Clinical trial results:
A 6-Week, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Lurasidone (SM-13496) in Acutely Psychotic Subjects with Schizophrenia

Summary

EudraCT number	2016-000060-42
Trial protocol	SK PL
Global end of trial date	06 November 2018

Results information

Result version number	v1 (current)
This version publication date	27 November 2019
First version publication date	27 November 2019

Trial information

Trial identification

Sponsor protocol code	D1001066

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	06 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 November 2018
Global end of trial reached?	Yes
Global end of trial date	06 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of lurasidone (SM-13496) 40 mg/day compared with placebo in acutely psychotic subjects with schizophrenia as measured by change from Baseline in Positive and Negative Syndrome Scale (PANSS) total score at Week 6.

Protection of trial subjects:

THE STUDY WAS CONDUCTED ACCORDING TO THE PROTOCOL, INTERNATIONAL COUNCIL FOR HARMONISATION (ICH) GOOD CLINICAL PRACTICE (GCP), ICH GUIDELINES, AND THE ETHICAL PRINCIPLES THAT HAVE THEIR ORIGIN IN THE DECLARATION OF HELSINKI.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 May 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: 9
Country: Number of subjects enrolled	Romania: 23
Country: Number of subjects enrolled	Japan: 107
Country: Number of subjects enrolled	Russian Federation: 147
Country: Number of subjects enrolled	Ukraine: 196
Worldwide total number of subjects	482
EEA total number of subjects	32

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)	472
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The Screening phase for each subject will begin at the time that the subject provides written informed consent. Subjects will be evaluated for eligibility during a screening period of up to 14 days, during which they will be tapered off all psychotropic medications(except as noted in this protocol)in a manner consistent with labeling recommendation

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	Investigator, Carer, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	lurasidone

Arm description:

Lurasidone 40 mg

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:

lurasidone 40mg dosed once daily

Arm title	Placebo

Arm description:

placebo

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:

placebo once daily

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

Dosage and administration details:

lurasidone 40mg dosed once daily

Number of subjects in period 1	lurasidone	Placebo
Started	247	235
Completed	199	175
Not completed	48	60
Consent withdrawn by subject	23	20
Adverse event, non-fatal	14	15
Lack of efficacy	10	24
need reason	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	lurasidone
Reporting group description: Lurasidone 40 mg	
Reporting group title	Placebo
Reporting group description: placebo	

Reporting group values	lurasidone	Placebo	Total
Number of subjects	247	235	482
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	241	231	472
From 65-84 years	6	4	10
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	41.0	39.3	
standard deviation	± 11.0	± 11.44	-
Gender categorical Units: Subjects			
Female	127	114	241
Male	120	121	241

End points

End points reporting groups

Reporting group title	lurasidone
Reporting group description: Lurasidone 40 mg	
Reporting group title	Placebo
Reporting group description: placebo	

Primary: Change from Baseline in PANSS total score

End point title	Change from Baseline in PANSS total score
End point description:	
End point type	Primary
End point timeframe: week 6	

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245[1]	233[2]		
Units: units on a scale				
least squares mean (standard error)	-19.3 (± 1.10)	-12.7 (± 1.15)		

Notes:

[1] - ITT population

[2] - ITT population

Statistical analyses

Statistical analysis title	primary endpoint
Comparison groups	lurasidone v Placebo
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	Mixed models analysis
Parameter estimate	Median difference (net)
Point estimate	-6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	-3.5

Notes:
[3] - the Kenward-Roger’s approximation will be used to calculate the denominator degree of freedom.

Secondary: Change from Baseline in PANSS total score at Weeks 1, 2, 3, 4 and 5

End point title	Change from Baseline in PANSS total score at Weeks 1, 2, 3, 4 and 5

End point description:

End point type	Secondary

End point timeframe:
up to week 5

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: units on a scale				
least squares mean (standard error)				
Week 1	-5.5 (± 0.57)	-4.5 (± 0.59)		
Week 2	-10.2 (± 0.75)	-6.6 (± 0.77)		
Week 3	-13.1 (± 0.85)	-8.6 (± 0.89)		
Week 4	-16.3 (± 0.95)	-10.8 (± 0.99)		
Week 5	-18.0 (± 0.99)	-11.9 (± 1.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PANSS Subscale Score - Positive Scale

End point title	Change from Baseline in PANSS Subscale Score - Positive Scale

End point description:

End point type	Secondary

End point timeframe:
up to week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: units on a scale				
least squares mean (standard error)				
Week 1	-1.8 (± 0.19)	-1.4 (± 0.20)		
Week 2	-3.3 (± 0.24)	-2.2 (± 0.25)		

Week 3	-4.3 (± 0.28)	-2.7 (± 0.29)		
Week 4	-5.1 (± 0.32)	-3.5 (± 0.33)		
Week 5	-5.6 (± 0.32)	-3.8 (± 0.33)		
Week 6	-6.1 (± 0.35)	-3.9 (± 0.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CGI-S Score at Weeks 1,2,3,4,5, and 6

End point title	Change from Baseline in CGI-S Score at Weeks 1,2,3,4,5, and 6

End point description:

End point type	Secondary

End point timeframe:

up to week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: units on a scale				
least squares mean (standard error)				
Week 1	-0.21 (± 0.036)	-0.19 (± 0.037)		
Week 2	-0.49 (± 0.045)	-0.33 (± 0.047)		
Week 3	-0.67 (± 0.048)	-0.48 (± 0.050)		
Week 4	-0.84 (± 0.053)	-0.59 (± 0.056)		
Week 5	-0.91 (± 0.057)	-0.63 (± 0.060)		
Week 6	-1.03 (± 0.063)	-0.66 (± 0.066)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PANSS Subscale Scores-Negative Scale

End point title	Change from Baseline in PANSS Subscale Scores-Negative Scale

End point description:

End point type	Secondary

End point timeframe:
up to week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: Units on a scale				
least squares mean (standard error)				
Week 1	-0.8 (± 0.16)	-0.7 (± 0.16)		
Week 2	-1.4 (± 0.19)	-0.9 (± 0.20)		
Week 3	-2.2 (± 0.21)	-1.6 (± 0.22)		
Week 4	-2.8 (± 0.23)	-1.7 (± 0.24)		
Week 5	-2.9 (± 0.25)	-1.9 (± 0.26)		
Week 6	-3.3 (± 0.26)	-2.5 (± 0.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PANSS Subscale Score -General Psychopathology Scale

End point title	Change from Baseline in PANSS Subscale Score -General Psychopathology Scale

End point description:

End point type	Secondary

End point timeframe:
up to week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: Units on a scale				
least squares mean (standard error)				
Week 1	-2.9 (± 0.33)	-2.4 (± 0.34)		
Week 2	-5.4 (± 0.41)	-3.6 (± 0.42)		
Week 3	-6.7 (± 0.45)	-4.5 (± 0.47)		
Week 4	-8.5 (± 0.49)	-5.8 (± 0.52)		
Week 5	-9.5 (± 0.53)	-6.5 (± 0.56)		
Week 6	-10.0 (± 0.53)	-6.8 (± 0.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PANSS 5-factor models scores-negative symptoms

End point title	Change from Baseline in PANSS 5-factor models scores-negative symptoms

End point description:

The PANSS 5-factor model was defined as follows:
- Negative symptoms: Blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, lack of spontaneity and flow of conversation, and active social avoidance.

The PANSS response defined as 20% or greater improvement from Baseline in PANSS total score.

End point type	Secondary

End point timeframe:

up to week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: Units on a scale				
least squares mean (standard error)				
Week 1	-0.8 (± 0.15)	-0.7 (± 0.15)		
Week 2	-1.6 (± 0.18)	-1.0 (± 0.18)		
Week 3	-2.3 (± 0.20)	-1.8 (± 0.21)		
Week 4	-2.8 (± 0.22)	-1.8 (± 0.23)		
Week 5	-3.0 (± 0.24)	-2.1 (± 0.25)		
Week 6	-3.4 (± 0.26)	-2.6 (± 0.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PANSS 5-factor model scores-Excitement

End point title	Change from Baseline in PANSS 5-factor model scores-Excitement

End point description:

The PANSS 5-factor model was defined as follows:
- Excitement: Excitement, hostility, tension, and poor impulse control.

End point type	Secondary

End point timeframe:

up to week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: Units on a scale				
least squares mean (standard error)				
Week 1	-0.8 (± 0.14)	-0.5 (± 0.14)		
Week 2	-1.5 (± 0.17)	-1.0 (± 0.17)		
Week 3	-1.7 (± 0.18)	-1.1 (± 0.19)		
Week 4	-2.1 (± 0.19)	-1.4 (± 0.20)		
Week 5	-2.4 (± 0.20)	-1.4 (± 0.21)		
Week 6	-2.5 (± 0.21)	-1.5 (± 0.22)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PANSS 5-factor model scores-Cognitive Disorders

End point title	Change from Baseline in PANSS 5-factor model scores-Cognitive Disorders

End point description:

The PANSS 5-factor model was defined as follows:
- Cognitive disorders: Conceptual disorganization, difficulty in abstract thinking, mannerisms and posturing, disorientation, and poor attention.

End point type	Secondary

End point timeframe:

up to Week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: Units on a scale				
least squares mean (standard error)				
Week 1	-0.5 (± 0.11)	-0.5 (± 0.11)		
Week 2	-1.1 (± 0.13)	-0.7 (± 0.14)		
Week 3	-1.5 (± 0.15)	-0.9 (± 0.16)		
Week 4	-2.0 (± 0.16)	-1.3 (± 0.16)		
Week 5	-2.2 (± 0.16)	-1.5 (± 0.17)		
Week 6	-2.4 (± 0.17)	-1.6 (± 0.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PANSS 5-factor model scores-Positive Symptoms

End point title	Change from Baseline in PANSS 5-factor model scores-Positive Symptoms

End point description:

The PANSS 5-factor model was defined as follows:
- Positive symptoms: Delusions, grandiosity, suspiciousness/persecution, and unusual thought content.

End point type	Secondary

End point timeframe:

up to Week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: Units on a scale				
least squares mean (standard error)				
Week 1	-1.0 (± 0.12)	-1.0 (± 0.12)		
Week 2	-1.9 (± 0.15)	-1.4 (± 0.16)		
Week 3	-2.5 (± 0.17)	-1.7 (± 0.18)		
Week 4	-3.0 (± 0.19)	-2.2 (± 0.20)		
Week 5	-3.4 (± 0.20)	-2.5 (± 0.21)		
Week 6	-3.7 (± 0.22)	-2.4 (± 0.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PANSS 5-factor model scores - Anxiety/Depression

End point title	Change from Baseline in PANSS 5-factor model scores - Anxiety/Depression

End point description:

The PANSS 5-factor model was defined as follows:
- Anxiety/depression: Somatic concern, anxiety, guilt feelings, depression, and preoccupation.

End point type	Secondary

End point timeframe:

Up to week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: Units on a scale				
least squares mean (standard error)				
Week 1	-1.5 (± 0.15)	-1.0 (± 0.16)		
Week 2	-2.2 (± 0.18)	-1.4 (± 0.19)		
Week 3	-2.7 (± 0.19)	-2.0 (± 0.20)		
Week 4	-3.4 (± 0.20)	-2.6 (± 0.21)		
Week 5	-3.7 (± 0.21)	-2.8 (± 0.22)		
Week 6	-4.0 (± 0.22)	-2.9 (± 0.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects who achieved a PANSS response Week 6 (LOCF)

End point title	Proportion of subjects who achieved a PANSS response Week 6 (LOCF)

End point description:

Proportion of subjects who achieve a response, defined as 20% or greater improvement from Baseline in PANSS total score at Week 6 last observation carried forward (LOCF) endpoint;of

End point type	Secondary

End point timeframe:

Week 6

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: percent of participants				
percentage	60	42		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in CDSS total score -Week 3

End point title	Change from baseline in CDSS total score -Week 3

End point description:

End point type	Secondary

End point timeframe:

Week 3

End point values	lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	233		
Units: Units on a scale				
least squares mean (standard error)	-1.43 (± 0.165)	-1.17 (± 0.175)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 6 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1
Reporting groups	
Reporting group title	lurasidone
Reporting group description: Lurasidone 40 mg	
Reporting group title	Placebo
Reporting group description: placebo	

Serious adverse events	lurasidone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 247 (0.81%)	4 / 235 (1.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 247 (0.00%)	1 / 235 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	2 / 247 (0.81%)	2 / 235 (0.85%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 247 (0.00%)	1 / 235 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	lurasidone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	114 / 247 (46.15%)	119 / 235 (50.64%)	
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 247 (6.07%)	11 / 235 (4.68%)	
occurrences (all)	17	12	
Anxiety			
subjects affected / exposed	8 / 247 (3.24%)	16 / 235 (6.81%)	
occurrences (all)	12	21	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	15 / 247 (6.07%)	27 / 235 (11.49%)	
occurrences (all)	16	32	
Schizophrenia			
subjects affected / exposed	13 / 247 (5.26%)	21 / 235 (8.94%)	
occurrences (all)	14	22	

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