Clinical trial results:
A 12-Week, Open-Label Extension Study of Lurasidone (SM-13496) in Subjects with Schizophrenia

Summary

EudraCT number	2016-000061-23
Trial protocol	SK PL
Global end of trial date	31 January 2019

Results information

Result version number	v1 (current)
This version publication date	26 January 2020
First version publication date	26 January 2020

Trial information

Trial identification

Sponsor protocol code	D1001067

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Sunovion Pharmaceuticals Inc.
Sponsor organisation address	84 Waterford Drive , Marlborough, United States, 01752
Public contact	CNS Medical Director, Sunovion Pharmaceuticals Inc., +1 866-503-6351, clinicaltrialdisclosure@sunovion.com
Scientific contact	CNS Medical Director, Sunovion Pharmaceuticals Inc., +1 866-503-6351, clinicaltrialdisclosure@sunovion.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	31 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2019
Global end of trial reached?	Yes
Global end of trial date	31 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the long-term safety of lurasidone (40 and 80 mg/day) in subjects with schizophrenia who have completed participation in Study D1001066.

Protection of trial subjects:

This study was conducted according to the protocol, International Council for Harmonization (ICH) Good Clinical Practice (GCP) and the ethical principles that have their origin in the Declaration of Helsinki

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 October 2016
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	Poland: 3
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Ukraine: 124
Country: Number of subjects enrolled	Russian Federation: 82
Country: Number of subjects enrolled	Japan: 71
Worldwide total number of subjects	289
EEA total number of subjects	12

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)	282
From 65 to 84 years	7

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

subjects must have completed the 6-week double-blind phase of study D1001066 and must have completed all required assessments on the final study visit

Pre-assignment

Screening details:

Change from Open-label and Double-bline Baseline in PANSS five-factor model scores (Anxiety/depression) at each post-baseline visit

Period 1

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

Arms

Arm title	lurasidone

Arm description:

Flexable doeses (40 or 80 mg/day)

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

Dosage and administration details:

flexable doese (40 or 80 mg/day)

Number of subjects in period 1	lurasidone
Started	289
Completed	235
Not completed	54
Consent withdrawn by subject	28
Adverse event, non-fatal	17
reason not given	4
Lack of efficacy	4
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Study-Open Label

Reporting group description: -

Reporting group values	Overall Study-Open Label	Total	
Number of subjects	289	289	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	282	282	
From 65-84 years	7	7	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	40.1		
standard deviation	± 11.23	-	
Gender categorical Units: Subjects			
Female	144	144	
Male	145	145	

End points

End points reporting groups

Reporting group title	lurasidone
Reporting group description: Flexable doeses (40 or 80 mg/day)	

Primary: Frequency of Adverse Events (AEs) or treatment related AEs, extrapyramidal AEs, SAEs, and AEs leading to study discontinuation

End point title	Frequency of Adverse Events (AEs) or treatment related AEs, extrapyramidal AEs, SAEs, and AEs leading to study discontinuation[1]
End point description:	

End point type	Primary
End point timeframe: Overall study	

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: this was an open label study - there was no statistical analysis required

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	289[2]			
Units: events				
Frequency of Adverse Events	146			
Frequency of treatment-related Adverse Events	100			
Frequency of extrapyramidal Adverse Events	28			
Frequency of Serious Adverse Events	14			
Frequency of AEs leading to study discontinuation	18			

Notes:

[2] - safety population

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of subjects using concomitant antiparkinsonian drugs

End point title	Proportion of subjects using concomitant antiparkinsonian drugs[3]
End point description:	

End point type	Primary
End point timeframe: overall study	

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: this was an open label study - there was no statistical analysis required

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	289[4]			
Units: participants				
Subjects using concomitant antiparkinsonian drugs	21			

Notes:

[4] - safety population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Open-label and Double-blind Baseline in Drug-Induced Extrapyramidal Symptoms Scale

End point title	Change from Open-label and Double-blind Baseline in Drug-Induced Extrapyramidal Symptoms Scale[5]

End point description:

Change from Open-label and Double-blind Baseline in Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS) total score (excluding the overall severity) at each post-baseline visit

End point type	Primary

End point timeframe:

Up to day 92 (follow-up)

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: this was an open label study - there was no statistical analysis required

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	289[6]			
Units: score				
arithmetic mean (standard deviation)				
Day 1	0.4 (± 1.15)			
Day 8	0.4 (± 1.18)			
Day 15	0.5 (± 1.28)			
Day 29	0.4 (± 1.08)			
Day 57	0.4 (± 1.17)			
Day 85	0.4 (± 1.13)			
Day 92 (follow-up)	0.3 (± 0.81)			

Notes:

[6] - safety population

Statistical analyses

No statistical analyses for this end point

Primary: Frequency of subjects with suicidal behavior and suicidal ideation

End point title	Frequency of subjects with suicidal behavior and suicidal ideation[7]

End point description:

Change from Open-label and Double-blind Baseline in Drug-Induced Extrapyramidal Symptoms Scale measured by Columbia-Suicide Severity Rating Scale (C-SSRS)

End point type	Primary

End point timeframe:

Overall study

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: this was an open label study - there was no statistical analysis required

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	289[8]			
Units: events				
Suicidial behavior	1			
Suicidal ideation	7			

Notes:

[8] - safety population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-blind baseline in (PANSS) score at each baseline visit

End point title	Change from Open-label and Double-blind baseline in (PANSS) score at each baseline visit

End point description:

Change from Open-label and Double-blind baseline in Positive and Negative Syndrome Scale (PANSS) score at each baseline visit

End point type	Secondary

End point timeframe:

Open-label (OL) Baseline, Double-blind (DB) Baseline, Week 1, Week 2, Week4, Week 8, Week 12, Week 1 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[9]			
Units: units on a scale				
least squares mean (standard error)				
Double-Blind Baseline	101.1 (± 11.00)			
Open-Label Baseline	80.5 (± 15.80)			
Week 1	79.0 (± 16.45)			
Week 2	75.9 (± 16.09)			
Week 4	73.9 (± 15.29)			

Week 8	71.5 (± 15.70)			
Week 12	68.9 (± 15.72)			
Week 12 (LOCF)	71.7 (± 18.22)			

Notes:

[9] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-blind Baseline in (CGI-S)score at each post-baseline visit

End point title	Change from Open-label and Double-blind Baseline in (CGI-S)score at each post-baseline visit

End point description:

Change from Open-label and Double-blind Baseline in Clinical Global Impression-Severity Scale (CGI-S)score at each post-baseline visit

End point type	Secondary

End point timeframe:

Open-label (OL) Baseline, Double-blind (DB) Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[10]			
Units: units on a scale				
least squares mean (standard error)				
Double blind baseline	4.9 (± 0.60)			
Open-label baseline	3.9 (± 0.89)			
Week 1	3.8 (± 0.87)			
Week 2	3.7 (± 0.84)			
Week 4	3.5 (± 0.85)			
Week 8	3.4 (± 0.82)			
Week 12	3.3 (± 0.82)			
Week 12 (LOCF)	3.4 (± 0.92)			

Notes:

[10] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-bline Baseline in PANSS subscale scores (Positive scale) at each post-baseline visit

End point title	Change from Open-label and Double-bline Baseline in PANSS subscale scores (Positive scale) at each post-baseline visit

End point description:

Positive scale

End point type	Secondary

End point timeframe:

Double-blind Baseline, Open-label Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[11]			
Units: units on a scale				
least squares mean (standard error)				
Double-blind baseline	25.3 (± 3.80)			
Open-label baseline	19.0 (± 5.31)			
Week 1	18.5 (± 5.42)			
Week 2	17.5 (± 5.06)			
Week 4	17.0 (± 4.73)			
Week 8	16.1 (± 4.56)			
Week 12	15.6 (± 4.68)			
Week 12 (LOCF)	16.4 (± 5.50)			

Notes:

[11] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-bline Baseline in PANSS subscale scores (Negative scale) at each post-baseline visit

End point title	Change from Open-label and Double-bline Baseline in PANSS subscale scores (Negative scale) at each post-baseline visit

End point description:

Negative scale

End point type	Secondary

End point timeframe:

Double-blind baseline, Open-label baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[12]			
Units: units on a scale				
least squares mean (standard error)				
Double-blind baseline	24.2 (± 4.08)			
Open-label baseline	20.7 (± 4.49)			
Week 1	20.4 (± 4.53)			
Week 2	19.7 (± 4.67)			
Week 4	19.3 (± 4.57)			
Week 8	18.8 (± 4.65)			

Week 12	18.3 (± 4.59)			
Week 12 (LOCF)	18.9 (± 4.95)			

Notes:

[12] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-bline Baseline in PANSS subscale scores (General psychopathology scale) at each post-baseline visit

End point title	Change from Open-label and Double-bline Baseline in PANSS subscale scores (General psychopathology scale) at each post-baseline visit

End point description:

End point type	Secondary

End point timeframe:

Double-blind baseline, Open-label baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[13]			
Units: units on a scale				
least squares mean (standard error)				
Double-blind baseline	51.5 (± 6.41)			
Open-label baseline	40.9 (± 8.29)			
Week 1	40.2 (± 8.56)			
Week 2	38.7 (± 8.46)			
Week 4	37.7 (± 8.01)			
Week 8	35.1 (± 8.33)			
Week 12	36.5 (± 9.58)			

Notes:

[13] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-bline Baseline in PANSS subscale scores (Negative symptom scale) at each post-baseline visit

End point title	Change from Open-label and Double-bline Baseline in PANSS subscale scores (Negative symptom scale) at each post-baseline visit

End point description:

End point type	Secondary

End point timeframe:

Double-blind baseline, Open-label baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[14]			
Units: units on a scale				
least squares mean (standard error)				
Double-blind baseline	21.1 (± 3.75)			
Open-label baseline	17.4 (± 4.09)			
Week 1	17.1 (± 4.16)			
Week 2	16.7 (± 4.16)			
Week 4	16.3 (± 4.12)			
Week 8	15.9 (± 4.24)			
Week 12	15.3 (± 4.10)			
Week 12 (LOCF)	15.8 (± 4.42)			

Notes:

[14] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-bline Baseline in PANSS five-factor model scores (Excitement) at each post-baseline visit

End point title	Change from Open-label and Double-bline Baseline in PANSS five-factor model scores (Excitement) at each post-baseline visit

End point description:

End point type	Secondary

End point timeframe:

Double-blind baseline, Open-label baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[15]			
Units: units on a scale				
least squares mean (standard error)				
Double-blind baseline	11.5 (± 2.90)			
Open-label baseline	8.9 (± 3.16)			
Week 1	8.7 (± 3.26)			
Week 2	8.4 (± 3.12)			
Week 4	8.1 (± 2.85)			

Week 8	7.7 (± 2.82)			
Week 12	7.5 (± 2.92)			
Week 12 (LOCF)	7.9 (± 3.29)			

Notes:

[15] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-bline Baseline in PANSS five-factor model scores (Cognitive disorders) at each post-baseline visit

End point title	Change from Open-label and Double-bline Baseline in PANSS five-factor model scores (Cognitive disorders) at each post-baseline visit

End point description:

End point type	Secondary

End point timeframe:

Double-blind baseline, Open-label baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[16]			
Units: units on a scale				
least squares mean (standard error)				
Double-blind baseline	16.3 (± 2.67)			
Open-label baseline	13.8 (± 3.15)			
Week 1	13.7 (± 3.14)			
Week 2	13.2 (± 3.29)			
Week 4	13.0 (± 3.00)			
Week 8	12.6 (± 2.90)			
Week 12	12.2 (± 3.29)			
Week 12 (LOCF)	12.6 (± 3.29)			

Notes:

[16] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-bline Baseline in PANSS five-factor model scores (Positive symptoms) at each post-baseline visit

End point title	Change from Open-label and Double-bline Baseline in PANSS five-factor model scores (Positive symptoms) at each post-baseline visit

End point description:

End point type	Secondary

End point timeframe:

Double-blind baseline, Open-label baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[17]			
Units: units on a scale				
least squares mean (standard error)				
Double-blind baseline	15.7 (± 2.38)			
Open-label baseline	15.7 (± 11.9)			
Week 1	11.5 (± 3.41)			
Week 2	10.9 (± 3.16)			
Week 4	10.5 (± 3.13)			
Week 8	10.0 (± 3.07)			
Week 12	9.6 (± 3.11)			
Week 12 (LOCF)	10.1 (± 3.52)			

Notes:

[17] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-bline Baseline in PANSS five-factor model scores (Anxiety/depression) at each post-baseline visit

End point title	Change from Open-label and Double-bline Baseline in PANSS five-factor model scores (Anxiety/depression) at each post-baseline visit

End point description:

End point type	Secondary

End point timeframe:

Double-blind baseline, Open-label baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[18]			
Units: units on a scale				
least squares mean (standard error)				
Double-blind baseline	16.1 (± 3.33)			
Open-label baseline	12.0 (± 3.51)			
Week 1	11.8 (± 3.48)			
Week 2	11.3 (± 3.43)			

Week 4	11.1 (± 3.24)			
Week 8	10.8 (± 3.30)			
Week 12	10.3 (± 3.46)			
Week 12 (LOCF)	10.8 (± 3.80)			

Notes:

[18] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Open-label and Double-blind Baseline in Calgary Depression Scale for Schizophrenia (CDSS) total scores at each post-baseline visit

End point title	Change from Open-label and Double-blind Baseline in Calgary Depression Scale for Schizophrenia (CDSS) total scores at each post-baseline visit

End point description:

End point type	Secondary

End point timeframe:

Double-blind baseline, Open-label baseline, Week 4, Week 12, Week 12 (LOCF)

End point values	lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	287[19]			
Units: units on a scale				
least squares mean (standard error)				
Double-blind baseline	4.1 (± 3.73)			
Open-label baseline	2.4 (± 2.85)			
Week 4	2.2 (± 3.02)			
Week 12	1.8 (± 2.70)			
Week 12 (LOCF)	2.0 (± 2.84)			

Notes:

[19] - ITT population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During the 12 week treatment period	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1
Reporting groups	
Reporting group title	lurasidone
Reporting group description: Flexable doeses (40 or 80 mg/day)	

Serious adverse events	lurasidone		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 289 (4.84%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	12 / 289 (4.15%)		
occurrences causally related to treatment / all	7 / 15		
deaths causally related to treatment / all	0 / 0		
Impulsive behaviour			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Anxiety			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	lurasidone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 289 (12.46%)		
Nervous system disorders			
Akathisia			
subjects affected / exposed	19 / 289 (6.57%)		
occurrences (all)	20		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	17 / 289 (5.88%)		
occurrences (all)	19		

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