Clinical trial results:
A Short-term Exploratory Study to Evaluate Safety, Tolerability, and Pharmacokinetics of Seltorexant as Adjunctive Therapy to Antidepressants in Adolescents with Major Depressive Disorder Who Have an Inadequate Response to an SSRI and Psychotherapy

Summary

EudraCT number	2021-000567-77
Trial protocol	Outside EU/EEA ES IT SE
Global end of trial date	08 April 2024

Results information

Result version number	v1
This version publication date	24 October 2024
First version publication date	24 October 2024

Trial information

Trial identification

Sponsor protocol code	42847922MDD1016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04951609
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202 South, Raritan, New Jersey, United States, 08869
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002746-PIP01-20
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	08 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective was to assess the safety and tolerability of seltorexant as adjunctive therapy to an antidepressant in adolescents with major depressive disorder (MDD), in short-term compared with placebo.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 September 2021
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: 5
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	United States: 22
Worldwide total number of subjects	30
EEA total number of subjects	7

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)	30
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 31 subjects were randomised, out of which only 30 subjects were treated with either study intervention or placebo. One subject was randomised to seltorexant treatment but was not treated with the study intervention.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.

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:

Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.

Arm title	Seltorexant 10 mg and 20 mg

Arm description:

Subjects with body weight greater than or equal to (>=) 45 kilograms (kg) received a single oral dose of seltorexant 20 milligrams (mg) tablet once daily at bedtime and subjects with body weight >=30 kg to less than (<) 45 kg received seltorexant 10 mg tablet once daily at bedtime from Day 1 to Week 6. Subjects continued with their baseline selective serotonin reuptake inhibitor (SSRI) antidepressant (fluoxetine or escitalopram) treatment at same dose as it was prior to entering the study.

Arm type	Experimental
Investigational medicinal product name	Seltorexant
Investigational medicinal product code	JNJ-42847922
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single oral dose of seltorexant 20 mg or 10 mg tablet once daily at bedtime based on the body weight from Day 1 to Week 6.

Number of subjects in period 1	Placebo	Seltorexant 10 mg and 20 mg
Started	7	23
Completed	6	22
Not completed	1	1
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.	
Reporting group title	Seltorexant 10 mg and 20 mg
Reporting group description:	
Subjects with body weight greater than or equal to (>=) 45 kilograms (kg) received a single oral dose of seltorexant 20 milligrams (mg) tablet once daily at bedtime and subjects with body weight >=30 kg to less than (<) 45 kg received seltorexant 10 mg tablet once daily at bedtime from Day 1 to Week 6. Subjects continued with their baseline selective serotonin reuptake inhibitor (SSRI) antidepressant (fluoxetine or escitalopram) treatment at same dose as it was prior to entering the study.	

Reporting group values	Placebo	Seltorexant 10 mg and 20 mg	Total
Number of subjects	7	23	30
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	7	23	30
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	15.9	15	
standard deviation	± 1.07	± 1.54	-
Title for Gender Units: subjects			
Female	5	17	22
Male	2	6	8

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.

Reporting group title	Seltorexant 10 mg and 20 mg

Reporting group description:

Subjects with body weight greater than or equal to (>=) 45 kilograms (kg) received a single oral dose of seltorexant 20 milligrams (mg) tablet once daily at bedtime and subjects with body weight >=30 kg to less than (<) 45 kg received seltorexant 10 mg tablet once daily at bedtime from Day 1 to Week 6. Subjects continued with their baseline selective serotonin reuptake inhibitor (SSRI) antidepressant (fluoxetine or escitalopram) treatment at same dose as it was prior to entering the study.

Primary: Double-blind Phase: Number of Subjects with Treatment Emergent Adverse Events (TEAEs)

End point title	Double-blind Phase: Number of Subjects with Treatment Emergent Adverse Events (TEAEs)[1]

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Treatment-emergent adverse events were any AE occurring at or after the initial administration of study intervention through 2 days after the last administration of study intervention. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention.

End point type	Primary

End point timeframe:

From start of treatment (Day 1) up to Week 6

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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	23		
Units: subjects	2	9		

Statistical analyses

No statistical analyses for this end point

Primary: Double-blind Phase: Number of Subjects with Treatment Emergent Adverse Event of Special Interest (AESIs)

End point title	Double-blind Phase: Number of Subjects with Treatment Emergent Adverse Event of Special Interest (AESIs)[2]

End point description:

An adverse event (AE) any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal

relationship with the intervention. Treatment-emergent adverse events were any AE occurring at or after the initial administration of study intervention through 2 days after the last administration of study intervention. AESIs were significant AEs that were judged to be of special interest because of clinical importance, known or suspected class effects, or based on nonclinical signals. Adverse events of special interest were cataplexy, sleep paralysis, complex, and sleep-related behaviors (parasomnias), new suicidal behavior or suicidal ideation. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention.

End point type	Primary

End point timeframe:

From start of treatment (Day 1) up to Week 6

Notes:

[2] - 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	23		
Units: subjects	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Double-blind Phase: Number of Symptoms as Assessed by Pediatric Adverse Event Rating Scale (PAERS)

End point title	Double-blind Phase: Number of Symptoms as Assessed by Pediatric Adverse Event Rating Scale (PAERS)[3]

End point description:

Number of symptoms as assessed by PAERS were reported. The PAERS was a patient-rated scale designed to assess adverse events occurring in pediatric subjects treated with psychotropic medication in clinical studies. Individual PAERS (patient-reported version) items rated on symptoms and severity of symptoms. PAERS scale consisted of 45 items (43 specific signs and symptoms and 2 to be specified). Individual items were rated on a scale of "0" (mild) to "4" (extreme). Safety analysis set included all randomised subjects who took at least 1 dose of study intervention.

End point type	Primary

End point timeframe:

Baseline, Day 15, Day 29, and end of double-blind phase (Week 6)

Notes:

[3] - 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	23		
Units: number of symptoms				
Baseline: Mild	55	177		
Baseline: Moderate	59	134		
Baseline: Severe	30	82		
Baseline: Extreme	21	43		
Day 15: Mild	79	172		

Day 15: Moderate	33	90		
Day 15: Severe	13	59		
Day 15: Extreme	9	26		
Day 29: Mild	83	154		
Day 29: Moderate	31	81		
Day 29: Severe	5	39		
Day 29: Extreme	2	19		
End of double-blind phase (Week 6): Mild	74	161		
End of double-blind phase (Week 6): Moderate	25	82		
End of double-blind phase (Week 6): Severe	9	35		
End of double-blind phase (Week 6): Extreme	2	16		

Statistical analyses

No statistical analyses for this end point

Primary: Double-blind Phase: Number of Subjects with Abnormalities in Clinical Laboratory Values

End point title	Double-blind Phase: Number of Subjects with Abnormalities in Clinical Laboratory Values[4]

End point description:

Number of subjects with abnormalities in clinical laboratory values (hematology, and serum chemistry) were reported. Only those categories in which at least one subject had data are reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Primary

End point timeframe:

From start of treatment (Day 1) up to end of double-blind phase (Week 6)

Notes:

[4] - 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	22		
Units: subjects				
Chemistry: Alkaline Phosphatase: high	0	1		
Chemistry: Cholesterol: high	1	3		
Chemistry: LDL Cholesterol: high	0	1		
Chemistry: Phosphate: high	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Double-blind Phase: Number of Subjects with Abnormalities in Electrocardiogram (ECG)

End point title	Double-blind Phase: Number of Subjects with Abnormalities in Electrocardiogram (ECG)[5]

End point description:

Number of subjects with abnormalities in ECG were reported. The ECG parameters included heart rate, PR interval, QRS interval, QT interval, and corrected QT (QTc). Only those categories in which at least one subject had data are reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

End point type	Primary

End point timeframe:

Pre-dose (Day 1) and end of double-blind phase (Week 6)

Notes:

[5] - 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	23		
Units: subjects				
Pre-dose (Day 1) (n=7, 23)	3	0		
End of double-blind phase (Day 43): (n=6, 23)	2	4		

Statistical analyses

No statistical analyses for this end point

Primary: Double-blind Phase: Number of Subjects with Abnormalities in Vital Signs

End point title	Double-blind Phase: Number of Subjects with Abnormalities in Vital Signs[6]

End point description:

Number of subjects with abnormalities in vital sign (blood pressure [systolic and diastolic blood pressure] and temperature) were reported. Only those categories in which at least one subject had data are reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Units for blood pressure: millimetre of mercury (mmHg).

End point type	Primary

End point timeframe:

From start of treatment (Day 1) up to end of double-blind phase (Week 6)

Notes:

[6] - 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	23		
Units: subjects				
Systolic Blood Pressure: >130 mmHg	0	3		
Systolic Blood Pressure: <90 mmHg	1	2		
Diastolic Blood Pressure: >80 mmHg	0	2		
Diastolic Blood Pressure: <50 mmHg	0	0		
Temperature: >37.7 Celsius (C)	0	0		
Temperature: <35.5 C	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Double-blind Phase: Change from Baseline in Physical Examination: Body Weight

End point title	Double-blind Phase: Change from Baseline in Physical Examination: Body Weight[7]

End point description:

Change from baseline in physical examination: waist circumference was reported. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline (Day 1), and end of double-blind phase (Week 6)

Notes:

[7] - 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	23		
Units: kilograms (kg)				
arithmetic mean (standard deviation)	-1.40 (± 1.333)	1.15 (± 1.736)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Suicidality Assessment Using the Columbia Suicide Severity Rating Scale (C-SSRS) Score

End point title	Number of Subjects with Suicidality Assessment Using the Columbia Suicide Severity Rating Scale (C-SSRS) Score[8]

End point description:

C-SSRS scale reported at least one occurrence of any suicidal behavior and ideation. Suicidal behavior:

reporting any of 5 items: suicide, actual attempt, interrupted attempt, aborted attempt, preparatory acts or behavior. Suicidal ideation: consists of 5 yes/no items: wish to be dead, non-specific active suicidal thoughts, active suicidal ideation with any methods (not plan) without intent to act, active suicidal ideation with some intent to act, without specific plan, active suicidal ideation with specific plan and intent. An event of suicidal ideation or behavior were scored on a scale of 0 (no suicidal ideation or behavior) to 10 (suicide) based on highest response at the given time point. Worsening of suicidal ideation indicated an increase in severity of suicidal ideation. Only those categories in which at least 1 subject had data are reported. Safety analysis set was analysed. Here, "n"(number of subjects analysed) signifies number of subjects analysed at specified categories.

End point type	Primary

End point timeframe:

Baseline (Day 1[D1]), Day 8, Day 15, Day 29, and end of double-blind phase (Week 6)

Notes:

[8] - 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	23		
Units: subjects				
D1: No suicidal ideation or behavior: n=7, 23	7	18		
D1: Wish to be dead: n=7, 23	0	1		
D1:Non-specific active suicidal thoughts:n=7, 23	0	3		
D1:Suicidal ideation without plan & intent: n=7,23	0	1		
D8:No suicidal ideation or behavior(n=7, 23)	7	21		
D8: Non-specific active suicidal thoughts(n=7, 23)	0	2		
D15: No suicidal ideation or behavior(n=7, 23)	7	20		
D15:Non-specific active suicidal thoughts:n=7, 23	0	2		
D15: Suicidal ideation intent without plan:n=7,23	0	1		
D29:No suicidal ideation or behavior (n=6, 23)	6	18		
D29: Wish to be dead (n=6, 23)	0	2		
D29:Non-specific active suicidal thoughts:n=6, 23	0	2		
D29:Suicidal ideation without plan & intent:n=6,23	0	1		
D43:No suicidal ideation or behavior(n=6, 22)	6	18		
D43: Wish to be dead (n=6, 22)	0	2		
D43:Non-specific active suicidal thoughts (n=6,22)	0	2		
D43:Non-suicidal self-injurious behavior(n=6, 22)	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Double-blind Phase: Menstrual Cycle Tracking: Duration of Menses and Length of Menstrual Cycle

End point title	Double-blind Phase: Menstrual Cycle Tracking: Duration of Menses and Length of Menstrual Cycle[9]

End point description:

Menstrual cycles were tracked during the study in female adolescents or subjects who have at least one menses' using a subject diary and subject's verbal report. Menstrual cycle duration was measured by the number of days subjects noted menstruating in their diary entry. Menstrual cycle length was assessed as the number of days between menstrual cycles (i.e., days between the start of a menstrual period and the start of the next consecutive menstrual period) from baseline to end of double-blind phase (Week 6). Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified categories.

End point type	Primary

End point timeframe:

From baseline (Day 1) up to end of double-blind phase (Week 6)

Notes:

[9] - 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	15		
Units: days				
arithmetic mean (standard deviation)				
Duration of menses (n=3, 13)	6.0 (± 1.00)	6.8 (± 3.06)		
Length of cycle (n=2, 15)	62.0 (± 2.83)	45.9 (± 19.12)		

Statistical analyses

No statistical analyses for this end point

Primary: Withdrawal Symptoms Assessment Using the Physician Withdrawal Checklist (PWC-20)

End point title	Withdrawal Symptoms Assessment Using the Physician Withdrawal Checklist (PWC-20)[10]

End point description:

PWC-20 was a reliable, sensitive instrument having 20-items used to assess potential withdrawal symptoms following cessation of treatment. Items were loss of appetite, nausea-vomiting, diarrhea, anxiety-nervousness, irritability, dysphoric mood-depression, insomnia, fatigue, poor coordination, restlessness, diaphoresis, tremor, dizziness, headaches, stiffness, weakness, increased acuity sound smell touch (IASST), paresthesia, difficulty concentrating-, remember, derealization. Each item score ranged from 0 (not present) to 3 (severe). Total score ranges from 0-60, where higher score indicates more severe symptoms. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

End point type	Primary

End point timeframe:

End of double-blind phase (Week 6), Follow-up 1 (Day 45), Follow-up 2 (Day 54)

Notes:

[10] - 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	23		
Units: Units on a scale				
arithmetic mean (standard deviation)				
End of double-blind phase (Week 6) (n=6, 23)	2.7 (± 3.78)	6.9 (± 6.43)		
Follow-up 1 (Day 45) (5, 22)	4.2 (± 3.90)	4.1 (± 6.57)		
Follow-up 2 (Day 54) (6, 23)	5.7 (± 6.65)	5.6 (± 5.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Children’s Depression Rating Scale (CDRS) Total Score

End point title	Change from Baseline in the Children’s Depression Rating Scale (CDRS) Total Score

End point description:

Change from baseline in the CDRS total score were reported. The CDRS-R was a validated 17-item, clinician-rated instrument that measured the severity of a subject's depressive symptoms. The CDRS-R total score was the sum of the responses to 17 questions, ranged from 17 to 113. Each scale item was scored from 1 to 5 or 1 to 7. The highest possible score is 113 (the most severe measure of depression), and the lowest is 17 (not suffering from depression). Higher scores represent a more severe condition. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and end of double-blind phase (Week 6)

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	22		
Units: Units on a scale				
arithmetic mean (standard deviation)	-22.0 (± 9.86)	-21.3 (± 12.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Score

End point title	Change from Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Score

End point description:

Change from baseline in MADRS score were reported. The MADRS scale score was a 10-item clinician-administered scale designed to measure depression severity and to detect changes due to antidepressant treatment using the 10 items followed: apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, & suicidal thoughts. Each item scored from 0 (no symptoms or normal) to 6 (symptoms of maximum severity), & the sum of scores of individual question items at a given time point ranged from 0 to 60. Higher scores indicated more severe condition. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and end of double-blind phase (Week 6)

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	22		
Units: Units on a scale				
arithmetic mean (standard deviation)	-17.2 (± 10.42)	-14.6 (± 9.22)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impression- severity (CGI-S) Score Over Time

End point title	Change from Baseline in Clinical Global Impression- severity (CGI-S) Score Over Time

End point description:

Change from baseline in the CGI-S score were reported. The CGI-S provided an overall clinician-determined summary measure of the severity of the subject's illness. The CGI scale is an investigator-rated evaluation that assesses the severity of a subject's illness on a 7-point scale, ranged from 1 (normal, not at all ill) to 7 (among the most extremely ill subjects). Considering total clinical experience with the depression population, a subject was assessed on severity of illness at the time of rating according to: 1=normal (not at all ill); 2=borderline ill; 3=mildly ill; 4=moderately ill; 5=markedly ill; 6=severely ill; 7=among the most extremely ill subjects. Higher scores indicated more severe condition. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here, "n"(number analysed) signifies number of subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 15, Day 29, end of double-blind phase (Week 6)

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	23		
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 15 (n=7, 23)	-1.7 (± 1.11)	-0.7 (± 0.75)		
Day 29 (n=6,23)	-2.0 (± 1.26)	-1.2 (± 1.00)		
Week 6 (n=6, 22)	-2.0 (± 1.26)	-1.6 (± 1.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Subjective Sleep Assessment (Patient Reported Outcome Measurement Information System-Pediatric-Sleep Disturbance [PROMIS-Pediatric-SD]

End point title	Change from Baseline in Subjective Sleep Assessment (Patient Reported Outcome Measurement Information System-Pediatric-Sleep Disturbance [PROMIS-Pediatric-SD]

End point description:

The PROMIS-Pediatric-SD was a static 8 item questionnaire used to assess self-reported perceptions of sleep quality. Each item has 5 responses scored on a 5 level Likert-type scale. The 8-item short form were used, in which responses were scored 1 to 5 for each item. For the 8-item form, the lowest possible raw score is 8; the highest possible raw score is 40. Lower scores indicate less sleep disturbance The "direction" of the responses was not the same for all questions, i.e., sometimes a response of "always" indicated more sleep disturbance and sometimes a response of "always" indicated less sleep disturbance. Safety analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and end of double-blind phase (Week 6)

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	22		
Units: Units on a scale				
arithmetic mean (standard deviation)	-3.93 (± 9.074)	-8.41 (± 8.618)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Total Sleep Time

End point title	Change from Baseline on Objective Sleep Assessment Actigraphy: Total Sleep Time

End point description:

Change from baseline on objective sleep assessment actigraphy: total sleep time were reported. Objective sleep parameters were measured using actigraphy. Total sleep time was defined as the number of scored sleep epochs (an epoch equals 30 to 60 seconds), in minutes. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	17		
Units: minutes (min)				
arithmetic mean (standard deviation)				
Week 1 (N=5, 17)	32.62 (± 48.351)	-25.22 (± 116.136)		
Week 2 (n=5, 14)	30.82 (± 76.472)	-20.64 (± 95.390)		
Week 3 (n=5,12)	11.44 (± 55.639)	5.61 (± 83.844)		
Week 4 (n=5,11)	17.98 (± 35.690)	10.14 (± 79.563)		
Week 5 (n=4,12)	-17.28 (± 30.116)	23.68 (± 68.934)		
Week 6 (n=4,12)	23.18 (± 51.956)	24.72 (± 38.304)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Number of Wake Bouts

End point title	Change from Baseline on Objective Sleep Assessment Actigraphy: Number of Wake Bouts

End point description:

Change from baseline on objective sleep assessment actigraphy: number of wake bouts were reported. Objective sleep parameters were measured using actigraphy. A wake bout was an epoch or continuous epochs (an epoch equals 30 to 60 seconds) scored as awake. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	17		
Units: number of wake bouts				
arithmetic mean (standard deviation)				
Week 1 (N=5, 17)	3.54 (± 10.971)	-2.29 (± 14.181)		
Week 2 (n=5,14)	8.96 (± 16.954)	-1.69 (± 11.511)		
Week 3 (n=5, 12)	5.72 (± 18.522)	2.92 (± 8.492)		
Week 4 (n=5, 11)	1.54 (± 12.002)	2.94 (± 12.360)		
Week 5 (n=4, 12)	-9.18 (± 15.027)	1.93 (± 8.405)		
Week 6 (n=4, 12)	1.93 (± 4.562)	2.76 (± 8.464)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Sleep Efficiency

End point title	Change from Baseline on Objective Sleep Assessment Actigraphy: Sleep Efficiency

End point description:

Change from baseline on objective sleep assessment actigraphy: sleep efficiency was reported. Objective sleep parameters were measured using actigraphy. Sleep efficiency was scored total sleep time divided by total time in bed minus total invalid time, multiplied by 100, in percentages. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	17		
Units: percentage				
arithmetic mean (standard deviation)				
Week 1 (N=5,17)	0.02 (± 0.045)	-0.01 (± 0.075)		

Week 2 (N=5,14)	0.00 (± 0.071)	0.01 (± 0.027)		
Week 3 (N=5,12)	0.02 (± 0.045)	-0.01 (± 0.051)		
Week 4 (N=5,11)	0.02 (± 0.045)	-0.01 (± 0.030)		
Week 5 (N=4,12)	0.03 (± 0.050)	0.01 (± 0.067)		
Week 6 (N=4,12)	0.08 (± 0.096)	-0.02 (± 0.039)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Sleep Onset Latency

End point title	Change from Baseline on Objective Sleep Assessment Actigraphy: Sleep Onset Latency

End point description:

Change from baseline on objective sleep assessment actigraphy: sleep onset latency was reported. Objective sleep parameters were measured using actigraphy. Sleep onset latency was time between the start of a given rest interval and the following sleep start time, in minutes. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	17		
Units: minutes				
arithmetic mean (standard deviation)				
Week 1 (N=5, 17)	-8.04 (± 25.258)	1.44 (± 33.390)		
Week 2 (n=5, 14)	-14.06 (± 19.382)	-6.25 (± 11.835)		
Week 3 (n=5, 12)	-11.56 (± 26.961)	-7.99 (± 12.198)		
Week 4 (n=5, 11)	-11.44 (± 22.834)	-7.75 (± 13.613)		
Week 5 (n=4, 12)	-7.85 (± 9.035)	-8.10 (± 16.855)		
Week 6 (n=4, 12)	-21.75 (± 21.807)	-7.41 (± 13.201)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on Objective Sleep Assessment Actigraphy: Wake After Sleep Onset

End point title	Change from Baseline on Objective Sleep Assessment Actigraphy: Wake After Sleep Onset

End point description:

Change from baseline on objective sleep assessment actigraphy: Wake after sleep onset was reported. Objective sleep parameters were measured using actigraphy. Wake after sleep onset was the number of epochs of the given sleep interval scored as wake by the actigraphy software, in minutes. Full analysis set included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint and "n"(number of subjects analysed) signifies number of subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Week 1, Week 2, Week 3, Week 4, Week 5, and Week 6

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	17		
Units: minutes				
arithmetic mean (standard deviation)				
Week 1 (N=5, 17)	10.56 (± 14.227)	-0.42 (± 19.384)		
Week 2 (N=5, 14)	20.56 (± 27.744)	0.76 (± 14.792)		
Week 3 (N=5, 12)	18.70 (± 15.566)	8.05 (± 14.490)		
Week 4 (N=5, 11)	14.06 (± 11.631)	8.88 (± 15.866)		
Week 5 (N=4, 12)	-3.28 (± 6.338)	2.30 (± 17.768)		
Week 6 (N=4, 12)	3.28 (± 11.261)	6.73 (± 17.272)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Subjective Sleep Related Impairment (PROMIS-Pediatric- Sleep-Related Impairment [SRI])

End point title	Change From Baseline in Subjective Sleep Related Impairment (PROMIS-Pediatric- Sleep-Related Impairment [SRI])

End point description:

Change from baseline in PROMIS-Pediatric-SRI were reported. The PROMIS-SRI 8 items score was used to assess self-reported daytime perceptions of alertness, sleepiness, and tiredness during usual waking hours, and the perceived functional impairments during wakefulness associated with sleep problems or impaired alertness and assessed on a 5 level Likert-type scale. The 8-item short form used in this study, scored 1 to 5 for each item. For the 8-item form, the lowest possible raw score is 8; the highest possible raw score is 39. Total raw score for a short form with all questions answered equals sum of the values of response to each question. Higher overall score indicated more sleep disturbance. Safety analysis set

included all randomised subjects who took at least 1 dose of study intervention. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1), and end of double-blind phase (Week 6)

End point values	Placebo	Seltorexant 10 mg and 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	22		
Units: units on a scale				
arithmetic mean (standard deviation)	-12.12 (± 8.055)	-6.60 (± 7.616)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Seltorexant and an Active Metabolite of Seltorexant

End point title	Plasma Concentration of Seltorexant and an Active Metabolite of Seltorexant[11]

End point description:

Plasma concentration of seltorexant and an active metabolite of seltorexant were reported. Population analysed included all subjects who received study intervention and had at least 1 plasma concentration data value after study intervention intake. Here "N" (Number of subjects analysed) signifies the number of subjects that were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From 8 to 14 hours post last dose in Week 6

Notes:

[11] - 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: Data for this endpoint was planned to be collected and analysed only for the arm "Seltorexant 10 mg and 20 mg.

End point values	Seltorexant 10 mg and 20 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: nanograms per millilitre (ng/mL)				
arithmetic mean (standard deviation)				
Total Seltorexant	42.7 (± 52.8)			
Active metabolite	54.5 (± 53.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of treatment (Day 1) up to end of double-blind phase (Week 6)	
Adverse event reporting additional description:	
Safety analysis set included all randomised subjects who took at least 1 dose of study intervention.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Seltorexant 10 mg and 20 mg
Reporting group description:	
Subjects with body weight greater than or equal to (>=) 45 kilograms (kg) received a single oral dose of seltorexant 20 milligrams (mg) tablet once daily at bedtime and subjects with body weight >=30 kg to less than (<) 45 kg received seltorexant 10 mg tablet once daily at bedtime from Day 1 to Week 6. Subjects continued with their baseline SSRI antidepressant (fluoxetine or escitalopram) treatment at same dose as it was prior to entering the study.	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single oral dose of placebo (matching to seltorexant) tablet once daily at bedtime from Day 1 to Week 6.	

Serious adverse events	Seltorexant 10 mg and 20 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 7 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Seltorexant 10 mg and 20 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 23 (26.09%)	2 / 7 (28.57%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 23 (13.04%)	1 / 7 (14.29%)	
occurrences (all)	5	1	
General disorders and administration site conditions			

Pyrexia subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	1 / 7 (14.29%) 1	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 3	1 / 7 (14.29%) 1	
Nausea subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 4	1 / 7 (14.29%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 March 2023	The purpose of the protocol amendment dated 27-Mar-2023 was to align the protocol criteria more with current clinical practices and to increase feasibility of the study conduct. Due to subject feedback to sites regarding length and number of visits, adjustments were made to the visits as noted in the protocol amendment to allow for visit flexibility through remote assessment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported