Clinical trial results:
An Open-Label, Single-Dose Study to Assess the Absolute Oral Bioavailability and Pharmacokinetics of JNJ-42847922 (Seltorexant) Administered as Oral Tablet and an Intravenous Microdose of 14C-seltorexant in Healthy Participants

Summary

EudraCT number	2021-004068-92
Trial protocol	
Global end of trial date	01 March 2022

Results information

Result version number	v1 (current)
This version publication date	16 March 2023
First version publication date	16 March 2023

Trial information

Trial identification

Sponsor protocol code	42847922MDD1019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05236868
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, B-2340
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)	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	03 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to determine the absolute bioavailability of seltorexant in healthy subjects following a single oral dose of seltorexant 20 mg and a 100 microgram (mcg) intravenous (IV) infusion dose of 14C-seltorexant.

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 Practice and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2022
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	Netherlands: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 10 subjects were enrolled and completed the study.

Period 1

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

Arms

Arm title	Seltorexant 20 mg Oral+14C-Seltorexant 100 mcg IV Infusion

Arm description:

Subjects received a single oral dose of seltorexant 20 mg tablet on Day 1 (0 hour). After 2 hours of oral dosing, subjects then received 14C-seltorexant 100 micrograms (mcg) as an IV infusion for 15 minutes.

Arm type	Experimental
Investigational medicinal product name	Seltorexant
Investigational medicinal product code	JNJ-4284792
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Seltorexant infusion was administered 2 hours after oral dose.

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:

Seltorexant was administered orally.

Number of subjects in period 1	Seltorexant 20 mg Oral+14C-Seltorexant 100 mcg IV Infusion
Started	10
Completed	10

Baseline characteristics

Reporting groups

Reporting group title	Seltorexant 20 mg Oral+14C-Seltorexant 100 mcg IV Infusion

Reporting group description:

Subjects received a single oral dose of seltorexant 20 mg tablet on Day 1 (0 hour). After 2 hours of oral dosing, subjects then received 14C-seltorexant 100 micrograms (mcg) as an IV infusion for 15 minutes.

Reporting group values	Seltorexant 20 mg Oral+14C-Seltorexant 100 mcg IV Infusion	Total	
Number of subjects	10	10	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	10	10	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	27.8		
standard deviation	± 8.99	-	
Title for Gender Units: subjects			
Female	6	6	
Male	4	4	

Subject analysis sets

Subject analysis set title	Seltorexant 20 Milligrams (mg) Oral
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects received a single oral dose of seltorexant 20 mg tablet on Day 1 (0 hour).

Subject analysis set title	14C-Seltorexant IV 100 Micrograms (mcg) Infusion
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects received 100 mcg 14C-Seltorexant (200 nanocuries [nCi]) as an IV infusion 2 hours post oral dose for over 15 minutes.

Reporting group values	Seltorexant 20 Milligrams (mg) Oral	14C-Seltorexant IV 100 Micrograms (mcg) Infusion	
Number of subjects	10	10	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	10	10	
From 65 to 84 years	0	0	

85 years and over	0	0	

Title for AgeContinuous Units: years arithmetic mean standard deviation	±	±	
Title for Gender Units: subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Seltorexant 20 mg Oral+14C-Seltorexant 100 mcg IV Infusion
Reporting group description:	
Subjects received a single oral dose of seltorexant 20 mg tablet on Day 1 (0 hour). After 2 hours of oral dosing, subjects then received 14C-seltorexant 100 micrograms (mcg) as an IV infusion for 15 minutes.	
Subject analysis set title	Seltorexant 20 Milligrams (mg) Oral
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects received a single oral dose of seltorexant 20 mg tablet on Day 1 (0 hour).	
Subject analysis set title	14C-Seltorexant IV 100 Micrograms (mcg) Infusion
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects received 100 mcg 14C-Seltorexant (200 nanocuries [nCi]) as an IV infusion 2 hours post oral dose for over 15 minutes.	

Primary: Absolute Bioavailability Calculated as the Ratio of Dose Normalized Area Under the Plasma Concentration Time Curve of Seltorexant From Time Zero to Time of the Last Quantifiable Concentration (AUC[0-last]) of Oral and Intravenous (IV) Administration

End point title	Absolute Bioavailability Calculated as the Ratio of Dose Normalized Area Under the Plasma Concentration Time Curve of Seltorexant From Time Zero to Time of the Last Quantifiable Concentration (AUC[0-last]) of Oral and Intravenous (IV) Administration
End point description:	
Absolute bioavailability calculated as the ratio of dose normalized AUC(0-last) of oral and IV administration. Pharmacokinetic (PK) analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.	
End point type	Primary
End point timeframe:	
Pre-dose up to 72 hours post-dose on Day 1	

End point values	Seltorexant 20 Milligrams (mg) Oral	14C-Seltorexant IV 100 Micrograms (mcg) Infusion		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: Hour*nanogram/milliliter (h*ng/mL)				
geometric mean (geometric coefficient of variation)	2113 (± 12.1)	3975 (± 12.1)		

Statistical analyses

Statistical analysis title	Seltorexant oral vs 14C-seltorexant IV infusion

Statistical analysis description:	
Subjects analysed in the assigned treatment was 10.	
Comparison groups	Seltorexant 20 Milligrams (mg) Oral v 14C-Seltorexant IV 100 Micrograms (mcg) Infusion
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mixed model analysis
Point estimate	53.15
Confidence interval	
level	90 %
sides	2-sided
lower limit	48.16
upper limit	58.65

Primary: Absolute bioavailability calculated as the ratio of dose normalized Area Under the Plasma Concentration Time Curve of Seltorexant from Time Zero to Infinite Time (AUC[0-Infinity]) of Oral and IV Administration

End point title	Absolute bioavailability calculated as the ratio of dose normalized Area Under the Plasma Concentration Time Curve of Seltorexant from Time Zero to Infinite Time (AUC[0-Infinity]) of Oral and IV Administration
End point description:	
Absolute bioavailability calculated as the ratio of dose normalized AUC(0-infinity) of oral and IV administration. PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.	
End point type	Primary
End point timeframe:	
Pre-dose up to 72 hours post-dose on Day 1	

End point values	Seltorexant 20 Milligrams (mg) Oral	14C-Seltorexant IV 100 Micrograms (mcg) Infusion		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	2120 (± 12.0)	3992 (± 12.0)		

Statistical analyses

Statistical analysis title	Seltorexant oral vs 14C-seltorexant IV infusion
Statistical analysis description:	
Subjects analysed in the assigned treatment was 10.	
Comparison groups	Seltorexant 20 Milligrams (mg) Oral v 14C-Seltorexant IV 100 Micrograms (mcg) Infusion

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mixed model analysis
Point estimate	53.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	48.13
upper limit	58.58

Secondary: Area Under the Plasma Concentration Time Curve of Seltorexant From Time Zero to Time of the Last Quantifiable Concentration (AUC[0-last]) For Oral Administration

End point title	Area Under the Plasma Concentration Time Curve of Seltorexant From Time Zero to Time of the Last Quantifiable Concentration (AUC[0-last]) For Oral Administration

End point description:

AUC(0-last) is defined as area under the plasma analyte concentration versus time curve from time zero to time of the last measurable (non- below quantifiable limit [BQL]) concentration of Seltorexant following oral administration. PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 72 hours post-dose

End point values	Seltorexant 20 Milligrams (mg) Oral			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: h*ng/mL				
arithmetic mean (standard deviation)	2296 (± 1087)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Analyte Concentration (Cmax) of Seltorexant For Oral Administration

End point title	Maximum Observed Plasma Analyte Concentration (Cmax) of Seltorexant For Oral Administration

End point description:

Cmax is defined as the maximum observed plasma concentration of Seltorexant after oral administration. PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 72 hours post-dose

End point values	Seltorexant 20 Milligrams (mg) Oral			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Nanogram/millilitres (ng/mL)				
arithmetic mean (standard deviation)	476 (± 188)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach the Maximum Observed Plasma Analyte Concentration (Tmax) of Seltorexant for Oral Administration

End point title	Time to reach the Maximum Observed Plasma Analyte Concentration (Tmax) of Seltorexant for Oral Administration

End point description:

Tmax is defined as the time to reach maximum observed plasma concentration of Seltorexant after oral administration. PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 72 hours post-dose

End point values	14C-Seltorexant IV 100 Micrograms (mcg) Infusion			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Hour				
median (full range (min-max))	1.71 (0.33 to 3.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time Curve From Time Zero to Infinite time (AUC[0-Infinity]) of Seltorexant For Oral Administration

End point title	Area Under the Plasma Concentration Time Curve From Time Zero to Infinite time (AUC[0-Infinity]) of Seltorexant For Oral Administration

End point description:

AUC(0-Infinity) is defined as the area under the plasma analyte concentration versus time curve from time zero to infinite time of seltorexant after oral administration. PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 72 hours post-dose

End point values	Seltorexant 20 Milligrams (mg) Oral			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Hour*nanogram/milliliter (h*ng/mL)				
arithmetic mean (standard deviation)	2304 (± 1088)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Elimination Half-life (t1/2) of Seltorexant For Oral Administration

End point title	Apparent Elimination Half-life (t1/2) of Seltorexant For Oral Administration

End point description:

t1/2 is time measured for the plasma concentration of seltorexant to decrease by half to its original concentration after oral administration. It is associated with the terminal slope of the semi logarithmic drug concentration-time curve, and is calculated as 0.693/lambda(z). PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 72 hours post-dose Day 1

End point values	Seltorexant 20 Milligrams (mg) Oral			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Hour				
arithmetic mean (standard deviation)	2.27 (± 0.546)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time Curve of 14C-Seltorexant from Time Zero to Infinite time (AUC [0-Infinity]) For IV Administration

End point title	Area Under the Plasma Concentration Time Curve of 14C-Seltorexant from Time Zero to Infinite time (AUC [0-Infinity]) For IV Administration

End point description:

AUC(0-Infinity) is defined as the area under the plasma analyte concentration versus time curve from time zero to infinite time of 14C-Seltorexant after IV administration. PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 70 hours post-dose

End point values	14C-Seltorexant IV 100 Micrograms (mcg) Infusion			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: h*ng/mL				
arithmetic mean (standard deviation)	21.1 (± 5.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time Curve of 14C-Seltorexant From Time Zero to Time of the Last Quantifiable Concentration (AUC[0-last]) For IV Administration

End point title	Area Under the Plasma Concentration Time Curve of 14C-Seltorexant From Time Zero to Time of the Last Quantifiable Concentration (AUC[0-last]) For IV Administration

End point description:

AUC(0-last) is defined as area under the plasma analyte concentration versus time curve from time zero to time of the last measurable (non- below quantifiable limit [BQL]) concentration of 14C-seltorexant after IV administration. PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 70 hours post-dose

End point values	14C-Seltorexant IV 100 Micrograms (mcg) Infusion			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: h*ng/mL				
arithmetic mean (standard deviation)	21.0 (± 5.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Analyte Concentration (Cmax) of 14C-Seltorexant For IV Administration.

End point title	Maximum Observed Plasma Analyte Concentration (Cmax) of 14C-Seltorexant For IV Administration.

End point description:

Cmax is defined as the maximum observed plasma concentration of 14C-Seltorexant following IV administration. PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 70 hours post-dose

End point values	14C-Seltorexant IV 100 Micrograms (mcg) Infusion			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
arithmetic mean (standard deviation)	10.3 (± 1.20)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach the Maximum Observed Plasma Analyte Concentration

(Tmax) of 14C-Seltorexant For IV administration

End point title	Time to reach the Maximum Observed Plasma Analyte Concentration (Tmax) of 14C-Seltorexant For IV administration

End point description:

Tmax is defined as the time to reach maximum observed plasma concentration of 14C-Seltorexant for IV administration. PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profi les allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 70 hours post-dose

End point values	14C-Seltorexant IV 100 Micrograms (mcg) Infusion			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Hour				
median (full range (min-max))	0.25 (0.25 to 0.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Elimination Half-life (t1/2) of 14C-Seltorexant For IV Administration

End point title	Apparent Elimination Half-life (t1/2) of 14C-Seltorexant For IV Administration

End point description:

t1/2 of 14C-seltorexant is time measured for the plasma analyte concentration to decrease by 1 half to its original concentration. It is associated with the terminal slope of the semi logarithmic drug concentration-time curve, and is calculated as 0.693/lambda(z). PK analysis set included all subjects who received at least 1 dose of active study intervention whose PK profiles allow for accurate calculation of at least 1 PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose up to 70 hours post-dose

End point values	14C-Seltorexant IV 100 Micrograms (mcg) Infusion			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Hour				

arithmetic mean (standard deviation)	2.80 (± 1.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point description:

Adverse Event (AE) is any untoward medical occurrence in a clinical study subject administered a pharmaceutical (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the study vaccine. TEAEs are defined as the AEs occurring after first study treatment administration up to end of study. Safety analysis set included all subjects who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Up to Day 7

End point values	Seltorexant 20 mg Oral+14C-Seltorexant 100 mcg IV Infusion			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Subjects	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Day 7	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0
Reporting groups	
Reporting group title	Seltorexant Oral + 14C-seltorexant Intravenous (IV) Infusion
Reporting group description:	
Subjects received a single oral dose of seltorexant 20 mg. At 2 hours after oral dosing, subjects received 14C-seltorexant as an IV infusion over 15 minutes.	

Serious adverse events	Seltorexant Oral + 14C-seltorexant Intravenous (IV) Infusion		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Seltorexant Oral + 14C-seltorexant Intravenous (IV) Infusion		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 10 (40.00%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
General disorders and administration site conditions			

Catheter Site Irritation subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Infusion Site Pain subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 November 2021	The purpose of the amendment was to include the following changes: updated the severe acute respiratory syndrome–related coronavirus-2 assessment frequency, temperature collection method, order of scheduled assessments, duration for abstaining from strenuous exercise, and dose of paracetamol to be used during study conduct to accommodate the clinical site's preference; removed reference to the use of a spermicide to complement local regulations; included a more stringent criterion related to enrollment of subjects; removed ketamine from the list of drugs to be evaluated as a drug of abuse; provided additional clarity to different aspects of study conduct; emphasized participant adherence to planned exclusion criteria on blood donation prior to dose administration; allowed some flexibility in enrollment of occasional tobacco users; provided consistency between different parts of the protocol; and removed ambiguity related to study conduct in certain sections of the protocol.
12 January 2022	The purpose of the amendment was to implement the feedback from the Central Ethics Committee to extend the duration of post-study contraception to 3 months instead of 1 month and incorporate consistency on alcohol restriction.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported