Clinical trial results:
Interventional, randomized, double-blind, placebo-controlled study of the efficacy and safety of initial administration of 25 mg vortioxetine intravenously with 10 mg/day vortioxetine orally in patients with Major Depressive Disorder

Summary

EudraCT number	2018-000992-34
Trial protocol	LV EE BG
Global end of trial date	28 August 2019

Results information

Result version number	v1 (current)
This version publication date	31 July 2020
First version publication date	31 July 2020

Trial information

Trial identification

Sponsor protocol code	17915A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03766867
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	Lundbeck Clinical Trials, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com
Scientific contact	Lundbeck Clinical Trials, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2019
Global end of trial reached?	Yes
Global end of trial date	28 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and safety of vortioxetine given as a single intravenous dose of 25 mg at initiation of an oral vortioxetine regimen of 10 mg/day for 7 days

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and ICH Good Clinical Practice (1996).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 44
Country: Number of subjects enrolled	Estonia: 25
Country: Number of subjects enrolled	Latvia: 12
Worldwide total number of subjects	81
EEA total number of subjects	81

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	79
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who met each of the inclusion and none of the exclusion criteria were eligible to participate in the study.

Period 1

Period 1 title	Placebo Lead-in
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Arm title	Placebo

Arm description:

one day single-blind treatment with placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

film-coated tablet, oral administration. one day single-blind treatment with placebo

Investigational medicinal product name	Placebo infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

concentrate for solution for infusion, 25 mL administered in 250 mL saline over 2 hours as single dose

Number of subjects in period 1	Placebo
Started	81
Completed	81

Period 2

Period 2 title	Double-blind Period (DBT)
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Vortioxetine

Arm description:

Double-blind Treatment (DBT) Period with vortioxetine

Arm type	Experimental
Investigational medicinal product name	Vortioxetine infusion 25 mg
Investigational medicinal product code	Lu AA21004
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vortioxetine – 25mg, IV infusion of 25mL 1mg/mL concentrate for solution for infusion on Day 0

Investigational medicinal product name	Vortioxetine tablets 10 mg/day
Investigational medicinal product code	Lu AA21004
Other name	Brintellix ®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg, tablets, oral administration once daily. 7 tablets for a duration of 7 days

Arm title	Placebo

Arm description:

Double-blind Treatment (DBT) Period with placebo

Arm type	Placebo
Investigational medicinal product name	Placebo tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

film-coated tablets, oral administration once daily. 7 tablets for a duration of 7 days

Investigational medicinal product name	Placebo infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

concentrate for solution for infusion, 25 mL administered in 250 mL saline over 2 hours as single dose

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 is the lead-in period of the study

Number of subjects in period 2[2][3]	Vortioxetine	Placebo
Started	39	41
Completed	38	40
Not completed	1	1
Consent withdrawn by subject	1	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: It is correct that not all the patients that enrolled the study started the double bind treatment period which explains that the numbers are not the same.

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: It is correct that the number of subjects starting the DBT period is not consistent with the number completing the preceding lead-in period: not all the patients that enrolled the study started the double bind treatment period which explains that the numbers are not the same.

Baseline characteristics

Reporting groups	
Reporting group title	Vortioxetine
Reporting group description: Double-blind Treatment (DBT) Period with vortioxetine	
Reporting group title	Placebo
Reporting group description: Double-blind Treatment (DBT) Period with placebo	

Reporting group values	Vortioxetine	Placebo	Total
Number of subjects	39	41	80
Age categorical Units: Subjects			
Adults (18-64 years)			0
From 65-84 years			0
Age continuous Units: years			
arithmetic mean	47.26	46.85	
standard deviation	± 11.03	± 13.65	-
Gender categorical Units: Subjects			
Female	28	30	58
Male	11	11	22
MADRS-6 subscale score Units: units on a scale			
arithmetic mean	23.41	22.85	
standard deviation	± 2.31	± 2.20	-
MADRS Total score Units: units on a scale			
arithmetic mean	35.59	34.66	
standard deviation	± 3.43	± 2.73	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: one day single-blind treatment with placebo	
Reporting group title	Vortioxetine
Reporting group description: Double-blind Treatment (DBT) Period with vortioxetine	
Reporting group title	Placebo
Reporting group description: Double-blind Treatment (DBT) Period with placebo	

Primary: Change from Baseline (Day 0) to Day 1 (24hours post-infusion) in Montgomery and Åsberg Depression Rating Scale (MADRS)-6 subscale score

End point title	Change from Baseline (Day 0) to Day 1 (24hours post-infusion) in Montgomery and Åsberg Depression Rating Scale (MADRS)-6 subscale score

End point description:

The Montgomery and Åsberg Depression Rating Scale (MADRS) is a ten-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at two-point intervals. This endpoint will be evaluated with MADRS-6 subscale score, calculated based on the scores on MADRS items 1, 2, 3, 7, 8, and 9 which cover core symptoms (apparent sadness, reported sadness, inner tension, lassitude, inability to feel, and pessimistic thoughts) and is more sensitive to the effect of treatment.

End point type	Primary

End point timeframe:

From baseline (Day 0) to Day 1 (24 h post-infusion)

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: units on a scale				
least squares mean (standard error)	-3.55 (± 0.58)	-2.76 (± 0.60)		

Statistical analyses

Statistical analysis title	Ratio vortioxetine vs placebo

Statistical analysis description:

The primary efficacy analysis was a mixed model for repeated measures (MMRM) of the change from Baseline to Day 1 in MADRS-6 subscore scale. The model included the following fixed effects: site, Day (1,3, and 7), and treatment; the Baseline MADRS-6 subscale score as a continuous covariate; and the treatmentby-Day interaction; and the Baseline score-by-day interaction. The analysis was based on the missed at random (MAR) assumption including all available observations (observed cases [OC])

Comparison groups	Vortioxetine v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2675
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.19
upper limit	0.61

Secondary: Change from Baseline (Day 0) to Day 3 in MADRS-6 subscale

End point title	Change from Baseline (Day 0) to Day 3 in MADRS-6 subscale

End point description:

The Montgomery and Åsberg Depression Rating Scale (MADRS) is a ten-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at two-point intervals. This endpoint will be evaluated with MADRS-6 subscale score, calculated based on the scores on MADRS items 1, 2, 3, 7, 8, and 9 which cover core symptoms (apparent sadness, reported sadness, inner tension, lassitude, inability to feel, and pessimistic thoughts) and is more sensitive to the effect of treatment.

End point type	Secondary

End point timeframe:

From baseline (Day 0) to Day 3

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: Units on a scale				
least squares mean (standard error)	-5.29 (± 0.79)	-5.23 (± 0.79)		

Statistical analyses

Statistical analysis title	Ratio vortioxetine vs placebo (Day 3)

Statistical analysis description:

The key secondary efficacy analysis of the continuous variables (change from Baseline in MADRS-6 subscale score), was performed using the same methodology (FAS, MMRM) as for the primary efficacy variable.

Comparison groups	Placebo v Vortioxetine

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (net)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.08
upper limit	1.97

Secondary: Change from Baseline (Day 0) to Day 7 in MADRS-6 subscale score

End point title	Change from Baseline (Day 0) to Day 7 in MADRS-6 subscale score

End point description:

The Montgomery and Åsberg Depression Rating Scale (MADRS) is a ten-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at two-point intervals. This endpoint will be evaluated with MADRS-6 subscale score, calculated based on the scores on MADRS items 1, 2, 3, 7, 8, and 9 which cover core symptoms (apparent sadness, reported sadness, inner tension, lassitude, inability to feel, and pessimistic thoughts) and is more sensitive to the effect of treatment.

End point type	Secondary

End point timeframe:

From baseline to day 7

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	41		
Units: units on a scale				
least squares mean (standard error)	-6.51 (± 0.93)	-7.27 (± 0.93)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MADRS total score at Day 1

End point title	Change from Baseline in MADRS total score at Day 1

End point description:

The Montgomery and Åsberg Depression Rating Scale (MADRS) is a ten-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at two-point intervals. This endpoint will be evaluated with MADRS total score.

End point type	Secondary

End point timeframe:

From Baseline to Day 1

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: units on a scale				
least squares mean (standard error)	-4.81 (± 0.77)	-4.20 (± 0.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MADRS total score at Day 3

End point title	Change from Baseline in MADRS total score at Day 3

End point description:

The Montgomery and Åsberg Depression Rating Scale (MADRS) is a ten-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at two-point intervals. This endpoint will be evaluated with MADRS total score.

End point type	Secondary

End point timeframe:

From Baseline to Day 3

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: units on a scale				
least squares mean (standard error)	-7.47 (± 1.01)	-7.81 (± 1.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MADRS total score at Day 7

End point title	Change from Baseline in MADRS total score at Day 7

End point description:

The Montgomery and Åsberg Depression Rating Scale (MADRS) is a ten-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items

in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at two-point intervals. This endpoint will be evaluated with MADRS total score.

End point type	Secondary

End point timeframe:

Change from Baseline in MADRS total score at Day 7

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	41		
Units: units on a scale				
least squares mean (standard error)	-9.38 (± 1.26)	-10.63 (± 1.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Response (defined as a >= 50% decrease in MADRS total score from Baseline) on Day 1

End point title	Response (defined as a >= 50% decrease in MADRS total score from Baseline) on Day 1

End point description:

The Montgomery and Åsberg Depression Rating Scale (MADRS) is a ten-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at two-point intervals. This endpoint will be evaluated with MADRS total score.

End point type	Secondary

End point timeframe:

From baseline to Day 1

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: patients	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Response (defined as a >= 50% decrease in MADRS total score from Baseline) on Day 3

End point title	Response (defined as a >= 50% decrease in MADRS total score from Baseline) on Day 3

End point description:

The Montgomery and Åsberg Depression Rating Scale (MADRS) is a ten-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. Items in the scale assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts. Symptoms are rated on a 7-point scale from 0 (no symptom) to 6 (severe symptom). Definitions of severity are provided at two-point intervals. This endpoint will be evaluated with MADRS total score.

End point type	Secondary

End point timeframe:

From baseline to Day 3

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: patients	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression-Global Improvement (CGI-I) score relative to Baseline at Day 1

End point title	Clinical Global Impression-Global Improvement (CGI-I) score relative to Baseline at Day 1

End point description:

The Clinical Global Impression (CGI) provides an overall clinician-determined summary measure that takes into account all available information, including knowledge of the patient's history, psychosocial circumstances, symptoms, behavior, and the impact of the symptoms on the patient's ability to function. The CGI consists of two clinician-rated subscales: severity of illness (CGI-S) and global improvement (CGI-I). The CGI-I provides the clinician's impression of the patient's improvement (or worsening). The clinician assesses the patient's condition relative to a baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). In all cases, the assessment should be made independent of whether the rater believes the improvement is drug-related or not.

End point type	Secondary

End point timeframe:

From baseline to Day 1

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: units on a scale				
least squares mean (standard error)	3.34 (± 0.13)	3.39 (± 0.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression-Global Improvement (CGI-I) score relative to Baseline at Day 3

End point title	Clinical Global Impression-Global Improvement (CGI-I) score relative to Baseline at Day 3

End point description:

The Clinical Global Impression (CGI) provides an overall clinician-determined summary measure that takes into account all available information, including knowledge of the patient's history, psychosocial circumstances, symptoms, behavior, and the impact of the symptoms on the patient's ability to function. The CGI consists of two clinician-rated subscales: severity of illness (CGI-S) and global improvement (CGI-I). The CGI-I provides the clinician's impression of the patient's improvement (or worsening). The clinician assesses the patient's condition relative to a baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). In all cases, the assessment should be made independent of whether the rater believes the improvement is drug-related or not.

End point type	Secondary

End point timeframe:

From baseline to Day 3

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: units on a scale				
least squares mean (standard error)	3.08 (± 0.14)	3.12 (± 0.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression-Global Improvement (CGI-I) score relative to Baseline at Day 7

End point title	Clinical Global Impression-Global Improvement (CGI-I) score relative to Baseline at Day 7

End point description:

The Clinical Global Impression (CGI) provides an overall clinician-determined summary measure that takes into account all available information, including knowledge of the patient's history, psychosocial circumstances, symptoms, behavior, and the impact of the symptoms on the patient's ability to function. The CGI consists of two clinician-rated subscales: severity of illness (CGI-S) and global improvement (CGI-I). The CGI-I provides the clinician's impression of the patient's improvement (or worsening). The

clinician assesses the patient's condition relative to a baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). In all cases, the assessment should be made independent of whether the rater believes the improvement is drug-related or not.

End point type	Secondary

End point timeframe:

From baseline to Day 7

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	41		
Units: units on a scale				
least squares mean (standard error)	2.84 (± 0.16)	2.90 (± 0.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: CGI-I response (defined as CGI-I score <= 2) on Day 1

End point title	CGI-I response (defined as CGI-I score <= 2) on Day 1

End point description:

End point type	Secondary

End point timeframe:

From baseline to Day 1

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: patients	3	5		

Statistical analyses

No statistical analyses for this end point

Secondary: CGI-I response (defined as CGI-I score <= 2) on Day 3

End point title	CGI-I response (defined as CGI-I score <= 2) on Day 3

End point description:

End point type	Secondary

End point timeframe:

From baseline to Day 3

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: patients	6	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impression-Severity of Illness (CGI-S) score at Day 1

End point title	Change from Baseline in Clinical Global Impression-Severity of Illness (CGI-S) score at Day 1

End point description:

The Clinical Global Impression (CGI) provides an overall clinician-determined summary measure that takes into account all available information, including knowledge of the patient's history, psychosocial circumstances, symptoms, behavior, and the impact of the symptoms on the patient's ability to function. The CGI consists of two clinician-rated subscales: severity of illness (CGI-S) and global improvement (CGI-I). The CGI-S provides the clinician's impression of the patient's current state of mental illness. The clinician uses his or her clinical experience of this patient population to rate the severity of the patient's current mental illness on a 7-point scale ranging from 1 (Normal - not at all ill) to 7 (among the most extremely ill patients).

End point type	Secondary

End point timeframe:

From baseline to Day 1

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: units on a scale				
least squares mean (standard error)	-0.28 (± 0.09)	-0.33 (± 0.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impression-Severity of Illness (CGI-S) score at Day 3

End point title	Change from Baseline in Clinical Global Impression-Severity of Illness (CGI-S) score at Day 3

End point description:

The Clinical Global Impression (CGI) provides an overall clinician-determined summary measure that takes into account all available information, including knowledge of the patient's history, psychosocial

circumstances, symptoms, behavior, and the impact of the symptoms on the patient's ability to function. The CGI consists of two clinician-rated subscales: severity of illness (CGI-S) and global improvement (CGI-I). The CGI-S provides the clinician's impression of the patient's current state of mental illness. The clinician uses his or her clinical experience of this patient population to rate the severity of the patient's current mental illness on a 7-point scale ranging from 1 (Normal - not at all ill) to 7 (among the most extremely ill patients).

End point type	Secondary

End point timeframe:

From baseline to Day 3

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: units on a scale				
least squares mean (standard error)	-0.66 (± 0.12)	-0.67 (± 0.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impression-Severity of Illness (CGI-S) score at Day 7

End point title	Change from Baseline in Clinical Global Impression-Severity of Illness (CGI-S) score at Day 7

End point description:

The Clinical Global Impression (CGI) provides an overall clinician-determined summary measure that takes into account all available information, including knowledge of the patient's history, psychosocial circumstances, symptoms, behavior, and the impact of the symptoms on the patient's ability to function. The CGI consists of two clinician-rated subscales: severity of illness (CGI-S) and global improvement (CGI-I). The CGI-S provides the clinician's impression of the patient's current state of mental illness. The clinician uses his or her clinical experience of this patient population to rate the severity of the patient's current mental illness on a 7-point scale ranging from 1 (Normal - not at all ill) to 7 (among the most extremely ill patients).

End point type	Secondary

End point timeframe:

From baseline to Day 7

End point values	Vortioxetine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	41		
Units: units on a scale				
least squares mean (standard error)	-0.90 (± 0.15)	-1.01 (± 0.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cav Day 0 (bed time)

End point title	Cav Day 0 (bed time)[1]

End point description:

average plasma concentration during a steady-state day

End point type	Secondary

End point timeframe:

Day 0

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No data available

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: ng/mL				
arithmetic mean (standard deviation)	9.51 (± 2.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cav Day 0 (2hrs post-IV)

End point title	Cav Day 0 (2hrs post-IV)[2]

End point description:

Average plasma concentration during a steady-state day

End point type	Secondary

End point timeframe:

Day 0

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No data available

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: ng/mL				
arithmetic mean (standard deviation)	13.91 (± 13.43)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cav Day 1

End point title	Cav Day 1[3]

End point description:

average plasma concentration during a steady-state day

End point type	Secondary

End point timeframe:

Day 1

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No data available

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: ng/mL				
arithmetic mean (standard deviation)	9.93 (± 2.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cav Day 7

End point title	Cav Day 7[4]

End point description:

average plasma concentration during a steady-state day

End point type	Secondary

End point timeframe:

Day 7

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No data available

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: ng/mL				
arithmetic mean (standard deviation)	11.93 (± 5.95)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 35 days	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	DBT: Vortioxetine IV 25 mg + Vortioxetine Oral 10 mg
Reporting group description: -	
Reporting group title	DBT: Placebo IV + Placebo Oral
Reporting group description: -	

Serious adverse events	DBT: Vortioxetine IV 25 mg + Vortioxetine Oral 10 mg	DBT: Placebo IV + Placebo Oral	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 39 (0.00%)	1 / 41 (2.44%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Major depression			
subjects affected / exposed	0 / 39 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	DBT: Vortioxetine IV 25 mg + Vortioxetine Oral 10 mg	DBT: Placebo IV + Placebo Oral	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 39 (53.85%)	15 / 41 (36.59%)	
Investigations			
Blood pressure increased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			

Dizziness			
subjects affected / exposed	4 / 39 (10.26%)	3 / 41 (7.32%)	
occurrences (all)	5	3	
Headache			
subjects affected / exposed	2 / 39 (5.13%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Sedation			
subjects affected / exposed	1 / 39 (2.56%)	3 / 41 (7.32%)	
occurrences (all)	1	4	
Somnolence			
subjects affected / exposed	1 / 39 (2.56%)	4 / 41 (9.76%)	
occurrences (all)	1	4	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 39 (5.13%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Nausea			
subjects affected / exposed	5 / 39 (12.82%)	7 / 41 (17.07%)	
occurrences (all)	7	7	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	4 / 39 (10.26%)	0 / 41 (0.00%)	
occurrences (all)	4	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 39 (5.13%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Insomnia			
subjects affected / exposed	3 / 39 (7.69%)	1 / 41 (2.44%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported