.6258
	Comments	A nominal p-value is provided.
	Method	Other [Adjusting for Baseline]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.13
	Confidence Interval	(2-Sided) 95% 0.70 to 1.81
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7178
	Comments	A nominal p-value is provided.
	Method	Other [Adjusting for Baseline]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.09
	Confidence Interval	(2-Sided) 95% 0.68 to 1.76
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8651
	Comments	A nominal p-value is provided.
	Method	Other [Adjusting for Baseline]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	0.96
	Confidence Interval	(2-Sided) 95% 0.59 to 1.55
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 4 ✓

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	0.8563
	Comments	A nominal p-value is provided.
	Method	Other [Adjusting for Baseline]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.05
	Confidence Interval	(2-Sided) 95% 0.65 to 1.69
	Estimation Comments	No correction for multiplicity was made.

8. 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 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally
Number of Participants Analyzed	145	154	155	151	148
Mean (Standard Error) Units: units on a scale	-9.57 (0.63)	-9.87 (0.61)	-10.7 (0.61)	-10.6 (0.62)	-11.0 (0.62)

▼ 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	0.1925
	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% -2.82 to 0.57
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.86
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2434
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.01
	Confidence Interval	(2-Sided) 95% -2.72 to 0.69
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.87
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7246
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.30
	Confidence Interval	(2-Sided) 95% -2.00 to 1.39
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.86
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 4 ✓

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	0.0981
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.45
	Confidence Interval	(2-Sided) 95% -3.16 to 0.27
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.87
	Estimation Comments	No correction for multiplicity was made.

9. 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 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally
Number of Participants Analyzed	145	155	154	151	149
Mean (Standard Error) Units: units on a scale	-1.64 (0.11)	-1.83 (0.10)	-1.81 (0.10)	-1.83 (0.10)	-1.82 (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	0.2285
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.17
	Confidence Interval	(2-Sided) 95% -0.46 to 0.11
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.14
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1794
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.20
	Confidence Interval	(2-Sided) 95% -0.48 to 0.09
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.15
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 3 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1741
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.20
	Confidence Interval	(2-Sided) 95% -0.48 to 0.09
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.14
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 4 ✔

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	0.2247
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.18
	Confidence Interval	(2-Sided) 95% -0.46 to 0.11
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.15

	Estimation Comments	No correction for multiplicity was made.

10. Secondary Outcome

Title:	Change From Baseline in ASEX Total Score After 8 Weeks of Treatment
▼ Description:	The Arizona Sexual Experience Scale (ASEX) is a 5-item, patient self-rated scale that evaluates a patient's recent sexual experience. Patients are asked to assess their own experience over the last week (for example, "How strong is your sex drive?", "Are your orgasms satisfying?") and respond on a 6-point scale for each item. The ASEX is used to identify individuals with sexual dysfunction. Possible total score ranges from 5 to 30, with the higher score indicating more patient sexual dysfunction. A negative change indicates a lower sexual dysfunction.
Time Frame:	Baseline and Week 8
Safety Issue?	Yes

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS; LOCF; ANCOVA

Arm/Group Title	Placebo	Vortioxetine 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 mg	Duloxetine 60 mg
▼ Arm/Group Description:	capsules; daily; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated tablets; orally	encapsulated capsules; orally
Number of Participants Analyzed	74	77	76	75	72
Mean (Standard Error) Units: units on a scale	-0.41 (0.65)	-0.53 (0.62)	-0.66 (0.64)	-0.62 (0.62)	-0.38 (0.64)

▼ 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	0.7789
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.24
	Confidence Interval	(2-Sided) 95% -1.93 to 1.45
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.86

	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 10 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8121
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.21
	Confidence Interval	(2-Sided) 95% -1.91 to 1.50
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.87
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Vortioxetine 2.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8918
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.12
	Confidence Interval	(2-Sided) 95% -1.82 to 1.59
	Parameter Dispersion	Type: Standard Error of the mean

		Value: 0.87
	Estimation Comments	No correction for multiplicity was made.

▼ Statistical Analysis 4 ✓

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	0.9720
	Comments	A nominal p-value is provided.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.03
	Confidence Interval	(2-Sided) 95% -1.69 to 1.75
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.87
	Estimation Comments	No correction for multiplicity was made.

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 2.5 mg	Vortioxetine 5 mg	Vortioxetine 10 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.	[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 2.5 mg**	**Vortioxetine 5 mg**	**Vortioxetine 10 mg**	**Duloxetine 60 mg**
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)

Total	3/148 (2.03%)	1/155 (0.65%)	3/157 (1.91%)	2/151 (1.32%)	2/155 (1.29%)
Ear and labyrinth disorders					
Middle ear effusion [A]	0/148 (0%)	0/155 (0%)	0/157 (0%)	0/151 (0%)	1/155 (0.65%)
Hepatobiliary disorders					
Jaundice cholestatic [A]	0/148 (0%)	0/155 (0%)	1/157 (0.64%)	0/151 (0%)	0/155 (0%)
Injury, poisoning and procedural complications					
Pelvic fracture [A]	0/148 (0%)	0/155 (0%)	0/157 (0%)	1/151 (0.66%)	0/155 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Gallbladder cancer [A]	0/148 (0%)	0/155 (0%)	1/157 (0.64%)	0/151 (0%)	0/155 (0%)
Nervous system disorders					
Serotonin syndrome [A]	1/148 (0.68%)	0/155 (0%)	0/157 (0%)	0/151 (0%)	1/155 (0.65%)
Psychiatric disorders					
Depression [A]	0/148 (0%)	0/155 (0%)	1/157 (0.64%)	1/151 (0.66%)	0/155 (0%)
Suicidal ideation [A]	0/148 (0%)	1/155 (0.65%)	0/157 (0%)	0/151 (0%)	0/155 (0%)
Suicide attempt [A]	0/148 (0%)	0/155 (0%)	1/157 (0.64%)	0/151 (0%)	0/155 (0%)
Reproductive system and breast disorders					
Adenomyosis [A]	1/103 (0.97%)	0/110 (0%)	0/104 (0%)	0/100 (0%)	0/105 (0%)
Respiratory, thoracic and mediastinal disorders					
Pulmonary embolism [A]	1/148 (0.68%)	0/155 (0%)	0/157 (0%)	0/151 (0%)	0/155 (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 2.5 mg**	**Vortioxetine 5 mg**	**Vortioxetine 10 mg**	**Duloxetine 60 mg**
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	64/148 (43.24%)	61/155 (39.35%)	63/157 (40.13%)	62/151 (41.06%)	93/155 (60%)
Gastrointestinal disorders					
Constipation [A]	6/148 (4.05%)	3/155 (1.94%)	5/157 (3.18%)	3/151 (1.99%)	10/155 (6.45%)
Diarrhoea [A]	10/148 (6.76%)	7/155 (4.52%)	3/157 (1.91%)	8/151 (5.3%)	7/155 (4.52%)
Dry mouth [A]	11/148 (7.43%)	6/155 (3.87%)	9/157 (5.73%)	6/151 (3.97%)	12/155 (7.74%)
Nausea [A]	13/148 (8.78%)	26/155 (16.77%)	26/157 (16.56%)	33/151 (21.85%)	52/155 (33.55%)
Vomiting [A]	5/148 (3.38%)	6/155 (3.87%)	6/157 (3.82%)	7/151 (4.64%)	11/155 (7.1%)
General disorders					
Fatigue [A]	3/148 (2.03%)	1/155 (0.65%)	3/157 (1.91%)	3/151 (1.99%)	8/155 (5.16%)
Infections and infestations					
Nasopharyngitis [A]	6/148 (4.05%)	12/155 (7.74%)	11/157 (7.01%)	4/151 (2.65%)	3/155 (1.94%)
Metabolism and nutrition disorders					
Decreased appetite [A]	2/148 (1.35%)	0/155 (0%)	2/157 (1.27%)	1/151 (0.66%)	12/155 (7.74%)

Nervous system disorders						
Dizziness	A	10/148 (6.76%)	7/155 (4.52%)	5/157 (3.18%)	6/151 (3.97%)	25/155 (16.13%)
Headache	A	24/148 (16.22%)	22/155 (14.19%)	16/157 (10.19%)	19/151 (12.58%)	22/155 (14.19%)
Somnolence	A	5/148 (3.38%)	5/155 (3.23%)	4/157 (2.55%)	5/151 (3.31%)	11/155 (7.1%)
Psychiatric disorders						
Insomnia	A	6/148 (4.05%)	8/155 (5.16%)	11/157 (7.01%)	3/151 (1.99%)	13/155 (8.39%)
Skin and subcutaneous tissue disorders						
Hyperhidrosis	A	1/148 (0.68%)	1/155 (0.65%)	4/157 (2.55%)	3/151 (1.99%)	10/155 (6.45%)

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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