

**Clinical trial results:****Interventional, Open-Label, Flexible-Dose Study of Vortioxetine on Emotional Functioning in Patients With Major Depressive Disorder With Inadequate Response to SSRI/SNRI Treatment****Summary**

EudraCT number	2017-004829-33
Trial protocol	FR ES LT IT
Global end of trial date	21 February 2020

Results information

Result version number	v1 (current)
This version publication date	07 March 2021
First version publication date	07 March 2021

Trial information**Trial identification**

Sponsor protocol code	17797A
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03835715
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Otillievej 9, Valby, Denmark, 2500
Public contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, 0045 36301311, LundbeckClinicalTrials@lundbeck.com
Scientific contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, 0045 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	21 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2020
Global end of trial reached?	Yes
Global end of trial date	21 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the effectiveness of 10-20 milligrams (mg) flexible-dose vortioxetine after 8 weeks of treatment on emotional functioning in participants with major depressive disorder (MDD) with inadequate response to selective serotonin reuptake inhibitor (SSRI)/serotonin-norepinephrine reuptake inhibitor (SNRI) treatment who were candidates for a switch and had a desire to change medication.

Protection of trial subjects:

This study was conducted in compliance with Good Clinical Practice and in accordance with the ethical principles described in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 2019
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	Spain: 68
Country: Number of subjects enrolled	France: 49
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Lithuania: 20
Worldwide total number of subjects	151
EEA total number of subjects	151

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)	147
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who met each of the inclusion and none of the exclusion criteria were eligible to participate in the study. A total of 151 participants were enrolled, out of which 150 participants were treated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Vortioxetine
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Arm description:

Participants received vortioxetine 10 mg tablet orally once daily. After the first week of treatment, the dose of vortioxetine could be adjusted (to 10 or 20 mg/day) up to Week 8. Participants were treated for 8 weeks.

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

Dosage and administration details:

Vortioxetine was administered per dose and schedule specified in the arm description.

Number of subjects in period 1^[1]	Vortioxetine
Started	150
Received at least 1 dose of study drug	150
Completed	131
Not completed	19
Consent withdrawn by subject	1
Adverse event, non-fatal	6
Other than specified	1
Lost to follow-up	6
Lack of efficacy	2
Protocol deviation	3

Notes:

[1] - 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: The number of participants reported in the baseline period are the participants who were enrolled and treated.

Baseline characteristics

Reporting groups

Reporting group title	Vortioxetine
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Reporting group description:

Participants received vortioxetine 10 mg tablet orally once daily. After the first week of treatment, the dose of vortioxetine could be adjusted (to 10 or 20 mg/day) up to Week 8. Participants were treated for 8 weeks.

Reporting group values	Vortioxetine	Total	
Number of subjects	150	150	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	47.1 ± 12.02	-	
Gender categorical Units: Subjects			
Female	105	105	
Male	45	45	

End points

End points reporting groups

Reporting group title	Vortioxetine
Reporting group description: Participants received vortioxetine 10 mg tablet orally once daily. After the first week of treatment, the dose of vortioxetine could be adjusted (to 10 or 20 mg/day) up to Week 8. Participants were treated for 8 weeks.	

Primary: Change From Baseline in Oxford Depression Questionnaire (ODQ) Total Score at Week 8

End point title	Change From Baseline in Oxford Depression Questionnaire (ODQ) Total Score at Week 8 ^[1]
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End point description:

ODQ: self-reported, 26-item questionnaire assessing 5 dimensions of emotional functioning (not caring[NC]; emotional detachment[ED]; positive reduction[PR]; general reduction[GR]; antidepressant as cause[AC]), comprised of 3 sections: Section 1(12 items) evaluated respondents' experiences during past week; Section 2(8 items) compared respondents' experiences during past week to the experience before their depression; Section 3(6 items) assessed participant's perception of a relationship between current antidepressant and emotional functioning. Each item rated on a 5-point likert scale:1 (disagree) to 5 (agree), summed into scores for each dimension and total score (range:26-130). Higher values=higher levels of emotional blunting. Full analysis set (FAS): all participants who received at least 1 dose of study drug, had a valid baseline assessment and at least 1 valid postbaseline assessment of ODQ total score. 'Number of participants analysed'=participants evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Baseline, Week 8

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis could not be presented for this single arm.

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: units on a scale				
arithmetic mean (standard error)	-29.84 (\pm 1.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Motivation and Energy Inventory (MEI) Total Score and Subscale Scores (Mental or Cognitive Energy, Social Motivation, and Physical Energy) at Week 8

End point title	Change From Baseline in Motivation and Energy Inventory (MEI) Total Score and Subscale Scores (Mental or Cognitive Energy, Social Motivation, and Physical Energy) at Week 8
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End point description:

The MEI is a 27-item, participant-rated scale initially developed and validated to evaluate interventions

to improve motivation and energy in participants with depression. The MEI is designed to assess 3 domains: mental or cognitive energy, social motivation, and physical energy. Respondents used scales ranging from 0 (indicating that the behaviour was never present) to 5 or 6 (a behaviour or feeling that was present very frequently or all of the time). All items used either a 5- or 7-point likert scale. Total score = sum of each item score (range: 0-144). Items 3-11, 13-15, 17, and 18 were reverse-scored to ensure that higher scores indicate greater levels of motivation and energy. FAS: all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score. Number of participants analysed' = participants evaluable for this endpoint. 'n' = participants evaluable for specified categories.

End point type	Secondary
End point timeframe:	
Baseline, Week 8	

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: units on a scale				
arithmetic mean (standard error)				
Total Score (n = 130)	34.28 (± 2.75)			
Mental or Cognitive Energy Score (n = 130)	14.98 (± 1.23)			
Social Motivation Score (n = 131)	9.55 (± 0.92)			
Physical Energy Score (n = 131)	10.30 (± 0.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ODQ Domain Scores (NC, ED, PR, GR, AC, PR-NC, and GR-ED) and ODQ Total Score (Calculated Only From Sections 1 and 2 of the Questionnaire [Excluding Items Related to the Antidepressants as Cause Domain]) at Week 8

End point title	Change From Baseline in ODQ Domain Scores (NC, ED, PR, GR, AC, PR-NC, and GR-ED) and ODQ Total Score (Calculated Only From Sections 1 and 2 of the Questionnaire [Excluding Items Related to the Antidepressants as Cause Domain]) at Week 8
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End point description:

ODQ: self-reported, 26-item questionnaire assessing 5 dimensions of emotional functioning (NC; ED; PR; GR; AC), comprised of 3 sections: Section 1 (12 items) evaluated respondents' experiences during past week; Section 2 (8 items) compared respondents' experiences during past week to the experience before their depression; and Section 3 (6 items) assessed participant's perception of a relationship between current antidepressant and emotional functioning. Each item rated on a 5-point likert scale: 1 (disagree) to 5 (agree) and summed into scores for each dimension and a total score (range: 26-130). Total score, calculated only from Sections 1 and 2 are reported in this endpoint. Higher values reflected higher levels of emotional blunting. FAS: all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score. 'Number of participants analysed'=participants evaluable for this endpoint.

End point type	Secondary
End point timeframe:	
Baseline, Week 8	

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: units on a scale				
arithmetic mean (standard error)				
ODQ NC Score	-5.98 (± 0.52)			
ODQ ED Score	-4.72 (± 0.46)			
ODQ PR Score	-7.81 (± 0.55)			
ODQ GR Score	-6.56 (± 0.44)			
ODQ AC Score	-5.08 (± 0.50)			
ODQ PR-NC Score	-13.65 (± 1.01)			
ODQ GR-ED Score	-11.20 (± 0.74)			
ODQ Section 1+2 Score	-24.73 (± 1.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Responded "No" (Absence of Emotional Effects) to Screening Question on Emotional Functioning

End point title	Percentage of Participants who Responded "No" (Absence of Emotional Effects) to Screening Question on Emotional Functioning
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End point description:

The participants were asked the following screening question on emotional functioning: Emotional effects vary, but may include, for example, feeling emotionally "numbed" or "blunted" in some way; lacking positive emotions or negative emotions; feeling detached from the world around you; or "just not caring" about things that you used to care about. Have you experienced such emotional effects during the last 6 weeks? FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score. Here, 'Number of participants analysed' signifies participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	138			
Units: percentage of participants				
number (confidence interval 95%)	49.3 (40.9 to 57.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disability Scale (SDS) Total and Individual Item Scores (Family Life/Home Responsibilities, Social Life, and Work/School) at Week 8

End point title	Change From Baseline in Disability Scale (SDS) Total and Individual Item Scores (Family Life/Home Responsibilities, Social Life, and Work/School) at Week 8
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End point description:

The SDS is a series of participant self-rated, 10-point visual analogue scales designed to measure the extent to which the participant's life is impaired by panic, anxiety, phobic, or depressive symptoms. The participant rated the extent to which his or her work, social life or leisure activities, and home life or family responsibilities were impaired by his or her symptoms. The sum of the 3 SDS items yielded a total score (possible range 0-30), with higher scores indicating worse functioning. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score. Here, 'Number of participants analysed' signifies participants evaluable for this endpoint. 'n' signifies participants evaluable for specified categories.

End point type	Secondary
End point timeframe:	Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: units on a scale				
arithmetic mean (standard error)				
Total Score (n = 131)	-7.73 (± 0.91)			
Family Life/Home Responsibilities Score (n = 131)	-2.54 (± 0.32)			
Social Life Score (n = 131)	-2.42 (± 0.30)			
Work/School Score (n = 90)	-3.19 (± 0.40)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Days Lost and Days Underproductive at Week 8 as Collected in the SDS Questionnaire

End point title	Change From Baseline in Days Lost and Days Underproductive at Week 8 as Collected in the SDS Questionnaire
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End point description:

The number of days lost and the number of underproductive days lost from work due to the symptoms were also captured in SDS questionnaire. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score. Here, 'Number of participants analysed' signifies participants evaluable for this endpoint.

End point type Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: days				
arithmetic mean (standard error)				
Days Lost	-1.86 (± 0.21)			
Days Underproductive	-2.21 (± 0.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression – Severity of Illness (CGI-S) Score at Week 8

End point title Change From Baseline in Clinical Global Impression – Severity of Illness (CGI-S) Score at Week 8

End point description:

CGI provides an overall clinician-determined summary measure of the severity of a participant's clinical condition and improvement or worsening that takes into account all available information, including knowledge of the participant's history, psychosocial circumstances, symptoms, behaviour, and impact of symptoms on participant's ability to function. CGI consists of 2 clinician-rated subscales: CGI-S and CGI-I. The CGI-S provides clinician's impression of the participant's current state of mental illness. Clinician rated the severity of participant's current mental illness on a 7-point scale ranging from 1 (normal not at all ill) to 7 (among the most extremely ill participants). Higher scores indicated worsened condition. FAS: all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid postbaseline assessment of the ODQ total score. Here, 'Number of participants analysed' signifies participants evaluable for this endpoint.

End point type Secondary

End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: units on a scale				
arithmetic mean (standard error)	-1.83 (\pm 0.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression – Global Improvement (CGI-I) Score at Week 8

End point title	Clinical Global Impression – Global Improvement (CGI-I) Score at Week 8
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End point description:

The CGI provides an overall clinician-determined summary measure of the severity of a participant's clinical condition and improvement or worsening that takes into account all available information, including knowledge of the participant's history, psychosocial circumstances, symptoms, behaviour, and impact of symptoms on participant's ability to function. CGI consists of 2 clinician-rated subscales: CGI-S and CGI-I. The CGI-I provides clinician's impression of the participant's improvement or worsening. Clinician assessed the participant's condition relative to baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). Higher scores indicated worsened condition. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid postbaseline assessment of the ODQ total score. Here, 'Number of participants analysed' signifies participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: units on a scale				
arithmetic mean (standard error)	2.01 (\pm 0.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Response Based on the CGI-I at Week 8

End point title	Number of Participants With Response Based on the CGI-I at Week 8
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End point description:

Response was defined as a CGI-I score of 1 or 2. The CGI provides an overall clinician-determined summary measure of the severity of a participant's clinical condition and improvement or worsening that takes into account all available information, including knowledge of the participant's history, psychosocial circumstances, symptoms, behaviour, and impact of symptoms on participant's ability to

function. CGI consists of 2 clinician-rated subscales: CGI-S and CGI-I. The CGI-I provides clinician's impression of the participant's improvement or worsening. Clinician assessed the participant's condition relative to baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). Higher scores indicated worsened condition. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score.

End point type	Secondary
End point timeframe:	
Week 8	

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: participants	96			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Remission Based on the CGI-S at Week 8

End point title	Number of Participants With Remission Based on the CGI-S at Week 8
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End point description:

Remission was defined as a CGI-S score of 1 or 2. The CGI provides an overall clinician-determined summary measure of the severity of a participant's clinical condition and improvement or worsening that takes into account all available information, including knowledge of the participant's history, psychosocial circumstances, symptoms, behaviour, and impact of symptoms on participant's ability to function. CGI consists of 2 clinician-rated subscales: CGI-S and CGI-I. The CGI-S provides clinician's impression of the participant's current state of mental illness. Clinician rated the severity of participant's current mental illness on a 7-point scale ranging from 1 (normal not at all ill) to 7 (among the most extremely ill participants). Higher scores indicated worsened condition. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score.

End point type	Secondary
End point timeframe:	
Week 8	

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: participants	63			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Digit-Symbol Substitution Test (DSST) Total Score at Week 8

End point title	Change From Baseline in Digit-Symbol Substitution Test (DSST) Total Score at Week 8
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End point description:

The DSST is a cognitive test designed to assess psychomotor speed of performance requiring visual perception, spatial decision-making, and motor skills. The DSST is sensitive to cognitive impairments affecting attention, processing speed, and executive function (including working memory). The DSST consists of 133 digits and requires the participant to substitute each digit with a simple symbol in a 90-second period. Each correct symbol was counted. The total score was the number of correct symbols and the total score ranged from 0 (less than normal functioning) to 133 (greater than normal functioning), higher scores indicating better cognitive performance. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score. Here, 'Number of participants analysed' signifies participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	130			
Units: units on a scale				
arithmetic mean (standard error)	7.83 (\pm 0.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Montgomery and Åsberg Depression Rating Scale (MADRS) Total Score at Week 8

End point title	Change From Baseline in Montgomery and Åsberg Depression Rating Scale (MADRS) Total Score at Week 8
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End point description:

The MADRS is a 10-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. The items in the scale are designed to assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Symptoms were rated on a 7-point scale from 0 (no symptoms) to 6 (severe symptom). The total score of the 10 items ranges from 0 to 60 with higher scores indicating worse symptom severity. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score. Here, 'Number of participants analysed' signifies participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: units on a scale				
arithmetic mean (standard error)	-13.77 (\pm 0.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MADRS Anhedonia Factor Score at Week 8

End point title	Change From Baseline in MADRS Anhedonia Factor Score at Week 8
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End point description:

The 5-item MADRS anhedonia subscale score was based on the following MADRS items: 1 (apparent sadness), 2 (reported sadness), 6 (concentration difficulties), 7 (lassitude), and 8 (inability to feel). Symptoms were rated on a 7-point scale from 0 (no symptoms) to 6 (severe symptom). The total score of the 5 items ranges from 0 to 30 with higher scores indicating worse symptom severity. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score. Here, 'Number of participants analysed' signifies participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline, Week 8

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: units on a scale				
arithmetic mean (standard error)	-8.86 (\pm 0.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Response Based on the MADRS at Week 8

End point title	Number of Participants With Response Based on the MADRS at Week 8
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End point description:

Response was defined as a \geq 50% reduction in MADRS total score compared to baseline. The MADRS is a 10-item rating scale designed to assess the severity of the symptoms in depressive illness and to be

sensitive to treatment effects. The items in the scale are designed to assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Symptoms were rated on a 7-point scale from 0 (no symptoms) to 6 (severe symptom). The total score of the 10 items ranges from 0 to 60 with higher scores indicating worse symptom severity. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score.

End point type	Secondary
End point timeframe:	
Week 8	

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: participants	81			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Remission Based on the MADRS at Week 8

End point title	Number of Participants With Remission Based on the MADRS at Week 8
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End point description:

Remission was defined as a MADRS total score of ≤ 10 . The MADRS is a 10-item rating scale designed to assess the severity of the symptoms in depressive illness and to be sensitive to treatment effects. The items in the scale are designed to assess apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Symptoms were rated on a 7-point scale from 0 (no symptoms) to 6 (severe symptom). The total score of the 10 items ranges from 0 to 60 with higher scores indicating worse symptom severity. FAS included all participants who received at least 1 dose of study drug and who had a valid baseline assessment and at least 1 valid post-baseline assessment of the ODQ total score.

End point type	Secondary
End point timeframe:	
Week 8	

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: participants	61			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 12

Adverse event reporting additional description:

All-patients-treated set (APTS) included all enrolled participants who took at least 1 dose of study drug.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	Vortioxetine
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Reporting group description:

Participants received vortioxetine 10 mg tablet orally once daily. After the first week of treatment, the dose of vortioxetine could be adjusted (to 10 or 20 mg/day) up to Week 8. Participants were treated for 8 weeks.

Serious adverse events	Vortioxetine		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 150 (0.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	1 / 150 (0.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Vortioxetine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 150 (30.00%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 150 (6.67%)		
occurrences (all)	10		
Headache			

subjects affected / exposed occurrences (all)	12 / 150 (8.00%) 13		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed occurrences (all)	9 / 150 (6.00%) 10		
Nausea			
subjects affected / exposed occurrences (all)	31 / 150 (20.67%) 38		
Vomiting			
subjects affected / exposed occurrences (all)	10 / 150 (6.67%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 July 2019	It included the following changes: - Inclusion criterion 5: sertraline added to list of allowed selective serotonin reuptake inhibitors (SSRIs) taken prior to the study. - Updated: Recent and Concomitant Medication, Disallowed or Allowed with restrictions to better reflect the participant population's medical treatment needs.
15 July 2019	It included the following changes: - Added: exploratory objective, endpoint, and assessment to explore the association between digital biomarkers/phenotypes and clinical features using the phone application discovery by Mindstrong. This amendment was never effectuated as no participant consented to using the phone application.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported