Clinical trial results:
Long-term, open-label, flexible-dose, continuation extension study with vortioxetine in child and adolescent patients with Major Depressive Disorder (MDD) from 7 to 17 years of age

Summary

EudraCT number	2015-002658-11
Trial protocol	BE GB LV HU EE ES IT DE BG PL FR
Global end of trial date	16 April 2020

Results information

Result version number	v1 (current)
This version publication date	21 October 2020
First version publication date	21 October 2020

Trial information

Trial identification

Sponsor protocol code	12712B

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03108625
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 36 3013 11, LundbeckClinicalTrials@lundbeck.com
Scientific contact	Lundbeck Clinical Trials, H. Lundbeck A/S, +45 36 3013 11, LundbeckClinicalTrials@lundbeck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000455-PIP02-10
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 April 2020
Global end of trial reached?	Yes
Global end of trial date	16 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the long-term safety and tolerability of vortioxetine in child and adolescent patients with a Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5™) diagnosis of MDD.

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	04 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Bulgaria: 11
Country: Number of subjects enrolled	Estonia: 7
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Latvia: 6
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Russian Federation: 35
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Serbia: 4
Worldwide total number of subjects	94
EEA total number of subjects	54

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)	21
Adolescents (12-17 years)	73
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The population enrolled in Study 12712B (78 weeks) were paediatric patients who had completed treatment in Study 12712A (26 weeks). Results are presented by duration of treatment relative to baseline in Study 12712A (104 weeks) and relative to baseline in Study 12712B (78 weeks).

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	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Vortioxetine

Arm description: -

Arm type	Experimental
Investigational medicinal product name	vortioxetine
Investigational medicinal product code	Lu AA21004
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5, 10, 15 or 20 mg/day oral tablets, 78 weeks of treatment

Number of subjects in period 1	Vortioxetine
Started	94
Completed	58
Not completed	36
Consent withdrawn by subject	4
Not specified	27
Non-compliant with IMP	3
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	94	94	
Age categorical Units: Subjects			
Children (2-11 years)	21	21	
Adolescents (12-17 years)	73	73	
Gender categorical Units: Subjects			
Female	55	55	
Male	39	39	

End points

End points reporting groups

Reporting group title	Vortioxetine

Reporting group description: -

Primary: Number of Participants With Treatment-Emergent Adverse Events (Safety)

End point title	Number of Participants With Treatment-Emergent Adverse Events (Safety)[1]

End point description:

Based on safety assessments (e.g. paediatric adverse event rating scale (PAERS), clinical safety laboratory tests (including reproductive hormones), vital signs, weight, height, Tanner score, menstrual cycle, ECG, and C-SSRS.

End point type	Primary

End point timeframe:

78 weeks

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: Only descriptive statistics

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	94			
Units: participants	48			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Children Depression Rating Scale (CDRS-R) total score to Week 104

End point title	Change in Children Depression Rating Scale (CDRS-R) total score to Week 104

End point description:

Children Depression Rating Scale, revised version. The CDRS-R is a clinician-rated scale to measure the severity of depression in children and adolescents. The CDRS-R is rated by a clinician following interviews with the child and parent and consists of 17 items out of which 3 items rate nonverbal observations (depressed affect, listless speech, and hypoactivity). Fourteen items are rated on a 7-point scale from 1 to 7, and 3 items (sleep disturbance, appetite disturbance, and listless speech) are scored on a 5-point scale from 1 to 5. The total score ranges from 17 (normal) to 113 (severe depression).

End point type	Secondary

End point timeframe:

Change from study 12712A baseline to Week 104

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: units on a scale				
least squares mean (standard error)	-21.67 (± 1.26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of relapses during the treatment period (78 weeks)

End point title	Number of relapses during the treatment period (78 weeks)

End point description:

CDRS-R total score ≥40 with a history of 2 weeks of clinical deterioration

End point type	Secondary

End point timeframe:

78 weeks

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Number of relapses	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Loss of remission during the treatment period (78 weeks)

End point title	Loss of remission during the treatment period (78 weeks)

End point description:

CDRS-R total score <28 with a history of 2 weeks of clinical deterioration

End point type	Secondary

End point timeframe:

78 weeks

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: patients	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Clinical Global Impression - Severity of Illness (CGI-S) score to Week 104

End point title	Change in Clinical Global Impression - Severity of Illness (CGI-S) score to Week 104

End point description:

Clinical Global Impression - Severity of Illness. 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:

Change from study 12712A baseline to Week 104

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: units				
least squares mean (standard error)	-2.36 (± 0.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression-Improvement (CGI-I) score at Week 78

End point title	Clinical Global Impression-Improvement (CGI-I) score at Week 78

End point description:

The Clinical Global Impression-Improvement (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).

End point type	Secondary

End point timeframe:

Week 78

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: units on a scale				
arithmetic mean (standard deviation)	1.35 (± 0.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Children (7-11 years): change in BRIEF using the Global Executive Composite score to Week 104

End point title	Children (7-11 years): change in BRIEF using the Global Executive Composite score to Week 104

End point description:

Behaviour Rating Inventory of Executive Function. The BRIEF® is a patient- and carer-rated scale designed to measure executive function behaviour in children and adolescents in an everyday environment. We use BRIEF (parent form) for children aged 7 to 11 years. The BRIEF contains 86 items. Items are rated on a 3-point scale, from N (never) to O (often). These items cover 8 non-overlapping clinical scales: 3 scales in the Behavioural Regulation Index (inhibit, shift, and emotional control) and 5 scales in the Metacognition Index (initiate, working memory, plan/organize, organization of materials, and monitor). The clinical scales also provide the Global Executive Composite score, which represents the child's overall executive function behaviour. There are 2 validity scales: negativity and inconsistency.

End point type	Secondary

End point timeframe:

Change from 12712A baseline to Week 104

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: units on a scale				
arithmetic mean (standard deviation)	-15.18 (± 14.48)			

Statistical analyses

No statistical analyses for this end point

Secondary: Children (7-11 years): change in BRIEF using the Metacognition Index to Week 104

End point title	Children (7-11 years): change in BRIEF using the Metacognition Index to Week 104

End point description:

Behaviour Rating Inventory of Executive Function. The BRIEF® is a patient- and carer-rated scale designed to measure executive function behaviour in children and adolescents in an everyday environment. We use BRIEF (parent form) for children aged 7 to 11 years. The BRIEF contains 86 items. Items are rated on a 3-point scale, from N (never) to O (often). These items cover 8 non-overlapping clinical scales: 3 scales in the Behavioural Regulation Index (inhibit, shift, and emotional control) and 5 scales in the Metacognition Index (initiate, working memory, plan/organize, organization of materials, and monitor). The clinical scales also provide the Global Executive Composite score, which represents the child's overall executive function behaviour. There are 2 validity scales: negativity and inconsistency.

End point type	Secondary

End point timeframe:

Change from study 12712A baseline to Week 104

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: units on a scale				
arithmetic mean (standard deviation)	-14.35 (± 14.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Adolescents (12-17 years): change in BRIEF-SR using the Global Executive Composite score to Week 104

End point title	Adolescents (12-17 years): change in BRIEF-SR using the Global Executive Composite score to Week 104

End point description:

Behaviour Rating Inventory of Executive Function, Self-report version. Behaviour Rating Inventory of Executive Function. The BRIEF® is a patient- and carer-rated scale designed to measure executive function behaviour in children and adolescents in an everyday environment. We use BRIEF-SR (self-report) for the adolescents aged 11 to 17 years. The BRIEF contains 86 items. Items are rated on a 3-point scale, from N (never) to O (often). These items cover 8 non-overlapping clinical scales: 3 scales in the Behavioural Regulation Index (inhibit, shift, and emotional control) and 5 scales in the Metacognition Index (initiate, working memory, plan/organize, organization of materials, and monitor). The clinical scales also provide the Global Executive Composite score, which represents the child's overall executive function behaviour. There are 2 validity scales: negativity and inconsistency.

End point type	Secondary

End point timeframe:

Change from study 12712A baseline to Week 104

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: units on a scale				
arithmetic mean (standard deviation)	-15.34 (± 15.27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Adolescents (12-17 years): change in BRIEF-SR using the Metacognition Index to Week 104

End point title	Adolescents (12-17 years): change in BRIEF-SR using the Metacognition Index to Week 104

End point description:

Behaviour Rating Inventory of Executive Function, Self-report version. Behaviour Rating Inventory of Executive Function. The BRIEF® is a patient- and carer-rated scale designed to measure executive function behaviour in children and adolescents in an everyday environment. We use BRIEF-SR (self-report) for the adolescents aged 11 to 17 years. The BRIEF contains 86 items. Items are rated on a 3-point scale, from N (never) to O (often). These items cover 8 non-overlapping clinical scales: 3 scales in the Behavioural Regulation Index (inhibit, shift, and emotional control) and 5 scales in the Metacognition Index (initiate, working memory, plan/organize, organization of materials, and monitor). The clinical scales also provide the Global Executive Composite score, which represents the child’s overall executive function behaviour. There are 2 validity scales: negativity and inconsistency.

End point type	Secondary

End point timeframe:

Change from study 12712A baseline to Week 104

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: units on a scale				
arithmetic mean (standard deviation)	-14.55 (± 15.18)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Pediatric Quality of Life Inventory Present Functioning Visual Analogue Scales (PedsQL VAS) score to Week 104

End point title	Change in Pediatric Quality of Life Inventory Present Functioning Visual Analogue Scales (PedsQL VAS) score to Week 104

End point description:

Pediatric Quality of Life Inventory Present Functioning Visual Analogue Scales. The PedsQL VAS is designed to measure at-that-moment functioning in children and

adolescents. The PedsQL™ VAS consists of 6 domains: anxiety, sadness, anger, worry, fatigue, and pain using visual analogue scales. The functionality for each domain is measured on a 10cm line with a happy face at one end and a sad face at the other. The patients are asked to mark on the line how they feel. The total score is the average of all 6 items, and the emotional distress summary score is the mean of the anxiety, sadness, anger, and worry items. A lower value represents a better outcome.

End point type	Secondary

End point timeframe:

Change from study 12712A baseline to Week 104

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: units on a scale				
arithmetic mean (standard deviation)	-1.85 (± 1.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Children’s Global Assessment Scale (CGAS) score to Week 104

End point title	Change in Children’s Global Assessment Scale (CGAS) score to Week 104

End point description:

Children’s Global Assessment Scale. The CGAS is a clinician-rated global scale to measure the lowest level of functioning for a child (4 to 16 years) during a specified time period. The CGAS contains behaviourally oriented descriptors at each anchor point that depict behaviours and life situations applicable to a child. The score ranges from 1 (most functionally impaired child) to 100 (the healthiest). A score >70 indicates normal function.

End point type	Secondary

End point timeframe:

Change from study 12712A baseline to Week 104

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: units on a scale				
arithmetic mean (standard deviation)	27.69 (± 10.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Children Depression Rating Scale (CDRS-R) total score to Week 78

End point title	Change in Children Depression Rating Scale (CDRS-R) total score to Week 78

End point description:

Children Depression Rating Scale, revised version. The CDRS-R is a clinician-rated scale to measure the severity of depression in children and adolescents. The CDRS-R is rated by a clinician following interviews with the child and parent and consists of 17 items out of which 3 items rate nonverbal observations (depressed affect, listless speech, and hypoactivity). Fourteen items are rated on a 7-point scale from 1 to 7, and 3 items (sleep disturbance, appetite disturbance, and listless speech) are scored on a 5-point scale from 1 to 5. The total score ranges from 17 (normal) to 113 (severe depression).

End point type	Secondary

End point timeframe:

Change from study 12712B baseline to Week 78

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: units on a scale				
arithmetic mean (standard error)	-8.88 (± 0.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of relapses during the treatment period (78 weeks)

End point title	Number of relapses during the treatment period (78 weeks)

End point description:

CDRS-R total score ≥40 with a history of 2 weeks of clinical deterioration

End point type	Secondary

End point timeframe:

78 weeks

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Number of relapses	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Loss of remission during the treatment period up to (78 weeks)

End point title	Loss of remission during the treatment period up to (78 weeks)

End point description:

CDRS-R total score <28 with a history of 2 weeks of clinical deterioration

End point type	Secondary

End point timeframe:

78 weeks

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: patients	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Clinical Global Impression - Severity of Illness (CGI-S) score to Week 78

End point title	Change in Clinical Global Impression - Severity of Illness (CGI-S) score to Week 78

End point description:

Clinical Global Impression - Severity of Illness. 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:

Change from study 12712B baseline to Week 78

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: units on a scale				
arithmetic mean (standard error)	-1.34 (± 0.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Children (7-11 years): change in BRIEF using the Global Executive Composite score to Week 78

End point title	Children (7-11 years): change in BRIEF using the Global Executive Composite score to Week 78

End point description:

Behaviour Rating Inventory of Executive Function. The BRIEF® is a patient- and carer-rated scale designed to measure executive function behaviour in children and adolescents in an everyday environment. We use BRIEF (parent form) for children aged 7 to 11 years. The BRIEF contains 86 items. Items are rated on a 3-point scale, from N (never) to O (often). These items cover 8 non-overlapping clinical scales: 3 scales in the Behavioural Regulation Index (inhibit, shift, and emotional control) and 5 scales in the Metacognition Index (initiate, working memory, plan/organize, organization of materials, and monitor). The clinical scales also provide the Global Executive Composite score, which represents the child's overall executive function behaviour. There are 2 validity scales: negativity and inconsistency.

End point type	Secondary

End point timeframe:

Change from 12712B baseline to Week 78

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: units on a scale				
arithmetic mean (standard error)	-8.65 (± 8.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Children (7-11 years): change in BRIEF using the Metacognition Index to Week 78

End point title	Children (7-11 years): change in BRIEF using the Metacognition Index to Week 78

End point description:

Behaviour Rating Inventory of Executive Function. The BRIEF® is a patient- and carer-rated scale designed to measure executive function behaviour in children and adolescents in an everyday environment. We use BRIEF (parent form) for children aged 7 to 11 years. The BRIEF contains 86 items. Items are rated on a 3-point scale, from N (never) to O (often). These items cover 8 non-overlapping clinical scales: 3 scales in the Behavioural Regulation Index (inhibit, shift, and emotional control) and 5 scales in the Metacognition Index (initiate, working memory, plan/organize, organization of materials, and monitor). The clinical scales also provide the Global Executive Composite score, which represents the child's overall executive function behaviour. There are 2 validity scales: negativity and inconsistency.

End point type	Secondary

End point timeframe:

Change from study 12712B baseline to Week 78

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: units on a scale				
arithmetic mean (standard error)	-7.88 (± 7.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Adolescents (12-17 years): change in BRIEF-SR using the Global Executive Composite score to Week 78

End point title	Adolescents (12-17 years): change in BRIEF-SR using the Global Executive Composite score to Week 78

End point description:

Behaviour Rating Inventory of Executive Function, Self-report version. Behaviour Rating Inventory of Executive Function. The BRIEF® is a patient- and carer-rated scale designed to measure executive function behaviour in children and adolescents in an everyday environment. We use BRIEF-SR (self-report) for the adolescents aged 11 to 17 years. The BRIEF contains 86 items. Items are rated on a 3-point scale, from N (never) to O (often). These items cover 8 non-overlapping clinical scales: 3 scales in the Behavioural Regulation Index (inhibit, shift, and emotional control) and 5 scales in the Metacognition Index (initiate, working memory, plan/organize, organization of materials, and monitor). The clinical scales also provide the Global Executive Composite score, which represents the child's overall executive function behaviour. There are 2 validity scales: negativity and inconsistency.

End point type	Secondary

End point timeframe:

Change from study 12712B baseline to Week 78

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: units on a scale				
arithmetic mean (standard deviation)	-11.47 (± 14.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Adolescents (12-17 years): change in BRIEF-SR using the Metacognition Index to Week 78

End point title	Adolescents (12-17 years): change in BRIEF-SR using the Metacognition Index to Week 78

End point description:

Behaviour Rating Inventory of Executive Function, Self-report version. Behaviour Rating Inventory of Executive Function. The BRIEF® is a patient- and carer-rated scale designed to measure executive function behaviour in children and adolescents in an everyday environment. We use BRIEF-SR (self-

report) for the adolescents aged 11 to 17 years. The BRIEF contains 86 items. Items are rated on a 3-point scale, from N (never) to O (often). These items cover 8 non-overlapping clinical scales: 3 scales in the Behavioural Regulation Index (inhibit, shift, and emotional control) and 5 scales in the Metacognition Index (initiate, working memory, plan/organize, organization of materials, and monitor). The clinical scales also provide the Global Executive Composite score, which represents the child's overall executive function behaviour. There are 2 validity scales: negativity and inconsistency.

End point type	Secondary

End point timeframe:

Change from study 12712B baseline to Week 78

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: units on a scale				
arithmetic mean (standard deviation)	-11.21 (± 13.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Pediatric Quality of Life Inventory Present Functioning Visual Analogue Scales (PedsQL VAS) score to Week 78

End point title	Change in Pediatric Quality of Life Inventory Present Functioning Visual Analogue Scales (PedsQL VAS) score to Week 78

End point description:

Pediatric Quality of Life Inventory Present Functioning Visual Analogue Scales. The PedsQL VAS is designed to measure at-that-moment functioning in children and adolescents. The PedsQL™ VAS consists of 6 domains: anxiety, sadness, anger, worry, fatigue, and pain using visual analogue scales. The functionality for each domain is measured on a 10cm line with a happy face at one end and a sad face at the other. The patients are asked to mark on the line how they feel. The total score is the average of all 6 items, and the emotional distress summary score is the mean of the anxiety, sadness, anger, and worry items. A lower value represents a better outcome.

End point type	Secondary

End point timeframe:

Change from study 12712B baseline to Week 78

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.70 (± 1.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Children’s Global Assessment Scale (CGAS) score to Week 78

End point title	Change in Children’s Global Assessment Scale (CGAS) score to Week 78

End point description:

Children’s Global Assessment Scale. The CGAS is a clinician-rated global scale to measure the lowest level of functioning for a child (4 to 16 years) during a specified time period. The CGAS contains behaviourally oriented descriptors at each anchor point that depict behaviours and life situations applicable to a child. The score ranges from 1 (most functionally impaired child) to 100 (the healthiest). A score >70 indicates normal function.

End point type	Secondary

End point timeframe:

Change from study 12712B baseline to Week 78

End point values	Vortioxetine			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: units on a scale				
arithmetic mean (standard deviation)	14.26 (± 10.63)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 82 weeks	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	Vortioxetine 5, 10, 15 or 20 mg/day

Reporting group description: -

Serious adverse events	Vortioxetine 5, 10, 15 or 20 mg/day		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 94 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Vortioxetine 5, 10, 15 or 20 mg/day		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 94 (31.91%)		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 94 (13.83%)		
occurrences (all)	15		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	8		
Vomiting			

subjects affected / exposed occurrences (all)	5 / 94 (5.32%) 6		
Endocrine disorders Hyperprolactinaemia subjects affected / exposed occurrences (all)	 5 / 94 (5.32%) 5		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Respiratory tract infection viral subjects affected / exposed occurrences (all)	 6 / 94 (6.38%) 6 5 / 94 (5.32%) 6		

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